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Clinical outcomes after magnetic resonance angiography (MRA) versus computed tomographic angiography (CTA) for pulmonary embolism evaluation

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Abstract

Purpose—To compare patient outcomes following magnetic resonance angiography (MRA) versus computed tomographic angiography (CTA) ordered for suspected pulmonary embolism (PE).

Methods—In this IRB-approved, single-center, retrospective, case-control study, we reviewed the medical records of all patients evaluated for PE with MRA during a 5-year period along with age- and sex-matched controls evaluated with CTA. Only the first instance of PE evaluation during the study period was included. After application of our exclusion criteria to both study arms, the analysis included 1173 subjects. The primary endpoint was major adverse PE-related event (MAPE), which we defined as major bleeding, venous thromboembolism, or death during the 6 months following the index imaging test (MRA or CTA), obtained through medical record review.

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Compliance with ethical standards:

This study was approved by the University of Wisconsin Health Sciences Institutional Review Board and adhered to regulations as outlined in the Health Insurance Portability and Accountability Act.

Logistic regression, Chi-square test for independence, and Fisher's exact test were used with a $p < 0.05$ threshold.

Results—The overall 6-month MAPE rate following MRA (5.4%) was lower than following CTA (13.6%, $p < 0.01$). Amongst outpatients, the MAPE rate was lower for MRA (3.7%) than for CTA (8.0%, $p = 0.01$). Accounting for age, sex, referral source, BMI, and Wells' Score, patients were less likely to suffer MAPE than those who underwent CTA, with an odds ratio of 0.44 [0.24, 0.80]. Technical success rate did not differ significantly between MRA (92.6%) and CTA (90.5%) groups ($p = 0.41$).

Conclusion—Within the inherent limitations of a retrospective case-controlled analysis, we observed that the rate of MAPE was lower (more favorable) for patients following pulmonary MRA for the primary evaluation of suspected PE than following CTA.

Keywords

Pulmonary embolism; magnetic resonance angiography; computed tomographic angiography; patient-oriented outcomes; clinical effectiveness

INTRODUCTION

Chest pain, shortness of breath, and syncope are frequent symptoms that lead physicians to evaluate patients for pulmonary embolism (PE) [1]. A missed diagnosis of PE can be fatal [1,2]. Unfortunately, symptoms are often non-specific, leading to heavy reliance on imaging, usually computed tomographic angiography (CTA), to make the diagnosis [3,4]. However, CTA has important drawbacks. First, CTA uses ionizing radiation, which recent literature suggests increases the lifetime risk of malignancy [5]. Second, CTA requires nephrotoxic iodinated contrast material. Recent evidence shows that PE is only present in 5–10% of the patients undergoing CTA, resulting in up to 19 patients being exposed to the risks of CTA for every PE detected [6].

Furthermore, there is growing concern that use of CTA may be resulting in the over-treatment of clinically insignificant subsegmental pulmonary emboli (SSPE) [7–9]. For example, in the setting of SSPE, multi-detector CTA is twice as sensitive as single detector CTA for PE, but there is no difference in the incidence of adverse venous thromboembolic (VTE) events at follow-up [7,8]. For this reason, *diagnostic efficacy studies using CTA as a reference standard for the detection of PE may not be the most clinically relevant approach*. In the setting of suspected PE, clinically relevant patient outcomes [10] can be measured by the incidence of major adverse PE-related events (MAPE) (e.g., death, VTE, or major bleeding events).

