
ORIGINAL ARTICLE

Diagnosis of Pulmonary Embolism by Computed Tomographic Pulmonary Angiography With and Without Optimal Contrast Enhancement: a Prospective Single Centre Audit

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ABSTRACT

Objectives: We aimed to establish whether there was a correlation between the diagnostic efficacy of computed tomographic pulmonary angiography for pulmonary embolism and the degree of pulmonary arterial enhancement measured objectively by main pulmonary artery attenuation level. Based on previous literature, we also evaluated the utility of setting a main pulmonary artery enhancement level of 211 Hounsfield Units (HU) as a minimum level for enhancement to optimise the number of determinate scans.

Methods: We performed an audit of the main pulmonary artery attenuation levels and reported patient outcomes of 416 computed tomographic pulmonary angiograms performed within our institution between January and April 2010. We then implemented a series of changes to our computed tomographic pulmonary angiography protocol aimed at optimising main pulmonary artery enhancement, before conducting a prospective re-audit of a further 100 computed tomographic pulmonary angiograms. Statistical analysis was performed to identify any correlation between enhancement and reported outcomes, using a main pulmonary artery attenuation level of 211 HU to denote adequate enhancement.

Results: Protocol changes resulted in an increase in main pulmonary artery enhancement and a corresponding decrease in the percentage of indeterminate examinations. There were significant differences between both the median main pulmonary artery attenuation levels of determinate and indeterminate scans ($p < 0.001$) and the percentages of determinate and indeterminate scans with main pulmonary artery attenuation levels of less than 211 HU ($p < 0.001$).

Conclusion: A significant correlation exists between pulmonary arterial enhancement level and whether or not computed tomographic pulmonary angiography is determinate for pulmonary embolism. Our audit validates the use of 211 HU as a minimum level of enhancement to optimise the number of determinate scans.

Key Words: Angiography/standards; Humans; Pulmonary embolism/diagnosis; Tomography, X-ray computed/methods; Tomography, X-ray computed/standards

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中文摘要

在有或無最佳對比度增強的情況下電腦斷層肺血管造影在診斷肺栓塞的效果：一項前瞻性單中心研究

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目的：探討電腦斷層肺血管造影對肺栓塞的診斷效果是否與肺動脈增強程度有關聯。根據過往文獻，嘗試把主肺動脈最低增強水平設定為211亨氏單位（HU）來評估是否能優化「確定診斷掃描」的數量。

方法：本研究回顧2010年1月至4月期間在本院進行的主肺動脈增強CT。研究期間共有416個電腦斷層肺血管造影結果。為優化主肺動脈增強掃描，我們把電腦斷層肺血管造影模式加以改良，然後重新進行一項前瞻性研究，檢視了100份電腦斷層肺血管造影。為確保主肺動脈有足夠的增強掃描，我們把最低水平設為211 HU，並進行統計分析來探討任何增強掃描與檢視結果之間的關係。

結果：掃描模式的改變使主肺動脈增強增加，同時令「不確定診斷掃描」的百分比相應減少。「確定診斷掃描」和「不確定診斷掃描」中的主肺動脈增強CT值的中位數有顯著差異（ $p < 0.001$ ），使用主肺動脈增強CT值為211 HU以下的「確定診斷掃描」和「不確定診斷掃描」的百分比亦有顯著差異（ $p < 0.001$ ）。

結論：肺動脈增強水平和電腦斷層肺血管造影用作診斷或排除肺栓塞有著明顯關係。本研究亦證明211 HU可以作為增強的最低水平，從而優化「確定診斷掃描」的數量。

INTRODUCTION

How does one judge the quality of computed tomographic pulmonary angiography (CTPA) to be confident that a scan is of sufficient quality to diagnose pulmonary embolism (PE)? A wide range of different methods for assessing CTPA quality have been employed to date. These range from the subjective assessment of vascular enhancement based on the experience of reporting radiologists to the more objective measurement of averages of central, segmental and sub-segmental pulmonary arterial attenuation levels and calculation of contrast-to-noise ratios.¹⁻¹⁰ However, to our knowledge, few large-scale recent studies have specifically looked into the correlation of an objective measurement of vascular enhancement with CTPA efficacy for the diagnosis of PE. Currently, there is also no consensus or formal guideline regarding the minimum level of pulmonary arterial enhancement to aim for in order to minimise the number of indeterminate scans.

