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ROLE OF CT PULMONARY ANGIOGRAPHY IN DIAGNOSIS OF CLINICALLY SUSPECTED ACUTE PULMONARY THROMBOEMBOLISM, ITS COMPARISON WITH CLINICAL (WELLS) CRITERIA AND BIOCHEMICAL (D-DIMER) STATUS

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ABSTRACT Since its introduction in 1992, computed tomography angiography (CTA) of the pulmonary arteries has become the main diagnostic test for the evaluation of pulmonary embolism (PE). With the advent of multi detector scanning, CTA has gained substantially in image acquisition speed and spatial resolution, which changed its diagnostic yield in many respects. Pulmonary embolism is the third most common acute cardiovascular disease after myocardial infarction and stroke and results in thousands of deaths each year because it often goes undetected. Pulmonary angiography, the diagnostic standard of reference for confirming or refuting a diagnosis of pulmonary embolism, remains underused. For each lung the main, lobar, segmental and subsegmental arteries are examined for pulmonary embolism. Acute pulmonary embolism cause intraluminal filling defects that should have a sharp interface with the intravascular contrast material. The vessels are seen as either normal, containing acute pulmonary embolism, or indeterminate. Aims of this study were to diagnose pulmonary thromboembolism on CT pulmonary angiography and compare the CT pulmonary angiography study results with Wells grade, D-dimer status. Total of 80 subjects were included irrespective of their age and sex. Comparison of results were done using 'Fisher's exact test'. In conclusion, Most of the emboli were seen at segmental (53.75%) and lobar (30.0%) levels. There is significant association between CTPA diagnosis and Wells grade (P value <0.05), no significant association between CTPA diagnosis and D-dimer status (P value >0.05). D-dimer had low specificity.

KEYWORDS : CT pulmonary angiography, Thromboembolism, Wells score, D-dimer

Introduction:
Since its introduction in 1992, computed tomography angiography (CTA) of the pulmonary arteries has become the main diagnostic test for the evaluation of pulmonary embolism (PE). With the advent of multi detector scanning, CTA has gained substantially in image acquisition speed and spatial resolution, which changed its diagnostic yield in many respects. Pulmonary embolism is the third most common acute cardiovascular disease after myocardial infarction and stroke and results in thousands of deaths each year because it often goes undetected.[1,2] Diagnostic tests for thromboembolic disease include (a) the D-dimer assay, which has a high sensitivity but poor specificity in this setting,[3] (b) ventilation-perfusion scintigraphy, which has a high sensitivity but very poor specificity,[4] and (c) lower limb ultrasonography, which has a high specificity but low sensitivity.[5] Computed tomographic (CT) pulmonary angiography has been evaluated has demonstrated sensitivities of 53%–100% and specificities of 83%–100% in wide ranges.[6]

Pulmonary angiography, the diagnostic standard of reference for confirming or refuting a diagnosis of pulmonary embolism, remains underused.[7,8] Standard diagnostic algorithm have described CT pulmonary angiography is crucial investigation for diagnosis of acute pulmonary thrombo-embolism. For each lung the main, lobar, segmental and subsegmental arteries are examined for pulmonary embolism. Acute pulmonary embolism cause intraluminal filling defects that should have a sharp interface with the intravascular contrast material. The vessels are seen as either normal, containing acute pulmonary embolism, or indeterminate. The reason for indeterminacy is reported, along with the extent of normalcy. For example, vessels may appear normal to the level of the segmental arteries; however, the presence of pulmonary embolism in sub-segmental arteries may remain indeterminate depending on the quality of the study.

The diagnostic criteria for acute pulmonary embolism include the following: 1. Arterial occlusion with failure to enhance the entire lumen due to a large filling defect; the artery may be enlarged compared with adjacent patent vessels, 2. A partial filling defect surrounded by contrast material, producing the “polo mint” sign on images acquired perpendicular to the long axis of a vessel and the “railway track” sign on longitudinal images of the vessel, 3. A peripheral intraluminal filling defect that forms acute angles with the arterial wall.

Clinical comparison will be done with Wells criteria.[9] Criteria includes multiple parameters like deep vein thrombosis, tachycardia, haemoptysis, history of surgery and malignancy [Table 1].

D-dimer value - D-dimer is the degradation product of cross-linked (by factor XIII) fibrin. It reflects ongoing activation of the haemostatic system. Results were expressed as positive when > 500 ng/ml FEU or negative when, < 500 ng/ml FEU.[10]

Aims of study were 1. To diagnose pulmonary thromboembolism on CT pulmonary angiography, 2. To compare the CT pulmonary angiography study results with Clinical status - Wells criteria, Biochemical marker – D-dimer status.

Study design: A cross sectional study.

Subjects and Methods: Total of 80 subjects were included irrespective of their age and sex with following inclusion and exclusion criteria.Complete history was taken and thorough physical examination was done in all recruited patients. D-dimer values were noted. Other haematological tests were observed.

Images of pulmonary vasculature were obtained in axial planes by bolus tracking and maximum intensity projection. Reformatting in axial, coronal and sagittal planes was done using software provided. Either positive or negative result obtained using standard parameter of CTPA. Comparison of results was made with clinical criteria (Wells) & biochemical marker (D-dimer).

