Comparison between Esophagogastric Adenocarcinoma and Squamous on Parameters of Spectral CT

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Abstract

Objective: The incidence of esophageal-gastric junction cancer has shown a clear upward trend worldwide. This study aimed to estimate the differences on Spectral CT parameters of squamous cell carcinoma and adenocarcinoma in the esophagogastric junction.

Methods: Thirty-five patients with squamous cell carcinoma and forty-five adenocarcinoma underwent spectral CT. Iodine concentration (IC), water content (WC), effective atomic number (Eff-Z) and slope of the spectral HU curve (λHU) of lesions were measured. The differences in measurements were compared using independent sample t-test, and parameters with significant differences were analyzed by ROC curve.

Results: The IC, Eff-Z, and λHU of squamous cell carcinoma patients in arterial phase were 1.38 ± 0.34 mg/mL, 8.49 ± 0.18 and 2.72 ± 0.65, respectively. The corresponding parameters of adenocarcinoma patients were 1.76 ± 0.41 mg/mL, 8.66 ± 0.23, and 3.35 ± 0.72, respectively. These parameters of squamous cell carcinoma patients were significantly smaller than those of adenocarcinoma patients (t = -4.433, 3.634, 4.007). The IC, Eff-Z, and λHU of squamous cell carcinoma patients in venous phase were 1.70 ± 0.21 mg/mL, 8.60 ± 0.10, and 3.23 ± 0.39, respectively. The corresponding parameters of adenocarcinoma patients were 2.20 ± 0.24 mg/mL, 8.85 ± 0.11, and 4.14 ± 0.43, respectively. These parameters of squamous cell carcinoma patients were significantly smaller than those of adenocarcinoma patients (t = -30.064, 10.368, 9.667; P < 0.01). The squamous cell carcinoma and adenocarcinoma patients had no statistically significant differences on WC in arterial and venous phase (P > 0.05). The ROC curve analysis was performed on parameters with significant differences in squamous cell carcinoma and adenocarcinoma. Arterial phase IC (AUC = 0.799), venous phase IC (AUC = 0.901), arterial phase Eff-Z (AUC = 0.661), and venous phase Eff-Z (AUC = 0.982), arterial phase λHU (AUC = 0.736), and venous phase λHU (AUC = 0.944) all had diagnostic value (AUC > 0.5, P < 0.01). And the parameters in venous phase were significantly higher than those in arterial phase, and AUC were all > 0.9.

Conclusion: Spectral CT can be used to differentiate squamous cell carcinoma from adenocarcinoma of esophagogastric junction, and it is worthy of application in clinical diagnosis.

Keywords: Spectral CT; Squamous Cell Carcinoma; Adenocarcinoma; Esophagogastric Junction

Abbreviations

CT: Computed Tomography; IC: Iodine Concentration; WC: Water Content; Eff-Z: Effective Atomic Number; λHU: Slope of the Spectral HU Curve; AUC: Area-Under-Curve; ROC: Receiver Operating Characteristic Curve

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Background

The esophagogastric junction cancer is a cancer whose center is within 5 cm of the anatomical boundary of the esophagus stomach. Unlike gastric cancer and esophageal cancer, it is more likely to have lymph node metastasis and hematogenous metastasis [1]. The early postoperative recurrence rate is high and the prognosis is poor. The incidence of esophageal-gastric junction cancer has shown a clear upward trend worldwide and has gradually attracted widespread attention and research at home and abroad [2,3]. The esophageal and stomach-associated cancers are mainly squamous cell carcinoma and adenocarcinoma and the pathological examination is the gold standard in diagnosing [4,5]. Endoscopic biopsy and intraoperative pathological examination are the main forms, but both have trauma to the patient. Spectral CT is of great value in the differential diagnosis of squamous cell carcinoma and adenocarcinoma of the esophagogastric junction, which can be used to accurately diagnose the tumor analogy with its parameter imaging and quantitative analysis.

