Diagnostic Accuracy of Multidetector Computed Tomography (MDCT) in Evaluation for Mediastinal Invasion of Esophageal Cancer

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Objective: *Determine diagnostic accuracy of evaluation for mediastinal invasion of esophageal cancer by multidetector computed tomography (MDCT) as compared with post-operative histopathology staging.*
Material and Method: *The present study retrospectively analyzed the 64-slice MDCT of twenty-one patient's diagnosis with esophageal cancer who received surgical treatment in Siriraj Hospital. Patients were enrolled between June 1, 2004 and Dec 31, 2009. Twenty-one CT images of chest were evaluated by two radiologists without knowing each patient's history as determined by surgical and pathology findings. Image analysis was determined for evaluating tumor location, wall appearance, findings of direct mediastinal extension. Accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were evaluated for tumor staging and nodal staging.*
Results: *Concordance between the two different readers for the interpretations with a kappa coefficient to assess interobserver variation of 0.2 to 0.9 suggests only slight agreement between the two readers. The overall sensitivity, specificity, PPV, NPV, and accuracy of CT T3 staging were 75%, 78%, 66.7%, 84.6%, and 77.3% respectively. The CT T4 staging had sensitivity 75%, specificity 85.7%, PPV 75%, NPV 85.7%, and accuracy 81.8%. In N staging, N0 staging from CT study had sensitivity 50%, specificity 33%, and accuracy 38%. N1 staging from CT study had sensitivity 33%, specificity 50%, and accuracy 38%.*
Conclusion: *64-slice MDCT can be evaluated for mediastinal tumor invasion of esophageal cancer with high sensitivity, specificity, and accuracy. The metastatic node and reactive lymphadenopathy in esophageal cancer were equivocal to discriminating from CT findings, especially using 1 cm in diameter of short axis as cut point.*

Keywords: *Esophageal cancer, Multidetector tomography, Picus' angle*

J Med Assoc Thai 2012; 95 (5): 704-11
Full text. e-Journal: *http://www.jmat.mat.or.th*

Esophageal cancer is the third most common gastrointestinal malignancy with poor long-term survival rates and high mortality[1]. In Thailand, esophageal cancer is found in the south of the country, with a higher incidence in elderly men than women. The disease is usually discovered in the first visit[2]. Esophagus is an organ that has no serosa layer, mainly causing direct extension of tumor to adjacent organ, especially in advanced disease. Treatment of esophageal cancer depends on accurate staging, which results in greater chance of complete curative treatment. Complete tumor resection is the first choice of curative treatment[1,3]. However, complete resection in locally advanced cases with resection adjacent malignant lymph node should be the curative treatment. In an operative procedure, a patient should not have adjacent organ invasion that causes an unresectable lesion and could cause serious complications from attempted resection.

Although endoscopic ultrasound (EUS) has high sensitivity and specificity in T1-T2 staging evaluation[4,5], computed tomography scan is superior in adjacent organ invasion, a non-passing scope in severe luminal stenosis from tumor, additional lymphadenopathy, and metastasis survey[6]. Multi-detector computed tomography (MDCT) is a good modality that can perform multiplanar reformation (MPR) image to confirm true lesion from three or more plane images.

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The need to confirm T staging of esophageal cancer is indicated for planning of treatment. Although there have been literature describing CT findings in the esophageal tumor and invasion[7,8], there are no articles on the role of MDCT for proving accuracy about mediastinal invasion and T staging of esophageal cancer from 64-slice multidetector CT scan with multiplanar reformation. Therefore, the aim of the present study was to determine the accuracy of evaluation for mediastinal invasion in esophageal cancer by multidetector computed tomography (MDCT) compared with post-operative histopathology staging.

