8-24-2009

The Effect of Left- Versus Right-Sided Contrast Infusion on Attenuation in Chest CT Angiograms

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The Effect of Left- Versus Right-Sided Contrast Infusion on

Attenuation in Chest CT Angiograms

A Thesis Submitted to the

Yale University School of Medicine

in Partial Fulfillment of the Requirements for the

Degree of Doctor of Medicine

by

Lars J. Grimm

Class of 2009
THE EFFECT OF LEFT- VERSUS RIGHT-SIDED CONTRAST INFUSION ON ATTENUATION IN CHEST CT ANGIOGRAMS

Lars J. Grimm, Daniel Cornfeld, Hamid R. Mojibian. Department of Diagnostic Radiology, Yale University, School of Medicine, New Haven, CT.

This study assesses if the arm of contrast infusion influences attenuation of the main pulmonary artery in CT angiograms to evaluate for pulmonary emboli.

With IRB approval, 407 consecutive CT angiograms performed to exclude pulmonary emboli were reviewed. Patient characteristics, study details, and interpretation results were collected. After exclusion criteria were applied, 100 studies from each of our three scanners (4, 16, and 64 slice) remained. A reader, blinded to injection side, reviewed the images and recorded the attenuation of the main pulmonary artery.

The average post-contrast attenuation in the main pulmonary artery was similar if infused through the right (275.4 HU) or left (275.0 HU) arm when controlling for confounders with a multiple regression analysis (p = 0.82). There was no statistical difference (p > 0.05) in the number of scans with attenuation less than 250 (45.9% right, 42.9% left), 200 (25.0% right, 29.0% left), or 150 HU (11.6% right, 12.3% left) and no difference in the number of scans interpreted as indeterminate (1% right, 4% left) or non-diagnostic (3% right, 3% left).

Main pulmonary artery attenuation is not dependent on the arm of infusion when evaluating mean attenuation, attenuation beneath thresholds of 250, 200, or 150 HU, or indeterminate or non-diagnostic interpretations for patients undergoing a CT angiogram of the chest to rule out pulmonary emboli.
I would like to acknowledge the guidance of my research mentors Dr. Daniel Cornfeld and Dr. Hamid Mojibian. This project would not have been possible without the support of the Office of Student Research: Dr. John Forrest Jr., Donna Carranzo, and Mae Geter. Funding for this research was made available through the Yale Endowed One Year Research Fellowship.
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INTRODUCTION

Pulmonary emboli (PE) are a major cause of morbidity and mortality. Autopsy studies list pulmonary emboli as a contributing underlying cause of death in as many as 33.9-37.3% of cases\(^1,2\). The incidence of pulmonary emboli has not changed in the last three decades, despite increased preventative measures and more routine anti-coagulation therapy. Unfortunately, pulmonary emboli are very difficult to diagnose clinically and are frequently only detected during autopsy. Although Well described a list of criteria for the diagnosis of deep vein thrombi (DVT) in 1995, which is the most common source location for pulmonary emboli, clinicians have continued to struggle with providing accurate diagnoses\(^3\). The difficulty in diagnosis frequently results from non-specific patient presentations and poor initial diagnostic tests. The classic clinical triad of dyspnea, tachycardia, and chest pain are collectively found in only a minority of patients, and are commonly the result of more benign processes. DVT are detected in less than half of confirmed cases of pulmonary emboli, and both electrocardiogram and chest x-ray abnormalities are equally poor indicators\(^4\). Although extremely sensitive, d-dimer assays are only approximately 50% specific. False positive results can be secondary to age, pregnancy, trauma, inflammatory disease, surgery, and liver disease. Unfortunately, these confounders exist in the patient population that is at greatest risk for developing a thromboembolism. As a result, without a test that is both sensitive and specific for pulmonary emboli, it is extremely difficult for clinicians to adequately determine if a patient has a pulmonary embolism.

Physicians must maintain a high index of suspicion for pulmonary embolism in any patient who suffers from a sudden onset unexplained major event, such as chest pain,
syncope, or arrhythmia, whether or not it appears cardiovascular in nature. The need for prompt diagnosis is magnified by the large discrepancy that exists between the treated and untreated mortality rates for patients who develop a pulmonary embolism. The untreated mortality rate is 5% among ambulatory patients, and up to 30% for hospitalized patients\(^5,6\). With prompt anticoagulation treatment the hospitalized mortality rate can be reduced to less than 8%. Treatment for pulmonary emboli is most commonly via anticoagulation therapy, usually with immediate short term heparin administration and then long term with warfarin. Patients subsequently require frequent monitoring of blood international normalized ratio (INR). Alternative treatment modalities for patients who are poor candidates for anticoagulation are inferior vena cava filter placement, clot thrombolysis, or surgical pulmonary thrombectomy. The initiation of anticoagulation requires a careful analysis of the risk-benefit ratio tailored to the individual patient. Patients undergoing anticoagulation therapy have a greatly increased risk of developing hemorrhagic complications, and thus must be carefully monitored. Fortunately though, the mortality rate for pulmonary emboli has declined dramatically over the last 20 years thanks to better diagnostic and treatment methodologies. Age adjusted mortality rates have reduced from 191 per million in 1979 to 94 per million in 1998\(^2\). As a result, it is especially important to ensure that the methods used to detect pulmonary emboli are both quick and accurate, because the potential complications of a false positive or false negative result may be fatal.

Although history, physical examination, and laboratory studies are the primary and most important steps towards diagnosing a pulmonary embolism\(^7\), there has been an increased reliance on imaging to provide more definitive diagnoses. Ventilation-
perfusion (V/Q) scans, pulmonary angiograms, and CT pulmonary angiography have become the most well known radiologic methods for diagnosis. V/Q scans are the traditional gold-standard methodology and as such, have been the most thoroughly investigated means of detecting pulmonary emboli. Unfortunately, V/Q scans require significant patient cooperation and are not readily available after normal hospital hours. The outcome of a V/Q scan is dependent on the pretest probability of the patient having a pulmonary embolism which is influenced by the primary care provider’s experience and thus provides a less objective means of diagnosis. Although V/Q scans are still used for patients who are especially sensitive to radiation, such as pregnant patients and young woman of childbearing age, and those for whom the administration of contrast is not possible, such as those with contrast allergies or renal failure, in most centers V/Q scans have become the second line modality. Nonetheless, the long established role of V/Q scans provides the basis upon which all subsequent studies and analysis are compared.

