Incidence of pulmonary embolism in patients with symptomatic lower limb venous thrombosis : An experience using ascending radionuclide phlebography and lung ventilation and perfusion scan.

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Venous thromboembolic disease is emerging as one of the leading cause of morbidity and mortality. The relationship between lower limb venous thrombosis and its most ominous sequelae, pulmonary embolism has often been written about in the past. However in the past decade post mortem studies on patients of sudden death have revealed that extent of the problem is possibly far more than was earlier defined. Estimates from the United States alone estimate about 120,000 to 150,000 deaths annually from venous thromboembolic disease. The clinical dilemma often rises because a large number of patients with pulmonary embolism do not present with the classical symptoms of the disease. Lung scintigraphic and angiographic abnormalities suggesting silent PE have been reported in 40-60% of patients with deep venous thrombosis. Most studies have been conducted on small groups of patients of whom have had secondary DVT and multiple risk factors. The need to evaluate the presence of PE in patients referred for primary DVT is critical particularly when outpatient treatment is considered. Because if therapeutic implications especially indications for insertion of inferior vena caval filters, comprehensive assessments of both the disease process (i.e., deep venous thrombosis) and the complication (i.e., pulmonary emboli) are important. The aim of this study was to define the incidence of pulmonary embolism in patients presenting with symptomatic lower limb venous thrombosis.

Study design

A prospective study was conducted between January 2001 and Feb 2003 in the Sir Ganga Ram Hospital, a large referral hospital in New Delhi as a collaboration between the departments of endovascular surgery and nuclear medicine. More than a thousand consecutive

patients with symptoms suggestive of lower limb venous thrombosis were enrolled in the study.
All patients underwent a combined ascending radionuclides venogram and lung perfusion scan . 4 mci of 99m Technetium albumin macroagregates divided in two equal doses kept in two syringes was administered through a 23 gauge butterfly inserted in the dorsal pedal veins of both feet as a slow continues infusion followed by a 10 ml saline wash. A tourniquet was tied tightly above each ankle below both knees and at mid thigh bilaterally. The transit of tracer was assessed simultaneously in the anterior and posterior projections in a dynamic whole body imaging, conducted on a dual head variable geometry gamma camera, using a high resolution parallel hole collimator.
The lung perfusion scan was performed immediately. A minimum of four view of anterior, posterior and right and left posterior oblique were taken, each acquired on a 256x256 matrix using a parallel hole high resolution collimator with a minimum of 500,000 Counts.
A ventilation scan was conducted if any abnormality was found on the lung perfusion scan. Patient were nebulised using 99m Tc DTPA aerosol. Lung ventilation images were conducted immediately using a parallel hole high resolution collimator with a minimum 200000 K counts. A minimum of four view of anterior, posterior and right and left posterior oblique were acquired.

The images were analysed by two experienced nuclear medicine physicians. Non or poor visualisation of a vein, visualisation of collateral veins and preobstruction accumulation of tracer (Pooling) were taken as indicator for deep venous thrombosis. The presence of two or more large segmental perfusion defects mismatched with the ventilation scan were taken as high probability for pulmonary embolism. One moderate to two large mismatched segmental perfusion defects or the arithmetic equivalent in moderate or large and moderate defect was categorized as intermediate probability and non segmental perfusion defect were categorized as low probability scans for pulmonary embolism.

Results

One thousand one hundred and one fifty patients with clinical suspicious of deep venous thrombosis were involved in the study. Two studies were excluded from the study due to technical inadequacy. 28% of the patients were female while 72% were male. The ages ranged between 18-76 years with a mean age of 36 years. 625 patients had venograms suggesting DVT . of these 412 patients has suprapopliteal involvement while 213 had isolated infrapopliteal

venous involvement. 172 patients showed evidence of DVT in both lower limbs.
Looking at the pulmonary perfusion scans 764 had normal lung perfusion scans while 383 had abnormal scans . 262 lung ventilation perfusion scans showed a high probability for pulmonary embolism while 121 showed an intermidate probability for pulmonary embolism. 259 patients (41%) with phleboscinitgrahic evidence of DVT showed a high probability scan for pulmonary embolism while 97(15.5%) patients showed an intermediate probability. 43.5% patients showed a low probability or a normal pulmonary perfusion scan. 44.3% patients with a high probability scan for PE had no chest symptoms.

