OPERAČNÍ PROGRAM PRAHA ADAPTABILITA

EVROPSKÁ UNIE

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HEART AND LUNGS

(a modern textbook of cardiology and pneumology)

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Projekt spolufinancuje Evropský sociální fond

Praha & EU: Investujeme do vaší budoucnosti“

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1. Introduction

(P. Widimský)

Cardiovascular disease and pulmonary diseases are among the most common diseases in medicine and are clearly the leading cause of death in most countries of the world. While, originally, this was believed to be the case of only industrialized nations, but with the rapid development witnessed by other regions, these diseases have become the most frequent cause of death all over the world (except for several poorest regions).

This textbook has been developed to meet the needs of medical students at the Charles University Third Medical School; however, we do believe that students of other medical schools across the Czech Republic will find it also useful as will junior physicians starting a two-year training program in any branch of medicine (specialization). Education and training programs provided at the Charles University Third Medical School are different from those available at other medical schools in the Czech Republic in that they are so-called problem-oriented. Hence, medical education/training is not based a format different from the traditional concept of education as it is more practical, and study relies on training in specific cases (case reports). When developing this new system of education/training in the 1990s, our subject was called “Dyspnoe and chest pain”. This title fits well the two most common symptoms of cardiovascular and pulmonary diseases as well as the fact that problem-oriented education is focused not on nosologic entities but, on the major symptom experienced by the patient presenting to the physician.

The textbook has been co-authored by lecturers at two departments of Charles University in Prague, Third Faculty of Medicine (Department of Internal Medicine/Cardiology and Department of Pneumology). In addition to cardiology and pneumology, the textbook occasionally refers to issues of interest in closely related specialties – angiology, cardiac surgery, thoracic surgery, and imaging techniques. Although (or just because) the authors gave utmost care and time to preparation of the textbook, they will appreciate any comments or suggestions of the reader (be they medical or physicians) that could possibly improve future editions. Given its electronic format, we plan to continuously update, make additions and/or revise the textbook. Any specific comments or suggestions can be e-mailed to the four main contributors/editors: dr. Pauk (pneumology), Associate Professor Moťovská (case reports), (junior lecturer) Osmančík (ECG), and Prof. Widimský (cardiology).

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2. Basic terms in the pathophysiology of the heart and circulation

(P. Widimský)

Heart rate and rhythm

***Heart rate*.** Under physiological conditions, heart rate is controlled by the sinus (sino-atrial) node functioning as a pacemaker. A normal heart rate is about 60 beats per minute. Spontaneous electrical sinus node activity is markedly influenced by the ratio of sympathetic to parasympathetic activity. In individuals with predominantly sympathetic activity (so-called sympathicotonics), the resting heart rate may be some 70 beats per minute and higher. By contrast, in individuals with predominant parasympathetic activity (so-called vagotonics), the resting heart rate is usually about 50 beats/min. and lower. Vagotonics include most endurance athletes (long-distance runners or swimmers, road cycling racers, cross-country skiers, etc.), with a resting heart rate of some being as low as 40 beats/min (the resting heart rate of the phenomenal professional cyclist Eddy Merckx was 36 beats/min). However, in the overwhelming majority of individuals, a heart rate below 45 beats/min should provide a reason for physical examination – at least having an electrocardiogram.

Pulse. Heart rate is usually measured by palpation on the radial artery. However, in under some circumstances, the pulse palpated on the wrist may not reflect the actual heart rate. In advanced shock (very low blood pressure levels) or in the event of radial or brachial artery occlusion, no pulse may be felt at the wrist and must instead be palpated on the large arteries, in the neck (carotid artery) or in the groin (femoral artery). While, in some arrhythmias (typically atrial fibrillation or frequent extrasystoles), pulse can be palpated on the radial artery, only some beats (stronger ones, with higher left ventricular diastolic filling) do propagate up to the periphery – this is referred to as peripheral deficiency (the heart rate measured by auscultation or ECG curve is higher than that measured by palpation at the wrist).

Tachycardia. Tachycardia is broadly defined as an abnormally faster heart rate. In fact, there is no cut-off point to identify a tachycardia. For example, while a resting heart rate of 75–80/ min. in a vagotonic with a resting heart rate of 48/min will be inadequate, it will be just normal in a a sympathicotonic. A resting heart rate over 100 beats/min is clearly a tachycardia. The most frequent causes of a physiological increase in sinus rhythm (physiological sinus tachycardia) include emotional upset, nervousness, physical exertion, and food. Under pathological conditions, sinus tachycardia will usually result from non-cardiac causes (fever, anemia, thyreotoxicosis, non-cardiac shock, etc.) or as a purposeful response (to maintain cardiac output) to some cardiac diseases (left ventricular dysfunction, heart failure, cardiogenic shock, etc.). Hence, we should not treat sinus tachycardia as such, instead, we should identify its cause and eliminate it. In cardiac

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patients, it has been shown that long-term presence of a higher heart rate is associated with a worse prognosis. It is less clear whether the same correlation exists in yet clinically healthy individuals.

Bradycardia. Just as with tachycardia, it is difficult to set a clearcut limit for a heart rate below which it can be referred as a bradycardia. Inter-individual differences have been commented on above. Nonetheless, it can be reasonably concluded that a heart rate below 50 beats/min is bradycardia. Physiological bradycardia is practically always due to predominant vagal activity (see above). So called vagal reaction (bradycardia + hypotension, sometimes even syncope) may in fact be a response to various stimuli, e.g., fear or pain.

Absolute arrhythmia (arythmia completa). The most common heart rhythm disorder in cardiac patients is atrial fibrillation. In this disorder, hundreds (perhaps as many as thousands – the exact number cannot be actually counted) of uncoordinated weak electrical impulses occur chaotically per minute which "bombard" the atrioventricular (AV) node. The AV node has (fortunately) the physiological property of conducting the stimuli more slowly than do the other parts of the cardiac conduction system. As a result, the AV node "lets go" farther to the ventricles only those stimuli which reach the node once the refractory phase is over. The passage of a random excitation through the AV node in atrial fibrillation can be compared with grains of sand falling randomly through the neck of the hourglass. Consequently, the ventricular rate in atrial fibrillation is as a rule irregular; hence the term arythmia completa. An experienced physician will be able to diagnose atrial fibrillation by mere palpation of the pulse.

Extrasystoles. Similar to atrial fibrillation, pulse palpation can also help identify (based on the absolutely irregular pulse) extrasystoles presenting as an occasional irregularity (a premature beat followed by a postextrasystolic pause) alternating with a period of regular pulse. Obviously, one cannot distinguish supraventricular from ventricular extrasystoles. Frequent or permanently present extrasystoles cannot be distinguished from atrial fibrillation or another type of arrhythmia without ECG.

Systemic blood pressure

Blood pressure. The term blood pressure (BP) refers (in the narrower sense of the word) to arterial blood pressure measured in the upper limbs. Of course, pressure levels can be measured (mostly invasively) at any point of the circulatory system (see subchapter 2.3). The term systemic blood pressure means specifically blood pressure in the arterial bed. The BP level is dependent on three factors: vascular filling, left ventricular performance and, first and foremost, arterial resistance at the level of arterioles (systemic vascular resistance). Normal BP levels are defined as 100–135/50–85 mmHg.

Hypertension (essential and secondary). Hypertension is usually defined as BP levels of 140/90 mmHg and over, measured repeatedly at rest in the physician's office. Hypertension is the most common cardiovascular disease and

insidious in that it may be present for decades asymptomatically until one of the following events occurs: stroke, myocardial infarction, heart failure, renal failure, or sudden death.

Hypotension. Lower BP levels (especially systolic BP levels of 85–100 mmHg) are commonly seen in asthenics or vagotonics and, unless associated with tachycardia or any symptoms, do not necessarily herald a pathological condition. By contrast, hypotension associated with tachycardia may be the first presentation of an incipient shock and should in no case be disregarded (see subchapter 2.3). A potentially useful measure to distinguish hypotension with and without tachycardia is so-called shock index (heart rate-to-systolic BP ratio). A shock index > 1.0 will almost invariably signal a pathological condition; already values > 0.8 should raise suspicion.

Left ventricle and heart failure

Left ventricular hypertrophy. The term left ventricular hypertrophy refers to an increase in left ventricular muscular mass. The condition usually develops as a compensatory response to a load (pressure or volume); less often "inadequately" (in the absence of an increased ventricular load) in genetically mediated hypertrophic cardiomyopathies. Normal left ventricular wall thickness at diastole is ≤ 12 mm and the anterior-posterior diameter of the left ventricle at diastole, as measured at the level of the mitral leaflet margin (tip), is ≤ 60 mm (of course, the left ventricular size also depends on overall body size, so, in small individuals with a lower body weight, the upper limit of the norm is ≤ 55 mm). Left ventricular volume overload (as in mitral insufficiency, aortic insufficiency, ventricular septal defect, or in endurance athletes such as marathon runners, road cycling racers, etc.) results in so-called ***eccentric hypertrophy*** (i..e, left ventricular dilatation without or with only small thickening of its wall). Left ventricular pressure overload (as in hypertension, aortic stenosis, coarctation of the aorta, or in power athletes such as weight lifters, etc.) results in so-called ***concentric hypertrophy*** (i.e., wall thickening without chamber dilatation or even with a decrease in chamber size). Left ventricular hypertrophy can be diagnosed by ECG (Sokolow index, McPhie index) or by echocardiograpy (direct measurement of wall thickness and chamber size).

Shock (cardiogenic, hypovolemic, anaphylactic, obstructive, septic) is defined as suddenly impaired organ perfusion due to circulatory collapse including, in clinical terms, hypotension (systolic blood pressure < 90 mmHg) with tachycardia (> 90 beats/min) and with clinical features of organ hypoperfusion (pale or cyanotic, clammy skin, oliguria, fear of death up to cognitive impairment in the more severe forms of shock, hypoxemia). Depending on its cause, there are a variety of types of shock:

Cardiogenic shock usually develops secondary to acute myocardial infarction: thrombotic occlusion of a coronary artery results in sudden akinesia of the ischemic myocardium in the coronary artery's bed followed by hypotension which, in turn, restricts blood flow through the remaining coronary arteries producing hypokinesia of the yet uninvolved parts of

the left ventricle making the hypotension still worse; this is a vicious circle eventually leading, if untreated, to death. The only effective therapeutic option is immediate (indeed every minute counts!) coronary angioplasty which breaks the vicious circle by restoring blood flow through the coronary artery in question. While, without angioplasty, mortality from cardiogenic shock in myocardial infarction is about 90%, with angioplasty, the death rate declines to some 40-45%. Despite adequate cardiac chamber and vascular bed filling in cardiogenic shock, the massive failure of left ventricular systolic function makes it impossible to generate sufficient systemic blood pressure.

Hypovolemic shock develops after a critical fall in circulating volume, with severe hypotension actually caused by inadequate vascular bed filling as a result of major bleeding, severe dehydration (e.g., severe prolonged diarrhea or massive removal of fluid to the extravascular space (as in the most severe form of allergy, i.e., ***anaphylactic shock***). While cardiac function is hypovolemic shock usually remains completely normal, the heart is constantly „empty“ working as it does without adequate filling pressures.

Obstructive shock is caused by a critical mechanical obstruction in the circulation, most often by massive pulmonary embolism, more rarely by cardiac tamponade (acute effusion of blood that will occur after perforation of the heart or a coronary artery, or rapidly forming pericardial exudate in pericarditis). While the vascular system before the heart (veins) is overfilled, the part of it behind the heart (arteries) is “empty”.

Septic shock is associated with serious infections (acute bacterial endocarditis, urosepsis in impaired urinary elimination, peritonitis secondary to gastrointestinal tract perforation, iatrogenic cannulation-related sepsis, etc.) or due to massive bacterial invasion to the vascular bed (most often in debilitated individuals). Development of shock is usually preceded by fever with chills.

***Pulmonary edema (cardiac, non-cardiac*)**. Pulmonary edema is a condition whereby fluid from the pulmonary capillaries enters the pulmonary interstitium (interstitial pulmonary edema) or pulmonary alveoli (alveolar pulmonary edema). Pulmonary edema is caused either by an increase in pulmonary capillary wedge pressure (normal level ≤ 12 mmHg) above oncotic pressure levels (i.e., approx. above 30 mmHg = cardiac pulmonary edema due to blood congestion before the left heart as a result of its pathology) or increased pulmonary capillary permeability (non-cardiac pulmonary edema developing in severe non-cardiac diseases). Cardiac pulmonary edema is the second most severe form of left ventricular failure (after cardiogenic shock). The diagnosis of pulmonary edema is based on a combination of clinical assessment + echocardiography + x-ray and, possibly, catheterization (pulmonary capillary wedge pressure measurement). A frequent occurrence in routine practice is mistaking mild pulmonary edema for bronchopneumonia, this is usually due to wrong description or interpretation of the x-ray image (a non-characteristic infiltrate on the x-ray scan can be both

bronchopneumonia or incipient or resolving pulmonary edema; the diagnosis must be based on the clinical presentation or, alternatively, on echocardiographic assessment).

Heart failure (acute, chronic, left-heart, right-heart, bilateral). The term heart failure denotes a condition when the heart is unable – whatever the cause of the heart disease – to pump blood to meet the needs of the body. Based on the rate of its development and duration, the condition is classified as acute heart failure (most typically, pulmonary edema) and chronic heart failure (a long-term, often permanent state with fluctuating intensity of complaints). Based on clinical symptoms, heart failure can be divided to right-sided (increased jugular vein filling, hepatomegaly, lower limb swelling up to generalized anasarca including ascites in the most severe forms) and left-sided (inspiratory pulmonary crackles, gallop rhythm) heart failure. The diagnosis of bilateral heart failure is established in the presence of both left- and right-sided heart failure. Most cases of heart failure are caused by a disease involving the left side of heart such as left ventricular dysfunction after myocardial infarction, dilated cardiomyopathy, acute myocarditis, aortic or mitral valve disease, long-standing or poorly controlled hypertension, and other conditions. Upon reaching a certain stage, all these conditions lead, via post-capillary pulmonary hypertension, to loading and eventual failure of the right heart; as a result, most cases of long-lasting left-sided heart failure develop progress to bilateral failure. Isolated right-sided heart failure develops in the presence of acute pulmonary embolism, severe chronic pulmonary hypertension (whatever its etiology), constrictive pericarditis, and restrictive cardiomyopathy.

Preload, afterload. ***Preload*** is a pathophysiological term referring to diastolic ventricular filling. Preload can be measured using the following parameters: ventricular filling pressure (i.e., left ventricular end-diastolic pressure), left ventricular end-diastolic volume or, most accurately, by relating the mutually dependent changes in both above values during a cardiac cycle (a most demanding technique employed only for research purposes). ***Afterload*** denotes the degree of resistance that the respective ventricle must overcome. It is more readily measured as vascular resistance (systemic, pulmonary), and can be roughly estimated – unless there is a valve stenosis – from the blood pressure (systemic, pulmonary) levels.

Left ventricular function. The left ventricle is the most important cardiac chamber playing a key role in the performance of the whole heart, making assessment of its function in clinical cardiology absolutely critical. Left ventricular function can be assessed by (i) evaluation of its wall motion over the cardiac cycle (echocardiography, ultrafast CT, magnetic resonance imaging, catheter-based left ventriculography, or radionuclide ventriculography); (ii) measurement of blood flow through the vascular bed (cardiac output, more accurately, cardiac index by relating the cardiac output to to body surface area); (iii) measurement of pressures in cardiac chambers and in the vascular bed (left ventricular filling pressure, left ventricular systolic pressure, pulmonary capillary wedge pressure, rate of pressure changes over time, the

latter parameters referred to as dP/dt+ and dP/dt-). Left ventricular dysfunction is sometimes divided into systolic (premature contractions) or diastolic (impaired relaxation and/or filling). In practice, both disorders most often co-exist; isolated diastolic dysfunction (devoid of contractual disorders) is a rare occurrence (e.g., in severe left ventricular hypertrophy in the presence of severe, long-term and long-untreated hypertension.

Ejection fraction is the parameter used to evaluate left ventricular function. It can be more readily determined by echocardiography, and most accurately using ultrafast CT or magnetic resonance imaging. It is used to express the relative proportion (fraction) of blood expelled during one contraction relative to its end-diastolic volume:

EF = SV / EDV

SV is the stroke volume (the volume of blood expelled from the aorta during one contraction; it is the difference between left-ventricular end-diastolic and end-systolic volumes, i.e., EDV – ESV) EDV stands for end-diastolic volume.

While normal EF values are > 55%, those of 45–55% are considered mild left ventricular dysfunction, EF of 35–45 % is classified as moderate dysfunction, and values EF <35% are associated with severe left ventricular dysfunction. The EF in full-blown cardiogenic shock is usually in the range of 10–20%.

Regional left ventricular wall motion. The most common cardiac disease – coronary heart disease – is associated with impaired left ventricular wall motion (weakening of contractions) in the vascular bed of an occluded or critically narrowed coronary artery. Occlusion of the left anterior descending artery (LAD; or anterior interventricular branch of the left coronary artery) results in impaired motion of the anterior wall, apex, and adjoining segments of the septum and the lateral wall (this is usually the most extensive wall motion impairment, i.e., most severe type of left ventricular dysfunction). Occlusion of the circumflex branch of the left coronary artery in patients with prevalent so-called right coronary predominance leads to posterolateral left ventricular wall motion impairment (in right coronary predominant patients, this is small vascular bed). A right coronary artery occlusion will impair the wall motion of the inferobasal wall motion of the left ventricle, posterior septal segment, and the right ventricle. In fact, three grades of wall motion impairment have been defined: hypokinesia (weaker contractions), akinesia (disappearance of contractions), and dyskinesia (disappearance of contractions with paradoxical bulging of the ventricle outward instead of inward in systole). In myocardial infarction, the uninvolved segments of the left ventricle will often show compensatory hyperkinesia.

Left ventricular filling pressure, Frank-Starling mechanism. According to the Frank-Starling law, the strength of contraction is proportionate to the degree of its passive stretching prior to contraction. While, up to a certain limit, the more the myocardial fibers become stretched in diastole, to stronger their contraction in systole. However, once this limit has been exceeded, the efficacy of the contraction begins to decline. In clinical practice, myocardial fiber stretching can

only be measured indirectly; a less appropriate, yet most accurate technique is measurement of the filling (end-diastolic) left (and/or right) ventricular pressure. In theory, measurement of end-diastolic volume is more appropriate (yet inaccurate in practice). Normal ventricular filling pressures are: left ≤ 12 mmHg, right ≤ 6 mmHg. Indeed, while increasing left ventricular filling pressure up to an approx. 18 mmHg will increase contractile strength, it becomes counterproductive and makes the situation worse once the above value has been exceeded. Unless a mitral valve disease is present, left ventricular filling pressure can be most readily measured by right heart (venous) catheterization indirectly using so-called wedge pressure (see subchapters 2.4 and 2.5). Needless to say, the most accurate value can be obtained by inserting a catheter directly to the left ventricle (left heart, or arterial, catheterization).

Pulmonary circulatory pressure, right ventricle

Pulmonary circulation is the part of the vascular system between the right ventricle and left atrium encompassing the pulmonary artery and its branches – pulmonary capillaries – pulmonary veins. Compared with the systemic circulation, pulmonary circulation is a low-pressure one. Normal blood pressure levels are: pulmonary artery ≤ 30/12/20 mmHg (systolic/diastolic/mean), pulmonary capillaries ≤ 12 mmHg (mean), pulmonary veins and the left atrium ≤ 12 mmHg (mean).

Pulmonary vascular resistance (PVR) refers to the resistance against offered by the pulmonary vascular bed to blood flow. This parameter can be calculated using the PVR = TPG / CO formula, where TPG is the transpulmonary pressure gradient (difference between mean pulmonary artery pressure and mean left ventricular pressure and/or wedge capillary pressure) and CO being the cardiac output. Normal PVR values are < 130 dyn/s/cm^{-5}.

Pulmonary hypertension (precapillary, postcapillary, mixed, primary, secondary). Pulmonary hypertension is defined as increased pressure in the pulmonary arteries over the above values. Pulmonary hypertension may be either "passive" (***postcapillary,*** beyond the pulmonary capillaries: the increase in pressure in the pulmonary circulation is carried over from a diseased left heart) or "active" (***precapillary,*** before the pulmonary capillaries: a pathological process in the pulmonary vascular bed itself and/or in the lungs). Occasionally, both forms may co-exist. (***mixed*** pulmonary hypertension). Examples of values measured in three hypothetical patients undergoing right-heart catheterization using a Swan-Ganz floating catheter (W. Ganz, a Czech cardiologist who spent much of his professional career in the USA) are shown in the table below:

	Pulmonary artery pressure (syst/diast/mean) in mmHg	Wedge pressure (mean) in mmHg	Explanation
Postcapillary PH	48/29/36	29	Increased diastolic pressure in the pulmonary artery is consistent with the increased mean wedged pressure (hence, left atrial pressure)
Precapillary PH	48/29/36	10	Pulmonary artery diastolic pressure is increased whereas mean wedged pressure is normal
Mixed PH	48/29/36	18	Mean wedge pressure is increased whereas pulmonary artery diastolic pressure is increased even more markedly (disproportionately)

Cor pulmonale refers to right ventricular hypertrophy (most often initially concentric and, later, also concentric) secondary to pulmonary hypertension due to chronic severe hypoxemia in the presence of long-term lung disease (typically chronic respiratory insufficiency co-existing with chronic obstructive lung disease or advanced pulmonary fibrosis). Right ventricular hypertrophy can be diagnosed by ECG (R>S in V1 and S>R in V5 or V6) or, more reliably, by echocardiography (right ventricular wall thickness > 5 mm, right ventricular dilatation > 30 mm).

Hemodynamics

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Intracardiac pressures. Intracardiac pressures are usually measured during cardiac catheterization, and their values serve as an invaluable and accurate marker of current heart function and the status of vascular bed filling. Normal intracardiac pressure and other important hemodynamic parameters are shown in the table below:

Cardiac chamber	**Systolic pressure**	**End-diastolic pressure**	**Mean pressure**
Right atrium (RA)	**„v“ ≤ 7**	**„a“ ≤ 8**	**≤ 6**
Right ventricle (RV)	≤ **30**	**≤ 6**	**N.A.**
Pulmonary artery (PA)	≤ **30**	**≤ 12**	**≤ 20**
Left atrium (PCW = pulmonary capillary wedge)	**„v“ ≤ 15**	**„a“ ≤ 12**	**≤ 12**
Left ventricle (LV)	≤ **140**	**≤ 12**	**N.A.**
Aorta (AO)	≤ **140**	**≤ 90**	N.A.

Parameter	**Normal values**	**Parameter**	**Normal values**
Cardiac output (CO)	4.5– 6.0 l/min.	Cardiac index (CI)	2.5–4.5 l/min./m^2
Oxymetry – Hb saturation in the right heart	< 75%	Oxymetry – Hb saturation in the left heart	> 95%
Qp/Qs (ratio of pulmonary-to-systemic flow)	1 : 1		

Cardiac output (CO), cardiac index (CI) Cardiac output is the volume of blood pumped by the heart per minute. Cardiac index is the cardiac output related to a patient’s body surface area.

Cardiac valve function, mechanism of development of murmur. Valves direct blood flow forward through the heart while precluding its backward leakage. In the presence of a valve stenosis, blood cannot flow adequately in the usual phase (in aortic stenosis, in systole; in mitral stenosis, in diastole, etc.), with pressure increasing before the stenotic valve, and

decreasing behind it (the result is a pressure gradient at the stenotic valve). The blood "struggling to make its way" through the stenotic valve runs in turbulent flow producing murmur. Hence, a stenotic valve murmur can be heard in the same phase of the cardiac cycle as with blood flowing through a normal cardiac valve. In incompetent valves, a pathological blood flow occurs in the phase when the valve should be completely closed (in aortic insufficiency, in diastole; in mitral insufficiency, in systole). Consequently, a murmur in the presence of valve incompetence occurs in that cardiac cycle phase when blood normally does not flow through the valve. The table below shows the most common auscultatory findings with the respective hemodynamic features:

	Auscultatory finding	**Examples of intracardiac pressures**
Aortic stenosis	Systolic ejection murmur (crescendo-decrescendo), right intercostal space adjacent to the sternum, radiating to the neck (in children with aortic stenosis, also an early systolic cklick)	LV 180 / 24 mmHg AO 120 / 80 mmHg PCW 24 mmHg PA 45/24/34 mmHg
Mitral stenosis	In the left lateral position, the first heart sound becomes more pronounced at the apex, mitral opening click, diastolic decrescendo murmur with presystolic crescendo (in sinus rhythm) or without crescendo (in atrial fibrillation)	LV 120 / 6 mmHg AO 120 / 80 mmHg PCW 24 mmHg PA 45/24/34 mmHg
Aortic insufficiency	Diastolic regurgitant murmur (decrescendo), right intercostal	LV 120 / 24 mmHg

	space, radiating downward to the left along the sternum	AO 120 / 80 mmHg PCW 24 mmHg PA 45/24/34 mmHg
Mitral insufficiency	Holosystolic regurgitant murmur, at the apex radiating to the axilla and Erb's point	LV 120 / 6 mmHg AO 120 / 80 mmHg PCW mean 24, wave „v" 38 mmHg PA 50/24/39 mmHg

Left atrial function. The atria contribute to optimizing ventricular filling in diastole. A diastole is divided into four phases: isovolumic relaxation – rapid ventricular filling – slow ventricular filling – atrial systole. In the absence of the atrial contribution (typical in atrial fibrillation), cardiovascular performance usually falls by an approx. 20%. Quite surprisingly, while younger patients will often tolerate this situation poorly, older ones (not already performing heavier physical activity) often cope well. The greatest risk associated with loss of atrial function is the formation of an atrial mural thrombus potentially resulting in embolism (the most feared complication is stroke caused by an embolus traveling from the left atrium to the central nervous system).

Valve disease quantification. When assessing the severity of valve disease (particularly in the decision-making process related to cardiac surgery), a host of factors should be taken into account: the clinical picture (most importantly, NYHA class), echocardiographic finding, hemodynamic assessment (by cardiac catheterization), associated disease, age, patient's own preference, etc. As regards hemodynamic assessment, cardiac catheterization should be performed and evaluated by an experienced interventional cardiologist well aware of the pitfalls associated with hemodynamic

measurements and carefully calibrate the measuring device prior to (and, possibly, also during) the procedure. Once all these requirements have been met, careful hemodynamic assessment will most reliably indicate the severity of the disease. With valve stenoses, the most accurate marker obtained by cardiac catheterization is the stenotic valve orifice area indexed to the patient's body surface area using the Gorling equation (based on the pressure gradient, cardiac output and duration of the respective phase of the cardiac cycle). Aortic stenosis is classified as severe if the aortic orifice area is smaller than 0.6 cm^2. Similarly, mitral stenosis is considered severe in cases where the mitral orifice area is smaller than 1.0 cm^2. Presence of regurgitation makes accurate measurement of stenosis severity most difficult as the increase (by regurgitating volume) in blood flow through the valve increases the pressure gradient to a level higher than consistent with actual stenosis severity.

Intracardiac shunts. Many congenital heart defects are associated with shunts between the left and right hearts (pulmonary and systemic circulation). A left-right shunt can be demonstrated during cardiac catheterization using so-called oxymetry run whereby blood samples are obtained from all heart chambers and large arteries. The presence of a left-to-right shunt is signaled by an abrupt rise in hemoglobin saturation in the respective heart chamber. The most frequent type of congenital heart disease in adults is atrial septal defect. The typical oxymetry finding in atrial septal defect associated with a left-to-right shunt is shown below:

	Vena cava inferior	**Vena cava superior**	**Mixed venous blood (3SVC + 1IVC) / 4**	**Right atrium**	**Right ventricle**	**Pulmonary artery**	**Capillary wedge pressure**	**Left ventricle**
Hb saturation (%)	73	66	68	81	81	81	97	97

An increase in saturation by 13% between the venae cavae (mixed venous blood) and the right atrium conclusively demonstrates a left-right shunt at the atrial level.

Peripheral and central cyanosis. Cyanosis is bluish discoloration of the skin (and, possibly, mucosal membranes) reflecting an increase in the volume of reduced hemoglobin in blood over 50 g/l. Central cyanosis is caused by non-oxidized blood mixing with atrial blood centrally (i.e., either a right-to-left shunt or inadequate blood oxygenation during transit

through the lungs). Cyanosis is clearly visible in the skin all over the body and in mucosal membranes. Peripheral cyanosis develops due to blood stagnation in the peripheral vascular bed and is evident in fingers, ears, nose, and lips.

Coronary blood flow. Myocardial ischemia

Anatomy of the coronary arteries. Normally, two coronary arteries originate from the aortic bulb (sinuses of Valsalva): the left coronary artery from the left coronary sinus, and the right coronary artery from the right coronary sinus, with no artery arising from the third (so-called non-coronary) sinus. The left coronary artery (LCA) typically runs for about 1 cm and then branches off into the left anterior descending (LAD) and the left circumflex branch (LCX). The section between the aorta and the bifurcation, known as the left main artery (LMA), is the most important part of the whole coronary bed: patients with a significant LMA stenosis usually show marked anginal symptoms (cave – occasionally, the pain associated with LMA stenosis may be experienced in between the scapulae and not in the anterior chest !!). Should thrombotic LMA occlusion develop, the patient usually died before receiving effective treatment as only a minority of individuals experiencing such an event live long enough to reach the cath lab. The reason for such a dramatic outcome is that the LMA supplies the left ventricle either by approx. 75% (in those with right coronary predominance) or completely the left ventricle (in those with left coronary predominance).

The LAD forks into septal (supplying the anterior part of the interventricular septum) and diagonal arteries (supplying the anterolateral part of the left ventricle), with the left ventricular apex supplied by the distal LAD segment. The LCX gives rise to the usually bigger left marginal artery (occasionally there may be several smaller ones) supplying the lateral and/posterolateral wall of the left ventricle In left coronary predominance, the LCX is normally large and gives rise also to the posterior left ventricular branch (posterolateral artery) and the posterior interventricular artery. In right coronary predominant patients, the right coronary artery gives rise to the right conus branch, right ventricular artery, right marginal artery and, distally, two main branches, the posterior right ventricular branch and the posterior interventricular artery. In left dominant patients, the latter two branches originate from the right circumflex artery; the right coronary artery is small and ends in the right ventricular region.

Coronary blood flow, coronary flow reserve. At rest, about 250 ml of blood flows per minute through the coronary arteries (i.e., approx. 5% of cardiac output). Even when at rest, the myocardium extracts as much as oxygen as possible from the blood flow. Consequently, any increased myocardial oxygen demand (during exertion, increase in blood pressure, tachycardia) must be met by increased blood flow. The maximum increase in blood flow through the coronary arteries above the normal resting volume (Qh/Qb) is termed coronary flow reserve. In other words, coronary flow reserve is the ability of the coronary arteries to raise blood flow rate in response to increased myocardial oxygen demand. Under normal conditions, coronary flow reserve is in the range of 4.0–10.0 (most often 4–6). A coronary stenosis greater than 50% will

restrict maximum blood flow; the more significant the stenosis, the more restricted hyperemic blood flow. In the presence of a 90% stenosis, an increase in blood flow in response to exercise is no longer possible – hence, coronary flow reserve equals 1 (Qh = Qb). The coronary arterial bed is the only part of the vascular bed in the body with blood flowing only in diastole. In clinical practice, coronary blood flow can only be measured indirectly by intracoronary Doppler techniques (measurement of coronary blood flow rate) or by an intracoronary catheter-tip manometer (measurement of trans-stenotic gradients in the coronary arteries).

Coronary stenoses. Narrowing of a coronary artery can be documented by coronary angiography (most accurately invasively by left heart catheterization; less accurately non-invasively by CT angiography) and is commonly expressed as the per cent of its luminal area: a normal coronary artery segment has a zero stenosis (however, narrowing smaller than 50% is not referred to as a stenosis), whereas complete artery occlusion equals a 100% stenosis (note that the condition is referred to as occlusion, not stenosis). In clinical terms, a stenosis is defined as a luminal narrowing in the range of 50–99%. Just as an example: a coronary artery with a 4mm lumen in its healthy part, and a 1mm lumen at the narrowest point of the stenosis; hence, the narrowing is from 4mm by 3mm, i.e., 75%. Stenoses <50% do not hinder blood flow and will not cause any problems. However, it should be noted that atherothrombosis (see below) is a dynamic process which, while usually progressing, may also regress should the mural thrombus dissolve or be removed by blood flow. Thus, even a patient (rarely) with a 30-40% "stenosis" may have occasionally experienced stenosis-related problems if a thrombus was attached to the lesion site or spasm occurred when reporting their complaints. Stenoses of 50-70% restrict blood flow on exertion and will typically not cause major problems. However, stenoses greater than 70% do pose a problem as they virtually always restrict hyperemia on exertion.

Coronary spasms were unduly attributed a greater role in the past than actually deserved. In fact, they occur frequently often than originally believed. Indeed, isolated coronary spasms (involving non-atherosclerotic arteries) are so rare that some cardiologists doubt that they occur at all. In contrast, arteries involved by atherosclerosis may be vulnerable to spasms. Spasms may make any stenoses worse; only rarely does a spasm result in stenosis or occlusion at the site of a non-stenotic plaque. A most rare form of coronary heart disease is so called ***variant (vasospastic, Prinzmetal's) angina*** presenting by resting (not exertional) anginal pain associated with transient ST-segment elevations (over the duration of anginal pain). Diagnosis of variant angina requires (in addition to transient ECG-documented ST segment elevations at the time of spasm) coronary angiography ruling out a morphological atherosclerotic stenosis or an intracoronary thrombus. The author of this chapter, with a practice in cardiology spanning 32 years, has encountered no more than 6 patients with true variant angina among tens of thousands of his patients. The smaller role of coronary spasms in the pathogenesis of various

forms of coronary heart disease is underlined by the absence of any prognostically relevant effects "antispastic" agents („coronary dilators"), i.e., nitrates, calcium antagonists, nicoradnil, and others. While these agents may be effective in reducing the incidence of anginal episodes, they do in no way lower the mortality rates of coronary heart disease patients.

Collateral blood flow. The myocardial vasculature is relatively well able to collateralize in response to multiple ischemic stimuli. As a result, when there is progressive slow narrowing of a coronary artery by the atherosclerotic process, collaterals begin to form so that the patient may not experience any major problems, and even a completely asymptomatic slow coronary artery occlusion may develop. However, as the affected coronary artery bed is by then supplied by collaterals from the other branches of the coronary vasculature, the occlusion may develop asymptomatically and without necrosis. In acute coronary syndromes (see below), there is usually no time for collaterals to form, and the myocardium will succumb to necrosis.

Atherothrombosis. Atherosclerosis *per se* (without thrombosis) would be a relatively benign condition with slow progression. What actually makes atherosclerosis the number one „killer" of our times is thrombus formation. The underlying mechanism is "rupture" of a vulnerable atherosclerotic plaque (plaque rupture, erosion, exulceration, etc.) followed, first, by platelet aggregation at the site of endothelial injury (white „platelet" thrombus) eventually becoming, by action of coagulation factors, the red (erythrocyte-rich) thrombus. The process is most dynamic and may proceed (i) either acutely resulting in sudden death or (ii) intermittently with a tendency to spontaneous resolution and be asymptomatic. Needless to say, there is a large variety of conditions between the above two extremes, ranging from mild unstable angina to extensive acute myocardial infarction with cardiogenic shock (see below). The pathophysiological processes contributing to, or precluding coronary thrombosis, are shown in the table below:

Factors promoting development and progression of coronary thrombosis	**Factors development and progression of coronary thrombosis**
Platelet hyperactivity	Inhibition of platelet activity
Hyperactivity of clotting factors	Spontaneous fibrinolytic activity of blood
Dehydration	Adequate hydration
Stress	Absence of stress
Presence of significant and/or complex coronary stenosis (turbulence + low post-stenotic perfusion	Absence of a stenosis, large arterial lumen (laminar flow + adequate perfusion pressure throughout the

pressure)	artery)
Stent not covered by the endothelium	Endothelium-covered stent
Hypotension	Normal or high normal blood pressure

Myocardial ischemia is a condition whereby a myocardial segment is not adequately supplied by oxygenated blood, with the myocardium quickly exhausting its energy reserve and failing to contract. This is followed, within several seconds of the onset of ischemia, by a decrease in the frequency, or even disappearance (due to complete arrest of blood flow) of contractions. The patient will most often perceive the ischemia (in about 80% of cases) as angina. Although most (approx. 90–95%) cases of ischemia are detectable by ECG (ST-segment elevations or depressions); the recording should be made while the ischemia is present. An ECG recording made just a couple of minutes once even a severe episode of ischemia will not necessarily document ischemia. Ischemia can almost invariably be detected by echocardiography (presenting as impaired left ventricular wall motion), the only problem is that echocardiography is unable to distinguish acute ischemia from earlier cases of wall motion impairment. Myocardial ischemia shorter than 10–20 minutes will not result in myocardial necrosis.

Myocardial necrosis, post-infarction scar. This issue has been addressed in detail in the Pathology section. From the clinical point of view, it is important that onset of necrosis does not begin until after 10–20 minutes of myocardial ischemia. In cases of acute complete coronary artery occlusion with no collaterals present, necrosis involving the whole ischemic focus will take about 12 hours to develop. However, collaterals and/or coronary artery occlusions may often be incomplete or intermittent in which case necrosis will take much longer, as many as several days, to develop completely. The earlier the therapeutic intervention (with acute coronary angioplasty) in the course of necrosis development, the greater area of the myocardium is saved from necrosis. Necrosis can be most reliably documented by serum troponin I (or T) determination or, alternatively, by ECG (pathological Q waves), echocardiography (akinesia up to dyskinesia often associated with left ventricular wall thinning) or other imaging techniques (CT, MRI, nuclear-based cardiology). In the acute phase of myocardial infarction (lasting mostly 12–24 hours; however, in the above – not rare – cases, it may last as many as several days). As a rule, the sooner coronary angioplasty is performed, the sooner progression of necrosis is stopped, the better the infarction heals, the better the left ventricular function and, most importantly, the patient's prognosis (the prognosis of post-infarction patients depends mainly from the left ventricular function post infarction).

