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Epidemiology, Diagnosis, and Therapy of Pulmonary Embolism

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Abstract: Pulmonary embolism is a frequently observed clinical symptom. Its mortality rate is ca. 10 % und occurs mainly in the acute phasis. Immobilization, surgery, old age, malignancies, hormonal factors as well as inherited or acquired thrombophilia are important risk factors. Spiral computed tomography and ventilation-perfusion-scintigraphy are the decisive imaging methods. Pulmonary angiography is still the gold standard. The risk of pulmonary embolism could be lowered by 50 % through prophylaxis with unfractioned or low-molecular-weight heparin. The therapy of pulmonary embolism stratifies the clinical grade and reaches from ambulant therapy with low-molecular-weight heparin to thrombolysis or embolectomy in massive pulmonary embolism. Long-term anticoagulation, usually with vitamin-K-antagonists, should be applied according to the individual risk profile of the patient.

Key words: Anticoagulation; embolectomy; heparin prophylaxis; spiral computed tomography; thrombolysis; ventilation-perfusion-scintigraphy

Pulmonary embolism is a frequently observed clinical symptom as well as a threat for death in association with deep venous thrombosis. On the following pages the crucial risk factors as well as the specialities of diagnosis, prevention, and therapy of this event are to be entered into. Because of the tight connexion with deep venous thrombosis, which in the English language is expressed more precisively than in German „venous thromboembolism“, at this point also data have to be discussed which are related to both aspects of the illness.

1. Epidemiology

There are no exact data for the incidence of pulmonary embolism. In the United States 600.000 acute events per year are estimated. Worldwide the mortality rate is 10 percent and more [14]. Especially in the acute phase of a pulmonary embolism mortality is a remarkable threat. About 20 percent of these patients die during the following two hours after pulmonary embolism, another 10 percent during the following first week [23]. The incidence of thromboembolic events has shown an increasing tendency in the past 25 years. This could reflect either better diagnostic procedures, an increase in the population at risk, e. g. an increase in the average population age and an increasing number of surgical interventions [54].

In large case-control studies immobilization has been identified as the main risk factor in more than 60 percent of thrombotic events, mainly after surgery but also to a large extent according to illnesses treated nonsurgically. Another 18 percent of patients suffer from a malignant disease. Only in about 5 percent of cases coagulopathy could be diagnosed.

No risk factor was found in about 25 percent of so-called idiopathic cases. Old age increases the risk for a thrombotic event drastically. Myocardial insufficiency or chronic obstructive pulmonary disease as accompanying illnesses are also to be considered [23].

Beside gravidity a small but clinically relevant part has to be related to other hormonal factors. Mainly oral contraception as well as postmenopausal hormonal supplementation lead to wide discussion during the past years [34, 53]. These currently shown constellations of clinical findings as well as the recently more frequently described thrombotic events after long-distance flights verify the importance ot the classical Virchow-trias. Stasis intima-injury and increased coagulopathy are described herein as predisposing factors for thrombogenesis.

Some special forms of pulmonary embolism will be treated in more detail because of their clinical relevance for according prophylaxis.

1.1. Postoperative Pulmonary Embolism

Postoperative pulmonary embolism frequently occurs during the first 10 to 20 days after surgery, the risk being increased for about 2 to 3 months. After complex orthopedic surgical intervention in the lower extremities the risk is twice as high as after other operations, whereas 75 percent of the initial thromboses manifest in the operated leg. Normally a thrombus in the proximal parts of the vein has to be expected which leads to pulmonary embolism [29].

1.2. Pulmonary Embolism in Malignancies

Venous thrombosis and pulmonary embolism occur as important complications in malignancies. During operations of a malignant tumor thromboembolic complications are more frequently observed than during operations of the according organs because of benign diseases. Autopsy findings of tumor patients also show to a higher degree pulmonary embolisms as in patients who died due to other causes. According to their worldwide occurrence pulmonary embolisms are specially mentioned in bronchial carcinoma, colon cancer and prostatic cancer. On the other side the relative frequency is much higher in patients with pancreatic cancer and ovarian cancer as well as brain tumor which might indicate that until now not specifically identified thrombogenic factors play a major role [33].

