Objective. The objective of our study was to estimate the mortality benefit-to-risk ratio of pulmonary CT angiography (CTA) by setting (ambulatory [emergency department or outpatient] or inpatient), age, and sex.

Materials and methods. A retrospective evaluation of 1424 consecutive pulmonary CTA examinations was performed and the following information was recorded: examination setting, patient age, patient sex, pulmonary CTA interpretation for pulmonary embolus (PE), and CT radiation exposure (dose-length product). We estimated mortality benefit of pulmonary CTA by multiplying the rate of positive pulmonary CTA examinations by published estimates of mortality of untreated PE in ambulatory and inpatient settings. We estimated the lifetime attributable risk of cancer mortality due to radiation from pulmonary CTA by calculating the estimated effective dose and using sex-specific polynomial equations derived from the Biological Effects of Ionizing Radiation VII report. We calculated benefit-to-risk ratios by dividing the mortality benefit of preventing a fatal PE by the mortality risk of a radiation-induced cancer.

Results. Pulmonary CTA diagnosed PE in 188 of 1424 patients (13.2%). Both inpatients (101/723, 14.0%) and emergency department patients (74/509, 14.5%) had significantly higher rates of PE than outpatients (13/192 [6.8%]). Males received significantly (p = 0.02451) higher radiation dose (9.7 mSv) than females (8.4 mSv), but males had a significantly (p < 0.0001) lower lifetime attributable risk of cancer mortality than females. Assuming an untreated PE mortality rate of 5% for ambulatory patients and 30% for inpatients, the benefit-to-risk ratio ranged from 25 for ambulatory patients to 187 for inpatients. Ambulatory women had the lowest benefit-to-risk ratio.

Conclusion. The benefit-to-risk ratio of pulmonary CTA in patients with suspected PE ranges from 25 to 187 and can be increased by optimizing the radiation dose.
would be lowest in young women. We hypothesized that the benefit-to-risk ratio of pulmonary CTA. Given the increased radiation-induced cancer risk in the form of lifetime attributable risk per milligray (mGy). This analysis has been performed for whole-body PET/CT [17] and coronary CTA [18].

The radiation risk associated with pulmonary CTA is often justified by the belief that untreated PE has a high mortality risk of approximately 30% [19]. However, as noted by Calder et al. [19], this risk estimate was derived from inpatient studies. They suggest that the mortality risk of untreated PE in ambulatory patients may be as low as 5%. Initial cohort studies of pulmonary CTA in the late 1990s were positive for PE in 25–30% of examinations. The widespread availability of CT has led to pulmonary CTA examinations of patients with lower clinical suspicion for PE. As a result, in some regions, PEs are found in approximately 5% of pulmonary CTA examinations [20, 21]. The combination of a lower mortality benefit than originally believed and the low yield of PE-positive examinations would substantially decrease the benefit-to-risk ratio of pulmonary CTA. Given the increased radiation sensitivity of younger patients and females, we hypothesized that the benefit-to-risk ratio would be lowest in young women.

Materials and Methods

Ethical approval for this retrospective cohort study was obtained from the institutional research board. The requirement for informed consent was waived on the basis of the retrospective design of the study and minimal risk profile. The finalized diagnostic report and the CT protocol page containing the commonly reported cumulative dose indicator, the dose-length product (DLP), were the only two documents reviewed for this investigation.

Using the common radiology information system of two academic teaching hospitals (hospitals 1 and 2) and one community hospital (hospital 3) within a single urban Canadian center, we reviewed 1424 consecutive pulmonary CTA reports and CT protocol pages from examinations performed from January 1, 2007, to December 31, 2007. Because this study is a retrospective cohort study approved by the ethics committee of the involved institutions, the authors were blinded to patient information except patient age, patient sex, examination DLP, examination setting, CT protocol, and pulmonary CTA interpretation. We recorded in a Microsoft Excel workbook the age and sex of the patient and the examination setting (ambulatory [emergency department or outpatient] or inpatient).

