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Research article

Is there association of gross tumor volume of adenocarcinoma of oesophagogastric junction measured on magnetic resonance imaging with N stage?

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ABSTRACT

Purpose: To determine whether gross tumour volume (GTV) of adenocarcinoma of oesophagogastric junction (AOG) measured on fat-suppression T_2-weighted imaging (FS-T_2WI) and diffusion-weighted imaging (DWI) correlates with regional lymph node metastasis and N stage.

Materials and methods: The study was approved by the institutional ethics committee, and written informed consent was obtained. Forty-six patients with AOG underwent preoperative magnetic resonance scans including FS-T_2WI and DWI with b-values of 500 and 800 s/mm^2. GTV was measured on FS-T_2WI and DWI. Statistical analyses were performed to determine association of GTV with N stage.

Results: Univariate analysis showed GTV measured on FS-T_2WI and DWI with b-values of 500 and 800 s/mm^2 were correlated with lymph node metastasis (all $Ps < 0.05$). Spearman rank correlation tests demonstrated a trend toward an increase in GTV obtained on previous sequences with increasing N stage (r = 0.578 to 0.591, all $Ps < 0.001$). Mann-Whitney *U* tests showed GTV obtained on previous sequences could distinguish grouped N stages (all $Ps < 0.05$). Receiver operating curve analyses demonstrated that GTV obtained on FS-T_2WI and DWI with b-value of 500 s/mm^2 and DWI with b-value of 800 s/mm^2 might differentiate stage N0 from stages N1-3 (cutoff, 19.70 cm^3, 16.70 cm^3 and 12.24 cm^3, respectively), stages N0-1 from N2-3 (cutoff: 22.16 cm^3, 17.54 cm^3 and 14.17 cm^3, respectively), stages N0-2 from N3 (cutoff: 25.57 cm^3, 29.27 cm^3 and 22.73 cm^3, respectively).

Conclusion: There is a trend toward an increase in GTV obtained on FS-T_2WI and DWI sequences with increasing N stage.

1. Introduction

The incidence of adenocarcinoma of oesophagogastric junction (AOG) has rapidly increased worldwide [1,2]. The symptoms of AOG appear relatively late, and most of the affected individuals present with lymph node metastasis at the onset [3]. Curative resection of primary tumour and regional lymph nodes is the mainstay for resectable AOG [4]. Lymph node metastasis is also an important prognostic factor, and extended lymphadenectomy is associated with the improved survival [5]. However, extended lymphadenectomy also increases the rate of surgical complications and mortality [6]. Surgery alone is now reserved for early T-stage node-negative disease and preoperative therapy seems to be more suitable for advanced AOG [7]. Accurately preoperative determining lymph node metastasis and identifying N stage of this tumour is important for treatment decision making so as to optimize the outcomes.

Computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET) and endoscopic ultrasound (EUS) have been used in diagnosing lymph node metastasis clinically. The diagnostic criterion for metastatic lymph node at CT or MRI is usually based on the size. Lymph nodes larger than 1 cm are considered abnormal [8]. As many metastatic lymph nodes are less than 1 cm in diameter whereas a number of nodes larger than 1 cm are benign, CT and MRI cannot reliably distinguish between benign and malignant

Abbreviations: GTV, gross tumour volume; AOG, adenocarcinoma of oesophagogastric junction; FS-T_2WI, fat-suppression T_2-weighted imaging; DWI, diffusion-weighted imaging; CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography; EUS, endoscopic ultrasound; AJCC, American Joint Committee on Cancer; ICC, intraclass correlation coefficient; ROC, receiver operating characteristic; AUC, area under the receiver operating characteristic curve