Material and Method

This retrospective review of database containing the patients' records at Siriraj Hospital was approved by a local institutional review board. The board determined that the present retrospective study could be done without acquiring a signed informed consent for each patient's image. The patient's data about symptom, admission records, surgical records, follow-up records, and pathologic finding were evaluated. The present study analyzed the 64 slice MDCT of 21 patients diagnosed with esophageal cancer who received surgical treatment in Siriraj Hospital. The pathologic tissue diagnosis that was obtained from surgical treatment was used as gold standard to confirm the lesions. CT image acquisitions of 21 patients were performed by 64 slice MDCT of chest before the operation. The patients were enrolled between January 1, 2004 and December 31, 2009. Twenty-one CT images of chest were evaluated by two radiologists without knowing the patient's history as determined by surgical and pathology findings. CT technique used the two 64-slice MDCT machines (LightSpeed VCT 64 scanner, GE Healthcare or Somaton Definition 64, Siemen) and protocal of chest (lung disease) that performed both non-contrast phase and contrast phase in supine position. Non-ionic, iodinated contrast material (about 80 cc) was administered intravenously, with injected rate about 3 ml/sec, after scan at 40 sec post-contrast administration. The CT images were obtained from supraclavicular region to upper abdomen (end of lower aspect of diaphragm), Somatom Dual source CT scan. The Siemens used the following scan parameters collimation, 64 x 0.625 mm; table feed/rotation, 0.5 mm; slice width 1.25 mm; volume pitch, 16; 120kVp; and 250 to 300 mAs. The additional one LightSpeed VCT GE healthcare used the following scan parameters: collimation, 64 x 0.6 mm; table feed/rotation, 0.5 mm; slice width 1.25 mm; volume pitch, 16; 120kVp; and 250 mAs. Standard mediastinal window images (window width, 400 HU; window level, 60 HU) were used for displaying the images when reviewed at the work station (picture archiving and communication systems) both transverse CT images and multiplanar reformation (MPR).

Image analysis was determined based on tumor location, wall appearance, and findings of direct mediastinal extension. The results from two radiologists' analyses were recorded in separate record forms. The data was determined by consensus in non-agreement finding. T staging parameter from CT findings[9] were characterized to T1 or T2 (indistinguish from CT image), T3 (defined as irregularities of the outer border, stranding of the paraesophageal fat, ill-defined abnormal soft-tissue density around the tumor) and T4 (defined as tumor invasion of adjacent structures). The adjacent organ invasion was assessed about thyroid gland invasion, tracheobronchial invasion, aortic invasion, pericardial invasion, and diaphragmatic invasion. Tracheobronchial invasion was determined with criteria as following, 0: no contact, 1: abutment only, 2: bulging or displacement, 3: extension to lumen of airway, 4: TE fistula. The criteria of invasion are 2: bulging or displacement, 3: extend to lumen of airway and 4: TE fistula. Aortic invasion was evaluated based on Picus' angle and triangular effacement. Picus' angle was defined as angle of contact of tumor and thoracic aortic circumference which was classified as the following ; 0: no contact or $< 45°$, 1: 45°-90°, 2: 90°-180°, 3: $> 180°$[7,10] which the criteria of invasion is angle more than 90°. Triangle effacement was defined as effacement of triangle fat space between esophagus, vertebral body and aorta by tumor, (0: no effacements, 1: Indeterminate, 2: effacements) which the criteria of invasion is effacements of triangle fat space. Pericardial invasions were evaluated as follows: 0: no contact, 1: absent fat plane between esophagus and pericardium, 2: convex inward deformity of heart without fat plane, 3: pericardial thickening, 4: pericardial effusion, 5: convex inward deformity of heart with fat plane[7] and the criteria of invasion are 2: convex inward deformity of heart without fat plane, 3: pericardial thickening and 4: pericardial effusion.

Each reviewer evaluated the presence of the tumor and assessed the images in location (classified as cervical/upper thoracic/middle thoracic/lower thoracic)[11], wall appearance (classified as smooth/

irregular), peritumoral fat stranding (classified as present/absent), focal tumor extension to peri-esophageal fat (classified as present/absent) and gastric extension.