Pulmonary CTA interpretations for PE were categorized as positive, negative, or indeterminate using the impression in the finalized report. In accordance with the literature, radiologists defined CTA findings as positive for PE if one or more low-density filling defects were seen within the contrast-enhanced lumen of central, segmental, or subsegmental pulmonary arteries. If the report impression was negative or was a qualified negative for PE (e.g., no central or segmental PE but subsegmental PE cannot be excluded), the pulmonary CTA interpretation was categorized as negative. If the impression stated that the examination was nondiagnostic because of excessive motion artifact or because of inadequate pulmonary arterial contrast density (< 200 HU) or if the report did not comment on the presence or absence of PE, it was categorized as indeterminate.

For this study, neither retrospective review of CT images nor a comparison of CT images with other imaging studies or patient follow-up was performed to determine the accuracy of the pulmonary CTA interpretation. The proximal extent of PEs (central, segmental, subsegmental) and the effect of PEs on the pulmonary vasculature as evidenced by indirect signs of right ventricular volume and pressure overload (right ventricular dilation, straightening of the intraventricular septum, reflux of contrast material into the inferior vena cava) were not recorded.

Non–cardiac-gated helical acquisitions were performed using five CT scanners (two Sensation scanners, Siemens Healthcare; one Definition scanner, Siemens Healthcare; one 8-MDCT scanner [LightSpeed Ultra, GE Healthcare]), and one MDCT scanner [LightSpeed Pro-16, GE Healthcare]). A range of pulmonary CTA acquisition parameters were used at the three hospitals: 120 kVp; 100–250 mA; 0.5–1-second rotation time; variable use of x-, y-, and z-axis tube current modulation; and scan range to cover the entire lung volume as defined by the performing medical technologist.

The contrast medium used was uniform across the three sites (ioversol [Optiray 320, Tyco Healthcare]) but the injection protocols varied. The total volume of contrast material ranged from 80 to 150 mL and the injection rate ranged from 2 to 4 mL/s. The scan delay was timed using both a test timing bolus and an automated tracking bolus triggered at the 200-HU enhancement level. The specific injection protocol varied among sites and among radiologists within sites. Specific details of the timing and injection protocols were not documented in the diagnostic report or on the protocol page in the PACS (Impax, Agfa Healthcare).

Contiguous images of 2–2.5 mm in thickness were reconstructed using intermediate- and high-spatial-frequency algorithms (hospitals 1 and 2) or an intermediate-spatial-frequency algorithm only (hospital 3). Coronal, sagittal, and oblique axis reformations were not routinely obtained but were generated on the review workstation as required by the interpreting radiologists. All images were interpreted on workstations attached to the regional PACS and were viewed at medistinal (width, 350–450 HU; level, 30–35 HU) and lung (width, 1200–1500 HU; level, 700–750 HU) window settings.

The images were initially interpreted by resident house staff or subspecialty training fellows and the images and report were reviewed and signed off by attending radiologists with 2–13 years of experience in pulmonary CTA interpretation at hospitals 1 and 2. The images were directly interpreted and signed off by attending radiologists with 3–13 years’ experience in pulmonary CTA interpretation at hospital 3. For the purpose of this retrospective study, these signed clinical reports were used to categorize the PE status of the patient.

Mortality Benefit of the Pulmonary CT Angiography Examination

The mortality benefit of the pulmonary CTA examination was defined as the avoidance of the risk of mortality secondary to untreated PE. The mortality risk of untreated PE was calculated by multiplying the rate of positive pulmonary CTA interpretations by published estimates of mortality risk for untreated PE. The probability of mortality due to untreated PE ranges from a low of 5% for ambulatory patients to 30% for inpatients [19]. Accordingly, the mortality benefit was calculated separately for ambulatory and inpatient cohorts. If the pulmonary CTA interpretation was negative or indeterminate, the mortality benefit of the pulmonary CTA examination was assigned a value of 0.

Pulmonary CT Angiography Radiation Risk

According to the institutions’ protocols, both the images and dose reports for all CT examinations were archived to the PACS. For each pulmonary

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CTA examination, the PACS workstation was used to retrieve the protocol page that had the total DLP and the total DLP was recorded in the Excel workbook. The total DLP was the sum of radiation delivered for the contrast timing scan, if used; the control scan; all pulmonary CTA acquisitions used to cover the scanned volume; and any repeated acquisitions acquired secondary to suboptimal image quality. If the pulmonary CTA examination was performed as part of a larger imaging request (e.g., pulmonary CTA and CTA of the abdomen or pelvis), only the DLP associated with pulmonary CTA was recorded. The estimated effective dose of pulmonary CTA was calculated for each patient by multiplying the total DLP by the chest-specific conversion coefficient of 0.017 mSv · mGy⁻¹ · cm⁻¹ determined from Monte Carlo simulations of chest CT [22]. Organ-specific energy deposition was not calculated.

