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ORIGINAL ARTICLE

Clinical impacts of magnetic resonance thoracic ductography on preventing postoperative chylothorax after thoracoscopic esophagectomy for esophageal cancer

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Abstract

Purpose The study aimed to determine whether magnetic resonance thoracic ductography (MRTD) is useful for preventing injury to the thoracic duct (TD) during thoracoscopic esophagectomy and for reducing the incidence of postoperative chylothorax.

Materials and method A total of 389 patients underwent thoracoscopic esophagectomy between September 2009 and February 2019 in Tokai University Hospital. Of them, we evaluated 228 patients who underwent preoperative MRTD (MRTD group) using Adachi's classification and our novel classification (Tokai classification). Then, the clinicopathological factors of the MRTD group ($n=228$) were compared with those of the non-MRTD group ($n=161$), and comparative analyses were conducted after propensity score matching (PSM).

Results The TD could be visualized by MRTD in 228 patients. The MRTD findings were divided into 9 classifications including normal findings and abnormal TD findings (Adachi classification vs Tokai classification; 5.3% vs 16.2%). After PSM, both groups consisted of 128 patients. The rate of postoperative chylothorax after thoracoscopic esophagectomy was significantly lower in the MRTD group (0.8%) than in the non-MRTD group (6.3%) ($p=0.036$). In the multivariate analysis for risk factors for chylothorax, the independent prognostic factors were preoperative therapy and the presence of MRTD.

Conclusions This study revealed that MRTD was useful for preventing of chylothorax after thoracoscopic esophagectomy for esophageal cancer.

Keywords Magnetic resonance thoracic ductography · Thoracoscopic esophagectomy · Chylothorax

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Introduction

Thoracoscopic esophagectomy was reported for the first time in 1992 [1], and it has since been widely adopted as a useful operative procedure in patients with esophageal cancer. According to a report from the National Clinical Database (NCD), in Japan, minimally invasive esophagectomy (MIE), including thoracoscopic esophagectomy, accounted for approximately 60% of all esophageal cancer surgeries in 2018 [2], and at our hospital, we adopt MIE in about 90% of cases [3]. The major complications of MIE include pneumonia, recurrent laryngeal nerve paralysis, anastomotic leakage, and chylothorax [4]. According to the data registered in the NCD, the incidence of chylothorax after MIE is approximately 2.2% [5], which is lower than the recorded incidences of recurrent laryngeal nerve paralysis and anastomotic leakage. The thoracic duct (TD) is involved in the drainage of approximately 75% of the whole-body lymph, and chylothorax caused by TD injury could potentially lead to marked dehydration or respiratory failure if it becomes serious. In addition, chylothorax, prolonged chylothorax may cause depletion of immunoglobulin or T cells and is associated with a high risk of sepsis [6, 7].

Some previous studies have reported that prophylactic TD ligation is useful to reduce the incidence of postoperative chylothorax [8]. However, according to a systematic review and meta-analysis by Lei et al. [9], there is currently no established evidence on the usefulness of prophylactic TD ligation during esophagectomy to reduce the incidence of postoperative chylothorax, and further accumulation of cases is required. In addition, it has also been reported that preoperative oral administration of olive oil and selective ligation of the TD in cases of intraoperative chyle leakage reduced the incidence of chylothorax [10]. On the other hand, regarding the risk factors for chylothorax, Ohkura et al. [11] reported that perioperative chemoradiotherapy and intraoperative fluid overload are independent risk factors for chylothorax. From the above, it is clear that while many studies have been conducted to identify useful measures for the prevention of chylothorax, there is currently no clear established evidence for any preventive measures. Our findings suggest that a clear understanding of the anatomical variations of the thoracic duct would be useful to prevent chylothorax as a postoperative complication, by reducing the risk of intraoperative injury to the thoracic duct and inappropriate manipulation of any abnormal branch.

Nomura et al. [12] successfully used a magnetic resonance imaging (MRI) technique, namely, preoperative magnetic resonance thoracic ductography (MRTD), to delineate the TD anatomy; MRTD enables three-dimensional (3D) construction of the TD and the surrounding blood vessels in the mediastinum by emphasizing water and blood components using the 3D-balanced turbo field echo sequence.

