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Mini Review

Triple Ultrasound in Diagnosis of Thromboembolism

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Abstract

Pulmonary embolism remains a challange and is the most frequent clinically nondiagnosed cause of death. Clinical symptoms are rare and tend to be quite harmless and unspecific. Clinical probabilty and classification are discussed.

In lung ultrasound (LUS) peripheral pulmonary embolisms are hypoechoic and largely homogenous on ultrasound. The lesions are mostly triangular, may be rounded towards the hilum. Two-thirds of lung infarctions are located dorsally in the lower lobes of the lung, more often on the right side than on the left side. In three recent meta-analyses of 5/10/13 studies on 652/887/1356 patients, the pooled sensitivity and specificity was 80% - 87% and 82 - 93%. In view of the increasing numbers of CT investigations and the increasing collective radiation dose for specific clinical situations, such als emergency, pregnancy, renal failure, and contrast allergy LUS serves as a diagnostic alternative to CT. Inability to compress the common femoral or popliteal vein is usually diagnostic of a first episode of deep venous thrombosis in symptomatic patients (positive predictive value of about 97%, negative predictive value of about 98%). In cases of suspected leg vein thrombosis, compression ultrasound has a median sensitivity of 95% and a median specificity of 97%. About 40% of patients with acute pulmonary embolism have a right heart load. This specifically includes patients at hemodynamic risk who have to undergo lysis or embolectomy as a life-saving measure. On echocardiography one can obtain a rapid overview of the degree of risk for the patient, establish the intensity of monitoring, and devise a treatment plan. A heart-lung-vessel-integrated triple ultrasonography according to clinical impression can help with the diagnosis of PE and should be a necesseray weapon fort he physicians, especially in emergency departements.

Keywords: *Pulmonary Embolism; Lung Ultrasound; Vein Compression Ultrasound; Echocardiography*

Introduction

As the pathologist Rudolf Virchow ca 1880 has described that thromboembolism is one disease: at the veins, the heart, and the lung. Venous thromboembolims (VTE) is a serious disease, with an overall annual incidence between 100 and 200 per 100,000 inhabitants [1]. Acute pulmonary embolism (PE) is the most severe outcome of VTE and may be life-threatening if not diagnosed and treated in time. Pulmonary embolism is the most frequent clinically nondiagnosed cause of death [2].

Clinical symptoms are rare and tend to be quite harmless and unspecific. Even in times of Multi-Slice-Computed-Tomography (MSCT), one most assume that 40% of fatal pulmonary embolisms remain undiagnosed in autopsy examinations [3]. When a patient presents with shortness of breath, pleuritic chest pain, tachycardia, or signs of right heart strain, clinicians are trained to think “pulmonary embolism”. Because these symptoms and signs are neither sensitive nor specific, several scoring systems have been developed to help clinicians decide which patients to further imaging prodedures, although in practice, many clinicians simply proceed with imaging to rule in or to rule out the diagnosis [4,5]. CT in patients with suspected PE has led to an increase in the diagnosis of PE without a corresponding decline in mortality [6]. On the other hand, some studies report a generally decreased mortality rate over the years. In particular, the detection of clinically insignificant patients can contribute to a decreased mortality rate. However, overtreatment with anticoagulant therapy lead to complications with increased morbidity and mortality. The main harm from overdiagnosis is unnecessary treatment, which in the diagnosis of pulmonary embolism means anticoagulation - a leading reason of medication related death [5,7]. Can we create a balance between these two ideas?

Clinical probability

Risk factors for PE include smoking, malignancy, obesity, age, hereditary thrombophilias, prolonged immobilization, and surgery. Major trauma, lower limb fractures and joint replacements, and spinal cord injury, are strong provoking factors for VTE. Cancer is a well-recognized perdisposing factor for VTE (well known since many years). Moreover, cancer is a strong risk factor for all-cause mortality following an episode of VTE.