The lifetime attributable risk of cancer mortality per milligram was obtained per decade for males and females using Table 12D-2 (Annex 12D, page 311) of the BEIR VII report [14]. Because the table values represent point estimates per decade, we converted these point estimates into a continuous function from the age of 10 to 80 years using a polynomial fitting function. This conversion allowed more accurate interpolation of lifetime attributable risk for a specific patient age (e.g., age = 47 years). Using the maximum $R^2$ value as a goodness-of-fit parameter, the lifetime attributable risk ($LAR$) as a function of age (where $x$ is age at the time of exposure in years) was best fitted to a third-order polynomial equation separately for females (equation 1: $LAR_{female} = 17.259 - 0.736x + 0.0144x^2 - 0.00000951x^3$; $R^2 = 0.996$) and males (equation 2: $LAR_{male} = 10.759 - 0.438x + 0.0888x^2 - 0.00000685x^3$; $R^2 = 0.996$), where lifetime attributable risk is per 100,000 per millisievert. Because we are simply fitting a function to observed data for the purpose of accurate interpolation to specific ages, the resultant fitting equation is dimensionless. We then estimated the lifetime attributable risk of cancer mortality from the estimated effective dose of the pulmonary CTA examination for each patient using sex- and age-specific values. Because the lifetime attributable risk values for each age were estimated using the fitting function, at ages greater than 80 years, the lifetime attributable risk values less than 0 could be generated. If this occurred, a value of 0 was assigned. The mortality risk attributable to the contrast injection (80–150 mL of Optiray 320) for the pulmonary CTA examination was estimated at approximately 1 in 1 million and was not considered in the risk estimate.

**Benefit-to-Risk Ratio**

The benefit-to-risk ratio was calculated by dividing the benefit (avoidance of the risk of mortality secondary to untreated PE) by the age- and sex-adjusted (female, equation 1; male, equation 2) lifetime attributable risk of radiation-induced cancer mortality as shown by equation 3. The benefit-to-risk ratio was calculated separately for ambulatory patients and inpatients assuming the risk of untreated PE was 5% and 30%, respectively. The average benefit-to-risk ratio was calculated per decade for males and females. Using this experimental design, the potential for false-positive diagnosis of PE was not assessed. Because the risk of anticoagulation is based on an international normalized ratio therapeutic range control and confounding conditions (e.g., gastritis, ulcers, hypertension), we have not considered the risk of complications from anticoagulation therapy in this analysis. The benefit-to-risk ratio ($BRR$) was calculated as shown in equation 3:

$$BRR = \frac{\text{risk of untreated PE}}{LAR_{sex, age, dose}}$$

Example calculations of the benefit-to-risk ratio are provided in Appendix 1.

**Results**

In this retrospective cohort, there was a significant difference ($p = 0.036$) in the frequency that pulmonary CTA examinations were performed between females (768/1424, 54%) and males (656/1424, 46%) (Table 1). The rate of positive PE diagnosis was not significantly different ($p = 0.55$) between females (97/768 [12.6%]) and males (91/656 [13.9%]). We performed 701 of 1424 (49%) pulmonary CTA examinations on ambulatory patients and 723 of 1424 (51%) on inpatients (Table 2). Overall, PE was diagnosed in 188 of 1424 cases (13.2%) with no significant difference observed in the PE rate ($p = 0.45$) between ambulatory patients (87/701 [12.4%]) and inpatients (101/723 [14.1%]). However, when subdividing ambulatory patients into emergency department patients and those referred from doctors’ offices (outpatients), emergency department patients had a significantly higher rate of PE (74/509 [14.5%]) than outpatients (13/192 [6.8%]). Twenty-one of 1424 studies (1.5%) were nondiagnostic, with no significant difference ($p = 0.88$) between ambulatory patients (10/701 [1.5%]) and inpatients (11/723 [1.5%]). There was no significant difference ($p = 0.39$) in the PE-positive rates between sites (hospital 1, 140/1012 [13.8%]; hospital 2, 14/93 [15.1%]; hospital 3, 34/319 [10.7%]).