Various anomalies of the TD are known to occur during the developmental process [13]. For the detection of anatomical abnormalities of the TD, our hospital reported that the original Tokai classification, according to which the patients are classified into 9 types, rather than the generally used Adachi classification, may be useful for reducing the incidence of chylothorax [14]. The purpose of this study was to demonstrate that the evaluation of TD anatomy by MRTD contributes to reducing the risk of chylothorax after MIE in further accumulated cases.

Materials and methods

Patient selection

The study involved 389 patients who underwent MIE at Tokai University Hospital between September 2009 and February 2019. Of these 389 patients, 161 underwent MIE between September 2009 and July 2014 prior to the introduction of preoperative MRTD (non-MRTD group), and 228 underwent MIE between August 2014 and February 2019 after undergoing preoperative MRTD (MRTD group).

Surgical procedure for esophagectomy

A right-sided approach with the patient in the prone position was generally used and thoracoscopy was performed using 5 trocars [15]. Before upper mediastinal dissection, the azygos arch was dissected, and the TD was identified on the dorsal side of the azygos arch. The TD was then detached toward the cranial side, and dissection with clipping was performed with the upper limit set at the cervicothoracic junction. In the middle and lower mediastinal dissections, the stratum disjunctum in the upper mediastinum was connected to the caudal side, and the TD was treated with the lower limit set just above the diaphragm. We usually simultaneously resect the TD in patients with Stage II or more advanced esophageal cancer. However, we preserved the TD in patients with liver dysfunction or malnutrition.

Magnetic resonance thoracic ductography (MRTD)

The MRTD imaging using a 3D-Balance turbo field echo sequence is described in detail by Nomura et al. [12]. However, special software is required for the imaging.

Images were obtained using a 1.5T-MRI device (Ingnia 1.5T; Philips, Best, The Netherlands) and a 3D-balanced turbo field echo sequence. The imaging parameters were

as follows: matrix = 256 × 294, slice thickness = 1.6 mm, and field of view (FOV) = 300 × 300 mm. Using images obtained under these conditions, 3D image reconstruction was performed using the image analysis software, Ziostation2 (Ziosoftware, Tokyo, Japan).

MRTD is performed preoperatively in all patients scheduled for esophageal cancer surgery, except in those with implanted MRI-incompatible intracorporeal or extracorporeal metallic devices, such as cardiac pacemakers and implantable cardioverter-defibrillators.

Thoracic duct evaluation using Tokai classification [14]

The classification of thoracic duct morphology is generally based on the classification by Adachi [13]. In our department, we use our own Tokai classification that it focuses on morphological abnormalities in the thoracic cavity and classifies into nine types, including the normal type shown in Fig. 1a, b. The categories as fellows. The Tokai classification differs from the Adachi classification, in that it focuses on abnormal branches in the thoracic cavity. In our series, 16% of patients were preoperatively diagnosed as having an abnormal TD by the Tokai classification and 5% were diagnosed as having an abnormal TD by the Adachi classification. In addition, Fig. 2 shows a comparison of the Adachi classification and Tokai classification for the MRTD group ($n = 228$).

1. Normal type. It ascends to the right side of the aorta and opens to the left venous angle.
2. Abnormal divergence type. The abnormal branching with no characteristic morphology.
3. Window formation type. The abnormal thoracic ducts join up to form a window.
4. Stitch formation type. The abnormal thoracic ducts form a mesh.
5. Knob formation type. There is a partial protrusion of the thoracic duct.
6. Flow into right clavicular vein type. The thoracic duct opens into the right of the neck.
7. Interruption type. Partial disruption of the thoracic duct.
8. Poor image type. Insufficient visualization of the thoracic duct.
9. False-negative type. The thoracic duct could not be visualized.

Postoperative management of chest tubes

Chest tubes were removed once the output was less than 200 mL per day for 2 consecutive days. We usually removed the chest tube on postoperative day 5 or 6. Chylothorax was suspected if there was a high-output pleural effusion and a change the color of the effusion from serous to milky.

Definition of chylothorax

At our hospital, we start enteral nutrition by the administration of 200 ml of Peptamen (1.5 kcal/m), which contains fatty acids (lipid content/200 ml 13.2 g) on the first postoperative day; the volume of administration is increased by 100 ml every day, which makes it possible to monitor the changes in the effusion properties and the drainage volume. When the chest tube output was more than 1000 mL per day, the effusion became milky in color, or the triglyceride level of the pleural effusion was more than 110 mg/dL or higher, we confirmed the diagnosis of postoperative chylothorax [16].