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Myocardial viability is the ability of heart muscle to contract (absence of necrosis). A normally contracting myocardium is clearly a viable one. Consequently, the issue of viability arises only in a non-contracting myocardium (severe hypokinesia, akinesia or, possibly, dyskinesia) and has to be taken into account only when considering revascularization (angioplasty or bypass) of the affected part of the myocardium. The term ***hibernating myocardium*** refers to a critically ischemic but not yet necrotic (minimal supply of oxygenated blood is preserved preventing development of necrosis, but it not sufficient for the myocardium to contract). It is a chronic condition lasting for days, weeks, or even months and is potentially reparable (resumption of contractions) by revascularization. A hibernating myocardium fails to contract as it has a critically limited blood flow. ECG signs may include (but are not specific for) ST-segment depressions.

Myocardial stunning is an acute postischemic (i.e., the ischemia has resolved and blood flow has been restored) contractile function disorder, which is transient and will disappear, when treated properly, within several hours or days. A stunned myocardium is unable to contract because it has not yet „recovered“ from acute severe ischemia. However, as the myocardium is not necrotic and its blood supply has been restored, contractions return spontaneously. In the a stunned myocardium, an ECG scan will show deep T-wave inversions. An example: a patient admitted to a hospital with already resolved anginal pain and their ECG scan on admission shows a negative T-wave in thoracic leads, the diagnosis is most likely to be myocardial stunning secondary to severe transient ischemia caused by critical LAD stenosis.

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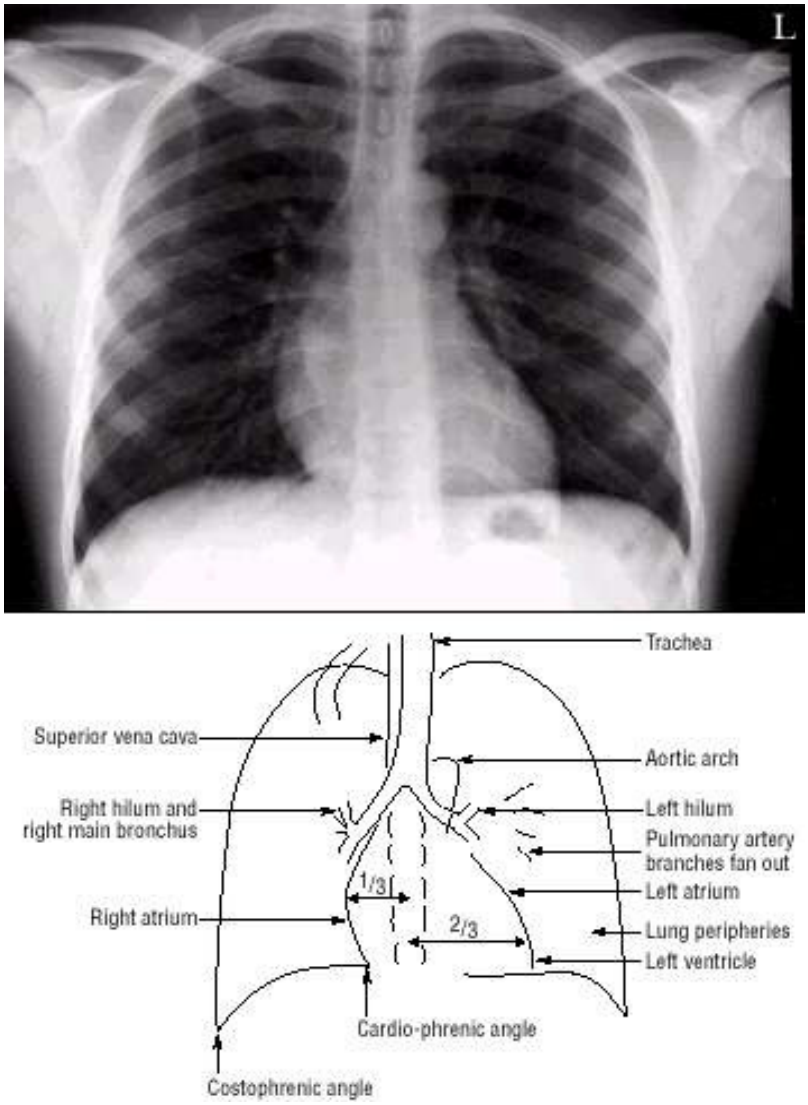
4. Examination methods in cardiology

(V.Kocka)

Chest X-Ray

Ideally taken in posteroanterior projection, standing or at least sitting, at maximal inspiration. X-rays taken in anteroposterior projection with patient lying can occasionally be performed in intensive unit setting but should be interpreted with caution. Structures and contours identifiable on Chest X-Ray are highlighted in Picture 1.



Picture 1. *Chest X-Ray normal finding, lower part is schematic with contours description*

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Heart size can be judged by cardiothoracic index, which is computed as maximal heart silhouette width divided by maximal inner width of patient chest, the upper limit of normal is 0.5. There are specific signs of dilatation of specific heart chamber again as per Picture 1, but echocardiography is more precise and the method of choice.

Dilated mediastinum can be suggestive of dilated ascending aorta.

Calcifications are generally well seen on X-ray, especially in lateral projection.

Lung fields are carefully studied. Pulmonary congestion can be divided into three stages: a) blood flow redistribution into upper lung fields is the initial stage; b) interstitial pulmonary oedema with fluid transuding into interstitial space is seen as Kerley B lines in the interlobar spaces, hazy contours of pulmonary hilae and mild shadowing of lung fields; c) intraalveolar "frank" pulmonary oedema with fluid in the alveoli is seen as dense symmetrical haziness of both lung fields close to hilae. Other findings detectable in lung fields are for example: consolidation typical for pneumonia or atelectasis; fluidothorax; round opacity suspicious of primary or secondary lung tumour; pneumothorax (chest X-ray is always recommended after central vein cannulation to rule out pneumothorax and confirm optimal position of inserted catheter).

Pulmonary oligaemia – absence of vascular structures – can be occasionally detected in patient with pulmonary embolism or pulmonary valve stenosis.

Bone structures must be examined and any pathology described (fracture etc.) can be key part of correct diagnosis.

Echocardiography

See separate textbook

Stress testing

Stress testing aims at detection of myocardial ischemia and/or viability. The most widely available and also cheapest option is exercise ECG using bicycle or treadmill. Bicycle use has the advantage of better ECG quality. The most common form of exercise is Bruce protocol using bicycle with exercise increases every 3 minutes. Every protocol should be adjusted according to patient level of fitness, level of exercise should rise gradually and exercise should last at least 8-10 minutes. At the end of every exercise stage blood pressure, heart rate and ECG are recorded.

There are several typical indications of stress testing:

a) evaluation of patient with chest pain regarding presence of coronary artery disease
b) evaluation of exercise capacity of patients with known coronary artery disease
c) screening of asymptomatic population
d) arrhythmia evaluation

Specificity and sensitivity of exercise ECG is around 70% and this test is therefore not suitable for testing of patients with either very low (below 10%) or very high (over 90%) pre-test probability of coronary artery disease based on analysis of age, sex and symptoms. It is best suited to evaluate patients with intermediate pre-test probability of coronary artery disease.

Pre-test probability (%) of coronary artery disease based on age, sex and symptoms						
	Typical AP		**Atypical AP**		**Bon-cardiac pain**	
Age	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**
30-39	70	26	22	4	5	1
40-49	87	55	46	13	14	3
50-59	92	79	59	32	22	8
60-69	94	90	67	54	28	19

Exercise ECG testing in patients with known coronary artery disease is indicated when symptoms progress, to evaluate prognosis after myocardial infarction and also before and during cardiac rehabilitation programme. Exercise ECG testing in safe hospital environment can reassure patient psychologically.

Exercise ECG testing of asymptomatic patient is indicated rarely, only in professions with large responsibility – i.e. firemen, aircraft pilots, bus driver.

Exercise stress testing contraindications

Exercise stress testing contraindications

Acute phase of myocardial infarction

Unstable angina pectoris (48 hours from last symptoms)

Severe arrhythmias, especially of ventricular origin

Hypertension

Symptomatic and haemodynamically significant aortic stenosis

Heart failure decompensation

Acute pulmonary embolism

Suspected aortic dissection

Acute non-cardiac disease which will prevent maximal exercise (i.e. infection, anemia, psychosis)

Every exercise testing is supervised by trained medical staff – complications include malignant arrhythmias, vaso-vagal reactions with bradycardia and/or hypotension. Beware of fall after exercise, we recommend to ask the patient to rest on his back during recovery phase.

Interpretation of exercise testing includes:

a) level of exercise, best expressed in metabolic equivalents (MET)
b) response of blood pressure and heart rate to exercise
c) ECG changes
d) Symptoms

ST changes on ECG are evaluated 80ms from the end of QRS complex; significant change is generally more than 0.1mV. We note the slope of ST segment with ascending slope usually considered benign finding. Exercise ECG is not able to localise ischemia, in other words we are not able to predict which coronary artery is affected. Reason of exercise termination should be recorded, for example limiting symptoms, maximal predicted heart rate reached, blood pressure drop or dangerous rise etc.

Interpretation summary should state clearly whether exercise stress testing was in relation to ischemia detection negative, positive or test non-diagnostic (typically heart rate did not reach 80% of predicted maximal rate).

Stress testing with cardiac imaging

These methods are extremely useful in patients where ECG is not easy to interpret, typically due to presence of pacemaker, left bundle branch block, LV hypertrophy with secondary ST and T changes, digoxin therapy, WPW syndrome etc. There are several imaging methods available – echocardiography evaluates wall motion abnormalities, nuclear scintigraphy evaluates myocardial perfusion and lately cardiac MRI emerged as possible new gold standard. Physical exercise with motion artefacts is not ideal for imaging methods and pharmacologically induced stress is preferred. There are two different forms of pharmacological stress: 1) dobutamine induces tachycardia and 2) dipyridamole or adenosine induce vasodilatation

(principle – coronary artery distal to significant stenosis is maximally vasodilated even at rest and will therefore not be able to dilate any more after vasodilating agent).

Myocardial viability can be tested after administration of small doses of dobutamine.

ECG Holter monitoring

Holter monitoring is basically 5 lead continuous ECG with 24-48 hours recording without any need for patient activation. Patient diary is useful to compare ECG recording with time of patient symptoms. In case of less frequent arrhythmia occurrence ECG monitoring can be longer but then not continuous, but patient triggered. After patient activation 20 minutes of ECG prior to activation is stored for later review. Similar ECG recorder can also be implanted subcutaneously in local anaesthesia; battery life is approx. 2 years. This can be useful in patients with syncope of unclear aetiology.

Blood pressure 24 hour monitoring

This device consists of standard arm tourniquet and automated barometer, blood pressure is measured every 30 minutes and recorded. The upper limit of normal for mean blood pressure is 130/85mmHg. This test is very helpful in patients with resistant hypertension and white coat syndrome.

Cardiac CT and MRI

Historically these methods played little role in cardiology due to heart motion artefacts. Advances in technology, especially the 64 and more slice CT and dual source CT have recently enabled application of CT technology in cardiology. This requires contrast agent injection into peripheral cannula. CT coronary angiography is improving every year; at this moment has acceptable negative predictive value. High radiation dose can be reduced by ECG gated image acquisition. Cardiac MRI is especially useful at tissue characterisation and this is clinically relevant in myocarditis, cardiac masses – tumours, thrombi, fat etc. There is no ionizing radiation; gadolinium can be used as MRI contrast agent with small risk of kidney damage. Metal implants are main contraindication of cardiac, or any, MRI.

Cardiac catheterization

Cardiac catheterization is routinely used to visualize coronary arteries. Evaluation of left ventricle or aorta, carotid or renal arteries can be easily performed at the same time. Right heart study can assess patient hemodynamic situation, measure cardiac output and valve gradients. Catheters are inserted by standard Seldinger over the wire technique. Both femoral and radial artery can be used. Radial access has less bleeding complications and enables outpatient coronary angiography. Femoral access has less radiation and enables use of larger devices. This procedure is usually performed in local

anaesthesia. Cardiac catheterization is very safe method in experienced hands. The most common complication is access site hematoma. The most feared is stroke which occurs in 0.1% of patients. Every patient is well and in advance educated about the procedure, benefits, risks and alternatives and signs written informed consent.

6. Principles of ECG

(P. Osmancik, V. Kocka)

Cardiomyocyte action potential

Action potential means the time course of the depolarization (and repolarization) of cardiomyocyte membrane. At rest, there is present a difference between electrical charge in and out of cardiomyocyte (so called resting membrane potential). It is because of the semipermeability of cardiomyocyte membrane, which is not permeable for Na, K and Ca), and active "pumping out" of K ions out of the cell. It results in a difference in the concentration of Na ions outside and inside the cardiomyocyte cell - the concentration outside the cell is much higher, which is called resting membrane potential. The value of resting membrane potential is about -70 mV (there is negative current inside the cell). When channels for Na opens, Na ions starts to flow inside (according their electrical and chemical gradient), which results in equilibrium between the difference. Is is called as phase 0 o faction potential, rapid depolarization. Rapid channels for Na are current - dependent. It means, if there is resting membrane potential of - 70 mV on the membrane, they are closed. If the membrane potential declines to a critical value (which is about 15 - 30 mV), rapid Na channels opens. On the top of phase 0, the is no change between the current inside and outside the cell, or inside the cell becomes even positive compared to the outside (which is called transpolarization). Cardiomyocytes are joined by gap junctions in the heart. If an action potential develops on one cell, it is conducted through gap junctions to neighboring cells, so the action potential is conducted through the whole myocardium. The velocity of action potential in the contractile myocardium is aprox. 0.3 - 0.5 m/s, however, in a specialized tissue of conducting system (Purkinje fibers) even 4 m/s. When the equilibrium between in and out current is reached, the flow in Na channels is stopped. This is a beginning of part I action potential, rapid repolarization. At that part, action potential decreases (for short time only) to its resting value. At the same time, so called slow Na and Ca channel are being opened. Na and Ca ions flows outside the cell, which leads to maintenance of depolarization on the membrane. This phase is called as plateau phase of action potential. Slow Na and Ca channels are closed, and Na ions are "pumped" out of the cell and exchanged with K ions. By this mechanism, the resting (originally present) state is reached (and that phases are called phase 3 and 4 of action potential; i.e. phase of slow repolarization.

In the cell of contractile myocardium between two actions potentials, a resting state is present (- 70 mV outside the cell with no oscillations). The cells of conducting system have an ability of so called spontaneous diastolic depolarization. During the resting phase, the value of action potential slowly decreases to 0 value. When the value on membrane reaches

an critical value, a new action potential develops. It is of great importance, because these cells determine the rate of contraction of the heart. These cells works as "pacemaker" of the heart.

Conduction system action potential

Resting action potential can be measured on the membrane of cardiomyocate by galvanometer. In the reality, it cannot be measured action potential of each single cardiomyocyte. The sum of all action potentials at one moment is base for ECG. This sum of all action potential changes its direction and size over time. Leads, which are connected to the body surface, can measure this sum of electrical activity of the whole heart. This is called ECG (electrocardiography). This sum can be at some time point zero (in no cell, either depolarization or repolarization is present). It means that you will see isoelectric line on ECG. Later, all cardiomyocytes of atria are contracting (however, ventricles are at rest). It means, on ECG, we will see sum electrical activity of atria (P-wave). And after that, the electrical impulse will be conducted into the ventricles and the leads on body surface will measure the electrical activity of both ventricles (QRS complex). This time course of sum electrical activity of heart is called ECG.

History and current standard of ECG recording

ECG was for the first time recorded by Dutch cardiologist W. Einthoven in Leiden in 1906. Einthoven measured by galvanometer the difference of voltage between leads connected on right (R) and left (L) arm. This bipolar lead is currently called as I. lead. Next lead was connected on left ankle (F). It led to two new leads: II. lead (the difference between voltage of right arm and left leg) and III. lead (the difference between voltage on left arm and left leg). This three leads together generated a triangle, which is called Einthoven triangle. Wilson added to this three bipolar leads new thee unipolar leads in 1934. He connected all three bipolar leads in one triangle. The sum of all voltages on all three leads is zero. Unipolar leads presents a difference between the voltage of each extremity lead (R, L, F) and „zero“ potential. This recording was later improved by Goldberger, he used as indifferent "zero" lead not the sum of all three triangle leads, but of only two of them. It resulted in an increase of amplitude recording and is now called as "augmented" lead (aVR, aVL, aVF). Later were to this 6 extremity leads added unipolar pectoral leads, which are recorded on chest.

Current standard ECG tracing contains 12 leads: three bipolar extremity leads (I, II, III), three unipolar extremity leads (aVR, aVL, aVF) and six unipolar pectoral leads (V1 – V6). Sometimes, when ECG of right half of thorax is needed (e.g. in case of the myocardial infarction of right ventricle), the unipolar pectoral leads are connected on the right half of thorax and these leads are called right pectoral leads (RV1 - RV6). The speed (x axis) is usually 25 mm /s. On y axis (voltage), one mm present one mV. However, other speeds can be used, especially when detailed analysis is needed (50 mm/s or even up to 400 mm/s during EP studies).

Placement of leads during ECG recording

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The placement of leads during ECG recording is shown on figure. Extremity leads are connected to the wrist of right (red) and left (yellow) limb and to the ankle of left (green) and right (black) leg. Pectoral leads are placed in 4th intercostal space just right of sternum (V1), in the 4th intercostal space left of sternum (V2), in the 5th intercostal space in the medioclavicular line (V4), in the middle between V2 and V4 (V3), in the 5th intercostal space in horizontal extension of V4 in anterior axillar line (V5) and in the middle axillar line (V6).

Anatomy of the conduction system

Physiologically, an electrical impulse is created in sinoatrial (SA) node. SA node is located in upper right atrium near superior caval vein. The rate of electrical impulses in SA node is aprox. 60 beats/min. The activity of SA node is under control of autonomic nervous system: sympaticus increases the creation of impulses in SA node and parasympaticus decreases it. During exercise, the rate of generated impulses is higher (maximum heart rate can be easily calculated as 220 – age). The ability of spontaneous depolarization is not property of only SA node, its ability is common for the whole conduction system. However, this ability decreases distally from SA node: the rate of spontaneous depolarization in SA node at rest is aprox. 60 bpm, in AV junction area (i.e. secondary pacemaker) 40 bpm and in the Purkinje system 20-30 bpm. Electrical impulses, which are normally generated in SA node, are conducted to atrio-ventricular (AV) node. AV node is the only place, where impulse could be conducted from atrium to ventricles. The rest of AV membrane is membranous (i.e. non-conductive). The electrical impulse is conducted further through His and Tawara bundle branches (right bundle branch, RBB, and left bundle branch, LBB) by Purkinje fibers to contractile myocardium.

SA node is called as primary pacemaker. The rate of impulses generated in SA node at rest is aprox. 60 bpm. The ability of generation of impulses decreases from SA node distally. However, if SA node is sick and does not generarate electrical impulses, the region of AV node can assume this role. The rate of impulses generate din AV node is aprox 40-50 bpm. and the final rhythm is called as juntional rhythm. QRS complexes are narrow , both ventricles are activated physiologically from AV node. P-waves are not present. If AV node is sick, the role of pacemaker would be assumed by the region of Tawara branches. It is called as i.e. tertiary pacemaker and its rhythm is called as idioventricular rhythm. Its rate is slow (aprox. 30/min), and QRS complexes are wide.

Waves and intervals on ECG tracing

On the ECG recording, you can describe waves, intervals or complexes. On physiological recording, there are present waves P, Q, R, S, and T, one complex (QRS) and more intervals (P-R, Q-T).

P-wave represent the electrical activity of atria. Its length is usually 80 ms and the amplitude is up to 0,25 mV (2,5 mm). P-wave is physiologically positive in inferior leads (II, III, aVF), and positive in left lateral leads (I, aVL) . In V1, it is biphasic or negative. P-wave is followed by short isoelectric interval, i.e. PR (or PQ) segment and its length is

physiologically 50 – 120 ms. it is not often measured in reality. On the other hand, **PQ (PR) interval** is measured routinely. It is the time between the onset of P-wave to the beginning of QRS complex. Its length is maximally influenced by the conduction through AV node. Physiologically, PQ (PR) interval is 120 to 200 ms.

QRS complex presents the electrical activity of ventricles. Physiologically, its length is from 80 to 120 ms. The first negative component us Q wave, the first positive component of QRS complex is R wave and the second negative component of QRS complex presents S-wave.

Physiologically, there is an increase of R waves from V1 to V6. In V1, there is only i.e. septal S, which presents activation of left ventricle. r wave in V1 is very small. In V3, typically, the R wave is as high as S wave. And in V6, there is almost only R wave with only very small s wave. **ST segment** follows QRS complex. The line is isoelectric, because it represent a period, where no de- or repolarization is present in the heart. ST segment is ended by T-wave. T-wave is physiologically of the same direction as QRS complex. The maximum lengt of T-wave is 200 msec. The period of electrical activity of ventricles (e.g. the sum of de- and and re-polarizations) represents **QT interval**. Its length is physiologically bellow 450 ms in men and 460 ms in women. However, the length of QT interval very depends on heart rate. During fast heart rate, QT becomes shorter. Therefore, QT is corrected to heart rate (so called QTc). QTc should be up 440 ms and is calculated by Bazettov´ s formula: QTc = (QT) / 2√ (R-R). At resting heart rate, at 60/min, when R-R interval is 1 s, QT reflects just QT. Qt interval shortens during faster heart rate. By increasing heart rate by 10 bpm, the QTc is shortened by 20 ms.

U-wave is physiologically not present on each ECG recording. If it is present, it is the same direction (i.e. concordant) with QRS complex and its amplitude is aprox. of 1/3 of QRS complex.

Electrical axis of the heart

In fact, the term electrical axis means the direction of the depolarization of ventricles in frontal plane, or in other words, the vector of QRS complex. Electrical and mechanical axis are different terms. Mechanical axis of normal heart is about 60°. It depends on the body type (it is different in tall and obese persons). If there conduction of an impulse in the heart in normal, the electrical axis is very similar to the mechanical one. However, if the heart is stimulated from the apex, the electrical axis is changed completely without changing of the mechanical axis. The assessment of electrical axis is important for the diagnosis of ventricular hypertrophy, for Tawara bundle blocks and hemiblocks assessment. Normal range of electrical axis is between -30° and + 105° and this axis is called as intermediate. If the axis is lower than -30° it is called as horizontal axis, o fit is more than 105°, it is called as vertical axis. Electrical axis of the heart is assessed from the limb leads. If the sum of waves of QRS complex is positive (i.e. the sum of Q + R + S is positive), the vector of depolarization of the ventricle runs to that lead. And vice versa, if the sum of waves of QRS complex is negative in a limb lead, the vector of QRS runs away from that lead.

Leads I and aVL are located by left hand. Leads II, III and aVF are located inferiorly (they look at heart from bellow). In patients with intermediate axis, the direction of sum vector of QRS complex runs just between I, aVL and II, III, aVF. Therefore, the QRS vector is positive in all these leads. Moreover, because the vector runs from right hand away, QRS is negative in aVR. Electrical axis can be calculated from leads I, II, III or aVL and aVF.

The pathology of P – wave

The duration of P – wave is physiologically up to 80 ms, the amplitude up to 0.25 mV (2.5 mm). Its axis in frontal plane is 0 - 75°. P – wave I therefore positive in inferior leads (II, III, aVF), in leads I, aVL and negative or biphasic with terminal negativeness in V1.

If the activation of atrium begins outside the SA node, the morphology of P-wave (i.e. the activation of atria) is different. Pathologic P-wave is also present, when atria (both or one of them) are hypertrophied or dilated. P – pulmonale occurs in patients with hypertrophy of right atrium, typically in patients with lung disease or tricuspid valve disease. P – pulmonale is high (higher than 2.5 mm), of normal duration (up to 80 ms) and is best seen in leads II, III and aAVF. P – mitrale occurs in patients with dilated left atrium (typically due to mitral valve disease). P – mitrale is “longer” than 80 ms, typically biphasic (consists of two peaks), but its height is not changed. It is best seen in leads I, II, aVL.

The pathology of PQ (PR) intervals

PQ (PR) interval represent the duration of depolarization of atria and conduction from atria to ventricles. It physiological duration is 120 - 200 ms. The prolongation of its duration occurs typically during AV node pathology and is called as AV block (1 – 3 grade).

The pathology of QRS complex

Changes of QRS complex typically present due to:

- bundle branch blocks
- ventricular hypertrophy
- scars within ventricular myocardium
- WPW syndrome

The physiological duration of QRS complex is 80 – 110 ms. QRS complex can be narrow only when the impulse comes through AV node to both bundle branches and further to both ventricles, and when there is not too much fibrosis (scars) within ventricular myocardium.

The most often cause of prolonged QRS complex is bundle branch block. In that case, the impulse can run in on ventricle only, and then through the septum to the other one. The “route” of electrical impulse is therefore prolonged. Moreover, the impulse must run through contractile myocardium, where the conduction speed is lower (0.4 m/s compared to 4 m/s in

Purkinje fibers). If both bundle branches are well, but there are too much fibrosis within ventricular myocardium, the "route" of electrical impulse if prolongs as well and the duration of QRS complex must be longer (it is called as non-specified intraventricular conduction delay).

The amplitude of QRS complex in precordial lead depends on the mass of ventricular myocardium bellow the lead. Of minor importance, there is a distance between the lead and the ventricle (which could be longer due to obesity or pericardial effusion). Lower amplitude can be therefore present in patients with pericardial effusion. High amplitude is typically present in patients with ventricular hypertrophy.

Right bundle branch block

In case of right bundle branch block, the activation of right ventricle occurs from the left bundle branch. The activation of interventricular septum is physiological, because interventricular septum is physiologically activated from left bundle branch, i.e. from the left to the right. QRS complex is wider (the most often cause of wide QRS complex is bundle branch block !): If the width of QRS complex is more than 120 ms, the RBBB is described as complete RBBB, if the width is more than 110 ms but less than 120 ms, it is called as incomplete RBBB. Typical patterns of RBBB are present in leads V1 and V2. In these leads, RSR´ (rsR´, Rsr´) pattern is present with T –wave negativeness (because of the change of depolarization; because of the change of depolarization, also the vector of repolarization is changed). In leads V5, V6, I and aVL, broad S waves are often present. RBBB occurs typically in patients with acute pulmonary embolism or right ventricular hypertrophy. However, sometimes it is present in otherwise healthy persons.

Left bundle branch block

In case of left bundle branch block, the whole activation of left ventricle is changed including interventricular septum. QRS complex is typically substantially wider. Typical ECG pattern are present in V5, V6 (and similar morphology is present in leads I and aVL). In that leads, broad R are present, typically with "notching", and negative T – wave. Further typical changes are present in leads V1 - V3. In those leads, broad and deep QS (or rS) with ascendant elevation of ST segment are present. Changes in V1 – V3 are similar to the ECG pattern of patients with scar (after myocardial infarction) on anterior wall. However, and in contrast to patients following myocardial infarction, also typical patterns in V5 and V6 are present.

Left ventricular hypertrophy

As mentioned above, the amplitude of QRS complex in precordial lead depends on the mass of ventricular myocardium bellow the lead. If the mass of left ventricle myocardium is larger, the amplitude of QRS complex above left ventricle must be larger as well. It is a base of so called "voltage" criteria of ECG signs of left ventricular hypertrophy. The

most often used is index Sokolow – Lyon, which is the sum of S in V1 and R in V6. If the sum is higher than 35 mm, it speaks for left ventricular hypertrophy. Similar criterion is index McPhie, which is the sum of largest S and largest R in precordial leads. If the sum is higher than 40, it is a sign of left ventricular hypertrophy. Index Cornell is the sum of S in V3 and R in aVL. The sum higher than 24 in men and 20 in women present ECG sign of left ventricular hypertrophy. Voltage criteria have a very good specificity (90%), but low sensitivity (20%). It means, when they are present, left ventricular hypertrophy is almost sure. However, their absence does not exclude left ventricular hypertrophy. To increase the sensitivity, voltage criteria are sometimes combined with other non – voltage criteria, such as the duration of QRC complex (the duration of QRS complex in patients with left ventricular hypertrophy slightly prolonged, especially the duration of the first part of QRS complex, i.e. QR) and left ventricular axis (left axis in hypertrophy). The combination of them is used in Roomhilt – Ester scoring system. The advantage of this criterion is high sensitivity, the disadvantage is of this system is its complexity.

Right ventricular hypertrophy

Physiologically, the mass of right ventricle is thinner than the mass of the left one. Therefore, the mass of right ventricle must be substantially more enlarged, to be seen on ECG. ECG has for right ventricular hypertrophy even lower importance than for left ventricular hypertrophy diagnostic (for both, echocardiography presents a gold standard). However, the principles of ECG signs of right ventricular hypertrophy should be known to all cardiologists. In general, in case of right ventricular hypertrophy, right axis deviation is present, and pathology of QRS complex in precordial leads. R is highest in leads above right ventricle (V1, V2), and, vice versa, it is low in leads V5, V6 (where large S is present). The amplitude of „R“ and „S“ waves is just in opposite to the physiological grow of R from V1 to V6. Also often, RBBB is present. Among particular signs of right ventricular hypertrophy belong: right axis deviation (> 110°), R/S > 1 in V1, R > 7 mm in V1, S < 2 mm in V2, qR in V1 and rSR´in V1 with R´> 10 mm.

Pathologic Q wave

Because QRS complex presents the activation of ventricles, its morphology must be changed in the presence of scar within ventricle myocardium .In leads above the scar, which is electrically “dumb”, so-called pathologic Q is present. It is wider than 0.04 s, deeper than 3 mm (or more than ¼ of R in QRS complex). Pathologic Q is present in leads above the scar. The scar of inferior wall is therefore visible in inferior leads II, III and aVF. The scar of anterior wall is visible (depending on its size and accurate location) in leads, I, aVL, V1 – V6.

WPW syndrome

The principle of WPW syndrome is the presence of accessory pathway between atrium and ventricle. Physiologically, the only electrical connection between atria and ventricles presents AV node. Accessory pathways present pathological “accessory” connections and can be present anywhere between (left or right) atrium and (left or right)

ventricle. The onset of QRS complex is substantially changed in WPW syndrome. The activation of ventricles does not start physiologically in the mass surrounding to Purkinje fibers, but in the contractile myocardium near the ventricular insertion of the accessory pathway. It results in so-called delta wave. Due to delta wave, QRS complex is prolonged, and PQ interval (correspondingly) shortened. The most typical arrhythmia in patients with WPW syndrome is AVRT. It is based on macro reentry circuit presenting due to accessory pathway. In contrast to AV node, the conduction through accessory pathway is fast, and often can conduct higher frequencies than AV node. Although AVRTR is the most typical arrhythmia in WPW patients, it is not the most dangerous one. The most dangerous (and sometimes event lethal) arrhythmia in WPW patients presents atrial fibrillation, which could lead due to high maximum of conduction to ventricles to ventricular fibrillation.

The pathology of ST segment and T wave

ST segment is physiologically isoelectric. ST segment and T wave is typically changed due to acute ischemia. Physiologically can be present ST segment elevation only in young, trained persons. However, these elevations are upwards concave, lower than 2 mm, and T wave is concordant (i.e. of the same direction as the vector of QRS complex).

Elevation of ST segment during acute myocardial infarction

ST segment is extremely important for the assessment of ischemia. Critical ischemia (typically total occlusion of coronary artery) leads to elevation of ST segment, sub –totally occlusion leads to depression of ST segment. The principle of ST segment elevation is so-called injury current, which is created by ischemic injury of ATP-sensitive potassium channels and shift of depolarization of ischemic segment to the ST segment. The vector of Injury current goes from endocardium to the epicardium. Therefore, it leads to an „increase“ of corresponding precordial lead, which is above ischemic area.

ST segment elevation during acute myocardial infarction were for the first time described by H. Pardee in 1920. ST segment elevations must be present in two neighboring leads, are higher > 2 mm in leads V1 – V4 or > 1 mm in remaining leads, typically, they are horizontal or descendent. In case of ischemia of inferior wall, ST segment elevations are present in inferior leads (II, III, aVF; typically occlusions of right coronary artery). For ischemia of anterior wall, ST segment elevations in I, aVL, V1 – V6 are pathognomic (and are caused typically by occlusion of ramus interventricular anterior). It is very difficult to correctly distinguish the signs of acute ischemia of posterior wall. The vector of injury current goes from endocardium to epicardium, as well. However, in case of posterior wall, the vector goes not to, but away from precordial lead. Therefore, elevations are present on leads V7 – V9 (which should be recorded, when suspicion on posteriori wall ischemia is present). In leads V1 – V6, depression (i.e. mirror elevations) are present.

The elevation of ST segment is not the only possible ECG sign of acute critical ischemia. Due to acute ischemia, also left bundle branch block (or bifascicular block, RBBB + LAH or RBBB + LPH) can develop. Therefore, all patients with clinical

suspicion on acute ischemia and all above mentioned ECG signs should be thought (and treated) urgently as acute ischemic patients.

Time course of myocardial infarction on ECG

The time course of acute ischemia has its typical ECG patterns. In the hyper-acute phase (minutes after coronary artery occlusion), T wave becomes very tall (Fig b). It is followed (10 min)by creation of ST segment elevation (fig c). ST elevation present the most typical sign of ischemia. Myocardium is ischemic, but not "dead", necrotic. If the coronary vessel is open, the myocardium will survive. If the occluded coronary artery is not opened, ischemic cell will be dying, which will lead to necrosis of affected area (hours). On ECG, pathological Q waves will be developed. As far as pathological Q waves are developed, ST segment goes back to isoelectric line ("dead" cell are no more electrically active; aprox 6 – 12 hours). T waves becomes inverted. Months or years after myocardial infarction, T waves can be normalized. However, pathologic Q (i.e. scar) will remain forever.

The elevation of ST-segment during acute pericarditis

The ECG signs of acute pericarditis is also elevation of ST segment. These ST segment elevations are of different morphology and occurrence. They are typically upwards concave, present in more non – neighboring leads (i.e. they do not reflect the territory of any coronary artery).

ST segment depression

ST segment depression presents always a pathology. According its morphology, we can divide ST segment depression to ascending, descending, horizontal or "scooped" ("navicular", i.e. downsloping depression with a "sagging" appearance).Horizontal depression are typical for acute myocardial ischemia. They are present in patients with unstable angina, non ST – elevation myocardial infarction, or during exercise test in patients with stable angina. During ischemia, they are typically deeper than 1 mm and present in at least two neighboring leads. Downsloping ST depression caused by digitalis are present in all leads and are best visible in leads with large R. Descending depression can be caused by myocardial ischemia. However, descending or ascending depression are present in patients with left ventricular hypertrophy.

The pathology of T – wave

T – wave represent the repolarization of ventricular myocardium. Change of the morphology of T – wave is non – specific and can be present by different causes. The most important pathology is symmetric, deep and negative T – wave, discordant to QRS complex in corresponding lead, which is present during ischemia. Tall and peaked T wave (typically higher than 5 mm in limb leads and even higher than 10 mm in precordial leads) is typical for hyperkalemia. In the

opposite, slow "flattened" T - wave is typical for hypokalemia. T – wave pathology often accompanies ventricular hypertrophy or bundle branch blocks.

The pathology of QT interval

QT represents the duration of repolarization of ventricles. Its duration depends on heart rate (and is decreasing with increasing heart rate). At 60 bpm, the QT duration should be up to 450 ms in men and 460 ms in women. To eliminate the effect of heart rate, so-called QTc (corrected QT)is calculated. QTc is calculated based on Bazzet´s formula: $QTc = QT/\sqrt{(R-R)}$. It men, at 60 bpm, QT = QTc. QT interval can be pathologically prolonged (more often) or shortened.

Long QT (LQT) syndrome

The prolongation of QT interval could be innate or acquired. Innate LQT is caused by known genetic mutations of genes important for repolarization (the most of them encoding potassium channels).Acquired LQT is often caused by drugs, which interact with potassium channels on the membrane and prolong the duration of repolarization. The most dangerous are combinations of antiarrhythmics, some psychoactive drugs and some antibiotics (macrolide antibiotics). Patients with LQT are at risk for ventricular tachycardia. Typical ventricular tachycardia for LQT is polymorphic VT called Torsades de piointes. The clinical manifestation are syncope and the patients are at risk for sudden cardiac death.

Short QT (SQT) syndrome

SQT presents genetic syndrome caused by mutation of genes, which encodes membrane channels, which are important for repolarization. The shortening of QT interval could be dangerous if QT reaches 330 ms or less. Persons with SQT are at risk for malignant ventricular tachycardia or fibrillation.

Elektronické srdce a plíce

CZ.2.17/3.1.00/33276

7. Arrhythmias, palpitation, synckope, sudden cardiac death

(P. Osmancik)

The term arrhythmias means all electrical disturbances of cardiac rhythm, i.e. disorders of either formation or conduction of electrical impulse within the heart. The only physiological rhythm is sinus rhythm. All other (regular or irregular) rhythms are arrhythmias.

According to the rate, arrhythmias are divided into bradyarrhythmias (heart rate lower than 50/min) and tachyarrhythmias (heart rate higher than 100/min). According to the origin, arrhythmias are divided into supraventricular (which origin is above AV node), arrhythmias using AV node and ventricular arrhythmias.

The etiology of arrhythmias can be quite different. In general, according to the etiology, we can divide arrhythmias to 1) arrhythmias of extracardiac etiology (outside the heart), 2) arrhythmias in patients with structural heart disease and 3) arrhythmias in patients without structural heart disease.

Ad 1) Typical exctracardiac disease, which is associated with cardiac arrhythmias, is hyperthyreosis. Overproduction of thyroid hormones is toxic for heart. Patients with hyperthyreosis suffer more often from atrial fibrillation. The treatment of hyperthyreosis leads to the treatment of atrial fibrillation. Anemia is accompanied by (compensatory) sinus tachycardia, similarly as others diseases, associated with hypoxia (such as chronic obstructic pulmonary disease or pulmonary embolism). An important group of extracardiac etiology of cardiac arrhythmias present drug intoxications. Significant number of drugs (beta – blockers, Ca channel blockers) have bradycardia effect. A lot of other drugs (not only antiarrhythmics) can prolong QT interval, which can lead to typical ventricular tachycardia, called as Torsades des pointes. Electrolyte abnormalities are associated with changing of duration of action potential and can indirectly “help” the creation or maintenance of arrhythmias. The most important is the level of potassium. Low potassium level facilitate ventricular fibrillation initiation. On the other hand, high potassium level, by prolonging action potential duration, has bradycardia effect. This effect can be very important at higher concentrations of potassium and can even lead to asystole and death.

Ad 2) Arrhythmias are often present in patients with structural heart disease. Almost all patients with mitral valve disease and dilated left atrium often suffer from atrial arrhythmias, especially from atrial fibrillation. Ventricular tachycardia is significant cause of sudden cardiac death in patients after myocardial infarction.

