UNIVERSITY OF MEDICINE AND PHARMACY CRAIOVA

MEDICINE

PNEUMOLOGY

MODERN APPROACH TO INTERRELATIONS BETWEEN DEEP VEIN PATHOLOGY AND PULMONARY EMBOLISM

Summary

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CONTENTS

Chapter 1. Introduction .................................................................................................................. 2

CHAPTER 2. Risk factors for venous thrombosis ................................................................. 3

CHAPTER 3. The clinical presentation of venous thromboembolism ............................... 3

CHAPTER 4. Diagnostic tests in venous thromboembolism ............................................. 3

CHAPTER 5. Initial treatment and long-term venous thromboembolism ............................. 5

CHAPTER 6. Chronic thromboembolic pulmonary hypertension ....................................... 6

CHAPTER 7. Personal study ........................................................................................................ 7

CHAPTER 8. Discussions ............................................................................................................. 8

CHAPTER 9. Conclusions ............................................................................................................ 9

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1. INTRODUCTION

Pulmonary thromboembolism is the third most common cardiovascular pathological entity, after acute coronary ischemic episodes and stroke and also the main cause of death in hospitalized patients over 65 and in pregnant. Deep vein thrombosis is a major complication in patients undergoing abdominal or orthopedic surgery within the oncological pathology and other chronic diseases. Improperly treated, deep vein thrombosis may be complicated by pulmonary thromboembolism. Therefore, the two pathological entities can be grouped and considered part of the same process: venous thromboembolism.

Fair treatment of venous thromboembolism, aiming relieving symptoms, avoiding extension of the thrombotic process, preventing complications and relapses, include anticoagulant therapy, elastic contention, endovascular treatment and surgery. We propose a modern therapeutic algorithm argued clinical and paraclinical, having effectiveness and easiness of administration.

All surgeries involve varying degrees of lesion tissue coagulation activation. The length of operation directly influence the risk of thrombosis. An intervention beyond 30-45 minutes is considered at risk. Continued development of surgical techniques and the increased, from year to year, number of surgical interventions and of patient age, highlights the importance of the problem addressed.
2. RISK FACTORS OF VEIN THROMBOSIS

Venous thrombosis is a multicausal pathology, that requires the presence of several risk factors for the disease to occur. Venous thrombosis recognize genetic and acquired causes, the first are related to stasis or hypercoagulability and the second almost invariably refers to hypercoagulability. Surgery is an important risk factor in the production of deep vein thrombosis. This risk is well defined and quantified, and the possibility of reduction it by adequate prevention has been proven in many studies. The work describes in detail each factor bet on producing venous thromboembolism. Impact of acquired causes of thrombosis decreased, due to the use of prophylactic anticoagulation, but they still cause a large number of thrombotic events.

3. THE CLINICAL PRESENTATION OF VENOUS THROMBOEMBOLISM

The diagnosis is often missed in clinical practice, as indicated by the high incidence of venous thromboembolism in autopsy studies. Thus, the clinical spectrum of venous thromboembolism ranges from asymptomatic cases to circulatory collapse, respectively, phlegmatic coerulea dolens, ie extreme clinical presentations of pulmonary embolism and deep vein thrombosis.

Signs and symptoms of deep vein thrombosis reflects the clinical situation of a clot causing vein obstruction, in one or more veins of the lower extremity and are represented by calf sensitivity or sensitivity on the path of the veins involved, painful dorsal flexion of the foot (Homans sign), unilateral leg swelling, heat and redness. Other signs include distended superficial veins and the appearance of collateral prominent veins. Rarely deep vein thrombosis of the leg is initially presented as a condition called phlegmatia caerulea dolens, when non-oxygenated hemoglobin can give cyanotic appearance of the affected limb. This situation, which is the most serious symptom in the clinical spectrum of deep venous thrombosis, requires immediate care to preserve the foot.

