

Application of low-dose hydro-CT using SAFIRE in the evaluation of esophageal cancer

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D – writing the article; E – critical revision of the article; F – final approval of the article

Advances in Clinical and Experimental Medicine, ISSN 1899–5276 (print), ISSN 2451–2680 (online)

Adv Clin Exp Med. 2023;32(10):1133–1138

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Funding sources

None declared

Conflict of interest

None declared

Received on October 12, 2022

Reviewed on December 19, 2022

Accepted on February 12, 2023

Published online on April 7, 2023

Abstract

Background. The esophageal cancer treatment strategy depends on the tumor stage according to the tumor, node and metastasis (TNM) classification. One of the methods recommended for esophageal cancer assessment is computed tomography (CT). The CT imaging is especially important for patients with contraindications for gastroscopy, which is the primary method used for assessing esophageal diseases.

Objectives. The aim of this retrospective study was to evaluate the inter-rater reliability of low-dose hydro-CT with a sinogram-affirmed iterative reconstruction algorithm (SAFIRE) used for the staging of esophageal cancer by 2 independent radiologists. We also evaluated the application of this method for the diagnosis of esophageal cancer.

Materials and methods. Low-dose hydro-CT was performed in 65 patients, and the raw data were reconstructed with SAFIRE. Obtained images were retrospectively interpreted by 2 independent and experienced radiologists. Histopathological results were used as the reference standard. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) in the diagnosis of esophageal cancer were calculated for hydro-CT. The examination of the inter-rater reliability level in the assessment of the esophageal cancer stage in the TNM classification was performed by calculating Cohen's kappa coefficient (κ) with square weights and standard errors (SEs) for kappa. Independence tests were also performed (Fisher's exact test – two-tailed, and Pearson's χ^2 test).

Results. For the diagnosis of esophageal cancer with hydro-CT, a sensitivity of 93%, a specificity of 100%, a PPV of 100%, and a NPV of 88% were observed. In the statistical analyses for the T, N and M stages, κ values greater than 0.90 and significance levels of $p < 0.001$ were obtained.

Conclusions. Hydro-CT using low-dose techniques may be a valuable diagnostic method for staging and diagnosis of esophageal cancer, especially in patients with contraindications for invasive procedures.

Key words: multi-detector computed tomography, esophageal diseases, esophageal neoplasms, TNM staging

Cite as

Celmer M, Międzybrodzki K, Patyk M, Pozowski P, Zaleska-Dorobisz U. Application of low-dose hydro-CT using SAFIRE in the evaluation of esophageal cancer.

Adv Clin Exp Med. 2023;32(10):1133–1138.

doi:10.17219/acem/161160

DOI

10.17219/acem/161160

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Background

The development of multi-detector computed tomography (MDCT) imaging in recent years has enabled high-resolution images to be obtained with a very short scan time. As a result, we have been given new, wide-ranging imaging capabilities for the gastrointestinal tract, including the esophagus.^{1–3}

According to the GLOBOCAN 2018 statistics, esophageal cancer ranks 7th on the list of the most common cancers in the world, and the MDCT study is one of the most important tools indicated for its evaluation.⁴ The use of water in MDCT hydrography (hydro-CT) as an oral neutral contrast agent allows for optimal distension of the esophageal walls and facilitates the diagnosis of small tumor lesions. It also improves the visual differentiation of pathological tumor tissues from the normal walls of the esophagus and surrounding structures in CT examinations with intravascular iodine contrast agents.^{1,2}

Due to the increasing use of MDCT in clinical practice, it was necessary to reduce radiation doses in accordance with the ALARA (as low as reasonably achievable) principle.^{5,6} Low-dose CT protocols are also used in hydro-CT studies. Obtaining high-quality images despite reduced radiation doses is possible thanks in part to improved raw data processing techniques (e.g., iterative reconstruction algorithms).⁷ Reducing exposure to ionizing radiation is particularly important for patients undergoing multiple CT scans and for patients undergoing radiotherapy.⁴ In patients with esophageal cancer, radiotherapy may be an important element of therapy, and CT examinations may be useful in the initial staging assessment and then during the follow-up.^{8,9}

Although endoscopic biopsy is the gold standard in esophageal cancer diagnosis,¹⁰ there is a group of patients with contraindications for endoscopy, including endoscopic ultrasound (EUS; uncooperative patients), or for biopsy (in the case of active bleeding, coagulopathy or patient instability). In these patients, low-dose hydro-CT with the use of iterative image reconstruction may be an alternative method for esophageal cancer diagnostics.