2. Diagnostic Procedures

Pulmonary embolism like deep vein thrombosis is not sufficiently diagnosed by only clinical examination. Today several modern apparative means of diagnosis are at hand but only a few of them fit for a part of the patients for a straightforward diagnosis whereas for many patients several steps have to be undergone.

For pulmonary embolism as an acute and life-threatening disease it is absolutely vital to come to objective results in a very short time in order to start immediately the necessary therapy [50]. Usually before starting examinations for a suspected pulmonary embolism, anticoagulation has to be induced considering the risk of hemorrhage (see below).

2.1. Symptoms and Signs

The symptoms and signs of pulmonary embolism are very heterogenic, from a course with hardly any symptoms to the complete picture of an acute right heart failure. For acute pulmonary embolism the typical symptoms are dyspnea, thoracic pain at breathing, often connected with anxiety, tachypnoea and tachycardia, occasionally fever and sometimes phases of syncopes are observed. The differential diagnosis of these symptoms reaches from pneumonia to coronary infarction up to pneumothorax and cerebral aplopexy. Concomitant diseases like COPD can cover the typical pattern of the complaint [2, 14, 9].

This clinical magnitude is the main reason for the vast discrepancy between the clinical diagnosis of a pulmonary embolism in affected patients (30%) and of pathological finding post mortem (60%). Therefore if acute pulmonary embolism is suspected, the anamnesis with comprehension of the individual risk profile might be the most important life saving diagnostic procedure. For important risk factors see Table 1.

Table 1. Risk factors for a thromboembolic event.

Age over 40
Surgery with anesthesia > 30 min
Surgery and fractures of the lower extremeties and the pelvis
Immobilization due to other reasons
Cerebrovascular diseases
Malign tumors
Remarkable obesity (adiposity)
Pregnancy and puerperium
Estrogen therapy
Inherited and acquired thrombophilia
– APC-resistance factor V
– prothrombin G20210A-mutation
– antithrombin-III-deficiency
– protein-C-deficiency
– protein-S-deficiency
– cardiolipin-antibody-syndrom
– Lupus anticoagulant

(modified after [14])

2.2. Clinical Findings

Usually there are no typical findings for pulmonary embolisms during the clinical examination. Occasionally dullness on percussion occurs indicating a pleural effusion. Auscultatory now and then rales or a stressed second heart tone with punctum maximum above the pulmonal segment are found.

2.3. Electrocardiogram, Blood gas Analysis

Classic ECG-alterations in pulmonary embolism are SI-QIII-type and SI-, SII-, SIII-type with p-pulmonale as well as a complete or incomplete RBB, only to be expected under massive right ventricular failure. More frequently unspecific alterations of the ST segment resp. of the T wave are observed. There is no typical time-related evidence for the alteration of the ECG to the embolism event, i. e. no substantial diagnosis is gained by these findings only. A large number of patients with pulmonary embolism exhibit hypoxia. Under oxygen insufflation typically there is no adequate rise of the pO_2 although initially the patient develops hypercapnia which despite an increased AMV turns into hypocapnia. In pulmonary embolism examinations of the pulmonary function show no characteristic changes and have no diagnostic value.

2.4. Chest Radiography

In pulmonary embolism pathological changes of the conventional radiography are common but no uniform picture is to be expected. Frequently infiltrate and atelectasis are visible (in about 60%), pleural effusion (in about 40%) or a combination of these phenomenons. The classical picture with a wedge-shaped infiltrate and accompanying pleural effusion occur in less than 10% of the cases. Only in patients with a massive pulmonary embo-

lism one has to expect a clearly reduced hypoperfusion of the lung segments in question together with hyperperfusion of the non-affected areas (Westermark-sign).