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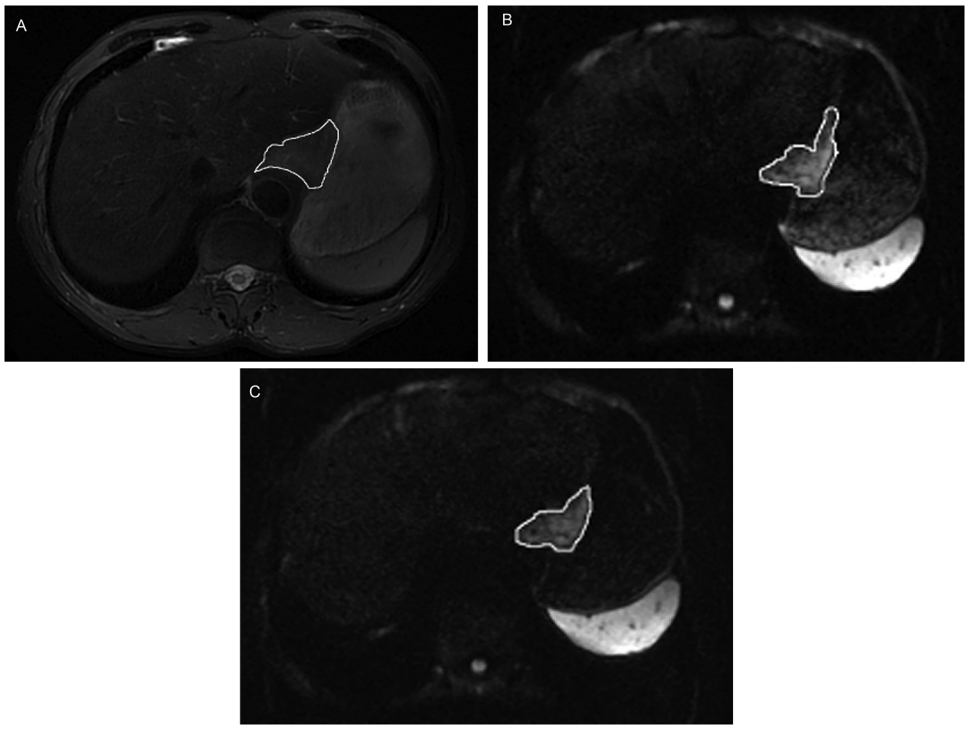

Fig. 1. Tumour Sectional Area Measurement. In a 61-year-old man with adenocarcinoma of oesophagogastric junction, tumour area is manually drawn along margin of tumour on axial fat-suppression T_2-weighted imaging (A) and on axial diffusion-weighted imaging acquired by using b values of 500 s/mm^2 (B) and 800 s/mm^2 (C), and values of this area are automatically derived by the software.

Table 1
Inter- and Intra-observer Agreements of GTV Measurements.

GTV	Differences between Two Measurements (Mean ± SD)	95% CI	95% Limits of Agreement	95% Inter- or Intra-observer Correlation Coefficient
Inter-Observer				
FS-T_2WI	1.68 ± 2.75	−3.71 to 7.07	−5.12 to 8.48	0.9825 (0.9684 to 0.9903)
DWI b = 500 s/mm^2	1.05 ± 2.31	−3.48 to 5.58	−4.65 to 6.75	0.9841 (0.9713 to 0.9912)
DWI b = 800 s/mm^2	0.14 ± 1.80	−3.39 to 3.67	−4.32 to 4.60	0.9896 (0.9812 to 0.9943)
Intra-Observer				
FS-T_2WI	−1.29 ± 2.35	−5.90 to 3.32	−7.11 to 4.53	0.9903 (0.9825 to 0.9947)
DWI b = 500 s/mm^2	−0.05 ± 1.73	−3.44 to 3.34	−4.34 to 4.24	0.9911 (0.9835 to 0.9951)
DWI b = 800 s/mm^2	−0.31 ± 1.76	−3.76 to 3.14	−4.66 to 4.04	0.9900 (0.9819 to 0.9945)

Notes: GTV = gross tumour volume, SD = standard deviation, CI = confidence interval, FS-T_2WI = fat-suppression T_2-weighted imaging, DWI = diffusion-weighted imaging, and b = diffusion-sensitive gradient b value.

lymph nodes on the basis of the size of lymph node [9]. Some researches have shown that EUS could be inaccurate in identifying lymph node metastasis for the limitation imposed by the detection depth of EUS, and the substantial reliance on the expertise and experience of the ultrasonographer as well as its size-based diagnostic criteria [10]. PET has a sensitivity of 71% to detect metastatic lymph nodes whereas the specificity is only 67% [11].

A previous research showed that gross tumour volume (GTV) of AOG measured with multidetector CT could be helpful for identifying regional lymph node metastasis and N stage [12]. However, CT cannot accurately show the boundary of this tumour and non-tumour area because normal tissue may accompanied with scirrhous invasion and tumour area may contain normal interstitial tissue, which can impact on the accuracy of GTV measurement. MRI can well show the contour of the tumour based on the thickening of the wall and the signal change of this lesion, suggesting that MRI can be more accurate than CT to measure GTV of AOG. Based on the previous CT study on the association of GTV with N stage [12], we could presume that GTV measured on MRI might be related to lymph node metastasis and N stage. As reported, both T_2-weighted imaging (T_2WI) and diffusion-weighted imaging (DWI) can provide important information for the degree of infiltrating depth of gastric cancer [13]. An addition of DWI could raise the accuracy of preoperative diagnosing oesophageal and gastric cancers, and could provide more information for staging than conventional MRI [14–16]. The purpose of this study was to explore whether GTV measured on T_2WI and DWI could distinguish regional lymph nodes metastasis and how to use it to differentiate N stages.

