**INTRODUCTION**

Chest pain is the 2nd most frequent cause of emergency room (ER) visits in the US, accounting for nearly 6 million visits. While the causes of chest pain can vary, pulmonary embolism (PE) is frequently in the differential diagnosis. PE in itself is one of the leading causes of mortality with estimates suggesting that about 100,000-200,000 patients die each year from pulmonary embolism.1 When PE is suspected, the current guidelines2 suggest the use of clinical criteria like modified Wells score, modified Geneva score for risk stratification. Diagnostic testing by computed tomographic pulmonary angiography (CTPA) or Ventilation-perfusion (VQ) scans is suggested based on clinical presentation, patient symptoms, d-dimer test, and pre-test probability. However, multiple prior studies have raised a concern about overutilization of CTPA and non-adherence to the use of clinical probability scores.3,4 The trends towards the use of CTPA is on the rise, with usage greater than 10 times over the last decade.5

The positive yield of CTPA has varied extensively, most studies showing a yield between 6%6 to 34%.3,7. However, a more recent study found a CTPA positive yield of <1% (0.2%) in a tertiary care center in the United States. This minimal positive yield is adds to the ever-rising concern of exposing these patients to unnecessary tests, radiation and contrast exposure. Increasing health-care costs are also an important implication of diagnostic tests, not only because of a negative yield but also because of recommendations for further management of ‘incidentals’.8,9 Moreover, overutilization of resources is both a source10 and a consequence of physician burn-out.11 The negative yield of CTPA is also not without individual patient harm. While the negative effects of radiation are difficult to measure, the incidence of contrast-induced nephropathy (CIN) has been shown to be 13-24%12,13 in studies.

Based on recent data highlighting the increased usage of CTPA with downtrend towards positivity of the study, the goal of our study was to measure the rate of CTPA positivity for pulmonary embolism in a tertiary care center in the US. The secondary goal of this study was to study the factors influencing the yield of CTPA. For this, we evaluated if the positive yield varies based on the referral unit (inpatient, outpatient, emergency department or intensive care unit), study order type (chest only or chest-abdomen-pelvis), or certain patient characteristics (age, sex, or body mass index).

**Materials & Methods:**

***Data collection***

This was a retrospective study approved by the local institutional review board. The patients that got CTPA between 2016 and 2018 were selected after accessing data from the hospital information system. Eligibility criteria included patients where requesting indication for CTA examination was to rule out pulmonary embolism. Any patient with CT angiography for other indications like aortic evaluation, pulmonary arteriovenous malformation, etc. was excluded. CTA double rule out studies (rule out pulmonary embolism and acute aortic syndrome) were however included. We aimed to detect differences in positivity rate based on admittance location and type of CTA procedure requested. Thus, all included patients were further subdivided based on their location of admittance (inpatients, outpatients, ICU patients, and ED patients) and CTA procedure request type (CTA chest only or CTA chest/abdomen/pelvis). We also aimed to analyze patient-related factors that would be predictors of CTPA yield hence parameters like age, gender, and body mass index (BMI) were recorded. Amount of intravenous contrast administered and radiation dose parameter dose length product (DLP) was also recorded for CTPA chest studies. Combined CTPA chest with CT abdomen and pelvis studies were excluded for contrast and radiation dose measurements.

Radiology report data were accessed from the radiology information system and final impressions were recorded for all eligible patients. Based on radiology impression list, patients were classified as positive or negative for PE. Patients who had non-diagnostic study due to technical factors were excluded. Patients with positive PE were further subdivided into central (if main, right or left pulmonary artery was involved), peripheral (beyond branch pulmonary arteries including segmental/subsegmental branches) or combined pulmonary embolism. Presence or absence of right heart strain was documented based on following criteria: flattening of the interventricular septum, enlarged right atrium or right ventricle (right ventricle to left ventricle ratio > 0.9), reflux of contrast in hepatic veins and inferior vena cava.

