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ORIGINAL ARTICLE

Accuracy of CT chest without oral contrast for ruling out esophageal perforation using fluoroscopic esophagography as reference standard: a retrospective study

Muhammad Awais[1,2] · Saqib Qamar[1] · Abdul Rehman[1,3] · Noor Ul-Ain Baloch[1,4] · Gulnaz Shafqat[1]

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Abstract

Purpose Esophageal perforation has a high mortality rate. Fluoroscopic esophagography (FE) is the procedure of choice for diagnosing esophageal perforation. However, FE can be difficult to perform in seriously ill patients.

Methods We retrospectively reviewed charts and scans of all patients who had undergone thoracic CT (TCT) without oral contrast and FE for suspicion of esophageal perforation at our hospital between October, 2010 and December, 2015. Scans were interpreted by a single consultant radiologist having > 5 years of relevant experience. Statistical analysis was performed using SPSS version 20. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of TCT were computed using FE as reference standard.

Results Of 122 subjects, 106 (83%) were male and their median age was 42 [inter-quartile range (IQR) 29–53] years. Esophageal perforation was evident on FE in 15 (8%) cases. Sensitivity, specificity, PPV and NPV of TCT for detecting esophageal perforation were 100, 54.6, 23.4 and 100%, respectively. When TCT was negative ($n = 107$), an alternative diagnosis was evident in 65 cases.

Conclusion Thoracic computed tomography (TCT) had 100% sensitivity and negative predictive value for excluding esophageal perforation. FE may be omitted in patients who have no evidence of mediastinal collection, pneumomediastinum or esophageal wall defect on TCT. However, in the presence of any of these features, FE is still necessary to confirm or exclude the presence of an esophageal perforation.

Keywords Esophageal perforation · Computed tomography · Contrast swallow · Fluoroscopy · Esophagography

Introduction

Esophageal perforation is a catastrophic event for most patients and can become a life-threatening condition in many cases [1]. Perforation of the esophagus can be iatrogenic, most commonly occurring after endoscopic procedures, but it may occur spontaneously or following blunt or penetrating chest trauma [2]. Mortality rates of esophageal perforation have been reported to be as high as 40% following spontaneous perforations, although outcome depends on the etiology, site of perforation and time of surgical intervention [3]. Patients generally present with non-specific signs and symptoms, such as chest pain, repetitive vomiting, retching and fever [4]. Physical examination may be notable for subcutaneous emphysema and plain radiographs may reveal a left-sided pleural effusion and/or pneumomediastinum [5]. A high index of suspicion is required for diagnosis and prompt

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✉ Muhammad Awais
awais_aku@yahoo.com

[1] Department of Radiology, The Aga Khan University Hospital, P.O. box 3500, Stadium Road, Karachi, Sindh 74800, Pakistan

[2] Department of Radiology, Dow University of Health Sciences, Ojha Campus, Suparco Road, KDA Scheme 33, Karachi, Sindh 75270, Pakistan

[3] Internal Medicine Section, Department of Medicine, Hamad Medical Corporation, P.O. box 3050, Doha, Qatar

[4] Department of Medicine, Rutgers-New Jersey Medical School, Newark, NJ, USA

recognition is essential to institute appropriate surgical management in a timely manner [6].

Fluoroscopic esophagography (FE) is generally considered the procedure of choice for diagnosis of patients with esophageal perforation [7]. This procedure requires the patient to swallow contrast material and trained personnel to capture proper radiographic images. This procedure can be technically difficult to perform in seriously ill patients and requires availability of a fluoroscopy suite with trained personnel [8]. Computed tomography is a rapid imaging modality that can be used in critically ill patients and provides an accurate assessment of thoracic and mediastinal structures [9, 10]. A number of abnormal findings may be detected by computed tomography that can suggest the presence of an esophageal perforation [8, 11].

Thoracic computed tomography (TCT) may be a useful imaging modality for patients with suspected esophageal perforation [12]. However, there is insufficient evidence available to justify its use as an imaging modality for patients with suspected esophageal perforation. We hypothesized that TCT may be sensitive for the detection of esophageal perforation. To test this hypothesis, we performed a retrospective cross-sectional study at our center to assess the diagnostic performance of TCT using FE as the reference standard. By evaluating the diagnostic performance of TCT, we may be able to justify or refute its use in patients with suspected esophageal perforation.