In this study, we reviewed the spectral CT data of 35 patients with squamous cell carcinoma and 45 patients with adenocarcinoma in the esophagogastric junction and explored the value of energy spectrum CT in the differential diagnosis of squamous cell carcinoma and adenocarcinoma in the esophagogastric junction.

Purpose of the Study

The purpose of this study was to compare iodine concentration (IC), water content (WC), effective atomic number (Eff-Z) and slope of the spectral HU curve (λHU) in patients with squamous cell carcinoma and adenocarcinoma using spectral CT imaging.

Methods

General information

A total of 80 patients who underwent spectral CT between January 2018 and February 2019 in the first affiliated hospital of Benbu were included in the study. The inclusion criteria were: A. a pathologically confirmed diagnosis of squamous cell carcinoma or adenocarcinoma; B. there were no hyperthyroidism and adjacent esophageal stomach disease on the patients; C. the clinical data of patients were complete. Exclusion criteria were: A. patients with other malignancies; B. previous allergic to the contrast agent; C. patients with AIDS, tuberculosis and other infectious diseases.

Imagining methods

All patients underwent dual-phase enhanced scans in the spectral imaging mode by Revolution CT (GE Healthcare, USA). High and low energy (140 and 80 kvp) instantaneous (0.5 ms) switching, automatic milliamperes, scanning layer thickness and layer spacing of 5.0 mm, X-ray tube rotation time of 0.5 s/week, collimator width of 40 mm, FOV36 cm x 36 cm, pitch 0.5/6. The contrast agent used for the enhanced scan was non-ionic contrast agent iohexol (containing iodine 300 mg/mL) injected via the middle elbow vein at a flow rate of 1.2 mL/kg and 3.0 mL/s using a high pressure syringe, Arterial phase scans in 28 seconds after contrast agent injection, Venous phase scan in 45 seconds.

The original data was reconstructed into a single-energy image with a slice thickness of 1.25 mm and was transmitted to a GE AW4.7 post-processing workstation. The image was post processed and data analysis was performed blindly by two high-level physicians using GSI Viewer software. Disagreement was discussed through consensus. The region of interest (ROI) was placed on the three dimensions of the cross-section of the lesion and its adjacent upper and lower layers, and the same lesion was used in the arterial and venous phase iodine diagrams, water base diagrams, and effective atomic number maps using the layer information and copy and paste functions. The location, shape, and area of the selected ROI are the same (the area of the selected ROI ranges from 15.33 to 79.57 mm). The solid components near the center of the tumor are selected as far as possible to avoid necrotic tissue, residual liniments, and blood vessels. We measured the iodine concentration (IC), water concentration (WC), and effective atomic number (Eff-z) of the ROIs at the arterial phase.
and venous phase on the aforementioned parameters, plot the ROI energy curve, and calculated the slope of the energy spectrum curve ($\lambda_{HU}$): $\lambda_{HU} = (CT_{40\text{ keV}} - CT_{70\text{ keV}})/|40\text{ keV} - 70\text{ keV}|$. Measurements of all ROIs were measured on three consecutive levels (3 times in total), and the measurement results were averaged.

**Observation indicators**

A. CT appearance of squamous cell carcinoma and adenocarcinoma in esophagogastric junction. B. CT scan parameters of squamous cell carcinoma and adenocarcinoma in arteriovenous gastroesophageal junction. C. Analysis of the diagnostic value of spectral CT in squamous cell carcinoma and adenocarcinoma of esophagogastric junction.

**Statistical analysis**

Statistical analysis in this study was performed using IBM SPSS 23.0 professional statistical analysis software: all the measurement data were expressed as mean ± standard deviation (± s) and were statistically analyzed using the two-sample t-test. A p-value < 0.05 was considered statistically significant. Receiver operating characteristic (ROC) analysis was carried out to establish threshold values and to calculate the area-under-curve (AUC) for ROC curves, and the larger the AUC is, the greater the diagnostic value of this parameter is.