Another modality for the detection of pulmonary emboli is pulmonary angiography which relies upon an interventionalist threading a catheter into the pulmonary artery and then injecting contrast material into the pulmonary artery underneath direct visualization. Although this provides a real time and directly modifiable method of detecting emboli, as well as the means to provide immediate treatment with target thrombolytics, it is associated with significant risks. The procedure is minimally invasive but still carries a risk of hematoma formation, arterial puncture, air embolism, catheter fracture and migration, and insertion site infection. Additionally, it involves a variable volume of contrast to be administered, and requires a significant level of personnel to be on call to provide appropriate patient care during and after the procedure. The risk benefit ratio of
the procedure is highly operator dependent, and therefore as the volume of conventional angiograms decreases the concomitant risk thus increases. In comparison to CT pulmonary angiograms, conventional angiograms today represent an increasingly small fraction of the diagnostic studies used to diagnose pulmonary emboli. As a result, pulmonary angiography has also become a second line modality for the detection of pulmonary emboli.

In most hospital centers, CT angiography has emerged as the first line modality for the detection of pulmonary emboli. The Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) II Study, whose results were initially published in The New England Journal of Medicine\textsuperscript{9} and jointly in The American Journal of Medicine\textsuperscript{10} and Radiology\textsuperscript{8}, was a prospective, multicenter investigation assessing the utility of CT angiography for the detection of pulmonary emboli. It is the largest and most current database for the analysis of diagnosing pulmonary emboli with CT angiography. Although the data is still being analyzed in further detail by additional investigators, the PIOPED II Investigators conclude that CT angiography, when combined with a sound clinical assessment, provides an excellent means of diagnosing pulmonary emboli with a sensitivity of 83% and a specificity of 95%. Furthermore, they provide a stepwise diagnostic tree which incorporates CT angiography into the workup of suspected pulmonary emboli that is becoming the standard of care in major hospitals. Numerous additional studies have established that when compared to V/Q scanning and catheter angiography, CT angiography provides rapid, cost-effective, non-invasive, and reliable diagnoses\textsuperscript{11-14}. Traditionally, the greatest limitation of CT angiography has been poor visualization of the peripheral pulmonary arteries, but the increased development and


availability of multidetector-row spiral CT equipment has helped compensate for this
deficit\textsuperscript{11}. The collective volume of literature supporting the use of CT angiography has
pushed it to become the current modality of choice for the diagnosis of pulmonary
embolism.

Although CT angiography is a powerful tool, there are still associated risks and
drawbacks. The visualization of a clot burden requires careful discrimination between
contrast enhanced blood and thromboembolism. This is achieved via a precisely timed
bolus of contrast material that is administered through a peripheral intravenous line.
Unfortunately, the administration of contrast carries an associated risk of contrast-
induced nephropathy\textsuperscript{15, 16}. Contrast-induced nephropathy is defined as a 25\% increase in
the serum creatinine level compared to baseline. Patients whose creatinine exceeds a
threshold level, usually between 1.5 and 1.8 mg/dL, are not usually eligible for a contrast
based study, since compromised renal function is the major risk factor for contrast-
induced nephropathy. The general risk of developing nephropathy after a radiologic
procedure is less than 3\%; however, in specific patient populations the risk may increase
to as much as 20\%\textsuperscript{17}. Patients with diabetes and those with pre-existing renal disease are
at greatest risk for developing nephropathy. The associated neuropathy and sedentary
lifestyle that frequently accompanies these conditions also places these patients at
increased risk for pulmonary embolism. Patients who develop contrast-induced
nephropathy are more likely to die in-hospital and their 1-year mortality rates are
increased beyond their underlying medical conditions\textsuperscript{16}. Although generally considered
routine, the administration of contrast material must be viewed as a calculated risk. The
benefit of detecting a pulmonary embolism in a moderate to high risk patient will usually
outweigh the potential for contrast nephropathy in most patients. However, even in 
patients with pristine renal function, contrast material will affect their renal function such 
that repeat scans require a washout period, usually at least 24 hours in most hospitals, to 
allow kidney function to return to baseline. As a result, it is important to maximize the 
information yield from a single CT angiogram for suspected pulmonary embolism, 
because serial scanning is associated with a serial increase in risk.

The other major concern with CT angiography is the radiation exposure. Although long known, there has been increased dialogue in both the academic literature and lay press\textsuperscript{18,19} recently regarding the quantity of radiation exposure, particularly from CT scanning, and the potentially associated increased risk of developing cancer. It is estimated that based on our current utilization of CT scans, 1.5-2\% of all cancers in the United States might be the result of CT-induced radiation exposure, up from 0.4\% in the period from 1991 to 1996\textsuperscript{20}. Furthermore, in large hospitals CT scanning accounts for approximately 75\% of the diagnostic radiation delivered to patients\textsuperscript{21}. Young patients and those who require repeat imaging are at greatest risk for developing radiation induced complications in the future, because radiation-induced genetic changes accumulate over the lifetime of an individual. As for contrast administration, the risk of radiation exposure must be compared to the risk of missing the diagnosis of pulmonary embolism. In the majority of situations, a single CT angiogram to detect a pulmonary embolism is worth the associated radiation exposure, but it is imperative to reduce the need for repeat imaging. Poor quality studies that provide indeterminate or non-diagnostic information do not provide a yes/no diagnosis and exposure the patient to needless radiation and contrast exposure. If patients have an inconclusive study, they are primarily at risk for
complications associated with an undiagnosed and untreated pulmonary embolism, but in many situations they will be subjected to repeat imaging at a later time which multiplies the previously described risks associated with CT scanning. To maximize the utility of a CT angiogram, it must be able to accurately detect a pulmonary embolism the first time. As a result, there is a great deal of emphasis on tweaking the operational parameters in order to optimize the information yield from a given study.

Identifying potential operational parameters for improvement is the first important step. Jones and Wittram reported in Radiology, in 2005, that the two major causes of a clinically indeterminate CT pulmonary angiogram study are motion artifact and poor enhancement of the pulmonary vasculature. In their study of 3612 CT pulmonary angiogram examinations there were 237 indeterminate studies (6.6%). Only 81 of these patients had follow up examinations of any sort within 5 days, defined as a repeat CT pulmonary angiogram, conventional pulmonary angiography, V/Q scan, or lower extremity ultrasound. 8% of those with indeterminate final interpretations were treated empirically without definitive imaging. They discovered that the mean attenuation of the main pulmonary artery was 339 HU +/- 88 in their control group, but only 245 HU +/- 80 in the group with indeterminate interpretations (p < 0.001). While motion artifact is usually the result of old, slower scanners or patients who are either non-compliant or in extremis, there are institutional protocols that can aid in patient compliance, including pain medication or low level sedation in certain circumstances. However, enhancement of the pulmonary vasculature can be maximized by optimizing certain operational parameters. The study authors theorized that the reduced attenuation in the main pulmonary arteries could be the result of technician error, anatomic variations, or
decreased perfusion secondary to low cardiac output. Of these factors, technician error is generally regarded to occur as a fixed percentage of cases, directly dependent on the experience of the operator. Reduced perfusion secondary to a low cardiac output state can be detected with a preliminary timing run, which is the standard protocol of choice on many scanners. However, anatomic factors are a poorly discussed, but potentially very influential means of altered attenuation values. If patients with certain anatomic conditions which predispose them to poor attenuation examinations could be identified, then compensatory mechanisms might be developed to overcome this obstacle.