An alternative to CTA is contrast-enhanced magnetic resonance angiography (MRA), which requires neither ionizing radiation nor nephrotoxic contrast material. The risks of gadolinium-based contrast agents (GBCA) are very low. The risk of anaphylaxis is lower for GBCAs than for iodinated contrast agents. For patients with end-stage chronic renal disease, there is a very small risk of developing nephrogenic systemic fibrosis using certain GBCAs [11], although based on improved understanding of NSF, no cases have been reported in almost a decade. Contrast-enhanced MRA has had variable levels of efficacy and technical

success for the diagnosis of PE [12–17]. The largest published study comparing MRA to CTA was the PIOPED III study, a prospective, multicenter study that evaluated the efficacy of MRA for the diagnosis of PE using CTA as the reference standard [18]. In that study, MRA demonstrated a modest sensitivity of 78% (95% CI: 67–86%) and excellent specificity 99% (95% CI: 96–100%). However, the clinical effectiveness of MRA compared with CTA, as measured by patient-oriented clinical outcomes, could not be assessed because all study subjects were treated on the basis of their CTA result and clinical outcomes were not measured.

For these reasons, since 2008, our institution has offered as a clinical service a focused 10-min MRA exam for the primary evaluation of pulmonary embolism [19]. This was initially intended for use with patients who were more susceptible to chest irradiation (e.g., younger and/or female) or those for whom CTA was contraindicated. However, the choice of MRA or CTA was left to the discretion of referring physicians. A recently published small retrospective cohort study showed that clinical outcomes following MRA as the primary imaging test for PE were similar to those reported in the literature following CTA [20].

Our purpose in this pragmatic, real-world retrospective study was to measure the 6-month patient outcomes following MRA and to compare these with an age- and sex-matched cohort of patients evaluated with CTA at the same institution over the same time period.

MATERIALS AND METHODS

Study Design and Population

This was a single-center, HIPAA-compliant, IRB-approved retrospective case-control study. We included all patients age 16 years or older who had been evaluated for PE using MRA as the primary imaging test during a 5-year period (April 1, 2008 – March 31, 2013). All of these MRA exams were performed using a previously published protocol [19,20]. Examples of the appearance of normal versus a scan with pulmonary embolism can be seen in the included Figure 1. These MRA exams were interpreted by the same process as CTA exams performed during the same period, with final interpretations provided by specialty-trained board-certified cardiothoracic radiologists. No *a priori* guidelines were used by referring physicians to select patients for MRA during this period. However, the primary reason the clinical MRA service was initiated was to provide an alternative approach for imaging those patients that referring physicians thought were at increased risk from ionizing radiation or renal toxicity. We suspected that this resulted in physicians ordering MRA more frequently in younger and female patients. Therefore, to control for these potential confounders, we used an automated search algorithm and the electronic medical record (EMR) to select age- (± 2 years) and sex-matched controls (1:1) from amongst all the patients who were evaluated for PE using CTA during the same time period. Due to technical and funding limitations, it was not feasible to automatically match for other possible confounders (e.g. referral source, comorbidities, Wells' score, or bleeding risk) or determine whether a case met exclusion criteria prior to manual medical records abstraction.

From these potential cases and controls, we excluded those for whom the identified imaging exam was not the first imaging exam performed for PE within the inclusion dates. We also

excluded all subjects with a pre-existing IVC filter, with atrial fibrillation, or who had been anticoagulated for at least 30 days prior to the index exam because these conditions could be risk factors for MAPE independent of the imaging exam chosen (Figure 2).

Data Abstraction

Study personnel performed data abstraction from the EMR in a randomized order, recording the data directly using electronic case report forms in the REDCap (Research Electronic Data Capture) system [21]. Due to the retrospective study design it was not feasible to follow-up directly with patients. Using the original data abstraction protocol, the primary data abstractor, a medical student with prior research experience, was trained on the first 80 cases, after which the data abstraction protocol was refined to address data abstraction uncertainties. The resulting data abstraction protocol and REDCap electronic case report form are included in Appendices S1–S2. The primary abstractor then trained two additional abstractors, both full-time research nurses, in the data abstraction protocol. The training cases were then re-evaluated using the final abstraction protocol. The same data abstraction protocol was followed for both MRA and CTA groups. It was not possible to blind the abstractors to the type of index exam because the radiology report for the index imaging exam had to be reviewed. The abstractors flagged ambiguous data for review by an expert panel of three investigators (two experienced cardiothoracic radiologists and an emergency medicine physician). The expert panel met in person 5 times during the 11-month data abstraction process to review ambiguous data and reached its decisions by consensus, with close reference to the *a priori* study protocol. The members of the expert panel re-abstracted (i.e. audited) a randomly selected sample of 92 (7.8%) of the records, blinded to the results of the primary abstraction, to monitor the performance of the abstractors.