2.5. Ventilation-perfusion-scintigraphy

Before establishing spiral computer tomography for many decades perfusion- or ventilation-perfusion-scintigraphy played a key role in the diagnostics of pulmonary embolism. The impact of this method is limited since the typical finding of hypoperfusion can also be related to a number of pulmonary diseases. The interpretation of relevant findings is made easier by comparison of the perfusion scintigraphy with the ventilation scintigraphy in relation to findings on the x-ray picture. The large multi center PIOPED study impressively showed that by including anamnestic and clinical data to scintigraphy findings the diagnostic statement could impressively be increased (for details see Table 2).

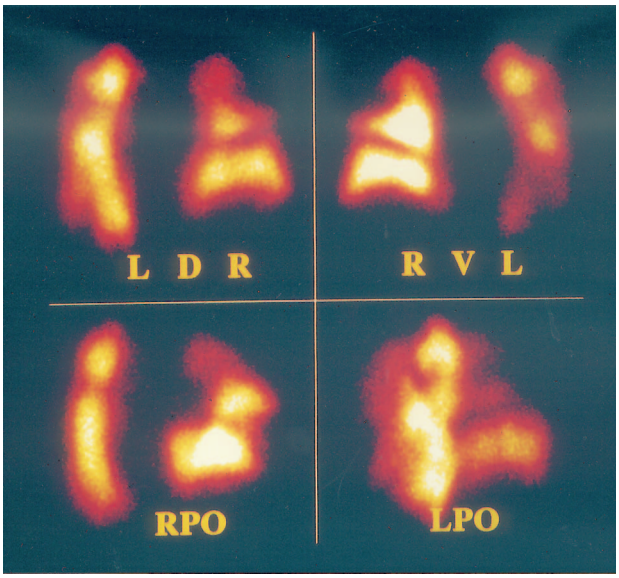

Fig. 1. Massive multiple pulmonary embolism (perfusion scintigraphy)
(with permission of Prof. K. H. Bohuslavitzki).

Under the strong suspicion of an embolic event without an affirming scintigraphy and even without any symptoms a Duplex-sonography should be made searching for a deep vein thrombosis. A positive finding would underline the clinical tentative diagnosis thus giving a valuably decisive factor for the start of anticoagulation therapy. If no thrombotic event in the deep veins is found, a spiral CT or a pulmonary angiography should follow according to the clinical state of the patient.

2.6. Computed Tomography

Only the establishment of the spiral technique helped the computed tomography to one of the top positions in the diagnostics of pulmonary embolism. As opposed to the conventional computed tomography with its sectional tomography in regular distances, by continuously scanning the patients' anatomical structures, especially vessels, can be judged in their total course. It takes only a few minutes examinationtime which is very valuable in the acute clinical situation. Risks and contraindications have mainly to do with the use of contrast medium and exposure to ionized radiation.

The spiral (helical) computed tomography implies two important benefits in comparison with the nuclear medical diagnostics: First the embolus in the pulmonary vessels is shown directly, so size and localisation can be estimated. And furthermore in the same procedure the surrounding structures can be valued thus finding or widely excluding other reasons for the patient's symptoms such as fibrosing lung diseases, bronchial carcinoma or enlargement of the lymph nodes.

The disadvantage of this method is the fact that the lung periphery cannot be judged as well as the central structures, thus making the localisation of the embolism very important for the diagnostic judgement of the spiral computer tomography. Thrombi in the main and segment arteries are shown in more than 90% of the cases whereas it drops to about 80% for embolisms in the subsegment arteries which after all come to about one third of all embolic events [2, 24, 42].

Table 2. Clinical probability and ventilation-perfusion scan probability.

	Clinical Probability		
V/Q Scan (Probability)	High Likely (80 – 100%)	Uncertain (20 – 29%)	Unlikely (0 – 19%)
High	28/29 (96%)	70/80 (88%)	5/9 (56%)
Intermediate	27/41 (66%)	66/236 (28%)	11/68 (16%)
Low	6/15 /40%)	30/191 (16%)	4/90 (4%)
Total	61/90 (68%)	170/569 (30%)	22/228 (9%)

(modified from [41])
Clinical and scintigraphic probability for the evidence of pulmonary embolism.

The limitations of the diagnostic statement influence to a great extent the practical approach. If an embolism is clinically suspected in a patient without cardiopulmonary instability and negative CT findings, a Duplex sonography of the leg vessel should follow. If the finding is positive, anticoagulation should be induced. A negative result in this context allows to initiate further diagnostic procedures to identify the thoracic disease.