Follow up of cases was made till patients were admitted.

Comparison of results of CT pulmonary angiography study with wells score probabilities and d-dimer results was done using 'Fisher's exact test' by means of Statistica software (StatSoft). Values of $p < 0.05$ were regarded as statistically significant.

Results:
Maximum numbers of patients were in age group of 61 to 70 years and followed by 71 to 80 years and 41 to 50 years. Males outnumbered females in most of the age group. In this study, majority of the patients were male (47). The gender ratio was found to be (Male: Female=1.4:1). There is unilateral thromboembolism in 52.27% of patients and bilateral involvement in 47.73% of patients. Most of the emboli were seen at segmental (53.75%) and lobar (30.0%) levels, followed by at subsegmental level (18.75%). Using the Wells score, 6.3 % of patients who were with low risk of PE, 67.5% with moderate risk and 26.3 % of patient with high risk of PE [Figure 4]. By using latex agglutination assay, 92.5% patients were positive for D-dimer and only 7.5% had showed negative results. Using the Wells score, out of 44, 1 patient who was with low risk of PE went to be diagnosed with PE on CTPA. 24 patients with moderate risk and 19 patients with high

risk on Wells score went to be diagnosed with PE on CTPA. By using Fisher's exact test, p-value < 0.05 therefore there is significant association between CT pulmonary angiography diagnosis and Wells grade [Table 2] [Figure 5]. 43 patients with positive d-dimer value went to diagnosed PE on CTPA.1 patient with negative d-dimer value went to diagnosed PE on CTPA.By using Fisher's exact test p-value > 0.05 therefore there is no significant association between CT pulmonary angiography diagnosis and D-dimer status.

In present study pulmonary thrombo-embolism were seen in 44 (55%) patients. In 36 (45%) patients non-embolic pathologies were demonstrated including interstitial lung disease (n=7), pneumonia(n=6), congestive cardiac disease (n=4), COPD (n=4) and pleural effusion in 1 patient. Search of origin of emboli was made. Deep vein thrombosis was seen in 24 patients, 5 patients shown IVC thrombosis on colour doppler while 2 patients were of right ventricular thrombus on ECHO. In remaining 13 patients cause of pulmonary thrombo-embolism was inconclusive. After 1 month follow up, out of 44 patients diagnosed and treated for pulmonary thromboembolism, 5 patients died in 2 to 8 days period after diagnosis.

Conclusions:

In our study, out of total sample of 80 patients, 44 (55%) patients were showed pulmonary thromboembolism on CTPA. Bilateral distribution of emboli was seen in 21(47.73%) patients. Thrombo-embolic material was observed in more than one region. Most of the emboli were seen at segmental (53.75%) and lobar (30.0%) levels, followed by at subsegmental level (18.75%). MDCT made the detection of subsegmental emboli which is difficult in single detector scanner. Usually, deep vein thrombosis originates in leg veins of the calf and propagates to the proximal leg veins.[19] Patients with deep vein thrombosis involving the proximal leg veins are considered at greatest risk for developing pulmonary embolism (as opposed to those with isolated calf vein thrombosis). It is hypothesized that isolated calf vein thrombosis may be a clinicallyUsing the Wells score, out of 44, 1 patient with low risk of PE went to be diagnosed with PE on CTPA. 24 patients with moderate risk and 19 patients with high risk on Wells score went to be diagnosed with PE on CTPA. There is significant association between CT pulmonary angiography diagnosis and Wells grade (*P value <0.05*). Out of 44 patients, 43 patients with positive d-dimer value went to diagnosed PE on CTPA. 1 patient with negative d-dimer value went to diagnosed PE on CTPA. There is no significant association between CT pulmonary angiography diagnosis and D-dimer status (*P value >0.05)*. D-dimer had very low specificity also.

Discussion:

Acute pulmonary embolism (PE) is characterised by partial or complete obstruction of central or peripheral arteries of the lungs by emboli. Not only the disease itself but also the anticoagulant treatment of PE may entail substantial morbidity.[11] There is a need for prompt and accurate diagnosis. However, the clinical diagnosis of PE has proven to be difficult, since clinical signs and symptoms are often non-specific.[12] In fact, in only up to one-third of patients clinically suspected of having PE is the diagnosis subsequently established.[13] Acute PE is the third most common cause of death after cardiovascular diseases and malignancies and also the third most-common cause of cardiovascular death after myocardial ischemia and stroke.[14] PE is the leading cause of maternal death in pregnancy.[15,16] PE is a common disorder, with an estimated annual incidence of 23 to 69 per 100,000 in a community.[1,17] The incidence of PE rises with age, approaching approximately 1 in 100 in the very old. In the absence of risk factors, PE is rare in children under 15 years of age (<5 per 100,000).[18] Pulmonary embolism usually arises from deep vein thrombosis of the lower extremities.[19] Further evidence that DVT and PE are distinct manifestations of the same disease process referred to as venous thromboembolism (VTE), comes from the observation that in the majority of patients with PE, DVT can be diagnosed using sensitive methods. In patients with proven leg vein DVT, 40% have asymptomatic PE.[20]