2. Materials and methods

2.1. Participants

The Institutional Ethics Committee of our hospital approved this prospective study. Written informed consent was obtained from each participant before the study.

Between January 2014 and December 2016, 51 patients with endoscopic biopsy-proved AOG were included according to the following inclusion criteria: (a) the patient did not receive any tumour-related treatment, such as radiation therapy or chemotherapy, prior to the MRI scans, (b) the tumour was considered resectable and there were no contraindications to surgery, and (c) patients desired to undergo surgical resection. The exclusion criteria were as follows: (a) the patient was treated with preoperative neoadjuvant radiation therapy and/or chemotherapy during the interval between MRI and surgery (n = 3), or (b) the MR images were of poor quality (n = 2). Consequently, 46 patients (39 males and 7 females; age range, 46–79 years; median age, 64

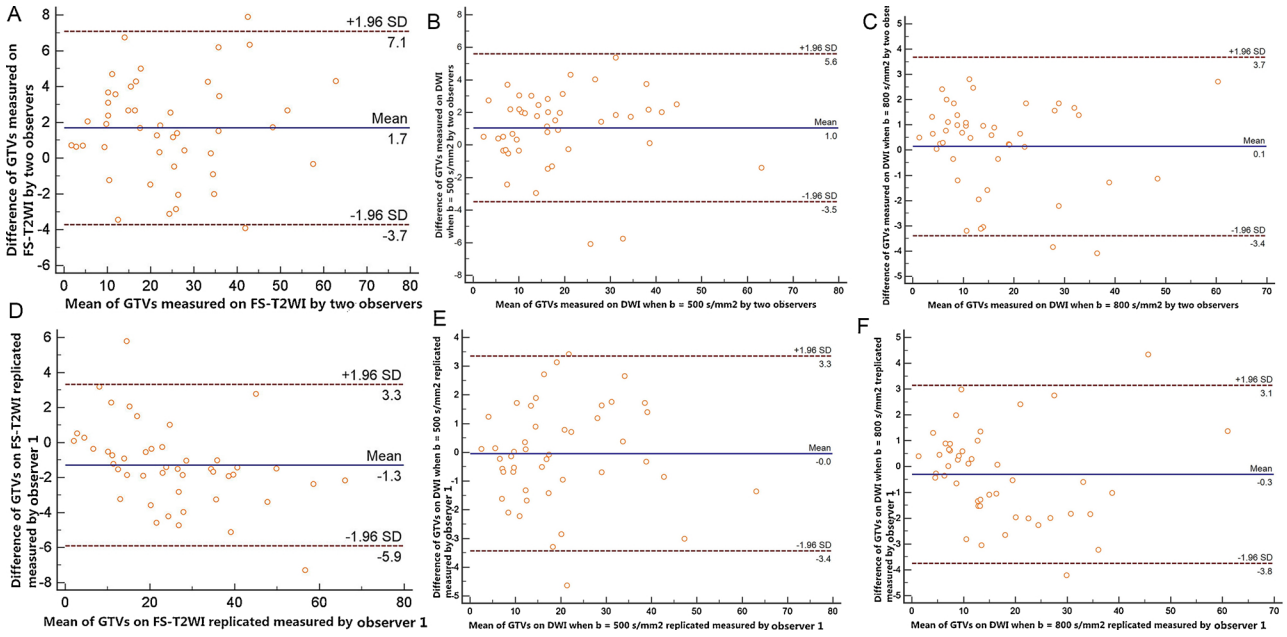

Fig. 2. Bland-Altman plots.
Bland-Altman plots show the inter-observer agreements of gross tumour volume (GTV) measured on axial fat-suppression T_2-weighted imaging (FS-T_2WI) (A) and on axial diffusion-weighted imaging (DWI) by using b-values of 500 s/mm^2 (B) and 800 s/mm^2 (C), and intra-observer agreements of GTV measured on FS-T_2WI (D) and on DWI with b-values of 500 s/mm^2 (E) and 800 s/mm^2 (F). b = diffusion-sensitive gradient b value.

Table 2
Univariate Analysis of Association between Regional Lymph Node Metastasis and GTV in the 46 Patients with Adenocarcinoma of Oesophagogastric Junction.