Objectives

The aim of this retrospective study was to evaluate the inter-rater reliability for the staging of esophageal cancer according to the tumor, node and metastasis (TNM) classification performed by 2 independent radiologists based on low-dose hydro-CT. We also evaluated the application of this method in the diagnosis of esophageal cancer.

Materials and methods

Study design

Low-dose hydro-CT was performed in 65 patients (44 men and 21 women, mean age: 64.3 years). The main indications for hydro-CT were the evaluation of benign lesions found in endoscopy or the staging of esophageal cancer in patients before treatment or after neoadjuvant radiotherapy. In our study, all endoscopies were performed by 3 different surgeons experienced in esophagoscopy (>8 years of experience) at our institution. In all cases, during the endoscopy, multiple biopsies (5–10 per procedure) were performed. Written informed consent was obtained from all patients, and this study was approved by the Bioethical Committee of Wrocław Medical University (Wrocław, Poland).

CT protocol and image analysis

All images were obtained with patients in the supine position using a 128-slice CT scanner (SOMATOM Definition AS+; Siemens Healthcare, Erlangen, Germany). The CT parameters were as follows: tube potential of 120 kV, tube current modulation (Care Dose 4D), collimation of 128 × 0.6 mm, a pitch of 0.8, and a gantry rotation time of 0.5 s. Raw data were reconstructed with a sinogram-affirmed iterative reconstruction algorithm (SAFIRE; Siemens Healthcare) and a strength setting of 3 using a high spatial resolution kernel (I30). The scan range covered the area of the thorax and the upper part of the abdominal cavity.

Before CT scanning, all patients ingested water orally in a volume of 0.75–1.0 L (within 10 min before starting the scanning), followed by 0.25 L (immediately before scanning) to distend the esophagus and gastroesophageal junction walls. They were also administered 20 mg of butylscopolamine intravenously (10 min before scanning) to reduce gastrointestinal tract motility. The ionic contrast medium (Ultravist 370; Bayer Healthcare, Leverkusen, Germany) was administered intravenously at a dose of 1.5 mL/kg of body weight, at a rate of 3.0–3.5 mL/s. Dynamic enhanced phases were then performed with scan delay times of 25 s and 50 s.

The obtained images were retrospectively interpreted by 2 independent and experienced (5 and 10 years of experience) radiologists who were blinded to the endoscopy results. They used a diagnostic workstation (Syngo.via; Siemens Healthcare) and maximum intensity projection reconstructions or multiplanar reconstructions for coronal, sagittal and axial images.

Statistical analyses

The results of the esophageal biopsy were treated as a standard of reference. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) in the diagnosis of esophageal cancer were calculated for hydro-CT

Table 1. Computed tomography (CT) criteria for tumor, node and metastasis (TNM) staging of esophageal cancer used in the study

Stage		Characteristics
T stage	T0	no visible changes in the wall of the esophagus; surrounding adipose tissue unchanged
	T1/2	esophageal wall thickening and transmural contrast enhancement with smooth external outlines; surrounding adipose tissue unchanged or visible desmoplastic reaction; no or slight stenosis of the esophagus
	T3	usually large tumor with contrast enhancement and significant thickening of the esophageal wall with irregular outer border; infiltration of the surrounding adipose tissue; moderate or severe stenosis
	T4	infiltration of surrounding organs
N stage	N0	no enlarged lymph nodes have been found (short-axis diameter of imaged lymph nodes less than 1 cm)
	N1	enlarged lymph nodes present (cervical, mediastinal, epigastric; short-axis diameter of lymph nodes at least 1 cm)
M stage	M0	no evidence of metastases
	M1	distant metastases present

The criteria are based on the studies by Ba-Ssalamah et al.³ and Prokop and Galanski.¹¹

(the calculations take into account the results obtained by the more experienced of the 2 radiologists). Additionally, we evaluated the compatibility level of the 2 independent radiologists in assessing the stage of esophageal cancers according to the TNM classification (presented in Table 1) using Cohen's kappa coefficient (κ) and independence tests (two-tailed Fisher's exact test and Pearson's χ^2 test). A value of $p < 0.05$ was considered statistically significant. The radiation dose was estimated using the volume CT dose index (CTDI_{vol}). CTDI is a standardized measure of radiation dose output of a CT scanner which allows the user to compare radiation output of different CT scanners. Calculations and statistical analysis of the results were performed using Microsoft Excel 2019 (Microsoft, Redmond, USA) and Statistica v. 13 (StatSoft Inc., Tulsa, USA).