In 2005, a retrospective review of 3612 CTPAs by Jones and Wittram³ found that the two most common causes of studies being reported as indeterminate for the presence of PE were motion artefact (74%) and

poor contrast enhancement (40%). The study used a main pulmonary artery (MPA) attenuation level of 250 Hounsfield Units (HU) as a threshold value for optimal pulmonary arterial enhancement and found that only 46% of CTPAs reported as indeterminate had attenuation levels which met or exceeded this level.³ Other studies considered enhancement levels of 150 HU as adequate, whereas some set 300 HU as the target for optimal enhancement.^{8,9}

A review by Wittram¹¹ in 2007 calculated the theoretical minimum attenuation levels of blood necessary to perceive all acute and chronic PEs. The values were derived from the published mean attenuation levels of acute and chronic PEs (33 and 87 HU, respectively), from which the highest possible attenuation levels of acute and chronic PEs were determined (the mean values plus 3 standard deviations [SDs]: 78 HU and 180 HU, respectively). Using the theoretical difference in attenuation required between a low-contrast lesion and its surroundings in order to be able to visualise the lesion (≥ 1 SD higher than the maximum attenuation level of the lesion), Wittram¹¹ then calculated the minimum attenuation levels of blood necessary to perceive all acute PEs as 93 HU, and for all chronic

PEs as 211 HU.¹¹⁻¹³ Despite the statistically valid basis on which these values have been derived, no currently published study has evaluated their use as minimum target levels of enhancement to optimise the diagnostic quality of CTPA.

Thus, the aim of this present study was to ascertain whether there was any correlation between the MPA enhancement level (an objective measure of CTPA image quality) and whether a scan was determinate or not for the presence of PE. To achieve our goal, we decided to examine the correlation between MPA enhancement level and diagnostic quality both before and after the introduction of changes to our CTPA protocol (specifically aimed at optimising pulmonary arterial enhancement).

Previous studies had demonstrated that increased pulmonary arterial enhancement levels in CTPA can be achieved by using higher concentrations of contrast media.¹⁴⁻¹⁷ CTPAs performed with contrast media of higher concentration have also been reported to be more diagnostic, based on subjective image quality rating.¹⁸

Instructing patients to “take a deep breath in and hold your breath” immediately prior to scanning has been reported to result in a transient interruption to the flow of contrast into the pulmonary arteries, leading to suboptimal enhancement and focal flow artefacts.^{4,10,11,19-22} No published studies have specifically compared the differences in pulmonary arterial enhancement for normal inspiration followed by breath-holding versus deep inspiration followed by breath-holding, to prevent these adverse effects. Many centres nevertheless advocate asking patients to “breathe normally” or “take a normal breath” before instructing them to hold their breath and starting the scan.^{11,22}

We hypothesised that implementing changes to the contrast media concentration and breath-hold instructions used in our institution’s CTPA protocol could optimise MPA enhancement. By these means we anticipated being able to confirm the relationship between MPA enhancement level and the diagnostic efficacy of CTPA for PE. Furthermore, by setting a standard value for adequate enhancement based on the calculations by Wittram,¹¹ we proposed it might be possible to assess the validity of a target / threshold MPA enhancement level for deciding whether a CTPA scan was or was not determinate for the presence of PE.

METHODS

Audit Criteria and Standards

Based on the calculations by Wittram in 2007,¹¹ we surmised that the theoretical minimum attenuation level of blood required for the detection of all PEs (acute and chronic) was 211 HU. In our audit, we set this value as the standard minimum level of MPA enhancement necessary when judging if the enhancement of a CTPA scan was adequate for the detection of PE. In the retrospective review of 3612 CTPAs by Jones and Wittram in 2005,³ approximately 3% of the total number of their CTPAs were reported as indeterminate due to poor contrast enhancement. To be comparable to this figure at our institution, we set our audit standard that a minimum of 97% of all CTPAs performed should have MPA attenuation levels greater than 211 HU.