Baseline Demographic and PE Risk Factors

We recorded baseline demographic data (age, sex, body mass index (BMI)) and referral source (inpatient, emergency department, clinic, or unknown). We compared the age and sex distribution of our study population with the population of all patients imaged with CTA for pulmonary embolism during the inclusion timeframe. We also collected data from the index encounter necessary to calculate two widely used clinical decision rules for PE risk stratification: Wells' Score and Revised Geneva Score [22,23]. Our institution does not follow rigid guidelines regarding the use of PE risk stratification scoring or D-dimer in the setting of suspected PE. The Wells' Score criterion "alternative diagnosis is less likely than PE" was assumed to be true since all patients were at high enough risk to warrant cross-sectional imaging and there was no reliable method for retrospectively determining the referring physicians' subjective assessment of pre-test probability. We also recorded results of D-dimer testing, if performed during the index encounter.

Primary Outcomes

Primary outcomes during the 6 months following the index encounter included all-cause mortality, major VTE events, or major bleeding events (collectively referred to as Major Adverse PE-related Events; or "MAPE"). This metric is analogous to the well-known Major Adverse Cardiac Events (MACE) metric used in the cardiology literature [24]. We ruled out mortality by the 6-month time point if the subject had an encounter recorded in the EMR

after this time point or if there was no record of death prior to this time point in the Social Security Death Index. Major VTE events included imaging-diagnosed new PE or deep venous thrombosis. Major bleeding events included symptomatic bleeding at a critical site (intracranial, intraspinal, intraocular, retroperitoneal, intra-articular, pericardial, or intramuscular with compartment syndrome), bleeding with a hemoglobin concentration decrease of at least 2 g/dL, or bleeding requiring a transfusion of at least 2 units of packed red blood cells [25].

Secondary Outcomes

We also recorded the index imaging results, based upon the radiology report (positive, negative, or equivocal for PE), and categorized the imaging exam as “technically limited” if the report impression included either the word “limited” or a recommendation for another imaging study to evaluate for PE. These pragmatic real-world definitions were used rather than formal retrospective image review because the radiology report represents the image-derived data that was actually used by referring clinicians in subsequent treatment decisions.

Data Analysis and Statistical Considerations

We analyzed the data using the R statistical package. All of the comparisons of proportions were performed using either a chi-square test for independence or Fisher’s exact test, depending on the counts in each cell. A p-value < 0.05 (two-sided) was used to determine statistical significance. We tested the association of study arm (MRA versus CTA) with demographic variables, PE risk (Wells’ and Revised Geneva scores), D-dimer, and referral source to assess how well the populations were matched.

We compared the occurrence of 6-month MAPEs between the MRA and CTA arms, both for all subjects as well as for only those who were outpatients (clinic, ED, or unknown referral source). Because ineligible subjects were excluded from the analysis after matching due to technical and budgetary limits, we first determined differences between the MRA and CTA groups independent of matching. We used logistic regression to predict occurrence of 6-month MAPE, accounting for age, sex, referral source (inpatient vs non-inpatient), and scan type.

In addition, we performed a paired analysis predicting adverse event, using the subset of pairs where both subjects (MRA and CTA) were eligible for the study. We used both McNemar’s test and conditional logistic regression. Conditional logistic regression treats the subject-pair as a stratum, allowing adjustment for other non-matching variables that may predict the outcome.

We also compared proportions of each type of adverse event, imaging results (positive, negative, or equivocal for PE), and technically limited exams between MRA and CTA arms.