**Results**

**CT appearance of squamous cell carcinoma and adenocarcinoma in esophagogastric junction**

Under spectral CT images, the esophagogastric junction showed a thickening of the wall of the esophagus or a visible soft-tissue mass in all the patients. Partial lumen stenosis and thinning were observed and enhanced scan lesions showed moderate to significant enhancement. Patient A was diagnosed with squamous cell carcinoma by surgery, 75-year-old, male. Patient B was diagnosed with adenocarcinoma by surgery, 70-year-old, male. Spectroscopic CT dual-phase enhanced scans were followed by post-processing to obtain the iodine profile, water concentration, water-based map, and effective atomic number of esophageal and gastric squamous cell carcinoma, adenocarcinoma arterial phase (Figure 1) and venous phase (Figure 2). Graphs and energy spectrum graphs and the image is clearly. We calculated the iodine concentration, the effective atomic number, and the energy spectrum of the two patients in the arterial and venous phases (Table 1).

(Table 1, figure 1 and 2)

**CT scan parameters of squamous cell carcinoma and adenocarcinoma in arteriovenous gastroesophageal junction**

IC, Eff-Z, and $\lambda_{HU}$ in arterial and venous phase of patients with squamous cell carcinoma were significantly smaller than those of adenocarcinoma patients, and the difference was statistically significant (P < 0.01). There was no statistical significance in WC in the arterial and venous phase between the squamous cell carcinoma and adenocarcinoma patients (P > 0.05) (Table 2).

<table>
<thead>
<tr>
<th>No.</th>
<th>Arterial phase</th>
<th>Venous phase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IC (mg/mL)</td>
<td>WC (mg/mL)</td>
</tr>
<tr>
<td>A</td>
<td>1.69</td>
<td>1 027.56</td>
</tr>
<tr>
<td>B</td>
<td>1.16</td>
<td>1 026.20</td>
</tr>
</tbody>
</table>

**Table 1:** Spectrum CT data of A, B patient.

*Abbreviations: IC: Iodine Concentration; WC: Water Content; Eff-Z: Effective Atomic Number; $\lambda_{HU}$: Slope of the Spectral HU Curve.*
**Figure 1:** Arterial phase energy spectrum CT: A–D are respectively iodine profile, water concentration, water-based map, effective atomic number map and energy spectrum. Patient A, 75 years old, male, squamous cell carcinoma. E–H are respectively iodine profile, water concentration, water-based map, effective atomic number map and energy spectrum, patient B, 66 years old, female, adenocarcinoma.

**Figure 2:** Vein energy spectrum CT: A–D are iodine profile, water concentration, water-based map, effective atomic number map and energy spectrum of Patient A with squamous cell carcinoma, 75 years old, male. E–H are iodine profile, water concentration, water-based map, effective atomic number map and energy spectrum of patient B with adenocarcinoma, 66 years old, Female.
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Table 2: Two groups of patients with spectral CT data.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Arterial phase</th>
<th>Venous phase</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IC (mg/mL)</td>
<td>WC (mg/mL)</td>
<td>Eff-Z</td>
<td>IC (mg/mL)</td>
<td>WC (mg/mL)</td>
</tr>
<tr>
<td>Squamous cell carcinoma (N = 35)</td>
<td>1.38 ± 0.34</td>
<td>1019.45 ± 9.48</td>
<td>8.49 ± 0.18</td>
<td>2.72 ± 0.65</td>
<td>1.70 ± 0.21</td>
</tr>
<tr>
<td>Adenocarcinoma (N = 45)</td>
<td>1.76 ± 0.41</td>
<td>1017.09 ± 8.85</td>
<td>8.66 ± 0.23</td>
<td>3.35 ± 0.72</td>
<td>2.20 ± 0.24</td>
</tr>
</tbody>
</table>

Analysis of the diagnostic value of spectral CT in squamous cell carcinoma and adenocarcinoma of esophagogastric junction

The ROC curve analysis was performed on parameters with significant differences in squamous cell carcinoma and adenocarcinoma of the arteriovenous gastroesophageal squamous cell carcinoma (Figure 3). Arterial phase IC, venous phase IC, arterial phase Eff-Z, and venous phase Eff-Z, arterial phase $\lambda_{HU}$ and venous phase $\lambda_{HU}$ all had diagnostic value (AUC > 0.5, P < 0.01), and the venous phase parameters were all significantly higher, and the AUC was > 0.9, which was of higher diagnostic value (Table 3).