Methods

Our tertiary care center is a 522-bedded hospital located in an urban city of a lower-middle income country with an estimated population of almost 27.5 million. After obtaining exemption from formal approval by the institutional ethics review committee, we performed a retrospective cross-sectional study. We retrieved reports of all FEs performed between October, 2010 and December, 2015 for a clinical suspicion of "esophageal perforation" using the institutional radiology information system (RIS). Patients were eligible for inclusion in the study if they had undergone TCT with intravenous contrast (but without oral contrast) for up to 48 h prior to the fluoroscopic examination. We excluded patients for whom FE was incomplete, or could not be performed satisfactorily. We also excluded patients who had undergone TCT after, or more than 48 h before the FE. Using a pre-designed, structured pro forma, each patient's chart was systematically reviewed and data relating to demographics, clinical features and subsequent work-up were collected. Personal identifiers or other identifiable information were not recorded. FE was performed using a digital fluoroscopic machine (FluoroSpeed 300®, Schimadzu, Japan) after asking the patient to swallow 50–100 ml of non-ionic contrast (Omnipaque®, Nycomed, Switzerland). Images were acquired in frontal and lateral projections. TCT was performed on either a 64-slice (Aquilion®, Toshiba, Japan) or 640-slice (Aquilion ONE®, Toshiba, Japan) multidetector CT scanner. After a scout film was obtained, 80 ml of non-ionic contrast (Omnipaque®, Nycomed, Switzerland) was injected intravenously and scanning was started by automatic bolus tracking technique. Oral contrast material was not used for any of these scans.

A single consultant radiologist with more than 5 years of experience in body imaging interpreted all scans. All scans were de-identified prior to re-interpretation for the purpose of this study. All FE scans were reviewed for evidence of esophageal perforation. For the purpose of this study, esophageal perforation on FE was defined as an extravasation of non-ionic contrast material outside the esophageal lumen (Fig. 1). All TCT scans were systematically reviewed for the presence of: (i) esophageal wall defect; (ii) pneumomediastinum; (iii) mediastinal collection or hematoma; (iv) pneumothorax or hydropneumothorax; (v) pleural effusion; (vi) subcutaneous emphysema; (vii) any other abnormality of the esophagus; (viii) any abnormal findings unrelated to the esophagus. For each TCT scan, the consultant radiologist also recorded if any alternative diagnosis was strongly suggested by the TCT scan findings (e.g., tracheal disruption or intra-abdominal viscus perforation). For the purpose of this study, we defined esophageal wall defect as a

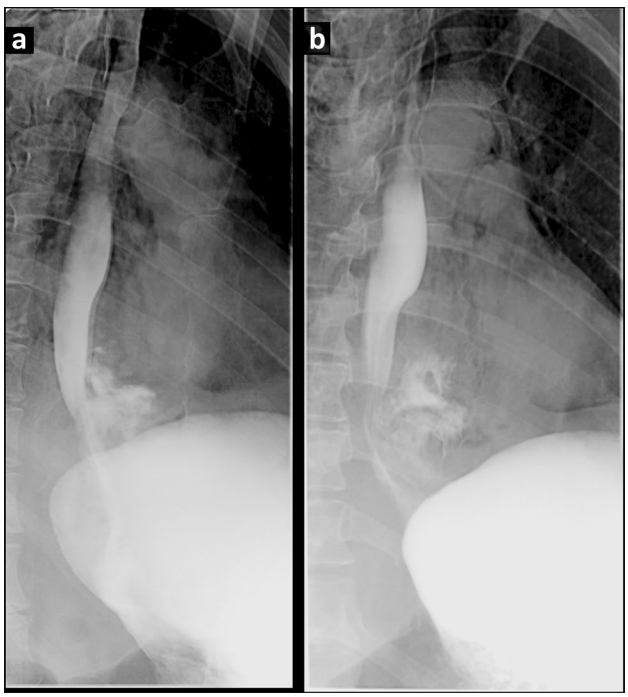

Fig. 1 **a**, **b** Fluoroscopic esophagograms demonstrating frank extravasation of contrast material from the distal esophagus consistent with an esophageal perforation