Statistical analysis

To adjust unbalanced covariates, a propensity score matching (PSM) method was used to generate two cohorts with a ratio of 1:1 between the MRTD group and the non-MRTD group. We performed PSM with pathological diagnostic factors to align oncological factors as much as possible. We included the depth of tumor invasion, lymph node metastasis, and preoperative therapy. To prevent poor matches, a caliper set at 0.30 of the standard deviation of the logit of the propensity score was used. The differences in the clinical findings between the MRTD group and the non-MRTD group were analyzed using the chi-square test, Fisher's exact test, and Student's *t* test before and after PSM. To assess the risk factors for chylothorax, multivariate logistic regression analysis was used for variable selection. Two-side *p* values were calculated and considered significant at $p < 0.05$. All statistical analyses were carried out using JMP Pro software (Version 15.0, SAS Institute Inc., Cary, NC, USA).

Results

Patient characteristics of all 389 patients

Table 1 shows the characteristics of the 389 patients who underwent MIE at our hospital between September 2009 and February 2019. Among all the patients, combined resection of the TD was performed in 205 patients (52.7%), and 8 of these patients (2.1%) developed chylothorax; on the other hand, the TD was preserved in 184 patients (47.3%), and 4 of these patients (1.0%) developed chylothorax. The difference in the incidence of chylothorax between the two groups was not statistically significant ($p = 0.38$). Staging was performed