The DLP was retrievable from PACS for 1389 of 1424 pulmonary CTA examinations (97.6%). The estimated effective dose (Table 1) was significantly lower in females (8.4 mSv) than in males (9.7 mSv). There was no significant difference ($p = 0.53$) in the mean age of females (58.3 ± 19.0 [SD] years) and males (59.5 ± 17.7 years). However, the dose- and sex-adjusted lifetime attributable risk of cancer mortality was significantly higher ($p < 0.0001$) in females (33/100,000) than in males (28/100,000). In both females and males, the lifetime attributable risk of cancer mortality increased with decreasing age at time of exposure.

There was a higher proportion of females in the ambulatory cohort (404/701, 57.6%) than in the inpatient cohort (364/723, 50.3%). Between ambulatory and inpatients, a statistical difference ($p = 0.00011$) was found between age (ambulatory, 57.0 ± 19.0 years; inpatient, 60.7 ± 17.7 years) but not for mean dose (ambulatory, 9.1 ± 3.2 mSv; inpatient, 8.9 ± 3.5 mSv) ($p = 0.19$). However, when accounting for the combined effect of sex, age, and dose using the polynomial fitting equation, the lifetime attributable risk of cancer mortality was significantly higher ($p = 0.0006$) in ambulatory patients (32/100,000) compared with inpatients (29/100,000).

Assuming a PE mortality rate of 5% for ambulatory patients and 30% for inpatients [19], benefit-to-risk ratios were calculated. The mean benefit-to-risk ratio was lower in ambulatory patients (25.3) than inpatients (187.2) and across all age groups, as shown in Figure 1. Among ambulatory patients, the benefit-to-risk ratio was lower in outpatients (12.7) than emergency department patients (30.1). Predicted benefit-to-risk ratios assuming a 5% PE rate and half of the radiation dose (4.5 mSv) are illustrated in Figure 2.

**Discussion**

We found that the lifetime attributable risk of cancer mortality and, consequently, the benefit-to-risk ratio of pulmonary CTA varied substantially with the estimated effective dose, age at exposure, and sex. The lifetime attributable risk of cancer mortality ranged from 57/100,000 for females 17–19 years old to 8/100,000 for males and females 80–89.
Risk-Benefit Analysis of Pulmonary CTA

TABLE I: Pulmonary CT Angiography (CTA) Data Categorized by Sex and Age Group at Exposure

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age Group (y)</th>
<th>No. of Studies</th>
<th>CTA Study Interpretation for PE</th>
<th>% CTA Studies With Positive Findings for PE</th>
<th>Dose (mSv)a</th>
<th>Mean Lifetime Attributable Risk of Cancer Mortalityb,c</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Positive</td>
<td>Negative</td>
<td>Indeterminate</td>
<td>Mean</td>
</tr>
<tr>
<td>Male</td>
<td>15–19</td>
<td>8</td>
<td>0</td>
<td>8</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>20–29</td>
<td>36</td>
<td>3</td>
<td>31</td>
<td>2</td>
<td>8.3</td>
</tr>
<tr>
<td></td>
<td>30–39</td>
<td>69</td>
<td>8</td>
<td>57</td>
<td>4</td>
<td>11.6</td>
</tr>
<tr>
<td></td>
<td>40–49</td>
<td>70</td>
<td>11</td>
<td>57</td>
<td>2</td>
<td>15.7</td>
</tr>
<tr>
<td></td>
<td>50–59</td>
<td>109</td>
<td>15</td>
<td>94</td>
<td>0</td>
<td>13.8</td>
</tr>
<tr>
<td></td>
<td>60–69</td>
<td>142</td>
<td>24</td>
<td>118</td>
<td>0</td>
<td>16.9</td>
</tr>
<tr>
<td></td>
<td>70–79</td>
<td>142</td>
<td>19</td>
<td>121</td>
<td>2</td>
<td>13.4</td>
</tr>
<tr>
<td></td>
<td>80–89</td>
<td>73</td>
<td>8</td>
<td>63</td>
<td>2</td>
<td>11.0</td>
</tr>
<tr>
<td></td>
<td>90–99</td>
<td>7</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>42.9</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>656</td>
<td>91</td>
<td>553</td>
<td>12</td>
<td>13.9</td>
</tr>
</tbody>
</table>