RESULTS

Patient Characteristics

Our institution performed 674 MRA exams for assessment of PE during the inclusion time period. Thus, an additional 674 matched CTA controls were randomly selected from

amongst the 6318 CTAs performed during the inclusion timeframe. The resulting study population was significantly younger than the pool of all patients scanned with CTA ($p<0.01$), with a significantly larger proportion of females ($p<0.01$), due to clinical practice patterns at our institution that result in younger patients and female patients more often being referred for MRA (Table S1). Of these, 82 MRA exams and 93 CTA exams were excluded due to presence of IVC filter, atrial fibrillation, pre-existing anticoagulation, or prior PE imaging exam during the study period. This resulted in the inclusion of 1173 unique subjects (592 MRA cases and 581 CTA controls) in the analysis (Figure 2).

Overall, the MRA and CTA groups did not differ significantly in demographics (age, sex, BMI) or Wells' Score. The groups differed slightly in their Revised Geneva Scores ($p=0.03$) and differed markedly in D-dimer testing ($p<0.01$) and referral source ($p<0.01$). The difference in D-dimer results was largely due to the fact that more D-dimer tests were obtained in the MRA group (56.3%) than in the CTA group (45.1%). Amongst those who underwent D-dimer testing, however, the positivity rates were very similar (87% of the CTA group and 86% of the MRA group). More of the MRA subjects were referred as outpatients (Emergency Department, clinic, or unknown) and more CTA subjects were referred as inpatients. Subgroup analysis of only those 866 subjects (491 MRA cases and 375 CTA controls) referred as outpatients showed no significant difference in any demographic feature or PE risk factor score (Table 1).

Primary Outcomes

The overall 6-month adverse event rate was 5.4% (95% CI: 3.8–7.6%) in the MRA group and 13.6% (95% CI: 11.0–16.7%) in CTA control group ($p<0.01$). Amongst outpatients, the 6-month adverse event rate was 3.7% (95% CI: 2.3–5.8%) following MRA and 8.0% (95% CI: 5.5–11.3%) following CTA ($p=0.01$). There was no significant difference in the distribution of types of adverse events between the groups ($p=0.35$ overall; $p=0.55$ for outpatients; Table 2).

Logistic regression accounting for age, sex, referral source, and scan type, showed an association of scan type with the odds of having a MAPE by 6 months (Table 3). Those receiving MRA were less likely to have a MAPE after adjusting for these factors (OR: 0.44 [0.24, 0.80] relative to outpatient CTA). Because there was insufficient EMR data for calculation of BMI or Wells' Score for all subjects, inclusion of these additional variables as predictors resulted in a smaller number of subjects ($n=959$) being included in this subanalysis. Despite this, when BMI and Wells' Score were included as predictors, the risk of experiencing a MAPE by 6 months following MRA remained lower than following outpatient CTA (OR: 0.36 [0.19, 0.66]).

We also performed a confirmatory paired analysis including only the 513 paired subjects who were both eligible for the study. The proportion of pairs with "MRA without MAPE" and "CTA with MAPE" was higher (12.5%) than the proportion of pairs with "MRA with MAPE" and "CTA without MAPE" (4.5%) with subjects matched by age and sex (McNemar $p<0.01$). Table 4 shows the conditional logistic regression of scan type and referral source as a predictor of event, accounting for matched pairs. Here, MRA was found

to be protective for MAPE (OR: 0.33 [0.13, 0.82], $p=0.02$) while referral source was not (OR: 1.82 [0.55, 6.02], $p=0.33$).

Of the 92 subjects whose records were re-abstracted by members of the expert panel, 3/92 (3.3%) had a MAPE. All over-reads agreed with the results of the primary abstraction.

Secondary Outcomes

The imaging results differed between the groups ($p=0.03$), with the CTA group having more positive (10.8% vs 8.8%) and equivocal (6.9% vs 3.9%) exams than the MRA group. Breakdown of MAPEs by imaging result is shown in Table S2. The rate of technically limited exams did not differ between the groups ($p=0.41$), with 9.5% of CTAs and 7.4% of MRAs categorized as technically limited by the interpreting radiologist. These comparisons were similar when limited only to outpatients (Table 2).