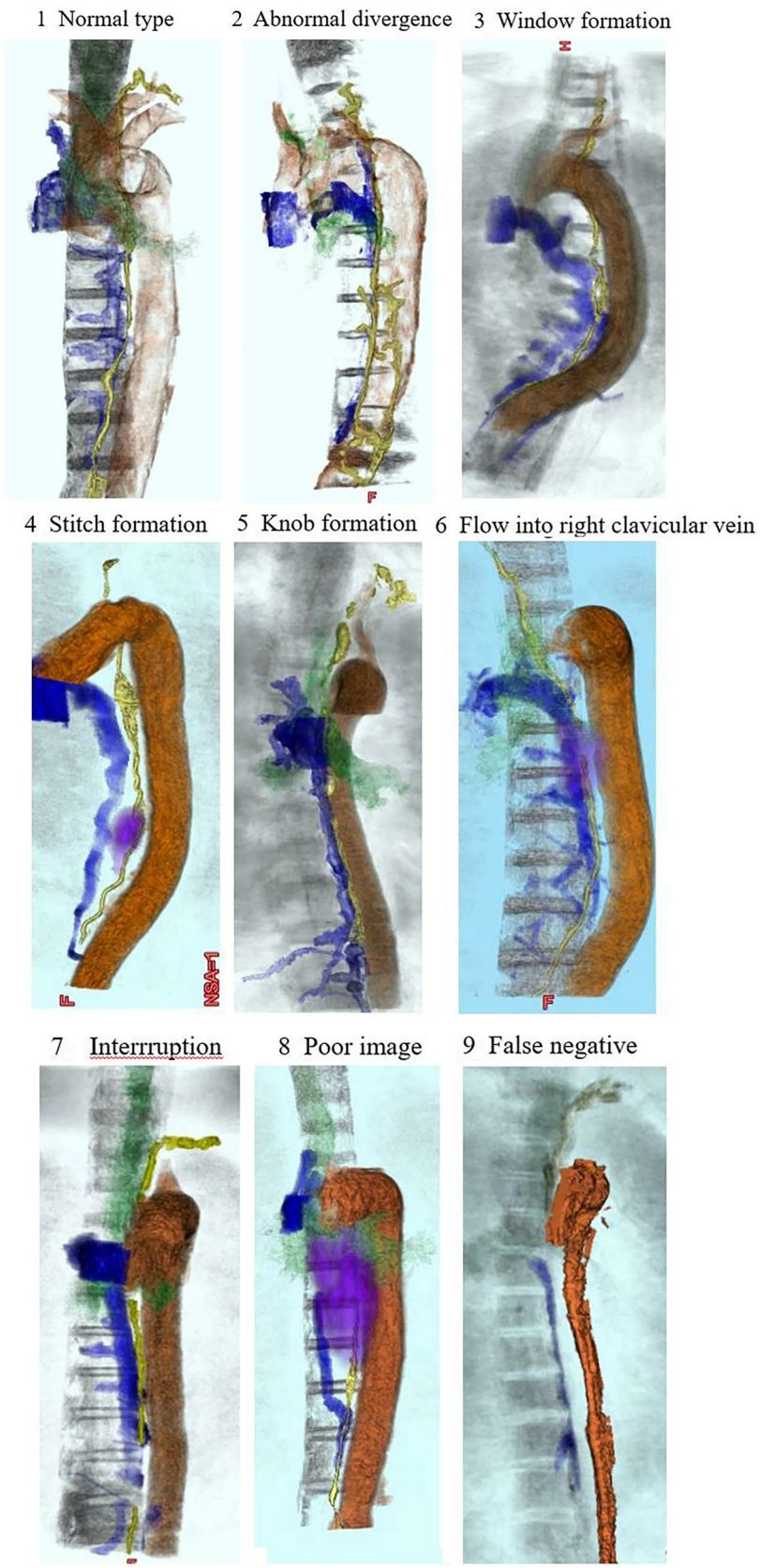
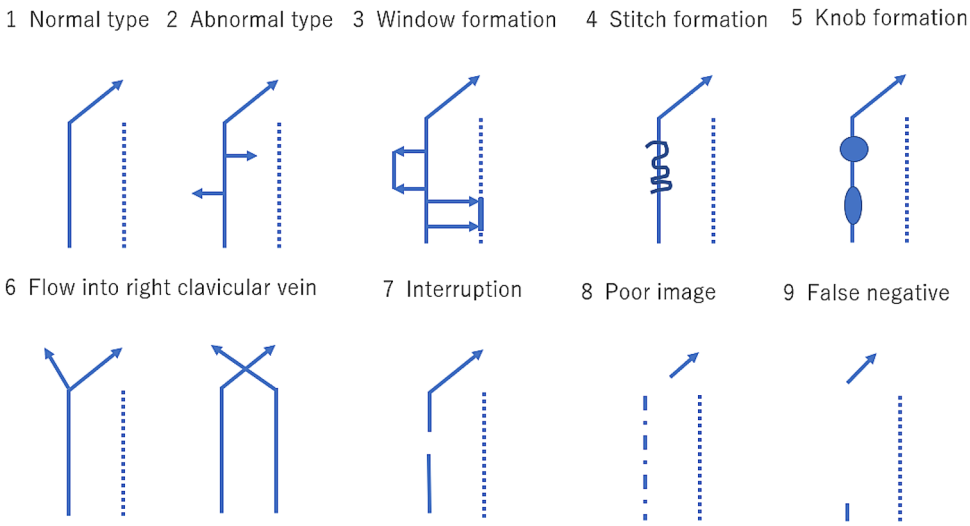


Fig. 1 **a** The Tokai classification of the thoracic duct morphology in the MRTD (yellow: Thoracic duct, red: Aorta, blue: Vein). **b** The Tokai classification schema of the thoracic duct morphology

Fig. 1 (continued)