Pulmonary embolism symptoms can vary on a wide range, depending on the size of the clot, the degree of obstruction of the pulmonary vascular bed and overall physical condition of the patient, especially in the presence or absence of an underlying pulmonary or heart disease. The main symptoms are chest pain (or precordial distress), dyspnea (hampered breathing, which is a subjective experience) and cough. When a productive cough contain streaks of blood is called hemoptysis and pulmonary embolism should be included in the differential diagnosis. As confirmed pulmonary embolism, hemoptysis is present only in a negligible number of patients. Circulatory collapse suggests massive pulmonary embolism, but this is not necessarily true in all patients.

4. TESTS DIAGNOSIS OF VENOUS THROMBOEMBOLISM

Blood-gas analysis is performed regularly in patients presenting with tachypnea or dyspnea.

Electrocardiogram (ECG) - is often the initial diagnostic test performed in patients presenting with dyspnea and is essential in the evaluation of patients with acute chest pain. However, ECG make a limited contribution to the evaluation of patients with suspected pulmonary embolism. A completely normal ECG does not exclude pulmonary embolism. S1Q3T3 is a triad consisting of a broad S wave in derivation I, a Q wave and a reversed T wave in derivation III. Although traditional, this pattern occurs in only 2-15% of patients with pulmonary embolism.
Chest X-ray - is still the most frequently requested radiological investigation, representing first-line examination in patients with signs or symptoms of heart or lung. Cardiomegaly, an ascending hemidiafragm or the extension of the pulmonary artery (Fleischner's sign) may be found on radiological examination.

Deep venous thrombosis ultrasound - has become the main tool for diagnosing patients with clinically suspected deep vein thrombosis. This paper presents a description of the ultrasound diagnostic criteria for deep vein thrombosis. Best ultrasound criterion valid for deep vein thrombosis is the lack of compressibility of a venous segment investigated. The true sign of recurrence is a clot in a vein segment previously unaffected. Another criterion of relapse is the growth in residual thrombus diameter of 4 mm or more, in the same vein segment. However, you need a detailed report on patient history, which even if present, does not provide a safe ultrasound recurrent deep vein thrombosis.

In the progress of venous thromboembolic disease, venous ultrasound documentation of the affected limb is very useful after 3 or 6 months, or at any time doctor deemed the disease as being stable and chronic. This allows the comparison in case of suspected relapse later.

D-dimer plasma - the positive predictive value for venous thromboembolism increases as the levels of D-dimer increased progressively over the chosen threshold. The most important limitation of D-dimer tests for diagnostic purposes is limited usefulness in specific patient or clinical conditions that are by definition correlated with increased plasma levels of D-dimers.

CT with contrast - has become the gold standard for the diagnosis of pulmonary embolism. CT diagnostic criteria for acute and chronic pulmonary embolism were well developed and standardized in the last decade. However, there are still pitfalls to avoid. CT angiography is now the most commonly used imaging examination for pulmonary embolism, it evolved from a promising procedure, the procedure of choice for the diagnosis of venous thromboembolism. Its popularity led to overuse, imposing the need of finding better strategies for triage and reduced radiation dose.

Digital subtraction pulmonary angiography - is reserved for the few patients who are considered eligible for surgery and in patients with high clinical probability of pulmonary embolism and inconclusive results of other diagnostic tests.

Echocardiography - transthoracic echocardiography (TTE) allows non-invasive determination of pulmonary arterial pressure, right ventricular volume and multiple functional parameters and, thus, assess the hemodynamic consequences of pulmonary embolism. It allows rapid risk stratification and guide therapy in many patients. However, better imaging standardization is necessary for a correct evaluation of the importance of echocardiography and track patients over time, particularly those with chronic pulmonary hypertension.

