Ann Mil Health Sci Res. 2026 March; 24(1): e156851 https://doi.org/10.69107/amh-156851

Published Online: 2026 March 31 **Research Article**

Comparison of Esophagography and Chest Computed Tomography and the Prognostic Value of Inflammatory Markers for Detecting Anastomotic Leakage After Esophageal Resection

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Received: 15 October, 2024; **Revised:** 16 December, 2025; **Accepted:** 21 February, 2026

Abstract

Background: Esophageal cancer poses substantial treatment challenges, particularly when esophagectomy is required. Despite advances in multimodality therapy, esophagectomy remains the primary curative approach. Anastomotic leakage (AL) after esophagectomy is associated with mortality rates of up to 40%–60%. Therefore, timely detection and intervention are essential to mitigate adverse outcomes.

Objectives: This study aimed to identify the gold standard for assessing AL after esophageal resection.

Methods: This prospective study was conducted at Imam Khomeini Complex Hospital, Tehran, Iran. From May to December 2022, a total of 46 patients who underwent esophageal or gastric resection for cancer were enrolled. Patients were evaluated using esophagography, chest computed tomography (CT), C-reactive protein (CRP) levels on postoperative days (within 30 days, as the gold standard of care), and clinical signs. Thirty patients underwent postoperative radiographic examination using a water-soluble contrast medium, and 16 underwent chest CT with oral and intravenous contrast medium during the same period. CRP levels were measured in all patients on the day of esophagography or chest CT.

Results: Ten patients exhibited clinical signs of leakage. Among the 30 patients who underwent radiographic examination, 27 (90%) had normal findings and 3 (10%) had AL, whereas clinical signs of AL were present in 10 patients (33.3%). Among the 16 patients who underwent chest CT, 9 (56.3%) had normal findings and 7 (43.8%) had AL. The sensitivity, specificity, and accuracy of radiographic examination were 30%, 100%, and 71.43%, respectively, compared with 71.43%, 66.67%, and 68.75%, respectively, for chest CT. The chi-square test showed no association between CRP levels and clinical signs of leakage ($P = 0.771$).

Conclusions: Esophagography demonstrated lower sensitivity than CT, although its accuracy was higher, indicating that both methods can be used to evaluate patients with clinical signs of AL. C-reactive protein levels were not associated with AL.

Keywords: Esophageal Resection, Computed Tomography, Esophagography, Anastomotic Leak

1. Background

Esophageal cancer poses significant challenges because of its high mortality rate and the complexity of treatments such as esophagectomy (1). Although advances in multimodality treatment have improved long-term survival, esophagectomy remains the primary curative approach (2). Nevertheless, esophagogastric resection is a high-risk surgical procedure and accounts for nearly 40% of postoperative deaths (3). Anastomotic leakage (AL) after esophagectomy is associated with substantial

How to Cite: Mirjavadi SH, Estaji M, Koopaee S, Pak F, Jalaeefar A, et al. Comparison of Esophagography and Chest Computed Tomography and the Prognostic Value of Inflammatory Markers for Detecting Anastomotic Leakage After Esophageal Resection. Ann Mil Health Sci Res. 2026;24(1):e156851. doi: https://doi.org/10.69107/amh-156851

morbidity, prolonged hospitalization, high health care resource utilization (4), and mortality rates of up to 40%-60% (5). Timely detection and intervention are therefore necessary to mitigate adverse outcomes. The clinically silent nature of some leaks underscores the need for vigilant diagnostic strategies.

Esophagography has traditionally been a mainstay for diagnosing leaks and facilitating prompt therapeutic intervention. However, the limited sensitivity of this method and the occurrence of clinically silent leaks, as reported by Sauvanet et al. (3), underscore the need for alternative diagnostic approaches.

Helical computed tomography (CT) has emerged as a valuable tool for identifying leaks after esophagectomy (6). Compared with esophagography, CT is easier to perform, particularly in patients with restricted mobility. Although some studies have examined the role of CT in detecting esophageal perforation (7-9), few have directly compared esophagography and CT for detecting leakage after esophagectomy.

The rapid response of C-reactive protein (CRP) to inflammation and tissue damage suggests that it may serve as an early indicator of leakage after esophagectomy. C-reactive protein is an acute-phase protein synthesized by hepatocytes in response to proinflammatory cytokines (10). Its level increases rapidly in the presence of infection, tissue damage, or ischemia and declines rapidly when these conditions resolve (11). In colorectal surgery, CRP has shown utility as a reliable marker of AL in multiple prospective studies (12-14) and 2 comprehensive meta-analyses. When CRP levels remain elevated or increase again after surgery, the priority is to control sepsis and secure the anastomosis rather than attempt to lower the CRP level directly.