*Data analysis*

The yield of CTPA examination (proportion of positive test results) was assessed for the entire group, and also according to admittance location as well as CTA study type. CTPA positivity rate was also determined for different age (under 18, 18-35, >35) and BMI groups (under 25, 25-40 >40). Effective dose (mSv) was calculated for chest only examinations by the following formula: DLP (mGy·cm) x 0.014.14

**Statistical Analysis**

Continuous variables were summarized as mean ± standard deviation (SD) with median and range; categorical data as number and percentage. Differences between positive or negative acute PE sub-groups; and between types of acute of PE were compared using Fischer’s exact test and Chi-Square test for categorical data. Statistical significance was assumed for p values of less than 0.05. A logistic regression model was fit to determine what factors affect the positivity rate of CT scans for PE. Data was analyzed using R software (R Foundation for Statistical Computing, Vienna, Austria).

**RESULTS:**

***Patient characteristics:***

A total of 2713 patients were included in the study, out of which 2412 patients got CTPA chest only while 301 patients got CTPA chest along with CT abdomen and pelvis. There were 1435 (53%) females and 1278 (47%) males in the total population. The mean age of the population was 58 years (SD 17.3, range 0-104). Mean BMI was 31.2 (SD 9.9, range 12-91.5), and a majority of patients had a BMI between 25-40 (1491/2713, 54.9%). Out of the entire patient population, 56.7% (1537/2713) were referred from the emergency room, 13.0% (352/2713) were referred by intensive care units (ICU), 22.6% (613/2713) were inpatients other than ICU, and 7.7% (211/2713) were outpatients. Table 1 shows the patient characteristics.

***Positivity rate and factors associated with positivity:***

In total, there were 296 positive test results resulting in an overall yield of 10.9% (296/2713). The mean effective radiation dose was 5.521 mSv (median dose 4.27 mSv; dose range 0.1-43.0 mSv). The mean contrast dose administered was 88.48 mL (median dose 95.0 ml; dose range 5.0-150.0 ml). Out of the positive test results, 79.7% (236/296) had a peripheral (segmental and subsegmental) location of thrombi, 5.7% (17/296) had a central location, and 14.2% (42/296) had both central and peripheral location of thromboembolism. Right heart strain was present in approximately one-third of positive cases (36.8%; 109/296). Table-2 and Table-3 shows pattern of the pulmonary embolism compared to patient location and the age group.

Type of CT order (CT Chest or CT chest with abdomen and pelvis):

Higher PE positivity rate was noted in studies ordered as CTPA plus abdomen and pelvis (12.3%; 37/301) as compared to CTPA chest only (10.7%; 259/2226).

Location of the patient:

Highest yield was found in CTPA examinations that were requested from ICU (15.3%, 54/352) followed by inpatients [other than ICU] (12.4%, 76/613), ED (9.6%, 148/1537), and outpatients (8.5%, 18/211). A chi-square test found these differences in the positivity rate to be statistically significant (p-value <0.01) [Figure-1].

Patient characteristics (age, sex, and BMI):

Patients were grouped together into three groups based on age: under 18 years old, 18-35, and over 35 years of age. Highest CT positivity was found in patients under 18 (16.0%, 4/25), followed by the 18-35 group (11.7%, 36/309) and patients over 35 (10.8%, 256/2379). Overall, the males had higher positivity (153/1278, 12.9%) as compared to females (143/1435, 10.0%). This difference was statistically significant (p = .048). The highest difference in positivity rate between males and females was seen in 18-35 age group (males= 18.7% vs females = 7.9%, p value= .002) [Figure-2]. The patient population was also grouped based on body mass: BMI under 25, between 25 and 40, and BMI over 40. Here we find the highest positivity rate in the BMI 25-40 group (11.9%, 178/1491), followed by the BMI over 40 (10.1%, 43/426) and BMI under 25 groups (9.4%, 71/757) (Figure-3 and 4). It is worth noting that these age and BMI groupings were constructed based on standard delineations, which resulted in groups containing a varying number of patients. As such, nearly half of all patients in the population belong to the age over 35 and BMI between 25 and 40 group (1336/2713).

***Positivity Predictive Model:***

A logistic regression model was fit to the data using the positivity of a patient’s CT scan as the response. The full model for rate of positive CT scans considered gender, age group, BMI group, type of procedure, and the location of admittance as variables of interest. After iterative variable selection, the final model found that BMI group and patient’s location of admittance were the only significant predictors of CT positivity. Coefficients and standard errors for this final model are given in Table-4. The default factor level for BMI group is the under 25 group, and the default for location is ED. Post hoc analyses to identify group differences within the BMI group and location variables were performed using a False Discovery Rate correction to reduce the chance of spurious significance.

