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Downstream Imaging Utilization After Angiography Versus CT Angiography for the Initial Evaluation of Pulmonary Embolism

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Abstract

Objective—To compare the proportion of emergency department (ED) patients who undergo subsequent chest CT/MR within one year of an initially negative scan for pulmonary embolism (PE).

Methods—This single-center, retrospective, observational study examined the use of chest CT/MR for ED patients with an MRA negative for PE during 4/2008–3/2013. We compared the 1-year scan utilization for these cases to an age- and sex-matched cohort of patients who underwent CTA. We also calculated time to first follow-up scan and mean radiation dose in each arm. Trained data abstractors used a standardized protocol and electronic case report form to gather all outcomes of interest. Results are reported as means or proportions with their associated confidence intervals.

Results—717 ED patients (430 MRAs and 287 CTAs) were included. At one year, the proportion undergoing subsequent imaging (MRA - 16.7%, CTA - 15.3%, difference =1.4% [95% CI -4.05–6.86%]) and time to first follow-up scan (difference =13 days, 95% CI -22.69–48.7) did not differ between arms. Mean radiation dose per patient at one year was significantly higher in the CTA arm (9.82 mSv [95% CI 9.12–10.53]), compared with 2.92 mSv (95% CI 1.86–3.98) with MRA. Those with an index MRA were more likely to undergo subsequent MRA (OR 3.68, 95% CI 1.22–11.12) than those with an index CTA. However, in both arms, the majority (85%) of subsequent scans were CTAs.

Conclusions—When comparing patients initially undergoing MRA versus CTA for the evaluation of PE, there was no difference in downstream chest CT/MR use at one year.

Introduction

Use of multi-detector computed tomography (CT) has continued to increase since its inception, particularly for the evaluation of pulmonary embolism (PE).(1) In a nationwide survey that asked physicians about their practices and experiences related to the evaluation of suspected acute PE, clinicians unequivocally preferred CT angiography (CTA) over other

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tests.(2) They identified availability, short interpretation times, relatively low rates of inconclusive examinations, and the possibility of identifying alternative diagnoses as contributing factors to this preference.(2)

However, CTA necessarily employs ionizing radiation, a known carcinogen, to generate images. Though the precise impact of this level of radiation exposure is not conclusively known, one study estimated that a new fatal malignancy will develop for every 2000 patients exposed to 10 mSv of radiation, a common dose for a CTA scan.(3) Another study estimated that in 2007, 1.5–2% of all cancers in the United States were directly attributable to medical imaging.(4) A newly tested alternative imaging modality for the diagnosis of PE is magnetic resonance angiography (MRA). Like CTA, it allows for a non-invasive evaluation of the pulmonary vasculature as well as the lung parenchyma, but lacks exposure to ionizing radiation.(5,6)

Since MRA avoids ionizing radiation, it likewise avoids the concomitant increase in lifetime risk of developing cancer. However, whether use of MRA will affect downstream imaging utilization is unknown. Patients evaluated for PE frequently have repeat visits for similar complaints.(7) One might posit that since MRA does not expose patients to ionizing radiation, physicians may order it more often, particularly in those patients who have previously undergone MRA. Understanding whether the chosen initial imaging modality affects subsequent imaging utilization will be of particular importance when calculating the cost-effectiveness of imaging algorithms for PE evaluation.

Therefore, the primary objective of this report is to compare the proportion of emergency department (ED) patients undergoing follow-up cross-sectional imaging of the chest (CT or MR) within one year of an initially negative imaging evaluation for PE using either CTA or MRA. We hypothesized that due to the lack of radiation exposure, patients who initially undergo MRA will have a significantly higher proportion of follow up scans than for patients who initially undergo CTA. Secondly, we sought to compare each arm (CTA versus MRA) with regard to the measured mean radiation exposure per patient, PE prevalence at one year, and time to first follow-up scan.

Methods

Study Design and Setting

This retrospective, observational study of ED patients undergoing cross-sectional imaging to evaluate for PE was conducted at an academic medical center with approximately 50,000 annual ED visits at the time. Our center has offered MRA for the diagnosis of acute PE since 2007, prior to the PIOPED III trial, and has continued this service given its observed reliability and high accuracy. We adhered to chart review guidelines to the fullest extent possible.(8) This is a sub-analysis of a parent study that compared six-month clinical outcomes of patients following pulmonary CTA versus MRA for the diagnosis of acute PE. All components of this study were HIPAA-compliant and IRB-approved.