5. INITIAL AND LONG-TERM TREATMENT OF VENOUS THROMBOEMBOLISM
The goals of treatment - in patients with deep vein thrombosis are:
1. Preventing deaths from pulmonary embolism
2. Relief of symptoms in the affected limb
3. Preventing morbidity from recurrent deep vein thrombosis, or pulmonary thromboembolism
4. Postthrombotic syndrome prevention or minimization of the symptoms of postthrombotic syndrome

Anticoagulant therapy - is the initial treatment of choice for most patients with symptomatic deep vein thrombosis. Initial administration of continuous IV heparin was the standard treatment of deep vein thrombosis during 1960-1990. Afterwards, the use 1-2 times daily of low molecular weight heparin has been shown - in clinical trials - have similar effect of heparin in continuous infusion. Unfractionated heparin administered iv replace low molecular weight heparins and fondaparinux in the initial treatment of deep vein thrombosis in patients with severe renal impairment.

Thrombolytic therapy - its role in the treatment of deep vein thrombosis is limited to cases with acute massive proximal thrombosis (eg. Phlegmatic coerulea dolens with impending venous gangrene), or selected cases with acute proximal extensive venous thrombosis, with symptoms installed up to 14 days, good functional status, life expectancy> 1 year and reduced risk of bleeding, in order to reduce acute symptoms and postthrombotic morbidity.

VCI filter – insertion of an inferior vena cava filter is reserved for patients with acute deep vein thrombosis who have contraindications to anticoagulant therapy and in rare cases patients with recurrence of venous thromboembolism undergoing appropriate conditions of anticoagulant therapy.

Long-term treatment of deep vein thrombosis - vitamin K antagonist therapy is started along with heparin, fondaparinux or low molecular weight heparins, the first day of treatment will interfere with the injection for 4-5 days until INR exceeds 2.0, after that heparin therapy is discontinued. Treatment should continue for at least 3 months in patients with a first episode of proximal deep vein thrombosis secondary to a temporary or reversible risk factor and will be administered indefinitely in patients with a second episode of idiopathic venous thromboembolism. Long-term treatment with subcutaneous low molecular weight heparin is as effective, and if neoplasms even better-than oral treatment with anti-vitamin K.

Side effects of anticoagulant therapy - bleeding, heparin-induced thrombocytopenia and osteoporosis and hepatotoxicity - are becoming increasingly rare.

Anticoagulant therapy is the mainstay of therapy in patients with acute pulmonary embolism. Development of new oral drugs, used both in initial and long-term therapy, can eliminate in the future, this differentiation. Patients with massive pulmonary embolism generally presents, respiratory failure and circulatory collapse, requiring specific means of symptomatic treatment. In these patients thrombolytic therapy and pulmonary embolectomy can be considered. Treatment of patients with circulatory collapse or respiratory failure combine symptomatic intervention with treatment leading to rapidly reduction of the degree of pulmonary vascular obstruction. Oxygen, fluid loading, inotropic and vasopressor substances - (isoproterenol, norepinephrine, epinephrine) - nitrous oxide are the most commonly used therapeutic means

Compressive therapy in prophylaxis and treatment of venous thromboembolism - is recognized as an effective treatment for lymphatic and venous disease management, and detailed information was obtained from published clinical series and randomized controlled trials.
6. CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

In the absence of surgical intervention, the prognosis for patients with chronic thromboembolic pulmonary hypertension is reserved. Natural history of chronic thromboembolic pulmonary hypertension is bleak and almost all patients die with progressive right heart failure. The most common symptom associated with chronic thromboembolic pulmonary hypertension is effort induced dyspnea. To ensure diagnosis in patients with chronic thromboembolic pulmonary hypertension, a standardized assessment is recommended for all cases presenting with unexplained pulmonary hypertension. This includes chest X-ray, electrocardiogram and pulmonary function tests necessary to exclude obstructive or restrictive pulmonary parenchyma as a cause of pulmonary hypertension. Computed tomography (CT), pulmonary angiography and magnetic resonance (MR) were considered as screening techniques for the diagnosis of chronic thromboembolic pulmonary hypertension. Medical treatment - chronic anticoagulation represent the mainstay of medical therapy. Inferior cava filters are typically used to prevent embolic recurrences. Immediate thrombolysis may be beneficial, but lytic agents are unable to modify chronic disease component. Right ventricular failure is treated with diuretics and vasodilators and, although, some improvements may occur, the effect is generally transient. Similarly, the prognosis is not affected by medical therapy, which should be regarded as only supportive.