Regardless of the etiology, every time a patient undergoes a CT angiogram that results in an indeterminate reading, the patient is exposed to needless contrast and radiation, without a concomitant increase in knowledge about their clinical status. Minimizing poor quality CT pulmonary angiogram studies is clinically important, because repeat or follow up scanning is not cost effective, delays a definitive diagnosis, and results in repeated exposure to the very real side effects of contrast enhanced CT examinations.

The precise timing and delivery of a contrast bolus is the most important modifiable factor affecting the information yield in a CT angiogram to evaluate for suspected pulmonary embolism. There is a great deal of literature attempting to determine which patient and study characteristics can maximize the information yield from a CT angiogram, including age, gender, patient weight, and catheter size or position. At our institution there has been increased discussion about the potential heterogeneity in contrast delivery based on the arm of infusion. Anatomically, there is a difference in the pathway of the left and right brachiocephalic veins as they cross from the shoulders to join the superior vena cava in the central chest. The right brachiocephalic vein has a
straight pathway from the shoulder to the superior vena cava, but as the left brachiocephalic vein crosses the thorax to join the superior vena cava, it must cross in front of the thick, muscular aortic arch. At this position, it is possible for the stiffer aortic arch to compress the thinner-walled left brachiocephalic vein. There is a fixed amount of space in the anterior-posterior diameter of the chest into which the aortic arch and the left brachiocephalic vein must fit. The two situations in which compression of the left brachiocephalic vein by the aortic arch might occur are via an increase in the area occupied by the aorta or a by a decrease in the potential anterior-posterior space available. Previous research has demonstrated that in patients with an elongated or ectatic aortic arch, such as elderly patients with hypertension, compression of the left brachiocephalic vein may occur. A compressed left brachiocephalic vein would limit the flow of blood from the left arm to the pulmonary arteries, and in the process reduce the rate of contrast delivery. This could dilute the volume of contrast received, reduce attenuation, and result in a poorly visualized examination of the pulmonary arteries, specifically in the periphery which is the region of greatest limitation for CT angiography.

Under ideal circumstances, contrast is administered in a rapid bolus that floods the anatomic region of interest in order to maximize attenuation of the vessel in question, with minimal attenuation of the surrounding vessels in order to reduce background noise. Figure 1a shows a theoretical attenuation over time curve under ideal circumstances. The rapid contrast bolus, if unrestricted in its passage, results in a steep attenuation curve. This value must cross a specific threshold to ensure that the vessels in question are adequately attenuated to be visualized by the radiologist. In this graph, the integral of the
curve is related to the total volume and rate of contrast administered, but in order to limit potential renal complications, the volume of contrast should be kept as low as possible. Increasing the rate of contrast delivery will increase the slope of the attenuation curve, but is technically limited by the route of administration (i.e. the bore of the intravenous line and the speed with which the contrast can be pushed) and the total volume to be given (i.e. injecting fast equates to injecting more). In order to maximize vessel attenuation while limiting potential renal complications, the minimal amount of contrast must be administered in as rapid a fashion as possible in order to keep the integral of the attenuation curve low and maximize the peak attenuation. If there is a delay in the delivery, for whatever etiology, then the value of the integral remains unchanged, but the slope decreases, causing the peak of the curve to be depressed and shift to the right. With a small delay in attenuated blood flow, there may be a subclinical reduction in peak attenuation, as shown in Figure 1b, because the peak attenuation value still crosses the attenuation threshold for the duration of the scan. As the delay increases, the slope of the attenuation curve flattens, leading eventually to a subclinical peak attenuation value in which the entirety of the scan is not above threshold, as shown in Figure 1c. Contrast administered from a peripheral intravenous line is continually mixed with non-attenuated blood as additional vessels join or as the central vessel merges with others. This results in a stepwise dilution first in the superior vena cava where the two brachiocephalic veins merge, and again in the right heart as blood from the inferior vena cava is introduced. This normal dilution is compensated by administering a volume of contrast large enough to ensure there is adequate attenuation in the distal region of interest. In the case of left brachiocephalic vein occlusion, compression by the aorta could reduce the flow of
attenuated blood into the superior vena cava. This reduction in blood flow is vessel specific, and not a systemic slowing, thus the proportional volume of attenuated blood entering the pulmonary vessels from the left brachiocephalic vein would be decreased. Since attenuation is dependent on the concentration within a vessel, this would lead to a decrease in the attenuation of the pulmonary vasculature, while still exposing the patient to the full volume, and the associated risks, of contrast administration. In certain circumstances, this reduction in flow may be severe enough to result in an attenuation peak that does not cross the attenuation threshold, or more likely, the attenuation is not above the threshold for the entire duration of the scan resulting in inconsistent image capture.

Although a theoretical risk for chest CT angiograms, there is a growing body of literature describing the influence of brachiocephalic vein occlusion in CT and MR imaging of the head and neck. Brachiocephalic vein compression influencing cross-sectional imaging was first reported in 1977 in the head and neck literature in the *Journal of Nuclear Medicine* as an incidental finding during brain flow imaging\(^{27}\). Although head and neck CT angiograms are subject to the same mechanistic, timing, and contrast delivery restrictions as chest imaging, the means of detecting occlusion are more readily apparent. Compression of the left brachiocephalic vein pools attenuated blood proximal to the merging of the vein with the superior vena cava\(^{28,29}\). In approximately 6% to 13% of the population, there exists either a congenital or acquired, usually the result of longstanding hypertension, absence of jugular venous valves\(^{30}\). Venous valves are designed to ensure unidirectional flow of blood, but when they are absent and there is downstream obstruction, then retrograde flow of contrast material from the
brachiocephalic vein up the left jugular vein and into the dural sinuses may occur. Upon image capture, the early arterial phase sequences are complicated by artifact from the refluxed venous contrast, leading to poor quality studies. In up to 9.1% of studies, increased artifacts and poor visualization were directly the result of left-sided brachiocephalic vein occlusion and retrograde flow.[31-33] This phenomenon has been extensively identified and described during both CT and MR imaging,[26, 30, 34, 35] and several published series propose that for head and neck imaging, right-sided contrast infusion should be the new standard of care. As a direct result of the anatomic region of coverage imaged, head and neck imaging is especially sensitive at detecting brachiocephalic vein occlusion.

To our knowledge, there are no published series that have looked at the impact of left-versus right-sided injections on attenuation of the pulmonary arteries in patients undergoing CT angiograms of the chest to evaluate for pulmonary emboli. Theoretically, the same process which limits left-sided contrast administration in CT angiograms of the head and neck may be apparent in CT angiograms of the chest, although the means of detection may by nature be more subtle because of the anatomic region imaged. In the authors’ experience, they have anecdotally witnessed occlusion of the left brachiocephalic vein by the aorta, and subsequent retrograde flow of contrast material up the left jugular vein. This has resulted in a poor quality bolus delivered to the pulmonary vasculature, requiring repeat imaging to allow for adequate visualization of the distal pulmonary arteries in order to rule out pulmonary emboli. Because of the time sensitive nature of identifying pulmonary emboli, as well as the associated risks of radiation and
contrast exposure, it is very important to identify any factors, such as arm of infusion, which may result in poor quality studies.