Female 17–19 9 1 8 0 11.1 7.1 10.3 4.3 57.4
20–29 61 7 53 1 11.5 7.5 20.7 3.6 48.7
30–39 73 5 65 3 6.8 7.9 18.9 3.2 40.4
40–49 106 9 95 2 8.5 8.1 24.2 3.6 37.8
50–59 124 18 106 0 14.5 8.6 23.1 3.3 38.7
60–69 148 25 122 1 16.9 9.0 38.0 2.2 37.2
70–79 142 21 120 1 14.8 8.5 22.6 3.0 25.1
80–89 86 11 74 1 12.8 8.7 16.6 3.3 8.5
> 90 19 0 19 0 0.0 6.8 11.6 3.6 0
Total 768 97 662 9 12.6 8.4 38.0 2.2 32.7
Grand Total 1424 188 1215 21 13.2 9.0 38.0 2.2 30.5

Note—Lifetime attributable risk for females and males were calculated using equation 1 and 2, respectively. PE = pulmonary embolus, Max = maximum, Min = minimum.
aCalculated for patients with dose data (1389/1424).
bPer 100,000 people corrected for mean mSv exposure, age, and sex.
cMean ± SD.

We note that one randomized clinical trial [23] comparing pulmonary CTA with nuclear medicine ventilation-perfusion scintigraphy using recurrent PE within 3 months as the outcome measure found no significant difference (p > 0.05) in outcome. However, an unanticipated finding was a significantly increased rate of venous thromboembolism diagnosis in the pulmonary CTA cohort. This finding suggests that pulmonary CTA might be identifying a milder form in the spectrum of PE disease [24] and raises questions regarding the mortality risk in pulmonary CTA–diagnosed PE, especially for patients with a limited burden of PEs (e.g., subsegmental PE). These findings further question mortality figures in the literature used in this analysis. Further research into this question is indicated.

The mean pulmonary CTA estimated effective dose was approximately 3.6 times the annual estimated effective dose from background radiation, which is about 2.4 mSv [1] in North America. In this study, the estimated effective dose in both males and females gradually increased with age until approximately 50–69 years and then declined. The pulmonary CTA estimated effective dose was significantly higher in males than females in each age group, likely secondary to the larger size of males, leading to both a larger scanned volume and a higher tube current–exposure time product (mAs). The mean estimated effective dose of a pulmonary CTA examination was 9.0 mSv and ranged from 2.2 to 38 mSv. For a female 20–29 years old, the mean estimated effective dose was 7.5 mSv, which corresponds to a lifetime attributable risk of cancer mortality of 0.084% or approximately 1 in 1190. The lifetime attributable risk of cancer mortality was significantly (p < 0.05) lower in males than females across all age groups even though the estimated effective dose was higher for males. This difference reflects the increased radiation sensitivity of females relative to males and highlights the need to correct-
could be addressed in a prospective study. This limitation previously shown to impact the survival rates of available for analysis, which has been previ-
ous nature of this study, ethnic data were not included. Because of the blinded, retrospec-
tive protocol for each pulmonary CTA study. Not record the CT scanner model or specif-
cals have multiple CT scanners and we did not record the CT scanner model or specific-
ly interpret both DLP and estimated effective dose measures. Both of these metrics are dose indicators and do not incorporate the important subject-specific risk factors of age and sex.

We note that in comparison with other imaging modalities, pulmonary CTA has a lower lifetime attributable risk of cancer mortality than whole-body PET/CT [17] and coronary CTA [18].

The retrospective cohort design of this study has several limitations. The retrospective study design did not allow any control of the clinical symptoms or signs leading to the request for a pulmonary CTA examination. In general, clinicians at these hospitals use the validated clinical decision rule, the Wells criteria, before ordering a pulmonary CTA examination. However, we cannot validate that all patients received this clinical evaluation before being imaged. All three hospitals have multiple CT scanners and we did not record the CT scanner model or specific protocol for each pulmonary CTA study. The attending radiologist’s pulmonary CTA interpretation was assigned as the gold standard for determination of PE. No clinical follow-up, additional imaging tests, or autopsy data were reviewed to determine the incidence of either false-positive or false-negative pulmonary CTA interpretations. Our study investigated only people who received medical attention; thus, the overall mortality of PE in the population was not assessed in this study. Because of the blinded, retrospective nature of this study, ethnic data were not available for analysis, which has been previously shown to impact the survival rates of patients with PE [25, 26]. This limitation could be addressed in a prospective study.