GTV	Positive lymph node (n = 34)	Negative lymph node (n = 12)	*P* value
FS-T_2WI			0.002
< 22.51 cm^3	12 (35.3)	11 (91.7)	
≥22.51cm^3	22 (64.7)	1 (8.3)	
DWI b = 500 s/mm^2			0.017
< 16.60 cm^3	13 (38.2)	10 (83.3)	
≥16.60 cm^3	21 (61.8)	2 (16.7)	
DWI b = 800 s/mm^2			0.017
< 12.24 cm^3	13 (38.2)	10 (83.3)	
≥12.24 cm^3	21 (61.8)	2 (16.7)	

Notes: Data are numbers of patients with percentages in parentheses. GTV = Gross tumour volume, FS-T_2WI = fat-suppression T_2-weighted imaging, DWI = diffusion-weighted imaging, and b = diffusion-sensitive gradient b value.

years) were enrolled into our study.

In this cohort, 5 of the 46 (10.9%) patients had a type I tumour, 22 (47.8%) patients had a type II tumour, and 19 (41.3%) patients had a type III tumour based on the endoscopic biopsy and double-contrast barium examinations according to the Siewert classification system [17]. All the patients with AOG underwent preoperative magnetic resonance scans. Subsequently, the enrolled patients were scheduled for surgery. The surgically removed tumour tissues and lymph nodes were sent to the pathology department for histologic examination. According to postoperative histopathologic examination and 8th edition of the American Joint Committee on Cancer (AJCC) criteria [18], the tumours were well, moderately and poorly differentiated in 8, 14 and 24 patients, respectively. Patients were considered as stage N0 disease if there were no metastatic lymph nodes; and the tumours were classified as stage N1, N2 and N3 disease if there were one to two, three to six and seven or more metastatic lymph nodes as shown by postoperative histopathology, respectively.

2.2. Magnetic resonance imaging

The MR data were acquired with a 3.0-T scanner (Discovery MR 750, GE Medical Systems, Milwaukee, WI, USA) with a 32 tunnel body phased-array coil with respiratory gating and cardiac gating. Before the MR image acquisition, at least 500 mL of water was given orally to distend the oesophagus and stomach. Patients were examined in the supine position. The scanning sequences included conventional axial T_1-weighted imaging (repetition time = 4 ms, echo time = 2 ms, flip angle = 12°, acquisition matrix = 260 × 192 mm, field of view = 300 × 300 mm, and slice thickness = 5 mm), T_2WI with fat suppression (repetition time = 3529 ms, echo time = 83 ms, flip angle = 110 deg, acquisition matrix = 384 × 320 mm, field of view = 300 × 300 mm, and slice thickness = 5 mm), and DWI (repetition time = 4800 ms, echo time = 66 ms, flip angle = 90°, acquisition matrix = 192 × 192 mm, field of view = 340 × 340 mm, and slice thickness = 5 mm). Diffusion-sensitive gradient b-values of 500 s/mm^2 and 800 s/mm^2 were applied for DWI. Additionally, conventional T_1-weighted imaging was performed to localize AOG, and fat suppression T_2-weighted imaging (FS-T_2WI) and DWI were performed for subsequent GTV measurement and data analysis.

2.3. Tumour volume measurement

The MRI data were reviewed on the work station (GE Advantage Workstation Version 4.4–09, Sun Microsystems, Palo Alto, CA, USA). The circumference of the AOG was manually drawn along the visible margins of this tumour (Fig. 1). Tumour measurement on FS-T_2WI can be done mainly based on the thickness and signal of the distal oesophageal and proximal gastric wall. The lesions showed iso-hyperintensity or slightly hyperintensity on FS-T_2WI. Tumour measurement on DWI could be done based on the remarkably high signal intensity owing to the restricted Brownian motion of water molecules within the tumour [19]. In each patient, the values of the areas were automatically derived by the software. GTV was then calculated by multiplying the sum of all the tumour areas by the section thickness.

In addition, the GTV was measured independently by two experienced radiologists including a radiology resident (Observer 1) with 3