2.7. Pulmonary Angiography

For the diagnosis of pulmonary embolism angiography of the pulmonary arteria is still the gold standard. It is the first-choice method for massive pulmonary embolism suspected in patients with cardiopulmonary instability. Reliable signs for an embolism are cut off at the radiopaque stream and filling defects. Apart from angiographic images hemodynamic parameters can be measured, especially the pulmonary artery pressure can be taken. As an additional benefit the pulmonalis catheter placed for the examination can be used for a local thrombolysis if necessary.

The pulmonary angiography is also indicated if undergone examinations do not offer any findings. It has to be considered that the diagnostic accuracy strongly depends on the experience of the examiner. Not only cardio-pulmonary complications can arise but also hematoma in the area of puncture, allergical reactions as well as renal insufficiency due to application of contrast medium. Up to 0.5% of patients die during examination, the number of deaths due to neglected pulmonary angiography, i. e. pulmonary embolism should be remarkably higher. Another advantage of the pulmonary angiography is the ability to differentiate between acute and older thrombi which makes this diagnostics unneglectable for the recurrent pulmonary embolism [2, 14, 15].

2.8 Echocardiography

One uncomplicated and non-invasive method for bedside investigation is the echocardiography for the diagnosis of the acute pulmonary embolism. Indirect signs can be the acute right ventricular failure, regional hypocontractility and dilatation at the pulmonary artery. If there is an insufficiency of the tricuspedalia valve, the systolic pressure gradient can be measured. Only in a small number of patients thrombi can be verified directly by echocardiography in the right heart or in the central pulmonary vessels. Another means is surface sonography for the diagnosis of pulmonary embolism if the finding lies near the thoracic wall or transesophageal sonography [31].

2.9 Laboratory Diagnostics

Over many years laboratory parameters played a inferior role in the diagnostics of pulmonary embolism. By establishing more sensitive tests the D-dimers, which give evidence of an increased fibrinolytic activity, prove their diagnostic importance. Nevertheless this test has only little specifity because increased D-dimer-levels occur not only in patients with embolism but also at older age, accompanying pregnancy or else in a magnitude of acute and chronic diseases. D-dimers play only a clinical role by excluding pulmonary embolism [52, 53]. Other parameters such as determinating prothrombin fragments F1 and F2 or cellular activation markers did not get any wide spreading in the diagnostics of thromboembolism as opposed to the D-dimers.

2.9.1. Thrombophilia Diagnostics

Top priority in the case of an acute pulmonary embolism is the immediate decision for treatment. Only after having started this accordingly, the search for inherited or acquired thrombophilia should be undergone though it is of great importance in order to evaluate the risk of a thrombus recurrence and to inform the patient about the individual problem as well as to decide on method and time of anticoagulation, as explained in this periodical at another part. Again it should be pointed out here that pulmonary embolism is still the most frequent cause of death during pregnancy and the puerperium. Women in this group are being found with the most frequent genetic alterations as is APC-resistance, which in most cases leads back to mutation of the factor-V-gene. Also in large numbers women with a prothrombin G20210A-mutation are affected. The discussion whether screening-examination of women in their age of parity makes sense or if under positive family anamnesis examinations at the beginning of the pregnancy is sufficient, has no finally been answered [4].

2.10. The Search for Occult Neoplasm

In this context the search for an occult neoplasm after initial manifestation of a thromboembolic event has to be mentioned. Although statistically up to 10 years after the initial manifestation of the event the risk of a malignancy is elevated, the intensive search for a tumorous disease does not seem sufficiently justified in this situation because according to survival time there was no significant difference between patients in controlled studies undergoing tumor-screening and a controlled cohort [14].

2.11. Risk Stratified Diagnostic Proceedings

The order in which different diagnostic proceedings will come into action, must consider the patient's individual risk profile, the actual physical situation as well as accompanying diseases.