Selection of Participants

No sample size calculation was performed; rather, the parent study used hospital billing data and the clinical indication listed for the MRA order to identify all patients 16-years-old who underwent pulmonary MRA for the evaluation of possible PE between April 1, 2008 and March 31, 2013. We then used an automated search algorithm to randomly select an age-matched (± 2 years) and sex-matched cohort of patients who underwent CTA for the diagnosis of PE during the same five-year period. Technical limitations precluded automated matching for other variables such as comorbidities, Wells' score, and referral source. Exclusionary criteria included: pregnancy, atrial fibrillation, presence of an inferior vena cava filter, or anticoagulation for at least 30 days preceding the index scan. We then limited this analysis to those patients with PE-negative imaging ordered from the ED. We excluded other referral sources (e.g. – inpatient and clinic) in order to enroll a more uniform incidence of PE and comorbidities (likely higher acuity/comorbidities in the inpatient cohort and lower in the clinic-based cohort). We excluded non-negative scans because we suspected the presence of PE would increase subsequent imaging utilization.

Interventions

MRA protocol—A full description of the MRA protocol has been previously published.⁽⁹⁾ The protocol consists of six breath-holds, each lasting 15–19 seconds. The total time in the scanner is less than 10 min (often as low as 5–6 min). The core angiographic acquisition is a rapid heavily T1-weighted 3D spoiled gradient echo (SGRE) sequence, which includes pre-contrast T1-weighted 3D SGRE, pulmonary arterial phase T1-weighted 3D SGRE, immediate post-contrast T1-weighted 3D SGRE, low flip angle post-contrast T1-weighted 3D SGRE, and T1-weighted 2D axial or 3D SGRE with fat saturation. Intravenous gadobenate dimeglumine (MultihanceTM, Bracco Diagnostics, Princeton, NJ) is administered at a dose of 0.1 mmol/kg after dilution to a total volume of 30 mL with saline. Injection rate via power injector is 1.5 mL/s.

CTA protocol—CTA images are generated using 64×0.625 mm detector configuration scanners (GE Healthcare, Waukesha, WI). Our CTA protocol consists of PA and lateral scout images followed by helical scanning from the lower neck to the diaphragm. Size-specific protocols for small, medium, and large body habitus range from 80–120 kVp with modulated mAs (smart mA with mA range 45–720 and noise index 41.5–56). Sagittal and coronal reformats of axial images are generated with 1.5 mm slice thickness at 0.75 mm intervals.

Methods and Measurements

Three trained data abstractors (two research nurses and a research associate), blinded to the study objective, used a standardized protocol and electronic case report form when reviewing patients' charts. The primary abstractor tested the protocol on 80 cases, after which it was refined, the other abstractors were trained, and the training cases were re-abstracted. Data of interest included: baseline demographic information, date and number of subsequent cross-sectional scans of the chest, accompanying radiation dose (if available), and scan interpretation. Radiation dose in CTA reports was reported as dose-length product

(mGy*cm), which we converted to milliSieverts (mSv). When unavailable, we imputed the value from the mean of all known values.

In an effort to validate the abstracted data, the primary data abstractor reviewed 10 randomly selected cases that were previously evaluated by the other two abstractors. He did find deviations from study protocol, so the research nurses were retrained and re-abstracted all of their cases. Subsequent to that re-abstraction, the primary abstractor evaluated another 10 randomly selected cases and found complete concordance on all outcomes. If an outcome of interest was unclear to the data abstractors, they flagged the case for adjudication by the three senior investigators (one emergency physician and two radiologists). Over the course of data collection, the primary abstractor and senior investigators met six times to review flagged cases and monitor abstraction quality. To further ensure data integrity, following the completion of data collection, the senior investigators abstracted a randomly selected sample of eight percent of the study cohort. They did not observe any differences.

Outcomes

The primary outcome was the proportion of patients who had subsequent cross-sectional imaging of the chest (MR or CT) at one year, though we also examined these proportions at 7, 14, and 30 days. Additionally, we compared each study arm (MRA vs CTA) with regard to the calculated mean radiation exposure per patient, PE prevalence at one year, and time to first follow-up scan. Through examining the radiologist's final scan interpretation, we defined a positive scan result as any new acute PE. These outcomes are amenable to chart review methodology since identification of subsequent scans and radiation doses are objective variables that do not rely on abstractor interpretation.

Analysis

We compared the aforementioned outcomes between those initially undergoing MRA versus CTA. The results are reported as means and proportions with confidence intervals. Differences were assessed for significance with the Mann Whitney U test, student's t-test, or Fisher's exact test, as appropriate, with $p < 0.05$ considered statistically significant. Data were analyzed using R statistical software.