Ad 3) Some arrhythmias are present in patients without structural heart disease (i.e. without CAD, valve disease, abnormal EF or dilation of cardiac chamber). There are often caused by innate electrical pathology of the heart, such as presence of abnormal electrical junction (accessory bypass or pathway) between atrium and ventricle (WPW syndrome, AVNRT).

Projekt spolufinancuje Evropský sociální fond

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BRADYARRTHMIAS are arrhythmias with final heart rate lower than 50 beats per minute (bpm). The heart rate is slow because of either slow formation of electrical impulse in SA node or the pathology of conduction of impulse (typically in AV node).

Sinus bradycardia The electrical impulse are generated in SA node. However, its rate is below 50 bpm. The morphology of P-wave is physiological. Sinus bradycardia can be physiologically present at night. In the daytime, it can be present at rest in well trained persons. In **SA arrest**, no electrical impulse are generated in SA node. It is evident on ECG as isoelectric line without P waves and QRS complexes.

SA blocks

SA node in located in the right atrium near the connection to the upper caval vein. The spontaneous diastolic depolarization is present in SA blocks. Electrical impulses are generated in SA node with normal rate. However, the conduction from SA node to the surrounding tissue of right atrium is diseased. SA blocks are divided, similarly as AV blocks, in three grades.

SA block grade I is characterized by prolonged conduction from SA node to the surrounding tissue. However, each impulse, which was created in SA node, is conducted to the atrium, although slower. SA block grade I can be recognized only by electrophysiological study and is not visible on surface ECG.

SA block grade II This type of SA block means, that not all impulses are conducted from SA node to the surrounding tissue. There exists two kinds of SA block grade II, similarly as in AV block grade II. In type I (Wenckebach), the conduction from SA node to the surrounding tissue is gradually prolonged, the conduction of each following impulse is longer and longer until the impulse is not conducted from SA node to the atrium On the surface ECG, there is present gradual shortening of P – P interval, followed by a loss of P wave (and corresponding QRS complex). The pause, which results from the loss of P wave and QRS complex is longer than two P-P- intervals before. Type II (Mobitz II type) is characterized by sudden absence of conduction of electrical impulse from SA node to the atrium without previous prolongation of SA – P interval. On the surface ECG, there is present an absence of P wave (of course with the corresponding QRS complex), and the resulting pause is just two P – P intervals before. Important is, that in SA blocks grade II (Wenckebach and Mobitz II type), both P waves and QRS complexes are absent. If there is a P-wave without following QRS complex, is not SA block, but AV block!

SA block grade III is characterized by a complete block of conduction between SA node and atria. Electrical impulses are generated in SA node, but not conducted to the surrounding tissue. On the surface ECG, there is isoelectric line, an absence of P – waves and corresponding QRS complexes. Most often, especially when the resulting pause is long, junctional rhythm (i.e. escape rhythm generated in the secondary pacemaker) is present. Whether the cause of isoelectric line is SA block or SA arrest is very difficult to recognize. And, not the cause of isolectric line (SA block or SA arrest), but its length and

symptoms (syncope, dizziness) are important. From the practical point of view it is important, that only SA blocks grade II can be recognized on surface ECG. SA blocks grade I and grade III can be recognize only during electrophysiological study. And because not the exact cause of pause, but its length and symptoms are important for clinical practice and treatment of patient, electrophysiological studies only for the diagnosis of type and level of SA blocks are not performed. Moreover, it is important to realize the difference between SA blocks and AV blocks: in SA blocks, both P – wave and QRS complex are absent, in AV block (grade II or III), only QRS complex is absent (on the ECG, there is present an P - wave without corresponding QRS complex).

AV blocks

All AV blocks are visible on surface ECG (in contrast to SA blocks). AV blocks are divided, similarly as SA blocks, in three grades.

AV block grade I The normal P - Q interval (i.e. the time of impulse conduction from atrial to ventricles) is from 120 to 200 ms. In AV block grade I, all impulses are conducted from atria to ventricles, only the conduction time is prolongs. In fact, the term "block" for AV block grade I is not correct, the conduction of no impulse is "blocked" in AV node. In fact, AV block grade I is a prolongation of conduction through AV node. On the surface ECG, AV block grade I is evident as prolongation of PQ (PR) interval, which is longer than 0.2 s (200 ms).

AV block grade I In AV block grade II, not all impulses are conducted from atria to ventricles. There exist two type of AV block grade II: type Wenckebach (or Mobitz I) and Mobitz II. In AV block grade II type Wenckebach (Mobitz I), there is a gradual prolongation of conduction through AV node until one impulse is not conducted from atria to ventricles. PQ intervals are longer and longer, until one P wave is not followed by QRS complex. On the surface ECG, there is prolongation of P-Q intervals and after that, there is one P wave not followed by QRS complex. Next P – Q interval after this non-conducted P – wave is typically the shortest PQ interval (it could be even longer than 200 ms, but the shortest from all P – Q intervals of particular patients). In both types of AV blocks, there are more P – waves than QRS complexes. For n P – waves, there is n – 1 QRS complexes. This ratio (e.g. 4/3) should be mentioned in the description of AV block (e.g. AV block grade II type Wenckebach 5/4). In AV block grade II type Mobitz, there is no prolongation of PQ interval. All PQ intervals are the same and suddenly, there is an absence of QRS complex following one P – wave. This type of AV block is more dangerous than type I. While AV block grade I type Wenckebach can be present in trained persons especially during night "physiologically". It means the presence of this type of AV block presents no risk for such patient and these patients needn´t to be treated by pacemaker. In contrast, AV block grade II type Mobitz presents worse pathology of AV node (with typically more distal location). Patients with this type of AV block are at risk for sudden death (due to progression to

sudden unexpected AV block grade III) and should be treated by permanent pacemaker implantation. If each second P – wave is not conducted, the AV block is described often as AV block 2/1 only.

AV block grade III means a complete absence of conduction from atria to ventricles. The rate of ventricles is done by secondary (or tertiary) pacemaker. Most often, junctional rhythm with rate aprox. 40 – 560 bpm is present. On surface ECG, there are QRS complexes independent of P waves.

Bundle branch blocks

Right bundle branch block (RBBB)

In case of right bundle branch block, the activation of right ventricle occurs from the left bundle branch. The activation of interventricular septum is physiological, because interventricular septum is physiologically activated from left bundle branch, i.e. from the left to the right. QRS complex is wider (the most often cause of wide QRS complex is bundle branch block !): If the width of QRS complex is more than 120 ms, the RBBB is described as complete RBBB, if the width is more than 110 ms but less than 120 ms, it is called as incomplete RBBB. Typical patterns of RBBB are present in leads V1 and V2. In these leads, RSR´ (rsR´, Rsr´) pattern is present with T –wave negativeness (because of the change of depolarization; because of the change of depolarization, also the vector of repolarization is changed). In leads V5, V6, I and aVL, broad S waves are often present. RBBB occurs typically in patients with acute pulmonary embolism or right ventricular hypertrophy. However, sometimes it is present in otherwise healthy persons.

Left bundle branch block (LBBB)

In case of left bundle branch block, the whole activation of left ventricle is changed including interventricular septum. QRS complex is typically substantially wider. Typical ECG pattern are present in V5, V6 (and similar morphology is present in leads I and aVL). In that leads, broad R are present, typically with “notching”, and negative T – wave. Further typical changes are present in leads V1 - V3. In those leads, broad and deep QS (or rS) with ascendant elevation of ST segment are present. Changes in V1 – V3 are similar to the ECG pattern of patients with scar (after myocardial infarction) on anterior wall. However, and in contrast to patients following myocardial infarction, also typical patterns in V5 and V6 are present.

Hemiblocks and bifascicular blocks

Left bundle branch composes of two fascicles, anterior and posterior. The term “hemiblock” means the block of only anterior or only posterior fascicle. In that case, QRS complex is only a bit wider (but shorter than 110 ms), because the activation of both ventricles occurs almost physiologically (from AV node to His and further to both ventricles at the same time). The main change in hemiblocks occurs in the axis. In case of left anterior hemiblock (LAH) a significant left axis deviation is present (more than - 30° or - 60°, according to different authors). You will find small r and deep S in leads II, III, and aVF. Moreover, deep S in V6 is also present. In case of left posterior hemiblock (LPH), which is less frequent, significant

right axis deviation is present (i.e. more than + 90°). The combination of RBBB with LAH or LPH is called as bifascicular block. In ECG, there are RBBB patterns with left or right axis deviation.

TACHYARRHYTHMIAS

are all arrhythmias with frequency faster than 100 /min. Physiologically, sinus tachycardia can occur, which is present in all healthy persons during physical activity, exertion or emotional stress.

Pathophysiologically, there exist three mechanisms, by which tachyarrhythmias can be caused:

1) abnormal automaticity

2) triggered activity

3) reentry mechanism

This division describes only the pathophysiological mechanisms of arrhythmias, not the location or even ECG characteristics of them. For example, reentry mechanism is the cause of some supraventricular arrhythmias (atrial flutter), ventricular arrhythmias (ventricular tachycardia in patients following MI) and all arrhythmias using AV node.

For clinical practice, the most useful division is to tachycardias with narrow and wide QRS complex. If QRS complex is narrow, the electrical impulse must go through AV node to the ventricles (and both bundle branches must be functional). Thus, all arrhythmias with narrow QRS complex must be supraventricular. If QRS complex is wide, it can be caused by three mechanisms: a) ventricular tachycardia (the electrical impulse is originated in the ventricles), b) supraventricular tachycardia with pre-existing bundle branch block, or c) antidromal AVRT.

The most often used division of arrhythmia is following:

1) supraventricular arrhythmias

2) tachyarrhythmias using AV node

3) ventricular tachyarrhythmias

1) Supraventricular tachyarrhythmias

Supraventricular arrhythmias are arrhythmias, which rise and maintain in atria. Of course, to the ventricles they are conducted through AV node. However, they do not need AV node for the maintenance.

QRS complex can be narrow or wide. If the conduction through AV node and bundle branches is preserved physiologically, final QRS complex will be narrow. If there is pre-existing bundle branch block, final QRS complex will be wide.

Atrial extrasystoles

Isolated atrial extrasytoles are typically originated in an ectopic focus anywhere in atria. The morphology of P – wave is abnormal (the vector of atrial activation is different compared to normal vector, because the place of creation is not SA

node). Following atrial extrasystole, non-complete compensatory pause is present. The corresponding QRS complex is narrow. Electrical impulse, generated anywhere in the atria, is conducted in the ventricle (through AV node), and to the SA node, where it leads to premature depolarization of SA node. After SA node is depolarized, new impulse is created in SA node. The sum of R-R intervals before and after atrial extrasystole is shorter than the sum of two normal R-R interval, which is just called as incomplete compensatory pause.

Atrial tachycardia

Atrial tachycardia has its origin in right or left atrium. Typically, there is an focus anywhere in the atrium, which can produce electrical impulses (by activity similar like SA node, but with faster rate). The pathophysiological mechanism could be abnormal automaticity or triggered activity. The morphology of P - waves is abnormal, the rate of abnormal P-waves is typically 100 - 240/min. QRS complex is narrow. The conduction to ventricles is controlled by AV node. Slower atrial tachycardias has often 1/1 conduction, faster 2/1 or can be even more blocked. Atrial tachycardias are often present in patients with structural disease of atrium(a) due to valve disease, COPD etc.

Atrial flutter (typical)

Typical atrial flutter is macro reentry right atrial tachycardia. Electrical impuls runs in a circuit around tricuspid anulus, typically in frequency of 250 – 350/min. The impulse runs around tricuspid annulus either clockwise or counter-clockwise. In each case, it must run in the area between tricuspid annulus and inferior caval vein. (so called cavo-tricuspid isthmus). As mentioned above, the frequency of flutter is typically 250 – 350 /min. It is higher than maximum conduction of AV node. Therefore, typically each second or even each third impulse is conducted to ventricle. (and it is called as flutter blocked 2/1, 3/1 etc.). Sometimes, the conduction to ventricle can be irregular. On surface ECG, there are typical patterns in leads II, III and aVF, where typical saw-tooth flutter waves are present.

Atypical atrial flutter

Atypical atrial flutter is, similarly as the typical one, macro reentry supraventricular arrhythmia. However, the circuit of atypical flutter is not around tricuspid annulus but anywhere else in the right or left atrium Typically it can occur in patients following atriotomy (which can had been done for example due to atrial septal defect surgery). The flutter circuit is in that case around the scar and it is called as post-incisional flutter. Flutter waves of atypical flutter differs from physiological P-waves and typical flutter waves, and their morphology can be quite different (according the location of flutter circuit).

Atrial fibrillation

Atrial fibrillation is the most often atrial tachyarrhythmia (and the most frequent arrhythmia even). It is very complex atrial tachyarrhythmia. Electrical impulses are irregular and chaotically conducted throughout the myocardium of atria in many reentry circuits. The frequency of atrial activity is irregular and varies between 350 – 500/min. In other above mentioned

supraventricular arrhythmias, an electrical impulse is created ectopically or runs in any circuit, however, the activation of atrium(a) has some "order". In case of atrial fibrillation, the activation of atria is chaotic and the activation does not have any order and is completely disorganized. Therefore, no mechanical contraction in AF is present. Pathophysiologically, all three mechanisms exercise in atrial fibrillation, abnormal automaticity (in some focuses typically within pulmonary veins), triggered activity and multiple reentry circuits. On surface ECG, there are either no visible P-waves, or there is present an "undulation" of isoelectric line. QRS complexes are narrow, however, the conduction from atria to ventricles varies very much and the R – R intervals (intervals between QRS complexes) are very irregular. The frequency of QRS complexes differs based on conduction capacity of AV node. If AV node is healthy, the resulting frequency of QRS complexes can be quite high (even 180 / min). Typically, due to drugs, the frequency is higher than in sinus rhythm, but not so high as mentioned (typically 100/min at rest).

Pathophysiologically, two mechanisms are needed for atrial fibrillation maintenance. The initiation of atrial fibrillation is often done by multiple extrasystole (typically originated in "sleeves" of atrial musculature within pulmonary veins) For the maintenance of arrhythmia, critical mass of diseased atrial myocardium is needed, which "helps" to maintain the arrhythmia in atrium in multiple reentry circuits. Especially fibrotic and scarred atrium presents a terrain, where atrial fibrillation is not difficult to maintain.

Atrial fibrillation can occur either paroxysmal, with sudden onset and termination, or can have longer duration. If the duration is longer than 1 week but shorter than 1 year, it is called as persistent atrial fibrillation, otherwise as long-lasting persistent atrial fibrillation. Typical symptoms of atrial fibrillation are palpitation, in case of long-lasting persistent atrial fibrillation then dyspnoe. Atrial fibrillation occurs substantially more in patients with dilated or diseased atrium(a),such as in patients with mitral valve disease (so called valvular atrial fibrillation). However, it can occur in patients without any structural disease of left atrium (so called "lone" atrial fibrillation).

2) Tachycardias using AV node

AV nodal reentry tachycardia (AVNRT)

The location of AVNRT is AV node. The base is so called duality of AV node. It means the presence of two pathways, which can conduct an electrical impulse from atria to ventricles and back. Both pathways differs in speed of conduction and refractority. The electrical impulse is conducted from atria to ventricles in one pathway and back from ventricles to atria in the other pathway in typical reentry circuit. The activation of atria and ventricles occurs almost simultaneously and atrial activity (P-wave) is hidden in QRS complex. On ECG, AVNRT is regular narrow-complex tachycardia with typical frequency of 150 - 200/min without visible P - waves. Paroxysms of AVNRT occurs typically paroxysmal, and vagal maneuvers can typically terminate arrhythmia.

Atrio – ventricular reentry tachycardia (AVRT)

AVRT is macro reentry arrhythmia which uses (needs) AV node for its maintenance. The base for this arrhythmia is pathological electrical connection between atrium and ventricle outside AV node (accessory pathway or accessory bypass). The situation, where two connection between atria and ventricles are present, can be recognized as delta wave on ECG (delta wave corresponds the part of ventricular myocardium, which is near the ventricular insertion of accessory pathway and so therefore activated earlier) and is called as WPW syndrome. This connection and AV node present the main parts of reentry circuit. The impulse run from atria through AV node to ventricle, than through the mass of ventricle to the ventricular insertion of accessory tract, through the accessory pathway back to atrium. If the impulse runs this direction, it is called as orthodromal AVRT. Sometimes (less often), the impulse can run in the opposite direction: from atria through accessory pathway to ventricle, then to AV node, and from ventricle to atria through AV node. It is called as antidromal AVRT is regular tachycardia with frequency of 150 – 220/min. QRS complex is either narrow (in orthodromal AVRT) or wide (antidromal AVRT). However, for patients with accessory pathway, the most dangerous arrhythmia is atrial fibrillation. Accesory pathway does not have the possibility of AV node to lower the impulse. If atrial fibrillation in patients with WVW presents, significant number of atrial impulses could be conducted to the ventricle through accessory pathway, which could lead to ventricular fibrillation.

3) Ventricular tachycardia

Ventricular extrasystoles

The cause of (isolated) ventricular extrasystoles is ectopic activity of a focus in the ventricle. QRS complex of ventricular extrasystole must be (ever) broad. Typically, the morphology of QRS complex is similar to a bundle branch block, opposite than the origin of extrasystole (i.e. if the origin of ventricular extrasystole is in left ventricle, it has RBBB pattern, and vice versa, if the origin is in the right ventricle, is has LBBB pattern). Most often, ventricular extrasystole does not lead to "discharge" of SA node (because it is not conducted through AV node retrogradelly to right atrium). The rate of impulse generation in SA node is therefore not changed. It results to so called complete compensatory pause, i.e. the sum of R-R intervals before and after the extrasystole is just two R – R intervals outside the extrasystole. It means, QRS complex of the extrasystole is earlier than QRS complex, that would come if there were no extrasystole. However, next QRS complex is comes after normal P-wave, which generation was not affected by extrasystole. Ventricular extrasystole can be monophorm (i.e. of the same morphology, if they are created always in the same focus in the ventricle) or polyphorm (if there are more foci, which have ectopic activity). In that case, there are more morphologies of QRS complex (each focus generates its own morphology). The term ventricular bigeminy means that each "normal" physiological QRS complex is followed by and ectopic one (and similarly, trigeminy means that there are two physiologic QRS complexes followed by one

ectopic QRS complex). Ventricular extrasystoles (non frequent) are often present in completely healthy persons However, there are more often in patients with structural heart disease.

Monomorphic ventricular tachycardia

The term ventricular tachycardia (VT) means three or more ventricular QRS complexes with frequency of 100 bpm or higher. If the duration of VT is longer than 30 sec or if it leads to hemodynamic instability, it is called sustained VT. If the duration if shorter than 30 sec and VT is not associated with mechanical instability, it is called non – sustained VT. The term monomorphic means that the morphology of all QRS complexes is the same. The pathophysiological background of almost all ventricular tachycardias is the presence of reentry circuit within the ventricle. Monomorhopic VT are typically present in patients after myocardial infarction. Within the scar, there are some surviving cells, which creates "channels" throughout the scar. The conduction of the impulse throughout these channels is lower compared to surrounding healthy myocardium. The channels works as "isthmus". Because the conduction of the impulse is low in the channel, when the impulse exits the channel, the surrounding myocardium is no more in refractory and can be activated. Action potential runs fast through the healthy myocardium to the entry to the channel. By entering the channel, the creation of reentry circuit is fulfilled. It results in monomorphic VT with broad QRS complex, where the morphology of all QRS complexes is the same. In patients following myocardial infarction, VT present the leading cause of death. Also in other patients with structural heart disease and regions of intraventricular fibrosis, those arrhythmias are often cause of sudden death. VT can be seldom present in otherwise healthy persons without structural heart disease. The cause of this VT is often ectopic activity in the right or left outflow tract. Such VT are often non - sustained, are not associated with hemodynamic instability and are called as idiopathic VTs or benign VTs.

Polymorphic ventricular tachycardia

Polymorphic ventricular tachycardia presents on surface ECG as tachycardia with broad QRS complex with changing morphology of QRS complexes. Sometimes it is difficult to distinguish polymorphic VT from ventricular fibrillation. Polymorphic VT does not run in reentry circuit like monomorphic VT. It is sometimes present in patients with ST – elevation myocardial infarction during acute phase and presents the most often cause of pre - hospital mortality of such patients. Furthermore, it typically occurs in patients with long QT syndrome.

Ventricular tachycardia "Torsades de pointes"

A special kind of polymorphic ventricular tachycardia is VT type Torsades de pointes. The vector of ventricular tachycardia has been changing periodically. On surface ECG, it is present as periodical increase and decrease of the amplitude of QRS complexes. VT type Torsades de pointes occurs typically in patients with long QT interval.

Ventricular fibrillation

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The electrical activity of ventricles during ventricular fibrillation (VF) is completely chaotic. Mechanical contractions, resulting from VF, are completely useless and hemodynamically, VF presents a rest of circulation (although on ECG some electrical activity is present, hemodynamically it is the same situation as during asystole). On ECG there are present irregular QRS complexes of completely different morphology and amplitude. Pathophysiologically, in the ventricles there are multiple reentry circuits and with different refractoriness. VF typically degenerates from VT. VF can occur (very rare) in patients without structural or other heart disease (which is called primary VF). Then, it occurs sometimes in patients without structural, but with "electric" heart disease (such as Brugada syndrome, LQT syndrome). In that patients, there is a genetic disorder of ion channels on the membrane of cardiomyocyte, which can lead to the initiation of VT or VF. However, most often, VF is present in patients with structural heart disease independent of etiology (coronary artery disease, dilated cardiomyopathy or hypertrophic cardiomyopathy). Typically, it is present in patients with coronary artery disease. In such patients, it can occur during acute phase of myocardial infarction as primary VF. Late after myocardial infarction, VF can occur as a degeneration from monomorphic VT.

Syncope is temporary blackout due to transient or global cerebral hypoperfusion. It is characterized by sudden beginning, short duration and spontaneous ending.

Syncope is quite frequent in general population. According to some sources, 10-20% of population suffer from some type of syncope during the whole life (not all of them are examined by physician). The pathophysiological mechanism of syncope is global transient cerebral hypoperfusion, which can be caused by blood pressure or heart rate fall. The impairment of consiousness occurs if the decrease of heart rate or blood presure achieve the critical point (mostly systolic pressure 60mmHg or asystolic pause more than 5 sec). The complete unconsiousness will not happen if the asystolic pause is short or the decrease of blood pressure is small. In this case, patients feel weakness and dizziness. We call this presyncope. It is important to distinguish the situations, which imitate the syncope but do not fulfill the definition of syncope. That include the states connected with partial or complete unconsciousness, which are not caused by global transient cerebral hypoperfusion, eg. epilepsy, intoxications, metabolic diseases (hypoglycaemia, hyperventilation with hypocapnia) or TIA. All these cases contain the impairment of consiousness, but the reason isn´t transient cerebral hypoperfusion. That's why we must differentiate these states at the beginning. Similarly we must distinguish the causes which imitate the syncope but aren't accompanied by unconsciousness (psychogenic pseudosyncopes or crashes).

The main diagnostic tool is anamnesis, which we often obtain by witnesses because of unconsciousness of patients during the syncope. It is not a syncope if the patient remembers the event (maximum it is a presyncope or may not). Because of cerebral hypoperfusion, even generalised convulsions of extremities which are analogous to grand-mal epileptic fit can occur during the syncope (the presence of convulsions depend on CNS state and the duration of hypoperfusion).

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Sometimes it is really difficult to distinguish the epileptic fit from syncope just by the informations from witnesses. The loss of consciousness in syncope is short and the consciousness returns very soon. We can observe confusion or desorientation immediately after awakening but it disappears early (it lasts seconds, minutes maximum). The more supposed diagnosis is epilepsy, if it persists longer (and the neurological examination and EEG helps us to validate the diagnosis). The presence of prodroms (the feelings foregoing the syncope) is important. These can be palpitation (because of tachycardia before syncope), state weakness, the feeling of beginning syncope (because of reflex origin of syncope), chest pain (warning of myocardial ischaemia). On the other hand, syncope can occur suddenly, without prodroms (typical for cardial syncope, eg. because of AV block). The conditions connected with syncope are also important (at rest or during excercise). Syncope after excercise is typicall for aortic stenosis, syncope during excercise occurs at hypertrophic cardiomyopathy, syncopes during micturition, defecation or pain are conclusive for situational syncope.

Syncopes are divided due to their etiology into reflective (so called neurally-mediated), orthostastic hypotension syncopes and cardiac syncopes.

Divison of syncopes:

Reflective (neurally mediated)

- Vasovagal – caused by emotional strain
- Situational – occur during situation typical for the patient
    - cough
    - irritation of GIT (swallowing, defecation, after eating, pain of GIT)

  Carotid sinus syncope – hyperreactivity of CS

  Atypical types

Orthostatic hypotenison

- Volume reduction – lack of fluids
- Drugs - diuretics, vasodilatators
- Autonomic nervous system insufficiency – primary (rare)
    - secondary (diabetes, amyloidosis, uremia)

Cardiac

- Arrhythmogenic - caused by bradycardia (AV blocks,..), tachycardia (ventricular tachycardias)
- Structural heart disease – aortic stenosis
    - acute coronary syndrome
    - hypertrophic cardiomyopathy

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- pulmonary embolism
- cardiac tamponade
- pulmonary hypertension
- heart myxoma

Reflective (neurally – mediated) syncopes are mediated by vagal mechanisms. This is the most common type of syncopes (about 60 % of syncopes). The etiology is the irritation of vagal reflexes resulting into bradycardia, hypotenison or the combination of both. The receptors responding to pain, temperature or mechanical irritation are sources of afferent signals, the efferent activations lead to hypotension and bradycardia. These syncopes have mostly very characteristic anamnesis. The vasovagal syncope is classical, appears especially at younger patients. Typically looks like this: young woman hurries to the work in the morning, she didn't eat and dring. During the travel to work, she stands in hot stale air in the bus and starts to feel the prodroms of presyncope, dizziness, nothing else. Suddenly she wakes up on the floor, wondering what happened, she is quite right in a few minutes. She still feels weak dizziness, but she is able to sit. We can make the diagnosis of vasovagal syncope just from the anamnesis very often. Situational syncope is very similar to vasovagal. It occurs during condition, which are characteristic for the one patient, eg. painful procedures, urination, ect. The carotid sinus syncope rises from the irritation of carotid sinus by the collar or tie for example. All of these syncopes are benign with good prognosis.

The orthostatic hypotension syncope developes typicaly in older patients during faster standing up. It is caused by insufficient rapid increase of blood pressure in carotid bed. The pathofysiology mechanism is often just gradual slowdown of naturally existing reflexes, which is sometimes supported by medication (diuretics, vasodilatators).

Cardiac syncope has the worst prognosis. The etiology can be the bradycardia, typically asystolic pauses longer than 5 seconds or bradycardia about 30/min. This syncope appears suddenly without prodromes. On the other hand, the tachycardia can be also the cause of syncope. Supraventricular tachycardias are felt very uncomfortable by patients but usually as palpitation or presyncope maximum. The main reason of tachycardial syncope is ventricular tachycardias. If the ventricular tachycardia terminates spontaneously, it manifestates clinically as syncope. If it doesn't terminates spontaneously, it presents as sudden cardiac death. The ventricular tachycardias are common for patients with ventricular dysfunction or with acute coronary syndrome. Genetically determined heart diseases are less frequent cause of ventricular arrhythmias (just because there exist more patients with ischemic left ventricular dysfunction). Genetically determined ventricular arrhythmias appear typicaly at younger patients with frequent syncopes and with family history of sudden deaths (that's why the family history has the great importance). These include hypertrophic cardiomyopathy or diseases

with mutations of genes encoding proteins of membrane channels participating in repolarisation (potassium channles), eg. Brugada syndrome, long QT syndrome. Syncope can be one of the symptoms of pulmonary embolism or aortic stenosis.

The differential diagnosis has to be focused on exclusion the syncope, which is connected with bad prognosis - cardiac syncope. The anamnesis is very important. The arrhythmogenic syncopes (because of ventricular arrhythmia, HKMP, long QT) occur during excercise, syncope because of aortic stenosis after excercie. Syncopes which appear in lying down are more suspected of cardiac etiology than syncopes appearing in standing. The physical examination follows the anamnesis (systolic murmur of aortic stenosis), thereafter ECG. We must focused on bradycardia (bundle branch blocks, AV blocks, sinus bradycardia), but also on structural heart diseases changes (pathological Q, hypertrophy of the heart walls). If we suspect the orthostatic hypotension, we can realize the simple test by measuring the blood pressure in a lying position and after fast verticalisation (the decrease of systolic blood pressure under 90 mmHg is typical for orthostatic hypotension). In the next step, we must use medical imaging for excluding organic heart disease and arrhythmias. It includes echocardiography (left ventricle dysfunction, aortic stenosis) and ambulant Holter ECG. The patient has good prognosis if we exclude organic infliction and bradyarrhythmia. Reflective syncopes can repeat but the patient isn't endangered by sudden death. On the other hand, the organic disease has to be treated causally (aortic stenosis by aortic valve replacement, acute coronary syndrome by revascularisation, ventricular arrhythmias by ICD implantation,...).

Suden death is death arrived not more than 2 hours after first symptomes arrising. The non-traumatic death is almost always cardiac origin. The malignant ventricular arrhythmias because of ischemic heart disease (acute coronary syndrome or left venctricular dysfunction after heart attack) are the most common cause of sudden cardiac detah in adult population. Also the patients with other type of left ventricular dysfunction (dilated cardiomyopathy, valvular disease) are proned to ventricular arrhythmias, but for the patiens with ischemic heart disease are absolutely typical. Genetical determined diseases often with familiar presentation are other less frequent cause of ventricular arrhythmias, which is mentioned in the syncope chapter. They appear most often by younger patients, where there is necessary to think. For example, the most common casue of sudden young athlethes death is ventricular tachycardia because of hypertrophic cardiomyopathy or genetic mutations of membrane channels (Brugada syndrome, long QT) or WPW syndrome. Less frequent cause of sudden death is pulmonary embolism or bradycardias (they often lead to syncope than sudden death).

PALPITATION. Palpitation means subjectively unpleasant perceived fast heart rate. The word subjectively is needed to highlighted. It is the situation when patient describes very uncomfortable feeling of heart rate. Sometimes he feels the speed of the heart rate, sometimes he describes it like „skipping" or „omission" of the heart rate. The basis is in some tachyarrhythmia (supraventricular or ventricular), typicaly paroxysms of AV nodal re-entry tachycardia or atrial fibrilation. The palpitation can occur as prodromal state before syncope, if the cause of palpitation is ventricular tachycyrdia. In other

cases, isolated extrasystoles are the correlates of palpitations. Sometimes the postextrasystolic contraction or compensatory pause are worse perceived than the extrasystole itselve. Sometimes the palpitation is just subjective without any ECG correlate. The basic examination in the diagnosis of palpitation is 24 hours ECG Holter.

8. Atherotrombosis. Acute coronary syndromes

(P. Widimský)

Acute coronary syndromes (ACS) is a term used for three different forms of coronary artery disease (CAD): **unstable angina pectoris, acute myocardial infarction without ST-segment elevations, acute myocardial infarction with ST-segment elevations**. Common pathophysiological substrate of all ACS forms is an unstable (exulcerated, eroded) atherosclerotic plaque with superimposed thrombus in the coronary arteries, which causes short acute ischemia without myocardial necrosis (unstable angina pectoris) or prolonged acute ischemia with myocardial necrosis (myocardial infarction). ACS represent wide spectrum of conditions with sudden death (acute ischemia causes ventricular fibrillation, and the patient dies before medical service is called) on one end and oligosymptomatic unstable angina, which the patient leaves untreated (atherosclerotic plaque becomes stable without myocardial infarction formation), on the other.

Symptoms of acute myocardial ischemia. The clinical presentation of acute myocardial ischemia is **chest pain (anginal pain)**. The typical presentation is pain localized on the anterior aspect of chest (most commonly retrosternal), which sometimes radiates between shoulder blades (cave: it can be mistaken for musculoskeletal back pain and such mistake may be fatal for the patient!!), or to the neck (it can be mistaken for angina tonsillaris), or epigastrium (cave: mistaking for acute abdominal pain can be ill-fated for the patient!). Eighty percent of patients with ACS have pain on the anterior aspect of chest, 10% of patients feel pain only in one of the other abovementioned areas (for example pain is felt between shoulder blades without pain on the anterior aspect of chest), and about 10% of patients (most often diabetics) do not feel any pain (silent ischemia). In about half of cases, anginal pain can be accompanied by other symptoms: dyspnea, diaphoresis, fatigue, nausea, or vomiting. In patients with silent ischemia, large ischemia (severe acute dysfunction of the left ventricle) presents only with sudden onset of dyspnea (without chest pain). If myocardial ischemia causes severe hypotension, extreme bradycardia, or ventricular arrhythmia (Torsade de Pointes), it can present with syncope. The more severe are symptoms, the more severe ischemia is, and poorer prognosis can be expected.

Definition and diagnostic criteria of myocardial infarction. Patophysiological definition: myocardial infarction is defined as regional ischemic necrosis of the myocardium in the territory of the occluded or critically narrowed coronary artery. **Clinical definition**: detection of a rise (above upper reference limit) and subsequent fall (within normal range) of cardiac biomarkers (troponin I, troponin T, or CK-MB) with at least one of the three following signs of ischemia:

(a) Medical history: typical symptoms (anginal pain), and/or

(b) ECG: new ST-segment-T wave changes, or new bundle branch block, or new pathological Q wave (see the ECG section of this textbook), and/or

(c) Imaging techniques: evidence of new regional wall motion abnormality of the left ventricle, or new loss of viable myocardium by imaging methods (echocardiography, CT scan, MRI, radionuclide imaging).

Diagnostic algorithm in patient with acute chest pain is shown below:

Patient with **suspected ACS** (angina pain and/or dyspnea): **prompt 12-lead ECG**

At least one of these criteria present:

ST-segment elevations >1 mm

ST-segment depressions >2 mm

New LBBB or RBBB

Symptoms of heart failure or shock

Severe arrhythmias

Ongoing chest pain

Administration of **antithrombotic medication**:

Heparin 100 IU/kg

Aspirin 250-500 mg

Prasugrel 60 mg (or Ticagrelor 180 mg or Clopidogrel 600 mg)

Prompt transfer in the cath lab

ECG is negative or **not specific**

Clinically stable patient (without heart failure, without hypotension, without arrhythmia, chest pain subsided)

Troponin positive

Coronary angiography within 72 hours or immediately, if symptoms reappears

Troponins are twice negative in 12 hours interval

If probability of CAD is low:

A stress test and discharge if the test is negative.

(If the stress test is positive, than coronary angiography.)

Conservative approach in elderly (≥75 years) without symptoms recurrence

In patients younger than 75 years, if probability of CAD is high (e.g. in diabetics):

Coronary angiography

Unstable angina pectoris. This term means any worsening of angina: (a) new onset angina, (b) sudden worsening of previously existing angina (of one CCS class at least), (c) angina occurring at rest. Apart from medical history, confirmation of ischemia by ECG during chest pain or during stress test and/or detection of a morphological substrate (significant coronary artery stenosis) by

angiography are necessary for definitive diagnosis of unstable angina. At the same time, biomarkers have to be negative at least twice in a row (if biomarkers were positive, it would be myocardial infarction). Availability and high sensitivity of modern biochemical methods, which detect even very small (<1 gram) myocardial necrosis, have changed spectrum of patients with unstable angina (many patients with this diagnosis in the past are now classified as little myocardial infarctions).

Acute myocardial infarction without ST-segment elevations (NSTEMI) / non-Q wave myocardial infarctions. It is smaller myocardial infarction (nontransmural, subendocardial) where the coronary artery with unstable plaque is usually not completely occluded, but critically narrowed. At presentation, working diagnosis is usually made according to patient's medical history (chest pain) and ECG (ST-segment depression, or negative T wave, or previous bundle brunch block). The diagnosis is confirmed by biomarker (troponin I or T) dynamics (rise with subsequent fall). Acute myocardial infarction without ST-segment elevations (admission diagnosis) with correct treatment results in non-Q wave myocardial infarction (discharge diagnosis). Although sometimes (especially, if coronary angiography was not carried out in time) even this type of myocardial infarction can progress in Q wave myocardial infarction (see below). The most typical ECG findings (ST-segment depressions) correspond with subendocardial myocardial ischemia.

Acute myocardial infarction with ST-segment elevations (STEMI) / Q wave myocardial infarction. It is larger myocardial infarction (transmural) where the coronary artery is usually completely occluded with a new thrombus. ECG shows ST-segment elevations (Parde waves) as signs of acute transmural myocardial ischemia. Without treatment or if the myocardial infarction is not treated within two hours of the symptom onset, myocardial infarction with ST-segment elevations (transmural ischemia) results in so called Q wave myocardial infarction (transmural necrosis). Q wave myocardial infarction is defined by presence of pathological (at least 40 ms wide) Q waves in at least two consecutive leads. With early (within two hours of symptom onset) and efficient treatment (recanalization of the coronary artery with thrombotic occlusion by angioplasty), it is almost always possible to prevent development of transmural necrosis (to prevent

development of Q waves), and the patient is discharged with much smaller (non-Q wave) myocardial infarction than initially threatened. Acute angioplasty for myocardial infarction is called primary percutaneous coronary intervention (primary PCI) – see below.

Localization of myocardial infarction. According to ECG, myocardial infarctions are traditionally classified as anterior (always V1-V4, sometimes also I, aVL, V5-V6), inferior (II, III, aVF) , and „true posterior" (III, aVF, V1, V6). This classification roughly corresponds with coronary anatomy: anterior infarction is caused by LAD occlusion, inferior one by RCA occlusion, and true posterior one by LCX occlusion. In up-to-date cardiology, all patients with myocardial infarctions undergo coronary angiography, so the infarct artery is identified at the beginning, and therefore, the most logical approach is to determine infarct location according to the occluded artery: myocardial infarction in the LAD territory, RCA territory, and LCX territory.