Patient Selection

We conducted an initial pilot audit aimed at identifying current practice, in which we retrospectively reviewed all CTPAs performed in our institution between January and April 2010 (316 separate CTPAs; 146 women and 170 men; median age, 68 years; age range, 19-97 years). Then we prospectively reviewed an additional 100 consecutive CTPAs performed within our institution in May 2010 (52 women and 48 men; median age, 69 years; age range, 23-100 years). As there had been no change in the CTPA protocol between the two audits, their populations were combined to add greater statistical significance to the data (total number of CTPAs = 416; 198 women and 218 men; median age, 71 years; age range, 19-100 years). We then implemented changes to our CTPA protocol as listed below, and then prospectively audited a further 100 CTPAs performed at our institution in January 2011 (58 women and 42 men; median age, 69 years; age range, 24-94 years):

1. The contrast media concentration was increased from 300 mg/ml of iodine to 350 mg/ml of iodine (Optiray 350 [Ioversol], Covidien Imaging Solutions).
2. The breath-hold instruction given to patients immediately prior to scanning was changed from “take a deep breath in and hold your breath” to “breathe normally, now hold your breath” (via a standard automated verbal breathing instruction).

All the CTPAs were performed on patients undergoing investigation for suspected PE and there was no change in referral guidelines during the study period. Both inpatient and outpatient CTPAs were included and

were performed both out-of-hours and during normal working hours. The protocol changes were implemented using an agreed departmental strategy as part of routine service delivery.

Computed Tomographic Technique

All CTPAs were performed using a General Electric Healthcare (GE Healthcare, Chalfont St. Giles, UK) Lightspeed VCT XT 64 section system with the following parameters: 120 kV tube voltage, 80-750 mAs tube current (auto mAs), 0.625 mm collimation, noise index 34.65, pitch factor 0.984:1, table speed 78.74 mm/rotation, rotation time 0.5s. Examinations were performed with patients in the supine position with their arms placed above their heads. Scans were acquired in a caudocranial direction, from the top of the diaphragm to the arch of the aorta. In all, 60 to 100 ml of non-ionic-iodinated intravenous contrast medium was administered through at least a 20-gauge cannula sited in the upper limb, delivered via an Optivantage pump injector (Covidien Imaging Solutions, Hazelwood, MO, USA) at a rate of 4 ml/s. Scanning was triggered via an automated bolus tracking technique (SmartPrep; GE Healthcare), with the region of interest (ROI) centred within the MPA, at the level of its bifurcation, and scanning was triggered 5 seconds after the attenuation level within the ROI reached 100 HU (Figure 1).

Image Analysis and Review of Reports

In both audit phases, the written report of every included

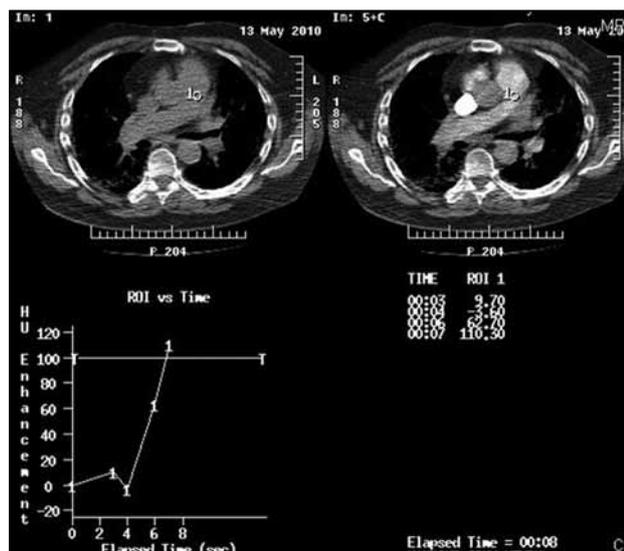


Figure 1. SmartSave image from SmartPrep (GE Healthcare) bolus tracking technique showing the region of interest centred within the main pulmonary artery (MPA), with the threshold MPA attenuation level for triggering the in-built 5-second scanning delay set at 100 Hounsfield Units.

CTPA examination was reviewed for documentary evidence that the reporting radiologist had judged the study to be positive, negative, or indeterminate/inadequate/non-diagnostic for the presence of PE. Any given reason for this judgement or additional reference to scan quality (e.g. “sub-optimal”) was also noted. All scans had been reported by consultant radiologists. All images had been reconstructed using Adaptive Statistical Iterative Reconstruction (ASIR; GE Healthcare) at a level of 40%. Images had been stored on a picture archiving and communication system (PACS; GE Healthcare) and viewed on a PACS monitor.

Using the axial images for each CTPA examination, two of the authors (SL and AS) independently measured the attenuation value of the MPA at the level of its bifurcation, using an ROI of maximum area that did not involve the vessel wall (minimum 150 mm²) [Figure 2]. Statistical analysis was performed by two independent statistical experts based at the Peninsula Deanery in the UK, in order to look for any correlation between the reported scan outcomes, the measured MPA attenuation values, and whether or not these attenuation values exceeded our audit standard of 211 HU.