In patients with high risk for pulmonary embolism a prompt evident imaging method should follow, i. e. either computed tomography or ventilation perfusion scintigraphy. If the result is not clear the diagnosis has to be secured by pulmo-

Table 3. Grading of pulmonary embolism.

	Grade I	Grade II	Grade III	Grade IV
Clinical symptoms	short-term symptoms dyspnea thoracic pain	symptoms continuing, dyspnea, tachypnea, thoracic pain, tachycardia	in add. to II: shock	in add. to III: shock
	probably: hemoptysis fever pleural effusion	probably: see I	severe dyspnea cyanosis anxiety, syncope	cardiac arrest
peripheral arterial pressure	normal	normal (slightly lowered)	lowered	extremely low
pulmonary artery pressure	normal	normal	25-30 mgHg (median)	> 30 mmHg (median)
pulmonary vessel involvement	periphery	segment arteries	pulmonary branch	pulmonary branch and lobar arteries

nary angiography if clinically necessary. In stable patients with limited symptoms (stage I – II) the therapy is sufficiently underminded by Duplex-sonography of the deep veins of the lower extremities. In contrast to this procedure measurement of D-dimers seems reasonable for patients with only discreet symptoms and low risk profile to rule out pulmonary embolism according to recently published studies [14].

The following considerations for a decision for computed tomography or ventilation perfusion scintigraphy have to be made:

Computed tomography should be favoured if accompanying pulmonary diseases are known since under these circumstances scintigraphy does not give much evidence (see above). This applies also if malignancies have to be ruled out. Even if pulmonary embolism is anamnestically known, computed tomography is to favour for differentiating between acute and older processes [44]. For patients with cardiopulmonary instability who are under intensive care, the bedside diagnosis has to be made according to the actual state where basic echocardiography usually precedes pulmonary angiography.

A helpful guideline for the decision of the matter of treatment is the staging of pulmonary embolism grade I to IV, as shown in Table 3.

3. Prophylaxis and Therapy of the Pulmonary Embolism

During the past 50 years dramatic improvements could be made in pharmacological prophylaxis and therapy of pulmonary embolism. On this way the study published in 1960 by Barritt and Jordan was a milestone which showed that mortality and frequency of recurrences could be lowered drastically by applying combined intravenous heparin and oral vitamin-K-antagonists [3]. Further innovations concerned finding out the optimal dose of anticoagulation extensively lowering the hemorrhage risk, the use of low-molecular-weight heparin and new pharmacological substances which are tested at the moment. At the same time in large epidemiological studies patients with high risk for thromboembolic events could be identified who will vastly gain from an intensive prophylaxis and therapy.

The therapy of pulmonary embolism pursues different diverging aims:

1. the prevention of pulmonary embolism in the sense of prophylaxis
2. the prevention of an apposition and a recurrence of a thrombus in the sense of anticoagulation
3. the specific treatment of a thrombus by thrombolysis or embolectomy
4. the surgical removal of organized thrombotic material (thrombendarterectomy)

3.1. Prophylaxis

3.1.1. Unfractioned Heparins

The value of unfractioned heparins for the prevention of thromboembolic events was impressingly proven by a large number of studies. There are comprehensive data for its effectiveness because of experience in decades with unfractioned heparin. It could be shown that under low-dose-heparin the risk for pulmonary embolism was lowered by 50% [9, 10, 12]. The reduction of mortality not only for surgical patients but also for

patients with malignant tumors, severe inflammatory and metabolic diseases could be demonstrated [9, 10, 21, 28].

3.1.2. Low-molecular-weight Heparins

As to unfractioned heparin the low-molecular-weight heparins show also a safe anticoagulative effect. With regard to there application they show remarkable advantages though, which are mainly based on bioavailability and pharmacokinetics. Because of the low affinity of low-molecular-weight substances to heparin-binding proteins and endothelial cells their effect is not directly related to the plasma concentration and exhibit a prolonged biological half-life. Therefore in most cases a once-daily-dose can be applied and there is no need for tight laboratory control during therapy [25].

Also the low-molecular-weight heparins proved their effectiveness for the prevention of thromboembolic events by numerous studies as well in the perioperative field as for trauma patients and in a large number of immobilized patients because of internal diseases [7, 8, 30, 38, 39].