Nodal staging was lymph node assessment about nodal station and metastasis node which short axis in maximum diameter more than 10 mm. N0 is defined as no regional LN metastasis and N1 is defined as regional LN metastasis[12]. Non-regional lymph node metastases are designated as metastasis[11]. The gold standard for definite T staging diagnosis was histopathology and gross intra-operative finding.

The statistical difference was assessed and its accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were evaluated, respectively. The general data included sex, age, date of chest CT study, curative-operative date, interval between imaging time and esophagectomy procedure time, diagnosis with cell type from histopathology. Results were reported as mean and standard deviation (SD) or percentage (%) when appropriate. Statistical analysis used SPSS statistical package version 13 (SPSS Inc. Chicago, Illinois, USA). The correction of T staging from CT compared to pathological T staging was performed by its accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) respectively. For all tests, statistical significance was set at $p < 0.05$ level. Kappa (K) used for disagreement with final interpretation were determined by consensus of both radiologists

Results

Twenty-one patients with 22 lesions were considered. One patient had two lesions. Age range of the patients was 45 to 90 years (mean 62.5). Six were women (2 adenocarcinoma, 4 squamous cell carcinoma) and the other fifteen men (4 adenocarcinoma, 12 squamous cell carcinoma). There were six adeno-carcinoma and 16 squamous cell carcinoma (one cervical, one upper third, 5 middle third and 15 lower third). T staging by MDCT presented nine T3 staging patients, eight T4 staging patients and five T1-2 staging patients. As compared with histopathology and operative staging, there were eight T4 staging patients, eight T3 staging patients and six T1-2 staging patients. Corrected CT evaluation staging were four patients in T1-2 staging (Fig. 1), six patients in T 3 staging (Fig. 2, 3) and six patients in T4 staging (Table 1).The overstating case were one patient in T3

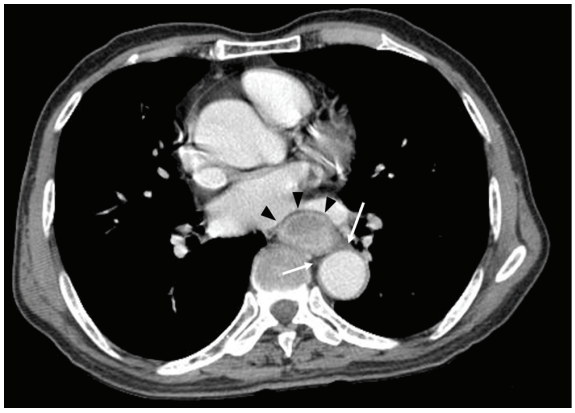

Fig. 1 Axial CECT of chest in A 64-year-old man with adenocarcinoma at lower esophagus showed convex inward deformity of the pulmonary vein with spare fat plane (black arrow head), no visualized periesophageal fat stranding (white arrow). The pathologic T staging was T2 stage