RESULTS

The percentages, median, and mean MPA attenuation levels of the CTPAs reported as positive, negative, or indeterminate for PE prior to the changes in protocol are detailed in Table 1. Those following the changes in protocol are shown in Table 2. In the post-change audit, the median MPA attenuation level increased from 275 HU to 301 HU, and the percentage of CTPAs that were

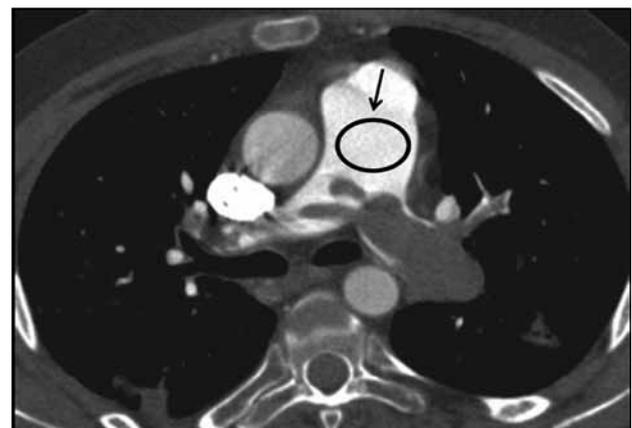


Figure 2. Representative depiction of main pulmonary artery (MPA) attenuation measurement with the region of interest (circled) at the level of the MPA bifurcation.

Table 1. Results of the first audit phase of 416 computed tomographic pulmonary angiograms, prior to the changes in protocol, showing correlations between main pulmonary artery (MPA) attenuation and reported diagnostic outcomes.

Reported outcome	% of scans with reported outcome	Median attenuation level of MPA (HU)	Mean attenuation level of MPA (HU)
Positive for PE	23	308	329
Negative for PE	61	309	326
Indeterminate for PE	16	200	215
All determinate for PE (positive + negative)	84	309	327

Abbreviations: HU = Hounsfield Units; PE = pulmonary embolism.

Table 2. Results of the re-audit phase of 100 computed tomographic pulmonary angiograms, following the changes in protocol, showing correlation between main pulmonary artery (MPA) attenuation and reported diagnostic outcomes.

Reported outcome	% of scans with reported outcome	Median attenuation level in MPA (HU)	Mean attenuation level of MPA (HU)
Positive for PE	18	301	359
Negative for PE	73	329	392
Indeterminate for PE	9	195	231
All determinate for PE (positive + negative)	91	311	385

Abbreviations: HU = Hounsfield Units; PE = pulmonary embolism.

reported as determinate (i.e. positive or negative for PE) increased from 84% to 91%. Although there was a slight decrease in the median MPA attenuation levels of scans reported as positive or indeterminate for PE, there was an increase in the median MPA attenuation level of all determinate CTPAs and the mean MPA attenuation levels of all categories of reported scan outcomes were higher following the protocol changes.

For both sets of scans, there was a significant difference between the median MPA attenuation levels of the three different categories of reported scan outcomes (Kruskal-Wallis; $p = 0.005$ for scans before the protocol changes, $p < 0.001$ for scans after the protocol changes [adjusted for ties]). A significant difference between the median MPA attenuation levels of determinate and indeterminate scans was also demonstrated (Mann-Whitney and two-sample T-tests; $p < 0.001$). The mean estimated difference in MPA attenuation level between determinate and indeterminate scans increased following the protocol changes, from 102 HU (95% confidence interval [CI], 77-126 HU) to 121 HU (95% CI, 72-169 HU). This thereby provides evidence to support the existence of a significant difference between determinate and indeterminate CTPAs in terms of MPA attenuation levels.

The range of MPA attenuation levels for each reported outcome and its relationship to the audit standard of 211 HU are depicted in Figures 3 and 4 for CTPAs

performed before and after the changes in protocol, respectively.

Before changes in the protocol, 82% of scans had MPA attenuation levels greater than our audit standard of 211 HU. Of these, 94% were reported as determinate for the presence of PE. Conversely, 18% of scans had MPA attenuation levels less than 211 HU, of which 58% were reported as indeterminate. The percentage of scans with MPA attenuation levels less than 211 HU that were reported as being indeterminate (57%) was significantly greater than those that were reported as being determinate (10.5%) [Pearson chi-square and Fisher's exact tests; $p \leq 0.001$].