discontinuation or an obvious defect within the wall of the esophagus. Pneumomediastinum was defined as the presence of free air specks within the mediastinal compartment but outside the lumen of the trachea or esophagus. Mediastinal collection or hematoma was defined as the presence of fluid (low density or mixed density material) in the mediastinal compartment outside the lumen of the trachea or esophagus (see Fig. 2). Pneumothorax was defined as the presence of air specks between the visceral and parietal pleura. Hydropneumothorax was defined as the presence of an air-fluid level within the pleural cavity (i.e., between the visceral and parietal pleura). Pleural effusion was defined as the presence of fluid (low density material) between the visceral and parietal pleura. Subcutaneous emphysema was defined as the presence of subcutaneous air in the fascial planes of the chest wall or the neck. If any other abnormal finding relating to the esophagus was evident (e.g., contrast enhancement of the wall, free specks of air outside the wall of the intra-abdominal part of the esophagus, etc.), it was also recorded.

For the purpose of this study, a TCT scan was considered "positive" for esophageal perforation if any of the following findings were noted: an esophageal wall defect, pneumomediastinum or mediastinal collection/hematoma. If neither of these findings were noted, a TCT scan was considered "negative". A TCT scan was considered a true positive if evidence of an esophageal perforation was confirmed by FE. A TCT scan was considered to be a true negative if esophageal perforation was excluded by an adequately performed FE. A TCT scan was considered false positive if esophageal perforation was excluded by FE but the TCT scan was positive. Likewise, a TCT scan was considered false negative if the TCT scan was negative, but FE showed evidence of esophageal perforation. Sensitivity of TCT was calculated as the number of true positive scans divided by the number of patients who were noted to have esophageal perforation on FE. Likewise, specificity of TCT was computed as the number of true negative scans divided by the number of patients who did not have evidence of esophageal perforation on an adequately performed FE. Positive predictive value (PPV) was calculated as the number of true positive TCT scans divided by the number of all TCT scans that were positive. Likewise, negative predictive value (NPV) was computed as the number of true negative TCT scans divided by the number of all TCT scans that were negative. Positive likelihood ratio was calculated as the ratio of sensitivity to (1 − specificity), while negative likelihood ratio was calculated as the ratio of (1 − sensitivity) to specificity.

To determine the optimal sensitivity and specificity of TCT, we computed the sensitivity and specificity of TCT by changing the definition of a "positive" scan using various combinations of esophageal abnormalities. We then determined sensitivity and specificity of TCT and plotted them on a graph with (1 − specificity) as the abscissa and sensitivity as the ordinate—analogous to a receiver operating characteristic curve [13]. Statistical Package for Social Sciences (SPSS) version 20.0 was used for performing statistical analysis. Frequencies were calculated for qualitative variables, while median [inter-quartile range (IQR)] was computed for