Results

The diagnosis of esophageal cancer was confirmed in a histopathological examination in 43 (66.2%) patients. In the remaining 22 cases (33.8%), benign lesions were diagnosed with endoscopy (7 cases of hernia hiatus esophagi, 2 cases of achalasia, 1 benign polyp, and 12 cases of esophagitis). In 40 cases (93%), a correct diagnosis of esophageal cancer was made using hydro-CT. For the diagnosis of esophageal cancer with hydro-CT, a sensitivity of 93%, a specificity of 100%, a PPV of 100%, and a NPV of 88% were observed.

In the statistical analyses for the T stage, $\kappa = 0.966$ and a significance level of $p < 0.0001$ (in Pearson's χ^2 independence test) were obtained. These results indicate the compatibility of the opinion of the 2 radiologists in the assessment of the T stage of esophageal cancer (Table 2). For the evaluation of enlarged lymph nodes (N stage), a statistically significant, very strong relationship was also observed between readers 1 and 2. In this case, $\kappa = 0.952$ and a significance level of $p < 0.001$ (two-tailed Fisher's exact test) were obtained (Table 3). In 100% of cases, the readers agreed in their assessment of distant metastases (M stage).

The CTDI_{vol} was in the range of 3.32–7.08 mGy per scan.

Table 2. Number classifications of tumor size (T stage) observed by the 2 radiologists and the estimated value of Cohen's kappa coefficient (κ) with square weights and standard errors (SEs)

Reader 1	Reader 2			
	T0	T1/2	T3	T4
T0	3	0	0	0
T1/2	2	17	0	0
T3	0	0	13	0
T4	0	0	0	8

$n = 43$; Cohen's kappa coefficient $\kappa = 0.966$; SE = 0.022; $p < 0.0001$.

Table 3. Number of classifications of the enlarged lymph nodes (N stage) observed by the 2 radiologists and the estimated value of Cohen's kappa coefficient (κ) with square weights and standard errors (SEs)

Reader 2	Reader 1	
	N0	N1
N0	25	0
N1	1	17

$n = 43$; Cohen's kappa coefficient $\kappa = 0.952$; SE = 0.048; $p < 0.001$.

Discussion

The main objective of the present study was to estimate the level of compatibility between 2 radiologists (inter-rater reliability) in the classification of the stage of esophageal cancer according to the TNM system. For this purpose, κ value was calculated. In the test materials for categories T, N and M, κ values of 0.90 were obtained, indicating very good compatibility between the 2 readers (Fig. 1–3). This result indicates the possibility of unambiguous assessments of the local stage of esophageal cancer in a hydro-CT study. Importantly, these results suggest that it is possible to accurately assess the stage of esophageal cancer, which is crucial in deciding on the proper therapeutic procedure.

Confirmation of these conclusions can be found in other studies. Ba-Ssalamah et al. evaluated the usefulness of MDCT hydrography in the assessment of category T in esophageal cancer.¹ In this study, images obtained