Pre-hospital diagnostic procedures and treatment in a patient with suspected myocardial infarction. A patient with symptoms resembling myocardial infarction should call directly the emergency medical service (telephone number in Czech Republic 155 or 112). They should dispatch an ambulance with a physician. The ambulance has to be equipped with resuscitation equipment including defibrillator and also a 12-lead ECG recorder. At the time of first medical contact, after a short assessment of medical history and physical exam, ECG should be obtained. Further steps are taken according to clinical findings and ECG:

Direct transport for coronary angiography (primary PCI) to catheterization laboratory of the nearest primary PCI center is indicated if (aa) ECG shows ST-segment elevations, or deep ST-segment depressions, or new LBBB or RBBB, and/or (ab) the patient has hypotension, signs of heart failure or shock. Before transport, three essential antithrombotic agents are administered: Kardegic i.v. (or other form of acetylsalicylic acid PO), Heparin 100 IU/kg i.v., Prasugrel 60 mg p.o. (or Ticagrelor 180 mg p.o., or Clopidogrel 600 mg p.o.). Fentanyl or Morfin are used during transport to relieved chest pain.

Transport to emergency department of the nearest hospital is indicated if ECG shows any other findings, and no signs of heart failure are present. During transport, diagnosis is uncertain in these cases, and clinical status of the patient is usually stable. Therefore pharmacotherapy is usually left after diagnosis is established at the hospital.

Myocardial infarction complications. Acute myocardial infarction (AMI) can have a wide variety of complications. The most common cause of death in patients with AMI in the pre-hospital setting are malignant arrhythmias (ventricular fibrillation or less often asystole) that are caused by electric instability in acute ischemia phase. After hospital admission, majority of arrhythmias are easy to manage, and most deaths are caused by hemodynamic instability (cardiogenic shock or other forms of acute heart failure). Other possible complications: pericarditis (pericarditis episthenocardiaca), cardiac tamponade due to ventricular free wall rupture, acute ventricular septal defect due to ventricular septal rupture, acute mitral

regurgitation due to rupture or severe dysfunction of papillary muscle, intracardiac thrombosis (usually in the apex of the left ventricle in anterior myocardial infarction with developing aneurysm) with possible systemic embolization (for example stroke), aneurysm (aneurysm of the left ventricle formed by scar tissue) , pseudoaneurysm of the left ventricle (aneurysm of the left ventricle covered by pericardium; it develops after slowly progressing and incomplete ventricular free wall rupture).

Differential diagnosis of myocardial infarction. At first medical contact, it is necessary to take into account the wide spectrum of other diseases that can cause similar symptoms: pulmonary embolism, acute myocarditis, acute pericarditis, dissecting aortic aneurysm, gastroesophageal reflux, peptic ulcer, acute abdominal pain, stress-induced cardiomyopathy (so called Tako-Tsubo), pneumothorax, etc. For establishing diagnosis, ECG, biomarkers, and echocardiography are essential. If the first ECG shows ST-segment elevations, diagnosis of STEMI is almost certain. Pericarditis and syndrome

of early repolarization (see ECG section of this textbook) has to be considered as well. Also, If a patient has typical chest pain a deep ST-segment depressions, diagnosis is easily established. In other cases echocardiography or ultrafast CT scan can help.

Antithrombotic treatment of acute coronary syndromes. Combination of fast and precise diagnosis (ECG, troponin, coronary angiography, echocardiography) with early antithrombotic treatment (dual antiplatelet therapy with acetylsalicylic acid + thienopyridine with anticoagulant – usually heparin) and early revascularization (PCI or bypass) is essential for successful treatment of ACS. The most common way of treatment currently is: **ASA + prasugrel (or ticagrelor) + heparin + urgent coronary angiography/ PCI**. Antithrombotic agents can be (in a simplified way) classified in three groups: drugs inhibiting platelet functions (antiaggregants), drugs targeting coagulation cascade (anticoagulants), and agents dissolving blood clots (thrombolytics, fybrinolytics). The class of oral **antiplatelet agents** includes: acetylsalicylic acid (aspirin, ASA, Anopyrin.), clopidogrel (Plavix.), prasugrel (Efient.), ticagrelor (Brilique.). So called dual antiplatelet therapy (ASA combined with one of the three abovementioned drugs) is used in patients with ACS. Injectable antiplatelet agents: Kardegic., abciximab (ReoPro.), epitifibatide (Integrilin.). Oral anticoagulants are not used in ACS. Parenteral **anticoagulants**: heparin (unfractionated, UFH), enoxaparin (Clexane.), bivalirudin (Angiomax.), fondaparinux (Arixtra.). **Fibrinolytics** (alteplase, reteplase, tenecteplase, streptokinase, urokinase) were formerly used in STEMI to achieve reperfusion. At present, they are not used where primary PCI is reachable (practically the whole area of Czech Republic). They are still indicated only if primary PCI is not reachable within 90 minutes from establishing the diagnosis, and at the same time, the patient has contacted medical service in the first three hours from symptom onset (“early presenters at long distance from PCI hospitals”). Trombolytics were never indicated in NSTEMI or unstable angina in the past.

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Reperfusion therapy of myocardial infarction. Reperfusion therapy is treatment modality aimed at re-establishing perfusion (reperfusion) in the coronary artery with thrombotic occlusion in acute phase of STEMI. Opening the occluded coronary artery can be achieved by two means: mechanically (by angioplasty) or pharmacologically (thrombolysis). Primary percutaneous coronary intervention (p-PCI, direct coronary angioplasty) has more than 90% efficacy in achieving reperfusion. Moreover, PCI eliminates coronary stenosis where thrombus was formed (so it minimalizes risk of myocardial infarction recurrence). Thrombolysis is effective only in about 50% of cases. Moreover, it does not influence preexisting coronary stenosis (so the risk of myocardial infarction recurrence is not negligible). Further thrombolysis limitation is the risk of serious bleeding (including 2% risk of cerebral hemorrhage). Many large randomized trials have proved much higher efficacy of p-PCI in comparison to thrombolysis in patients with STEMI. Czech cardiologists (in 51 Czech hospitals) have published two important pioneering studies: PRAGUE (published in 2000) and PRAGUE-2 (published in 2003). Both trials have proved that p-PCI is better than thrombolysis not only for patients coming

with myocardial infarction right in the primary-PCI capable center, but even for those coming in other smaller hospitals who need transfer for p-PCI by ambulance service from remote places up to 100 km away from the referral center. Similar outcomes showed also the smaller study called VINO (published in 2002) in patients with NSTEMI. These findings (later confirmed by similar studies abroad) have changed fundamentally management of patients with AMI: practically all these patients get in PCI capable centers where coronary angiography and PCI can be performed.

Indications for reperfusion therapy with p- PCI and thrombolysis in STEMI are listed in the table:

Primary PCI **Thrombolysis**

ST-segment elevations ≥2 mm in at least 2 consecutive leads in patients **0-12 hours** from symptom onset if estimated time from establishing diagnosis till the beginning of coronary angiography/PCI is **<90 minutes**

ST-segment elevations ≥2 mm in at least 2 consecutive leads in patients **0-3 hours** from symptom onset if estimated time from establishing diagnosis till the beginning of coronary angiography/PCI is **>90 minutes**

New (or presumed new if older ECGs are not available) **LBBB or RBBB**, other as above

ST-segment elevations ≥2 mm in at least 2 consecutive leads in patients **0-12 hours** from symptom onset in countries or areas where PCI is not available

STEMI with **thrombolysis contraindications** (regardless estimated time to PCI)

STEMI with **heart failure, hypotension, or cardiogenic shock** 0-48 hours from symptom onset

AMI with recurrent ischemia (**reinfarction**)

STEMI with ongoing ischemia after unsuccessful thrombolysis (**rescue PCI**)

AMI with **ST-segment depressions >2 mm** and ongoing/recurrent anginal pain or hemodynamic or electric instability

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Other pharmacological agents in acute coronary syndromes. Apart from above mentioned antithrombotics, patients with ACS are given statins, betablockers, and angiotenstin-converting enzyme inhibitors (ACE-I) as standard treatment. Statins (e.g. atorvastatin, rosuvastatin, simvastatin) improves blood cholesterol levels and stabilize atherosclerotic plaques. Betablockers decrease risk of reinfarction and sudden cardiac death. ACE-I lower risk of heart failure progression. Other drugs have not been proved to influence prognosis of patients with ACS, but they can improve their symptoms (if they have any in further clinical course).

Revascularization treatment of acute coronary syndromes (percutaneous coronary intervention, coronary artery bypass grafting (CABG)). The term includes two methods: PCI is a transarterial catheterization procedure and CABG is a surgical procedure. **PCI** is performed via femoral or radial approach. The advantage of radial approach is greater patient comfort (he leaves cath lab "by foot" and he can be discharged in a few hours) and the disadvantages is higher radiation dose for the patient and personnel. Less hematomas have been reported after use of radial approach. As far as serious **complications of PCI**, both approaches are similar: death after PCI has been reported in 0.1-0.5%, clinically apparent periprocedural myocardial infarction in about 3-5% (most often cause is occlusion of lateral branch in dilated segment), cerebrovascular accident in 0.1-0.2%, serious hemorrhage requiring transfusion and/or surgical treatment in 2%. It has been proved that PCI in ACS unambiguously improves prognosis of patients (extends life span, decreases mortality rate). This is different from PCI in patients with chronic forms of CAD where symptoms are improved after PCI, but prognosis does not change. During PCI procedure, at first, a guiding catheter is advanced to a stenosed (or occluded) artery, than a thin intracoronary wire with a soft tip is passed through its lumen, than a balloon catheter is passed over the wire into stenosis. Stenosis is than dilated with the balloon and a coronary stent is implanted in this place. There are two types of stents: bare metal stents (BMS, the best BMS are from alloy of chrome and cobalt) and drug eluting stents (DES, the best current stents are those eluting everolimus – drug preventing restenosis). The risk of clinically apparent repeat narrowing so called restenosis is about 3-5% in patient with an implanted stent (DES). Restenosis is slow process (hypertrophic scaring of the artery at the place of a stent). It manifests clinically as gradual recurrence of exertional angina and we usually have enough time to treat it (re-PCI or CABG). To the contrary, stent thrombosis has much more dramatic clinical course (as peracute STEMI). Risk of stent thrombosis after BMS or everolimus eluted stent implantation is about 1-3%. Stent thrombosis is usually consequence of dual antiplatelet therapy interruption. Coronary artery bypass grafting is surgical method using vein or arterial grafts to bypass the stenosed or occluded segment of the coronary artery. The risk of this procedure depends on patient's overall health status, age, comorbidities, etc. Mean mortality rate in connection with CABG is about 2%, the risk of

perioperative stroke is about 5%, serious bleeding rate is about 10-15%, infections are reported in about 2-3%. Particularly, patient with extensive coronary atherosclerosis (three vessel
disease, i.e. LAD, LCX and RCA or left main coronary artery disease + two other arteries) and patients with systolic dysfunction benefit from CABG. Prognosis of those patients (e.g., three vessel disease + systolic dysfunction) is poor without surgery. PCI is indicated in patients with less extensive disease (one or two vessel disease) or if the risk of surgery is too high (patients with much comorbidities, patients with AMI and hemodynamic instability, very old patients, all patients with STEMI).

Sekundární prevence po infarktu myokardu. It is utterly essential to adhere to principles of secondary prevention after myocardial infarction: do not smoke, meticulous treatment of diabetes mellitus and hypertension, reduce overweight, eat diet with low quantity of animal fat and high in plant-based foods, and use drugs that are proved to lower the risk of death and reinfarction: aspirin, clopidogrel (or prasugrel, or ticagrelor), statin, betablocker, and alternatively ACE-I. Nowadays, also implantable cardioverter-defibrillators, which are implanted in patients with significant dysfunction of left ventricle after myocardial infarction, are embodied in secondary prevention of sudden cardiac death.

Short- and long-term **prognosis after myocardial infarction.** AMI mortality in pre-hospital phase is not well explored considering difficulties with establishing of diagnosis in individuals who die before hospital admission. Figures from literature stating up to 30% mortality rates are difficult to verify. In contrary, data on in-hospital mortality are very precise. Mortality rate of STEMI is 4-8% after p-PCI, 6-18% with thrombolysis, and about 25-30% without reperfusion treatment. After hospital discharge, 3-5% of patients after STEMI die during the first year, and about 2% a year die in following years. NSTEMI has in-hospital mortality rate 1-3% after PCI and 6-9% without revascularization treatment. After hospital discharge, 7-11% of patients after NSTEMI die during the first year of follow-up. The mortality rate in patients with unstable angina (repeatedly negative troponin) who undergo PCI treatment is similar as in stable angina patients (i.e. <1%). It is higher without PCI.

10. Systemic hypertension

(P.Gregor)

Prevalence of Hypertension, Definition, Classification, Key Terms

Systemic hypertension is the most common disease of cardiovascular system. Its prevalence ranges between 20 to 50% in developed countries and remains serious public health problem. It is one of the major risk factor for stroke, ischemic heart disease and peripheral artery disease beside diabetes, dyslipidemia, smoking and obesity.

Hypertension is defined as a blood pressure (BP) of 140/90 mm Hg or higher. Closer it can be specified as an optimal, normal, higher (prehypertension) and stage 1, 2 and 3 hypertension (Tab. 1).

Other terms related to hypertension: *Resistent* hypertension is considered when the blood pressure cannot be reduced below 140/90 even with combination of at least three antihypertensive drugs. *Hypertensive crisis* is an acute, life-threatening condition associated with sudden increase in BP (diastolic BP usually exceeding 130mmHg). When the rapid rise of BP is accompanied by acute damage of target organs or their function it is called emergent hypertensive crisis. These include hypertensive encephalopathy, heart failure, acute coronary syndromes, cerebrovascular events, subarachnoid hemorrhage or aortic dissection.

We talk about "*white coat hypertension"* when the blood pressure is higher only in medical institute - physician´s office, while in other cases the measurement of BP is normal. The opposite may be *masked hypertension* when the values measured in physician´s office are normal while in all other cases (including home monitoring) are higher.

Measurement Technique

The blood pressure should be measured with the patient seated, after 10 minutes of rest, in bare arm at heart level (for the first visit in both arms) (1). For arm circumference 33 cm or more, wider cuffs are used. Systolic pressure is read at the appearance of heart sounds, diastolic in their disappearance. In some cases of hyperkinetic circulation, where the phenomenon of endless tone is evident, we read diastolic BP at the time of sudden attenuation of sounds. Measurements should be performed three times and it is considered taking the average of 2nd and 3rd. In elderly and in diabetics we perform measurement even while standing (orthostatic hypotension possibility).

When aneroid manometer is used including variety of semi-automatic monitors for laics, these devices must be calibrated more frequently compared to values obtained by classical mercury tonometer. Ambulatory BP monitoring is

performed in patients with large fluctuation in BP values, in suspected white coat phenomenon or masked hypertension, or in patient with resistance to treatment (1). The length of monitoring is usually 24 hours with a mean normal value ≤ 130/80, while daily average is ≤135/85 and ≤120/70 at night. The measurement of BP is performed automatically. In terms of etiopathogenesis hypertension is divided into primary (essential) and secondary.

Essential Hypertension

It is a typical multifactorial disease and represents 95% of all hypertensions. In pathogenesis are reflected genetic influences, as well as certain dietary habits (increased salt intake), obesity, regular intake of greater amounts of alcohol (over 30g/day), stress. It also occurs more frequently in people with insulin resistance (increased insulin levels, lipid disorders and obesity defined by waist circumference determines metabolic syndrome). There is also a number of other factors such as failure of regulatory mechanisms with various vasoconstrictor factors (sympathetic activity, catecholamines, tromboxanes, renin-angiotensin-aldosterone system, endothelin, etc.).

Secondary Hypertension

Although it occurs in only 5% of hypertensive patients its differentiation from essential hypertension is necessary for option of specific therapy with causes elimination which may lead to full recovery. Overview of secondary hypertension types shows Tab. 2, some of them are simply discussed below, others are discussed in other relevant chapters (coarctation of aorta, congenital heart diseases etc.).

Renovascular Hypertension

It is frequent cause of secondary hypertension. The cause is atherosclerotic disease or fibromuscular dysplasia of renal artery. As a result of renal ischemia renin and angiotensin II are overproducted. Another ischemic affections can be often found when examinated (especially ischemic peripheral artery disease), sometimes systolic abdominal vascular murmur can be obtained. Gold standard for renal artery stenosis evaluation is angiography. Sometimes renal scintigraphy after captopril administration or assessment of renin blood level during captopril test can be non-invasive alternative. The main therapeutic approach is percutaneous transluminal renal angioplasty.

Renal Hypertension

Hypertension may cause virtually any more severe renal parenchymal disease, so the diagnosis is very broad. For therapy are preferably used antihypertensives which does not reduce renal flow (selective betablockers, calcium channel blockers, centrally acting antihypertensives…), for patients with severe chronic renal failure certainly diuretics (furosemide from creatinin level 200 μmol/l). ACE inhibitors slow disease progression, especially in diabetic neuropathy and other renal diseases with proteinuria.

Primary Hyperaldosteronism (Conn Syndrome)

The most common cause of endocrine hypertension and it is responsible for nearly 20% of resistant hypertension. The cause is autonomous aldosterone overproduction from adenoma or andrenal cortex hyperplasia respectively. The most often warnings are resistant hypertension with hypokalemia, often at young age. Clinically muscle weakness and polyuria can be observed. In laboratory findings is typical increased plasmatic aldosterone in ng/dl (not always expressed) and decreased plasma renin or plasma renin activity in ng/ml/hod (always reduced to varying degrees). The most sensitive marker in screening is plasma aldosterone/plasma renin activity ratio above 30. Further we should focus on imaging of anatomical substrate – tumor or hyperplasia (sonography, CT, MRI). It can be treated by adrenalectomy (adenoma) or aldosterone antagonists for hyperplasia (spironolactone in initial dose of 100 to 200 mg, maintenance 25 to 70 mg/day or eplerenone).

Pheochomocytoma

Tumor of adrenal medulla chromaffinic tissue or localized extraadrenally in abdominal cavity. thorax or neck. In 10% the tumor is malignant. Clinically may be typical paroxysms with severe hypertension and signs of increased metabolism (tachycardia, tremor, pallor, abdominal pain, hyperglycemia), but more often it comes to sustained hypertension with significant myocardial hypertrophy and retina changes. Diagnosis is based on hormonal overproduction of metanephrines (metanephrin and normethanephrine in urine, total plasmatic metanephrines) or original plasmatic catecholamines in urine and timor imaging (sonography, CT, MRI). For extraadrenal timors can be performed isotop-labeled test with metajodbenzylguanidin (MIBG). Treatment consist of adrenalectomy, when surgery impossible (and when preparing for surgery) phenoxybenzamine or doxazosine. Betablockers can be used after previous administration of alphablockers.

Cushing Syndrome

Hypertension is caused by an overproduction of cortisone with sodium retention and increased vascular sensitivity to vasopressor hormones. Central form is caused by an overproduction of ACTH (known as Cushing´s disease, mostly pituitary adenomas), peripheral form (Cushing´s syndrome) by adrenal tumors (adenomas). Ectopic form (e.g. at lung cancer, pancreatic cancer, etc.) and mainly iatrogenic form caused by corticosteroid therapy also exist. Typically we can found central type of pbesity, moon-like face, reddish purple striae, osteoporosis and more. For laboratory assessment is used free cortisol level in urine or ACTH, details about suppression tests can not be discussed here.

Hypertension Associated to Drug Use

It is relatively new group of hypertension developing after the use of certain drugs (amphetamine, LSD, cocaine, ecstasy).

Hypertension in pregnancy

It is necessary to distinguish between pre-existing hypertension ongoing in pregnancy and new onset of hypertension in pregnancy (gestational). It usually appears after 20th week of pregnancy – it is mostly preeclampsia which is associated with proteinuria.

Effects of Hypertension

Untreated hypertension causes hypertensive vascular changes affecting the arterioles. It leads to vessels remodeling which then have thicker wall (hypertrophy of media) and narrower lumen resulting in increased peripheral vascular resistance. Left ventricle responds to pressure overload with myocardial hypertrophy development which further worsens the prognosis (higher incidence of sudden death caused by arrhythmia, heart failure - mainly diastolic dysfunction).

Prognosis of Hypertension

It depends on the BP level (especially systolic), presence of other risk factors (smoking, lipids, diabetes mellitus, obesity), target organ damage and presence of other comorbidities. From the damages of target organs are prognostically important especially left ventricle hypertrophy, sonographically proven thickening of arterial wall (thickness of intima – media of common carotic artery 0.9mm or more), peripheral artery disease, advanced retinopathy (haemorrhages, exudates, papilloedema, resp.). Significant prognostic sign is occurrence of strokes (ischemic or aemorrhagic) or TIA. Microalbuminuria (30-300 mg/24 h) and decline in renal functions are also important prognostic factors. When determioning total cardiovascular risk, it is recommended to use SCORE nomograms, which allow to predict probability of cardiovascular death in next 10 years (Fig. 1). Evaluated risk higher than 5% is assumed to be significant.

Treatment

Treatment leads to decrease in mortality from stroke by 30-40%, morbidity and mortality from ischemic heart disease by 20-30%, incidence of heart failure by 50% (2). The aim of treatment is to achieve values of BP below 140/90 in all patients with hypertension. The target value of BP for diabetics, patients with history of myocardial infarction or stroke, those with metabolic syndrome, SCORE more than 5%, renal dysfunction or proteinurua is < 130/80.

Nonpharmacological Treatment

is summarized in Table 3.

Pharmacological Treatment

Situations in which we start pharmacological treatment are summarized in Table 4. It includes five principal antihypertensive agents of "1st line". These represent angiotensine converting enzyme inhibitors (ACE-I), AT1 receptor blockers, calcium channel blockers (Ca-B), betablockers, diuretics.

The different types of antihypertensives are chosen preferably in situations where they are indicated from other causes (Table 5).Other aspects of hypertension treatment using different agents are summarized in Table 6 – 15, treatment of hypertensive crisis in Table 16.

Table 1. Definition and Classification of Blood Pressure Categories (1).

	Systolic	*Diastolic*
optimal	< 120	< 80
normal	120 – 129	80 – 84
high normal	130 – 139	85 – 89
mild hypertension	140 – 159	90 – 99
moderate hypertension	160 - 179	100 – 109
severe hypertension	≥ 180	≥ 110
isolated systolic	≥ 140	< 90

Table 2. Simplified Causes of Secondary Hypertension

Renal causes	-	Renovascular (stenosis of a. renalis)
		Renal: glomerulonephritis, interstitial nephritis, diabetic nephropathy, polycystic degeneration etc.
Endocrine syndrom	-	Adrenal cortex: primary hyperaldosteronism, Cushing´s

	-	Adrenal medulla (pheochromocytoma)
	-	Other: hyperthyreosis, primary hyperparathyreosis, acromegaly
Coarctation of aorta		
Medicaments	-	Hormonal contraceptives, glucocorticoides, tricyclic antidepresives, anorectics….
Drugs	-	Amphetamines, cocain, LSD, ecstasy
Pregnancy	-	Late pregnancy gestosis (preeclampsia)
Neurogenic	-	Tumors or inflammation of brain or meninges
Others	-	Hypertension after transplantations (heart, kidney), sleep apnea syndrome

Figure 1. SCORE – European system for 10-years risk stratification of cardiovascular mortality

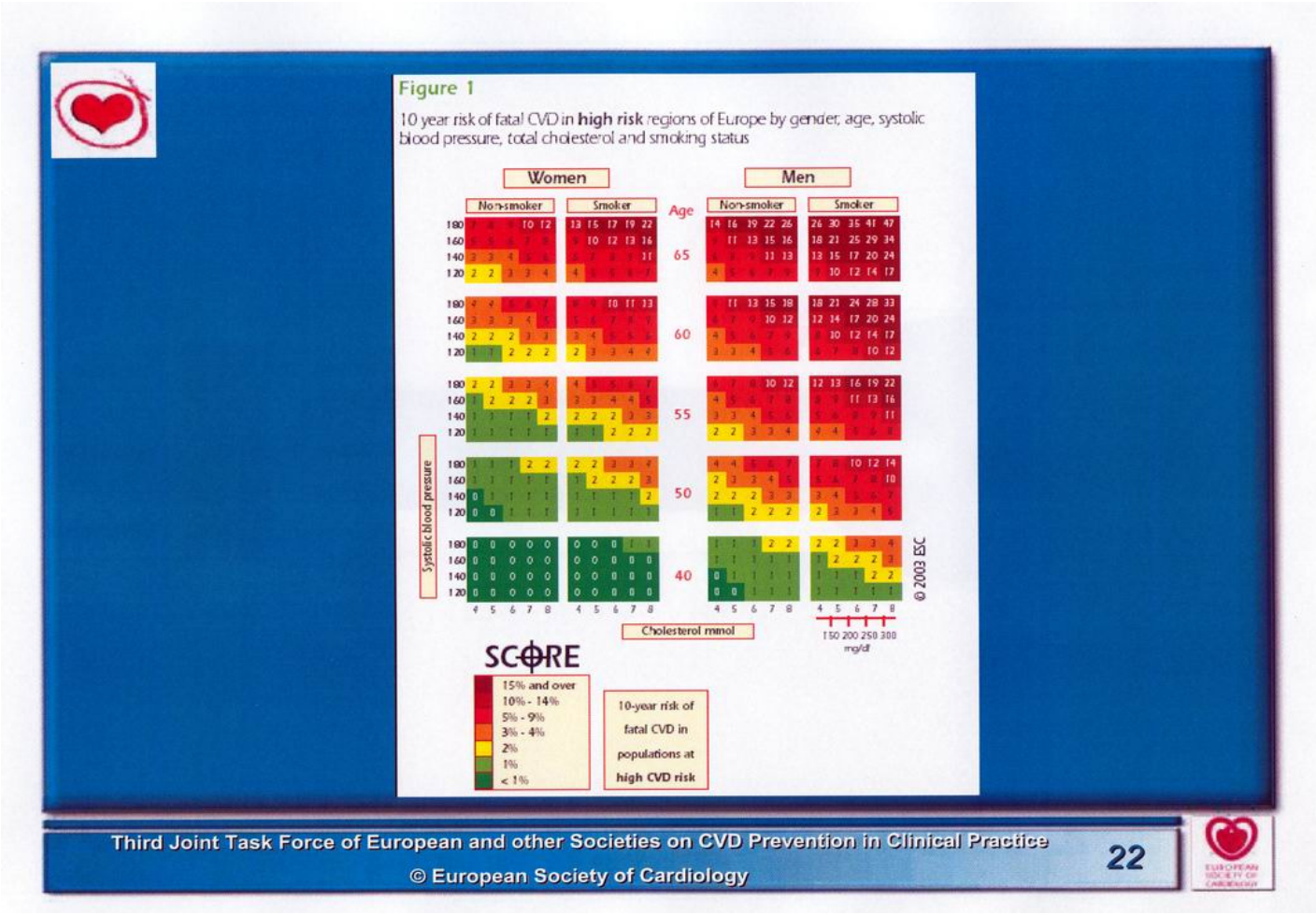


Table 3. Nonpharmacological Treatment of Hypertension (2)

Activity	***Aim***
Stop smoking	Decrease in cardiovascular mortality
Weight reduction	BMI 18,5 – 25
Physical activity	Aerobic, fast walking 30min/day
Reduce in salt intake	5-6 g/24hours
Alcohol reducing	Less than 30 g/day for men and 20 g/day for women
Increase in consumption of fruit, vegetables, fat (especially unsaturated).	

Table 4. When is The Pharmacological Treatment Indicated?

Blood pressure: > 180/110 mm Hg - always > 140/90 in SCORE more than 5%or damage of target organs 130 - 139/85 - 89 – history of stroke, ischemic heart disease, DM, cumulation of risk factors

Table 5. Which type of antihypertensive drugs are preferably used

Ischemic heart disease, heart failure:	BB, ACE-I, (diuretics)
Diabetes mellitus:	ACE-I, Ca-B
Elderly people:	Ca-B, BB, ACE-I
Renal diseases with proteinuria:	ACE-I

(BB – betablockers, ACE-I – angiotensin – converting enzyme inhibitirs, Ca-B – calcium channel blockers

Table 6. Therapy of Hypertension – ACE inhibitors

Cardioprotective, vasoprotective and renoprotective effects Preferably for: - Chronic heart failure - Left ventricle dysfunction (even asymptomatic) - DM with neuropathy - Hypertensive crisis (first aid – captopril)

Table 7. Summary of ACE-I used for Treatment of Hypertension
Simplified according to guidelines of the Czech Society of Hypertension (1)

Generic name	**Daily dosage**
Long-acting	
Cilazapril	2.5 - 5 mg
Fosinopril	10 - 20 mg
Imidapril	5 - 20 mg
Lisinopril	20 - 40 mg
Perindopril	5 - 10 mg
Quinapril	5 – 20mg
Ramipril	2.5 -10 mg
Spirapril	6 mg
Trandolapril	2 – 4 mg
Moderate-acting	
Enalapril	5 – 20 mg
Short-acting	
Captopril	12.5 – 50 mg

Table 8. Summary of AT1 blockers used for treatment of hypertension
Simplified according to guidelines of the Czech Society of Hypertension (1)

Generic name	**Daily dosage**
Candesartan*	8–32 mg
Irbesartan*	150–300 mg
Losartan	50–100 mg
Olmesartan*	10–40 mg
Telmisartan	40–80 mg
Valsartan	80–160 mg
* – currently not available in the Czech republic	

Table 9. Calcium Channel Blockers – effect, indication

Decrease in peripheral vessel´s resistance
positive influence on renal and peripheral vessels blood flow
Without orthostatic hypotension, bronchoconstriction, influence on lipid metabolism, glycides, K, Na
Recommended for DM, COPD, renal insufficiency, ischemic disease of peripheral arteries, isolated systolic hypertension, supraventricular tachycardia (verapamil)

Table 10. Summary of Calcium Channel Blockers used for Treatment

Simplified according to guidelines of Czech society of hypertension (1)

Drug	**Daily dosage**
Amlodipine	5–10 mg
Felodipine	5–10 mg
Isradipine SRO	5–10 mg
Lacidipine 1	2–6 mg
Nitredipine	10–40 mg
Verapamile SR	120 – 140 mg

Table 11. Treatment of Hypertension – betablockers

Preferably for ischemic heart disease, left ventricle dysfunction
Preferably selective, without ISA (or light ISA)
Alone or in combination

Table 12. Sumarry of Betablockers Used for Therapy of Hypertension

Simplified according to guidelines of Czech society of hypertension (1)

Generic name	**Daily dosage**
Selective:	
Atenolol	50–100 mg
Betaxolol	10–20 mg
Bisoprolol	5–10 mg
Metoprolol	50–200 mg
Selective with ISA:	
Acebutolol	400–800 mg
Nonselective with ISA:	
Bopindolol	1–2 mg
Combined alfa and beta effect	
Carvedilol	12,5–25 mg
Labetalol*	100–200 mg

* – currently not available in the Czech republic

Table 13. Therapy of Hypertension – diuretics.

Indication: age, retention of Na or water, congestive heart failure	
Types of drug:	
Thiazides: HCHTZ 12.5 – 25mg/day	
Chlortalidone 12.5 mg /day	
Furosemide	- only for renal insufficiency (GFbelow 0,5, creatinine below 200)
	- hypertensive crisis, left ventricle failure
Metipamide, indapamide	– DM, hyperlipoproteinemia

Table 14. Summary of Diuretics Used for Therapy of Hypertension

Simplified according to guidelines of Czech society of hypertension (1)

Name	**Daily dosage**
Thiazides and related diuretics	
Hydrochlorothiazide tbl.	12,5 – 25 mg
Chlorthalidone	12,5 mg
Indapamide	1,25 – 2,5 mg
Metipamid	1,25 – 2,5 mg
Loop diuretics (only for hypertension associated to heart failure or renal insufficiency (creatinine > 200 umol/l)	
Furosemide	20 – 1 000 mg
Kalium sparing diuretics	
Amiloride**	5 – 10 mg
Spironolaktone***	12,5 – 50 mg
Eplerenone***	50 – 100 mg

**Usually in combination with other diuretics
***Preferably in chronic heart failure in combination with look diuretik and in primary hypertaldosteronism

Table 15. Adrenergic alfa receptor blockers

Central (+ peripheral): alpha – metyldopa, clonidine, urapidil

Imidazole receptors blockers – moxonidin, rilmenidin

Peripheral: prazosin (resistant hypertension, first dose syndrome)

Table 16. Treatment of Hypertensive Crisis

Nitrates:	ISDN 2-10 mg/h, NTG 0,5-10 mg/h
Nitroprusside:	0,3… (max.8) μg/kg/min.
Urapidil:	mg i.v. (continuously up to 100 mg i.v.)
Labetalol:	bolus of 20-40 mg i.v., than 1-2 mg/min.
Labetalol:	(first aid – physician´s office)
The aim: Decrease in BP of 20 %/ hour.	

11. Pulmonary hypertension

(V. Kočka)

Definition

Pulmonary hypertension (PH) is defined by mean pulmonary artery pressure (PAP) 25mmHg and higher. Values between 20-24mmHg are considered borderline. Exercise leads to PAP rise even in healthy volunteers and is no more used for PH diagnosis. Right sided heart catheterization is necessary for exact quantification of PH, echocardiography derived estimates of PAP are commonly used as well. There are two types of PH based on hemodynamic parameters like PAP, pulmonary capillary wedge pressure and cardiac output (table 1): precapillary and postcapillary. Table 2 presents another approach with groups more based on clinical picture. Please note that large majority of PH has secondary aetiology and only small minority of patients sufers from primary pulmonary hypertension – this is in contrast to systemic hypertension. Pulmonary hypertension can be mild, moderate or severe.

Table 1. Hemodynamic types of pulmonary hypertension					
		Pulmonary capillary wedge presure (mmHg)	**Transpulmonary gradient**	**Cardiac output**	**Clinical group**
Precapillary PH		≤15		Low or normal	1,3,4,5
Postcapillary PH		>15			
	Pasive		≤12	Low or normal	2
	Reactive, formerly mixed PH		>12	Low or normal	2
Hyperkinetic		≤15	>10	High (pulmonary flow)	Part of 1.4

Table 2. Clinical types of pulmonary hypertension (Dana Point, 2008)

1. Pulmonary arterial hypertension (PAH)

1.1. Idiopathic – primary

1.2. Hereditary

1.3. Drug or toxin induced

1.4. Secondary to: cardiac shunting, connective tissue disorders, HIV, portal hypertension

1' Pulmonary capillary haemoangiomatosis and pulmonary veno-occlusive disease

2. Pulmonary hypertension due to left heart disease

3. Pulmonary hypertension due to pulmonary disease and/or hypoxia

4. Chronic thromboembolic pulmonary hypertension

5. Pulmonary hypertension with unknown or multifactorial cause

Table 3 Severity of pulmonary hypertension			
	Mild	***Moderate***	***Severe***
Mean pulmonary artery pressure (mm Hg)	26-35	36-45	>45
Systolic pulmonary artery pressure (mm Hg)	36-45	46-60	>60

Clinical picture

Symptoms are often non-specific and occur rather late at the stage of severe PH. The most common complaints are dyspnoea and fatigue. Angina pectoris type of chest pain can be caused by right ventricle ischemia and syncope can be a sign of low cardiac output. Loud second heart sound over pulmonary area and gallop can be detected on heart auscultation. Regurgitant systolic murmur in the left parasternal area increasing in loudness in inspiration is typical of tricuspid regurgitation. Elevated jugular venous pressure, oedema and ascites are clear signs of right heart failure.

Examination methods

Examination methods are needed for diagnosis of PH as well as evaluation of its severity and aetiology. Echocardiography plays a key role:

- maximal velocity of tricuspid regurgitation jet can be used to derive pressure difference between right ventricle and right atrium.
- right atrial pressure can be estimated from the diameter and respiratory variation of vena cava inferior
- by simple adding those two values one can get a good estimate of right ventricle systolic pressure which (in the absence of pulmonary valve stenosis) is equal to pulmonary artery systolic pressure

Width of free wall of right ventricle over 5mm is suggestive of hypertrophy. Non round, asymmetric, moon-like shaped geometry of right ventricle make evaluation of size and systolic function difficult even for experienced imagers. Echocardiography will evaluate left heart disease as well, intracardiac shunting usually requires transoesophageal imaging.

ECG can occasionally demonstrate right ventricle hypertrophy. Chest X-ray can show dilated pulmonary arteries. CT pulmonary angiography is the method of choice to exclude pulmonary embolism, with the advantage of lung parenchyma evaluation at the same time. Invasive pulmonary angiography is performed rarely.

Pathophysiology and clinical classification of pulmonary hypertension

1. Pulmonary arterial hypertension (PAH) is primary disease of pulmonary arterioles. Arteriolar obliteration, tunica media hypertrophy, plexiform lesions are typical findings at histology. Pulmonary veins are typically spared. This disease is rare; prevalence is 15 patients per 1 million population. Idiopathic form constitutes 40%, hereditary less than 10% and the majority are secondary causes as per Table 2. Only 0.5% of HIV positive patients have pulmonary hypertension. Untreated PAH has poor prognosis, median survival is 2.8 years from diagnosis. Supportive therapy consists of home oxygen, flu vaccination and anticoagulation. Specific therapy is best concentrated in specialised centres of excellence, vasodilatin therapy can be chosen between calcium channels antagonists, i.v. prostanoids and recently orla medication like bosentan or sildenafil. This vasodilating therapy seems to improve patient prognosis. *Pulmonary capillary haemoangiomatosis and pulmonary veno-occlusive disease are very rare and not easy to differentiate from PAH. Severe hypoxia and severe reduction in CO diffusion capacity are typical, CT images are diagnostic and prognosis is poor, occasionally lung transplantation can be considered.
2. Pulmonary hypertension due to left heart disease, i.e. postcapillary form, is the most common form of chronic pulmonary hypertension. The incidence rises with age and it is estimated that it is present in 70% with left ventricle dysfunction – be it systolic or diastolic. It is a marker of worse prognosis. In the early phases the pulmonary capillary wedge pressure and pulmonary artery pressure rise in linear fashion, later transpulmonary gradient rises due to reactive pulmonary arterioles vasoconstriction resulting in mixed form of pulmonary hypertension. Therapy concentrates on primary disease; clinical trials with sildenafil are ongoing.

3. Pulmonary hypertension due to pulmonary disease and/or hypoxia is the second most common form of PH. Pulmonary hypertension is often mild and contrary to frequent belief only 10% of patients with COPD has pulmonary hypertension. Oxygenotherapy slows progression of the disease, probably due to better tissue oxygenation, lower haemoglobin levels and better rheological blood properties. The other causes of PH in this group include interstitial pulmonary disease and sleep apnoe syndrome.
4. Chronic thromboembolic pulmonary hypertension develops in 2-4%of survivors of acute pulmonary embolism. There are probably genetic predispositions. CT pulmonary angiography is diagnostic test of choice and is best evaluated in specialised centre. Prognosis correlates with the severity of PH, patients with severe PH have 80% mortality at two years. Effective anticoagulation is main therapy, should significant pulmonary hypertension persists after several months then surgical therapy (pulmonary artery endarterectomy) can be considered in experienced centres.
5. Pulmonary hypertension has been described in patients with myeloproliferative disorders, hystiocytosis etc.