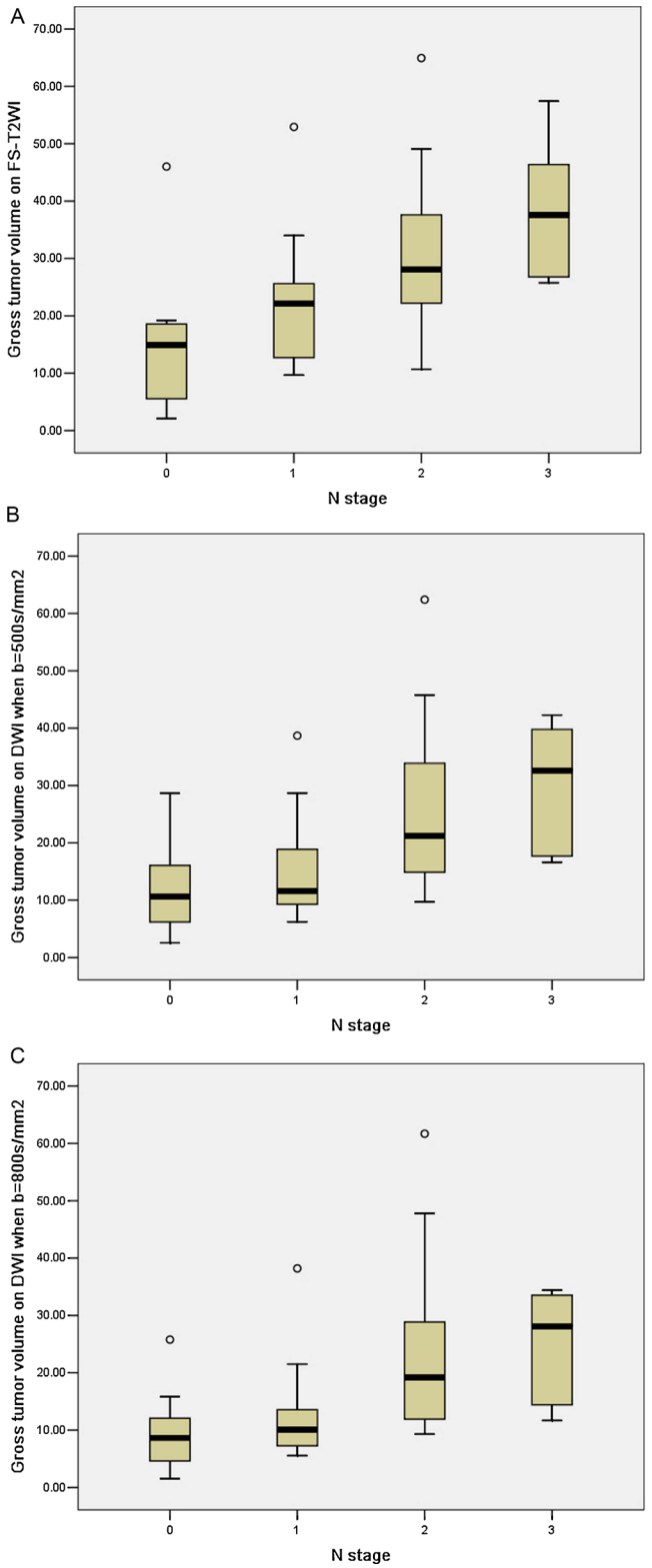

Fig. 3. Boxplots. Boxplots show distributions of gross tumour volume of adenocarcinoma of oesophagogastric junction measured on fat-suppression T_2-weighted imaging (FS-T_2WI) (A) and on diffusion-weighted imaging (DWI) with b-values of 500 s/mm^2 (B) and 800 s/mm^2 (C) corresponding to N stages.

years of radiology expertise and an experienced radiology professor (Observer 2) with 20 years of abdominal radiology expertise without any knowledge of the histologic results to test the interobserver variation in measuring GTV. One month later, repeated measurement was performed by Observer 1 to test the intraobserver variation in measuring GTV.

2.4. Statistic analysis

Statistical analyses were performed by using SPSS software (version 13.0 for Windows, SPSS Inc., Chicago, IL, USA) and the MedCalc statistical software (version 13.0 for Windows, SPSS Inc.). The intraclass correlation coefficient (ICC) was calculated and Bland-Altman plots [20] were conducted to determine the interobserver variation in measuring GTV by the two observers, and the intraobserver variation in the two measurements by Observer 1. ICCs less than 0.5, between 0.5 and 0.75, between 0.75 and 0.9, and greater than 0.90 could be indicative of poor, moderate, good and excellent reliability, respectively [21]. If good agreements were achieved between the two replicated measurements by Observer 1, and between the first measurements by two observers, values of the first measurement by Observer 1 were regarded as the final results for further analyses.

The univariate analysis was performed to determine whether GTV could predict lymph node metastasis by Fisher's exact test. The correlation between GTV and N stage was tested based on the Spearman rank correlation test. The Mann-Witney *U* test was conducted to compare GTV among different grouped N stages. Receiver operating characteristic (ROC) analysis was then performed to determine the cutoff value of GTV for predicting N stage. The level of significance was set at a *P* value less than 0.05.