Following changes in protocol, 91% of scans had MPA attenuation levels greater than our audit standard of 211 HU, of which 97% were reported as determinate for the presence of PE. Conversely, 9% of scans had MPA attenuation levels less than 211 HU, of which the proportion reported as indeterminate (two-thirds) was significantly greater than the proportion reported as determinate for the presence of PE (Pearson chi-square and Fisher's exact tests; $p < 0.001$). Thus, the changes in protocol were associated with both a larger percentage of scans with MPA attenuation levels greater than 211 HU (91% vs 82%) and more scans with MPA attenuation levels greater than 211 HU being reported as determinate for the presence of PE (97% vs 94%) [Figure 5].

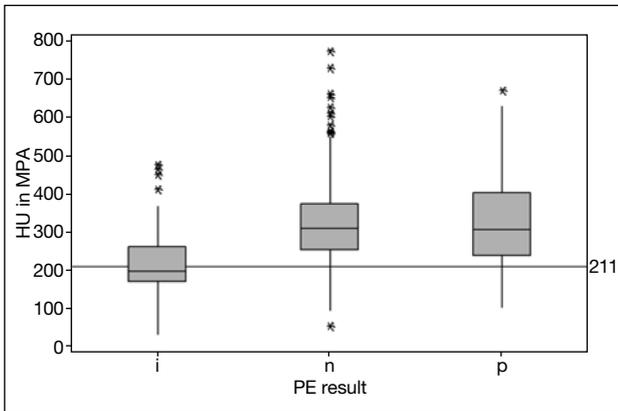


Figure 3. Boxplot of main pulmonary artery attenuation levels for indeterminate, negative, and positive computed tomographic pulmonary angiography examinations performed before changes in the protocol, with a line drawn at 211 HU to represent our audit standard. The asterisks indicate outliers. The horizontal lines within the boxes represent the medians, the lower and upper bounds of the boxes represent the 25th and 75th percentiles, and the vertical lines of the boxes represent the 5th and 95th percentiles.

Abbreviations: i = indeterminate for pulmonary embolism (PE); n = negative for PE; p = positive for PE; MPA = main pulmonary artery; HU = attenuation level in Hounsfield units.

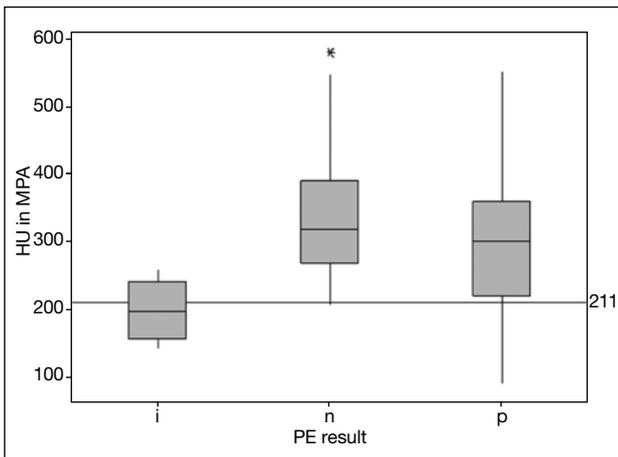


Figure 4. Boxplot of main pulmonary artery attenuation levels for indeterminate, negative, and positive computed tomographic pulmonary angiography examinations performed after the changes in the protocol, with a line drawn at 211 HU to represent our audit standard. The asterisk indicates an outlier. The horizontal lines within the boxes represent the medians, the lower and upper bounds of the boxes represent the 25th and 75th percentiles, and the vertical lines of the boxes represent the 5th and 95th percentiles.

Abbreviations: i = indeterminate for pulmonary embolism (PE); n = negative for PE; p = positive for PE; MPA = main pulmonary artery; HU = attenuation level in Hounsfield units.