Pulmonary hypertension due to congenital heart disease is part of group 1 but deserves special attention. It is less common now due to early diagnosis of congenital heart disease. Left-to-right shunting leads to increased flow in pulmonary circulation, initially mild PH progresses with advancing age and increasing pulmonary vascular resistence. Eisenmenger syndrome is extreme form of PH due to cardiac shunting when severe PH and high pulmonary vascular resistence lead to reversal of shunting to right-to-left or bidirectional form and development of cyanosis. This syndrome is contraindication of operative correction and marker of poor outcome.

Summary

Pulmonary hypertension is frequent complication of left heart disease or pulmonary disease, primary causes are less frequent. It is generally marker of worse prognosis. Less common forms, especially with severe pulmonary hypertension, are best evaluated and treated at specialised centres.

THROMBOEMBOLIC DISEASE

Definition and epidemiology

Deep vein thrombosis and pulmonary embolism are two clinical presentations of the same disease. Pathologist Rudolf Wirchow identified three basic conditions which predispose to thrombosis already in the mid 19th century: vessel wall trauma, blood stasis and hypercoagulable state. Thromboembolic disease is the third most common cardiovascular disease, estimated incidence is 6-10 thousand patients per 10 million population of Czech Republic per year. However this number may be underestimated due to non specific symptoms and difficult diagnosis of this disease.

Pathophysiology

Majority (90%) of vein thrombosis originates in the lower extremities, however number of patients with thrombosis in the upper extremities or superior vena cava is increasing due to widespread use of central cannulae or pacing electrodes. Vessel wall trauma may be due to local factors like trauma, plaster or bloodstream factors causing endothelial damage. Blood stasis can by caused by external vein compression, longer immobilisation, heart failure or venous insufficiency. Hypercoagulable state has several known genetic causes listed in Table 1; these are found in 30-50% of patients. Generally speaking these predispositions can be due to patient (age, thrombophilia, cancer, heart failure) and these are usually permanent or due to temporary circumstances like trauma, postoperative period, immobilisation etc.

Table 1. Genetic causes of thrombophilia known in 2012
Factor V Leiden station – activated protein C resistence
Prothrombin gene mutation
Protein C and S deficiency
Antithrombin III deficiency
Hyperhomocysteinemia
Antiphospholipid syndrome

Clinical significance of pulmonary embolism (PE) depends on the degree of pulmonary artery tree obstruction – it is necessary to obstruct 50% of pulmonary artery tree to cause pulmonary hypertension in healthy individuals. However please note that patients with pre-existing heart or lung disease may develop severe symptoms much earlier. Thin walled right ventricle (RV) cannot cope with sudden increase of pulmonary pressure in patients with acute pulmonary embolism; this leads to RV dilatation and failure. Acute RV dilatation leads to compression of left ventricle due to pericardial constraint, this leads to poor filling of left ventricle and later to hypotension. High wall stress of RV plus hypotension (lower perfusion pressure of coronary arteries) results in RV ischemia.
Significant PE leads to hypoxemia. At the same time there is "stretch" receptor mediated hyperventilation resulting in lower partial pressure of CO2. This combination of hypoxemia and respiratory alkalosis is typical for PE.

Examination methods

Quantitative measurement of D-dimer levels by ELISA method is very simple way how to exclude thromboembolic disease. There is excellent negative predictive value over 95% and this is clinically used to exclude PE. It has been demonstrated that patients with clinical suspicion of PE and negative D-dimer testing can be safely discharged home without further testing. **Genetic testing** is often indicated but remember: medical knowledge is evolving and positive family history may be more accurate than genetic testing. Table 2 summarizes situations when genetic testing may be useful.

Table 2. Which patiens should be considered for genetic testing for thrombophilia ?
Proven thromboembolic disease at the age of 45 years or less
Reccurrent vein thrombosis
Trombosis in unusual localisation
Positive family history
Idiopathic pulmonary embolism

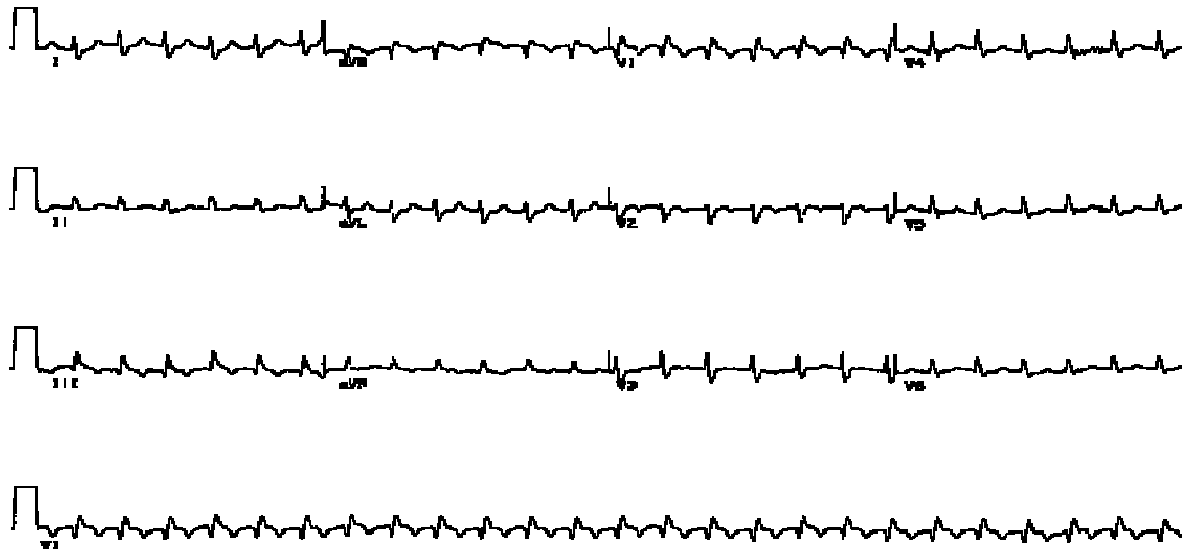
Elektronické srdce a plíce

CZ.2.17/3.1.00/33276

Females with thrombosis in pregnancy prior to second pregnancy

Duplex ultrasound of lower extremities veins is the basic screening method for diagnosis of deep vein thrombosis. Loss of compressibility of the vein (normal vein can be compressed, thrombus cannot be fully compressed) is diagnostic. Ultrasound can define the localization and extent of vein thrombosis. It is very accurate in pelvic and femoral veins, below the knee veins are more difficult to evaluate. Occasionally MRI imaging may be needed.

Every patient with clinical suspicion of PE should have **ECG and chest X-Ray** performed quickly. Tachycardia, S wave in lead I and Q wave and negative T in lead III (Picture 1) are typical. Often there is ischemia of right ventricle with negative T in leads V1-4 (Picture 2); this can be misdiagnosed as unstable angina in the left anterior descending territory.



Picture 1. ECG typical for acute PE. Tachycardia, S wave in lead I and Q wave and negative T in lead III

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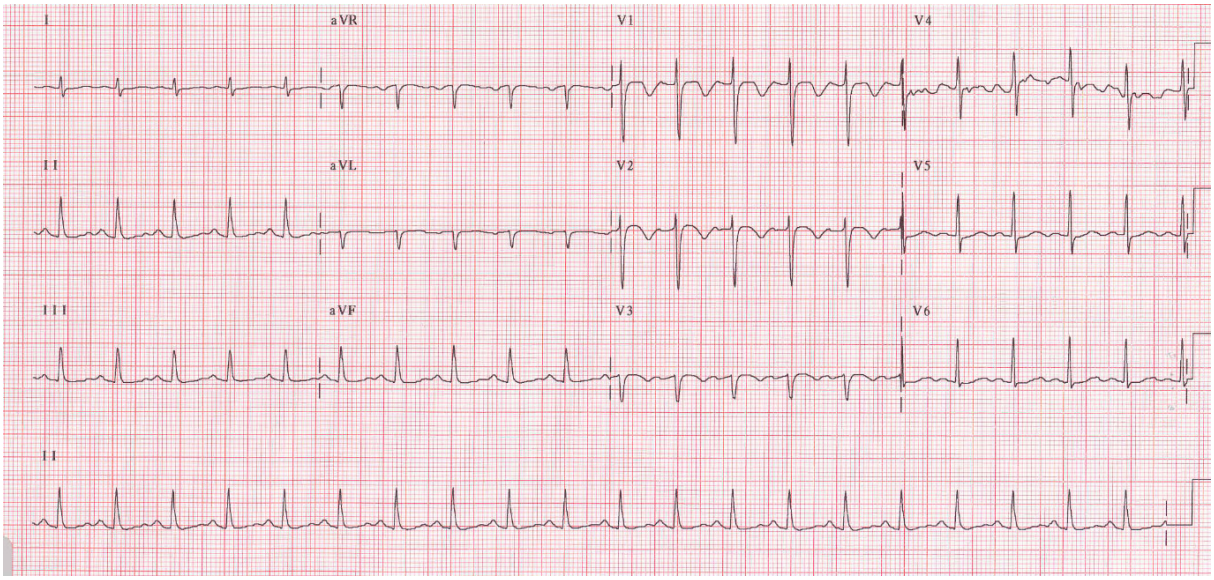

Picture 2. Sinus tachycardia 120/min., negative T in leads V1-3 due to RV ischemia

Chest X-Ray can occasionally be diagnostic of PE – in case of peripheral pulmonary infarction and typical wedge shaped consolidation on X-ray (Picture 3). Much more common is situation when patient with dyspnoea has normal chest X-ray and therefore by excluding pulmonary congestion and pneumonia the diagnosis of pulmonary embolism is more likely.

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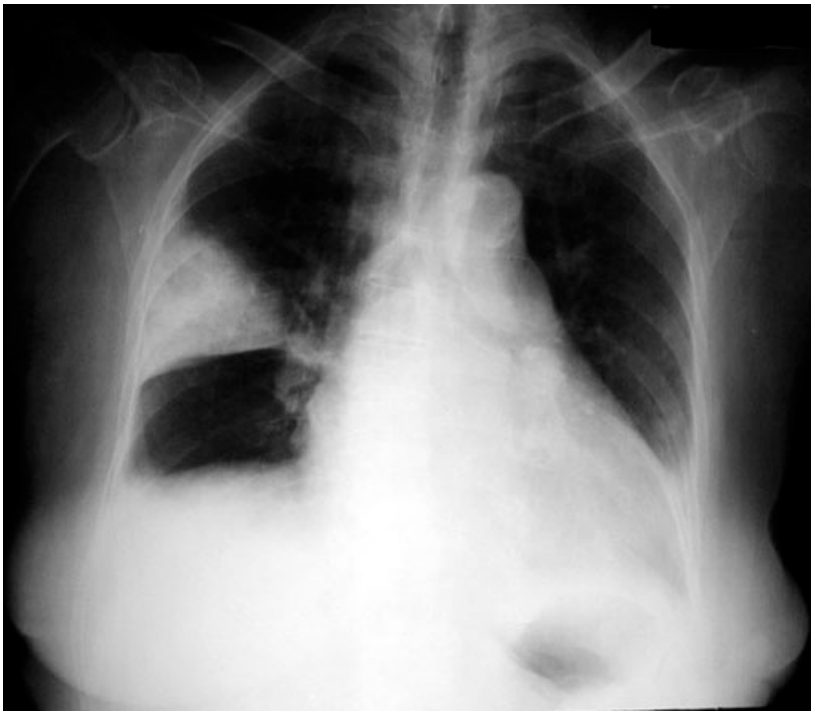
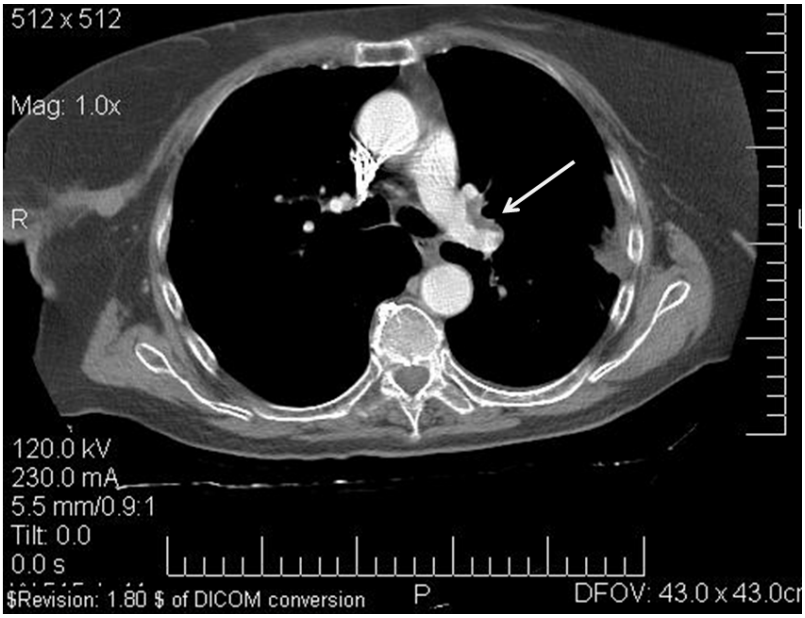


Picture 3. Chest X-Ray with Westermark sign – pulmonary infarction with typical wegde shaped density

Lung scanning – ventilation/perfusion scintigraphy – used to be performed frequently. Radionuclide isotope is given i.v. and perfusion study is performed. In case of detected defects of perfusion ventilation scan is done and localization of defects compared. However ventilation scans are logistically difficult (air tight chambers are required) and typically are replaced by chest X-Ray. Less than 50% of lung scans are diagnostic, the majority of patients has nondiagnostic scan.

CT pulmonary angiography has become the method of choice in the last decade. It is noninvasive, available 24 hours a day, both sensitivity and specificity are over 90%. 70-100ml of X-ray contrast agent is needed. Picture 4 demonstrated visible thrombus in main branch of pulmonary artery.



Picture 4. CT pulmonary angiography. Arrow shows thrombus (less dense structure).

Pulmonary angiography is still considered a gold standard but due to invasive character is rarely indicated. At our institution it is occasionally performed in critically ill patients, who are already in cardiac catheterization laboratory and acute myocardial infarction has been excluded. In this situation it is easier and quicker to do invasive angiography than transport patient to CT suite.

Echocardiography is rarely diagnostic but will evaluate size and function of right ventricle – very important parameters in therapeutic decision making. The advantage of echocardiography is its availability at patient bedside.

Ultrasound or CT of abdomen and pelvis are often indicated to rule out malignancy. The usefulness of tumour markers is still controversial; we would recommend PSA testing in males.

Clinical picture of deep vein thrombosis

Unilateral, painful swelling of lower extremity, either whole or below knee is typical. Pain is usually dull, sharp pain is rare. The extremity is warm; the extent of oedema is best quantified by measurement of limb circumference and comparison with healthy leg. One may see dilated

superficial veins serving as collateral venous drainage. Homans sign – calf pain on dorsiflexion – is not too reliable. Complete pelvic vein thrombosis may result in cyanosis of markedly swollen limb, this syndrome is called phlegmasia coerulea dolens. Marked oedema and resulting interstitial pressure higher than capillary perfusion pressure may lead to limb ischemia and pallor. Extensive or recurrent vein thrombosis may damage venous valves and result in post-thrombotic syndrome – venous insufficiency with chronic hard oedema and pigmentation. Differential diagnosis consists of limb trauma, cellulitis, baker cyst rupture, erysipel.

Clinical picture of pulmonary embolism

Clinical manifestation depends of thrombus size and extent of pulmonary artery tree obstruction. Massive PE may result in syncope or even sudden death. Frequency of symptoms is: dyspnoea 80%; tachypnoe over 20 breaths/min 60%; chest pain 50%; tachycardia 40%. Smaller, more peripheral thrombi can lead to infarctions and typical symptoms are cough, haemoptysis and pleuritic chest pain. It is important to note signs of right heart failure – elevated jugular venous pressure, liver congestion, accented second heart sound over pulmonary artery. Differential diagnosis is summarized in Table 3.

Table 3. Differential diagnosis of pulmonary embolism – how to differentiate	
Myocardial infarction	ECG, troponin, ECHO
Pneumonia	Fever, Chest X-Ray, productive cough
Asthma bronchiale	Exspiratory wheeze, spirometry
Left heart failure	Auscultation, Chest X-Ray, ECHO, BNP
Pericarditis	Auscultation – friction rub, ECHO, EKG
Pneumothorax	Lung auscultation and percussion, Chest X-Ray
Muskulosceletal chest pain	Palpation tenderness, negative CT angiography
Rib fracture	Chest X-Ray
Pulmonary arterial hypertension	Nonsegmental defects at CT angiography

Therapy

Hospital mortality of untreated pulmonary embolism can reach 25%, effective therapy can reduce this to approximately 10%. Below the knee deep vein thrombosis can be treated on a outpatient basis, all other forms of thromboembolic disease require admission to hospital. Elastic stockings are routine. Anticoagulation is the mainstay of therapy, unfractionated heparin or low molecular weight heparin can be used, the latter has several advantages: more predictable effect, subcutaneous administration without the need of frequent APTT monitoring, lower risk of heparin induced thrombocytopenia. Oral anticoagulation therapy can be started once patient condition is stable, usually after 2-3 days. Thrombolytic therapy carries at least 2% risk of intracranial haemorrhage and is therefore reserved only for patients where potential benefit is large – indications are summarized in Table 4.

Table 4. Severity of pulmonary embolism and therapy

Severity of PE	Presentation	Pulmonary obstruction	RV dilatation	Thrombolytic therapy	Early mortality
Massive	Syncope, dyspnoe, cyanosis, hypotension	Over 50%	Yes	Clearly indicated	40-50%
Large	Dyspnoe	30-50%	Yes	Possible	5-15%
Small	Pleuritic chest pain, haemoptysis	Under 30%	No	Not indicated	2-3%

Prevention

All in-hospital patient who are immobilized or after operation should receive small dose of low molecular weight heparin. This simple recommendation is still not followed in 40% of suitable patients!!

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Reference

Guidelines on the diagnosis and management of acute pulmonary embolism, The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC), European Heart Journal (2008) 29, 2276–2315

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13. Valvular heart disease in adults

(H. Línková)

During the past 50 years there has been a dramatic shift in the causes of valvular heart disease, with a marked decline in the incidence of rheumatic valve disease and
a corresponding increase in the age – related degenerative valve disease.

Valve problems may be congenital (inborn) or acquired (due to another cause later in life). Echocardiography is the gold standard method used to confirm the diagnosis of valvular heart disease as well as to assess its severity and prognosis. It is indicated in any patient with a murmur, unless no suspicion of valve disease is raised after the clinical evaluation.

Cardiac catheterization – the measurement of pressures and cardiac output or aortography are restricted to situations where non-invasive evaluation is inconclusive or discordant with clinical findings. Given the potential risks, cardiac catheterization to asses hemodynamics should not be done routinely with coronary angiography. Coronary angiography is indicated for the detection of coronary artery disease when cardiac surgery is planned.

Treatment may be conservative (medical treatment), but often, depending on the severity, involves valve repair or replacement (insertion of an artificial heart valve).

The optimal timing of surgical intervention is indicated when symptoms occure or it is based on objective parameters. The valve replacement is indicated in patients who in addition to moderate valvular heart disease undergo cardiac surgery for another disease (most often
CABG for coronary artery disease).

There is no perfect valve substitute. Two types of valve replacements are currently used, in particular mechanical replacements and bioprothesis. Mechanical replacements have unlimited durability but require anticoagulation therapy, while bioprothesis do not require anticoagulation therapy but they are subject to structural deterioration over time.

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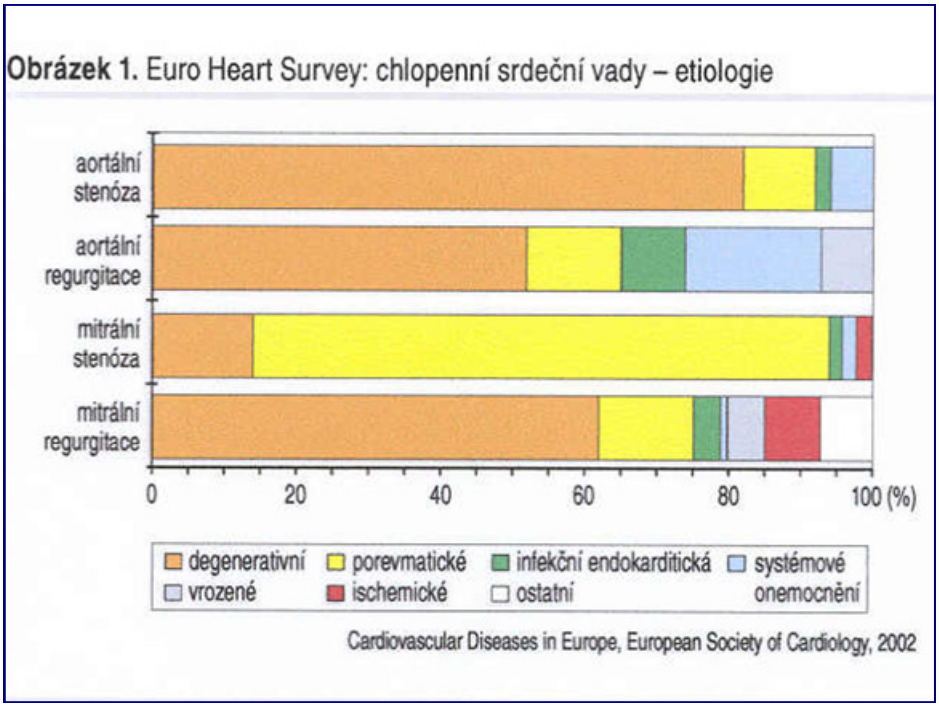
Figure 1: current spectrum of valvular heart disease



Aortic regurgitation

The total prevalence of aortic regurgitation is about 13% in men and 8,5% in women, the maximum incidence is between 40-60 years of age. Moderate aortic regurgitation has a prevalence of about 4,9% and severe aortic regurgitation of about 0,9%.

Etiology

a/ lesion of aortic cusps (congenital - bicuspid aortic valve, postrheumatic changes , endocarditis – healed or acute, degenerative changes, lupus erythematoides, revmatoid artitis, trauma)

b/ enlargement of the aorta or of aortic anulus because of high blood pressure or hardening of the arteries (the valve is normal)

c/ lesion of aortic anulus, cusps or root (Marfan syndrome, Ehlers – Danlos syndrome, syphilis)

Aortic regurgitation is divided into acute and chronic, their causes are different :

Chronic aortic regurgitation:

a) congenital - bicuspid aortic valve

b) postrheumatic valvular disease

c) enlargement of the aorta or of aortic anulus (because of high blood pressure, Marfan syndrome etc.)

Acute aortic regurgitation

a) infective endocarditis (destructon of leaflets or paravalvular abscess)

b) aortic dissection

c) acute dysfunction of valve replacement (thrombosis, endocarditis, release- dehiscence of valve replacement)

Pathophysiology

In aortic regurgitation (AR), when the pressure in the left ventricle falls below the pressure in the aorta, the aortic valve is not able to completely close. This causes a leaking of blood from the aorta into the left ventricle. This means that some of the blood that was already ejected from the heart is regurgitating back into the heart. The percentage of blood that regurgitates back through the aortic valve due to AR is known as the regurgitant fraction. For instance, if an individual with AR has a stroke volume of 100 ml and during ventricular diastole 25 ml regurgitates back through the aortic valve, the regurgitant fraction is 25%. This regurgitant flow causes a decrease in the diastolic blood pressure in the aorta, and therefore an increase in the pulse pressure (systolic pressure - diastolic pressure). Thus, physical examination will reveal a bounding pulse, especially in the radial artery.

Since some of the blood that is ejected during systole regurgitates back into the left ventricle during diastole, there is decreased effective forward flow in AR.

Note that while diastolic blood pressure is diminished and the pulse pressure widens, systolic blood pressure generally remains normal or can even be slightly elevated. This is because the sympathetic nervous system and the renin-angiotensin-aldosterone axis of the kidneys compensate for the decreased cardiac output. Catecholamines will increase the heart rate and increase the strength of ventricular contraction, directly increasing cardiac output. Catecholamines will also cause peripheral

vasoconstriction, which causes increased systemic vascular resistance and ensures that core organs are adequately perfused. Renin, a proteolytic enzyme, cleaves angiotensinogen to angiotensin I, which is converted to angiotensin II, which is also a potent vasoconstrictor. In the case of chronic aortic insufficiency with resultant cardiac remodeling, heart failure will develop, and it is possible to see systolic pressures diminish.

Aortic regurgitation causes both volume overload (elevated preload) and pressure overload (elevated afterload due to increased stroke volume) of the heart.

The pressure overload (due to elevated pulse pressure and the systemic effects of neuroendocrine hormones) causes left ventricular hypertrophy (LVH). There is both concentric hypertrophy and eccentric hypertrophy in AR. The concentric hypertrophy is due to the increased left ventricular systolic pressures associated with AR, while the eccentric hypertrophy is due to volume overload caused by the regurgitant fraction.

The hemodynamic sequelae of AR are dependent on the rate of onset of AR. Acute AR and chronic AR will have different hemodynamics and individuals will have different signs and symptoms.

Acute aortic regurgitation

In acute AR, as may be seen with acute perforation of the aortic valve due to endocarditis, there will be a sudden increase in the volume of blood in the left ventricle. The ventricle is unable to deal with the sudden change in volume. On the Frank-Starling curve, the end-diastolic volume will be very high, such that further increases in volume result in less and less efficient contraction. The filling pressure of the left ventricle will increase. This causes pressure in the left atrium to rise, and the individual will develop pulmonary edema.

Severe acute aortic insufficiency is considered a medical emergency. There is a high mortality rate if the individual does not undergo immediate surgery for aortic valve replacement. If the acute AR is due to aortic valve endocarditis, there is a small risk that the new valve may become seeded with bacteria.

Acute AR usually presents as florid congestive heart failure, and will not have any of the signs associated with chronic AR since the left ventricle had not yet developed the eccentric hypertrophy

and dilatation that allow an increased stroke volume, which in turn causes bounding peripheral pulses. On auscultation, there may be a short diastolic murmur and a soft S_1. S_1 is soft because the elevated filling pressures close the mitral valve in diastole (rather than the mitral valve being closed at the beginning of systole).

Chronic aortic regurgitation

In chronic aortic regurgitation the left ventricle adapts by eccentric hypertrophy and dilatation of the left ventricle and the volume overload is compensated for. The left ventricular filling pressures will revert to normal and the patient will no longer have overt heart failure. In this compensated phase, the subject may be totally asymptomatic and may have normal exercise tolerance.

Eventually (typically after a latency period) the left ventricle will become decompensated, and filling pressures will increase. As the disease progresses and ventricular dimensions and systolic pressure increase, the degree of wall thickening fails to keep pace, and end- systolic wall stress increases. Hemodynamic decompensation ensues, with a decline in ejection performance related to the excessive aferload. With continued volume and pressure overload of the left ventricle, depression of myocardial contractility follows and the ejection fraction is reduced. These patients may have irreversibile systolic dysfunction of the left ventricle and are less likely to improve after surgical correction.

While most patients would complain of symptoms of congestive heart failure to their physicians, some enter this decompensated phase asymptomatically. Proper treatment for AR involves aortic valve replacement prior to this decompensation phase.

Symptoms:

Symptoms of aortic regurgitation are similar to those of heart failure and include dyspnea on exertion, orthopnea and paroxysmal nocturnal dyspnea. Palpitations and angina pectoris may also be felt. In acute cases there may be cyanosis and circulatory shock.

Objective:

Physical examination:

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The physical examination of an individual with aortic regurgitation involves auscultation of the heart to identify the murmur of aortic regurgitation and the S3 heart sound (S3 gallop correlates with development of LV dysfunction). The murmur in chronic aortic regurgitation is typically described as early diastolic and decrescendo, which is best heard in the third left intercostal space and may radiate along the left sternal border. If there is increased stroke volume of the left ventricle due to volume overload, an ejection systolic 'flow' murmur may also be present when auscultating the same aortic area. Unless there is concomitant aortic valve stenosis, the murmur should not start with an ejection click.

There may also be an Austin Flint murmur, a soft mid-diastolic rumble heard at the apical area. It appears when regurgitant jet from the severe aortic regurgitation causes partial closure of the anterior mitral leaflet.

Peripheral physical signs of aortic regurgitation are related to the high pulse pressure and the rapid decrease in blood pressure during diastole due to blood returning to the heart from the aorta through the incompetent aortic valve, although the usefulness of some of the eponymous signs has been questioned:

- large-volume, 'collapsing' pulse also known as: Corrigan's pulse (rapid upstroke and collapse of the carotid artery pulse)
- low diastolic and increased pulse pressure
- Musset's sign (head nodding in time with the heart beat)
- Quincke's sign (pulsation of the capillary bed in the nail)
- Duroziez's sign (systolic and diastolic murmurs heard over the femoral artery when it is gradually compressed with the stethoscope)

In acute aortic regurgitation there is typically a weak early diastolic murmur and it may lead to a wrong diagnosis.

ECG

The electocardiographic findings include voltage criteria for left ventricular hypertrophy and associated repolarization abnormalities. A strain pattern on the resting ECG correlates strongly with

abnormal left ventricular dimensions, mass and wall stress. In acute aortic regurgitation tachycardia is often present.

Chest X ray

Chest X ray shows an enlarged cardiac silhouette due to left ventricular dilatation in chronic disease. Aortic root dilatation is frequently present either due to primary disease of the aorta or due to secondary dilatation.

Echocardiography

Echocardiography is the most important method to diagnose AR as it estimates the mechanism of aortic regurgitation and the hemodynamic parameters. Doppler and 2D echocardiographic methods allow semiquantitative and quantitative evaluation of the severity of the regurgitation. Echocardiographic evaluation of valve anatomy and severity of the regurgitation, size of left ventricle and the function of the left ventricle are key to deciding which patients have disease that merits further evalutation and may require medical or surgical intervention.

Transesophageal echocardiography is the most important method to diagnose aortic dissection.

Catheterization

Invasive examination (aortography) is needed only in cases in which echocardiographic data are nondiagnostic or not consistent with other clinical data. Coronary angiography is usually needed prior to aortic valve surgery (men older then 40 years and women older then 45 years).

Catetherization is not a standard method for patients with aortic dissection, in these cases a CT scan is performed instead.

Therapy:

Aortic regurgitation can be treated either medically or surgically, depending on the acuteness of presentation, the symptoms and signs associated with the disease process, and the degree of left ventricular dysfunction. Surgical treatment is controversial in asymptomatic patients, however it has been recommended if the ejection fraction falls to 50% or below, in the face of progressive and severe left ventricular dilatation, or with symptoms or abnormal response to exercise testing. For both groups of patients, surgery before the development of worsening ejection fraction/LV

dilatation, is expected to reduce the risk of sudden death, and is associated with lower peri-operative mortality. Also, surgery is optimally performed immediately in acute cases. Patients with bacteremia with aortic valve endocarditis should not wait for treatment with antibiotics to take effect, given the high mortality associated with the acute AR.

Chronic aortic regurgitation

Medical treatment

Medical therapy of chronic aortic regurgitation that is stable and asymptomatic involves the use of vasodilators. Small trials have shown a short term benefit in the use of ACE inhibitors or angiotensin II receptor antagonists, nifedipine, and hydralazine by improving left ventricular wall stress, ejection fraction, and mass. The use of these vasodilators is only indicated in patients who suffer from hypertension in addition to AR. The goal in using these pharmacologic agents is to decrease the afterload so that the left ventricle is somewhat saved. The regurgitant fraction may not change significantly, since the gradient between the aortic and left ventricular pressures is usually fairly low at the initiation of treatment.

Other rather conservative medical treatments for stable and asymptomatic cases include diuretics, digoxin, calcium blockers and avoiding very strenuous activity.

Surgical treatment

The surgical treatment of choice at this time is an aortic valve replacement. In the case of severe acute aortic regurgitation, all individuals should undergo surgery if there are no absolute contraindications for surgery. Patients with bacteremia with aortic valve endocarditis should not wait for treatment with antibiotics to take effect, given the high mortality associated with the acute AR. Instead, replacement with an aortic valve homograft should be performed if possible. A percutaneous approach to aortic valve replacement is now feasible, but the main experience has been in the treatment of aortic stenosis.

Aortic stenosis:

Aortic stenosis has become the most frequent type of valvular heart disease in Europe and in North America. It primarily presents as calcified aortic stenosis in adults of advanced age

(2-7% of the population older than 65 years).

Etiology

a) the most frequent cause of aortic stenosis is degenerative aortic stenosis and is caused by age-related progressive calcification of a normal (three-leafed) aortic valve (>50% of cases) the mean age of the patients at presentation is 65 to 70 years .

b) Other causes include calcification of a congenital bicuspid aortic valve (30-40% of cases, 2% of general population), it is twice as common in males as in females. In many cases, a bicuspid aortic valve will cause no problems. However bicuspid aortic valve may become calcified later in life, which may lead to varying degrees of severity of aortic stenosis.

c) rheumatic aortic stenosis has become rare (less than 10% of cases). The severity of posthreumatic aortic stenosis is often only moderate, however the valve may become calcified later in life, which may lead to varying degrees of severity.

d) congenital disease in young patients (frequent late restenosis after commisurotomy in chilhood)

Pathophysiology:

Initially, the LV compensates the pressure overload by thickening its walls (myocardial hypertrophy) in order to maintain adequate pumping pressure. The type of hypertrophy most commonly seen in AS is concentric hypertrophy, in which the walls of the LV are (approximately) equally thickened. Initially the function of LV is normal. In the later stages, the left ventricle dilates, the wall thins, and the systolic function deteriorates.

Symptoms

Symptoms related to aortic stenosis depend on the degree of valve stenosis. Most people with mild to moderate aortic stenosis do not have symptoms. Symptoms are usually present in people with severe aortic stenosis (aortic valve area < 1,1 cm2), although they can exist in those with mild to moderate severity as well. The initial presenting symptoms include progressive shortness of breath on exertion. More worrisome symptoms include syncope, chest pain and sudden death

Congestive heart failure

Congestive heart failure (CHF) carries a grave prognosis in patients with AS. Patients with CHF that is attributed to AS have a 2 year mortality rate of 50%, if the aortic valve is not replaced. CHF in the setting of AS is due to a combination of systolic dysfunction (a decrease in the ejection fraction) and diastolic dysfunction (elevated filling pressure of the LV).

Syncope

Syncope (fainting spells) from aortic valve stenosis is usually exertional. In patients with syncope, the 3 year mortality rate is 50%, if the aortic valve is not replaced.

It is unclear why aortic stenosis causes syncope. One popular theory is that severe AS produces a nearly fixed cardiac output. When the patient exercises, their peripheral vascular resistance will decrease as the blood vessels of the skeletal muscles dilate to allow the muscles to receive more blood to allow them to do more work. This decrease in peripheral vascular resistance is normally compensated for by an increase in the cardiac output. Since patients with severe AS cannot increase their cardiac output, the blood pressure falls and the patient will faint due to decreased blood perfusion to the brain.

A second theory as to why syncope may occur in AS is that during exercise, the high pressures generated in the hypertrophied LV cause a vasodepressor response, which causes a secondary peripheral vasodilation that, in turn, causes decreased blood flow to the brain. Indeed, in aortic stenosis, because of the fixed obstruction to bloodflow out from the heart, it may be impossible for the heart to increase its output to offset peripheral vasodilation.

A third mechanism may be possible due to the hypertrophy of the left ventricle in aortic stenosis, including the consequent inability of the coronary arteries to adequately supply blood to the myocardium , arrhythmias may develop. These can lead to syncope.

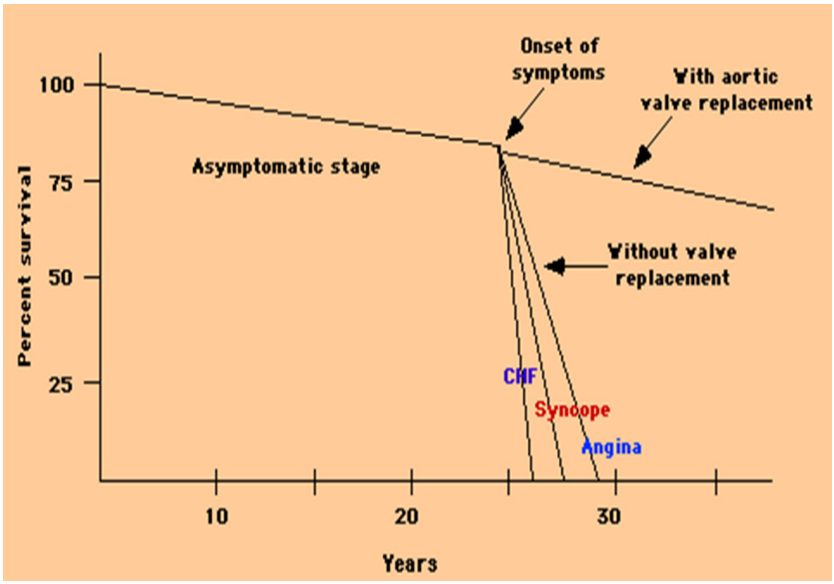
Finally, in calcified aortic stenosis at least, the calcification in and around the aortic valve can progress and extend to involve the electrical conduction system of the heart. If that occurs, the result may be heart block - a potentially lethal condition of which syncope may be a symptom.

Angina

Angina in the setting of heart failure also increases the risk of death. In patients with angina, the 5 year mortality rate is 50%, if the aortic valve is not replaced.

Angina in the setting of AS is secondary to the left ventricular hypertrophy (LVH) that is caused by the constant production of increased pressure required to overcome the pressure gradient caused by the AS. While the myocardium of the LV gets thicker, the arteries that supply the muscle do not get significantly longer or bigger, so the muscle may become ischemic (it does not receive an adequate blood supply). The ischemia may first be evident during exercise, when the heart muscle requires increased blood supply to compensate for the increased workload. The individual may complain of exertional angina. At this stage, a stress test with imaging may be suggestive of ischemia.