For the BMI groups, a significant difference was found between the under 25 and between 25-40 (OR = 1.342, Z =1.980, p = .024). This means that the odds that an individual with a BMI between 25-40 has a positive CT scan are 34.2% greater than the odds of a positive test result for someone with a BMI under 25. No other pair-wise differences were significant (over 40 and under 25: OR = 1.113, Z = 0.525, p-value = .300; over 40 and between 25 and 40: OR = 0.889, Z = 1.037, p-value = 0.15).

For the location variable, significant differences were found between ICU patients and ED patients (OR = 1.721, Z = 3.150, p < .001), in-patients and ED patients (OR = 1.343, Z = 1.951, p = .026), and between ICU patients and out-patients (OR = 1.994, Z = 2.396, p = .008. This indicates that the odds of an ICU patient having a positive CTPA scan are 99.4% greater than the odds for an out-patient, and 72.1% higher than the odds for an ambulatory (ED) patient. Also, the odds of a non-ICU inpatient testing positive for PE are 34.3% higher than the odds of a positive coming in from ED. No other pairwise differences were significant (OUT and ED: OR = 0.863, Z = 0.94, p = .174; OUT and IN: OR = 1.556, Z = 0.36, p = .360; ICU and IN: OR = 1.281, Z = 1.288, p = .099). The predicted CT positivity based on patient location and patient’s BMI is shown in Figure-5.

**DISCUSSION:**

Our study shows that the detection of pulmonary embolism on CTPA in a tertiary care center in the US is 10.9% and not as low (<1%) as recently shown15 in a similar tertiary care center in the US. The positivity in our study is similar to other previous studies which showed a yield ranging from 6-34%.16,17 Most of the studies with less than 10% yield are from the US,18 with at least two studies showing positivity less than 2%.15,19 This is in strike contrast to European studies showing a yield well over 10%.20-22 These again reflect the overuse of CTPA examination in the United States. Previous research has shown that the main reason for overutilization appears to be non-adherence to the established guidelines and ever-increasing concern of litigations leading to practice of defensive medicine.23,24 CTPA may also help to find other reasons for patient’s symptoms even when CTPA is negative for PE. This may also be contributing to increased utilization. While existing data suggest that CTPA can help find the cause of CP or shortness of breath in approximately 1/3rd of cases,25 this data may have changed over years due to increased overutilization of CTPA. Although there is no robust analysis behind this, the overall CTPA positivity of more than 10% is generally considered acceptable.26 Various strategies have been attempted to improve the yield of CTPA. Hoo et al showed that adherence to clinical decision support (CDS) with mandatory D-dimer testing results in increased CTPA yield by 15% over the course of 6 years.27 This approach is also endorsed by the American College of Emergency Physicians.28 However, the guidelines acknowledge and various other studies have shown that these recommendations are not routinely employed in clinical practice and the CTPA utilization remains high.28-30 An international multicenter trial has also shown that the US physicians perform CTPA more often than physicians from other countries in patients with low or moderate pre-test probability combined with negative D-Dimer.31

While the overutilization remains high, it does not come without potential harm. The “Choose Wisely” campaign endorsed by the American College of Chest and Emergency physicians calls for judicious use of CTPA examinations, recommending against CTPA for low clinical probability and negative D-dimer assay.32 Our study shows that with each CTPA exam patients receive a mean radiation dose of 5.5 mSv, approximately 1.8 times the mean background radiation to a person in the US. Any unnecessary or added radiation exposure is associated with increased cancer risk.33-35 Also, the mean intravenous iodinated contrast exposure was approximately 88.5 mL. In this study, we did not evaluate the risk of contrast-induced nephropathy (CIN), but it has been studied previously with reported CIN incidence between 14-24% of all CTPA studies.12,36,37 Other potential harms include directly increased healthcare costs, increased downstream testing because of imaging incidentals8, and work-force burnout.10 With approximately 90% negativity among approximately 2700 examinations in a 2-year period in a single tertiary care center in the US and some studies showing > 99% negativity among CTPA studies, the impact of overutilization in a broader and global perspective is enormous.