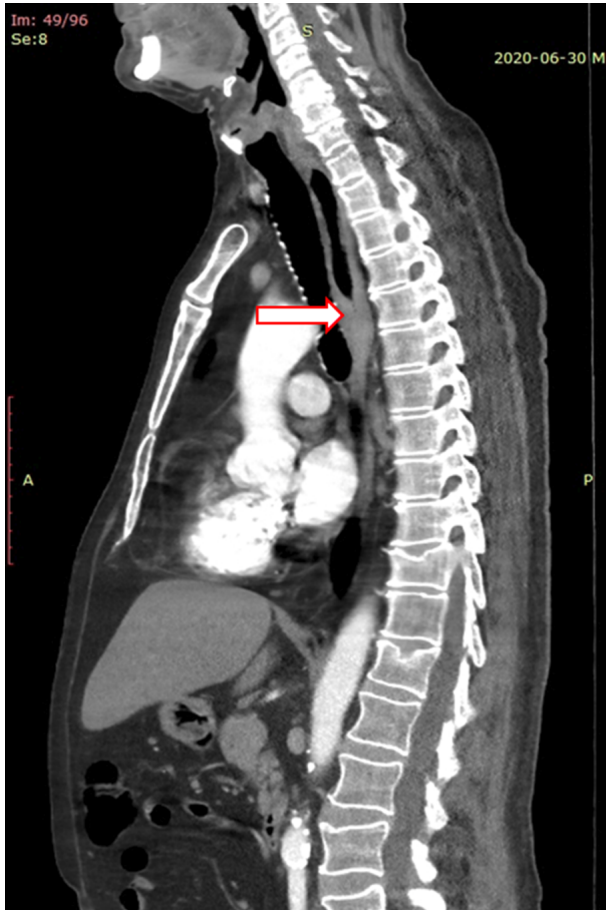


Fig. 1. Hydro-computed tomography (CT) image in sagittal reconstructions in a patient with T1/2 esophageal cancer shows the esophageal wall thickening 10 mm in depth with a smooth outer border in the thoracic part of the esophagus

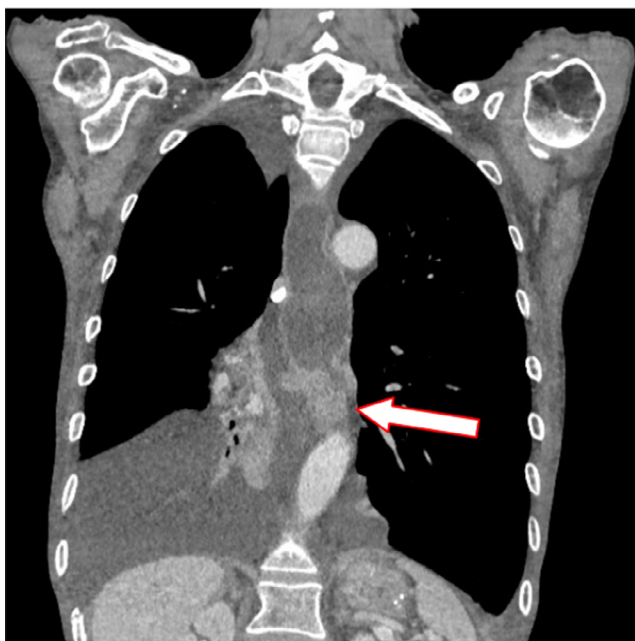


Fig. 2. Hydro-computed tomography (CT) image of the esophagus in coronal reconstruction shows an irregular, circumferential wall thickening up to 11 mm in depth in the proximal and middle third of the esophagus, with inhomogeneous enhancement and blurred outer borders in terms of the T3 tumor

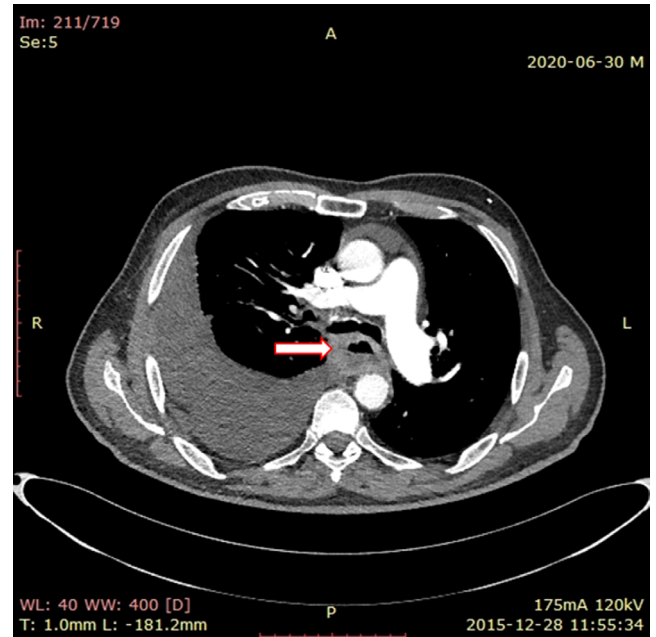


Fig. 3. Hydro-computed tomography (CT) image of the esophagus in axial reconstruction in a patient with a T4 stage of esophageal cancer and a large esophageal diverticulum filled with content located supravascularly on the right side. The tumor causes a concentric thickening of the esophageal wall at the level of the tracheal bifurcation with proximal dilatation of the esophagus, with a broad contact with the thoracic aorta and the Th8 vertebra, and with infiltration of the right intermediate bronchus (causing atelectasis in the right lower lobe), the pericardium and the outflow of the pulmonary veins

