**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 likely to add 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’. The negative yield of CTPA is also not without harmful effects. While the negative effects of radiation are difficult to measure, the incidence of contrast-induced nephropathy (CIN) has been shown to be 13-14%8,9 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 and evaluate if the positive yield varies based on the referral unit (inpatient, outpatient, emergency department or intensive care unit). The secondary objective was to measure the change in positive yield if a study was ordered as chest only or chest-abdomen-pelvis as one of the hypotheses for overordering CTPA is that physicians are increasingly ordering these studies due to constraints with an increased focus on turnaround time and an increased patient load limiting the ability to risk-stratify patients. The third objective of this study was to measure the radiation and contrast dose to the patients getting CTPA studies.

**Materials & Methods:**

***Data collection***

This was a retrospective study approved by local institutional review board. The patients that got CTPA between 2016 and 2018 were selected after accessing data from 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. were excluded. 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 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 factor were excluded. Patients with positive PE were further subdivided into central (if main, right or left pulmonary artery was involved) or peripheral (beyond branch pulmonary arteries including segmental/subsegmental) pulmonary embolism. Presence or absence of right heart strain was documented based on following criteria: flattening of 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, 25-35 >35).

Effective dose (mSv) was calculated for chest only examinations by the following formula: DLP (mGy·cm) x 0.014.10

**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 2369 patients got CTPA chest only while 301 patients got CTPA chest along with CT abdomen and pelvis. There were 1435 (53%) female 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. 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:**

Out of all patients, there were 296 positive test results resulting in an overall yield of 10.9%. 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 peripheral (segmental and subsegmental) location of thrombi, 5.7% (17/296) had 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). 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).

**Patient characteristics (age 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). 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). 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, location of admittance, type of scanner used, and administered effective dose 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 8. 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 = .300; over 40 and between 25 and 40: OR = 0.889, Z = 1.037, p = 0.15).

For the location variable, significant differences were found between in-patients and ED patients (OR = 1.343, Z = 1.951, p = .026), ICU patients and out-patients (OR = 1.994, Z = 2.396, p = .008), and between ICU patients and ED patients (OR = 1.721, Z = 3.150, p < .001). This indicates that the odds of a non-ICU in-patient testing positive for PE are 34.3% higher than the odds of a positive result from an ED patient. Moreover, The odds of an ICU patient having a positive CT scan are 99.4% greater than the odds for an out-patient, and 72.1% higher than the odds that an ambulatory (ED) patient tests positive. 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).

**DISCUSSION:**

Our study highlights that detection of pulmonary embolism on CTPA in a tertiary care center in the US is 10.9% and not as low as recently shown (<1%) in a similar tertiary care center in the US. The positivity in this study is similar to few other previous studies which showed a yield ranging from 6-34%.11,12 Most of the studies with less than 10% yield are from the US,13 with at least two studies showing positivity less than 2%.14,15 This is in strike contrast to European studies showing a yield well over 10%.16-18 These again reflect the over use of CTPA examination in 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.19,20 Although there is no robust analysis behind this, the overall yield of more than 10% has been generally considered acceptable.21 Stratigies to improve the diagnostic yield of CTPA examinations has been debated and studied extensively. In a study comparing the benefits of using clinical decision support (CDS) guidelines , Yan et al found that the CDS improved the yield from 4.2% to 11.2%.22 Hoo et al reported that adherence to decision guidelines with mandatory D-dimer testing results in increased CTPA yield reporting an average yield of 15% over the course of 6 years.23 Hence, this approach has been endorsed by the American College of Emergency Physicians.24 However, the guidelines also acknowledge that this recommendation is not routinely employed in clinical practice. Raja et al reported that performance feedback reports result in modest increase in adherence to these guidelines. However, they didn’t find any significant change in the use and yield of CTPA.25 Previous studies have mentioned that these scoring system guidelines have not been routinely implemented in the clinical practice and CTPA utilization remains high.26,27 The proposed reasons for lack of improvement with CDS include CTs ability to find other causes of CP or shortness of breath, physician’s desire to know cause of symptoms, increasing availability of CT scanners in ED, patient preference and fear of litigation. It has been shownis28Another reason for lack of reliance on d-dimer testing is relatively poor specificityand reliability 29-32 Mandatory reporting of CDS scoring has been found to increase adherence to these guidelines, however with no significant change in yield and CT utilization rates.27 While existing data suggest that CTPA can help find the cause of CP or shortness of breath in approximately 1/3 rd of cases,33 this data may have changed over years due to increased overutilization of CTPA.