***Factors affecting the CTPA positivity:***

Patient Location:

An interesting finding of this study is the significant differences in the positivity rate of CTPA between ICU and out-patients, in-patients and ED patients, and between ICU patients and out-patients. Our study showed significantly higher odds of having a positive test in ICU and inpatients compared to ED and outpatients. In one of the largest analysis (of 1677 patients), Costa et al38 didn’t find any significant difference in CTPA yield among ED, ICU and inpatients.38 In a different study, no significant difference was seen in the CTPA positivity rate between in- and outpatients.27 However, in a separate study by Woo et al, a significant difference was found between inpatients and ED patients as compared to outpatients.39 The higher yield for CTPA in ICU and in-patients likely reflects high pre-test probability due to multiple high-risk and comorbid conditions such as prolonged immobility, acute medical illness, sepsis, hypoxemia, infection, heart disease, cancer, and chronic obstructive pulmonary disease. This study, by showing significantly less incidence of PE in ED patients and outpatients highlight that it may be imperative to mandate the use of CDS and D-dimer testing to improve CTPA yield. The d-dimer testing invariably has relatively poor reliability and specificity in hospitalized patients and elderly population.40-43 Hence, given inherent high pre-test probability and high incidence as shown by this data, strict adherence to d-dimer testing and CDS may be relaxed in this patient-group.

Type of study requested:

Our results didn’t show any significant difference in the yield between chest only and combined chest, abdomen, and pelvis group. All double rule out procedures were negative for PE, which may suggest that these procedures are being overused without any additional benefit. The studies ordered as chest, abdomen, and pelvis were associated with a slightly higher CTPA positivity as compared to the chest only studies (12.3% vs 10.7%), however, this difference is not statistically significant. A possible explanation for this finding may be that the patients which get chest, abdomen, and pelvis studies are likely sicker and need more extensive imaging evaluation versus patients getting chest only studies.

Patient characteristics:

We found BMI to be a significant predictor of a positive test result with a higher probability in the group between 25-40 than under 25. Very few studies have been performed to understand obesity as a risk-factor for PE. In a recently published study using Nationwide Inpatient Sample Database, Movahed et al44 showed that obese patients have significantly higher incidence of pulmonary embolism as compared to non-obese patients. In another recent study in post-orthopedic surgery patients, Sloan et al45 showed that both over-weight and obese patients had increased risk of PE. However, the risk of extremity venous thromboembolism was not elevated in these patients. Our study shows increased incidence of PE in BMI > 25 (overweight, class-I, and class-II obesity) irrespective of patient age, sex, location, or diagnosis. Interestingly, morbidly obese patients (BMI > 40) had relatively less CTPA positivity as compared to BMI 25-40. No apparent reason for this finding could be ascertained from this study and further prospective studies may be required for further evaluation. Age and sex were not a significant predictor of PE positivity rate in our study. This was also consistent with multiple prior studies.46-48

The retrospective design of this study is the primary limitation of this study. Other limitation of this study is that the CTPA yield in our study was determined based on existing radiology reports and we didn’t do a second read to verify the findings. These CTPA studies were interpreted by board-certified sub-specialized thoracic radiologists and as such may not be generalized to other facilities. Also, we didn’t evaluate if CTPA ordering was based on any CDS scoring system (appropriateness criteria) and no follow-up data was recorded on patients that had a negative CTPA study. The strength of our study lies in large sample size and inclusion of all CTA exams performed for PE evaluation over a period of two years without any exclusions (except for non-diagnostic studies). The study design was adequate to answer the questions that we raised.

***Conclusion:***

In summary, the overall CTPA yield of 10.9% may be within acceptable limits as compared to some recent studies showing exceptionally low (less than 2%) positivity, it is still below the CTPA yield from majority of European studies reflecting relative overutilization and non-adherence to CDS guidelines in the US. This leads to unnecessary radiation and contrast exposure in these patients. Our study showed that patient location and BMI are significant predictors of CTPA positivity in PE patients. Given higher yield in ICU and in-patient as well as 25-40 BMI subgroup, these patients may be subjected to a different pre-test CDS and thromboembolism prevention anticoagulation recommendations. However, this should be validated in future prospective studies.

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