Fig.2 .natural course of aortic stenosis



Physical examination

The systolic murmur of aortic stenosis has a crescendo- decrescendo pattern of amplitude and most often is loudest at the base, over right second intercostal space. In general, the loudness of the murmur correlates with the jet velocity or pressure gradient. The presence of a systolic thrill in the aortic region is highly specific for severe valvular obstruction. Conversely, even in the case of a patient with severe aortic stenosis, the murmur can be soft if cardiac output is

low or if obesity or lung disease diminish transmission to the chest wall .

The murmur of aortic stenosis radiates to the karotid arteries in the majority of patients . In the minority of patients, the murmur radiates to the apex, a pattern referred to as the Gallavardin phenomenom. Normal splitting of the second heart sound depends on flexibile pulmonic and aortic leaflets that „snap " shut at end- systole and on normal timing of right and left ventricular ejection. The second heart sound in severe aortic stenosis is typically single because the aortic component is inaudible due to the impaired motion of the thickened valve leaflets.

Electrocardiography:

ECG manifestations of left ventricular hypertrophy (LVH) are common in aortic stenosis and arise as a result of the stenosis having placed a chronically high pressure load on the left ventricle (with LVH being the expected response to chronic pressure overload on the left ventricle no matter what the cause).

Chest X- ray

Chest X ray can also assist in the diagnosis, showing the calcified aortic valve, and, in longstanding disease, an enlarged left ventricle and atrium.

Echocardiography

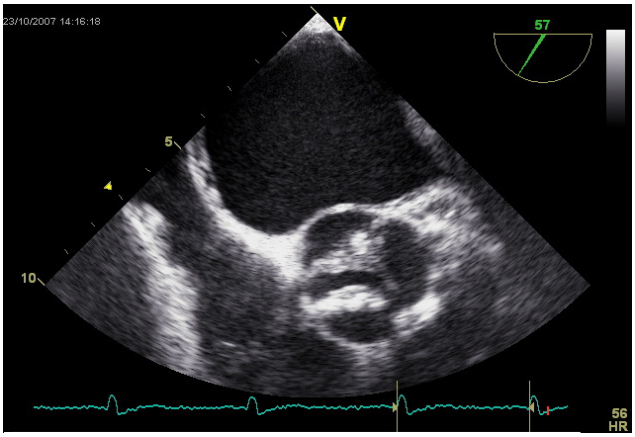
Echocardiography is the best non-invasive method to evaluate the aortic valve anatomy and function.

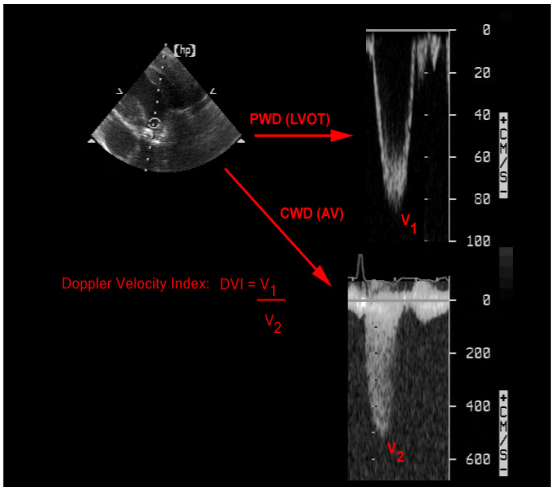
2D echocardiography visualizes the entire aortic valve structure, the degree of valvular calcification, the size of aortic anulus and the supravalvular ascending aorta. Futhermore, 2D echocardiography is useful for determining the degree of LV hypertrophy , LA enlargement, ventricular function and the integrity of other valves. The aortic valve area can be calculated non-invasively using echocardiographic flow velocities.

Doppler echocardiography: Using the velocity of the blood through the valve, the pressure gradient across the valve can be calculated using the modified Bernoulli's equation: Gradient = 4(velocity)^2 mmHg. A normal aortic valve has a gradient of only a few mmHg. A decreased valvular area causes increased pressure gradient, and these parameters are used to classify and grade the aortic stenosis

as mild, moderate or severe. The pressure gradient can be abnormally low in the presence of other coexisting valvular diseases or heart failure and dysfunction of left ventricle. A more accurate method to classify the severity of aortic stenosis is the assesment of aortic valve area by the continuity equation. The aortic stenosis is usually severe when peak aortic velocity is ≥ 4 m/s, mean pressure gradient is ≥ 40 mm Hg, and the aortic valve area is 0,6 ≤ cm^2/m^2

Figure 3. Echocardiographic diagnosis of aortic stenosis





Severity of aortic stenosis:

Degree of aortic stenosis	**Mean gradient (mmHg)**	**Aortic valve area (cm^2)**
Mild aortic stenosis	<25	>1.5
Moderate aortic stenosis	25 - 40	1.0 - 1.5
Severe aortic stenosis	>40	< 1.0
Critical aortic stenosis	>70	< 0.6

Cardiac catheterization:

In nearly all patiens with valvular aortic stenosis, diagnostic data (incl. quantification of stenosis severity) can be obtained by echocardiography. Invasive measurement of the transaorthic gradient and calculation of valve area (using the Gorlin formula) is needed only in cases in which echocardiographic data are nondiagnostic or not consistent with other clinical data. Coronary angiography is usually needed prior to aortic valve surgery (men older then 40 years and women older then 45 years) and is often indicated to differentiate whether anginal symptoms are due to coexisting coronary disease in patients with mild to moderatce aortic stenosis.

Fig 4:

Catetherization in aortic stenosis

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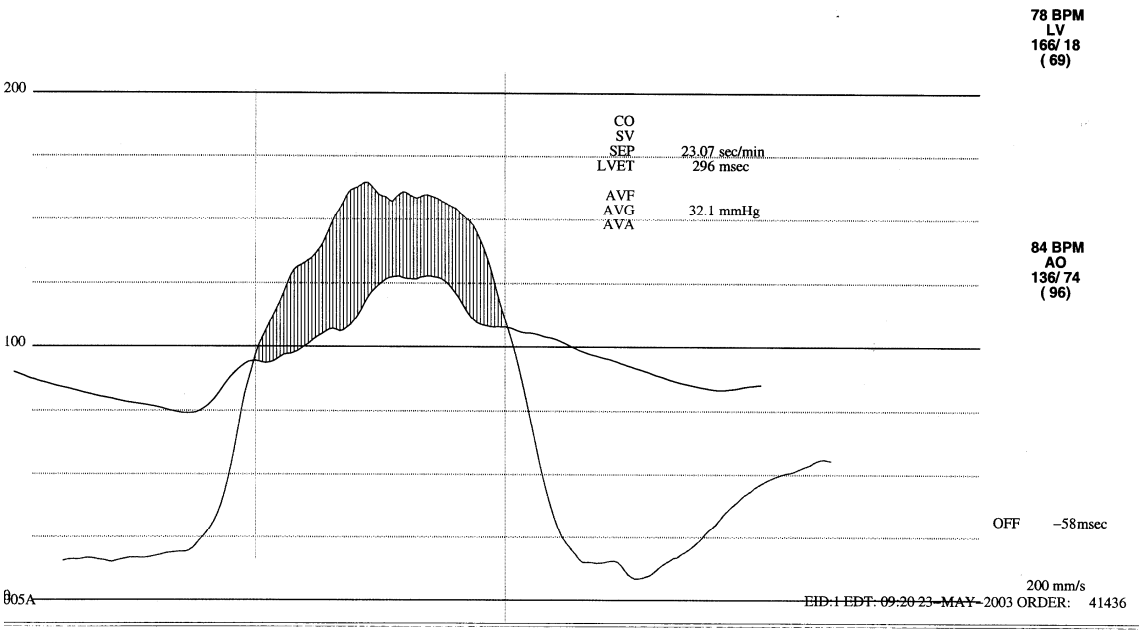

Therapy:

Medical therapy:

Symptomatic patients require early intervention, because no medical therapy is able to improve outcome. However, patients who are unsuitable candidates for surgery or are currently awaiting a surgical or TAVI procedure may be treated with digoxin, diuretics, ACE inhibitors or ARBs if they experience heart failure symptoms. Co- existing hypertension should be treated. However , therapy should be carefully titrated to avoid hypotension. Maintenance of sinus rhytmus is important.

Surgical therapy:

Aortic valve replacement is the definitive therapy for severe symptomatic aortic stenosis in patients with some of the symptoms : exertional dyspnea, angina or exertional syncope. Other indications are as follows :

- in patients with severe or moderate aortic stenosis ungergoing CABG or intervetion on another valve
- in asymptomatic patients with systolic LV dysfunction

- in asymptomatic patients with abnormal exercise testing showing symptoms on exercise clearly related to aortic stenosis

While AVR has been the standard of care for aortic stenosis for several decades, currently aortic valve replacement approaches include open heart surgery or minimally invasive catheter-based (percutaneous) aortic valve replacement. Aortic valve is most commonly replaced using a surgical procedure with either a mechanical or a tissue valve. The choice of valve replacement (mechanical or bioprothesis) is based on durability of the valve versus the patient life expectancy and the risks associated with chronic anticoagulation. In younger patients (< 65 years) we usually use mechanical valve replacement, in elderly patients (> 65 years) mechanical valve replacement is used. The procedure is done as an open-heart surgical procedure .In the young patient, the transfer of pulmonary autograft in the aortic position (Ross procedure) may be considered.

Percutaneous (Transcatheter) Aortic Valve Replacement: For patients who are not candidates for surgical valve replacement, transcatheter valve replacement may be a suitable alternative. When selecting the optimal therapy for individual patients, the percutaneous (transcatheter) approach must be carefully weighed against the excellent results achieved with conventional surgery.

Balloon aortic valvuloplasty:

Is reserved for infants and children with congenital aortic stenosis . In adults, however, it is generally ineffective, as the valve tends to return to a stenosed state and is only uses as bridge therapy.

Mitral regurgitation

A trivial amount of MR is present in up to 70 percent of adults. Significant (moderate to severe) mitral regurgitation is much less common. Significant mitral regurgitation can develop as a result of an abnormality in a heart valve or another cardiac disease.

Etiology:

When mitral regurgitation is present, blood flows backwards through the mitral valve when the heart contracts. This reduces the amount of blood that is pumped out to the body.

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The mitral valve apparatus is a complex anatomic and functional unit composed of the mitral annulus, valve leaflets, chordae, papillary muscles, and the underlying left ventricular wall. Normal function depends on both normal anatomy of each of these components and on the overall three dimensional relationships of these structures to each other, including the effects of overall left ventricular size, shape, and systolic function. Diverse mechanisms of mitral regurgitation are associated with different clinical outcomes. In addition, medical or surgical treatment is directed at the specific mechanism of regurgitation in each individual patient. Mitral regurgitation caused by an anatomic abnormality of the leaflets and chordae is termed primary regurgitation, while mitral regurgitation caused by a process primarily affecting the left ventricle is termed secondary mitral regurgitation.

Mitral regurgitation includes the following etiology::

Chronic mitral regurgitation:

a/primary MR: includes myxomatous mitral valve disease which results in mitral regurgitation caused by leaflet prolapse and/or chordal rupture, rheumatic disease which typically causes increased leaflet stiffness with chordal shortening and fusion, and endocarditis with leaflet deformation or destruction.

b/ secondary MR: includes ischaemic disease that affects the function of the papillary muscles and underlying left ventricular wall, and dilatated cardiomyopathy that alters the normal angle between the papillary muscles and mitral annulus

Acute mitral regurgitation:

Acute mitral regurgitation may occur due to the sudden rupture of a chorda tendinae or papillary muscle caused by endocarditis. Acute ischaemic mitral regurgitation may occur due to rupture of a chorda tendinae or papillary muscle and/or with developement of left ventricular dysfunction usually few days after myocardial infarction.Acute mitral regurgitation (may occur due to the sudden rupture of a chorda tendinae or papillary muscle) causes a sudden volume overload of both the left atrium

and the left ventricle. The left ventricle develops volume overload because with every contraction it now has to pump out not only the volume of blood that goes into the aorta (the forward cardiac output or forward stroke volume), but also the blood that regurgitates into the left atrium (the regurgitant volume). The combination of the forward stroke volume and the regurgitant volume is known as the total stroke volume of the left ventricle.

In the acute setting, the stroke volume of the left ventricle is increased (increased ejection fraction). However, as it progresses the LV volume increases and the contractile function deteriorates and thus leading to dysfunctional LV and a decrease in ejection fraction. The increase in stroke volume is explained by the Frank–Starling mechanism, in which increased ventricular pre-load stretches the myocardium such that contractions are more forceful. The regurgitant volume causes a volume overload and a pressure overload of the left atrium. The increased pressures in the left atrium inhibit drainage of blood from the lungs via the pulmonary veins. This causes pulmonary congestion.

Chronic mitral regurgitation

If the mitral regurgitation develops slowly over months to years or if the acute phase cannot be managed with medical therapy, the individual will enter the chronic compensated phase of the disease. In this phase, the left ventricle develops eccentric hypertrophy in order to better manage the larger than normal stroke volume. The eccentric hypertrophy and the increased diastolic volume combine to increase the stroke volume (to levels well above normal) so that the forward stroke volume (forward cardiac output) approaches the normal levels.In the left atrium, the volume overload causes enlargement of the chamber of the left atrium, allowing the filling pressure in the left atrium to decrease. This improves the drainage from the pulmonary veins, and signs and symptoms of pulmonary congestion will decrease.These changes in the left ventricle and left atrium improve the low forward cardiac output state and the pulmonary congestion that occurs in the acute phase of the disease. Patients in the chronic compensated phase may be asymptomatic and have normal exercise tolerance. The patients may be in the compensated phase of mitral regurgitation for years, but will eventually develop left ventricular dysfunction, the hallmark for the chronic decompensated phase of mitral regurgitation. In this phase, the ventricular myocardium is no longer

able to contract adequately to compensate for the volume overload caused by mitral regurgitation, and the stroke volume of the left ventricle will decrease. The decreased stroke volume causes a decreased forward cardiac output and an increase in the end-systolic volume. The increased end-systolic volume translates to increased filling pressures of the left ventricle and increased pulmonary venous congestion. The patient may again have symptoms of congestive heart failure. The left ventricle begins to dilatate during this phase. This causes a dilatation of the mitral valve annulus, which may worsen the degree of mitral regurgitation. The dilatated left ventricle causes an increase in the wall stress of the cardiac chamber as well. As the left ventricle enlarges and contracts efficiently, the left atrium progressively enlarges, abnormal heart rhythms occur, and the blood pressure in the pulmonary artery (the blood vessel from the heart to the lungs) increases; this is called pulmonary hypertension. Over time, these changes become irreversible as the signs and symptoms of heart failure develop.

Symptoms:

Findings on clinical examination depend on the severity and duration of mitral regurgitation. The symptoms associated with mitral regurgitation are dependent on which phase of the disease process the patient is in.

Patient with acute mitral regurgitation will have the signs and symptoms of decompensated congestive heart failure (i.e. shortness of breath, pulmonary edema, orthopnea, and paroxysmal nocturnal dyspnea), as well as symptoms suggestive of a low cardiac output state (i.e. decreased exercise tolerance). Palpitations are also common. Cardiovascular collapse with shock (cardiogenic shock) may be seen in patiens with acute mitral regurgitation due to papillary muscle rupture or rupture of a chorda tendinea.

Patient with chronic compensated mitral regurgitation may be asymptomatic, with a normal exercise tolerance and no evidence of heart failure, but they may be sensitive to small shifts in their intravascular volume status, and are prone to develop volume overload (congestive heart failure).

The mitral component of the first heart sound is usually soft and with a laterally displaced apex beat.

The first heart sound is followed by a high-pitched holosystolic murmur at the apex, radiating to the

back or clavicular area. It is holosystolic. In chronic mitral regurgitation, the loudness of the murmur correlates with the severity of MR. A systolic thrill (gr. 4 or greater murmur) can be heard in severe MR, whereas a murmur less than gr.2 indicates mild disease. However, the severity of regurgitation varies widely in patients with the grade 2 to 3 murmur, which is present in the majority of patients. With acute regurgitation, severe mitral regurgitation may be present despite a soft murmur.

Commonly, atrial fibrillation is found. In acute cases, the murmur and tachycardia may be the only distinctive signs.

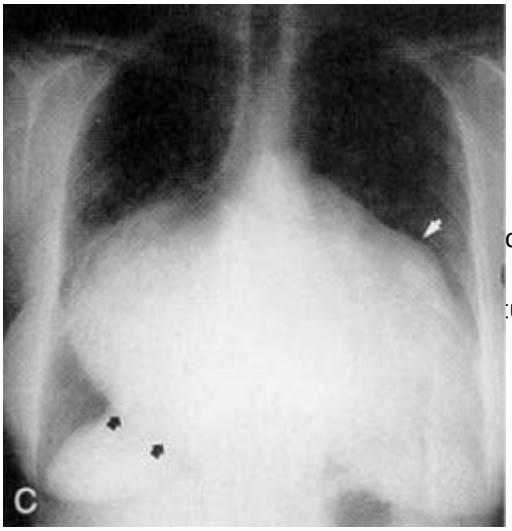
Electrocardiography

The electrocardiogram (ECG) in long standing mitral regurgitation may show evidence of left atrial enlargement and left ventricular hypertrophy. P mitrale is a broad, notched P wave in several or many leads with a prominent late negative component to the P wave in lead V_1, and may be seen in mitral regurgitation, but also in mitral stenosis, and, potentially, any cause of overload of the left atrium. Atrial fibrillation may also be noted on the ECG in patients with chronic mitral regurgitation. The ECG may not show any of these finding in the setting of acute mitral regurgitation.

Chest X ray

Although the heart may not be enlarged in patients with acute mitral regurgitation, severe pulmonary edema is frequently present as a result of left-sided cardiac failure. In cases involving chronic mitral regurgitation, the LA and the LV border appears enlarged, and it may be massive because of volume overload and increased pressure. When the LA is enlarged, it may extend toward the right side, and it may appear as a double shadow along the right atrial border. Co-existent pulmonary arterial hypertension or tricuspid regurgitation may cause dilatation of the right atrium and ventricle, as well as enlargement of the pulmonary arteries.

Figure 5. Chest X ray of severe mitral regurgitation



Echocardiography:

Echocardiography allows identification of the presence, severity and mechanism of mitral regurgitation, left ventricular size and systolic function, left atrial size, pulmonary artery pressure and any associated abnormalities. When transthoracic imaging is suboptimal, transoesophageal images provide excellent visualisation of mitral valve anatomy, and allow an accurate assessment of the etiology of valve disease. The severity of mitral regurgitation can be quantified by several approaches, including evaluation of regurgitation severity by colour flow imaging in multiple views, calculation of regurgitant volumes and fraction from calculation of volume flow rate at two intracardiac sites, from the proximal isovelocity surface area, or by measurement of the vena contracta on colour flow imaging.

Assessment of the haemodynamic consequences of regurgitation is very important.

Figure 6. Organic mitral regurgitation – deep prolapse of posterior mitral leafflet and severe regurgitation in colour doppler examination

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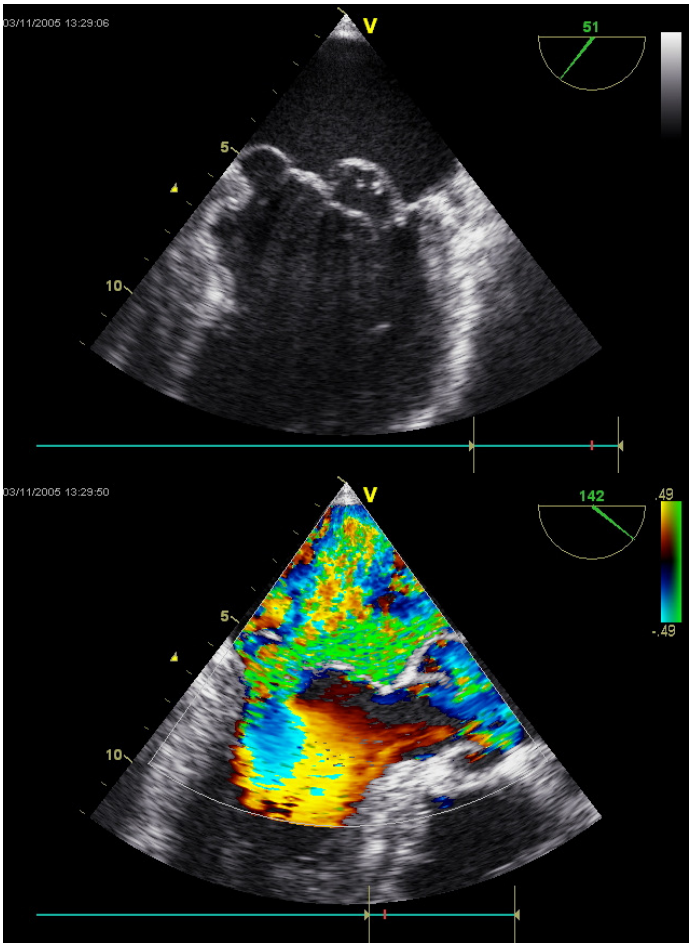

Cardiac catheterization:

In patients older than 40 years or in those with symptoms suggestive of coronary disease, cardiac catheterization should include coronary angiography. The main indications for catheterization include the need to evaluate a discrepancy between echocardiographic findings and the clinical presentation, the need to detect other associated valvular lesions and to assess the severity of those lesions, and the need to determine whether coronary artery disease is present and, if so, to assess the extent of disease. Ventriculography may be performed to evaluate mitral regurgitation.

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The immediate appearance of contrast material in the LA after its injection into the LV indicates mitral regurgitation. The regurgitant volume may be determined from the difference between the total LV stroke volume, which is estimated invasively, and the simultaneous measurement of the effective forward stroke volume, which is determined by using the Fick method.

In patients with severe mitral regurgitation, the regurgitant volume may approach the effective forward stroke volume; in rare instances, it may even exceed this volume. Qualitative but clinically useful estimates of the severity of mitral regurgitation may be made by means of angiographic observation of the degree of opacification of the LA and the pulmonary veins after the injection of contrast material into the LV.

The cause of the regurgitation i.e. MVP or a flail leaflet may often be distinguished using angiography. Mitral regurgitation secondary to rheumatic heart disease is angiographically characterized by a central regurgitant jet and by thickened leaflets that have reduced motion. In regurgitation resulting from other conditions, particularly dilatation or calcification of the mitral annulus or ruptured chordae tendineae and papillary muscles, the systolic jet may be eccentric; in such cases, the valves consist of thin filaments that display excessive motion.

Therapy

In patients with chronic mitral regurgitation, medical treatment is directed at preventing the secondary complications of the disease. The patients can be treated with vasodilators to decrease afterload. In the chronic state, the most commonly used agents are ACE inhibitors and hydralazine. Endocarditis prophylaxis is indicated based on accepted guidelines. In patients with rheumatic valve disease, guidelines for prevention of recurrent rheumatic fever should also be implemented. Since many patients with mitral regurgitation will eventually need surgical intervention, and since operative risk increases when coronary artery disease is present, it is especially important to evaluate and treat coronary artery disease risk factors. If atrial fibrillation occurs, treatment with anticoagulation and cardioversion or rate control of the arythmia is indicated.

In acute mitral regurgitation secondary to a mechanical defect in the heart (i.e. rupture of a papillary muscle or chordae tendineae), the treatment of choice is urgent mitral valve replacement. If the patient is hypotensive prior to the surgical procedure, an intra-aortic balloon pump may be inserted

in order to improve perfusion of the organs and to decrease the degree of mitral regurgitation. If the patient with acute mitral regurgitation is normotensive, vasodilators may be used to decrease the afterload of the left ventricle and thereby decrease the regurgitant fraction. The vasodilator most commonly used is nitroprusside.

Surgical therapy

The surgical options for treatment of mitral regurgitation include mitral valve replacement, with or without chordal preservation, and mitral valve repair. Mitral valve repair offers several advantages including avoidance of longterm anticoagulation and, most importantly, preservation of the continuity between the mitral annulus and papillary muscles. This annular–papillary muscle continuity helps maintain normal left ventricular geometry and systolic function. When annular–papillary continuity is preserved, ejection fraction typically remains stable or improves after mitral surgery. The average operative mortality for mitral valve repair is 1–2% compared to 5–10% with valve replacement. When mitral valve repair is not feasible, the next option is mitral valve replacement with chordal preservation. Various surgical techniques are used to ensure that the residual mitral valve tissue does not interfere with the function of the valve prosthesis. Typically, a mechanical valve is used because of concerns about longevity of tissue valves in the mitral position and because many patients require long term anticoagulation for chronic atrial fibrillation in any case.

There is also a non-surgical option for the treatment of mitral regurgitation. Mitral-valve repair can be accomplished with an investigational procedure that involves the percutaeneous implantation of a clip that grips and approximates the edges of the mitral leaflets at the origin of the regurgitant jet, although this method is less effective at reducing mitral regurgitation than conventional surgery.

In acute mitral regurgitation secondary to a mechanical defect in the heart, the treatment of choice is urgent mitral valve replacement. If the patient is hypotensive prior to the surgical procedure, an intra-aortic balloon pump should be considered.

Mitral stenosis

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Almost all cases of mitral stenosis are caused by rheumatic fever and the consequent rheumatic heart disease. Uncommon causes of mitral stenosis include calcification of the mitral valve leaflets, and congenital heart disease. Mitral stenosis can also be caused by infective endocarditis.

Pathophysiology

The normal mitral valve orifice area is approximately 4-6 cm^2. As the orifice size decreases, the pressure gradient across the mitral valve increases to maintain adequate flow.

Patients will not experience valve-related symptoms until the valve area is 2-2.5 cm^2 or less, at which point moderate exercise or tachycardia may result in exertional dyspnea from the increased transmitral gradient and increased left atrial pressure. Severe mitral stenosis occurs with a valve area of less than 1 cm^2. As the valve progressively narrows, the resting diastolic mitral valve gradient, and the left atrial pressure increase. This leads to transudation of fluid into the lung interstitium and dyspnea at rest or with minimal exertion occurs. Hemoptysis may also be present. Left atrial dilatation increases the risk of atrial fibrillation and subsequent thromboembolism.

Pulmonary hypertension may develop as a result of retrograde transmission of left atrial pressure, pulmonary arteriolar constriction, interstitial edema, or by obliterative changes in the pulmonary vascular bed (intimal hyperplasia and medial hypertrophy). As pulmonary arterial pressure increases, right ventricular dilation and tricuspid regurgitation may develop, leading to elevated jugular venous pressure, liver congestion, ascites, and edema of the legs.

Left ventricular end-diastolic pressure and cardiac output are usually normal in patients with isolated mitral stenosis. As the severity of the stenosis increases, the cardiac output becomes subnormal at rest and fails to increase during exercise. Approximately one third of patients with rheumatic mitral stenosis have decreased left ventricular systolic function as a result of chronic rheumatic myocarditis. The presence of concomitant mitral regurgitation, systemic hypertension, aortic stenosis, or myocardial infarction can also adversely affect left ventricular function and cardiac output.

Symptoms:

Symptoms of mitral stenosis usually manifest during the third or fourth decade of life and nearly half of the patients do not recall a history of acute rheumatic fever.

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Patients are generally asymptomatic at rest during the early stage of the disease. However, factors that increase heart rate such as fever, severe anemia, thyreotoxicosis, exercise, excitement, pregnancy, and atrial fibrillation may result in dyspnea.

Nearly 15% of patients develop embolic episodes that are usually associated with atrial fibrillation. Rarely, embolic episodes may occur even in the patient with sinus rhythm. Systemic embolization may lead to stroke, renal failure, or myocardial infarction.

Hoarseness can develop from compression of the left recurrent laryngeal nerve against the pulmonary artery by the enlarged left atrium. Also, compression of bronchi by the enlarged left atrium can cause persistent cough.

Hemoptysis may also occur, but it is usually not fatal.

Pregnant women with mild mitral stenosis may become symptomatic during the second trimester because of the increase in blood volume and cardiac output.

Physical examination:

The physical examination of the patient with MS is characteristic and usually diagnostic. In advanced disease, the pulse pressure may be reduced, which indicates reduced stroke volume. There may be typical “mitral” facies with plethoric cheeks punctuated by bluish patches, a condition probably related to impaired cardiac output. Jugular vein distention is seen in accompanying right sided heart failure. On lung examination, rales may be present. During cardiologic examination, if pulmonary hypertension is present, the heart apex is shifted to the left, and systolic rising of the sternum can be found.A diastolic thrill may be palpated in the left lateral decubitus position. There is increased intensity of the S_1 that occurs because the transmitral gradient holds the mitral valve open in diastole, so that ventricular systole closes the mitral valve later. In far-advanced disease, S_1 may become soft because the valve is so diseased it neither opens nor closes well. The pulmonary component of the second sound will be increased if pulmonary hypertension is present. After S_2, the mitral valve opens with a snap. The distance from S_2 to the opening snap is a good clue to MS severity. The higher the left atrial pressure (and the more severe the stenosis), the sooner the mitral valve opens. An S_2-opening snap interval <0.08 seconds usually indicates severe disease. A low-pitched mitral rumble follows the opening snap and may be punctuated by presystolic accentuation if

the patient is in sinus rhythm. A high-pitched blowing murmur (Graham Steell) may be heard at the cardiac base. Although often this murmur is thought to be secondary to the pulmonary regurgitation or pulmonary hypertension, in reality the murmur is more often due to concomitant aortic regurgitation. In patients with pulmonary hypertension, other findings may include a tricuspid murmur, hepatomegaly, ascites, and edema.

Electrocardiograpy:

Classical ECG findings in patient with mitral stenosis include left atrial enlargement, right axis deviation, and , in severe cases right ventricular hypertrophy. A broad notched P wave is a classic finding in mitral stenosis but may also be seen in patients with other cardiac diseases. Probably the most common electrocardographic abnormality in patients with mitral stenosis is atrial fibrillation.

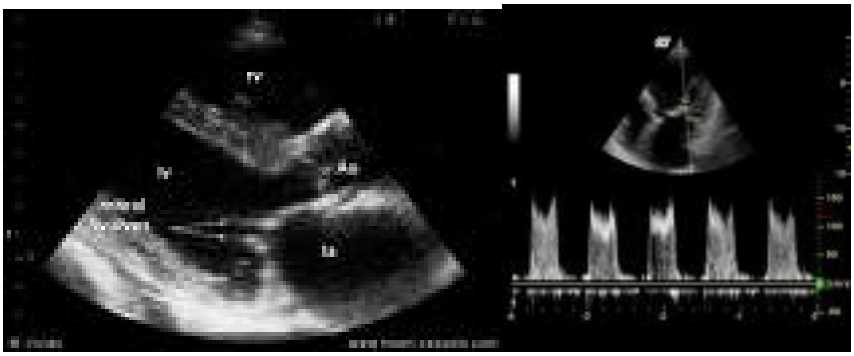
Chest X ray:

Early in the disease, the X ray shows a normal size cardiac silhouette. Later, there may be evidence of left atrial enlargement. Pulmonary vascular redistribution and interstitial and alveolar edema may be seen if elevated left atrium pressures have led to hemodynamic decompensation. Right dilatation and failure lead to evidence of right ventricular and right atrial enlargement. The radiographic abnormalities correspond to the severity of the disease process.

Echocardiography

Echocardiography is used to establish the anatomy of the valve, confirming a typical “rheumatic” or “hockey stick” appearance. Stenosis severity is determined in 3 ways. First, the valve area can be measured by plaimetry. Second, doppler interrogation of the valve can establish the pressure gradient, where gradient=4 v^2 and v=transmitral flow velocity. Third, valve area may be obtained by the pressure half-time technique. This empirical method divides the constant 220 by the time it takes for transmitral flow velocity to decrease from peak velocity to that velocity divided by the square root of 2. The more severe the MS, the slower the emptying into the left ventricle and the longer the pressure half-time will be, which enlarges the denominator and reduces the calculated valve area.

Figure 7. echocardiography image of mitral stenois, 2D and doppler imaging



Cardiac catheterization

Cardiac catheterization may be necessary to determine the severity of the stenosis. Cardiac output and transvalvular gradient measurements are used to calculate valve area with the Gorlin formula to reassess stenosis severity. In most cases, the pulmonary capillary wedge pressure is substituted for left atrial pressure.

Another method of measuring the severity of mitral stenosis is simultaneous left and right heart chamber catheterization. The right heart catheterization (Swan-Ganz catheterization) marks the mean pulmonary capillary wedge pressure, which is a reflection of the left atrial pressure. The left heart catheterization shows us the pressure in the left ventricle. By simultaneously taking these pressures, it is possible to determine the gradient between the left atrium and left ventricle during ventricular diastole, which is a marker for the severity of mitral stenosis. This method of evaluating mitral stenosis tends to overestimate the degree of mitral stenosis, however, because of the time lag in the pressure tracings seen on the right heart catheterization and the slow Y descent seen on the wedge tracings. If a trans-septal puncture is made during right heart catheterization, however, the pressure gradient can accurately quantify the severity of mitral stenosis

Treatment

Treatment is not necessary in asymptomatic patients. The treatment options for mitral stenosis include medical management, mitral valve replacement by surgery, and percutaneous mitral valvuloplasty.

Medical treatment

The medical treatment possibilites for patients with MS and sinus rhythm are relatively limited. In general, all patients with MS should undergo appropriate antibiotic prophylaxis against infective endocarditis for those procedures known to cause bacteremia. Diuretics are useful for treating mild symptoms.

AF commonly accompanies MS and is more related to age than to the severity of the stenosis. When AF occurs acutely, it is often associated with a rapid ventricular response. Because increased heart rate primarily reduces diastole, the arrhythmia causes further impairment in left ventricular filling, which leads to abrupt left atrial hypertension and reduced cardiac output. Immediate rate control is imperative and can be accmplished by the administration of β-blockers or rate-affecting calcium channel blockers. If these therapies are ineffective in controlling the heart rate and the patient is unstable, immediate DC cardioversion is indicated.

The patient with MS and chronic AF is at risk of embolic stroke (at a rate of between 7% and 15% per year). Accordingly, all such patients require warfarin anticoagulation therapy with a target international normalized ratio of 2.5 to 3.5. Chronic rate control for such patients is usually managed by digoxin, a β-blocker, a calcium channel blocker, or some combination of these agents.

Surgical treatment:

The indication for invasive treatment with either a mitral valve replacement or balloon mitral valvuloplasty is NYHA functional class III or IV. To determine which patients would benefit from percutaneous balloon mitral valvuloplasty, a scoring system has been developed. Scoring is based on 4 echocardiographic criteria: leaflet mobility, leaflet thickening, subvalvular thickening, and calcification. Patients with a score of ≥ 8 tend to have suboptimal results. Superb results with valvotomy are seen in patients with a crisp opening snap, score < 8, and no calcium in the commissures. In cases in which mitral valve replacement the operative risk is 3% to 8% in the

absence of pulmonary hypertension and other comorbidities. The choice of prosthesis is based on patient age, the risk of anticoagulation, and patient and surgeon preference.

Tricuspid regurgitation

Tricuspid regurgitation refers to the failure of the heart's tricuspid valve to close properly during systole. As a result, with each heart beat some blood passes from the right ventricle to the right atrium, the opposite of the normal direction. Tricuspid regurgitation occurs in roughly less than 1% of the population and is usually asymptomatic.

Tricuspid valve regurgitation occurs mainly from annular dilation and right ventricular enlargement, which is often secondary to left heart failure from myocardial or valvular causes, right ventricular volume and pressure overload, and dilatation of cardiac chambers. Less common causes of tricuspid valve pathology include rheumatic, congenital, or other causes (endocarditis, leaflet tear/prolapse, chordal rupture, papillary muscle rupture, or myxomatous degeneration of the tricuspid valve). With isolated TR, patients may experience fatigue and decreased exercise tolerance as a result of decreased cardiac output. They may also experience the classic symptoms of “right-sided heart failure” from elevated right atrial pressures, such as ascites, congestive hepatopathy, peripheral edema, decreased appetite, and abdominal fullness. The assessment of intravascular volume status in a patient with severe TR can be difficult because of the pulsatile jugular venous pressure on physical examination. Atrial fibrillation is common as a result of right atrial enlargement. A unique cause of TR is the result of pacemaker or defibrillator leads, which cross from the right atrium into the right ventricle and may directly interfere with leaflet coaptation.

Pathophysiology:

The hemodynamic changes in patients with tricuspid regurgitation include an elevated right atrial mean pressure with a systolic v- wave and also a decreased cardiac output at rest. These hemodynamic changes depend on the acuteness as well as severity of valvular lesion.

Symptoms

Tricuspid insufficiency may be asymptomatic, especially if right ventricular function is well preserved. Symptoms are generally those of right-sided heart failure, such as ascites, hepatomegaly, edema and

jugular venous distension. Vague upper abdominal discomfort (from a congested liver), and fatigue (due to diminished cardiac output) can also be present to some degree.

Signs

On examination, the jugular venous pressure is usually elevated, and 'CV' waves can be seen. Prominent V waves and rapid y descents in jugular venous pressure are found. The liver may be enlarged and is often pulsatile (the latter finding being virtually diagnostic of tricuspid regurgitation). Peripheral edema is also often found. In severe cases, there may be ascites and even cirrhosis (so-called 'cardiac cirrhosis').

Physical examination.

Tricuspid insufficiency may lead to the presence of a pansystolic heart murmur. Such a murmur is usually of low frequency and best heard low on the lower left sternal border. It tends to increase with inspiration, and decrease with expiration and the Valsalva maneuver. However, the murmur may be inaudible reflecting the relatively low pressures in the right side of the heart. A third heart sound may also be present, also heard best with inspiration at the left lower sternal border. Parasternal heave may be felt along the left lower sternal border as well.

Electrocardiography:

Atrial fibrillation is usually present.

Figure 8. tricuspid regurgitation in colour flow mapping

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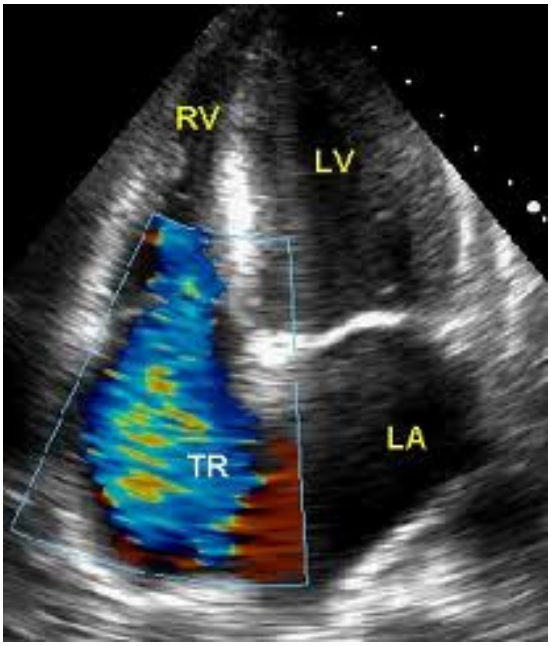

The main therapy is treatment of underlying cause. In most cases, surgery is not indicated since the root problem is a dilated or damaged right ventricle. Medical therapy with diuretics is the treatment of choice. Unfortunately, this can lead to volume depletion and decreased cardiac output. Indeed, one must often accept a certain degree of symptomatic tricuspid insufficiency in order to prevent a decrease in cardiac output. The reduction of cardiac afterload is also beneficial, but a similar risk of depressed cardiac output applies.