In our calculation of the benefit-to-risk ratio for pulmonary CTA, the benefit and risk were strictly defined. The mortality benefit of pulmonary CTA was defined as the probability of preventing a fatal PE at the positive PE rate found in this study. Because this study failed to identify a single positive PE in males 15–19 years old, the mortality benefit according to our model is 0. For this sex and age group, the benefit-to-risk ratio cannot be established because the sample size is limited. A single positive PE case was also not found in our study for females 90–99 years old. For this sex and age group, the calculation of the benefit-to-risk ratio is indeterminate given that the extrapolated lifetime attributable risk for all persons older than 90 years is 0 because of their limited life expectancy and the latency of radiation effects.

Our definition for mortality benefit assumed all positive PE cases resulted in uniform risk of either 30% or 5% with no adjustment for age or sex. To our knowledge, in comparison with the Life Span Study [16], no equivalent, large-cohort, long-term population-based study assessing the impact of age and sex on PE mortality exists. We are aware of only two published studies that provide age- and sex-specific survival rates for PE, studies by Siddique et al. [25] and Anderson et al. [27]. Siddique et al. provided survival functions only for patients older than 65 years old, limiting the ability to apply their results to our patient data for patients 65 years old or younger. Anderson et al. provided survival functions for patients older than 10 years with both deep vein thrombosis and PE but only a 4-year outlook in comparison with more than 50 years of data from the Life Span Study [16]. Given these limitations, neither model can be appropriately adapted to our model.

In addition, we did not account for other benefits secondary to diagnosing PE. These

<table>
<thead>
<tr>
<th>Patient Setting</th>
<th>Age (y)</th>
<th>No. of Studies</th>
<th>CTA Study Interpretation for PE</th>
<th>% CTA Studies With Positive Findings for PE</th>
<th>Dose (mSv)</th>
<th>Mean</th>
<th>Max</th>
<th>Min</th>
<th>Mean Lifetime Attributable Risk of Cancer Mortality</th>
<th>Benefit-to-Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient</td>
<td>60.7 ± 17.7</td>
<td>723</td>
<td>101</td>
<td>611</td>
<td>11</td>
<td>14.0</td>
<td>8.9</td>
<td>31.0</td>
<td>2.2</td>
<td>29.0</td>
</tr>
<tr>
<td>Ambulatory</td>
<td>57.0 ± 19.0</td>
<td>701</td>
<td>87</td>
<td>604</td>
<td>10</td>
<td>12.4</td>
<td>9.1</td>
<td>25.2</td>
<td>3.0</td>
<td>32.0</td>
</tr>
<tr>
<td>ED</td>
<td>57.5 ± 19.1</td>
<td>509</td>
<td>74</td>
<td>428</td>
<td>7</td>
<td>14.5</td>
<td>9.3</td>
<td>25.2</td>
<td>3.3</td>
<td>32.5</td>
</tr>
<tr>
<td>Outpatient</td>
<td>55.7 ± 18.7</td>
<td>192</td>
<td>13</td>
<td>176</td>
<td>3</td>
<td>6.8</td>
<td>8.5</td>
<td>16.4</td>
<td>3.0</td>
<td>30.6</td>
</tr>
<tr>
<td>Total</td>
<td>58.9 ± 18.4</td>
<td>1424</td>
<td>188</td>
<td>1215</td>
<td>21</td>
<td>13.2</td>
<td>9.0</td>
<td>31.0</td>
<td>2.2</td>
<td>30.5</td>
</tr>
</tbody>
</table>

Note—Lifetime attributable risk for females and males were calculated using equation 1 and 2, respectively. PE = pulmonary embolus, Max = maximum, Min = minimum, ED = emergency department.