Discussions

Several studies have shown a high prevalence of pulmonary embolism in patients of lower limb DVT even when signs are symptoms of lung involvement are lacking. Symptoms and signs of PTE are non specific with standard clinical traid of tachypnea., hemoptysis and chest pain being present in less than 30% patient. Untreated clinically apparent PET has been associated with a 30% hospital mortality rate. In patient who do not die early of massive PTE, delayed death may result from recurrence of previously unsuspected PTE, delayed death may result from recurrence of previously unsuspected PTE. Monreal et al have found that DVT patients with silent PE have a higher rate of scinitgarphic PE recurrences during initial therapy with heparin than those with DVT alone [18]. These findings were subsequently confirmed in a larger group which showed that 3% of patient with silent PE developed new symptomatic PE events as compared to only 0.5% of patients with DVT alone. In our study eleven patients had recurrent pulmonary embolism. All except one had pulmonary perfusion defects in the baseline study. The importance of determining the prevalence of silent PE is even more important in ambulatory outpatients where the strategies of therapy have to be adapted to the extension of the thrombotic diseases and findings positive evidence of PE may be a critical point to ensure adequate therapeutic and prophylaxis strategies [20].
Since the signs and symptoms of PE are non specific the diagnosis of PE relies heavily on imaging techniques. Many investigative modalities have been used to define DVT and Pulmonary emboli Contrast venography and pulmonary angiography still remain the gold standard in this respect. However due to many adverse reactions of contrast these tests are seldom practiced in clinical medicine today. The Dupleix scan because of its ease of performance is often the first investigation to evaluate the presence of venous thrombosis. However Dupleix scanning while a sensitive technique for diagnosing DVT , fails

to define a subgroup of patients at higher risk for PE. Data from numerous ultrasound studies shows that anticoagulation should not be graded on US findings.

Other investigative modalities such as MR venography and high resolution CT have also been used. While on one hand these investigations provide a very precise evaluation of the extent of thrombosis of the deep venous system their use is often limited by the high economics of the investigation. In addition in all the aforementioned investigations a separate additional investigation has to be conducted to evaluate pulmonary perfusion.

Radionuclide phlebography using 99m Tc MAA has been established as a reliable investigation for detecting deep veneous thrombosis , establishing its proximal extent and diagnosing pulmonary embolism. Mangkharak et al compared radionuclide venography to contrast venography which is still considered as gold standard and found comparable sensitivities , specificities and predictive values. The results were even more consistent when the infrapopliteal DVT were excluded suggesting a slightly lower sensitivity of radionuclide venography in detecting isolated calf vein thrombosis [29]. However compared to conventional contrast venography there are no adverse reactions reported due to contrast medium and the total radiation exposure is shown to be significantly less. None of the patients in our study suffered any adverse reaction due to the procedure. Radionuclide venography shows a high accuracy in detecting pelvic and IVC thrombosis . The most attractive philosophy behind radionuclide venography is the simultaneous assessment of both peripheral and pulmonary thromboembolism and this has been shown to be particularly useful in many studies.[32,33,34,35]

Lung perfusion scans have long been accepted as the most useful tool to rule out Pulmonary embolism . No other method has been proven to have the same efficacy in detecting PE and in non invasively quantitating flow reduction [22]. The effectiveness of lung perfusion scintigraphy is highest in young patients in whom non diagnostic scans are less frequent and in whom the use of perfusion scans alone may be employed to diagnose Pulmonary embolism [25,26]. A number of studies have also been conducted to establish the relation of the location of the thrombus in the lower limb and its association with the incidence of Pulmonary embolism. The hypothesis that the consequences of a more cephalad extend of primary extremity thrombus should be more ominous makes intuitive sense. As the host vein increases in diameter, large potential emboli might be more likely to obstruct major pulmonary artery segments. Therefore if the incidence of severity of PE varies according to its anatomic source a proximal localisation of DVT should increase its clinical significance. In

our study of the 259 patient with DVT and high probability scan for PE, 231(89%) had suprapopliteal venous involvement. These 231 patient constituted 56% of the 412 patients showing suprapopliteal DVT. This data is in close concurrence to the study by Borst-Krafek et al which showed the incidence of silent PE to be 51% of iliac and 50% in femoral vein DVT [27.] However 28 patients with high probability pulmonary scans for pulmonary embolism had only infrapopliteal venous involvement suggesting that isolated calf DVT has a small yet defined risk of pulmonary embolism. The treatment strategies however may differ with patients with distal DVT alone needing a lower level of anticoagulation [28.] One interesting observation in our study has been that the incidence of pulmonary embolism does not increase with IVC involvement . 21 patients during the course of our study are found to have IVC thrombosis on phleboscintigraphy. However only four of these patients had evidence of perfusion on lung scans. Since the difficult to hypothesize regarding the reason for such an observation. More studies in the future will probably be needed to seek an explanation for the same.

In conclusion it can be summarised that pulmonary emboli caused by deep venous thrombosis may be clinically silent. Because of therapeutic implications especially indications for insertion of inferior venacaval filters comprehensive assessments of deep venous thrombosis even in the absence of symptoms or signs in the lower extremities involving the popliteal or superficial femoral vein is the presenting process, correlative assessment of the pulmonary circulation even when no pulmonary symptoms or signs are present may be of therapeutic significance. The aim of this study is to evaluate the prevalence of clinically occult scintigraphically proven pulmonary embolism (PE) in a group of patient with deep venous thrombosis (DVT) to determine the relationship between prevalence of PE and DVT extension as seen on radionuclide venography and to establish the impact of the information provided by this investigation on the therapeutic management of such patients.

Refereces:

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