Where surgery has to be performed, the following alternatives are available:

Tricuspid valvular repair or valve replacement (rarely performed)

Tricuspid stenosis

Tricuspid valve stenosis is a rare clinical condition, with rheumatic disease accounting for aproximately 90% of all cases. Unusual causes of tricuspid stenosis include metastatic carcinoid

disease and congenital anomalies of valvular structure, infective endocarditis and Whipple's disease or right atrial myxoma.

Physical examination

On physical examination tricuspid stenosis is characterized by an opening snap followed by a diastolic rumbling murmur at the right sternal border. ECG often shows atrial fibrillation. X ray shows an enlarged right atrium but normal pulmonary artery size and clear lung fields.

Tricuspid stenosis can be evaluated by catheterization with measurement of the transvalvuvlar pressure gradient and calculation. Tricuspid valve area less than 1,5 cm2 is associated with symptoms.

Echocardiography allows definitive diagnosis of the cause and severity of tricuspid stenosis.

Like mitral stenosis, tricuspid valve obstruction is the result of a chronic, slowly progressive disease .

Therapy: medical therapy is usually ineffective since diuresis to improve systemic venous congestion futher reduces cardiac output. An intervention shoud be considered for patients with significant stenosis.

Pulmonary stenosis

While the most common cause of pulmonary valve stenosis is congenital heart disease, it may also be due to rheumatic heart disease or a malignant carcinoid tumor. Both stenosis of the pulmonary artery and pulmonary valve stenosis are causes of pulmonic stenosis.

Symptoms include jugular vein distension, cyanosis (usually visible in the nailbeds), right ventricular hypertrophy, and general symptoms of lowered oxygenation of the blood. When the stenosis is mild, no symptoms may be present. If the stenosis is severe, syncope or dizziness may occur on exertion. An enlarged liver (hepatomegaly) and swelling in the legs (edema) may also be present. The initial evaluation of pulmonary valve stenosis involves echocardiography. The degree of stenosis is typically determined by the peak pressure gradient across the valve. Pulmonary stenosis is moderate if the trans-valvular gradient is 20-40 mmHg, the stenosis is severe if the trans-valvular gradient is 50-80 mmHg and velocity is more than 4m/s.

Treatment

Valve replacement or surgical repair (depending upon whether the stenosis is in the valve or vessel) may be indicated. If the valve stenosis is of congenital origin, balloon valvuloplasty is another option, depending on the case.

Pulmonary regurgitation

In adults, pathologic pulmonary regurgitation is most often the consequence of prior interventions for congenital heart disease. Other causes include rheumatic valve disease, carcionoid disease, trauma and endocarditis. Pulmonary regurgitation in adults may be due to pulmonary artery and annular dilatation secondary to pulmonary hypertension.

A soft decrescendo murmur can sometimes be identified early in diastole, heard best over the left lower sternal border. Severe regurgitation may contribute to right ventricular hypertrophy, and in later stages, cause right heart failure.

The diagnosis is often initially made by echocardiography.Cardiac catheterization is only minimally helpful in the diagnosis of pulmonary regurgitation. However catheterization is essential for calculation of pulmonary vascular resistance in patients with pulmonic regurgitation due to pulmonary hypertension.

Mild pulmonary regurgitaton is usually asymptomatic. Chronic severe pulmonary regurgitation is often well tolerated for many years. However, the right ventricle may dilatate and develop systolic dysfunction, analoguos to the effect of chronic aortic regurgitation on the left ventricle. Severe right ventricle dilatation is also associated with the increased risk of sudden death.

Medical and surgical treatment

No specific therapy is needed for most adults with pulmonic regurgitation because the it is usualy mild.With severe regurgitation and evidence of progression of right ventricular enlargement or right ventricular dysfunction , surgical treatment should be considered.

14. Cardiomyopathies

(P. Gregor)

Definition: Cardiomyopathies (CMP) are diseases in which the heart muscle is structurally and functionally abnormal in absence of ischemic heart disease, hypertension, valvular or congenital heart disease which could be the cause of myocardial disorder.

The classification is shown in Table 1.

Table 1. Classificatin of the Cardiomyopathies

Dilated
Hypertrophic
Restrictive
Arrhythmogenic right ventricular cardiomyopathy
Unclassified (non-compaction, stress…)

Dilated cardiomyopathy

Brief description: Dilatation of left ventricle (and often other cardiac chambers) associated with impaired left ventricle systolic function.

Etiology and pathogenesis: Mostly idiopathic conditions without a known cause, in some patients due to underlying genetic abnormalities.

In other patients the pervious viral infection leading to dilated cardiomyopathy is proved, but the whole issue is much more complex – there may some abnormalities in cytosceletal genes etc.

In a broader sense also inflammatory cardiomyopathies – myocarditis (discussed in appropriate chapter), alcoholic or tachycardia-induced cardiomyopathies and number of other conditions belong to dilated cardiomyopathies ***. Alcoholic cardiomyopathy*** is predominatly caused due to a toxic effect of alcohol with an expected consumption about 80 g of alcohol for a period of 10 years (smaller amount for women). ***Tachycardia-induced cardiomyopathy*** is caused by impact of prolonged tachycardia on myocardial muscle (usually with frequency ≥ 120/min). These include various supraventricular tachycardias (rarely also ventricular arrhythmias) and a cure of the tachycardia (in any different way) leads in gradual restore of left ventricle systolic function.

Prevalence is about 26/100000 inhabitants (increasing).

Clinical presentation in a full developed form is the same as symptoms of systolic left ventricle heart failure e.g. dyspnea, lung crackles, often gallop and also symptoms of right ventricle insufficiency when the duration is longer and postcapillary pulmonary hypertension is developed.

Echocardiography shows dilatation and dysfunction of left ventricle, dilatation of other heart chambers (esp. left atrium) and mitral valve insufficiency are also common.

ECG: LBBB is very common in dilated cardiomyopathy (Figure 1).

The prognosis is usually poor – there is a gradual deterioration of left ventricle function and consequent worsening of heart failure presentation. However, the most often mortality cause is sudden death due to malignant arrhythmia.

The therapy should follow the current guidelines for treatment of chronic heart failure. Betablockers and ACE inhibitors have major prognostic importance, for symptomatic treatment diuretics and digitalis cardiotonics are available. Biventricular pacemaker, ICD or heart transplantation is indicated for some patients in advanced stages.

Hypertrophic cardiomyopathy

Brief description: it is characterized by myocardial hypertrophy, especially of interventricular septum (Figure 2). The size and systolic function of left ventricle is normal (contractility may be even increased with "hypernormal" ejection fraction)and the diastolic filling is impaired. There can be also a presence of obstruction – dynamic subaortic senosis, whose significance is affected by changes

in preload, afterload and myocardial contractility. It is caused probably on the basis of the Venturi effect with a suction of mitral valve apparatus in a left ventricle outflow tract (outflow tract itself is narrowed by myocardial hypertrophy, blood velocity is higher there and so sucks in components of mitral valve apparatus and mitral valve itself).

Etiology and pathogenesis: it is a typical genetic determinate disease (autosomal dominant), that is caused by mutation of genes responsible for coding of cardiac sarcomeric proteins. There were described mutations of 10 genes totally (the first in 1990 – mutation of beta-myosine heavy chains coding which represents the most frequent type of mutation in HCMP).

In a broad sense, different types of familiar hereditary diseases causing myocardial hypertrophy can meet criteria for hypertrophic cardiomyopathy (e.g. Fabry disease, different types of infiltrative disorders etc.)

Clinical presentation is in advanced forms given by congestive symptoms of left ventricle diastolic dysfunction, e.g. dyspnea, lung crackles and even syncope can occur (mostly based on arrhythmias). The most remarkable finding in obstructive form is precordial systolic murmur which is typically amplified while Valsave maneuver is performed.

The *ECG* shows signs of left ventricle hypertrophy, pathological Q waves resembling myocardial infarction are also common.

Echocardiography shows myocardial hypertrophy, especially interventricular septum, while left ventricle has normal size and contractility (norm or even “hypernormal” ejection fraction). A forward movement of mitral chordae tendineae is the cause of the systolic murmur discussed above in obstructive forms, mitral regurgitation is also common.

Prognosis is worse in patients with evidence of ventricle tachycardias, syncopes, family history of sudden death, greater thickness of myocardium (≥ 30 mm), decrease in blood pressure after exercise (≥ 20 mm Hg) or those with cardiopulmonary resuscitation history. The main cause of death is a sudden death caused by arrhythmias, only in a small number of patients a dysfunction of left ventricle as a pump is terminally developed.

Betablockers and calcium channel blockers (verapamil, diltiazem) are used in *therapy*. For the obstructive form accompanied by severe subjective symptoms percutaneous septal ablation

(instillation of small amount of concentrated alcohol into the first septal branch of left anterior descending artery) or surgical procedure (septal myotomy - myectomy) or even implantation of pacemaker (decrease in obstruction) should be considered. Implantation of cardioverter – defibrillator is indicated in patients threatened by sudden death (see above).

Restrictive cardiomyopathy

Brief description: restrictive filling together with reduce in left or even in right ventricle volume.

Etiology and pathogenesis: idiopathic or associated with other diseases (amyloidosis, endomyocardial eosinophilic disease etc.).

Currently the main cause of restrictive cardiomyopathies in adults is primary (AL) amyloidosis which is associated with myeloma. It results from the deposition of immunoglobulin light chains produced by monoclonal population of plasmatic cells.

Clinical presentation: the disease usually manifests by symptoms of congestion from diastolic dysfunction and by systolic murmurs from mitral and tricuspidal regurgitation.

The prognosis is very poor (median survival is 1 year).

Treatment is symptomatic and also high dose chemotherapy is administered.

Arrhythmogenic right ventricular cardiomyopathy

Brief description: typically progressive fibro-fatty replacement of the right ventricular myocardium. Familiar disease is common, usually with autosomal dominant inheritance.

Etiology and pathogenesis: inflammation is accused (chronic myocarditis)

Clinical presentation: persistent ventricular arrhythmias (especially ventricular tachycardia shaped as left bundle branch block), epsilon wave can be found on ECG (special wave following the QRS complex).

The diagnosis is based on the wall thinning and also frequent dilatation of right ventricle (magnetic resonance, echocardiography) together with its dysfunction, aneurysm of right ventricle wall can be often found.

Treatment is medical (betablockers, different types of antiarrhythmics) and non-medical consisting in an attempt to influence life-threatening arrhythmias (ICD implantation, sometimes cryoablation or resection of the part of right ventricle wall)

Unclassified cardiomyopathies

Here is an example of the recently two best known –non-compaction and stress.

Non-compaction cardiomyopathy

It is a congenital defect in production of compacta from spongiosa in embryonic development. The disease impresses as hypertrophic cardiomyopathy, but in fact it is not real hypertrophy but preserved spongiform layer of myocardium. The prognosis is usually worse – it can demonstrate as heart failure, systemic embolism and different arrhythmias. The diagnosis is made by echocardiography or magnetic resonance.

Stress cardiomyopathy ("takotsubo")

Initially it impressed as ST elevations myocardial infarction but there is normal angiography of coronary arteries. Echocardiography usually shows akinesia or dyskinesia of apical part of the left ventricle.

The disease affects mostly elderly women after emotional or physical stress in which the chest pain with suspicion of myocardial infarction appears. The disease is usually benign with normalization of left ventricle function within 2-4 weeks. It is assumed that this is a "stunned" myocardium due to high levels of catecholamines released during stress

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Figure 1. ECG – left bundle branch block in dilated cardiomyopathy

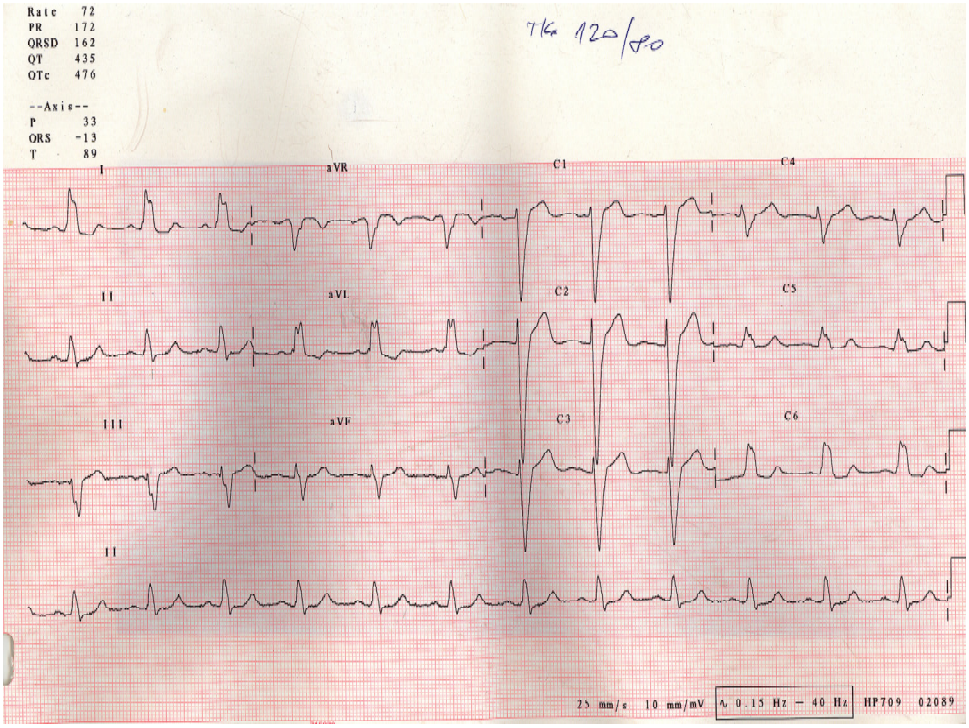

Figure 2. Typical pathological – anatomical morphology of the hypertrophic cardiomyopathy. Severe myocardial septal and free wall hypertrophy of left ventricle (lenght of the line on the paper indicates 1cm).

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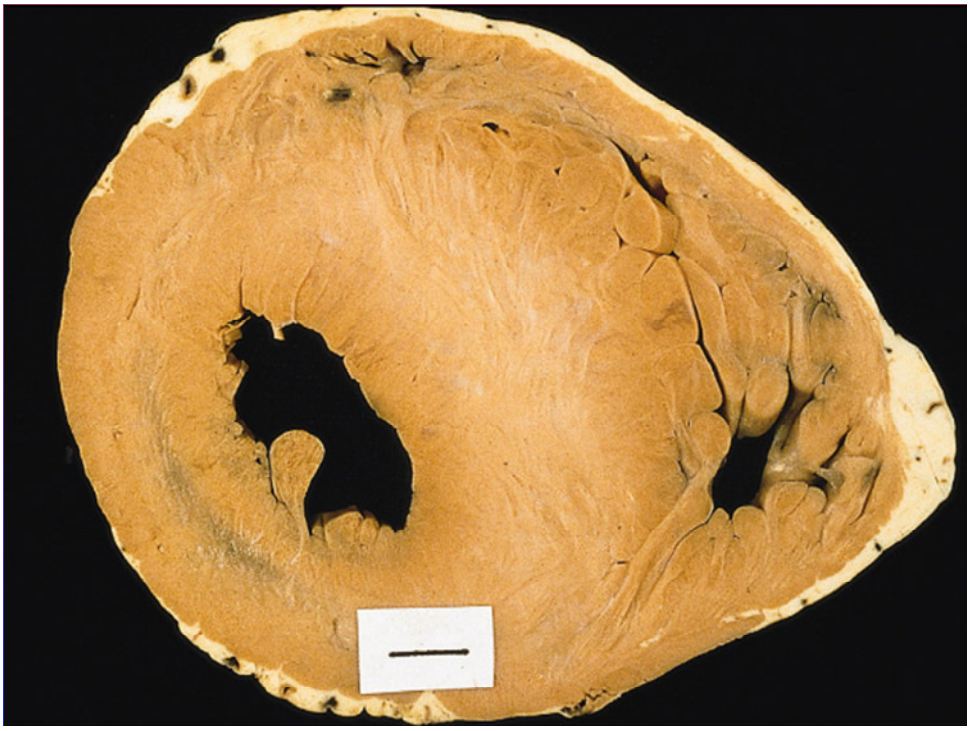

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15. Inflammatory heart diseases (myocarditis, pericarditis, endocarditis)

(P. Gregor)

Myocarditis

Myocarditis is defined as diffuse or local inflammation of myocardium. According to current classification it belongs to dilated cardiomyopathies. They can occur in 0.3 – 10% of autopsies but reaches 20% in persons who died by sudden death, in patients with new onset of heart failure up to 10%. Etiology of myocarditis captures Figure 1. In experimental conditions, disease caused by Coxsackie viruses often has two phases – at the beginning (5^{th} to 7^{th} day) it is reversible inflammation of cardiomyocytes (curable), later (from about 9^{th} day) there is a interstitial (often monocyte) infiltration which does not disappear. In pathogenesis of viral myocarditis is applied multiplication of the virus in myocardium with subsequent infiltration of macrophages and NK cells with their cytokines production, leukocytes activation and subsequent autoimmune process with antinuclear antibodies formation.

Prior to clinical presentation often nonspecific viral prodromes are manifested. Cardiac symptoms as chest pain (often atypical), tachycardia (or other arrhythmias), systolic murmurs (from AV valves regurgitation) can appear later. In extreme cases, however, the disease may present with cardiogenic shock or subclinically at the opposite side. In many cases the infection may resemble the image of myocardial infarction with corresponding ECG changes (mostly changes in repolarization ST-T phase as well as pathological Q waves) surprisingly with normal coronary angiography. Only a few myocarditis have their typical clinical manifestation (e.g. diphteric, Chagas disease).

Laboratory in acute phase shows elevation of troponin (in contrast to myocardial infartction it can preserve several weeks). Various inflammatory markers are frequently positive (leukocytosis, elevated CRP). In many patients also different immunological parameters indicating the presence of immunoalterative response may be found (rheumatoid factor, myocardial antibodies). Serological testing may help identify the etiological agents.

Echocardiography often shows regional wall motion abnormalities that do not match to regional coronary disease; also reversible myocardial hypertrophy may occur (inflammatory edema).

The cardiac catheterization is important mainly to distinguish ischemic heart disease and myocardial infarction, respectively. Endomyocardial biopsy has also important diagnostic value. The assumption is, however, access to excellent imunohistochemistry and microbiological tests (PCR, electrone microscope) with an option of precise indentification of e.g. viral agents.

Treatment of acute myocarditis: A rest is necessary in acute phase (approx. 2 weeks) with a gradual loading afterwards. Antibiotics are certainly administered in acute phase when the disease is caused by microbes that can be positively affected by antibiotics (this applies of course mainly for bacterial infections). Corticosteroids and immunosuppressants may have good results in "immunohistochemically positive" patients with no evidence of virus in myocardium or in some special forms of myocarditis with poor prognosis (giant cell myocarditis, myocarditis in systemic diseases). Of course there is a need of symptomatic therapy according to clinical presentation (diuretics in heart failure, vasodilatans, cardiotonics, antiarrhytmics in some patients).

Betablockers and NSAIDs should not be administered in acute phase of viral myocarditis (they may enhance the viral replication).

The prognosis is uncertain. It mainly depends on the dynamic of clinical, ECG and echocardiographic findings. E.g. the degree of dilatation and left ventricle dysfunction is an important prognostic factor but decisive, however, is their dynamics rather than the initial value.

Figure 1. Etiology of Myocarditis, part 1

Etiology of myocarditis

Viruses

- Parvovirus
- Coxsackie B
- Adenovirus
- Enterovirus
- Influenza, parvo, hepatitis C, AIDS…

Bacteria

- Diphtheria, streptococcus, staphylococcus, pneumococcus….
- Borrelia
- Chlamydia
- Mycoplasma

Fungi (mycosis, rickettsia)

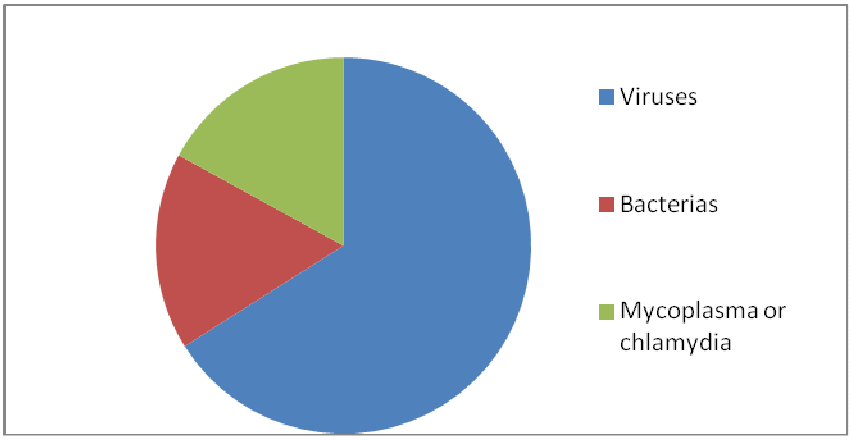
Protosoa (Chagas disease)

Parasits (echinococci, trichinosis, philariosis)

Figure 2. Etiology of Myocarditis, part 2

Infectious: 38 – 47% (etiological agents can be proved)

Non-infectious: 53 – 62% (only histological signs of myocardial inflammation, infectious etiological agents cannot be found



Pericarditis

Etiological types of pericarditis are shown in Fig. 1 and 2. The most common is acute benign idiopathic pericarditis – it affects health people in which fever, pericarditis type chest pain and other signs of pericarditis that are summarized in Figure 3. The attribute “benign” does not necessarily reflect the reality because it may recur (and frequently even repeatedly) or it may forestall

constrictive pericarditis. Viral pericarditis behaves similarly (in contrast to previous form the etiological agent can be identifie; the clinical presentation is identical). Bacterial pericarditis may be in substance caused by any type of bacterial infection. Very deceitful – especially while we do not think about it – may be tuberculous pericarditis ongoing unrecognizable for a long time. Treatment of proven TBC pericarditis is long-term (6 to 12 months) using a combination of tuberculostatics.

Pericarditis associated to myocardial infaction is the most often. The most common type – pericarditis epistenocardiaca – is a bordered inflammatory reaction above the necrotic part of myocardium that affects the patients 3th to 5^{th} day after transmural myocardial infarction. It is usually benign disease that can be proved by ECG and/or echocardiography. Pericarditis in postinfarctional Dressler syndrome represents entirely different disease arising from immunoalergic background. It could be associated with pleuritis and pneumonic infiltrates and it appears approximately one month after the attack; it is very rare currently.

Pericarditis associated to postpericardiotomy syndrome is frequent due to large number of patients undergoing cardiosurgical procedure and it is manifested by recurrent effusions (often in combination with pleuritis and pleural effusions). Post-traumatic pericarditis may be associated ith perforating or non-perforating injury (in the first case there is a danger of contamination and developemnet of severe purulent pericarditis with a rapid development of constriction; these are usually very severe conditions accompanied by cardiac tamponade). Other types of pericarditis are included cancer, metabolic, pericarditis in systemic diseases. Among pericarditis from allergic causes and hypersensitivity could include lupus like syndrome (today almost absent). From physical causes mainly high doses irradiatin is associated to acute pericaritis with an effusion and early followed with constriction.

Acute pericarditis usually manifests with pericardial type of pain (Figure 3). It is a chest pain which is often atypical and remains musculoskeletal pain. We often find pericardial friction murmur. There are typical concave ST elevations on ECG which normalize after recovery. The most sensitive method for detection of pericardial effusion is echocardiography that allows detecting even small limit amount of fluid in pericardium (from 20 mL). Laboratory testing often shows leukocytosis and

elevation of inflammatory markers. Elevation of cardiospecific enzymes indicates subepicardial myocardial damage.

The treatment of acute pericarditis is based on therapy of underlying cause (if possible). When it causes significant chest pain, NSAID´s may be administered (acetylsalicic acid, indomethacin). Colchicine or corticosteroids can be given when prolonged or recurrent pericarditis (mainly in idiopathic, postpericardiotomy etc.). Anticoagulants administration may be problematic therefore there are mostly avoided.

Constrictive pericarditis occurs when fibrotic scars are developed in pericardium that leads to the gradual restriction in diastolic filling and often continued with storage of calcium in pericardium with ongoing gradual restriction in filling of all cardiac chambers (Figure 4 to 6). Diastolic pressures in both ventricles are becoming equalized, the cardiac output progressively decreases and vicious circle is closed. Clinically in more advanced forms the manifestation of advanced heart failure occurs with swelling, hepatomegaly, frequent ascites (it may resemble cirrhosis including gynecomstia, loss of hair, palmary erytema etc. – Figure 6). The only possible treatment is surgical pericardiotomy.

Figure 1. Types of pericarditis due to etiology, part 1

- Acute benign idiopathic pericarditis
- Viral (coxsackie, echo…)
- Bacterial: direct transfer of infection in empyema, pneumonia or indirect in septicemia (streptococcus, pneumococcus, staphylococcus…., TBC)
- Post-myocardial infarction: epistenocardiaca, Dressler syndrome
- Postpericardiotomy syndrome

Figure 2. Types of pericarditis due to etiology, part 2

- Posttraumatic
- Connective tissue diseases (SLE, RA…)
- Metabolic diseases (uremia, dialysis-associated, hypothyroidism)
- Cancer

- Allergic and hypersensitivity disease(lupus-like syndrome, drugs – hydralazines, minoxidile)
- Physical and chemical factors

Figure 3: Pericarditis – diagnosis and treatment

Acute pericarditis

- Sicca, effusive
- Pain
- Friction murmur
- Laboratory findings: inflammatory signs, enzymes
- ECG: concave ST elevations, later T wave inversions
- Echocardiography: RTG, CT
- Treatment: daccording to underlying cause

Figure 4: Constrictive pericarditis – development

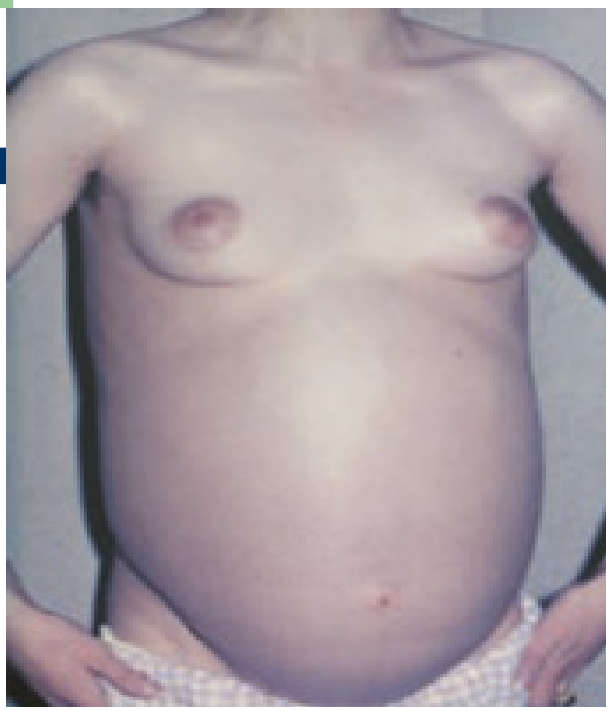
- Thick and scared pericardium presses the heart and restricts its diastolic filling despite high filling pressures, calcium storage resp.
- Generalized process – equal restriction in filling of all cardiac chambers, rarely localized pericardium thickening

Figure 5: Constrictive pericarditis – pathophysiology

- Rigid pericardium inhibits the diastolic filling of all cardiac chambers – increasing and equalizing of diastolic pressures in cardiac chambers
- At the beginning the diastolic filling is unlimited, suddenly interruption of filling (cardiac volume reaches borders defined by pericardium) – in both ventricles *dip* and *plateau*
- Reduce of cardiac output, tachycardia, normal or decreased kinetics

- Therapy: pericardiotomy

Figure 6: Constrictive pericarditis – clinical presentation with ascites reminding liver cirrhosis



Endocarditis

Definition

Disease caused by various types of microorganisms that affects endocardium, preferably valvular.

It affects primarily patients with preexisting valvular heart disease or those with implantation of valve prosthesis; affection of intravenous drugs abusers is also frequent. Dividing in acute and subacute (lenta) is no longer used.

Pathogenesis, etiology, types of infective endocarditis (IE).

In places with blood turbulence presence (e.g. preexisting heart disease) microtombi can settle and subsequently may be infected by bacteria from bacteraemia caused by various reasons (it may be due to physiological activities such as brushing teeth, coitus, strenuous defecation through various surgical interventions, particularly in the oral cavity). These masses are called vegetations (Fig. 1), which further damage the endothelium mechanically and by action of cytokines and toxins. Microorganisms "protected" in these masses consist of platelets and fibrin fibers cannot be destroyed by immune system, leukocytes cannot penetrate the fibrin net while inside the microorganisms may multiply rapidly and the vegetation grows. They may even cause obstruction of valvular orifice but more often leads to partial or total destruction of the valve or disruption of chordae tendineae resulting in insufficiency of the valve. They can embolized and artificial valves can be partially or fully released (1).

In addition to native valves IE often IE of valvular prosthesis appears today (a large number of operated patients in developed countries). They are divided into type with early onset or late onset – Tab 1. Both types differ mainly in connection to procedure, type of microbe and prognosis. Early onset IE has an obvious relation to surgical procedure; it is therefore nosocomial infection where S. aureus and gram-negative rods usually apply (Tab 2), often with considerable resistance; the prognosis is unfavorable. The spectrum of agents of late onset type is near to etiology of native valve IE. The original boundary for its formation of two months has shifted to 12 months (nosocomial infections can manifest even after 12 months), the mortality rate is lower (about 20% compared to 40% in early).

IE in intravenous drug abusers (IDA) is a common disease together with hepatitis B, C and HIV infection. The mortality rate is lower (approx. 10%). Vegetations are usually localized on tricuspid valve.

Clinical presentation

Beginning is usually very unspecific especially in typical subacute endocarditis (e. lenta) – fever, sweating, weakness, arthralgia and other nonspecific signs. In a physical examination splenomegalia, Osler nodes (small, slightly painful nodules on the acres of limbs, disappear spontaneously), splinter hemorrhages under nails or petechiae can be found. There can be also found mycotic aneurysms (their origin is in small embolisms in vasa vasorum, they are not related to fungal infections). Less specific signs are Janeway lesions (small groups of painless hemorrhages under the skin of soles, palms or calf) and Roth spots in retina (retinal hemorrhage with pale centers).

Heart murmurs are typically found (often as a result of preexisting valvular heart disease).

In acute endocarditis preferably appear prolonged signs of sepsis with high fever, symptoms of septic embolization, rapid progression of valvular damage and even septic metastasis. However, as mentioned above, differences between those two types disappear and their division is not currently universally accepted. A picture of pneumonia migrant indicates right sided endocarditis.

Laboratory findings

Blood cultures (3/24 hours) and echocardiography (transesophageal optimally) belong to essential diagnostic methods.

Other routine laboratory tests should be undoubtedly performed such as blood count (usually normochromic normocytic anemia and leucocytosis with left shift can be found), inflammatory markers (CRP), renal parameters (CAVE immune complex glomerulonephritis with possible renal failure and hematuria), as well as some immunological parameters (theumatoid factor, circulating immunecomplexes, etc.).

For the diagnosis are mostly used criteria created by Durack and his colleagues at Duke University – Tab. 3.

As mentioned above, IE affects preferably patients with preexisting heart disease (valvular diseases as stenosis or regurgitations, congenital – mainly circuit disorders). The risk stratification of IE for different type of disease is shown in Table 4.

Therapy

It should be noted that without treatment 100% of patients dies – not only a single case of spontaneous recovery has been described. Bactericidal antibiotics are administered sufficiently long period (4 – 6 weeks), intravenously, at sufficient doses (difficult penetration of antibiotics into vegetations). Antibiotic therapy is usually chosen due to sensitivity obtained from blood cultures and close cooperation with antibiotic center is desirable. In patients with infection that is not able to control with antibiotics (including especially fungal infections), those with heart failure, extravalvular dissemination (abscess, fistula), recurrent embolism, or with large vegetations (more than 10mm), surgical treatment is recommended. It is of course indicated while the valve or chordae tendineae are significantly destroyed (e.g. perforation).

Prophylaxis

Since the IE threatens particularly those with valvular heart disease or other disposition, it is necessary to take care about their optimal hygiene especially oral hygiene (often presence of viridians streptococci in oral cavity as normal saprophytes threaten such persons with bacteremia). Especially in high risk patients (Fig. 4) even higher doses of antibiotics before any procedure is required. One dose is usually enough – e.g. before procedures in oral cavity 2g of amoxycilin is administered, details can be found e.g. in guidelines of the Czech Society of Cardiology (3). It should be noted that none of the recommended practice has ever been verified by broad clinical trial and it would probably never happen.

Table 1. Types of the Infective Endocarditis

Native valve IE
Prosthetic valve IE
Early onset (up to 2 moths from surgery, it is associated with the procedure, worse prognosis)
Late onset (2-12 moths from surgery, better prognosis)
IE of intravenous drugs abusers

Table 2. Etiology of Endocarditis (simplified according to 1)

	Native valve	IDA	Valvular prosthesis early onset	Late onset
Sttreptococci	+++	+	+	+
Enterococci	+	+	+	+
Staphylococci				
S. aureus	++	+++	+++	++
Coagulase - negative	(+)	(+)	+++	++
Gram - negative bacilli	+	+	+	+
Fungi	-	+	+	(+)

Table 3: Diagnosis of IE due to Duke Criteria (2).