In fertile woman, oral contraception ist he most frequent predisposing factor factor for VTE. When occuring during pregnancy, VTE is a major cause of maternal mortality. The risk is highest in the third trimester of pregnancy and over 6 weeks of the postpartum period, being up to 60 times higher 3 months after delivery, compared with the risk of non-pregnant women.

For the purpose of clinical management, "confirmed PE" is defined as a probability of PE high enough to indicate the need for PE-specific treatment, and "excluded PE" as a probability of PE low enough to justify withholding PE-specific treatment with an acceptably low risk [2].

Clinical classification

The clinical classification of the severity of acute PE is based on the estimated PE-related early mortality risk defined by in-hospital or 30-day mortality. This initial risk stratification has important implications for the diagnostic and therapeutic strategies. High-risk PE is suspected or confirmed in the presence of shock or persistent arterial hypotension and not high-risk PE in their absence [2].

D-dimer levels are elevated in the presence of acute thrombosis, but also in a wide varity of diseases such as cancer, inflammation, bleeding, trauma, surgery and necrosis. D-dimer testing should only be performed in patients with not high risiko for PE [4].

Lung ultrasound (LUS)

Peripheral pulmonary embolisms are hypoechoic and largely homogenous on ultrasound. The lesions are triangular, may be rounded towards the hilum or polygonal in shape. The margin may be initially somewhat blurred, but is usually sharp. Two-thirds of lung infarctions are located dorsally in the lower lobes of the lung, more often on the right side than on the left side. This is because of anatomical factors and because of hemodynamics. In cases of pulmonary embolism, on average 2.4 infarctions are seen on sonography. Given two or more lesions and the clinical likelihood of pulmonary embolism, the specificity of sonography is up to 99%. The mean size of pulmonary infarctions is 12 mm × 16 mm (range 5 - 70 mm) (Figure 1 and 2). Lesions less than 5 mm in size should not be taken into account because they might be merely scars. If clinical suspicion is given, their progress should be monitored. Pleuritis may be marked by a similar appearance with small subpleural consolidations. In some cases one finds an anechoic band of vessels on the B-mode image. The band of vessels is oriented from the tip of the lesion towards the hilum. In approximately half of cases the investigator finds small pleural effusions either focally above the lesion or in the pleural sinuses. In few cases is the investigator able to visualize, on color-coded duplex sonography, a circulation stop caused by embolism [8,9].

A large multicenter study comprising 352 patients in the ordinary clinical setting round the clock, which included less experienced investigators, showed that three-fourths of patients with pulmonary embolism have typical peripheral lesions on sonography. A surprisingly high specificity of 95% was achieved in this study [10]. These figures concur with those reported for the demonstration of peripheral pulmonary embolisms in pathological studies. The results are worse, if the dorsal region is not examined [11].

Three recent meta-analyses of 5/10/13 studies on 652/887/1356 patients, the pooled sensitivity and specificity was 80% - 87% and 82-93%. The authors conclude that, in view of the increasing numbers of CT investigations and the increasing collective radiation dose for specific clinical situations, such als emergency, pregnancy, renal failure, and contrast allergy chest ultrasound serves as a diagnostic alternative to CT [12-14]. This is recommended it actual consenses and guidelines [4,15].

Compression Ultrasound of Leg Veins

Much more than half of pulmonary embolisms originate from leg veins. Inability to compress the common femoral or popliteal vein is usually diagnostic of a first episode of deep venous thrombosis in symptomatic patients (positive predictive value of about 97%). Com-

plete compressibility of both of these points excludes proximal deep venous thrombosis in symptomatic patients (negative predictive value of about 98%). Compression sonography is a safe procedure to confirm that an embolism is originating from a deep vein thrombosis (well known). In cases of suspected leg vein thrombosis the median sensitivity is 95% and the median specificity is 97% (it is right and cited). Even in cases of the relatively frequent isolated lower leg thrombosis the median sensitivity is > 90% and the median specificity is 95%. Patients who have anticoagulation withheld following a negative or inconclusive whole-leg compression ultrasound for suspected deep vein thrombosis have a low rate of adverse events [16-19].