STATEMENT OF PURPOSE

This study is an outcomes based analysis that seeks to determine if the side of contrast infusion influences the attenuation of the main pulmonary artery in patients undergoing a CT angiogram of the chest to evaluate for pulmonary emboli. Although a mechanism for a difference has been discussed based on previous published research, our analysis seeks to determine if a difference exists rather than to identify any potential etiologies. The primary outcomes are post-contrast attenuation in Hounsfield Units (HU) of the main pulmonary artery. The secondary outcomes are the number of studies beneath an attenuation threshold of 250, 200, and 150 HU, and the number of studies interpreted as non-diagnostic or indeterminate. Tertiary analysis will seek to determine if there is an age dependent shelf affect that results in an attenuation difference. *We hypothesize that there exists a difference in the attenuation of the main pulmonary artery based on the arm of infusion in patients undergoing a CT angiogram of the chest to evaluate for pulmonary emboli.*

MATERIALS AND METHODS

This retrospective study was performed solely at the Yale-New Haven Hospital. Approval for the study was obtained through the institutional Human Investigation
Committee (HIC). The study was compliant with the guidelines of the Health Insurance Portability and Accountability Act (HIPAA) and a waiver of informed consent was obtained. All work was undertaken by the primary author except when noted otherwise, as in the image review section.

Study Selection

A list of studies was generated from our institutional computer database (IDX, GE Medical Systems) by searching for the billing code for CT pulmonary angiograms performed on each of our three CT scanners beginning June 1, 2006. This date was chosen to predate the increase in institutional dialogue regarding the potential heterogeneity in arm of infusion attenuation. To our knowledge, there have been no systemic efforts to insert intravenous lines in a specific arm as a result of this dialogue, but we cannot rule out non-institutionalized preferences. Consecutive studies were evaluated from each scanner. A sample size of 300 was chosen based on preliminary power calculations that showed this would allow us to detect attenuation differences of 25 HU with a $p = 0.05$ at a power of 80%.

Exclusion Criteria

Studies were excluded for a variety of technical, procedural, or structural reasons. If the full bolus of contrast was not administered due to technical or mechanical failure, then the study was excluded because the exact volume and rate of infusion could not be determined. This most commonly occurred as a result of extravasation of contrast at the intravenous line site and frequently resulted in a repeat examination, both of which were
ineligible for inclusion. Residual contrast material that had not been adequately cleared by the initial bolus could create artificially elevated attenuation readings. Less commonly, mechanical malfunction resulted in only a partial bolus of contrast administration. Although a strict protocol guideline associated with the volume of contrast to be administered was in place, if the quantity of contrast injected was not recorded by the CT technician, we did not assume homogenous contrast volume administration and the study was excluded. Finally, if a patient had a repeat CT scan to evaluate for pulmonary embolism and both studies were within the eligibility time frame, only the first study was considered eligible for inclusion in the final analysis, so as to prevent duplicate assessment of an individual’s anatomy.

Dialysis patients were excluded because of the high probability for iatrogenic changes in their peripheral vasculature secondary to shunt placement or repeated vascular manipulation, which may lead to altered flow patterns. The field of view of the CT scan does not include the full length of the arm vasculature so it was impossible to determine which patients had altered vasculature. Also, repeated prior catheter insertion could result in local stenosis. Patients with a central venous thrombus have reduced flow of contrast material to the pulmonary vessels that was unrelated to the structural phenomena we were trying to assess and were excluded if identified by the primary radiologist’s interpretation. Although all patients are supposed to have contrast administered via a peripheral intravenous line, in rare situations a central line was used and these studies were excluded. Central lines bypass the subclavian and brachiocephalic vessels and administer contrast directly to the superior vena cava or the right atrium, thus removing any potential brachiocephalic occlusion from consideration. Finally, patients with a
repair from congenital heart disease may have completely distorted structural anatomy and flow patterns and could not be standardized in our analysis.

Hardware and Technique

Scans were performed on our three institutional CT scanners. Scanner 1 was a 4-slice GE LightSpeed (GE Medical Systems). A smartprep, in which low-dose scanning is performed in a designated region of interest (ROI) until an attenuation threshold is breached, was performed at the level of the main pulmonary artery. Scanning of the chest began 3 seconds after the technologist detected a pulmonary artery enhancement of 100 HU in the designated ROI. A total of 100 cc of contrast was administered at a rate of 4 cc/sec followed by 10 cc saline at 4 cc/sec. 2.5 mm thick images were acquired using 120 kVP and SmartMA dose modulation with the noise index set to 15.

Scanner 2 was a 16-slice GE LightSpeed. A timing run was performed at the level of the main pulmonary artery using 25 cc of contrast injected at 4 cc/sec followed by 10 cc saline at 4 cc/sec. Timing was determined by peak pulmonary artery enhancement as measured by ROI analysis. CT angiogram images were obtained following a second injection of an additional 90 cc of contrast at 4 cc/sec followed by a 10 cc saline at 4 cc/sec. 1.25 mm thick images were acquired using 120 kVP and SmartMA dose modulation with the noise index set to 11.

Scanner 3 was a 64-slice GE VCT. A timing run was performed at the level of the main pulmonary artery using 25 cc of contrast injected at 4 cc/second followed by 10 cc saline at 4 cc/sec. Timing was determined by peak pulmonary artery enhancement as measured by ROI analysis. CT angiogram images were obtained following a second
injection of an additional 90 cc of contrast at 4 cc/sec followed by a 10 cc saline at 4 cc/sec. 1.25 mm thick images were acquired using 120 kVP and SmartMA dose modulation with the noise index set to 20.

All scans used Omnipaque 350 (Amersham, Piscataway NJ) contrast material injected through an 18 gauge or larger upper extremity peripheral intravenous line.

**Chart Review**

One researcher was designated to perform the initial chart review to screen for eligible studies from among the computer generated list of CT pulmonary angiograms. Studies were reviewed chronologically. Potential exclusion criteria were identified in either the formal radiology report or the study order form completed by the requesting clinician. Studies that met eligibility criteria were assigned a unique study identifier for subsequent use. The following variables were recorded from the radiology report and order form: age, gender, history or diagnosis of congestive heart failure (CHF), scanner used, contrast quantity, pacemaker presence, and radiologist study interpretation, recorded as positive, negative, indeterminate, or non-diagnostic. In our experience, indeterminate and non-diagnostic interpretations are reader specific means of indicating that the study was not performed adequately to justify a formal reading. No reinterpretations of the images were made.