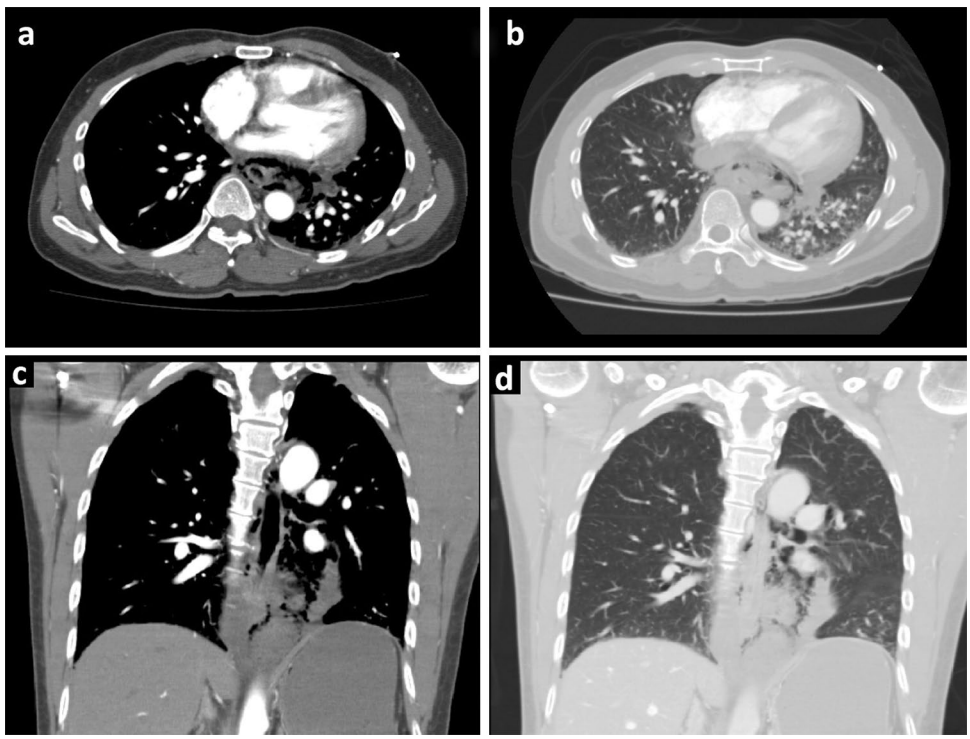

Fig. 2 **a, b** Axial and **c, d** coronal images at mediastinal and lung windows (respectively) demonstrating a thick-walled esophagus with surrounding mediastinal hematoma and pneumomediastinum

quantitative variables. Chi-square (χ^2) or Fisher's exact test was used for comparison of proportions. For all comparisons, a *P* value of less than 0.05 was considered statistically significant.

Results

Of a total of 700 FE, only 321 were performed for a suspicion of esophageal perforation. Of these patients, only 128 had undergone TCT within the preceding 48 h. We excluded another 5 patients from analysis, as they had an inconclusive (or incomplete) FE, leaving 123 patients for final analysis (Fig. 3). Median age of included subjects was 42 (IQR 29–53) years and 106 (86.2%) were men. Most patients were referred from the emergency department ($n=105$, 85.4%), while a few were referred from the in-patient admission units ($n=18$, 14.6%). The most common indications for performing FE were firearm injuries ($n=68$, 55.3%), road traffic accidents ($n=21$, 17.1%) or following endoscopic or surgical procedures ($n=15$, 21%). Thirteen (10.6%) patients had a history of malignancy. These results are summarized in Table 1.

The prevalence of esophageal perforation on FE in our sample was 12.2% (15/123). The most common findings noted on TCT were pneumo- or hydropneumothoraces ($n=67$, 54.5%), pneumomediastinum ($n=58$, 47.2%) and pleural effusions ($n=48$, 39%). Esophageal wall defect was noted in 3 (2.4%) scans, while mediastinal collections or hematoma were noted in 17 (13.8%) TCT scans. Another 36 (29.3%) patients had evidence of subcutaneous emphysema. Other esophageal abnormalities were evident on 13 (10.6%) TCT scans. Moreover, 98 (79.7%) scans had abnormal findings unrelated to the esophagus. Among patients with negative TCT, an alternative diagnosis was evident in 65 (52.8%) cases. Findings of TCT in patients who had evidence of esophageal perforation on FE are given in Table 2.

Using our standard definition of a positive TCT scan (i.e., pneumomediastinum or mediastinal collection/hematoma *or* esophageal wall defect), 64 (52%) TCT scans were positive for esophageal perforation. Table 3 provides data in a 2×2 table format with depiction of true positive, false positive, true negative and false negative findings. Using our standard