Another 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. The regression model demonstrated higher odds of having a positive test in ICU and inpatients compared to ED and outpatients. The existing data on this question varies and most studies have shown no significant difference in CTPA yield among several subgroups. In one of the largest analysis (of 1677 patients), Costa et al28 didn’t find any significant difference in CTPA yield among ED, ICU and inpatients.34 In a different study, no significant difference was seen in the CTPA positivity rate between in- and outpatients.23 However, in a separate study by Woo et al, significant difference was found between inpatients and ED patients as compared to outpatients.35 Though we didn’t evaluate the individual patients, the higher yield in ICU and in-patients likely reflects high pre-test probability in these patients due to multiple high-risk risk and comorbid conditions including but not limited to 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. 2,30,313334-37

**Diagnostic yield and type of study requested**

Our results didn’t show any significant difference in the yield between chest only and combined chest/abdomen/pelvis group. Interestingly all double rule out procedures were negative for PE, which may suggest that these procedures are being overused without any additional benefit.

**Diagnostic yield and age/BMI:**

We found BMI to be significant predictor of a positive test result with higher probability in the group between 25-40 than under 25. Multiple previous studies have reported increased incidence of PE in obese patients.38,39 Stein et al found higher prevalence of pulmonary embolism in hospitalized patients compared to non-obese patients.38 These studies again highlight the fact that obese hospitalized patients may undergo CTPA testing without applying CDS scoring and D-dimer testing, though prospective randomized studies may be required for further evaluation. Age was not a significant predictor of PE positivity rate in ours study. This was also consistent with multiple prior studies.41-43

**Contrast and radiation exposure:**

We found a quadratic relationship between age and Contrast. This is likely due to some quadratic relationship between age and BMI, where young and old patients tend to weigh less than patients between 30 and 60. Figure 4 overlays the relationship between age and BMI onto the relationship between age and contrast so that we can compare. In this graph we do see similar relationships with age for BMI and contrast, which seems to support our theory that there is a quadratic relationship between patient age and BMI that can explain the quadratic nature of the relationship between patient age and the amount of contrast administered prior to the CT scan. Previous studies have also mentioned increase in radiation dose with increasing BMI, total adipose tissue and abdominal fat thickness.44,45

Contrast induced nephropathy (CIN) is another concern that needs attention. Though we didn’t evaluate the same in the current study, prior studies have mentioned increased risk of CIN.8,46,47 Similarly, radiation related cancer and mortality risk is an area of major concern.48-50 This again calls for reduction of unnecessary CTPA examinations by adhering to CDS guidelines to reduce risks related to radiation and contrast. “Choosing Wisely” campaign as endorsed by American college of Chest and Emergency physicians also calls for judicious use of CTPA examinations, recommending against CTPA for low clinical probability and negative D-dimer assay.49

The retrospective design of this study has several inherent limitations, primarily related to reliance on already recorded data. CTPA yield in our study was determined based only on available radiology reports and we didn’t include a second read to verify the findings. The radiology reports were produced by board-certified thoracic radiologists and as such may not be generalized to other facilities. We counted all indeterminate CTPA results as negative. However, this would have only increased the yield if some of those cases were found to be positive on second read. We didn’t evaluate if CTPA ordering was based on any CDS scoring system (appropriateness criteria). We didn’t perform any retrospectively calculation of these scoring systems either that may have predicted change in overall CTPA yield and change in yield based on admittance location. We didn’t include any follow up (clinical or imaging) examinations or additional imaging tests performed especially in patients who had no PE on CTA. Due to study performed in large tertiary care academic center, our findings may not be generalizable. We didn’t identify alternative diagnosis/incidental findings especially in patients without PE and thus could not measure the impact of alternative CT diagnosis on patient management. We didn’t perform analysis of factors predicting radiation and contrast dose administration and are unable to evaluate harms associated with radiation exposure. This may be addressed in a future study. The strength of our study lies in inclusion of all CTA exams performed for PE evaluation over a period of two years without any exclusions. The study design was adequate to answer the questions that we raised.

**Conclusion:**

In summary, our study showed that patient location and BMI are significant predictors of CTPA positivity in PE patients. Though the overall yield of 10.9% is within acceptable limits, it is still below the CTPA yield from majority of European studies, reflecting relative overutilization and non-adherence to CDS guidelines. This again reflects risk of unnecessary radiation and contrast exposure in such patients. The use of double rule out studies also appears overutilized. There is significantly higher yield in ICU and in-patient subgroups, and in 25-40 BMI subgroup. This raises a possibility that CDS guidelines and D-dimer testing could be avoided in high risk inpatient and ICU population subgroup. However, this hypothesis should be validated in future prospective studies.

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