Usually, deep vein thrombosis originates in leg veins of the calf and propagates to the proximal leg veins.[19] Patients with deep vein thrombosis involving the proximal leg veins are considered at greatest risk for developing pulmonary embolism (as opposed to those with isolated calf vein thrombosis). It is hypothesized that isolated calf vein thrombosis may be a clinically self-limiting condition and patients become at risk for pulmonary embolism if the thrombus propagates to the proximal venous system.[19,20] self-limiting condition and patients become at risk for pulmonary embolism if the thrombus propagates to the proximal venous system.[19,20]

With time, the thrombosis will extend in a contiguous fashion to involve the more proximal venous system of the legs; the popliteal, superficial femoral, and common femoral veins. Less commonly, deep vein thrombosis originates in the iliac veins and, with time, will spread distally. Ilio-femoral or pelvic deep vein thrombosis tends to occur in certain settings such as pregnancy or in the presence of pelvic masses and post surgery in gynaecological, urological or abdominal procedures. The thrombus dislodges from the deep veins, travelling through the inferior vena cava and the right heart to finally lodge in the pulmonary arterial system or paradoxically to the systemic arterial circulation via a patent foramen ovale or atrial septal defect.[19,21-23]

PE may less commonly originate from other venous sources. Particularly, with the chronic use of upper extremity indwelling catheters, pulmonary embolism may arise from the veins in the upper extremities. The de novo development of pulmonary embolism is thought to be uncommon.[19,24,25] The most feared long-term consequence of untreated or poorly treated acute PE is chronic thrombo-embolic pulmonary hypertension, a severely debilitating and potentially fatal condition.[26-28] According to the PIOPED II study, signs and symptoms are similar in both the young and the elderly except that dyspnoea or tachypnoea is less frequent in the elderly, who have no history of cardiopulmonary disease. Typical symptoms and signs may even be absent in patients with severe PE. The haemoptysis/pleuritic pain syndrome, uncomplicated dyspnoea syndrome or circulatory collapse syndrome typical of PE are more common in proximal artery PE (94% of patients) than segmental artery PE (72% of patients).[29] While certain symptoms and signs are more commonly observed in PE than in other conditions, it is not possible to confirm a diagnosis of PE on clinical features alone. The diagnosis of PE must be confirmed or refuted on the basis of a conclusive imaging test.[30,31]

Wells et al[32] performed a comparative analysis of a randomized study where it was deducted that although CTPA is more effective at preventing overall mortality. An ideal scoring system aimed at assessing the pretest probability of any disease requiring prompt therapeutic intervention (such as acute PE), should be designed so as to keep to a minimum the proportion of patients classified as "intermediate probability".[33] The Wells and co-workers model[34] has been used in at least 12 studies, and more than 10,000 patients have been evaluated, including 5 studies with a total of more than 5800 patients in which the authors used the dichotomous scoring system of PE unlikely (score < 4) or PE likely (score >4). Simply posting the model in the clinic area has proven useful in one centre.[32] The Wells model seems better suited to rule out rather than to rule in the diagnosis of PE, and its performance is likely to be better in clinical settings where the prevalence of the disease is expected to be low.[32]

D-dimer is a specific breakdown product of cross-linked fibrin in blood clots. D-dimer is thus elevated in the setting of deep venous thrombosis and pulmonary embolism.[35] The plasma D-dimer latex agglutination test and enzyme-linked immunosorbent assay (ELISA) have become recognized as a sensitive screening tests for excluding acute pulmonary thromboembolism. Quantitative assay of D-dimer, based on a rapid ELISA method, has a high sensitivity (about 95%) for venous thromboembolism.[36]

Multi-detector Computed Tomography (MDCT) scanners with 4, 8, 16, 32, and 64 detector-rows are now several years old and have solved most of the problems concerning single-slice CT angiography. The collimation or slice thickness used today is commonly at or near 1-mm, with sub-second gantry rotation speeds of 0.3 to 0.5 seconds resulting in improved spatial and temporal resolution as well as increasing the number of subsegmental (fourth-order pulmonary arterial branches and smaller) arteries that can be evaluated, enhancing the interpretation of the spiral CT scan[37,38] and improving observer agreement.[39] CT can also demonstrate other conditions that clinically mimic PE, such as acute pneumonia, lung abscess, pneumothorax, pneumo-mediastinum, pleural or pericardial effusion, aortic dissection, cardiovascular disease, mediastinitis, mediastinal abscess, esophageal rupture, malignancy and interstitial pulmonary fibrosis. On

CTPA, the location of embolic material was classified as: Main pulmonary arteries, lobar branches, segmental arteries and sub-segmental branches.

Primary therapy consists of thrombolysis using thrombolytic agents and/or embolectomy (surgery or catheter) which is reserved for high risk patients i.e. those with hemodynamic instability, right ventricular dysfunction, or elevated troponin levels secondary to right ventricular microinfarction and elevated brain natriuretic peptide (BNP) values.[23] The preferred thrombolytic agent is recombinant tissue plasminogen activator (tPA).

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