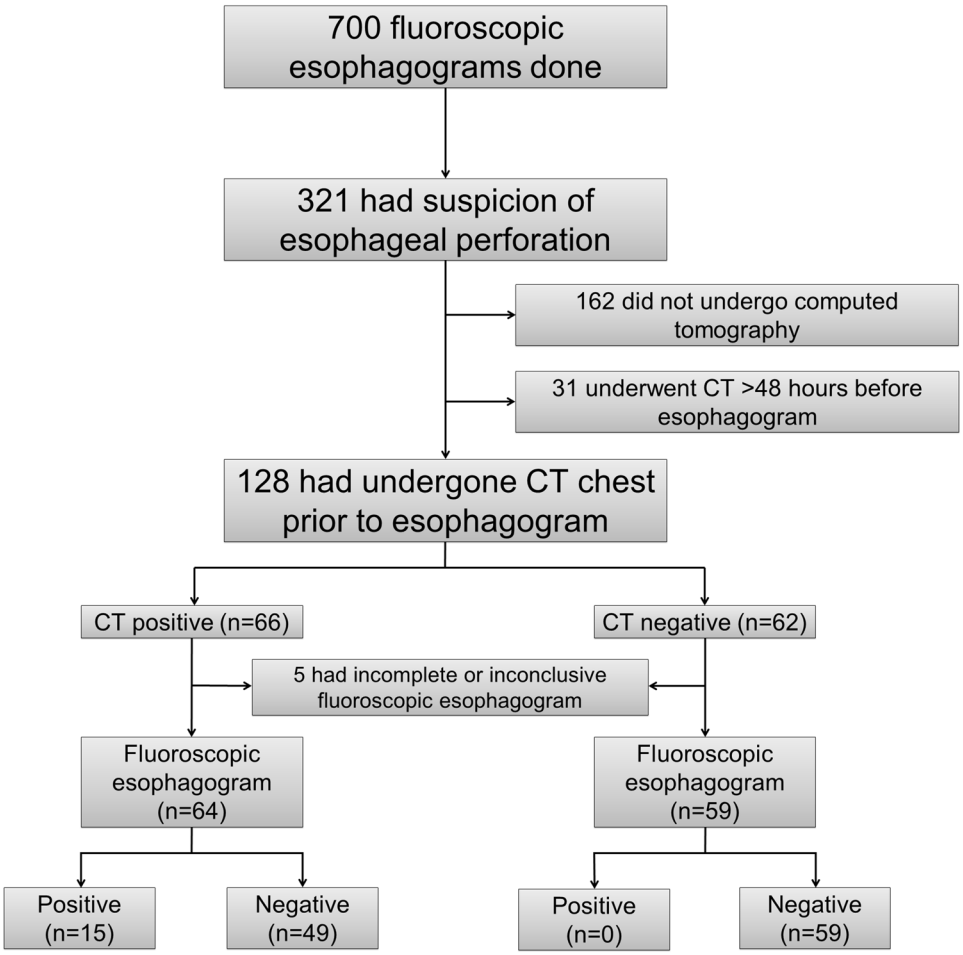

Fig. 3 Flow diagram depicting the inclusion of patients in our study and performance of index (thoracic computed tomography) and reference tests (fluoroscopic esophagography). *CT* computed tomography

Table 1 Characteristics of subjects included in our study

Characteristics	All subjects ($n=123$)	Subjects with esophageal perforation[a] ($n=15$)
Sex		
Female	17 (13.8%)	2 (13.3%)
Male	106 (86.2%)	13 (86.7%)
Age [median (IQR)], years	42 (29–53)	55 (51–62)
Source of referral		
Emergency department	105 (85.4%)	11 (73.3%)
In-patient units	18 (14.6%)	4 (26.7%)
Clinical indication		
Firearm injuries	68 (55.3%)	7 (46.7%)
Road traffic accidents	21 (17.1%)	0 (0.0%)
Post-procedure[b]	15 (12.2%)	4 (26.7%)
Stab wounds	4 (3.3%)	1 (6.7%)
Blunt trauma (NOS)	3 (2.4%)	0 (0.0%)
Corrosive ingestion	1 (0.8%)	1 (6.7%)
Other	11 (8.9%)	2 (13.3%)
History of malignancy		
Yes	13 (10.6%)	2 (13.3%)
No	110 (89.4%)	13 (86.7%)

IQR inter-quartile range, *NOS* not otherwise specified

[a]As evidenced by active contrast extravasation on fluoroscopic esophagography

[b]Surgical or endoscopic procedures

Table 2 Results of computed tomography vis-à-vis those of fluoroscopic esophagography

Computed tomography	Fluoroscopic esophagography		Total
	Negative	Positive	
Negative	59	0	59
Positive	49	15	64
Total	108	15	123

Table 3 Findings of thoracic computed tomography among study subjects

Radiologic findings[a]	All subjects ($n=123$)		Subjects with esophageal perforation[b] ($n=15$)	
	n	%	*n*	%
Esophageal wall defect	3	2.4%	3	20.0%
Pneumomediastinum	58	47.2%	11	73.3%
Mediastinal collection/hematoma	17	13.8%	9	60.0%
Pneumo- or hydropneumothorax	67	54.5%	5	33.3%
Pleural effusion	48	39.0%	7	46.7%
Subcutaneous emphysema	36	29.3%	6	40.0%
Other esophageal abnormalities	13	10.6%	6	40.0%

[a]See the "Methods" section for definitions of each of these radiologic findings

[b]Esophageal perforation as evidenced by active extravasation of contrast material on an adequately performed fluoroscopic esophagogram

definition, sensitivity and specificity of TCT for detection of esophageal perforation were 100 and 54.6% respectively. PPV and NPV were 23.4 and 100% with positive and negative likelihood ratios of 2.2 and 0, respectively. Data for subgroups of patients with trauma, penetrating trauma and blunt trauma are provided in Tables 4, 5 and 6 respectively. The sensitivity of TCT for detection of esophageal perforation was 100% in the subgroup of patients with trauma (Table 4).