Table 3: Analysis of the diagnostic value of spectral CT in squamous cell carcinoma and adenocarcinoma of esophagogastric junction.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Youden Index</th>
<th>95% CI (Lower Bound, Upper Bound)</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial phase IC</td>
<td>1.725</td>
<td>(0.702, 0.896)</td>
<td>0.799</td>
</tr>
<tr>
<td>Venous phase IC</td>
<td>2.085</td>
<td>(0.836, 0.967)</td>
<td>0.901</td>
</tr>
<tr>
<td>Arterial phase Eff-Z</td>
<td>8.445</td>
<td>(0.5340, 0.781)</td>
<td>0.661</td>
</tr>
<tr>
<td>Venous phase Eff-Z</td>
<td>8.755</td>
<td>(0.959, 1.000)</td>
<td>0.982</td>
</tr>
<tr>
<td>Arterial phase $\lambda_{HU}$</td>
<td>3.175</td>
<td>(0.624, 0.848)</td>
<td>0.736</td>
</tr>
<tr>
<td>Venous phase $\lambda_{HU}$</td>
<td>4.025</td>
<td>(0.898, 0.989)</td>
<td>0.944</td>
</tr>
</tbody>
</table>

Discussion

The significance of IC and WC in the diagnosis of squamous cell carcinoma and adenocarcinoma in esophagogastric junction

The IC value of spectral CT mainly reflects the blood supply status of the lesion. The higher the IC value is, the richer the blood supply of the lesion tissue is [6]. The results of this study suggest that the IC value of the adenocarcinoma lesion tissue is higher than that of the squamous cell carcinoma tissue, indicating the gastroesophageal junction adenocarcinoma is richer in blood supply than squamous cell carcinoma. After analyzing the reasons for this, the main considerations are as follows: the adenocarcinoma and the squamous cell carcinoma of the esophagogastric junction is similar to lung adenocarcinoma and squamous cell carcinoma [7-9]. The adenocarcinoma has more neovascularization than squamous cell carcinoma, and the microvessel density is greater. However, the adenocarcinoma tends to spread the growth, squamous cell carcinoma tends to accumulate and grow, and the pressure within the general adenocarcinoma mass is smaller, which is favorable for the opening of new blood vessels. Therefore, the adenocarcinoma’s vascular richness and openness are significantly higher than that of squamous cell carcinoma, and its blood supply richness is better for squamous cell carcinoma, so the IC
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Figure 3: ROC curve of parameters with significant differences in squamous cell carcinoma and adenocarcinoma: A: ROC curve of arterial phase IC; B: ROC curve of venous phase IC; C: ROC curve of arterial phase Eff-Z; D: ROC curve of venous phase Eff-Z; E: ROC curve of arterial phase λHU; F: venous phase λHU The ROC curve (IC: Iodine Concentration; Eff-Z: Effective Atomic Number; λHU: Slope of the Spectral HU Curve; ROC: Receiver Operating Characteristic Curve).

value of adenocarcinoma is higher than that of squamous cell carcinoma. The author summarizes the actual operation in the clinical examination, if the ROI contains a necrotic area or small blood vessels and the size of the ROI will affect the accurate measurement of the IC value, the ROI should be accurately selected and kept the same size.

We also statistically analyzed the WC of gastroesophageal junctional adenocarcinoma and squamous cell carcinoma. The arterial phase and venous phase WC of adenocarcinoma patients were slightly lower than those of squamous cell carcinoma, but neither of the two groups had statistical significance in the middle arterial phase and venous phase WC. We analyzed the reason may be that the adenocarcinoma of the mesenchyme is more abundant than the squamous cell carcinoma, and the tumor cell density per unit volume is smaller, but WC cannot be used for the differential diagnosis of gastroesophageal junction adenocarcinoma and squamous cell carcinoma [4,10].