2. Objectives

By assessing the diagnostic performance of esophagography and CT and examining the correlation between CRP levels and AL, both individually and in combination, this study aimed to improve the diagnostic approach for identifying AL after esophagectomy.

3. Methods

3.1. Study Design and Participants

This prospective study was approved by the review board of Tehran University of Medical Sciences. The sample size for each method was determined based on previous studies in this field. Alvandipour et al. reported that 2.8% of 72 patients experienced AL. Accordingly, this estimated proportion was used in the Cochran formula to calculate the required sample size. In this formula, n represents the sample size, p is the estimated proportion, d is the allowable error (usually 0.05 - 0.08), and Z is obtained from the standard normal distribution for the desired confidence level (type I error). With an allowable error of d = 0.06, the required sample size for each method was n = 29. Therefore, 30 samples were used for each modality.

A total of 46 patients who underwent esophageal or gastric resection for cancer at Imam Khomeini Complex Hospital, Tehran, Iran, from May to December 2022 were enrolled. All patients provided written informed consent to participate.

Patients had no history of esophageal surgery before study enrollment. Medical histories unrelated to the patients' current conditions were not considered.

Age is a recognized risk factor for AL after esophagectomy. Both very young and older patients may be at increased risk, although this relationship is complex and interacts with other comorbidities and technical factors (15). Therefore, no age criterion was applied.

Patients who were unable to swallow the contrast medium, experienced contrast aspiration, died, or declined to participate were excluded from the analysis.

3.2. Clinical Monitoring and Management

During the 30-day postoperative period (16), patients were monitored for nausea, vomiting, early satiety, dysphagia, and elevated CRP levels. Recorded data included sex, age, medical history, surgical method, primary cancer, and surgical indication. When a patient's symptoms suggested an abnormality, the patient was recalled for further evaluation. Patients without abnormalities within 5 days were discharged and instructed to monitor symptoms closely and report any suspicious symptoms.

If the CRP level was high (a CRP level of 170 mg/L on postoperative day 3 was considered indicative of leakage) or did not decline as expected, and clinical signs were present, including fever, tachycardia, pain, ileus, sepsis, or dysphagia, the usual steps were as follows:

1) Prompt imaging to confirm or exclude AL or an intra-abdominal collection.

2) Source control tailored to the findings, including percutaneous drainage of collections, endoscopic stenting or endoscopic vacuum therapy for contained