Major criteria

Echocardiography (typical vegetation, abscess, new regurgitation or dehiscence of prosthetic valve

Positive blood culture with an evidence of typical microorganism (Streptococcus viridans or bovis, Staphylococcus aureus, Enterococcus, HACEK group) or persistently positive blood cultures with the same microorganism

Minor criteria

Preexisting valve disease, i.v. drug use, fever more than 38°C, vascular phenomena (arterial emboli, mytocit aneurym, septic pulmonary emboli, hemorrhage - intracranial, conjunctival, Janeway lesions, imunological phenomena (glomeruloephritis, Osler nodes, Roth spots, positive rheumatoid factor), positive blood cultures or untypical echocardiographic findings

Definite IE = 2 major criteria or 1 major and 3 minor criteria or 5minor criteria

Table 4: Risk stratification of IE development depending on the type of heart disease

High risk: prosthetic valve, st.p. IE, ductus arteriosus patens, aortic valve disease with calcifications, defect of interventricular septum, coarctation of aorta
Medium risk: mitral prolapse with regurgitation, mitral stenosis, hypertrophic obstructive cardiomyopathy, degenerative valve diseases in elderly
Low risk: defect of interatrial septum, mitral prolapse without regurgitation

Fig.1: Vegetations on mitral valve in pathological – anatomic preparation

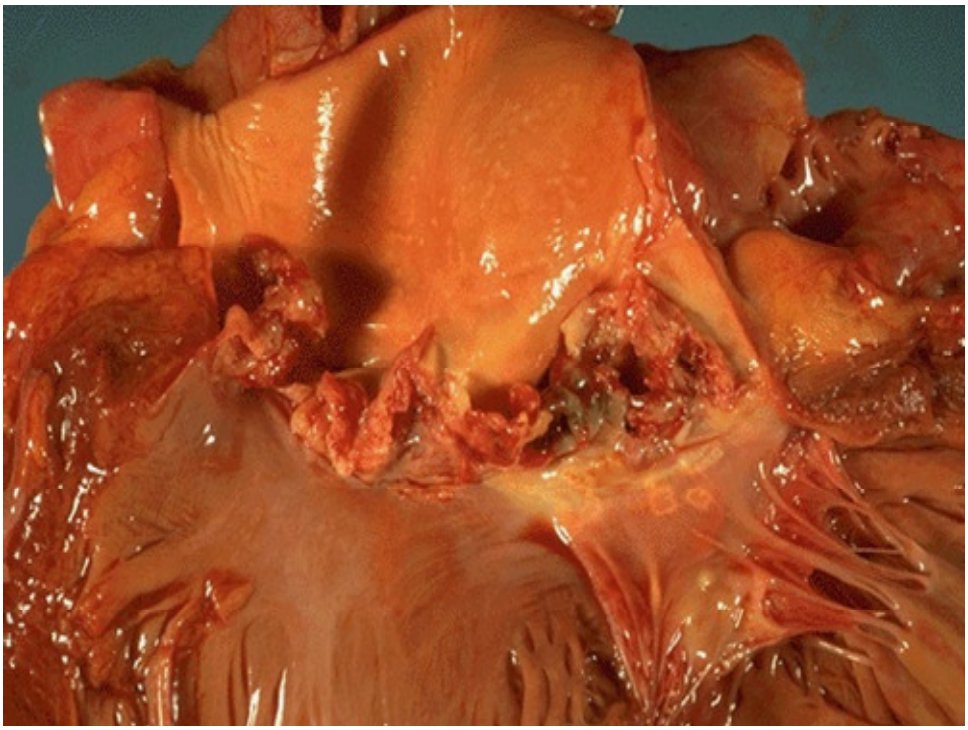


Figure 2: Large vegetation on the tricuspid valve (under the sign PS) in transesophageal echocardiography. PS – right atrium, LS – left atrium, Ao – aorta, PK – right ventricle

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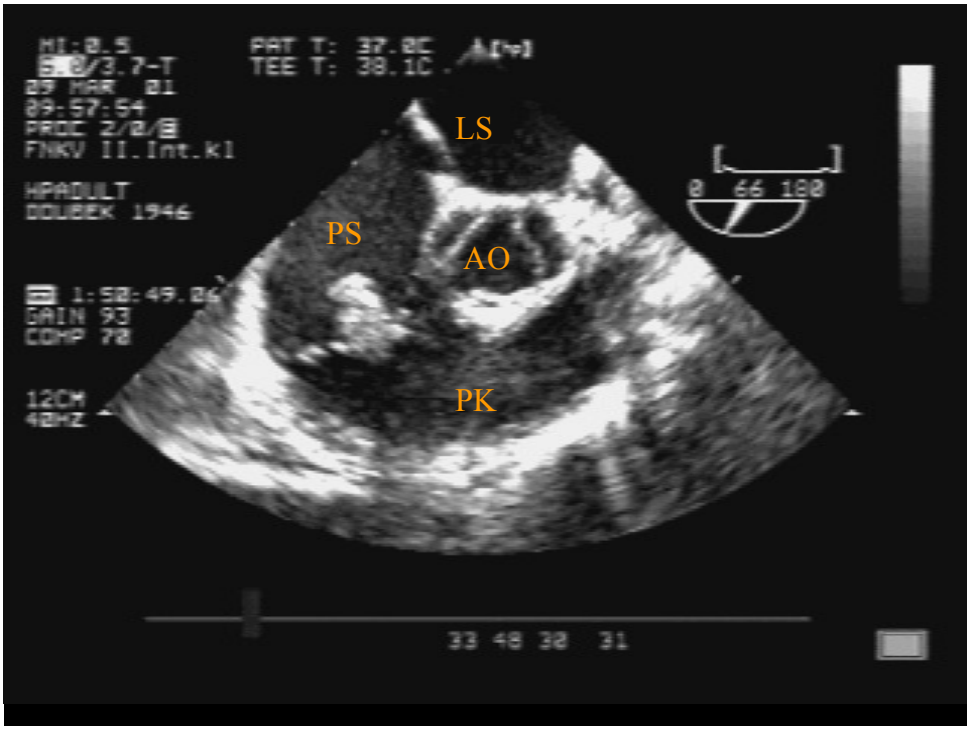

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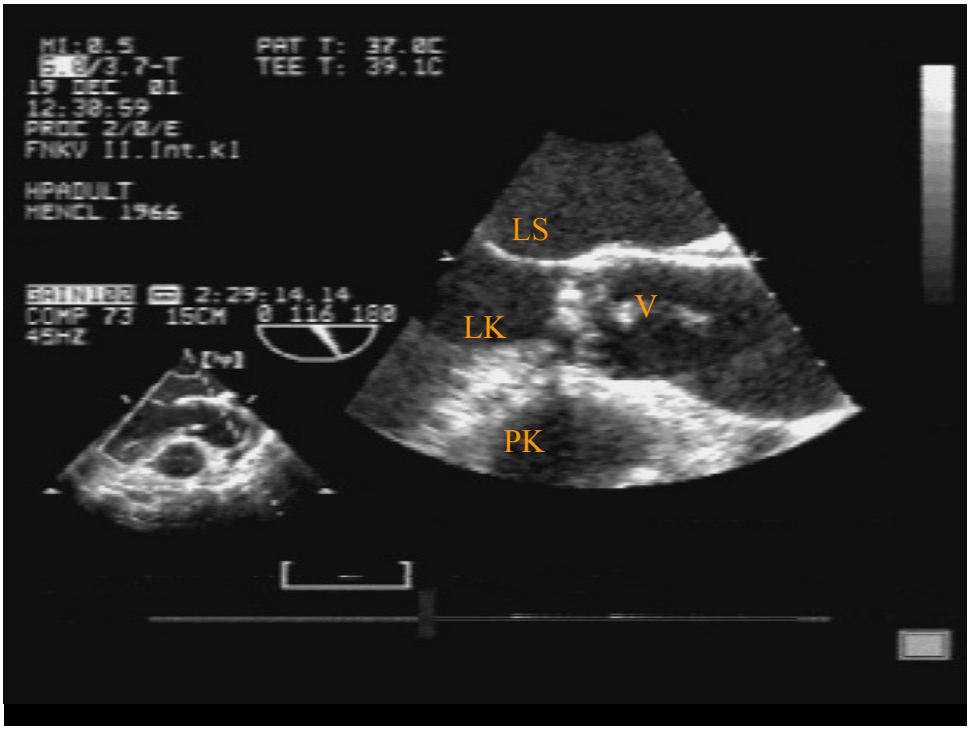
Figure 3: Vegetation on the aortic valve (V) in transesophageal echocardiograpyhy



16. Pericardial Diseases

(P.Gregor)

Pericardium is composed of two layers (Fig. 1). External - parietal layer (pericardium in the strict sense) has ligamentous attachments to the sternum, diaphragm and merges into adventitia of large vessels (fixed position of the heart). Internal – visceral (epicardial) layer covers the heart. There is a space between them, under normal circumstances rather virtual, containing 15 to 50 ml of serous fluid.

It is a paradox that the existence of pericardium has been known for a long time but we do not understand its function in details (Fig 1). It is assumed that it is a membrane allowing smooth movement of structures in mediastinum, representing a barrier against infection and preventing dilatation of the heart indiastole (important mainly for thin-walled chambers in the right ventricle). Its removal, however, results in an increased cardiac output because of tachycardia.

The pressure in pericardial cavity is similar as in pleural cavity (-5 to +5 mm of water column) and it is influenced by the interpleural pressure. If the pressure rises to (or above) the pressure in the right atrium or the diastolic pressure in the right ventricle it leads to cardiac tamponade.

The major part of pericardial diseases consists of the pericarditis. In this chapter we discuss only some aspects related to pericardial effusion (especially cardiac tamponade) and issues of pericardial tumors, the other is concentrated in Chapter 15.

Pericardial effusion

Under normal circumstances, pericardial cavity contains 15 to 50 ml of serous fluid, which is ultrafiltrate of plasma and allows a smooth gliding of two pericardial layers. Pericardial effusion in a meaning of disease is formed when there is greater amount of pericardial fluid than can be absorbed. Three situations may occur in this case:

insignificant effusion without any impact on hemodynamics (Figure 3).

effusion compressing the heart, but its hemodynamical influence is avoided or substantially reduced by compensatory mechanisms.

effusion associated with severe compression of the heart that gets out of compensation mechanisms – cardiac tamponade.

Pericardial effusion may be clinically with no symptoms at all (more about in cardiac tamponade and Chapter 16 about pericarditis). The most sensitive method for the detection is echocardiography. It may detect effusions with boundary quantities of fluid in pericardial cavity (approx. 20 ml), RTG may reveal effusion more than 200 ml (tent like configuration of the heart with smooth contours). ECG may show in case of large effusions lower voltage in all leads or electrical alternans (oscillating of QRS voltage – see below). CT and magnetic resonance imaging also allow detection of pericardial effusions.

Cardiac tamponade (Fig. 2).

It is a term referring the compression of the heart due to excessive accumulation of fluid in the pericardial cavity associated with severe impairment of diastolic filling and cardiac output gradually. Then critical hypoperfusion of myocardium and other organs is developed and electromechanical dissociation occurs. The patients usually have hypotension, increased venous pressure and silent beats (this triad was described by Beck in 1935). Fairly typical (but not sensitive) sign is pulsus paradoxus. It is a quietness or even disappearance of pulse during inspiration on peripheral and also central arteries. The quietness of the arterial pulses was called paradox by Kussmaul in 1873 (over persistence heartbeats the arterial pulse weakens or disappears). Actually, it is not paradox but physiological response of the blood pressure which is graduated by tamponade. Normally, the volume of right ventricle increases, the volume of left ventricle decreases and the velocity of blood flow from caval veins to the right atrium increases during the inspiration (due to decrease in intrapleural pressure). ECG findings have explicitly auxiliary character – there is

sometimes low voltage in all leads or electric alternans (regular oscillation of QRS complexes configuration which is the sign of "swinging" movements of the heart in a large amount of pericardial fluid).

The cause of tamponade may be rupture (of myocardium, aorta), tumors with pericardial metastasis and also various types of pericarditis or postpericardiotomy syndrome. The treatment is pericardiocentesis with draining of the fluid by special needle, usually under echocardiographic control. Subxiphoidal surgical endoscopic drainage in local anesthesia or surgical pericardiotomy may be also performed.

Pericardial tumors

Primary tumors are very rare. These are mesothelioma, fibro – or angiosarcoma. More frequent secondary affections occur especially metastasis of lung, breast, stomach or other types of carcer and even mediastinal lymphoma is not rare. Tumor pericarditis stay asymptomatic for a long time. Only when the amount of the fluid is larger dyspnea, weakness and development of tamponade may present – therefore pericardiocentesis is indicated. The therapy is only palliative.

Also cysts may occur in pericardium and they may resemble as circumscribed pericardial effusions at echocardiography.

Figure 1. Pericardium – layers, function.

Pericardium

- Parietal (external) – pericardium, visceral – epicardium.
- Smooth movement of structures, barrier against infection, prevention against heart distension ("p. constraint").
  After removal – only increased cardiac output

Figure 2. Cardiac tamponade – symptoms.

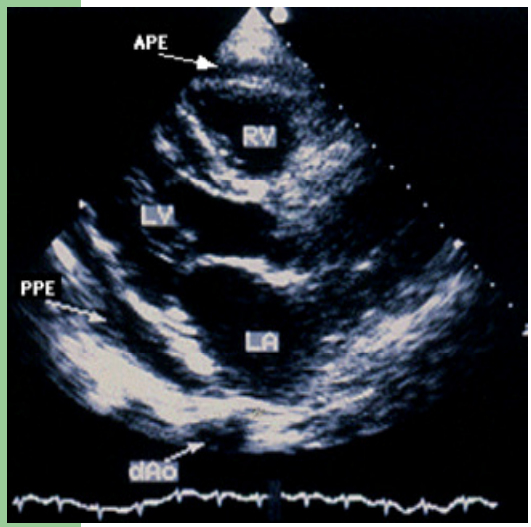
Cardiac tamponade

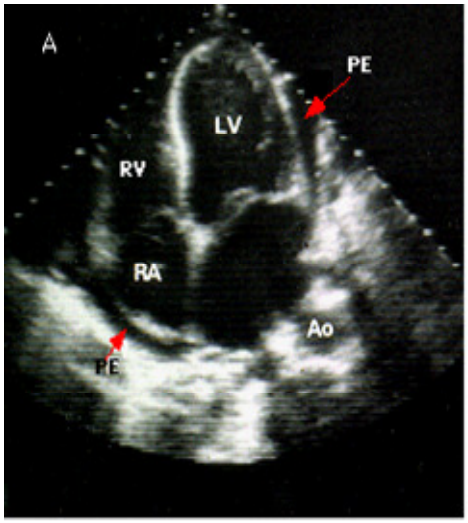
- Gradually hypoperfusion (incl. coronary), myocardial ischemia with decrease of cardiac output, hypotension, eletromechanical dissociation
- Clinically: hypotension + increased venous pressure + silent heartbeats (Beck 1935). Tachycardia, tachypnoea….shock.

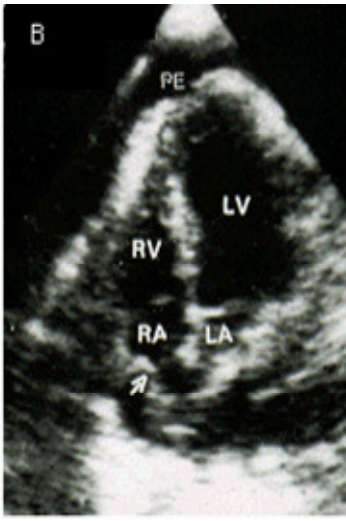
- Pulsus paradoxus – it disappears in insipiration (Kussmaul 1873). Low sensitivity, high specifity.
- Low voltage of QRS, pulsus alternans (swinging heart)
- RTG: enlargement of the cardiac shadow, tent-like configuration

Figure 3. Pericardial effusion (PE) in echocardiographic picture

Echokardiografie







Projekt spolufinancuje Evropský sociální fond

Praha & EU: Investujeme do vaší budoucnosti“

19. Asthma bronchiale

(Norbert Pauk)

Asthma is a disorder that causes the airways of the lungs to swell and narrow, leading to wheezing, shortness of breath, chest tightness, and coughing.

Causes

Asthma is caused by inflammation in the airways. When an asthma attack occurs, the muscles surrounding the airways become tight and the lining of the air passages swells. This reduces the amount of air that can pass by.

In sensitive people, asthma symptoms can be triggered by breathing in allergy-causing substances (called allergens or triggers).

Common asthma triggers include:

- Animals (pet hair or dander)
- Dust
- Changes in weather (most often cold weather)
- Chemicals in the air or in food
- Exercise
- Mold
- Pollen
- Respiratory infections, such as the common cold
- Strong emotions (stress)
- Tobacco smoke

Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) provoke asthma in some patients.

Many people with asthma have a personal or family history of allergies, such as hay fever (allergic rhinitis) or eczema. Others have no history of allergies.

Symptoms

Elektronické srdce a plíce

CZ.2.17/3.1.00/33276

Most people with asthma have attacks separated by symptom-free periods. Some people have long-term shortness of breath with episodes of increased shortness of breath. Either wheezing or a cough may be the main symptom.

Asthma attacks can last for minutes to days, and can become dangerous if the airflow is severely restricted.

Symptoms include:

- Cough with or without sputum (phlegm) production
- Pulling in of the skin between the ribs when breathing (intercostal retractions)
- Shortness of breath that gets worse with exercise or activity
- Wheezing, which:
    - Comes in episodes with symptom-free periods in between
    - May be worse at night or in early morning
    - May go away on its own
    - Gets better when using drugs that open the airways (bronchodilators)
    - Gets worse when breathing in cold air
    - Gets worse with exercise
    - Gets worse with heartburn (reflux)
    - Usually begins suddenly

Emergency symptoms:

- Bluish color to the lips and face
- Decreased level of alertness, such as severe drowsiness or confusion, during an asthma attack
- Extreme difficulty breathing
- Rapid pulse
- Severe anxiety due to shortness of breath
- Sweating

Other symptoms that may occur with this disease:

- Abnormal breathing pattern --breathing out takes more than twice as long as breathing in

- Breathing temporarily stops
- Chest pain
- Tightness in the chest

Exams and Tests

Allergy testing may be helpful to identify allergens in people with persistent asthma. Common allergens include:

- Cockroach allergens
- Dust mites
- Molds
- Pet dander
- Pollens

Common respiratory irritants include:

- Fumes from burning wood or gas
- Pollution
- Tobacco smoke

The doctor will use a stethoscope to listen to the lungs. Asthma-related sounds may be heard. However, lung sounds are usually normal between asthma episodes.

Tests may include:

- Arterial blood gas
- Blood tests to measure eosinophil count (a type of white blood cell) and IgE (a type of immune system protein called an immunoglobulin)
- Chest x-ray
- Lung function tests
- Peak flow measurements

Treatment

The goal of treatment is to avoid the substances that trigger your symptoms and control airway inflammation. You and your doctor should work together as a team to develop and carry out a plan for eliminating asthma triggers and monitoring symptoms.

Elektronické srdce a plíce

CZ.2.17/3.1.00/33276

For information on treating asthma in children, see: Pediatric asthma.

There are two basic kinds of medication for treating asthma:

- Control drugs to prevent attacks
- Quick-relief drugs for use during attacks

Control drugs for asthma control your symptoms if you don't have mild asthma. You must take them every day for them to work. Take them even when you feel okay.

The most common control drugs are:

- Inhaled corticosteroids (such as budesonid, fluticasone, ciclesonide) prevent symptoms by helping to keep your airways from swelling up.
- Long-acting beta-agonist inhalers also help prevent asthma symptoms. Do not take long-acting beta-agonist inhaler drugs alone. These drugs are almost always used together with an inhaled steroid drug. It may be easier to use an inhaler that contains both drugs.

Other control drugs that may be used are:

- Leukotriene inhibitors (such as montelucast)
- Omalizumab (Xolair)
- Aminophylline or theophylline (rarely used anymore)

Quick-relief drugs work fast to control asthma symptoms:

- You take them when you are coughing, wheezing, having trouble breathing, or having an asthma attack. They are also called "rescue" drugs.
- They also can be used just before exercising to help prevent asthma symptoms that are caused by exercise.
- Tell your doctor if you are using quick-relief medicines twice a week or more to control your asthma symptoms. Your asthma may not be under control, and your doctor may need to change your dose of daily control drugs.

Quick-relief drugs include:

- Short-acting bronchodilators (inhalers), such as salbutamol, terbutaline

- Your doctor might prescribe oral steroids (corticosteroids) when you have an asthma attack that is not going away. These are medicines that you take by mouth as pills, capsules, or liquid. Plan ahead. Make sure you do not run out of these medications.

A severe asthma attack requires a check-up by a doctor. You may also need a hospital stay, oxygen, breathing assistance, and medications given through a vein (IV).

ASTHMA CARE AT HOME

- Self-care skills that are important in taking care of your asthma are
- Know the asthma symptoms to watch out for
- Know how to take your peak flow reading and what it means
- Keep the phone number of your child's doctor or nurse with you.
- Know which triggers make your asthma worse and what to do when this happens.
- Children with asthma need a lot of support at school. They may need help from school staff to keep their asthma under control and to be able to do school activities.

Asthma action plans are written documents for anyone with asthma. An asthma action plan should include:

- A plan for taking asthma medications when your condition is stable
- A list of asthma triggers and how to avoid them
- How to recognize when your asthma is getting worse, and when to call your doctor or nurse

A peak flow meter is a simple device to measure how quickly you can move air out of your lungs.

- It can help you see if an attack is coming, sometimes even before any symptoms appear. Peak flow measurements can help show when medication is needed, or other action needs to be taken.
- Peak flow values of 50% - 80% of a specific person's best results are a sign of a moderate asthma attack, while values below 50% are a sign of a severe attack.

Outlook (Prognosis)

There is no cure for asthma, although symptoms sometimes improve over time. With proper self management and medical treatment, most people with asthma can lead normal lives.

Possible Complications

The complications of asthma can be severe. Some include:

- Death
- Decreased ability to exercise and take part in other activities
- Lack of sleep due to nighttime symptoms
- Permanent changes in the function of the lungs
- Persistent cough
- Trouble breathing that requires breathing assistance (ventilator)

When to Contact a Medical Professional

Call for an appointment with your health care provider if asthma symptoms develop.

Call your health care provider or go to the emergency room if:

- An asthma attack requires more medication than recommended
- Symptoms get worse or do not improve with treatment
- You have shortness of breath while talking
- Your peak flow measurement is 50% - 80% of your personal best

Go to the emergency room if the following symptoms occur:

- Drowsiness or confusion
- Severe shortness of breath at rest
- A peak flow measurement is less than 50% of your personal best
- Severe chest pain
- Bluish color to the lips and face
- Extreme difficulty breathing
- Rapid pulse
- Severe anxiety due to shortness of breath

Prevention

You can reduce asthma symptoms by avoiding known triggers and substances that irritate the airways.

- Cover bedding with "allergy-proof" casings to reduce exposure to dust mites.
- Remove carpets from bedrooms and vacuum regularly.

- Use only unscented detergents and cleaning materials in the home.
- Keep humidity levels low and fix leaks to reduce the growth of organisms such as mold.
- Keep the house clean and keep food in containers and out of bedrooms -- this helps reduce the possibility of cockroaches, which can trigger asthma attacks in some people.
- If a person is allergic to an animal that cannot be removed from the home, the animal should be kept out of the bedroom. Place filtering material over the heating outlets to trap animal dander.
- Eliminate tobacco smoke from the home. This is the single most important thing a family can do to help a child with asthma. Smoking outside the house is not enough. Family members and visitors who smoke outside carry smoke residue inside on their clothes and hair -- this can trigger asthma symptoms.

Persons with asthma should also avoid air pollution, industrial dusts, and other irritating fumes as much as possible.

Chronic obstructive pulmonary disease (COPD)

Norbert Pauk

Epidemiology of COPD

- Globally, ~10% of people older than 40 have airflow limitation of GOLD stage 2 or worse (FEV1 < 80% predicted); up to 25% may have GOLD stage 1 (FEV1 ≥ 80% predicted but FEV1/FVC < 0.7).
- Up to 60-85% of people with COPD (mostly mild/moderate severity) are undiagnosed.
- Besides tobacco smoking, biomass exposure (wood burning stoves), secondhand smoke, air pollution and work exposures to fumes and dusts cause COPD in susceptible people.
- COPD is the 4th leading cause of death worldwide; its mortality is rising, while cardiovascular disease's is falling; COPD is expected to be the 3rd leading cause of death in the next 20 years.

Pathophysiology of COPD

COPD is characterized both by destruction of lung parenchyma with loss of elastic recoil (causing emphysema) and infiltration of the walls of the small airways by inflammatory cells (causing chronic

bronchiolitis / bronchitis). Although students are still taught these two broad phenotypes are distinct entities, in truth they coexist and overlap in varying degrees in virtually everyone with COPD. The reasons for these variable phenotypes and their clinical importance are poorly understood.

Alpha-1 antitrypsin deficiency is present in 1-2% of people with COPD, and is likely underrecognized. Genome-wide association studies have identified various gene polymorphisms associated with increased (and a few with decreased risk) for developing COPD.

COPD continues to be frequently described as chronic and progressive, and this is so in many patients. However, COPD is a highly heterogeneous disease, and this applies to its progression between individuals. Among people with COPD who stop smoking, some will continue to experience accelerated decline in lung function compared to healthy non-smokers; however, **recent evidence suggests** the majority will experience FEV1 declines no more rapid (and in some cases, less rapid) than the average nonsmoker.

COPD Exacerbations

Many (not all) patients with COPD experience days-long episodes of increased dyspnea, cough, and sputum production, called COPD exacerbations. Most COPD exacerbations occur at home, resulting in increased use of bronchodilators, impaired function and enjoyment of life; more severe COPD exacerbations require systemic steroids, antibiotics, and sometimes hospitalization.

People with moderate COPD have one exacerbation per year on average; those with severe COPD have 2 on average. However, these averages mask wide heterogeneity: many patients with COPD have exacerbations never or very infrequently; a few experience them almost every month.

Recent research using invasive sampling of sputum from patients with COPD exacerbations strongly suggests that infections cause the majority (~80%) of COPD exacerbations, especially severe exacerbations. Common-cold bacteria and viruses including *H. influenzae, S. pneumoniae, M. catarrhalis*, rhinovirus, coronavirus, and parainfluenza cause the majority of infectious exacerbations (or about 50-60% of all COPD exacerbations), with less common organisms like Pseudomonas aeruginosa, S. aureus, and atypical bacteria (*Mycoplasma, Chlamydia pneumonia*) causing a minority of COPD exacerbations.

Congestive heart failure, systemic infections, pulmonary embolism, pneumonia, air pollution, cold air, allergies, and smoking are thought to cause 20-40% of COPD exacerbations.

Treatments for COPD

The **GOLD guideline treatment table** is the most well-known and accepted guideline for the treatment of COPD. It can be summarized as follows:

Stage:*	1 (mild)	2 (moderate)	3 (severe)	4 (very severe)
FEV1/FVC	<0.70	<0.70	<0.70	<0.70
FEV1	>= 80% pred.	50-80% pred.	30-50% pred.	<30% pred., or <50% pred. w/chronic respiratory failure
Treatment	Short-acting bronchodilator as needed for all patients with COPD.			
		Consider pulmonary rehabilitation.	Consider pulmonary rehabilitation.	Consider pulmonary rehabilitation.
		One or more long-acting bronchodilators.	One or more long-acting bronchodilators.	One or more long-acting bronchodilators.
			Inhaled corticosteroid, if repeated exacerbations.	Inhaled corticosteroid, if repeated exacerbations.
				Long-term oxygen if needed; consider lung volume reduction surgery

** All patients should receive smoking cessation counseling and influenza vaccination.*

Long-acting Bronchodilators, Inhaled Corticosteroids, and Tiotropium

Long-acting bronchodilators (formoterol, salmeterol) and long-acting anticholinergics (tiotropium) have similar efficacy:

- Improvements in post-bronchodilator FEV1 (~50-100 mL)
- Improvements in dyspnea (~3 points on the St. George's questionnaire)
- Reduction in daily short-acting beta-agonist use by ~1 inhalation.
- Tiotropium prevented COPD exacerbations better than salmeterol in **one randomized trial**, but the effect was quite small.

Long-acting beta agonists have cardiac effects, but have not been found to cause cardiovascular events, and don't have the very slightly increased risk of death associated with LABA monotherapy for asthma.

Tiotropium has been suspected of causing cardiovascular events based on observational trials, but the current consensus (based mainly on UPLIFT randomized trial data and a meta-analysis) is that Spiriva does not cause cardiovascular events.

Inhaled corticosteroid/LABA combination products cause pneumonia in a tiny proportion of patients; however, combination products may also reduce mortality slightly (based on the just-barely-negative TORCH trial). ICS/LABA combination products do not seem to cause an increased risk of death from pneumonia. Inhaled corticosteroids probably cause osteoporosis in a small number of susceptible patients.

The evidence is inconclusive as to whether any drug treatments for COPD modify (slow) the disease course or reduce mortality, but data from several clinical trials suggests that both inhaled corticosteroid/LABA combination products and tiotropium may reduce decline in FEV1 and slightly reduce mortality risk.

An **observational study** also suggested a benefit of "triple therapy" with inhaled corticosteroid, long-acting beta-agonist, and tiotropium.

Roflumilast and Cilomilast

The role of these new phosphodiesterase inhibitors is unclear. They have not been included in GOLD or other society treatment guidelines. Roflumilast only improved postbronchodilator FEV1 by ~50 mL and reduced exacerbation frequency by a relative 17%, among selected patients with GOLD stage 3-4 COPD who had cough with sputum changes and a history of exacerbations. The Cochrane

Collaboration published an **analysis** on these new agents in 2011. Postmarketing data will be essential to determine the new agents' real-world efficacy and risk of adverse events.

Azithromycin

A **randomized trial** of 1,577 patients treated with azithromycin or placebo for a year showed a 27% reduction in exacerbations in the azithromycin group, but may also have caused hearing loss. Erythromycin had a similar effect in another trial, but has poor gastrointestinal tolerability.

Lung Volume Reduction Surgery

Consideration for lung volume reduction surgery is recommended for all patients with very severe COPD. The surgery provides a **mortality reduction** and improvement in quality of life, especially in patients with upper-lobe predominant disease and poor exercise capacity. For unclear reasons, however, lung volume reduction surgery has never caught on: only 105 Medicare beneficiaries underwent LVRS in 2006.

Non-Surgical, Bronchoscopic Lung Volume Reduction

Because of the morbidity and risk associated with lung volume reduction surgery, and its subsequent unpopularity, numerous companies and investigators have sought to produce a medical device that could be placed bronchoscopically and that would reduce dead space ventilation — lung volume reduction surgery without the surgery, if you will. To date, none of these devices have worked effectively enough to recommend their use outside clinical trials. The most recent example was the **EASE trial,** published in *Lancet* 2011, showing that bronchoscopically-placed airway stents with one-way valves (the **Exhale device**) did not improve airway mechanics or dyspnea.

Why haven't these bronchoscopically placed devices worked? The most likely answer is collateral ventilation, or interalveolar air drift through the pores of Kohn. These are miniscule anatomic intercommunications that allow air to fill back into emphysematous areas after air is removed through the implanted device.

Treatment of COPD Exacerbations

Guidelines are available for treatment of COPD exacerbations; they mainly recommend:

- Increasing the dose of short acting bronchodilators (salbutamol and/or ipratropium).
- Adding oral corticosteroids if bronchodilators are not successful.

- Oxygen and ventilatory support for respiratory failure. A **recent review** showed that non-invasive positive pressure ventilation is likely improving outcomes from COPD exacerbations.
- Consider theophylline for severe exacerbations.

20. Lung tumors

(P. Zatloukal, L. Havel)

Tumors of lung are common in routine clinical praxis, both primary lung carcinoma, and metastatic involvement of lung in primary extrapulmonary cancers.

Benign lung tumors

are relatively unfrequent and usually asymptomatic. Histological types include bronchial adenomas, hamartomas, leiomyomas, hemangiomas and chondrohamartomas.

Treatment of choice is surgical resection /enucleation/

Malignant lung tumors

The most frequent is bronchogenic carcinoma, further malignancies are bronchial carcinoids or lung sarcomas

Bronchogenic carcinoma

was uncommon disease in the beginning of last century, but in since third decade if it is incidence rapidly increasing. Nowadays is lung cancer worldwide health problem and cause 1,1 millions deaths annually. Czech republic is a country with high incidence and mortality of lung cancer with annually incidenceof approximatelly 5500 cases /3977 males and 1478 females in 2009/. Majority of patient are recognised with advanced disease, so 5 years survival is less than 10%.

Risk factors

Smoking. Association between smoking and lung cancer is well documented, risk increases with number of cigarettes, lower age of smoking onset. Relative risk is 13.3 whem compared to non-smokers. Smoking of cigars or pipe is associated with lower risk. Also passive smoking increse risk RR 1.5

Asbestos usually professional exposude increases RR to 1.4-2.6

Radon is radioactive gas in the soil, concentration could be increased in mainly older buildings. When

inhaled causes alpha irradiation of bronchial epithelium.

Air pollution

Is increasing worldwide-e.g. exhaust gases, heating systems, heavy metals and other industry pollutants

Professional risks

Includes exposure to ionizing irradiation, chemicals, asbestos and other mutagens and cancerogens as occupational load

Cummulation of risk factors

Exposition to more risk factors produces higher risk than simple sum of single RR. Cigarette smoking and asbestos exposition increases RR of lung cancer to 28,8.

Classification

At the time of diagnosis includes description of tumor extent using TNM system / T describes extent of primary tumor, N involvement of regional lymph nodes and M distant metastases/ and histological classification.

Most frequent are non –small cell lung cancer, which includes squamous cell carcinomas,adenocarcinomas and large cell carcinomas. Small cell carcinomas have decreasing incidence /15%/, on the contrary adenocarcinomas have increasing incidence.

Signs and symptoms

Small intrapulmonary tumors are usually asymptomatic. When symptoms occured is a sign of advanced disease and poorer prognosis.

Main symptoms are:

-cough

-hemoptysis

-dyspnea

-chest pain

-weight loss

-hoarseness

-dysphagia

-superior vena cava obstruction

-bone pain

-clubbing of the fingernails

Diagnostics methods

Consist of assessment of intrathoracic invasion of tumor, spread into regional lymph nodes and detection of distant metastases.Diagnostic algothitm includes PA and lateral chest X-ray, CT of chest and upper abdomen, brain CT or MRI, bone scintigraphy, also PET/CT scan if possible. Biopsy samples should be taken by bronchoscopy, peripheral tumors could be biopted by percutaneous fine-needle under CT control. Further possibilities includes surgical techniques / videothoracoscopy, mediastinoscopy or thoracotomy.

Therapy

Treatment depends from tumor type, extent of disease, other comorbidities and general performance status of patient. Therapeutic options are surgery, radiotherapy, chemotherapy, targeted treatments or their combinations. Palliative care is also very important.

Small cell lung cancer:

Main modality is systemic chemotherapy, radiotherapy should be added to patient without distant metastases. Prophylactic cranial irradiation shoud be offered to responding patients. Preferred regimens are platinum based + etoposide, or cyclophosphamide,doxorubicin,vincristin.

Non-small cell cancers:

Only chance for cure is radical surgical resection, which is feasible only in minority of patients. Treatment of choice is lobectomy. If lobectomy is not feasible,minor resections shoud be performed /wedge resection/. Pneumonectomy should be avoided, but sometimes is only chance for radical resection.

Chemotherapy is used in adjuvant setting after resection. In locoregionally advanced tumors is used in combination with radiotherapy. In metastatic disease provide chemotherapy survival prolongation and symptoms palliation. Usual regimen consist of platinum and paclitaxel,gemcitabine,docetaxel, vinorelbine or pemetrexed.

Palliative therapy includes pain control, treatment of malignant pleural effusions , bronchial desobliteration /laser, stents/.

Results of treatment are unsatisfactory. 5 year survival in NSCLC is approximetely 10%, and less than 5% in SCLC.

Bronchial carcinoids

Are originated from APUD systém /Amine Precursor Uptake and Decarboxylation/. Lung affection is second after gastrointestinal systém.

Approximately 1% of lung tumors are carcinoids.

Usually rise centrally, clinical signs are mainly recidiving pneumonias due to bronchial obstruction. Carcinoid syndrome is less fraquent in lung them gastrointestinal tumors.Standard assesment include analysis of 5-hydroxyindol acid/ which could be a biochemical marker of relaps.

Treatment of choice is surgical resection, radiotherapy and chemotherapy are only of minimal importance.

Survival is much more better than in other types of lung malignancies. 5 year survival is 90%

Mesenchymal lung malignancies

Are very rare. Crucial for diagnosis is accurate histopathology and exclusion of extrathoracic primary tumor. Sarcomas metastasing to lungs is common.

Traeatment is surgical resection, but recurrence rate is high and general prognosis is poor.

Secondary lung tumors

30-40% extrapulmonary tumors develops in some phase of their growht pulmonary metastases.

Metastases could be solitary or multiple nodules of different size, or diffuse infiltrates /carcinomatous lymphangiitis/. Usually, primary tumor is diagnosed based on specific symptoms and lung metastases are found at routine diagnostic work-up. Sometimes are lung metastases first sign of malignancy recognized finally later. Sometimes is bioptic verification required to exclude non-malignant etiology of lesions /rheumatoid nodules, tuberculosis, grananulomatoses, mycotis infections/

22. Interstitial lung dinase (ILD)

(Norbert Pauk)

ILD is a common term that includes 130 to 200 chronic lung disorders, which may be:

- chronic
- nonmalignant (non-cancerous)
- noninfectious

Interstitial lung diseases are named after the tissue between the air sacs of the lungs called the interstitium - the tissue affected by fibrosis (scarring).

Interstitial lung diseases may also be called interstitial pulmonary fibrosis or pulmonary fibrosis.

The symptoms and course of these diseases may vary from person to person, but the common link between the many forms of ILD is that they all begin with an inflammation.

- bronchiolitis - inflammation that involves the bronchioles (small airways)
- alveolitis - inflammation that involves the alveoli (air sacs)
- vasculitis - inflammation that involves the small blood vessels (capillaries)

Most interstitial lung diseases are diagnosed as pneumoconiosis, a drug-induced disease, or hypersensitivity pneumonitis. The other types are:

- sarcoidosis
- idiopathic pulmonary fibrosis
- bronchiolitis obliterans
- histiocytosis X
- chronic eosinophilic pneumonia
- collagen vascular disease
- granulomatous vasculitis
- Goodpasture's syndrome
- pulmonary alveolar proteinosis

How does interstitial lung disease occur?

In interstitial lung disease, the lung is affected in three ways:

1. Lung tissue is damaged in some known or unknown way.
2. The walls of the air sacs in the lungs become inflamed.
3. Scarring (fibrosis) begins in the interstitium.

Fibrosis results in permanent loss of that tissue's ability to breathe and carry oxygen. Air sacs, as well as the lung tissue between and surrounding the air sacs, and the lung capillaries, are destroyed by the formation of scar tissue.

The diseases may run a gradual course or a rapid course. People with ILD may notice variation in symptoms - from very mild, to moderate, to very severe. The condition may remain the same for long periods of time or it may change quickly. The course of ILDs is unpredictable. If they progress, the lung tissue thickens and becomes stiff. The work of breathing then becomes more difficult and demanding. Some of the diseases improve with medication if treated when inflammation occurs. Some people may need oxygen therapy as part of their treatment.

What are the symptoms of interstitial lung diseases?

The following are the most common symptoms for interstitial lung diseases. However, each individual may experience symptoms differently. Symptoms may include:

- shortness of breath, especially with exertion
- fatigue and weakness
- loss of appetite
- loss of weight
- dry cough that does not produce phlegm
- discomfort in chest
- labored breathing
- hemorrhage in lungs

The symptoms of interstitial lung diseases may resemble other lung conditions or medical problems. Consult your physician for a diagnosis.

What causes interstitial lung diseases?

The cause of interstitial lung disease is not known, however, a major contributing factor is thought to be inhaling environmental pollutants. Other contributing factors include:

- sarcoidosis
- certain drugs or medications
- radiation
- connective tissue or collagen diseases
- family history

How are interstitial lungs diseases diagnosed?

In addition to a complete medical history and physical examination, the physician may also request the following tests:

- pulmonary function tests - diagnostic tests that help to measure the lungs' ability to exchange oxygen and carbon dioxide appropriately. The tests are usually performed with special machines into which the person must breathe.
    - Click Image to Enlarge

      spirometry - a spirometer is a device used by your physician that assesses lung function. Spirometry, the evaluation of lung function with a spirometer, is one of the simplest, most common pulmonary function tests and may be necessary for any/all of the following reasons:
        - to determine how well the lungs receive, hold, and utilize air
        - to monitor a lung disease
        - to monitor the effectiveness of treatment
        - to determine the severity of a lung disease
        - to determine whether the lung disease is restrictive (decreased airflow) or obstructive (disruption of airflow)
    - peak flow monitoring (PFM) - a device used to measure the fastest speed in which a person can blow air out of the lungs. During an asthma or other respiratory flare up, the large airways in the lungs slowly begin to narrow. This will slow the speed of air leaving the lungs and can be measured by a PFM. This measurement is very important in evaluating how well or how poorly the disease is being controlled.

- chest x-rays - a diagnostic test which uses invisible electromagnetic energy beams to produce images of internal tissues, bones, and organs onto film.
- blood tests - arterial blood gas to analyze the amount of carbon dioxide and oxygen in the blood.
- high-resolution computed tomography scan (Also called an HRCT or CAT scan.) - a diagnostic imaging procedure that uses a combination of x-rays and computer technology to produce sharper and more detailed cross-sectional images (often called slices), both horizontally and vertically, of the body. An HRCT scan shows detailed images of any part of the body, including the bones, muscles, fat, and organs. CT scans are more detailed than general x-rays.
- bronchoscopy - the examination of the bronchi (the main airways of the lungs) using a flexible tube (bronchoscope). Bronchoscopy helps to evaluate and diagnose lung problems, assess blockages, obtain samples of tissue and/or fluid, and/or to help remove a foreign body.
- bronchoalveolar lavage - to remove cells from lower respiratory tract to help identify inflammation and exclude certain causes.
- lung biopsy - to remove tissue from the lung for examination in the pathology laboratory.

Treatment for interstitial lung diseases:

Specific treatment will be determined by your physician based on:

- your age, overall health, and medical history
- extent of the disease
- your tolerance for specific medications, procedures, or therapies
- expectations for the course of the disease
- your opinion or preference

Treatments may include:

- oral medications, including corticosteroids, cyclophosphamice pulmonary rehabilitation
- influenza vaccine
- pneumococcal pneumonia vaccine
- oxygen supplementation from portable containers

- lung transplantation