3. Results

3.1. Intra- and inter-observer variability of GTV measurements

The mean values of GTV measured on FS-T_2WI and DWI with b-values of 500 and 800 s/mm^2 by Observer 1 were 24.84 ± 14.76 cm^3, 19.57 ± 12.98 cm^3 and 16.74 ± 12.33 cm^3, respectively. Values obtained on FS-T_2WI and DWI with b-values of 500 and 800 s/mm^2 by Observer 2 were 23.17 ± 14.62 cm^3, 18.52 ± 12.99 cm^3 and 16.60 ± 12.53 cm^3, respectively. The replicated measurements on FS-T_2WI and DWI with b-values of 500 and 800 s/mm^2 by Observer 1 were 26.14 ± 15.77 cm^3, 19.62 ± 12.94 cm^3 and 17.05 ± 12.49 cm^3, respectively. There were excellent agreements in terms of GTV on FS-T_2WI and DWI with b-values of 500 and 800 s/mm^2 between the two independent observers or between the two measurements by Observer 1 (Table 1), and Bland-Altman plots are shown in Fig. 2. The values of the initial measurements by Observer 1 were regarded as the final GTV for the subsequent analysis.

3.2. Association of GTV with lymph node metastasis

The association of GTV with the status of lymph node metastasis is shown in Table 2. The median value of GTV measured on FS-T_2WI and DWI with b-values of 500 and 800 s/mm^2 were 22.51 cm^3, 16.60 cm^3 and 12.24 cm^3, respectively. According to univariate analysis, GTV measured on FS-T_2WI and DWI with b-values of 500 and 800 s/mm^2 were all related to lymph node metastasis (all $Ps < 0.05$). There was a trend toward an increase in GTV measured on FS-T_2WI and DWI with b-values of 500 and 800 s/mm^2 (Fig. 3) with lymph node metastasis according to the Spearman rank correlation test (r = 0.591, 0.582 and 0.578, respectively; all $Ps < 0.001$).

3.3. Association of GTV with N stage

Based on the postsurgical pathologic examination and the AJCC classification system, we found 12 (26.1%) patients had stage N0 disease, 15 (32.6%) patients had stage N1 disease, 13 (28.3%) patients had stage N2 disease, and 6 (13.0%) patients had stage N3 disease. As for the tumour stage, 4, 5 and 37 patients had T1, T2 and T3 disease,

Table 3
GTV of Adenocarcinoma of Oesophagogastric Junction according to N stage (in cm^3).

N stage	GTV on FS-T_2WI	GTV on DWI b = 500 s/mm^2	GTV on DWI b = 800 s/mm^2
N0	14.65 ± 3.40 (7.15, 22.14)	11.77 ± 7.31 (7.12, 16.41)	9.74 ± 6.49 (5.62, 13.86)
N1	22.44 ± 2.96 (16.08, 28.79)	15.43 ± 9.19 (10.34, 20.52)	12.72 ± 8.46 (8.04, 17.41)
N2	30.69 ± 4.23 (21.47, 39.91)	26.62 ± 15.51 (17.24, 35.99)	24.01 ± 15.64 (14.56, 33.47)
N3	38.60 ± 4.91 (25.97, 51.22)	30.27 ± 11.01 (18.71, 41.82)	25.02 ± 10.15 (14.37, 35.67)

Notes: Data are means ± standard deviations. Numbers in parentheses are 95% confidence intervals of the volume. GTV = gross tumour volume, FS-T_2WI = fat-suppression T_2-weighted imaging, DWI = diffusion-weighted imaging, and b = diffusion-sensitive gradient b value.

Table 4
The *P* Values for Statistical Comparisons of Gross Tumour Volume of Adenocarcinoma of Oesophagogastric Junction among Grouped N stages.

N stage comparisons	FS-T_2WI	DWI b = 500 s/mm^2	DWI b = 800 s/mm^2
N0 vs. N1-3	0.002[a,b]	0.006[a,b]	0.007[a,b]
N0-1 vs.N2-3	0.001[a,b]	0.000[a,b]	0.000[a,b]
N0-2 vs. N3	0.007[a,b]	0.016[a,b]	0.024[a]

Notes: Data are *P* values calculated using the Mann-Whitney test.
FS-T_2WI = fat-suppression T_2-weighted imaging, DWI = diffusion-weighted imaging, and b = diffusion-sensitive gradient b value.
[a] denotes significant *P* values < 0.05.
[b] denotes significance after Bonferroni correction.

respectively. The relationship between GTV and N stage is illustrated in Table 3. As for the grouped stages, GTV measured on FS-T_2WI and DWI with b-values of 500 and 800 s/mm^2 could help differentiate stage N0 from stages N1-3, stages N0-1 from N2-3, and stages N0-2 from N3 (all *Ps* < 0.05) (Table 4).