The different reasons cited for scans being reported as suboptimal prior to the protocol changes are shown in Figure 6. Poor contrast enhancement was the most common (64% of all suboptimal scans; 15% of all

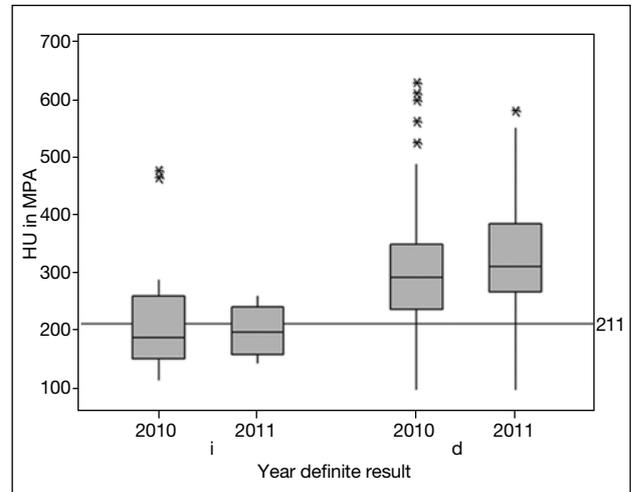


Figure 5. Direct comparison of main pulmonary artery attenuation levels for indeterminate and determinate (positive + negative) computed tomographic pulmonary angiography examinations performed before the changes in protocol (2010) and after the changes in protocol (2011). The asterisks indicate outliers. The horizontal lines within the boxes represent the medians, the lower and upper bounds of the boxes represent the 25th and 75th percentiles, and the vertical lines of the boxes represent the 5th and 95th percentiles.

Abbreviations: i = indeterminate for pulmonary embolism (PE); d = determinate (positive + negative) for PE; MPA = main pulmonary artery; HU = attenuation level in Hounsfield units.

416 scans performed prior to the protocol changes). Combining the number of scans that were reported as indeterminate with the number of scans reported as determinate but of poor quality (for any reason), the percentage of scans reported as suboptimal (whether determinate or not) decreased from 24% to 12% following the protocol changes. Correspondingly, the percentage of scans reported as being suboptimal due to poor contrast enhancement decreased from 15% to 9%. Both before and after the changes in protocol, two-thirds of the scans reported as being suboptimal due to poor contrast enhancement had MPA attenuation levels less than our audit standard of 211 HU.

Combining the data for all 516 scans performed both before and after the changes in protocol, the median MPA attenuation level of all indeterminate CTPAs was 192 HU, and the median MPA attenuation level of all determinate scans was 302 HU (Figure 7). A Mann-Whitney test demonstrated that this difference was strongly significant ($p < 0.001$, adjusted for ties).

DISCUSSION

It is important that we have an accepted and accurate means of assessing CTPA quality to confidently state

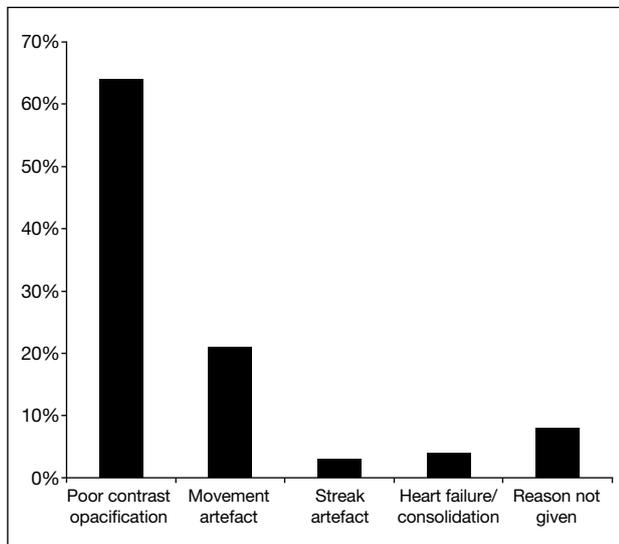


Figure 6. Reasons cited for suboptimal computed tomographic pulmonary angiography examinations prior to the changes in protocol.

whether or not a CTPA scan is of sufficient quality to be of diagnostic value. There are obviously a large number of factors that influence whether a scan is judged to be of diagnostic quality, not least the expectations of the reporting radiologist, but also their experience and ability to discern the presence of PE. There is therefore a large subjective component to the overall assessment of diagnostic quality in CTPAs and this is necessary because so many factors having an impact on the quality have to be addressed.^{3,4,7-11} It is necessary to take all of these factors into account when making a decision as to whether a scan is diagnostic, but this is clearly open to interobserver variation.