Results

Characteristics of Study Participants

Of the 1,410 patients with an MRA or CTA identified in this five-year span, 136 met at least one exclusion criterion. Of the remaining 1,274 cases, 829 came from the ED, 717 of whom had a negative scan interpretation (430 MRAs, 287 CTAs). Notably, limiting this analysis to ED cases eliminated more CTAs than MRAs since a higher proportion of CTAs came from non-ED settings (i.e. – inpatient or clinic). Figure 1 illustrates the patient selection processes. For the combined study cohort, the mean patient age was 36 (SD 15.4) years and 84.5% (606/717) were female. Table 1 displays further details regarding the patients included in this analysis, particularly the mean Wells' Score for each group as well as the individual elements of the Wells' Score and the proportion of patients who had d-dimer testing performed.

Main Results

At one year, the proportion of patients undergoing subsequent imaging did not significantly differ between the index MRA versus index CTA cohorts (respectively, 16.7% [72/430] versus 15.3% [44/287]; difference = 1.4% [95%CI -4.05–6.86%]). When evaluated at 7, 14, and 30 days, the proportions with follow-up scans were 4.2%, 6.7%, and 9.3% in the index MRA cohort and 1.1%, 2.1%, and 2.8% in the index CTA cohort, respectively. The difference between proportions at each of these time intervals were 3.14% (95%CI 0.9–5.4%), 4.65% (95%CI 1.76–7.54%), and 6.5% (95%CI 3.2–9.8%), respectively, indicating that MRA had more follow up scans during each time interval. When assessing all subsequent scans, regardless of index scan, 15% (28/191) were MRAs. Stratified by index scan type, we found that 19% [24/125] of subsequent scans in the index MRA arm were MRAs compared to only 6% (4/66) of subsequent scans being MRAs in the CTA arm (OR 3.68, 95%CI 1.22–11.12).

Secondary Results

Radiation dose was available in 83.1% of cases; we imputed the value for the remainder from the mean of all available cases (10.0 mSv). Per patient, mean (95%CI) cumulative radiation exposure was 2.92 mSv (95%CI 1.86–3.98) and 9.82 mSv (95%CI 9.12–10.53) for patients in the MRA and CTA arms, respectively (difference = 4.35 mSv [95%CI 2.71–5.99]). Mean and median time in days to first subsequent scan was 101 days (95%CI 82–121; range 0–351) and 75 days (interquartile range: 10–163) in the MRA arm and 115 days (95%CI 86–143; range 0–349) and 93 days (interquartile range: 38–152) in the CTA arm (difference = 13 days, 95%CI -22.69–48.7) respectively. Figure 2 displays the Kaplan-Meier curves for any follow-up scan (2a), follow-up CTA scans (2b), and follow-up MRA scans (2c). At one year, overall prevalence of subsequent PE was 0.6% (4/717). All of these subsequent PEs were identified in the index MRA arm, though the difference between arms (0.9% versus 0%) was not statistically significant ($p=0.26$).

Discussion

In this report of subsequent chest imaging utilization following an initially negative MRA or CTA for the evaluation of PE, we found no significant difference between groups at one year of follow-up. Moreover, the mean time to first subsequent scan was also not statistically different (102 days for MRA versus 115 days for CTA). This was contrary to our working hypothesis; we initially suspected that a radiation-free imaging alternative to CTA, which incurs the same cost to patients, would lower the threshold for providers to order subsequent scans, specifically subsequent MRAs. In fact, only a minority of follow-up scans (15%) were MRAs; even in the index MRA arm, only 19% of follow-up scans were MRAs. This may indicate physician preference for CTA over MRA, echoing the results of the previously mentioned nationwide survey,⁽²⁾ or simply physician ignorance of the availability of MRA for the evaluation of PE at our center.

In line with our hypothesis, patients were more likely to have a subsequent MRA if their index scan was an MRA (19% in the index MRA arm versus 6% in the index CTA arm). However, of those re-scanned within one month, the preferred imaging test was CTA in both

arms, which was counter to our hypothesis. This suggests that physicians may not trust a negative MRA result, a finding potentially rooted in the results of the PIOPED III trial, which reported that the sensitivity of MRA for the diagnosis of PE was inferior to CTA.(10) Our own institutional data, however, showed that MRA has a negative predictive value of 97%, in line with published values for CTA imaging.(6) Alternatively, physicians may have been interested in identifying alternative pathologies that they felt were not as well elucidated on MRA.