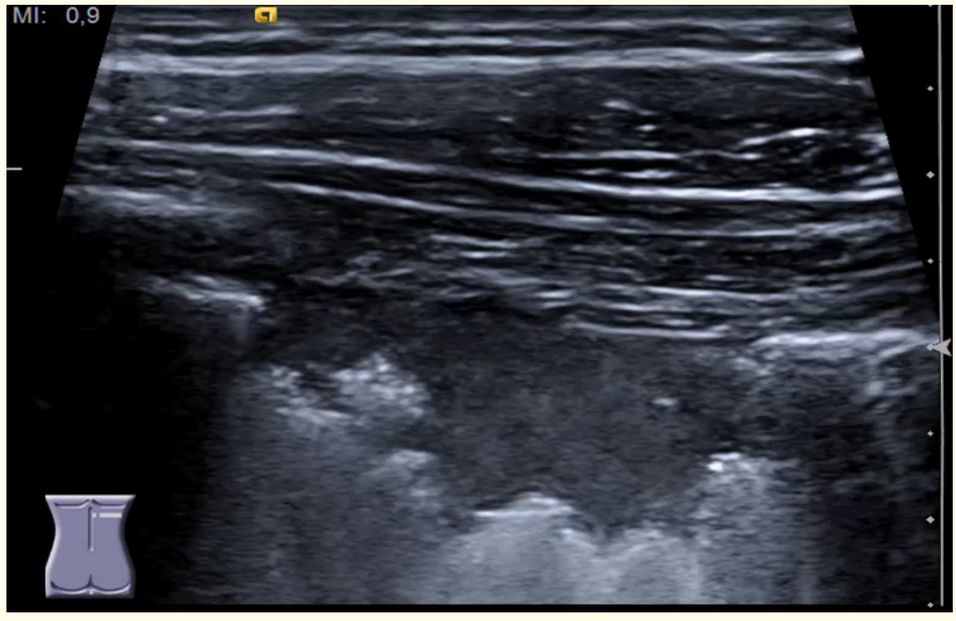

Figure 1: *A 25 year old with a triangular/polygonal lung infarction.*

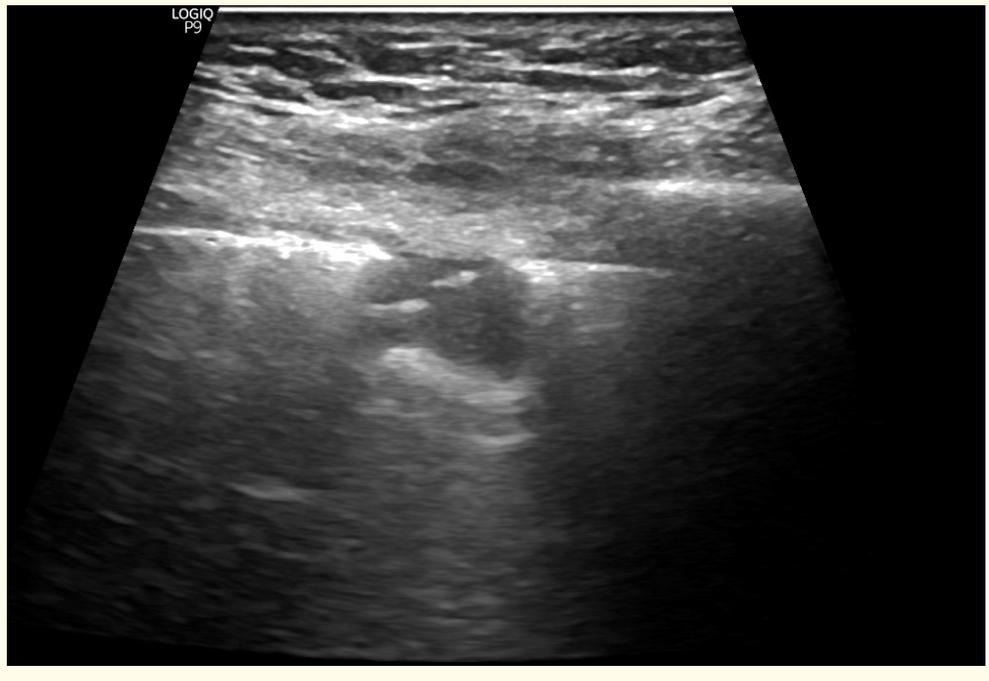

Figure 2: *A 62 year old man with lung cancer an a rounded lung infarction.*

Visualization of the thrombus and the absence of flow are direct signs of leg vein thrombosis. Detection of the thrombus in the B-mode is indirectly improved by the application of color-Doppler sonography. The thrombosed vein is not compressible or is only partially compressible, which is indicative of an occluding coagulation (Figure 3). However, signs of compressibility are only reliable when they are found in the inguinal or popliteal region. The vena cava and pelvic veins are not sufficiently compressible. In cases of calf thrombosis the compression is painful on palpation. The respiratory phase of venous flow is lost at a location distal to any hindrance of flow. In cases of acute thrombosis the vein is markedly dilated and valvular movements are absent.