**Image Review**

The selected study image series were transferred from the hospital PACS system (Synapse, FujiFilm; Stamford CT) to a Vitrea graphics workstation (Vital Images;
Minnetonka MN) by the initial chart reviewer. This researcher then recorded the side of injection by identifying the attenuated brachiocephalic and subclavian vessels at the imaging workstation. A consecutive stack of images through the main pulmonary artery and its bifurcation were then selected and saved to the workstation, as shown in Figure 2. The remaining images in the series were deleted from the workstation. The saved images did not include the superior aspect of the series, thus removing the brachiocephalic vessels. From the saved images, it was not possible to determine from which side the contrast was injected upon subsequent review. A new de-identified list of these prepared images was created, which did not contain any of the previously collected information from the chart review.

A separate researcher with 7 years of experience reading CT pulmonary angiogram examinations received the list of prepared images. The researcher was thus blinded to the side of infusion and to all clinical information regarding the saved images. An ROI was placed within the center of the main pulmonary artery, as determined by drawing lines along the long and short axis of the vessel and placing the ROI at the intersection, as shown in Figure 3. The diameter of the ROI was made equal to the radius of the artery. The researcher ensured that there was no volume averaging by checking that the slice immediately above and below also contained the main pulmonary artery. The average attenuation value in Hounsfield Units of the ROI and the area of the ROI were recorded.

Statistical Analysis

After the chart review and the image analysis, the two lists were merged. The mean attenuation of the main pulmonary artery for the right and left arm cohorts were
calculated and 95% confidence intervals were determined. Statistical significance was computed using a two tailed, non-paired t-test. Multiple regression analysis was performed to control for potential confounders: gender, age, contrast volume, region of interest area, CHF status, and pacemaker presence.

The number of scans beneath the 250, 200, and 150 HU thresholds and the number of studies interpreted as non-diagnostic or indeterminate were compared using a Chi-squared analysis. The threshold value of 250 HU was determined based on a review of the literature regarding adequate attenuation for CT pulmonary angiograms to rule out pulmonary emboli. The addition of 200 and 150 HU threshold values were made based on preferences of multiple readers at our institution. A p value of less than 0.05 was considered statistically significant. Data was collected and analyzed using the software programs Excel (Microsoft; Seattle WA) and SPSS (SPSS; Chicago IL).

RESULTS

Figure 4 shows the distribution of studies included and excluded in the analysis. 407 total studies were reviewed to obtain a sample of 300 studies, with 100 from each scanner. The most common etiology of exclusion was failure by the technician to record the volume of contrast material delivered in the study, followed by infiltrated intravenous lines, central line delivery, dialysis, and congenital heart disease repair. No central venous thrombi were identified.
The baseline study sample characteristics are shown in Table 1 for each scanner and in aggregate. There was no statistically significant difference in the distribution of age, gender, CHF status, pacemaker presence, ROI area, or contrast volume administered for the left- and right-sided injection groups on any individual scanner or across the study sample as a whole.

Table 1 – Study baseline characteristics. P values are > 0.05 based on Chi-squared analysis. ROI = region of interest, CHF = congestive heart failure

<table>
<thead>
<tr>
<th></th>
<th>All Scanners Total = 300</th>
<th>Scanner 1 Total = 100</th>
<th>Scanner 2 Total = 100</th>
<th>Scanner 3 Total = 100</th>
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<tbody>
<tr>
<td></td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>Studies (%)</td>
<td>146 / 300 (48.7)</td>
<td>154 / 300 (51.3)</td>
<td>47 / 100 (47)</td>
<td>53 / 100 (53)</td>
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<tr>
<td>Age, years (SD)</td>
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<td>57.5 (17.3)</td>
<td>55.5 (22.1)</td>
<td>58.8 (18.0)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>93 / 146 (64)</td>
<td>84 / 154 (55)</td>
<td>27 / 47 (57)</td>
<td>32 / 53 (60)</td>
</tr>
<tr>
<td>CHF (%)</td>
<td>2 / 146 (1)</td>
<td>0 / 154 (0)</td>
<td>0 / 47 (0)</td>
<td>0 / 53 (0)</td>
</tr>
<tr>
<td>Pacemaker (%)</td>
<td>2 / 146 (1)</td>
<td>0 / 154 (0)</td>
<td>0 / 47 (0)</td>
<td>0 / 53 (0)</td>
</tr>
<tr>
<td>ROI Area, mm² (SD)</td>
<td>193.5 (77.5)</td>
<td>201.8 (73.8)</td>
<td>155.0 (42.6)</td>
<td>166.3 (39.4)</td>
</tr>
<tr>
<td>Contrast, mL (SD)</td>
<td>101.6 (7.8)</td>
<td>101.4 (7.2)</td>
<td>100.0 (0)</td>
<td>101.3 (7.3)</td>
</tr>
</tbody>
</table>
The average attenuation of the main pulmonary artery and the 95% confidence intervals are shown in Table 2 for each scanner and in aggregate. The distribution of the attenuation values for the left- versus right-sided injection groups broken down into 25 HU increments are shown in Figure 5. There was no statistically significant difference in the average attenuation between patients injected with contrast from the left or the right arm. The average attenuation of the main pulmonary artery in patients injected in the right arm was 275.4 HU (95% CI 255.6 to 295.1 HU). The average attenuation of the main pulmonary artery in patients injected in the left arm was 275.0 HU (95% CI 257.3 to 292.8 HU). Multiple regression analysis showed no confounding factors among the baseline characteristics collected and shown in Table 1.

Table 2 – Mean scanner attenuation values. P values are > 0.05 based on t-test analysis.

<table>
<thead>
<tr>
<th></th>
<th>All Scanners</th>
<th>Scanner 1</th>
<th>Scanner 2</th>
<th>Scanner 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>Attenuation, HU (95% CI)</td>
<td>275.4 (255.6 – 295.1)</td>
<td>275.0 (257.3 – 292.8)</td>
<td>244.7 (219.2 – 270.1)</td>
<td>229.7 (206.2 – 253.2)</td>
</tr>
</tbody>
</table>

Table 3 displays the values of the secondary endpoints under consideration: threshold attenuations and study interpretation results. There was no statistically significant difference in the number of scans below threshold attenuation values of 250 HU (67 (45.9%) right, 66 (42.9%) left), 200 HU (37 (25.3%) right, 45 (29.2%) left), and 150 HU (17 (11.6%) right, 19 (12.3%) left). There was no statistically significant difference in the number of scans interpreted as non-diagnostic (4 (2.7%) right, 4 (2.6%) left) or
indeterminate (2 (1.4%) right, 6 (3.9%) left). Although not a primary or secondary endpoint, there was incidentally also no statistically significant difference in the number of positive (20 (13.7%) right, 31 (20.1%) left) or negative (120 (82.2%) right, 113 (73.4%) left) study interpretations.

Table 3 – Outcomes of analysis. P values are > 0.05 based on Chi-squared analysis.