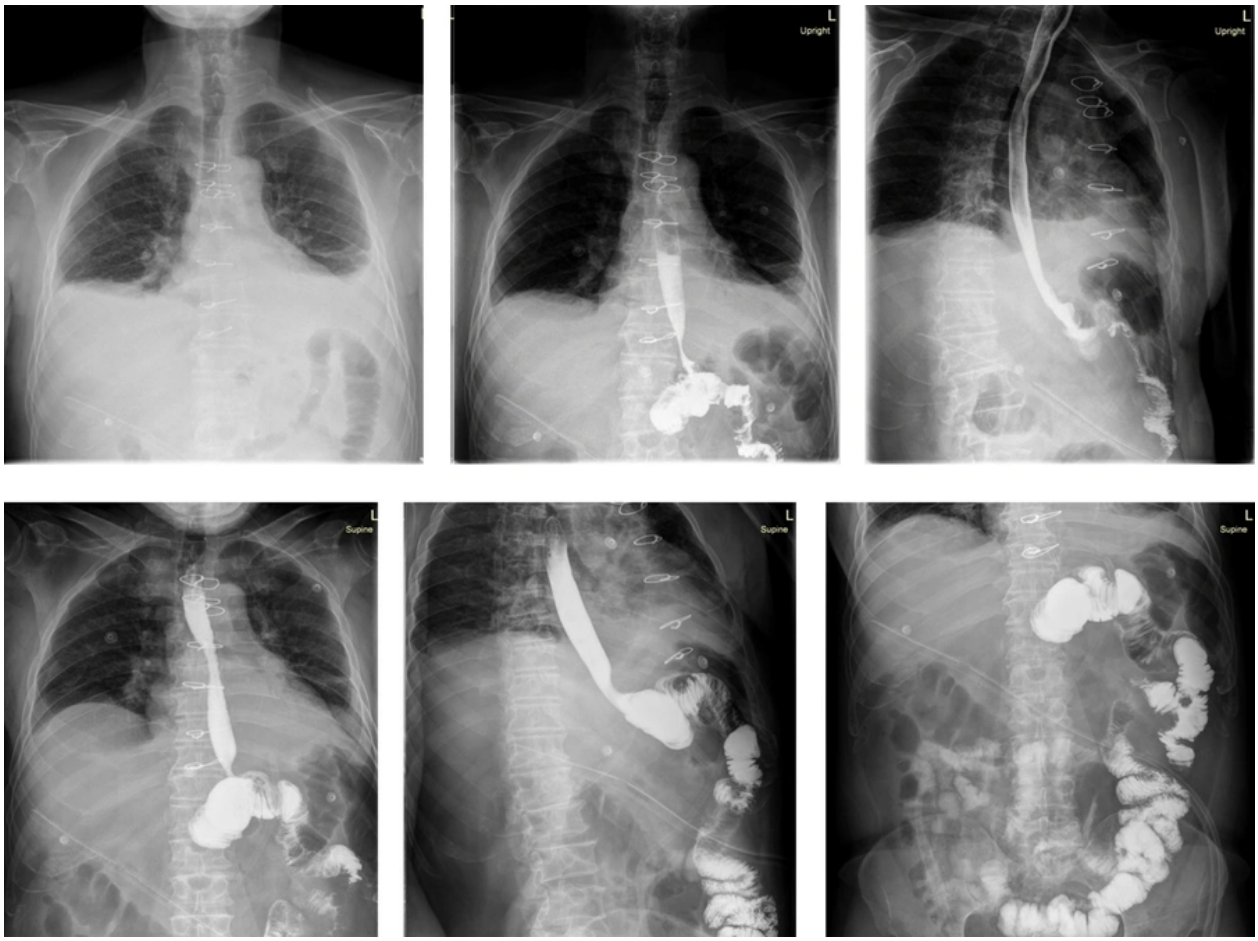

Figure 1. A 56-year-old man after total gastrectomy and partial esophagostomy, with an elevated C-reactive protein (CRP) level of 58 mg/L but no evidence of anastomotic leakage on radiographic evaluation

leaks, or reoperation for uncontrolled sepsis or major disruption.

3) Broad-spectrum antibiotics, hemodynamic stabilization, and organ support as needed for sepsis.

Patients were assessed using esophagography and chest CT to rule out AL.

3.3. Esophagography

Thirty patients underwent postoperative radiographic examination using a water-soluble contrast medium (Visipaque-320). The examinations included a chest radiograph without contrast as a scout view, followed by radiography with contrast medium to detect leakage, fistula, or stricture (Figure 1).

3.4. Computed Tomography

Sixteen patients underwent postoperative chest CT both with and without oral and intravenous (IV) contrast medium. The examinations were performed in the Imaging Department of Imam Khomeini Complex Hospital using a 16-slice Philips CT system. Scans were obtained in the portal phase, 55 seconds after injection, at a rate of 2.5 mL/s, using 1.5 mL/kg of Visipaque-320. Three-dimensional reconstructions were created in the sagittal, coronal, and axial planes; the axial and coronal views were the most informative for diagnosing leakage (Figure 2).

3.5. C-Reactive Protein Measurement

Figure 2. A 51-year-old woman with clinical signs of leakage, an elevated C-reactive protein (CRP) level of 50 mg/L, and computed tomography-confirmed anastomotic leakage after total gastrectomy and partial esophagostomy

C-reactive protein levels were measured in all patients using blood samples and a Hitachi 917 analyzer (Japan). The laboratory reported CRP levels in mg/L on the day of esophagography or chest CT.

3.6. Statistical Analysis

Descriptive analyses and cross-tabulation were used to calculate the sensitivity, specificity, and accuracy of the 2 diagnostic methods. These measures were used to assess the effectiveness of the diagnostic tests in detecting postoperative leakage.

Quantitative data were analyzed using the chi-square test. Statistical analyses were performed using SPSS, version 20. A P value of less than 0.05 was considered statistically significant.

4. Results

A total of 46 patients were recruited, including 32 men and 14 women. The mean age was 62.8 ± 9.2 years (range, 34 - 90 years).

Fourteen patients were excluded from the analysis because of an inability to swallow the contrast medium, contrast aspiration, death, or refusal to participate.

Patients underwent diagnostic procedures during the 30-day postoperative period, including esophagography, chest CT, clinical assessment, and measurement of CRP levels.

Of the 46 patients, 10 had clinical signs of leakage, including elevated CRP levels and other significant clinical findings.

Among the 30 patients who underwent radiographic examination, 27 (90%) had normal findings and 3 (10%) had AL. Clinical signs of AL were present in 10 patients (33.3%).