The subject of repeated CTA examinations for the evaluation of PE and resultant radiation exposure is concerning. In 2008, Kline et al. completed a similar longitudinal study of follow-up scans for PE. Although that analysis was limited to only follow-up CTAs, those authors concluded that nearly one-third of all patients with one CTA will have a second scan with a negative read for PE.(7) Their findings highlight our concern about downstream scan utilization. Indeed, we found significantly higher mean radiation exposure in our CTA cohort, with a measured difference of 4.35 mSv (95%CI 2.71–5.99). The mean CTA scan dose for values that were not imputed was 10 mSv, which is actually the value used to estimate the lifetime risk of malignant transformation in the article by Dixon and colleagues.(3)

Limitations

There are a number of limitations to this study. First, we conducted it at a single academic medical center, which limits the generalizability of our findings. Moreover, our center routinely performs MRA well when evaluating for PE, as recommended by PIOPED III, but this is not representative of centers universally.(10) Secondly, data collection was retrospective and limited to that included in the electronic health records, potentially introducing information bias. Additionally, we were unable to control for comorbidities, which may have influenced the number of subsequent scans. However, we found not statistical difference in the prevalence of cancer between groups. Further, the indication for subsequent imaging was not always clear, which could bias our findings. Finally, some CTA imaging records did not include radiation dose, so we imputed missing values (16.9%) from the mean of reported doses.

Conclusions

While we found no difference in downstream imaging utilization at one-year follow-up comparing patients initially undergoing MRA or CTA, overall radiation exposure was significantly higher for those initially undergoing CTA. Additionally, within a month, additional scans were more likely for those initially undergoing MRA, suggesting physicians may be reticent to accept a negative MRA result in patients returning to the ED with ongoing symptoms referable to PE. These findings should be considered in the risk-benefit analysis of what scan to order for patients with possible PE.

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Take Home Points

1. At one year of follow-up, there was no difference in subsequent chest CT/MR use when comparing patients who initially underwent either MRA (16.7%) or CTA (15.3%) for the evaluation of PE.
2. In the first 30 days after an index ED visit with a negative scan for PE, more patients had a repeat chest scan if they initially underwent MRA (9.3%) versus CTA (2.8%).
3. Mean radiation dose for patients undergoing subsequent chest imaging was higher for those initially undergoing CTA (9.82 mSv) versus MRA (2.92 mSv).
4. Though follow-up MRAs were more common in patients who initially underwent MRA (OR 3.68), follow-up CTAs were more common in both groups (85% of follow-up scans).

Figure 1. STROBE flow diagram

The potentially eligible patients refers to those patients who were potentially eligible for the parent study. Those who met inclusion criteria for the parent study were considered “enrolled in research cohort.” This analysis focuses on only those enrolled from the emergency department (ED) and had a negative scan, so non-ED sources and those with non-negative index scans were excluded from our analysis. This left 717 patients, 430 in the MRA index arm and 287 in the CTA index arm.

Figure 2a

Figure 2b

Figure 2c

Figure 2.

Figure 2a. Kaplan-Meier Curve – The proportion of patents who did not undergo subsequent chest imaging (MRA or CTA), plotted against time through one year of follow-up, categorized by index scan arm.

Figure 2b. Kaplan-Meier Curve – This plot displays the proportion of patients without follow-up chest CT imaging over time, up to one year of follow-up.

Figure 2c. Kaplan-Meier Curve – Similar to 2b, this plot displays the proportion of patients without follow-up chest MR imaging over time, up to one year of follow-up.

Table 1
Patient Demographics and Wells' Score

Usual demographic information as well as individual elements of the Wells' Score and whether d-dimer was performed are listed by patient cohort.

	MRA (n = 430)	CTA (n = 287)	p-value
Age: Mean (SD)	36 ($\pm$ 15)	36 ($\pm$ 16)	1.00
% Female	85.1% (366/430)	83.6% (240/287)	0.59
Wells' Score	4.11 (SD 1.34)	4.16 (SD 1.26)	0.62
Highest Recorded HR 100	29.8% (128/430) values 100 Mean: 114 (SD 13)	40.1% (115/287) values 100 Mean: 114 (SD 15)	0.005
Surgery or Immobility for 3 Days within 4 weeks of Scan	8.4% (36/430)	10.1% (29/287)	0.43
Previous PE?	10.5% (45/430)	9.4% (27/287)	0.64
Hemoptysis	1.6% (7/430)	4.9% (14/287)	0.01
Malignancy	5.1% (22/430)	5.9% (17/287)	0.64
D-Dimer Performed	63.3% (272/430)	65.2% (187/287)	0.60