3.1.3. Low-dose Aspirin

Low-dosed aspirin only or in combination with heparin also showed in a number of controlled studies its effect for the prophylaxis of pulmonary embolism. The oral take is an advantage which for patients with high risk makes longer ambulant therapy possible, only having to check on hemorrhage complications in the case of contraindication [40].

3.2. Therapy of Pulmonary Embolism with Heparins

3.2.1 Acute Phase Therapy

The intravenous application fo unfractioned heparin is the standard therapy of the acute pulmonary embolism. After the bolus application of 5.000 IU heparin a body-weight-adjusted dose of about 500 IU/kg (usually between 30.000 and 50.000 IU) will follow [5, 45]. This therapy requests monitoring of the PTT and the number of thrombocytes and because of the continuous infusion it is reserved for in-patients until the oral anticoagulation will show its effect (see below).

As for the prophylaxis low-molecular-weight heparins also offer an important alternative treatment for acute pulmonary embolism. Comparative studies including patients with stable disease (grade I – II) not needing lysis or embolectomy, showed a positive effect of this therapy as with unfractioned heparins and comparable side-effects (ca. 7% heavier hemorrhage, 2% thromboembolism recurrence). Because of no permanent infusion and reduced frequency of laboratory controls inhospitalization could be reduced by three days thus meaning a considerable cost reduction for the treatment [11, 16, 17, 26, 48].

Furthermore a meta analysis based on 11 randomized studies comparing therapies with unfractioned and low-molecular-weight heparins could show that patients treated with low-molecular-weight heparin suffered from significantly less frequences of hemorrhage complications ($p = 0.02$) without significant differences in recurrences [18].

3.2.2. Therapy and Secondary Prophylaxis of Pulmonary Embolism with Vitamin-K-antagonists

For the longer lasting treatment and secondary prophylaxis of thrombosis and pulmonary embolism the oral intake of vitamin-K-antagonists is the appropriate answer. The effect of the coumarin derivatives depends on the inhibition of 4 vitamin-K-depending coagulation factors (factor II, VII, IX and X) as well as of the vitamin-K-depending factors protein C and protein S. Phenprocoumon which is frequently used in Germany (e. g. Marcumar® or Falithrom®) shows a biological half-life of 100 to 150 hours which is significantly longer then for Warfarin being used in anglosaxon countries (30 to 40 hours) on which essential studies for this topic base [5, 6].

As explicitly described in this issue above the induction of therapy with the initial heparin dose and overlapping oral anticoagulation is common. Related to the body weight a low dose has to be chosen (ca. 9 to 12 mg). The median maintenance dose for phenprocoumon is 1.5 to 3 mg/die and for warfarin 4 to 5 mg/die. The monitoring runs under the standardized INR-value which allows the advantage against determining the prothrombin time (Quick's value) that values measured in different laboratories can be compared. The aim is an INR-value of 2.0 to 3.0, having proved a satisfactory anticoagulative effect with acceptable risk of hemorrhage (1.5 to 2%) [5].

Based on multiple studies the standard recommendation for the treatment of pulmonary embolism after first event is 6 months. A shorter regime makes sense if the risk for a thrombosis is limited, e. g. during immobilization of the patient after surgery, for other reasons such as hormone therapy or on the other hand if a risk for bleeding appears [20, 46].

Recurrent pulmonary embolisms require a prolonged anticoagulation, mainly if pulmonary hypertension occurs, and also patients with known risks for coagulopathy or recurrent deep venous thrombosis need special regard [13, 15].

3.2.3. Long-term Anticoagulation with Heparins

Under special clinical circumstances a long-term anticoagulation with heparin, mainly low-molecular-weight heparin, should be carried out deviating from the standard therapy with oral vitamin-K-antagonists mainly applying to patients with clearly higher risk for hemorrhage because of serious accompanying diseases of liver or kidney, inflammatory bowel diseases or malignancies. Low-molecular-weight heparins are to be favoured be-

cause of the more favourable side-effect profile, especially considering osteoporosis and thrombocytopenia. Interestingly, in a number of studies it was reported that tumor patients treated with low-molecular-weight heparin had a higher survival time than those treated with a coumarin derivative [32].