Using different thresholds for a positive TCT scan yielded differing results of sensitivity and specificity (see Fig. 4). When individual abnormal findings were used alone to define a positive TCT scan, presence of a mediastinal collection or hematoma was 40% sensitive and 92.6% specific for detecting an esophageal perforation (positive likelihood ratio: 8.1, negative likelihood ratio: 0.43). Likewise, presence of an esophageal wall defect was 100% specific, but only 20% sensitive for detection of an esophageal perforation (positive likelihood ratio: ∞, negative likelihood ratio: 0.8). Moreover, pneumomediastinum provided a sensitivity of 73.3% and a specificity of 56.5% for detecting an esophageal perforation.

Table 4 Results of computed tomography vis-à-vis those of fluoroscopic esophagography among patients with a history of blunt or penetrating trauma

Computed tomography	Fluoroscopic esophagography		Total
	Negative	Positive	
Negative	53	0	53
Positive	46	12	58
Total	99	12	111

Table 5 Results of computed tomography vis-à-vis those of fluoroscopic esophagography among patients with a history of penetrating trauma

Computed tomography	Fluoroscopic esophagography		Total
	Negative	Positive	
Negative	44	0	44
Positive	31	12	43
Total	75	12	87

Table 6 Results of computed tomography vis-à-vis those of fluoroscopic esophagography among patients with a history of blunt trauma

Computed tomography	Fluoroscopic esophagography		Total
	Negative	Positive	
Negative	9	0	9
Positive	15	0	15
Total	24	0	24

Discussion

Our results show that TCT had a high sensitivity and NPV for detecting esophageal perforation. The overall specificity and PPV of TCT was relatively poor, although presence of esophageal wall defect or mediastinal collection was highly specific for esophageal perforation. Highest sensitivity of TCT was noted when a positive scan was defined by presence of any of the following: mediastinal collection, pneumomediastinum or esophageal wall defect. Given the high sensitivity and NPV of TCT for detecting esophageal perforation, FE may be unnecessary in cases when a TCT is negative.

Some previous studies have attempted to determine the sensitivity and specificity of CT for detecting esophageal leaks or perforation. Fadoo and colleagues evaluated the use of helical CT esophagography for detection of esophageal rupture [8]. They administered an aqueous solution (consisting of a mixture of 10% iohexol [Omnipaque 300®, Nycomed, Switzerland] and effervescent granules [sodium bicarbonate and tartaric acid]) per orally or through a nasogastric tube. Helical CT esophagography accurately identified 5/5 patients with an esophageal perforation and excluded esophageal perforation in 5/5 cases. Our study was different from that of Fadoo et al. in that we used TCT without any oral contrast medium. In another study, Wu and co-workers demonstrated that TCT (without oral contrast) provided a sensitivity of 100% and NPV of 100% for ruling out esophageal injury [14]. Our results are largely in concordance with the findings reported by Wu et al. in that the sensitivity and NPV of TCT was also 100% in our study.