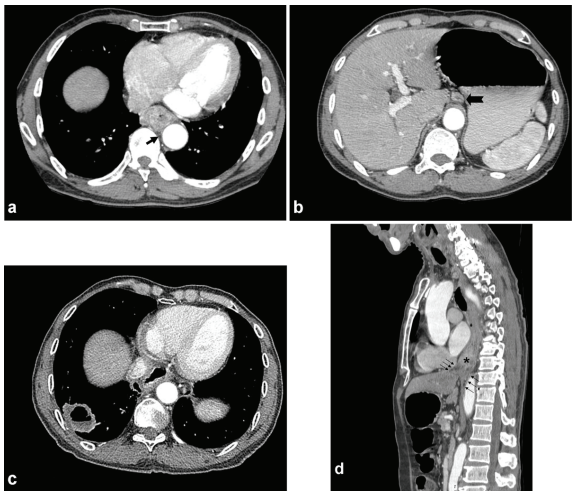

Fig. 2 A 68-year-old man with squamous cell carcinoma at mid to lower esophagus (a) axial CECT of chest showed irregular circumferential soft tissue enhancement lesion at lower esophagus, abutting to aorta with Picus' angle less than 90° and no triangle effacement (black arrow). (b) The enlarged left gastric node (black arrow) that indicates suspected metastasis lymph node, which is a positive metastasis node in histopathiologic finding. (c) The esophagus had periesophageal fat stranding with small focal extension from wall, suspected T3 staging that pathologic findings denoted T3 staging and cavitating lesion at right lower lung. (d) Sagittal view MPR showed tumor at distal esophagus (*) with thin hypodensity line between tumor-heart and tumor-aorta (thin black arrow)

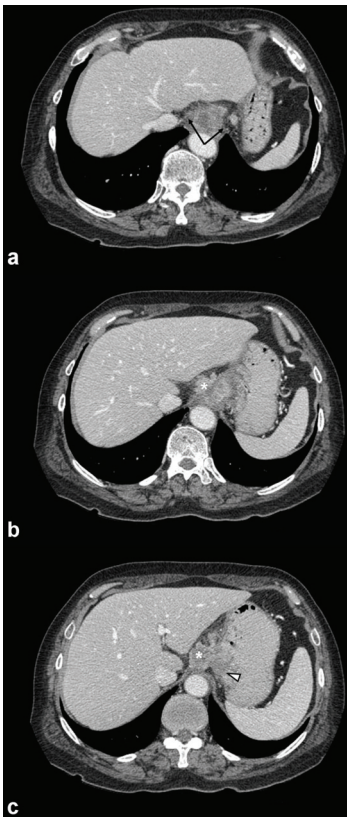

Fig. 3 A 58-year-old woman with adenocarcinoma at lower esophagus (a) axial CECT of chest showed irregular circumferential soft tissue enhancement lesion at lower esophagus abutting to aorta with Picus' angle less than 90°. (b) Axial CECT, soft tissue density near gastric wall is enlarged lymph node (*). (c) Axial CECT in a lower slice than in picture a and b showed esophageal tumor with gastric wall extension (white arrow head) and soft tissue density near gastric wall extension which suggested left gastric node metastasis (*). The pathologic T staging was T3, N1 stage

to T4 and T1-2 to T4 staging. The under staging were two patients in T4 toT3 and T3 to T1-2 (Table 2).

CT T4 staging cases were evaluated by Picus' angle 90° and 180° (two cases), effacement of aortic triangle (three cases), convex inward to pericardium without spare fat plane (one case) and both Picus' angle 90°-180° with effacement of aortic triangle (one case). All of them which confirmed with pathologic finding showed invade thoracic organ; One effacement of aortic triangle (pathological finding of tumor invade azygos vein and left main bronchus), one Picus' angle 90° and 180° with effacement of aortic triangle (pathological finding of tumor invade left main bronchus and aortic invasion), one convex inward to pericardium without spare fat plane (pericardial involvement). One of two cases of Picus' angle 90° and 180° from CT had positive invasion of aorta from histopathology. One case with Picus' angle 90° and 180° and effacement of aortic triangle was positive in histopathology. One case convex inward to pericardium without spare fat plane was corresponding to pericardial involvement (Fig. 4). One case had posterior bulging of bronchus with azygos vein invasion (Fig. 5).

Pathologic T4 staging were detected in 8 cases (2 middle and 6 lower segment) which CT finding about 2 cases of intrathoracic organ invasion are evaluated as effacement aortic triangle and Picus' angle 90° and 180°.

Tumors were most frequently located in the lower esophagus (15 patients). The most common histopathology in the present study was squamous cell carcinoma. The overall sensitivity, specificity, PPV, NPV, and accuracy of CT T3 staging were 75%, 78%, 66.7%, 84.6%, and 77.3%, respectively. The CT T4 staging had sensitivity of 75%, specificity 85.7%, PPV 75%, NPV 85.7%, and accuracy 81.8%.