The significance of $\lambda_{\text{HU}}$ in the differential diagnosis of squamous cell carcinoma and adenocarcinoma in esophagogastric junction

In this study, we found that the energy spectrum curve of enhanced gastroesophageal junction cancer has a large change in the slope of the low-energy segment. With the increase of KeV, the curve gradually flattens, which is related to the large X-ray absorption coefficient and X-ray attenuation at low energy levels [11]. So, this study uses the slope of the 40 - 70 KeV energy level as a quantitative analysis to compare squamous cell carcinoma with adenocarcinoma. The results showed that the $\lambda_{\text{HU}}$ of adenocarcinoma was higher than that of

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squamous cell carcinoma, and the difference between the two was statistically significant. It was considered that the IC value of adenocarcinoma was higher than that of squamous cell carcinoma, and the low keV condition and iodine contrast agent enhanced the mass absorption coefficients of the two groups. Therefore, the performance of adenocarcinoma in $\lambda_{\text{HU}}$ is greater than that of squamous cell carcinoma [6,12].

**Eff-Z differential diagnosis of esophageal gastric squamous cell carcinoma and adenocarcinoma significance**

The results of this study indicate that the Eff-Z value of adenocarcinoma is higher than that of squamous cell carcinoma, and the difference is statistically significant. We consider this is mainly due to the substance composition of iodine in squamous cell carcinoma and adenocarcinoma after enhanced scavenging and introduction of iodine contrast agent and the absorption and distribution caused by the difference [13]. Subsequent ROC curve analysis showed that Eff-Z had a threshold value of 8.755 at the venous phase, which was the highest diagnostic efficiency for squamous cell carcinoma and adenocarcinoma. We analyzed that the reason was that the various parameters of the energy spectrum CT and the material component analysis were determined by the material Eff-Z, so its comparative material separation quantitative analysis method may be more sensitive or stable to the determination of material composition [14,15].

**The arterial and venous phase energy spectrum identification of squamous cell carcinoma and adenocarcinoma significance**

The results of this study indicate that IC, Eff-Z, and $\lambda_{\text{HU}}$ in the arterial phase have diagnostic value for adenocarcinoma and squamous cell carcinoma of the esophagogastric junction, and the diagnostic efficacy of IC, Eff-Z, and $\lambda_{\text{HU}}$ at the venous phase is higher than those at arterial phase, Eff-Z and Eff-Z at venous phase for the differential diagnosis of esophageal gastric squamous cell carcinoma and adenocarcinoma greater significance. We consider that the CT scan of the arterial phase spectrum of patients in this study is earlier, which resulting in insufficient iodine uptake in squamous and adenocarcinoma in the arterial phase [16-18]. However, the intravenous perfusion is more adequate at the venous phase, causing the above-mentioned parameters that are closely related to iodine (IC, Eff-Z) to be associated with greater differences than those in the arterial phase.

**Conclusion**

In conclusion, this study preliminarily shows that the multi-parameter quantitative analysis of spectroscopic CT has certain value in the differential diagnosis of squamous cell carcinoma and adenocarcinoma of the esophagogastric junction. Preoperative routine spectral CT scan can provide patients with esophagogastric junction cancer is of greater valuable.

**Ethics Approval and Consent to Participate**

This study was performed in accordance with the ethical guidelines of the Declaration of Helsinki (version 2002). And the study was approved by the Ethical Committee of the First Affiliated Hospital of Bengbu Medical College. Written informed consent was obtained from all participants.

**Consent for Publication**

Not applicable.

**Availability of Data and Material**

All data generated and analysed during the current study are available from the corresponding author on reasonable request.

**Competing Interests**

The authors declare that they have no competing interests.

**Authors’ Contributions**

YM participated in the design of the study, performed the study and drafted the manuscript. SZ participated in the design of the study, conducted the data analysis and drafted the manuscript. All authors have read and approved the final version of the article.

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