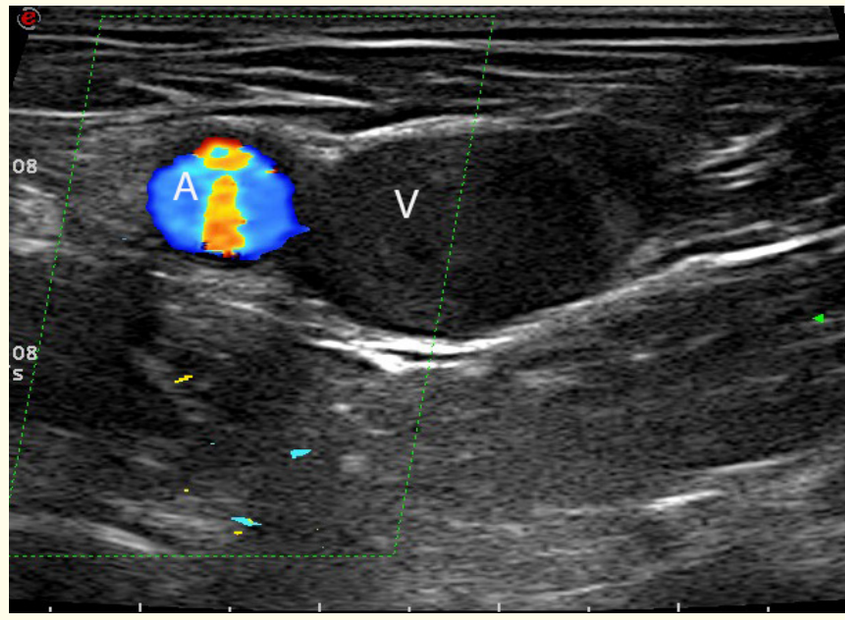

Figure 3: *A 22 years old pregnant women with deep vein trhombosis. V: Vena femoralis: enlarged, non compressible, filled with thrombisis, A: Arteria femoralis.*

Lower limb compression ultrasound is studied as an optimal diagnostic tool for both unstable and stable PE patients, since that a proximal positive result of the test has a high positive value for PE [16].

Echocardiography

About 40% of patients with acute pulmonary embolism have a right heart load. This specifically includes patients at hemodynamic risk who have to undergo lysis or embolectomy as a life-saving measure. The first hours after the onset of symptoms are of decisive importance for the prognosis of hemodynamically relevant pulmonary embolism. Right ventricular (RV) failure due to pressure overload is considered the primary cause of death in severe PE.

On echocardiography one can obtain a rapid overview of the degree of risk for the patient, establish the intensity of monitoring, and devise a treatment plan.