The statistical analysis of lymphadenopathy in esophageal cancer was considered in N0 staging from CT staging showed sensitivity 50%, specificity 33%, PPV 23%, NPV 62.5%, and accuracy 38% (Table 3). Some patients showed non-regional lymph

Table 1. T staging from MDCT and post operative pathological T staging

CT T staging	Pathologic T staging			
	T1-2	T3	T4	Total
T1-2	4	0	1	5
T3	2	6	1	9
T4	0	2	6	8
Total	6	8	8	22

Table 2. Result of comparison of MDCT with post-operative T staging

	Post-operative pathologic staging	Correct staging	Over staging	Under staging
T1-2	6	4	2	-
T3	8	6	2	-
T4	8	6	-	2

node involvement that was classified to metastasis (M staging) (Fig. 3 b, c).

Duration of pre-operative CT to surgical treatment (esophagectomy) is an important factor in evaluation significant T staging. Interval between pre-operative CT image and surgery showed varied interval time (15-270 days). The missed diagnoses were found to be about two months long duration (Table 4). Discordant results in CT findings between the two radiologists assessments were solved by consensus and Kappa in each characteristic of CT findings had been calculated (Table 5).

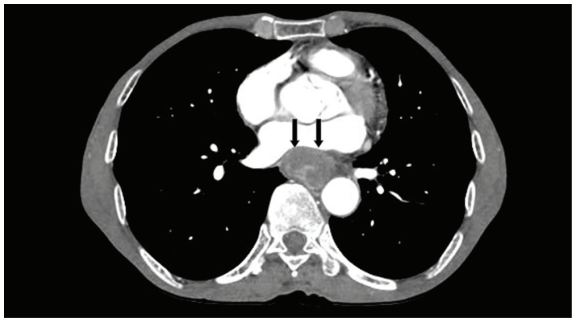

Fig. 4 Axial CECT scan of chest in 57-year-old man with squamous cell carcinoma at distal thoracic esophagus showed convex inward deformity of the heart with loss of fat plane (black arrow) between tumor and posterior portion of heart, compatible with pericardial invasion. The pathologic T staging was T4 stage

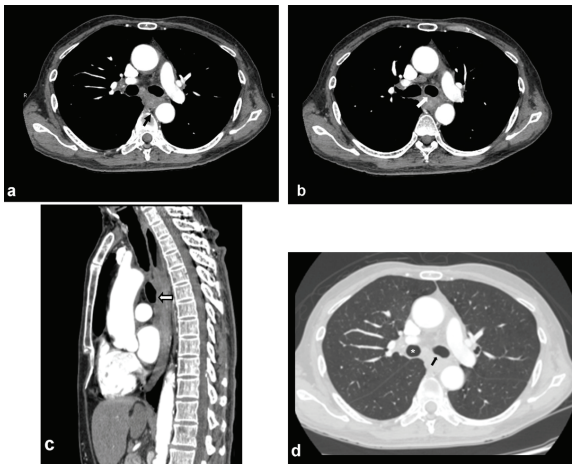

Fig. 5 (a) Axial CECT scan of chest in 57-year-old man with squamous cell carcinoma at mid thoracic esophagus showed bulging or displacement of airway with irregular wall, effacement of triangle fat (black arrow head) and not visualized azygos vein. (b) Surgical finding founded tumor invaded azygos and left bronchus (white arrow). (c) MPR sagittal view shows posterior bulging of left main bronchus (white arrow). (d) Axial lung window algorithm showed the posterior bulging of left main bronchus (black arrow) when compare to patent right main bronchus (*). The pathologic T staging was T4 stage

Discussion

Because of prognosis after treatment, the protocols of treatment in esophageal cancer were

Table 3. Diagnostic statistics of MDCT for N staging esophageal cancer

CT N staging	Pathologic N staging		
	N0	N1	Total
N0	3	10	13
N1	3	5	8
Total	6	15	21