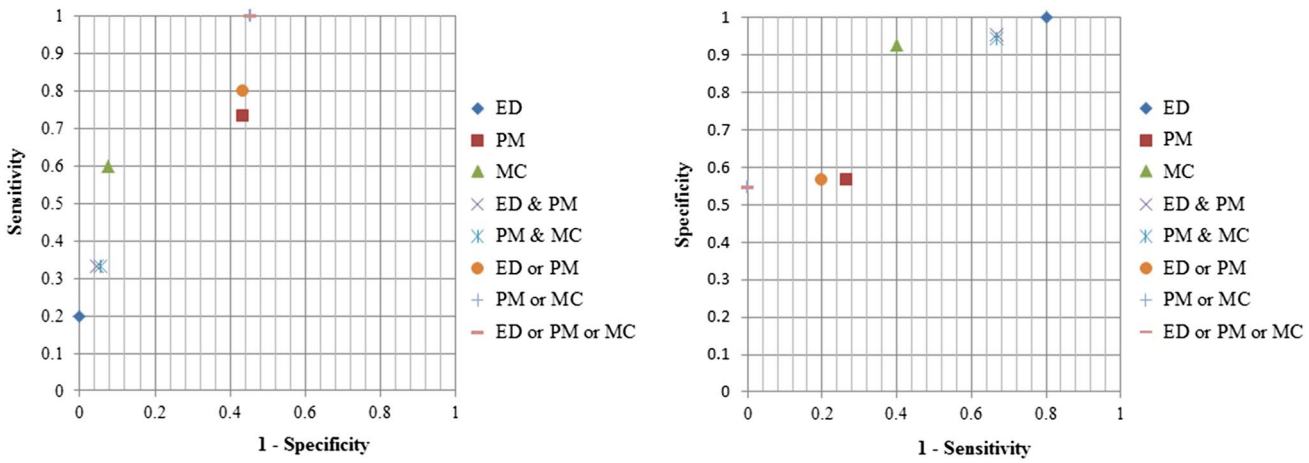

Fig. 4 A graph depicting the sensitivity and specificity of thoracic computed tomography for detection of esophageal perforation using different criteria for a "positive" scan

However, in our study, presence of esophageal wall defect or other esophageal abnormalities alone were specific but not sensitive for the detection of esophageal perforation. This may be attributed to the fact that our cohort had a larger number of patients with firearm injuries; in contrast, none of the patients included in the cohort of Wu et al. had firearm injuries [14].

Anatomically, the esophagus has three portions viz. the cervical, thoracic and abdominal parts [15]. Radiological signs of esophageal perforation differ based on the anatomic site of perforation [16]. A rupture of the cervical esophagus can lead to subcutaneous emphysema in the neck, which would be evident on TCT. An injury to the abdominal part of esophagus may be expected to cause pneumoperitoneum. Perforation of the thoracic esophagus can lead to pneumomediastinum with or without the development of a mediastinal collection, pleural effusion, or hydropneumothorax. Moreover, the patterns of injury to the three portions of esophagus also differ considerably [17]. The cervical esophagus is commonly injured (iatrogenically) during endoscopic procedures, although it may be damaged in stab wounds as well. The abdominal esophagus is often damaged (iatrogenically) during surgical procedures. On the other hand, the thoracic esophagus is more prone to spontaneous rupture (Boerhaave's syndrome) or penetrating trauma (firearm injuries). In our cohort, most patients had a history of firearm injuries and this explains the relatively high prevalence of pneumo- or hydropneumothorax (54.5%), pneumomediastinum (47.2%) and pleural effusion (39%) in our study. However, only a small number of patients (15/123) were subsequently found to have esophageal perforation; this precluded us from calculating sensitivity and specificity separately for each anatomic portion of the esophagus. Nevertheless, the frequency of esophageal perforation noted in our study was comparable to that of previous studies [8, 14].

We noted a high number of false positive TCT scans in our study, which accounted for the low specificity of TCT. Moreover, the frequency of false positive TCT scans differed considerably based on the definition of a "positive" scan. As mentioned before, our study cohort consisted of a large number of patients who presented with firearm injuries or road traffic accidents. Such patients were more likely to have injuries to other mediastinal and thoracic structures, such as aortic branches, azygous vein, trachea, thoracic duct and/or other structures [18]. Injury to the trachea alone can lead to pneumomediastinum, which may be mistaken for an esophageal perforation [19]. Likewise, injury to the thoracic duct, aorta or its branches, the azygos vein or other vessels may lead to the formation of a mediastinal hematoma or collection [20]. This may also mimic an esophageal perforation on a TCT scan and lead to a false positive scan. Another possible explanation for a false positive TCT may be that a small esophageal injury could spontaneously occur prior to the performance of FE. However, we only included patients who had undergone TCT within 48 h of FE. Lastly, some previously published studies have reported that FE may be rarely negative in patients with an esophageal perforation [14, 21].