<table>
<thead>
<tr>
<th>Attenuation &lt; 250 HU (%)</th>
<th>All 300 scans</th>
<th>Scanner 1 100 scans</th>
<th>Scanner 2 100 scans</th>
<th>Scanner 3 100 scans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>67 / 146 (45.9)</td>
<td>66 / 154 (42.9)</td>
<td>28 / 47 (59.6)</td>
<td>30 / 53 (56.6)</td>
<td>32 / 51 (62.7)</td>
</tr>
<tr>
<td>Attenuation &lt; 200 HU (%)</td>
<td>37 / 146 (25.3)</td>
<td>45 / 154 (29.2)</td>
<td>15 / 47 (31.9)</td>
<td>22 / 53 (41.5)</td>
</tr>
<tr>
<td>Attenuation &lt; 150 HU (%)</td>
<td>17 / 146 (11.6)</td>
<td>19 / 154 (12.3)</td>
<td>6 / 47 (12.8)</td>
<td>8 / 53 (15.1)</td>
</tr>
<tr>
<td>Positive (%)</td>
<td>20 / 146 (13.7)</td>
<td>31 / 154 (20.1)</td>
<td>9 / 47 (19.1)</td>
<td>11 / 53 (20.8)</td>
</tr>
<tr>
<td>Negative (%)</td>
<td>120 / 146 (82.2)</td>
<td>113 / 154 (73.4)</td>
<td>36 / 47 (76.6)</td>
<td>37 / 53 (69.8)</td>
</tr>
<tr>
<td>Non-Diagnostic (%)</td>
<td>4 / 146 (2.7)</td>
<td>4 / 154 (2.6)</td>
<td>1 / 47 (2.1)</td>
<td>1 / 53 (1.9)</td>
</tr>
<tr>
<td>Indeterminate (%)</td>
<td>2 / 146 (1.4)</td>
<td>6 / 154 (3.9)</td>
<td>1 / 47 (2.1)</td>
<td>4 / 53 (7.5)</td>
</tr>
</tbody>
</table>

Table 4 displays the tertiary analysis for age bracketed outcomes. Primary and secondary outcomes under consideration are broken down for patients greater than 60, 70, 80, and 90 years of age. There was no statistically significant difference in the arm of infusion, mean attenuation, scans beneath threshold attenuation values of 250, 200, and 150 HU, or indeterminate and non-diagnostic readings for any of the age groupings. The
total number of studies included in each age group progressively shrinks to only 6 subjects for the greater than 90 year age bracket.

**Table 4** – Age bracketed outcomes. P values are >0.05 based on Chi-squared analysis.

<table>
<thead>
<tr>
<th>Age, years</th>
<th>&gt; 60</th>
<th>&gt; 70</th>
<th>&gt; 80</th>
<th>&gt; 90</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>Total</td>
<td>Total</td>
<td>Total</td>
<td>Total</td>
</tr>
<tr>
<td>Right</td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>All Scanners (%)</td>
<td>59 / 127 (46.5)</td>
<td>68 / 127 (53.5)</td>
<td>40 / 76 (52.6)</td>
<td>36 / 76 (47.4)</td>
</tr>
<tr>
<td>Attenuation, HU (95% CI)</td>
<td>304.6 (265.9 – 343.4)</td>
<td>305.1 (274.0 – 336.2)</td>
<td>334.4 (282.3 – 386.5)</td>
<td>338.3 (295.0 – 381.6)</td>
</tr>
<tr>
<td>Attenuation &lt; 250 HU (%)</td>
<td>23 / 59 (38.9)</td>
<td>24 / 68 (35.2)</td>
<td>14 / 40 (35.0)</td>
<td>8 / 36 (22.2)</td>
</tr>
<tr>
<td>Attenuation &lt; 200 HU (%)</td>
<td>14 / 59 (23.7)</td>
<td>19 / 68 (27.9)</td>
<td>9 / 40 (22.5)</td>
<td>7 / 36 (19.4)</td>
</tr>
<tr>
<td>Attenuation &lt; 150 HU (%)</td>
<td>6 / 59 (10.2)</td>
<td>5 / 68 (7.4)</td>
<td>3 / 40 (7.5)</td>
<td>1 / 36 (2.8)</td>
</tr>
<tr>
<td>Non-Diagnostic (%)</td>
<td>2 / 59 (0.3)</td>
<td>2 / 68 (3.0)</td>
<td>0 / 40 (0)</td>
<td>0 / 36 (0)</td>
</tr>
<tr>
<td>Indeterminate (%)</td>
<td>0 / 59 (0)</td>
<td>2 / 68 (3.0)</td>
<td>0 / 40 (0)</td>
<td>0 / 36 (0)</td>
</tr>
</tbody>
</table>
DISCUSSION

Our analysis demonstrates no statistically significant difference in the mean post-contrast attenuation of the main pulmonary artery between patients receiving a contrast injection through the left or right arm. The baseline distribution of potential confounding factors was similar between these two groups and the multiple regression analysis demonstrated that age, gender, CHF status, pacemaker presence, contrast volume, and ROI area were not independently confounding factors. We were also not able to discern a statistically significant difference in the secondary endpoint attenuation thresholds or study interpretations results. Tertiary analysis did not reveal an age dependent shelf effect for attenuation variation.

There are no established minimum attenuation criteria for CT angiograms to rule out pulmonary emboli currently available in the literature. In our experience, most radiologists do not have a specific Hounsfield Unit requirement. They will attempt to read the examination and instead report that it is a poorly attenuated study which may not completely rule out emboli and if clinically suspicious might warrant a repeat examination. Our decision to use a 250 HU threshold was based on the work of Wittram et al. who recently presented in Radiology a series of chest CT angiograms positive for pulmonary emboli. They discerned that the average attenuation was 33 HU with a standard deviation of 15 for acute pulmonary emboli and 87 HU with a standard deviation of 31 for chronic pulmonary emboli. This increased attenuation of chronic pulmonary emboli was attributed to clot organization, calcification, or local hemoglobin iron concentration. To reach a value of 250 HU, they statistically extrapolated their results to minimize false negatives. Three standard deviations above the mean would
include 99.75% of all emboli, and then an additional standard deviation would be needed to differentiate clot from surrounding blood. For acute thrombi, with a maximum attenuation of 78 HU, the blood must be attenuated to 91 HU, and for chronic thrombi, with a maximum attenuation of 180, the blood must be attenuated to 211 HU. From this value, 250 HU and 200 HU were deemed appropriate thresholds for our study, with 150 HU providing a more restricted outlier. Although Wittram et al.’s results provide a very useful starting point, their sample size of 39 warrants additional investigation before more concrete criteria can be established. In our study population we did not differentiate between chronic and acute emboli; however, from the perspective of the radiologist who is blinded to the duration of any potential clot the higher attenuation value seems to be more clinically appropriate.