Table 4. Duration between pre operative CT and surgical treatment in misdiagnosis T staging

No.	T staging (CT)	T staging (patho)	Duration (month)
1	T4	T3	1.44
2	T3	T2	1.74
3	T4	T4	1.44
4	T1-2	T4	2.30
5	T1-2	T4	2.00

Table 5. Kappa between reviewers in each CT finding

CT findings of esophageal tumor	Kappa
CT staging of two reviewer	0.525
Segmental involvement	0.909
Tumor border appearance	0.199
Periesophageal fat stranding	0.394
Focal tumor bulging	0.645
Aorta invasion:	
Picus' angle	0.694
Triangle effacement	0.507
Pericadial invasion	Uncounted
Tracheal invasion	Uncounted
Gastric invasion	0.891
Diaphragmatic invasion	0.450
Lymphadenopathy	0.320

considered in different ways for different T staging. The recent 64-slice MDCT and multiplanar reformation techniques (MPR), which optimized the visualized esophagus and adjacent anatomic structures and discovered the extension of tumor to intrathoracic or intraabdominal structure, were helpful in delineating anatomy and identifying an invasive point and degree of invasion with confidence and realization. Furthermore, the fast speed of scanning optimizes the evaluation of patient because thoracic movement artifacts caused by respiration and heart beats were minimized. The presence of all esophageal cancers depicted at CT had been correctly determined about T staging and N staging from the surgical finding and specimens. At MDCT, twenty-two lesions using multiplanar reconstruction (MPR), had 77.3% accuracy in T3 staging and 81.1% accuracy in T4 staging and determined the significant improved sensitivity and specificity of tumor extension to adjacent organs, especially in the mediastinum region, using MPR, sagittal and coronal reformation images that had been shown to increase the confidence of the two radiologists.

In the understaging group from CT evaluation, T3 from CT staging, gross pathology from intraoperative findings revealed invasion of tumors to the bronchus and main pulmonary artery. In the overstaging group, as T4 from CT staging, CT finding criteria of mediastinal invasion was depicted (loss of triangle effacement, convex deformity of heart with loss of fat plane). Finding of effect of fat plane between organs is a non-reliable sign for evaluating mediastinal invasion because of the paucity of body fat composition, both in the mediastinal and intraabdominal part in groups of these cancerous patients.

From the prior study[6,13], CT showed no suitable role to evaluation T1-T2 staging of esophageal cancer, difference from T3 staging. The CT finding that found in almost all of T3 staging compared to T1-T2 staging were irregular wall appearance, peritumoral fat stranding, focal tumor extension to periesophageal fat. The intrathoraicic finding is that significances in evaluation suggest Picus' angle 90° and 180°, convex inward to pericardium with loss of fat plane, and both Picus' angle 90° and 180° with effacement of aortic triangle. However, finding effacement of aortic triangle alone has no significance for evaluating of mediastinal invasion, which occurs if a tumor has large size and minimal intrathoracic fat of the patient.

Invasive esophageal cancer CT findings to mediastimun that limited evaluation in the present study were aortic invasion due to small of sample size, thus the confidence in the CT finding is less. However, convex deformity of the heart with loss of fat plane in one case of the present study was the helpful finding to be concern about pericardium invasion.

There are multiple limitations in the present study. First, the population included in the present study was small which affected sensitivity, specificity, and accuracy. Second, for basis of a retrospective study is unable to prepare patients about appropriate esophageal dilatation, phase of scanning images and position of patient in CT chest protocol. Third, an obvious case of mediastinal invasion was not included as a candidate for surgery that influenced the evaluation of statistical significance of mediastinal invasion sign in the present study. Fourth, the small number of T4 patient population and findings was present. Fifth, the esophageal cancer in the present population study is mostly found in the distal thoracic location, which influences researchers to record CT findings for mediastinal organ invasion.