A standardised method to objectively assess the quality of arterial enhancement in CTPAs might reduce the interobserver variation associated with subjective assessment. Our results provide strong evidence to support the existence of a correlation between MPA enhancement and the diagnostic efficacy of CTPAs for PE detection or exclusion. For CTPAs performed both before and after the changes in our protocol, there was a significant difference between the median MPA attenuation levels of determinate and indeterminate scans ($p < 0.001$ in both audit phases). The estimated difference in MPA attenuation level between determinate and indeterminate scans was also significant: 102 HU (95% CI, 77-126 HU) for scans performed before the protocol changes; 121 HU (95% CI, 72-169 HU) for scans performed after the protocol changes.

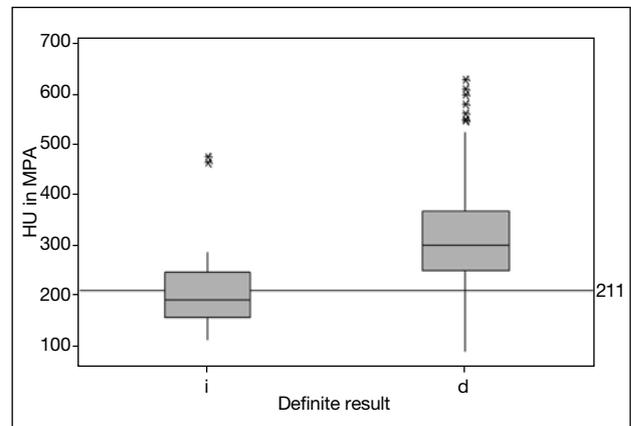


Figure 7. Boxplot of main pulmonary artery attenuation levels for all indeterminate and determinate computed tomographic pulmonary angiography examinations performed both before and after the changes in the protocol. The asterisks indicate outliers. The horizontal lines within the boxes represent the medians, the lower and upper bounds of the boxes represent the 25th and 75th percentiles, and the vertical lines of the boxes represent the 5th and 95th percentiles.

Abbreviations: i = indeterminate for pulmonary embolism (PE); d = determinate (positive + negative) for PE; MPA = main pulmonary artery; HU = attenuation level in Hounsfield units.

Our results also provide evidence to support the use of an MPA attenuation level of 211 HU as a minimum / target level of enhancement in order to increase the number of determinate CTPAs. However, following our protocol changes, one-third of the 9% of scans with MPA attenuation levels below 211 HU were still determinate, and 3% of the 91% of scans with MPA attenuation levels above 211 HU were still indeterminate. Therefore we cannot use a threshold value of 211 HU as a threshold value to infer that all scans with MPA levels less than 211 HU will be non-diagnostic. Clearly large PEs may be conspicuous at lower enhancement levels, and Wittram¹¹ calculated that the minimum attenuation level of blood required to perceive all acute PEs was only 93 HU. Similarly, we cannot use 211 HU as a threshold value in order to state that all scans with MPA levels above this value will be diagnostic. Obviously other factors need to be taken into account when deciding whether a scan is diagnostic or not, but our results show that a scan with an MPA attenuation level of greater than 211 HU appeared diagnostic 97% of the time, thus providing evidence to support the use of 211 HU as a minimum / target level of enhancement.

Setting a higher target level may further optimise the number of diagnostic scans, and our results show that this seems to be true. However, higher MPA attenuation levels may be less attainable. Following our changes in

protocol, 91% of examinations had MPA attenuation levels greater than 211 HU, but our audit standard of 97% was still not achieved. To further increase the number of determinate scans, additional work is still needed to determine the optimal, achievable target level. We therefore need to explore other ways of increasing pulmonary arterial enhancement levels within our own institution.

One limitation of our study was inter-reporter variability and the fact that a non-standardised volume of contrast (60-100 ml) was administered to patients through a non-standardised size of cannula (minimum, 20 gauge). These factors were applicable to all CTPAs performed both before and after the protocol changes. Thus, as an audit of our routine service delivery, they were acceptable limitations for our type of study and more reflective of our practices.

Our results prove that there was a highly significant correlation between the level of MPA enhancement in CTPAs and whether or not the examination was determinate for the presence of PE. Clearly, objectively assessing CTPA quality is of use in studies assessing the impact of variables on pulmonary enhancement, but our results show that it correlates well with overall diagnostic utility and therefore also has the potential to be of value in everyday practice. Our results also provide evidence to support the theoretical basis of using 211 HU as a minimum level of enhancement to optimise the number of determinate scans. When judging the overall diagnostic quality of a CTPA examination, the use of this level as a threshold value for deciding whether a scan is diagnostic must, however, be put into context with an assessment of factors other than enhancement level.

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