The following parameters are used to assess acute right heart load:

- Size of the right ventricle
- Contraction of the free right-ventricular wall
- Movement of the interventricular septum
- Size of the right atrium
- Are embolisms seen in the right heart?
- Exclusion of atrial myxoma.

These parameters are frequently assessed, determined individually, but not conclusively. This "over-view" focussed echocardiogram provides important subjective impressions, a few measured data, and occasionally an inadequate range of differential diagnoses concerning the various causes of right heart load (Figure 4).

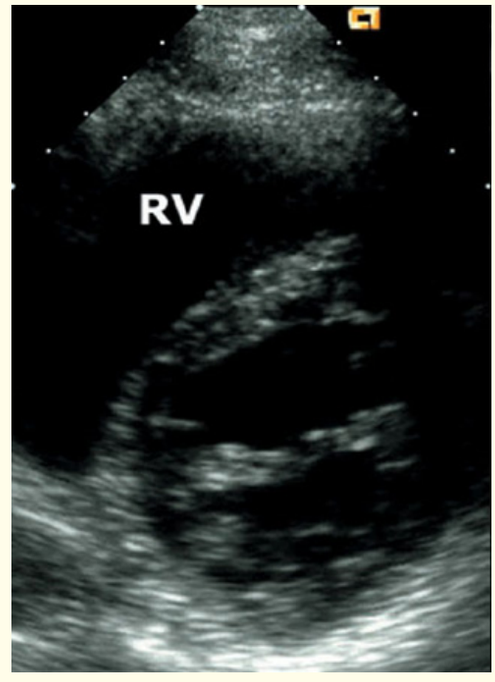

Figure 4: *Right heart dilatation (RV) in a 42 years old patient with submassive pulmonary embolism after appendectomy.*

Right-ventricular dysfunction typically occurs in basal location and is more pronounced medially in cases of acute right heart failure while the kinetics of the apex of the heart is relatively intact [20]. In cases of chronic right heart load the right ventricle is uniformly adynamic and dilated. Measurement of the tricuspid annulus plane systolic excursion (TAPSE) may also be useful.

Echocardiographic examination is not recommended as part of the diagnostic work-up in haemodynamically stable, normotensive patients with suspected (not high-risk) pulmonary embolism. This is in contrast to suspected high-risk PE, in which the absence of echocardiographic signs of RV overload or dysfunction practically excludes PE as the cause of haemodynamic instability. In the latter case, echocardiography may be of further help in the differential diagnosis of the cause of shock, by detecting pericardial tamponade, acute valvular dysfunction, severe global or regional LV dysfunction, aortic dissection, or hypovolaemia [2,21,22].

Since the introduction of transesophageal echocardiography, the source of embolism is increasingly looked for in the heart as well. Transthoracic echocardiography may disclose sessile and floating thrombi in the right atrium. In transesophageal location, one may also find riding thrombi in the central main trunks of the pulmonary arteries.

Triple Ultrasound - Conclusion

The clinician is called upon to use any method that improves the diagnosis of thromboembolism and reduces mortality. A heart-lung-vessel-integrated triple ultrasonography according to clinical impression can help with the diagnosis of PE and should be a necesseray weapon fort he physicians, especially in emergency departements. Computed tomography pulmonary angiography is overused to diagnose pulmonary embolism [23,24]. A major advantage of triple ultrasound investigation of thromboembolism is its manifold applicability and its availability at the bedside, whether in the emergency department or in the intensive care unit. It is a noninvasive, widely available, cost-effective method which can rapidly performed. LUS combinded with echocardiography and leg vein compression sonography yield

a sensitivity of more than 90% and a specificity of 95% for pulmonary embolism [11,24-26]. A negative US study cannot rule out PE with certainty, but positive US findings with suspicion for PE may prove a valuable tool in diagnosis of PE. Alternative diagnosis more likely than PE can be detected.

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