DISCUSSION

In this retrospective, case-control study of 1173 subjects, the overall 6-month rate for MAPE following MRA (5.4%) was lower than the rate following CTA (13.6%). This is the first large study of its kind comparing the clinically relevant 6-month outcomes of patients who underwent MRA versus those who underwent CTA as the first-line test for the diagnosis of PE. In the population assessed at our single site, we found that that MRA was a safe, technically robust, and clinically effective test for the primary detection of PE.

Technical success rates and equivocal interpretation rates for MRA and CTA in our study did not differ significantly. The technical success rate of MRA in our study (92.6%) was markedly higher than that reported in the PIOPED III study (75%) [18]; however, direct comparison is problematic due to markedly different methods for assessing technical adequacy. Our high technical success rate is likely due to a combination of maturing scanner technology, including improved phased array coils, advanced 2D versus 1D parallel imaging algorithms, use of diluted contrast, and triphasic acquisitions [14,19,20,26,27].

The MRA protocol used in this study can be implemented using commercial software on MRI scanners made by all of the major manufacturers. While there has been some concern that MRA may not show alternative diagnoses to PE as well as CTA, a recent publication showed that MRA also enables the diagnosis of a wide range of alternative pathologies, very similar to CTA [28].

This study has limitations. First, it was a retrospective study at a single institution where MRA is performed and interpreted by radiologists experienced in the technique. Second, our study population was biased towards younger and female patients due to clinical practice patterns at our institution, which limits generalizability. MRAs are preferentially requested when the treating physician is especially concerned about the potential risks of ionizing radiation. Third, it is possible that subjects experienced an adverse event that was not recorded in our institution's EMR and was therefore not captured by our study design. Fourth, there may have been uncontrolled differences in comorbidities between groups. We attempted to control for these potential biases through comparison with a CTA control arm

that closely matched the MRA arm in terms of risk for pulmonary embolism, age, sex, and body mass index. However, there were more inpatients in the CTA group, and the adverse event rate following a negative imaging exam was greater in the CTA group than in the MRA group (11.9% vs 4.3%, $p<0.01$), suggesting that the CTA arm had more comorbidities. Despite this, PE was detected in 8.8% of MRAs, comparable to the rate of PE both in our CTA arm (10.8%) and as reported in the literature [6].

In summary, based on this single center review of 6-month clinical outcomes, we found that the clinical effectiveness following contrast-enhanced pulmonary MRA for the primary imaging evaluation of suspected PE was similar to that following CTA. Our results support the need for a prospective, multicenter, randomized clinical effectiveness trial of MRA versus CTA for primary evaluation of PE using clinical outcomes (MAPE) instead of imaging-focused outcomes. Doing so will mature our knowledge base beyond that of a traditional diagnostic efficacy study and into the realm of true comparative effectiveness research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Coronal (A) and axial (B) images of an example of PE MRA image quality. In this PE MRA examination, the pulmonary arteries are well seen to the subsegmental level. In addition, some lung perfusion is seen due to fortuitous timing of the imaging with the arrival of the contrast bolus, increasing the confidence of the interpreting radiologist that there are no pulmonary emboli present. The right four panes display an example of pulmonary embolism on PE MRA in coronal (C, E) and axial (D, F) configurations. In this case of multiple pulmonary emboli (arrows), the filling defects created by pulmonary emboli within the pulmonary arteries are clearly depicted.

Figure 2.
Study flow diagram.

Table 1

Demographics and pulmonary embolism risk factors. Baseline demographics did not significantly differ between the groups, as expected based upon our matching protocol. However there was a significant difference in referral source – more emergency department (ED) patients in the MRA group and more inpatients (IP) in the CTA group. While there was a difference in Revised Geneva Score between the groups, there was no significant difference in Wells' Score. Amongst outpatients (ED, clinic, and unknown referral sources), there was no significant difference between MRA and CTA groups with respect to either clinical decision rule (Wells' Score or Geneva Score), demonstrating that the MRA and CTA arms were well-matched.