3.4. ROC analyses of GTV of AOG in the determination of grouped N stages

As shown by the ROC analyses of all the 46 AOG patients, when measured on FS-T_2WI, GTV cutoffs of 19.70 cm^3, 22.16 cm^3 and 25.57 cm^3 could differentiate stage N0 from grouped stages N1-3, stages N0-1 from stages N2-3, and stages N0-2 from stage N3, respectively; when measured on DWI with b-values of 500 s/mm^2, GTV cutoffs of 16.60 cm^3, 17.54 $cm^3$and 29.27 cm^3 could differentiate stage N0 from grouped stages N1-3, stages N0-1 from N2-3, and stages N0-2 from stage N3, respectively; and when measured on DWI with b-value of 800 s/mm^2, the corresponding cutoffs were 12.24 cm^3, 14.17 cm^3 and 22.73 cm^3, respectively. The area under the ROC curve, sensitivity, specificity, predictive values, and accuracy of GTV in the differentiation of grouped N stages of AOG are summarized in Table 5.

4. Discussion

For the investigation of the association of GTV with lymph node metastasis and N stage, we chose FS-T_2WI and DWI of MRI sequences for GTV measurement in our study for the reason that boundary of the tumour could be clearly shown on the previous MRI sequences without any invasive enhancement, and MRI can be superior to CT in detecting the thickening of the oesophagogastric wall [13,22]. Tumours are generally more cellular than normal tissues, which contributes to the high signal of the tumour on DWI. As for the choice of b-value, DWI with high b-value is more sensitive to water molecule diffusion than with low b-value which enables visualization of gastrointestinal cancer [14,15,22]. Because of the recommended b value of less than 1000 s/mm^2 for body DWI, b-values of 500 s/mm^2 and 800 s/mm^2 were chosen for performing this DWI study [23]. In this series, all tumours presented isohyperintense or slightly hyperintense on FS-T_2WI and significant hyperintense on DWI. Based on the signal difference between this tumour and normal distal oesophageal or proximal gastric wall, tumour boundary delineating the visible margin was possible for the GTV measurement. The inter- and intra-observer reproducibility for GTV measurement on FS-T_2WI and DWI with b-values of 500 s/mm^2 and 800 s/mm^2 were all excellent in our study, suggesting that FS-T_2WI and DWI could be feasible for the GTV measurement.

As shown in our practice, GTV values measured on FS-T_2WI and DWI with b-values of 500 and 800 s/mm^2 were related to regional lymph node metastasis, and there was a trend toward an increase in GTV with the increasing N stage. The potential mechanism for the inner relationship between GTV and lymph node metastasis may be explained by the location of AOG and the lymph duct supply. According to Aikou et al. [24], when the tumour was located in the distal oesophagus, the main lymphatic pathway tended to advance upward to lower oesophageal nodes and downward to upper gastric lymph nodes; and when the tumour was located in the gastric cardia, the lymphatic pathway was mainly towards upper gastric lymph nodes with far less findings in lower mediastinal lymph nodes. We can conclude that the potential

Table 5
Receiver Operating Characteristic Analysis of GTV in the Determination of Grouped N Stage.

Cutoff GTV	Comparison	AUC	Sen. (%)	Spe. (%)	PPV (%)	NPV (%)	Acc. (%)
FS-T_2WI							
19.70 cm^3	N0 vs N1-3	0.806	73.5 (25/34)	91.7 (11/12)	96.1 (25/26)	55 (11/20)	78.3 (36/46)
22.16 cm^3	N0-1 vs N2-3	0.797	84.2 (16/19)	70.4 (19/27)	66.7 (16/24)	86.4 (19/22)	76.1 (35/46)
25.57 cm^3	N0-2 vs. N3	0.842	100 (6/6)	70 (28/40)	33.3 (6/18)	100 (28/28)	73.9 (34/46)
DWI b = 500 s/mm^2							
16.60 cm^3	N0 vs N1-3	0.767	61.8 (21/34)	83.3 (10/12)	91.3 (21/23)	43.4 (10/23)	67.4 (31/46)
17.54 cm^3	N0-1 vs N2-3	0.828	73.7 (14/19)	77.8 (21/27)	70.0 (14/20)	80.8 (21/26)	76.1 (35/46)
29.27 cm^3	N0-2 vs. N3	0.808	66.7 (4/6)	85.0 (34/40)	40.0 (4/10)	94.4 (34/36)	82.6 (38/46)
DWI b = 800 s/mm^2							
12.24 cm^3	N0 vs N1-3	0.762	61.8 (21/34)	83.3 (10/12)	91.3 (21/23)	43.4 (10/23)	67.4 (31/46)
14.17 cm^3	N0-1 vs N2-3	0.834	73.7 (14/19)	81.5 (22/27)	73.7 (14/19)	81.5 (22/27)	78.2 (36/46)
22.73 cm^3	N0-2 vs. N3	0.788	66.7 (4/6)	82.5 (33/40)	36.4 (4/11)	94.3 (33/35)	80.4 (37/46)