Indications for surgery - when the diagnosis of chronic thromboembolic pulmonary hypertension has been firmly established, the decision for surgery is based on the severity of symptoms and general condition of the patient. Surgical technique is described in detail on the paper and consists in pulmonary trombendarteriectomia, that on all cases must be performed bilaterally. The only surgical alternative for these patients is lung transplantation.

Postoperative Care - Postoperative management is essential to the success of this intervention. All patients are mechanically ventilated for at least 24 h and all patients are subjected to a sustained diuresis in order to reach the patient's preoperative weight within 24 hours. Patients are exposed to all the complications associated with heart or lung interventions (arrhythmias, atelectasis, wound infection, pneumonia, mediastinal bleeding, etc.), but also can develop specific complications for assistance. These include persistent pulmonary hypertension, pulmonary reperfusion and neurological disorders related to deep hypothermia.

Results - after this intervention a reduction in pulmonary pressure and resistance to normal levels and the corresponding improvement of pulmonary blood flow and cardiac output arises immediately, and changes are permanent. Survival after pulmonary endarterectomy was 75% at 6 years or more, a percentage that exceeds the rate of survival after single or double lung transplantation for chronic thromboembolic pulmonary hypertension.

7. PERSONAL STUDY - I proposed for analyze:

• establishing the prevalence of each entity analyzed, determining risk factors involved in the production of venous thromboembolism with direct application of preventive measures
• updating diagnostics of deep vein thrombosis and pulmonary embolism
• adopting an effective therapeutic algorithm for the treatment of deep vein thrombosis, able to minimize complications
• modern therapeutic approach of pulmonary thromboembolism
current management of the public health chapter described, having the final visa the improvement of quality of life

We conducted a prospective study, including started on January 1, 2008, for a period of 24 months. The study group consisted initially selected 438 people with the following characteristics:

- age of patients over 18 years
- presented ambulatory or admitted to Emergency Hospital Floreasca
- diagnosed with venous thromboembolism

We divided the group of patients in the following subcategories:

I. patients who had been diagnosed ambulatory with and deep vein thrombosis - 314 cases
II. patients undergoing surgery in hospital Floreasca frequency of deep vein thrombosis following, coupled with prophylactic treatment applied - 87 cases. This group will be divided into 2 subgroups:
   a general surgery patients ask - 31 cazuri
   b ask orthopedics patients - 56 cases
III. patients in the first 2 categories that triggered pulmonary thromboembolism - 25 cases
IV. patients presented with pulmonary thromboembolism, without obvious triggering cause - 37 cases

We performed a classification of patients according to risk level:

1. **low risk patients** - 271 cases, we have included here ambulatory presented patients, without a family history of venous thromboembolism, in age group below 60 years.
2. **moderate risk patients** - 70 cases; includes age group patients over 61 years, who underwent non-oncologic surgery or presented ambulatory, without a family history of venous thromboembolism
3. **high-risk patients** - 45 cases; here are included ambulatory patients with a family history of pulmonary thromboembolism and coagulation abnormalities (14 cases)
4. **very high-risk patients** - 52 cases, we have enrolled cases of hip replacement and leg fractures, representing 15% of these interventions during the period.

Inclusion of patients in the study was based on the following diagnostics:

- clinical examination of the lower limbs, electrocardiogram, heart-lung radiography, Doppler ultrasonography of the leg veins, CT scan with contrast angiography and CT venography and autopsy.

Curative treatment efficiency was evaluated by the same methods at predetermined intervals in which the 1½, 3, 6, 12 and 24 months. In the interval we analyzed all patients undergoing surgery, enclosed in the appropriate risk group. Additional data were obtained from the patient observation chart. There were no exclusion criteria, the departments concerned are, as I said, those of internal medicine (including cardiology), general surgery, orthopedics and vascular surgery, the number of admissions in these four sections in the two years studied exceeding 62,000 (62,444 admissions).