	ALL SUBJECTS		OUTPATIENTS ONLY	
	MRA	CTA	MRA	CTA
N	592	581	491	375
Age	p = 0.94		p = 0.97	
16–25	163 (27.5%)	166 (28.6%)	144 (29.3%)	116 (30.9%)
26–35	165 (27.9%)	152 (26.2%)	148 (30.1%)	104 (27.7%)
36–45	89 (15.0%)	93 (16.0%)	81 (16.5%)	57 (15.2%)
46–55	64 (10.8%)	66 (11.4%)	46 (9.4%)	40 (10.7%)
56–65	61 (10.3%)	59 (10.2%)	41 (8.4%)	34 (9.1%)
66–75	32 (5.4%)	33 (5.7%)	19 (3.9%)	15 (4.0%)
76–91	18 (3.0%)	12 (2.1%)	12 (2.4%)	9 (2.4%)
Sex	p = 0.46		p = 0.29	
Male	110 (18.6%)	119 (20.5%)	76 (15.5%)	69 (18.4%)
Female	482 (81.4%)	462 (79.5%)	415 (84.5%)	306 (81.6%)
Body Mass Index	p = 0.86		p = 0.32	
(13,18.5]	13 (2.2%)	14 (2.4%)	10 (2.0%)	10 (2.7%)
(18.5,25]	165 (27.9%)	143 (24.6%)	136 (27.7%)	89 (23.7%)
(25,30]	130 (22.0%)	134 (23.1%)	107 (21.8%)	70 (18.7%)
(30,35]	96 (16.2%)	94 (26.2%)	76 (15.5%)	55 (14.7%)
(35,73]	123 (20.8%)	132 (22.7%)	97 (19.8%)	90 (24.0%)
Unknown	65 (11.0%)	64 (11.0%)	65 (13.2%)	61 (16.3%)
Wells' Score	p = 0.78		p = 0.38	
3–6	484 (81.8%)	477 (82.1%)	411 (83.7%)	312 (83.2%)
7+	57 (9.6%)	50 (8.6%)	33 (6.7%)	19 (5.1%)
Unknown	51 (8.6%)	54 (9.3%)	47 (9.6%)	44 (11.7%)
Revised Geneva Score	p = 0.03		p = 0.15	
0–3	188 (31.8%)	143 (24.6%)	182 (37.1%)	112 (29.9%)
4–10	342 (57.8%)	377 (64.9%)	258 (52.5%)	216 (57.6%)
11+	11 (1.9%)	7 (1.2%)	4 (0.8%)	3 (0.8%)
Unknown	51 (8.6%)	54 (9.3%)	47 (9.6%)	44 (11.7%)
D-dimer	p < 0.01		p = 0.24	
Negative	48 (8.1%)	34 (5.9%)	47 (9.6%)	31 (8.3%)
Positive	285 (48.1%)	228 (39.2%)	267 (54.4%)	188 (50.1%)
Unknown	259 (43.8%)	319 (54.9%)	177 (36%)	156 (41.6%)

	ALL SUBJECTS		OUTPATIENTS ONLY	
	MRA	CTA	MRA	CTA
Referral Source	p < 0.01			
IP	101 (17.1%)	206 (35.5%)		
ED	451 (76.2%)	321 (55.2%)		
Clinic	29 (4.9%)	41 (7.1%)		
Unknown	11 (1.9%)	13 (2.2%)		

Table 2

Univariate Outcomes Analysis. Overall adverse event rates following MRA were lower than following CTA amongst all patients (5.4% vs 13.6%, $p < 0.01$) and within the subset of patients presenting as outpatients (3.7% vs 8.0%, $p < 0.01$). A breakdown by imaging result (positive, negative, or equivocal) is provided in Table S2. There was no significant difference in the technical success rate of MRA versus CTA.