using hydro-CT performed before and after surgery in 131 patients were evaluated by 2 independent radiologists and compared with the results of a histopathological examination of the material removed during the operation. Very good compatibility was achieved between the readers, with a weighted κ ratio of 0.93 and κ unbalanced at 0.89. The results obtained by both readers showed a high sensitivity for hydro-CT (95%) and a high PPV (96%) in the assessment of the T stage. Staging was properly assessed in 76.3% and 68.7% of patients by investigators 1 and 2, respectively.

In this study, we also evaluated the application of low-dose hydro-CT using SAFIRE in the diagnosis of esophageal cancer. Our results suggest a high utility for this imaging modality. However, it should be noted that the assessment of the T stage and diagnosis of esophageal cancer using hydro-CT may have some limitations.^{3,12} One of them is the poor contrast of the different layers of the esophageal wall, which makes it difficult to identify early forms of esophageal tumors and differentiate them from benign esophagitis. Due to this limitation, endoscopy with biopsy should be performed in each patient, and hydro-CT may be considered a useful method in the diagnosis of esophageal cancer only for patients with a contraindication to endoscopy or biopsy.

The latest, 8th edition of the American Joint Committee on Cancer/International Union Against Cancer (AJCC/UICC) guidelines recommends EUS as a method

of choice for the clinical evaluation of the T stage.¹³ Shim et al. presented a comparison of the accuracy of EUS and CT examinations in the assessment of esophageal cancer advancement.¹⁴ In the conclusions of their report, they suggest that EUS examination is not superior to chest CT for diagnosing the T stage in esophageal cancers. Other authors report that EUS is less accurate in staging cancer after radiotherapy and chemotherapy. It is also limited by the inability to assess lumen-occluding tumors in the esophagus.^{15–17} At the same time, the advantage of hydro-CT in detecting distant metastases, such as lung or liver metastases (stage M), should be emphasized. Thus, it allows for a complete assessment of esophageal cancer advancement according to the TNM system.

According to the AJCC/UICC guidelines, EUS, MDCT and fluorodeoxyglucose positron emission tomography are basic imaging techniques that do not differ significantly in accuracy, sensitivity or specificity in the assessment of regional lymph nodes in patients with esophageal cancer.¹²

It is commonly accepted that hydro-CT scans are performed in the supine or prone position, depending on the location of the lesion, on the dependent side.^{1,18} Our experience shows that the supine position for scanning is better tolerated and more comfortable for patients whose stomach is bloated with a large amount of water. Some authors claim that there is no need to use the prone position for scanning in clinical practice.^{11,19–21} Therefore, in our study, the scanning was performed only in the supine position.

Limitations

Our study has some limitations. These include the inability to compare the results obtained from hydro-CT with the intraoperative and postoperative histopathological evaluation of tumor tissues. The patient group was heterogeneous and some patients were treated only with radiotherapy.

The study group was relatively small and consisted mainly of patients with advanced cancer lesions, as esophageal cancer screening is not performed in our population. Therefore, it should be noted that our results confirm the usefulness of hydro-CT in the diagnosis and evaluation of esophageal cancer, usually only in advanced cases.

In this study, we used the low-dose scanning technique, which in some cases may reduce the quality of the obtained images and affect the evaluation of the primary tumor and metastatic lesions, especially in the liver. Some authors, based on objective and subjective analyses of image quality, suggest that a combination of Care Dose 4D and SAFIRE reduces the radiation dose by an average of 74.85% while maintaining image quality.⁷ However, they noted the unclear impact of different imaging conditions and the use of post-processing techniques on the accuracy of the diagnosis, which led them to believe that research into the use of this method should be continued.

Conclusions

In conclusion, hydro-CT using low-dose techniques may be a valuable diagnostic method for staging and diagnosis of esophageal cancer, especially for patients with contraindications to invasive procedures (endoscopy, biopsy or EUS). Conducting studies on a larger group of patients using the latest low-dose techniques and iterative algorithms (third-generation CT scanners) may contribute to the wider use of MDCT for the evaluation of esophageal cancer in the future.

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