As stated, patients diagnosed with deep vein thrombosis and undergoing treatment were regularly called for clinical and paraclinical reassessment. Each patient received at least three Doppler ultrasound examinations - 1½, 3,
6, 12 and 24 months – and were automatically excluded from the study patients not presented on reevaluation - 64 cases of deep vein thrombosis. We also excluded patients who did not follow rigorous treatment prescribed with anticoagulant treatment interruption more than 7 days - 71 cases of deep vein thrombosis. We considered important the presentation o each stage of the study group - not just the patients remained under observation at the end of two years - because of the important implications of this pathology health problem, involving every aspect emerged during therapy.

Research program was conducted in accordance with ethical rules concerning: participation of human subjects in research studies (clinical or experimental), personal data protection, the use of biological samples, copyright and related rights, etc.

8. DISCUSSION - on the end of the paper we discussed the results of our study, trying to refer to the literature data.

If, at present, re and more studies refer to ambulatory treatment of pulmonary embolism, in our study we have a high percentage of patients admitted in hospital for a diagnostic and therapeutic closer supervision. Another reason for the high number of admissions is the use of unfractionated heparin, with the possibility of monitoring therapeutic response. However, 31% of the cases included on study received outpatient treatment.

I noticed the large number of patients with venous thromboembolism included in group age 41-80 years, over 80%, which correlated with increased incidence of associated pathologies including neoplasia or illness with visa of major surgery

Another detail is worthy to note - large number of highly localized venous thrombosis, iliac and cava - 18% of cases included-representing the most severe forms, with high potential for lung embolisation and also high risk of death.

Unfractionated heparin was used mainly in hospitalised cases, administered IV and therapeutic outcome was monitored by APTT test, while oral anticoagulant therapy was monitored by INR test. Combination antiplatelet therapy, venotonic medication and use of elastic contention have been used in line with recommendations made in the literature.

In our study, we paid special attention to a high risk cases and very large bet on all 97 patients, from abdominal surgery, urology, gynecology and orthopedic hip arthroplasty bet on special. For rapid diagnosis and rapid establishment of appropriate therapy had provided all necessary imaging methods, which simplified the procedure for sorting the cases.

9. CONCLUSIONS

In terms of symptoms, pain is noted in most cases, so any leg/arm pain should be investigated, especially in the context of joint swelling member.

Lower/upper limb venous ultrasound as the main tool for diagnosing patients with medium-high clinical probability of deep venous thrombosis. CT with contrast angiography (CTPA) is believed to be the choice excurrently, providing reliable evidence of pulmonary embolism and other lung disease.
Low molecular weight heparins may be used instead of unfractionated heparin for the initial treatment of hospitalized patients with deep vein thrombosis. Both unfractionated and low molecular weight heparins are acceptable for initial treatment of patients with pulmonary embolism.

Ambulatory treatment of deep venous thrombosis with low molecular weight heparin is safe and effective for carefully selected patients. We recommend it in location of thrombosis below the popliteal vein and in pregnancy. Oral anticoagulation should be administered 6 months after the first episode of deep vein thrombosis or pulmonary embolism. Regarding the recurrent venous thromboembolism it requires oral anticoagulation for indefinite period. Low molecular weight heparins represents safe and effective long-term treatment of venous thromboembolism in selected persons and may be preferable for patients with cancer.

In patients with acute pulmonary embolism, thrombolytic therapy should be used in the presence of significant hemodynamic instability or sustained hypotension.

Installation of a recurrence of venous thromboembolism, or absence of a complete resolution at 6 months of therapy requires anticoagulant treatment correctly performed indefinitely.

It is increasingly evident that chronic pulmonary hypertension caused by pulmonary embolism is an under-recognized condition, that carries a poor prognosis, without specific surgery.