Notes: Data in parentheses are numbers of patients. GTV = Gross tumour volume, AUC = area under the receiver operating characteristic curve, Sen. = sensitivity, Spe. = specificity, PPV = positive predictive value, NPV = negative predictive value, Acc. = accuracy, FS-T_2WI = fat-suppression T_2-weighted imaging, DWI = diffusion-weighted imaging, and b = diffusion-sensitive gradient b value.

lymphatic pathway may expand with the tumour grows and spreads across the oesophagogastric junction. As reported, with the increase of oesophagogastric invasion length and tumour depth of AOG, the risk of lymph nodes metastasis would also increase [25,26]. Because GTV is mainly determined by both the length and the depth of the tumour invasion, we could presume an increasing trend of the number of metastatic lymph nodes with the increase of GTV.

Our study demonstrated that the combination of FS-T_2WI and DWI to measure GTV of AOG could be helpful for predicting lymph node metastasis and grouped N stage. The ROC analyses showed that GTV values measured on FS-T_2WI and DWI with b-values of 500 s/mm^2 and 800 s/mm^2 could distinguish AOG without lymph node metastasis (N0) from those with this metastasis (N1-3), stages N0-1 from N2-3 disease, and stages N0-2 from stage N3 disease. Our findings showed that FS-T_2WI was the best sequence for GTV measurement to discriminate stage N0 disease from stage N1-3 because of the area under the receiver operating curve (AUC) from FS-T_2WI sequence more than 0.8 and the AUC from DWI sequences less than 0.77, and FS-T_2WI was also the best sequence for discriminating stages N0-2 disease from stage N3 because of the AUC from FS-T_2WI sequence more than 0.84 and the AUC from DWI sequences less than 0.81. Previous researches suggest that DWI with higher b-value may underestimate tumour size, and the measured tumour length may become short with the increase of b-value [23,27]. We could deduce that GTV values measured on FS-T_2WI and DWI with lower b-value may get close to the true tumour size, thus reflecting information more related to the tumour. For differentiating between stages N0-1 and N2-3, AUCs of GTV measured on FS-T_2WI, DWI with b-value of 500 s/mm^2 and DWI with b-value of 800 s/mm^2 were 0.797, 0.828 and 0.834, respectively, suggesting that DWI with b-value of 800 s/mm^2 could be the best sequence for discriminating stage N0-1 from stage N2-3 disease.

The present study has several limitations. Firstly, the N stage was determined by the number of metastatic lymph nodes, but the location of involved lymph node was not considered according to the AJCC criteria. However, the location of lymph node metastases is an independent predictor for survival of patients with AOG [28]. We will take the location of positive lymph node into account to obtain more practical information to benefit the patients. Second, we did not perform MRI examination of lymph nodes but of AOG in this study. We will carry out MRI study in lymph nodes in the future to determine possibility of MRI for differentiation positive and negative lymph nodes including small changes of cellularity visualized on scans. Third, dynamic contrast-enhanced MRI might be of help in delineating small and superficial tumours for measuring GTV, but we did not perform dynamic contrast-enhanced MRI in this study. We will carry out the relevant study in the future. Last, although the sample size was relatively small, some useful information of GTV associated with N stages has still been obtained. In the future, we will expand the sample size to confirm these results.

5. Conclusions

There is a trend toward an increase in GTV obtained on FS-T_2WI and DWI with increasing N stage. Combining FS-T_2WI and DWI for the measurement of GTV can be used to predict regional lymph node metastasis and N stage of AOG. FS-T_2WI can be the best sequence for differentiating stage N0 from stages N1-3 and stages N0-2 from N3, and DWI with b-value of 800 s/mm^2 can be the best sequence for distinguishing between stages N0-1 and N2-3. The results of our study could be useful for differentiating grouped N stages of AOG to determine appropriate therapy approach.

Conflict of interest

There were no conflicts of interest to declare in this study.

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