During pregnancy the use of oral vitamin-K-antagonists is contraindicated because they pass the placental barrier and to a large extent teratogenic effects were described after their use. For risk patients with thrombophilia or status after thromboembolism and also for the therapy of pulmonary embolism during gravidity low-molecular-weight heparins are the treatment of choice because of the more benevolent side-effect profile and the simplier application. Nevertheless therapy and dose recommendations must still be given with special care at this time because for the time being there exists only a limited number of data for effectivity and safety during pregnancy [5, 22, 35].

3.3. Thrombolysis

In the case of massive pulmonary embolism (grade III to IV) the thrombolysis will be the appropriate treatment for an immediate recovery of the cardiovascular and respiratory symptoms. The following substances are admitted for therapy: streptokinase, urokinase and tissue-plasminogen-activator (tPA). Standard protocols consider the delivery of the dose for the thrombolytic agent for up to 24 hours. Alternatively the so-called short-lysis with the application of a high dose for 2 hours can be chosen which in a number of studies showed a faster recovery ot the cardio-pulmonary symptoms [27, 37].

The hemorrhage risk is up to 10% which means before starting a therapy several diseases undergone before have to be outruled. Essential contraindications are intracerebral hemorrhage as well as brain tumors and neurosurgical operations in the immediate past. Relative contraindications apply to those of systemic heparin therapy, i. e. tumors, apoplex, hypertension, gastrointestinal hemorrhage, etc.

The clinical picture of pulmonary embolism in the acute phase could be remarkably improved under thrombolysis but no advantage for the long-time survival was found. Nevertheless in a number of studies was shown that pulmonary pressure and respiratory parameters such as diffusion capacity normalize in the long run more than just after sole heparin therapy [47], though the part of the spontaneous thrombolysis which is more intensive in the lung than in the peripheral veins practically cannot be judged.

3.4. Surgical Treatment

3.4.1. Embolectomy

As emergency treatment of the acute pulmonary embolism the embolectomy which was initiated in 1908 bei Trendelenburg and at first successfully carried out by Kirschner in 1924, was accompanied by an extremely high letality (more than 80%) which could be reduced to between 20 to 50% through establishing extracorporal circulation. On one side this is the ultima ration, on the other side as an alternative to thrombolysis, mainly in patients having hemorrhage complications as contraindication [19]. Nevertheless this method in the acute event is limited because it requires the highest standard of the operation team and of the perioperative care.

3.4.2. Thrombendarterectomy

In the case of severe pulmonary hypertension the removal of thrombotic material in connection with the intima wall can be administered during the interval [15].

3.5. Vena cava inferior-barriers

Vena cava-filters or surgical clips are a sensible option of therapy if heparin and/or lysis are contraindicated, e. g. in the case of massive hemorrhage tendency, for trauma patients and if floating thrombi are evident in the femuric or pelvic veins. Although their efficacy has been proved, the application is not without a remarkable risk, mainly for local thrombi, thus in practice only in exceptional situations temporal filters are relevant, being implanted for up to 14 days [12, 43].

Outlook

An improvement of the prevention strategies for thrombotic events is to be expected by further optimization of diagnostics of inherited and acquired thrombophilia. Individual measures of thrombosis prophylaxis could decisively lower incidence and mortality of pulmonary embolism in phases of increased risk. The development of imaging methods can help diagnose and even find small embolisms in time thus counteract recurrences accordingly. Several studies showed for a number of synthetical anticoagulants as for example fondaparinux that similar to low-molecular-weight heparin after subcutaneous application worked as effective as systemic heparin therapy [36]. Even for Dermatan sulfate promising results were documented [51].

Summarizing these options the diagnosis and therapy of localized pulmonary embolism might become clearly easier and more specific. A big challenge will remain in future the massive pulmonary embolism with its high mortality mainly during the first hours which can only be encountered through immediate diagnosis and the induction of the necessary emergency treatment.

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