Among the 16 patients who underwent chest CT, 9 (56.3%) had normal findings and 7 (43.8%) had AL.

The sensitivity, specificity, and accuracy of radiographic examination were 30%, 100%, and 71.43%, respectively. The corresponding values for CT were 71.43%, 66.67%, and 68.75%.

The mean CRP level among all patients was 43.31 ± 26.07 mg/L. During postoperative days 2 - 10, the mean CRP level was 43.31 ± 26.07 mg/L. The mean CRP levels in patients with and without AL were 53.33 ± 15.2 mg/L and 38.35 ± 25.79 mg/L, respectively.

Among patients with clinical signs of leakage, CRP levels ranged from 35 - 85 mg/L, with a mean of 53.33 ± 15.2 mg/L. Only 1 patient had a CRP level of 105 mg/L; however, this patient showed no leakage on esophagography or CT.

Chi-square analysis showed no correlation between CRP levels and clinical leakage (P = 0.771).

5. Discussion

Anastomotic leakage is one of the most serious complications after esophagectomy (17-19), with a high mortality rate of 35% and a substantial contribution to post-esophagectomy deaths (25% - 50%) (5). Diagnosing AL before resuming an oral diet is essential (17).

Although esophagography is routinely used to diagnose leaks (3), it demonstrated relatively low sensitivity (30%), a high number of false-negative results (8 patients), and high specificity (100%) in this study. These results are consistent with a literature review by Fabbi et al. (20), which reported sensitivity values ranging from 33% - 52% and a specificity of 100%. Other authors have reported similar findings. Mejia-Rivera et al. reported a sensitivity of 43% (21), and Boone et al. reported a sensitivity of 52% for detecting AL using a contrast-enhanced swallow study (22). The accuracy of this method for identifying leaks has therefore been questioned because of false-negative results and the need for interpretation by experienced radiologists (23). Accordingly, discontinuation of its routine use has been recommended, although it may remain useful when leakage is clinically suspected and its extent must be assessed (22, 24).

Computed tomography is a noninvasive, safe, and widely available technique for investigating leakage (25). In this study, CT had higher sensitivity than esophagography (71.43% vs 30%). Upponi et al. reported CT sensitivity and specificity of 100% and 80%, respectively (6), compared with fluoroscopy. Although CT was compared with esophagography in the present study, both fluoroscopy and esophagography have lower sensitivity, and CT is better tolerated by severely ill patients. Helical CT can more readily detect small periesophageal air collections indicative of esophageal perforation. Such collections may be the most useful finding for suggesting esophageal rupture (6).

In this study, CRP levels were not correlated with AL. The mean interval between surgery and postoperative CRP measurement was 5.73 ± 1.68 days, and the mean CRP level was 43.31 ± 26.07 mg/L. The mean CRP levels in patients with and without AL were 53.33 ± 15.2 mg/L and 38.35 ± 25.79 mg/L, respectively. Although the value was slightly higher in patients with AL, the difference was not significant. In contrast to some studies of colorectal surgery (26), the present study found no significant correlation between CRP levels and AL after esophageal resection (27). Although some research has supported CRP as an early biomarker of leakage, these findings are consistent with conflicting results from previous studies (28-30).

These findings suggest that esophagography remains valuable for detecting leakage because of its high specificity, although its sensitivity is limited. Computed tomography appears to be a more sensitive alternative but has lower diagnostic accuracy and specificity for detecting leakage after esophagectomy.

5.1. Conclusions

This study provides insight into the diagnosis of AL after esophagectomy, highlighting the limitations of esophagography and the potential benefit of CT as a more sensitive diagnostic tool. Further research and clinical efforts are needed to optimize diagnostic strategies and improve patient outcomes associated with this serious postoperative complication.

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

Authors' Contribution: Study concept and design: S. M., A. J., and M. E. Acquisition of data: S. M. Analysis and interpretation of data: S. K. Drafting of the manuscript: E. J. Critical revision of the manuscript for important intellectual content: M. E. Statistical analysis: S. K. Administrative, technical, and material support: M. E. and F. P. Study supervision: E. J. All authors reviewed and approved the final manuscript.

Conflict of Interests Statement: The authors do not declare any conflicts of interests for this study.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after its publication. The data are not publicly available due to privacy or ethical restrictions.

Ethical Approval: This study is approved under the ethical approval code of IR.TUMS.SPH.REC.1400.190 (webpage of ethical approval code is: https://ethics.research.ac.ir/PortalCommittee.php?code=IR.TUMS.SPH.REC)

Funding/Support: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Informed Consent: All patients provided written informed consent to participate.

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