The differential attenuation threshold identified by Wittram et al. does raise the issue of whether patients should be triaged to receive different infusion protocols. Since nephrotoxicity is directly related to the volume of contrast administered, it is important to utilize the least amount of contrast appropriate to receive adequate attenuation. Although the majority of patients who are diagnosed with a pulmonary embolism do not present with the classically described symptoms, for the subset of the population who are at low risk for chronic embolism and who have a clearly timed symptomatic onset it might be appropriate to utilize a protocol with a smaller volume of administration. Based on Wittram et al.’s calculations, the maximum acceptable attenuation for identifying acute thrombi is less than half that of chronic thrombi, 91 HU versus 211 HU. The lower risk of nephrotoxicity must be balanced against the risk of repeating the examination secondary to lower than acceptable attenuation.
There are two possible scenarios in which compression of the left brachiocephalic vein might influence CT angiogram results. Compression might occur on a systemic basis, such that in every examination there is a reduction in flow with left-sided injections to varying degrees. In this situation, we would expect to see a difference in the average attenuation between left and right arm injections, with the magnitude of the difference equal to the consistency in the degree of obstruction. However, the mean post-contrast attenuations of the main pulmonary artery were nearly identical, with significant overlap when confidence intervals are taken into consideration, as shown in Figure 6. Additionally, we would expect to find a differential increase in the number of studies that are below the threshold attenuation values. However, there is not only no difference in the distribution of studies beneath the 250, 200, and 150 HU thresholds, there is also no appreciable difference on a course visual analysis of the scan attenuation distribution, as shown in Figure 5. These surrogates indicate that compression does not appear to be occurring on a consistent basis.

The other scenario is if compression of the left brachiocephalic vein occurs sporadically, such that only in certain circumstances is flow reduction present. In this case we might not find a difference in the mean attenuation, but we would expect to see a difference in the number of studies beneath the different attenuation thresholds for individuals injected via the left or right arm. As noted above, this is not the case. Furthermore, we would expect to find a difference in the number of indeterminate or non-diagnostic interpretations, which are the clinical expressions of low attenuation examinations. However, this difference is not apparent indicating that even if there is a difference on the anatomic level, this difference is not significant enough to translate
clinically into non-decisive radiology reports. Therefore, it is unlikely that compression is occurring sporadically to a degree which our mechanisms can identify.

Interestingly, despite the difference in the scanner protocols, there was no identifiable difference between the attenuation values for the individual scanners. Scanner 1 relies on a single contrast administration with ROI threshold triggering to initiate scanning, whereas scanners 2 and 3 both utilize timing runs with two phase contrast administration. Although this resulted in mean global attenuation differences between scanners, it resulted in a statistically insignificant difference within scanners for left versus right arm of infusion. Brachiocephalic vein occlusion should result in a delay in the upstroke of the attenuation over time curve, leading to a wider and flatter curve as opposed to the ideal brisk upstroke, as shown in Figure 1a-c. If the slope of the curve is shallow enough, then the peak attenuation might never reach a clinically significant level, despite an equal area under the curve. Presumably, timing runs should better accommodate upstream occlusion because they look at the entire spectrum of the contrast bolus delivered, and even if there is a delay they will still be able to pace the scanner to accommodate the peak attenuation value. However, triggering protocols assume a continual rate of increase in attenuation. They are set for a lower than peak attenuation value on the assumption that the attenuation curve is on the rapid upslope and will continue to increase after the set value is breached. In the case of a slower attenuation upstroke, then this could result in a scan time that either precedes the peak attenuation or misses it, and may thus be beneath the attenuation threshold necessary for an adequate clinical examination. However, the lack of a statistically significant difference for both protocols presumes that there is neither a decrease in the maximum peak of the attenuation over time curve, nor a
decrease in the slope of the upstroke component under the conditions monitored in our study.

The difference in identifiable outcomes between the pulmonary vasculature in our study and that found in the head and neck literature, as described in the introduction, could be the result of several factors. First of all, retrograde flow of small amounts of contrast material into the jugular vein and dural sinuses causes venous artifact of the arterial structures, thus making the head and neck very sensitive to regurgitation. Based on our results, even if there is some reflux up the internal jugular vein, it is not significant enough to affect the attenuation in the main pulmonary artery (i.e. it does not cripple the utility of the contrast bolus). Additionally, the volume of contrast and tissue imaged is grossly different between the two regions. Head and neck CT angiograms typically use 60 – 80 mL of contrast, rather than the 100 mL used in chest imaging, and by the time this contrast reaches the head and neck it has been diluted to a greater extent than in the pulmonary vasculature. Brachiocephalic vein occlusion should have a fixed impact on contrast flow, thus producing a disproportionately larger influence on the head and neck vessels. As such, it is possible that our mechanisms of detecting brachiocephalic vein occlusion are not as sensitive as in the head and neck. We were unable to detect a clinically significant difference though in terms of inconclusive study interpretations, unlike the head and neck literature, which advocates that even if the effect is too small for our tools of detection then it is not clinically important.

It is also possible that occlusion is occurring during head and neck imaging but not during chest CT angiograms. This may be the result of procedural factors occurring during imaging that are different between the two protocols utilized. Several authors
have hypothesized that brachiocephalic vein compression may be reduced during deep inspiration because of the increase in the anterior to posterior diameter of the chest, thus reducing aorta-brachiocephalic compression\textsuperscript{26}. During cross-sectional imaging of the head and neck, patients are asked to respire at a tidal volume, whereas during imaging of the chest, patients are asked to inspire deeply and hold their breath for the duration of the scan. The difference in the depth of inspiration could be enough to reduce the compression of the brachiocephalic vein to a subclinical level. Additionally, the positioning of the patient’s arms during the two studies is different. In cranial imaging, the patients are told to keep their arms at the side, but during chest imaging the arms are raised overhead. Although one might hypothesize that upraised arms might induce a thoracic outlet-like effect, this effect should be equally influential for both arms, and not susceptible to the arm of infusion.

The results indicate several possibilities regarding the phenomena of brachiocephalic vein occlusion. If brachiocephalic vein compression occurs in the setting of CT pulmonary angiograms for PE evaluation, it appears to have a subclinical effect, either because the brachiocephalic vein diameter is not sufficiently occluded to diminish flow or the volume of contrast administered is enough to overcome any restriction in flow. Future research focusing on the brachiocephalic vein as it crosses the arch of the aorta would be necessary to further clarify this possibility. Either real time, direct visualization of the vessel diameter during simulated conditions or a comparison of the vessel attenuation immediately before and after it crosses the arch of the aorta might provide useful insights, rather than the surrogate indicators used in this study and others.
Despite the negative outcomes found in this study, it is possible that there may be subgroups of patients that our analysis was not extensive enough to cover but for whom a difference in clinical outcome might still be apparent. Patients who are unable to produce an appropriate inspiratory effort or who are unable to hold their breath might not increase the anterior-posterior diameter of their chest enough to escape aorta-braciocephalic compression. Patients with absent venous valves, narrow anterior to posterior chest wall anatomy, and exceptionally ectatic aortic arches may still be at risk for insufficient contrast delivery to the pulmonary vasculature if infusion is through the left arm.