Conclusion

The 64-slice MDCT has high sensitivity and specificity in determining T3 and T4 staging of esophageal cancer. Specificity of 64-slice MDCT in T4 staging is more effective than in T3 staging. In the present study, N staging in 64-slice MDCT has low accuracy. The metastatic node and reactive lymphadenopathy in esophageal cancer is equivocal to decide from CT findings, especially when using 1 cm in diameter of short axis as cut point. The additional CT findings of wall appearance, peritumoral fat stranding and focal tumor extension to periesophageal fat are also benefit for differentiating between T2 and T3 staging of esophageal cancer.

Acknowledgments

The authors wish to thank Ms. Julaporn Pooliam for statistical analysis. This article was supported by research funding from the Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand.

Potential conflicts of interest

None.

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การประเมินความถูกต้องของการลุกลามของมะเร็งหลอดอาหารสู่อวัยวะในช่องทรวงอกโดยใช้เอกซเรย์คอมพิวเตอร์ 64 สไลด์

โสภา พงศ์พรทรัพย์, สุธินี โพธิ์ศรี, กันยารัตน์ โตธนะรุ่งโรจน์

วัตถุประสงค์: *เพื่อศึกษาลักษณะภาพเฉพาะในการประเมินการลุมลามของมะเร็งหลอดอาหารสู่อวัยวะในช่องทรวงอก โดยใช้การตรวจเอกซเรย์คอมพิวเตอร์ 64 สไลด์ เทียบกับผลการผ่าตัด และผลทางพยาธิวิทยา*

วัสดุและวิธีการ: *ศึกษาย้อนหลังจากผู้ป่วยที่ได้รับการตรวจเอกซเรย์คอมพิวเตอร์ 64 สไลด์จากผู้ป่วยจำนวน 21 คน ได้รับการวินิจฉัยว่าเป็นมะเร็งหลอดอาหารได้รับการผ่าตัดในโรงพยาบาลศิริราชตั้งแต่เดือนมิถุนายน พ.ศ. 2547 ถึง ธันวาคม พ.ศ. 2552 โดยรังสีแพทย์ 2 คนที่ไม่ทราบผลการผ่าตัด และพยาธิวิทยา โดยประเมินตำแหน่ง, ขอบนอกของก้อนมะเร็ง, ลักษณะภาพที่ลุกลามสู่อวัยวะในทรวงอก, และหาความไว ความจำเพาะ ความแม่นยำของการตรวจ*

ผลการศึกษา: *ค่า kappa ของผู้อ่าน 2 คนอยู่ระหว่าง 0.2-0.9 ค่าความไว, ความจำเพาะ, PPV, NPV และความถูกต้องในการประเมินภาวะ T3 เท่ากับ 75%, 78%, 66.7%, 84.6% และ 77.3% ตามลำดับ ค่าความไว, ความจำเพาะ, PPV, NPV และความถูกต้องในการประเมินภาวะ T4 เท่ากับ 75%, 85.7%, 75%, 85.7% และ 81.8% ตามลำดับ ค่าความไว, ความจำเพาะ และความถูกต้องในการประเมินต่อมน้ำเหลือง N0 เท่ากับ 50%, 33% และ 38% ค่าความไว, ความจำเพาะ และความถูกต้องในการประเมินต่อมน้ำเหลือง N1 เท่ากับ 33%, 50% และ 38% ตามลำดับ*

สรุป: *การประเมินภาวะกระจายของมะเร็งหลอดอาหารสู่อวัยวะในทรวงอกโดยใช้การตรวจเอกซเรย์คอมพิวเตอร์ 64 สไลด์ มีค่าความไว, ความจำเพาะ และความถูกต้องสูง แต่อย่างไรก็ตามการประเมิน ต่อมน้ำเหลือง โดยใช้เส้นผ่านศูนย์กลางในแนวสั้นมากกว่า 1 ซม. อาจแยกภาวะมะเร็งกระจายสู่ต่อมน้ำเหลืองกับภาวะ reactive node ได้ยาก*