	ALL SUBJECTS		OUTPATIENTS ONLY	
	MRA	CTA	MRA	CTA
N	592	581	491	375
Adverse Event	$p < 0.01$		$p < 0.01$	
None	560 (94.6%)	502 (86.4%)	473 (96.3%)	345 (92.0%)
Event	32 (5.4%)	79 (13.6%)	18 (3.7%)	30 (8.0%)
Adverse Event Type	$p = 0.35$		$p = 0.55$	
DVT/PE	3/32 (9.4%)	6/79 (7.6%)	3/18 (16.7%)	3/30 (10.0%)
Major Bleed	12/32 (37.5%)	41/79 (51.9%)	6/18 (33.3%)	15/30 (50.0%)
Death	17/32 (53.1%)	32/79 (40.5%)	9/18 (50.0%)	12/30 (40.0%)
Test Result	$p = 0.03$		$p = 0.05$	
Clearly Positive	52 (8.8%)	63 (10.8%)	37 (7.5%)	40 (10.7%)
Clearly Negative	517 (87.3%)	478 (82.3%)	437 (89.0%)	313 (83.5%)
Equivocal	23 (3.9%)	40 (6.9%)	17 (3.5%)	22 (5.9%)
Technically Limited	$p = 0.41$		$p = 0.42$	
“limited” in interpretation	30 (5.1%)	35 (6.0%)	20 (4.1%)	19 (5.1%)
Additional imaging recommended to rule out PE	14 (2.4%)	20 (3.4%)	11 (2.2%)	13 (3.5%)
Not technically limited	548 (92.6%)	526 (90.5%)	460 (93.7%)	343 (91.5%)

Table 3

Multivariate Outcomes Analysis. Logistic regression of predictors for MAPE by 6 months shows that MRA was protective of MAPE relative to outpatient CTA when the variables of age, sex, Wells' score, BMI and inpatient status are taken into consideration. Missing Wells' Score or BMI data decreased the number of subjects included in the analysis that incorporated all of these predictors. Reference group: Outpatient CTA, OR=1.00

Accounting for age, sex, referral source and scan type (n=1173)				
	Estimate	Std. Error	OR [95% CI]	p-value
Intercept	-3.2583	0.31	0.04 [0.02–0.07]	<0.01
Age (per year)	0.0195	0.01	1.02 [1.01–1.03]	<0.01
Male	0.2626	0.24	1.30 [0.80–2.06]	0.27
MRA	-0.8180	0.31	0.44 [0.24–0.80]	<0.01
IP	1.2148	0.25	3.37 [2.06–5.59]	<0.01
MRA:IP	-0.0343	0.46	0.97 [0.39–2.36]	0.94

Accounting for age, sex, referral source, BMI, Wells Score and scan type (n=959)				
	Estimate	Std. Error	OR [95% CI]	p-value
Intercept	-2.9364	0.60	0.05 [0.02–0.17]	<0.01
Age (per year)	0.0197	0.01	1.02 [1.01–1.03]	<0.01
Male	0.1779	0.25	1.19 [0.72–1.94]	0.48
MRA	-1.0297	0.32	0.36 [0.19–0.66]	<0.01
IP	0.7161	0.27	2.05 [1.21–3.49]	<0.01
BMI (per unit)	-0.0308	0.01	0.97 [0.94–1.00]	0.03
Wells' Score (per point)	0.2031	0.07	1.23 [1.07–1.40]	<0.01
MRA:IP	0.1580	0.48	1.17 [0.45–2.99]	0.74

Table 4

Paired Multivariate Outcomes Analysis. Paired analysis confirms the results of the primary unpaired analysis, showing the MRA is predictive of lower incidence of MAPE by 6 months. Reference group: Outpatient CTA, OR=1.00

Matched Pairs Conditional Logistic Regression (n=1026)			
	Estimate	OR [95% CI]	p-value
MRA	-1.116	0.33 [0.13–0.82]	0.02
IP	0.597	1.82 [0.55–6.02]	0.33
MRA:IP	0.934	2.54 [0.46–14.22]	0.29