The causes of esophageal perforation or rupture can be broadly divided into traumatic or non-traumatic categories. Traumatic esophageal perforation usually occurs secondary to penetrating trauma as in the case of a foreign body, iatrogenic trauma (surgical or endoscopic), or shrapnel injuries [22]. Non-traumatic or spontaneous esophageal rupture is also known as Boerhaave syndrome and may be precipitated by a variety of causes [23]. In the cohort of Wu and colleagues, esophageal perforation was traumatic in 75% (12/15) of cases [14]. Our findings are similar to their findings in that 75% (12/15) of patients had a traumatic esophageal perforation. Regardless of the cause of esophageal perforation, it is always considered an emergency condition and requires rapid diagnosis and management [2]. Most patients undergo TCT as part of their work-up either to exclude thoracic injuries (as is the case with trauma) or evaluate for alternative diagnoses. Moreover, TCT is useful in that it can be rapidly performed in acutely ill patients and does not require a dedicated fluoroscopy suite. In our study, TCT was noted to have a high sensitivity and NPV for detecting esophageal perforation. Among patients who had a negative TCT scan for esophageal perforation, none had evidence of esophageal perforation on FE. Moreover, among patients with a negative TCT scan ($n = 59$), an alternative diagnosis was evident in 94.9% (56/59) of cases. These results imply that in patients who present with a suspicion of an esophageal perforation (whether traumatic or non-traumatic), TCT can be used as a first step to exclude an esophageal perforation and look for alternative diagnoses. If TCT does not reveal any signs of esophageal injury, patients do not need to undergo further evaluation for esophageal perforation. On the other hand, patients who have highly specific signs of esophageal injury on TCT (such as esophageal wall defect) should be managed as having an esophageal perforation. In our study, esophageal wall defect was 100% specific for esophageal perforation, while mediastinal collection was 92.6% specific for esophageal perforation. In these patients, it is reasonable to skip FE and proceed directly to their definitive management (endoscopic, surgical or conservative). It is advantageous to obviate the need of FE in such cases as many patients are seriously ill and cannot be transported to the fluoroscopy suite for an adequate FE. Moreover, patients with traumatic injuries may have cervical spine instability, which can preclude the performance of an adequate FE [24]. Additionally, many critically ill patients have altered mental status and are at risk of aspirating iodinated contrast material with hazardous consequences [25]. In these cases, TCT can provide significant benefits in terms of time, cost and procedural risks to the

patient. One peculiar aspect of our study was that adequate FE was performed in most patients (123/128), i.e., only 5/128 could not have a satisfactory FE. This observation holds true for most tertiary care centers with a dedicated fluoroscopy suite, where performing FE is not difficult at all. However, this may not always be the case, especially in smaller centers of lower-middle income countries where patients often need to be transported to a separate imaging center for FE [26]. Our study suggests that in at least 48% of such cases, FE may be obviated altogether. This observation is not only useful for smaller hospitals, but it can also benefit larger tertiary care centers by reducing cost and resource utilization. Having said all this, patients, who are noted to have some signs of possible esophageal injury (other than esophageal wall defect or mediastinal collections) on TCT, will still need to undergo FE to accurately assess the esophagus.

The results of this study are encouraging, but they come with a number of caveats. This study was a retrospective study performed at a single-center tertiary care center with a limited sample size, although the prevalence of esophageal perforation in our sample (12.2%) was comparable to that of previous studies [8, 14]. Second, some patients were excluded from this study due to inadequate or incomplete FE, which may have introduced selection bias. Third, as we had a small number of patients, this precluded us from performing any meaningful subgroup analysis of sensitivity and specificity. However, there is no evidence to suggest that sensitivity and specificity would be different for particular sites or types of esophageal perforation. Lastly, we used FE as the reference standard for diagnosis of esophageal perforation; this may have underestimated the accuracy of TCT in some cases, as FE can be false negative in case of small perforations [21].

Conclusion

TCT had a sensitivity of 100% and NPV of 100% for esophageal perforation. Moreover, presence of an esophageal wall defect or mediastinal collection was highly specific for esophageal perforation. These findings suggest that FE may be omitted in patients who have no evidence of mediastinal collection, pneumomediastinum or esophageal wall defect on TCT. However, in the presence of any of these features, FE is still necessary to confirm or exclude the presence of an esophageal perforation.

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Compliance with ethical standards

Conflict of interest Muhammad Awais, Saqib Qamar, Abdul Rehman, Noor Ul-Ain Baloch and Gulnaz Shafqat have no conflict of interests to disclose.

Ethical standards All procedures related to this study were performed in accordance with ethical standards of the institutional ethics review committee and with the most recent version of the Declaration of Helsinki (1964).

Informed consent As this was a retrospective study, formal consent was not required and requirement of informed consent was waived.

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