Attempts to address this issue were made through repeat subgroup analysis. We used patient age bracketing to see if there is a shelf effect that may not have been detected by the multiple regression analysis because of the smaller sample size available for these extremes of age. We might expect to identify an attenuation difference secondary to changes that are acquired over the lifetime of an individual: aortic ectasia, incompetent valves, reduced forward flow of blood, and restricted chest wall motion. Table 4 shows the primary and secondary endpoints distributed over different decades of life. Although there were no statistically significant differences identified, these calculations are limited by the sample sizes, and some conclusions can still be reached. The average attenuation for the over 80 and 90 age brackets begin to diverge between arms of infusion with right-sided infusions attenuating more than left-sided. Additionally, there is an increase in the number of patients who are beneath the various attenuation thresholds for the over 70, 80, and 90 age brackets; however, right-sided infusions make up a larger share. There was no difference in the number of indeterminate or non-diagnostic interpretations. Ultimately though, the average attenuation values in the main pulmonary artery in these
more senior age groups are all well above even the most stringent threshold values for a diagnostic study (250 HU).

From an outcomes standpoint, our data indicate that it does not matter which side a patient receives the contrast bolus for a CT pulmonary angiogram to evaluate for PE. Anecdotally, we are aware of some clinicians and institutions that mandate that patients have a right-sided intravenous line, except in emergent cases. Our analysis demonstrates that there is no need to delay the time to diagnosis and treatment for pulmonary embolism by insisting that patients have venous access on a specific side.

There are several limitations to our study. There exists the potential for systemic bias regarding why a particular arm was chosen for infusion. In our experience, most patients present to the CT scanner with an intravenous line already inserted in only one arm, thus removing the CT technologist from consideration. The arm of insertion is influenced by patient or provider preference, as well as limitations to access such as the layout of furniture or other obstacles at the bedside in crowded Emergency Departments. Patients may prefer one side over the other as a result of hand dominance, previous intravenous line insertion experiences, or other less definable reasons. In our study population though, there was no difference between the number of left and right-sided infusions, despite the increased population prevalence of right-handed individuals. To remove this potential confounder we could have prospectively enrolled patients and mandated that they have intravenous access on a specific randomly determined side before they came to the CT scanner.

Another limitation in our data collection process is the absence of patient weight and the apparent discrepancy between the volumes of contrast recorded versus the amount
dictated by the protocol. We chose not to collect or include patient weight as a potential confounding variable in our analysis. Although our hospital’s order entry system requires clinicians to input the patient’s weight, this value is commonly not provided. Additionally, it is our experience that patient weight, when present, is only an estimate since most patients are not weighed on admission or initial presentation to the Emergency Department. It is unclear why the volume of contrast recorded is sometimes different from the protocol volume. We hypothesize that this is most likely related to an error in recording rather than an error in following the structured protocol. However, it is safe to assume that all cases were injected at a fixed rate of 4 cc/sec. Furthermore, the baseline volume characteristics are equal across groups, and the multiple regression analysis confirmed there was no statistically significant difference. Patient weight and contrast volume are generally considered to influence vessel attenuation, but for a first pass arterial study their influence is less important than the rate of contrast injection and blood flow. Since all scan times were less than 25 seconds and the bolus of contrast was running during the entirety of the scanning, the final volume of contrast administered should not influence the attenuation. Furthermore, the protocols on all three scanners utilize SmartMA dose modulation which attempts to compensate for variations in body habitus, and should thus lessen attenuation changes secondary to differences in patient weights. As a result, we feel that the weight absence and contrast volume discrepancy would have a minimal, if any, influence on our outcomes, and certainly not enough to change the central conclusions reached by our analysis.

Another potential confounding variable is CHF status. As previously discussed, the rate of blood flow has a major impact on the rate of contrast delivery, the slope of the
attenuation curve, and thus the peak attenuation value. CHF patients have reduced forward flow of blood which could allow for contrast pooling proximal to the site of imaging. In our sample the prevalence of CHF was 1% versus the 2.5% estimated by the American Heart Association\textsuperscript{39}. We might have predicted a higher than normal average, since CHF is an independent risk factor for the development of deep vein thrombosis\textsuperscript{40}. We recorded CHF status as positive if it was included in the brief clinical history inserted by the requesting clinician or if the diagnosis of CHF was made based on the clinical interpretation of the scan made by the radiologist. We recognize that the ordering clinician may not have obtained a complete history or included all relevant history when placing the order. Additionally, the scans were not re-interpreted during the image review to ensure whether a diagnosis of CHF was appropriate. However, the low reported prevalence of CHF was evenly distribution between the two arms. CHF prevalence is also directly proportional to age, and there was no statistically significant difference in age between the two infusion groups. Although our data indicate that a number of CHF patients might not have been appropriately classified as such, there is no reason to suspect that there is a systemic absence of classification for one particular arm of infusion. As a result, we do not believe that this would have a major impact on our principal outcomes.

A final identified limitation of this study is the inability to control for the location of the intravenous access within the arm. Our records do not indicate the size of the intravenous needle or its location on the arm of infusion. The CT pulmonary angiogram protocol calls for an 18 gauge or larger IV to be placed in an upper extremity vein, so that an injection rate of 4 cc/sec can be obtained. Antecubital access with a 20 gauge IV may
provide a better bolus than hand access with an 18 gauge IV, even if both are injected at the same rate. Given the lack of available data we are unable to control for this possibility, although again there is no reason to suspect a systemic difference between the arms of infusion.

In conclusion, our data and analysis indicate that the side of contrast injection did not affect the post-contrast attenuation within the main pulmonary artery when performing CT pulmonary angiogram examinations to evaluate for pulmonary emboli. Additionally, the number of studies with main pulmonary artery attenuations of less than 250, 200, or 150 HU and the number of studies interpreted as indeterminate or non-diagnostic was independent of the side of contrast injection. Finally, we were unable to identify a shelf effect demonstrating attenuation divergence with increasing age. While in patients with known central venous occlusions or structurally altered anatomy it may be wise to choose the side of injection to correlate with the side of least resistance, this was not the case for patients in the general population.

REFERENCES


Fig. 1 a-c – Attenuation over time curves for contrast infusion based on ideal conditions (a), clinically insignificant delays (b), and clinically significant delays (c).
**Fig. 2** – Coronal reformat of a CT angiogram demonstrating series trimming to remove evidence of arm of infusion.

**Fig. 3** – Transverse slice of a CT angiogram with a region of interest (ROI) placed within the main pulmonary artery. Attenuation values and cross-sectional area are shown.
Fig. 4 – Flow diagram of included studies.

Fig. 5 – Left versus right arm attenuation distribution.
Fig. 6 – Attenuation in Hounsfield units in the right vs. left arm with 95% confidence intervals shown.