FIG. 1—Benefit-to-risk ratio of pulmonary CT angiography (CTA) in female and male ambulatory patients and inpatients. Higher benefit-to-risk ratios better justify use of ionizing radiation to diagnose pulmonary embolus (PE). Note that PE mortality rate was 0 for ambulatory males (age, 10–29 years), inpatient males (age, 10–19 years), and inpatient females (age, 10–19 years). For these groups, benefit-to-risk ratio calculation is 0 and thus cannot be determined using study sample size.
benefits include the benefit of preventing pulmonary hypertension caused by chronic PE, which has been reported in approximately 1% of PE patients [28]. We did not account for the benefit of detecting ancillary findings at CT such as pneumonia, cardiovascular disease, pulmonary fibrosis, trauma, malignancy, pleural disease, and post-operative changes. In patients without PE, previous studies have reported ancillary CT findings accounting for presenting signs and symptoms at rates ranging from 33% to 67% [5, 29, 30]. We note that the ability of CT to provide alternate explanations for a patient’s presenting complaints contributes to its wide popularity as a diagnostic tool in this clinical setting [31].

The risk of pulmonary CTA was defined as the lifetime attributable risk of cancer mortality. We did not account for the risk of nonfatal cancer induction, which is approximately twice the lifetime attributable risk of cancer mortality [14]. The risks of allergic and nonallergic reactions to iodinated contrast media, interstitial extravasation of contrast material, and contrast nephropathy were also not incorporated into the benefit-to-risk ratio.

As the term implies, “estimated effective dose” has inherent uncertainty. It is most inaccurate for small and very large subjects because it is a metric designed to predict risk in a 70-kg hermaphrodite reference subject. However, despite the acknowledged inaccuracy of this metric, this method of dose estimation is highly practical because it can be easily calculated by multiplying the total scanner-reported DLP by a chest conversion coefficient [32]. Although we used a chest conversion coefficient of 0.017 mSv · mGy⁻¹ · cm⁻¹ based on the 2000 European Commission guidelines [32], a chest conversion coefficient of 0.014 mSv · mGy⁻¹ · cm⁻¹ has also been proposed in Appendix C of the 2004 guidelines [24]. However, estimated effective dose derived from organ doses, calculated on the basis of the methods recommended by the International Commission on Radiological Protection (ICRP) in ICRP publications 103 [33] and 60 [15], suggests that the actual effective dose in a specific patient may be between 30% and 200% of the estimated effective dose calculated by the aforementioned method [34, 35].

Finally, we acknowledge that the lifetime attributable risk estimate of cancer mortality also has inherent uncertainty and is not supported by randomized clinical experimental data. Although there is no firm experimental evidence to conclude that the linear no-threshold model for low-dose radiation risk is valid, the results of epidemiologic studies of Japanese survivors of the atomic bomb explosions [36] and the largest occupational study of nuclear workers [37] are consistent with this extrapolation. Furthermore, most authorities agree that the linear no-threshold model for low-dose radiation risk estimation is a reasonable assumption. A full discussion of the scientific debate surrounding the use of the linear no-threshold extrapolation is beyond the scope of this article. Further information about the scientific controversy surrounding this issue can be found in two recently published reviews [38, 39].

In summary, sex-specific third-order polynomial equations can be used to estimate the lifetime attributable risk of cancer mortality as a function of age at exposure. Pulmonary CTA was found to have the lowest benefit-to-risk ratios for females 17–39 years old in all settings studied, female outpatients 50 years or older, and female emergency department patients in general. Reducing the radiation dose by half in these cohorts would double the benefit-to-risk ratio of pulmonary CTA. Substantial advances in chest CT radiation dose reduction including multi-axis tube current modulation, adjustment of tube voltage based on patient size, limitation of z-axis coverage, collimator shutter action to eliminate z-axis overscanning, and iterative reconstruction algorithms have the potential to reduce radiation dose by at least a factor of 2 with minimal decrease in image quality. Because halving the radiation dose results in a doubling of the benefit-to-risk ratio, utilization of these dose reduction strategies should be routine, especially in younger patients. Alternatively, in the correct clinical setting, imaging investigations using either lower ionizing radiation dose (ventilation-perfusion scintigraphy [31]) or no ionizing radiation dose (lower leg Doppler ultrasound or pulmonary MR angiography and venography) should be considered. Awareness of the intrinsic benefit-to-risk ratio for pulmonary CTA examinations will enhance the utilization of dose reduction strategies, assist in the appropriate application of this radiologic investigation, and facilitate substitution of pulmonary CTA with lower-dose examinations in the appropriate clinical setting.

References
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(Appendix 1 follows on next page)
Risk-Benefit Analysis of Pulmonary CTA

APPENDIX 1: Detailed Calculation of the Benefit-to-Risk Ratio

This appendix is intended to provide readers with a method to calculate the benefit-to-risk ratio. The lifetime attributable risk (LAR) of induced cancer mortality is defined as the number of excess deaths per 100,000 people from a single exposure of 100 mGy [14]. The risk is both age and sex dependent, with point estimates per decade listed in Table 12-D2 of the BEIR VII report [14].

A continuous function for each sex was developed fitting a third-degree polynomial to the point estimates for patient between 10 and 80 years old. These equations are referenced in the article as equation 1 and equation 2 for females and males, respectively. Because the LAR is defined as the excess number of cancer deaths in a population of 100,000 exposed to 100-mGy dose, the LAR from a pulmonary CT angiography (CTA) examination must be adjusted for the estimated effective dose received from the examination. This adjustment is achieved by converting the DLP to the estimated effective dose by multiplying the DLP by an examination region-specific conversion factor. For chest examinations, this conversion factor is 0.017 mSv · mGy–1 · cm–1. Please note the effective dose (mSv) is equivalent to a full-body absorbed dose (mGy) for x-ray radiation.

After adjusting the LAR for estimated effective dose received by the patient, the benefit-to-risk ratio is calculated as the quotient of the risk of untreated PE (5% for ambulatory patients, 30% for inpatients) by the dose-adjusted LAR (equation 3). The following two examples illustrate the calculation process.

Example 1: A 25-year-old woman underwent pulmonary CTA; the recorded DLP for the examination was 440 mGy · cm.

Step 1—Calculate estimated effective dose ($E$):

$E = \text{DLP} \times 0.017$

$E = 440 \times 0.017$

$E = 7.48 \text{ mSv}$

Step 2—Calculate the LAR per 1 mSv exposure:

$LAR_{\text{female}} = 17.259 - 0.736x + 0.0144x^2 - 0.0000951x^3$

$LAR_{\text{female}} = 17.259 - 0.736(25) + 0.0144(25)^2 - 0.0000951(25)^3$

$LAR_{\text{female}} = 6.37$

Step 3—Calculate LAR for specific examination exposure:

$LAR = \frac{LAR_{\text{per mSv}} \times E}{6.37 \times 7.48} = 47.6$

Step 4—Calculate the benefit-to-risk ratio for ambulatory ($BRR_{\text{amb}}$) and inpatient ($BRR_{\text{inpatient}}$) cohorts, 5% and 30%, respectively:

$BRR_{\text{amb}} = \frac{0.05}{LAR} = 0.0011$

$BRR_{\text{inpatient}} = \frac{0.3}{LAR} = 0.0063$

Example 2: A 58-year-old man underwent pulmonary CTA; the total DLP was 588 mGy · cm.

Follow the same steps shown in Example 1.

Step 1—Calculate estimated effective dose ($E$):

$E = \text{DLP} \times 0.017$

$E = 588 \times 0.017$

$E = 10.0 \text{ mSv}$

Step 2—Calculate the LAR per 1-mSv exposure:

$LAR_{\text{male}} = 10.759 - 0.438x + 0.0888x^2 - 0.0000608x^3$

$LAR_{\text{male}} = 10.759 - 0.438(58) + 0.0888(58)^2 - 0.0000608(58)^3$

$LAR_{\text{male}} = 3.36$

Step 3—Calculate LAR for specific examination exposure:

$LAR = \frac{LAR_{\text{per mSv}} \times E}{3.36 \times 10} = 33.6$

Step 4—Calculate the benefit-to-risk ratio for ambulatory ($BRR_{\text{amb}}$) and inpatient ($BRR_{\text{inpatient}}$) cohorts, 5% and 30%, respectively:

$BRR_{\text{amb}} = \frac{0.05}{LAR} = 0.0015$

$BRR_{\text{inpatient}} = \frac{0.3}{LAR} = 0.0089$