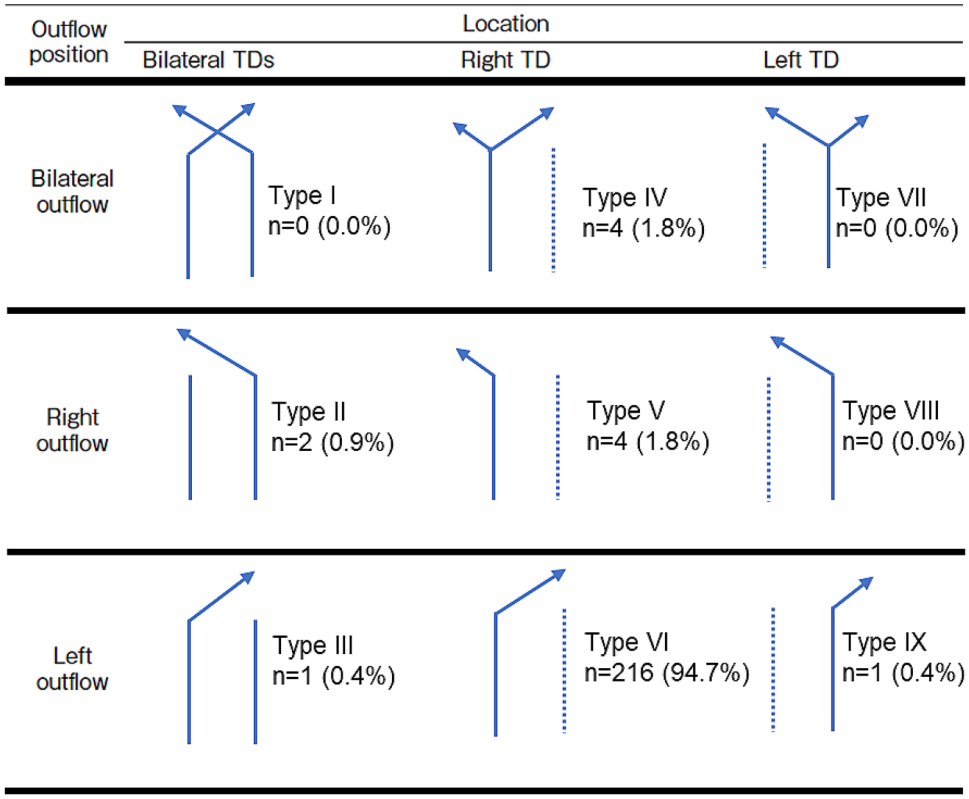


Fig. 2 The Adachi classification of the thoracic duct morphology in the MRTD

according to the 8th edition of the TNM classification of the Union for International Cancer Control (UICC).

Patient characteristics after PSM

PSM was performed for the MRTD and non-MRTD groups to match the baseline patient characteristics so as to analyze the incidence of postoperative chylothorax as the outcome. As a result of matching, the patients could be divided into two cohorts of 128 patients each; there was no significant difference in the percentage of patients who had/had not received preoperative chemotherapy among the matched cases, unlike among the unmatched cases ($p < 0.001$), and there were more cases of TD resection in the MRTD group, but the bias was eliminated by matching. There were also no significant differences in any of the other patient characteristics (Table 2).

Table 1 Demographics and characteristics of 389 patients

Variables	*n* (%)
Age (mean ± SD)	66.6 ± 9.0
Sex	
Male	332 (85.3)
Female	57 (14.7)
Location of tumor	
Upper	50 (12.9)
Middle	214 (55.0)
Lower	125 (32.1)
MRTD	
Yes	228 (58.6)
No	161 (41.4)
Preoperative therapy	
Yes	147 (37.8)
Neoadjuvant chemotherapy (NAC)	141 (95.9)
Neoadjuvant chemoradiotherapy (NACRT)	6 (4.1)
No	242 (62.2)
Resection of TD	
Yes	205 (52.7)
No	184 (47.3)
Operative time for thoracic procedure (min)	235.1 ± 56.0
Blood loss for thoracic procedure (mL)	45.2 ± 80.3
Pathological T	
0	55 (14.1)
1a	8 (2.1)
1b	118 (30.3)
2	50 (12.9)
3	154 (39.6)
4a	4 (1.0)
Pathological N	
0	184 (47.3)
1	87 (22.4)
2	79 (20.3)
3	39 (10.0)
Pathological Stage	
0	46 (11.8)
IA	8 (2.1)
IB	74 (19.0)
IIA	21 (5.4)
IIB	64 (16.5)
IIIA	31 (8.0)
IIIB	100 (25.7)
IVA	32 (8.2)
IVB	13 (3.3)
Metastasis of LN around TD	
Yes	7 (1.8)
Invasion to TD	
Yes	6 (1.5)
Chylothorax	
Yes	12 (3.1)

TD thoracic duct

[a]Date expressed as mean ± SD

Comparison of postoperative chylothorax incidence using PSM in groups examined with or without MRTD

The incidence of postoperative chylothorax was compared between MRTD and non-MRTD groups before (unmatched) and after (matched) PSM (Table 3). The incidence of chylothorax was significantly lower in the MRTD group than in the non-MRTD group when examined with or without PSM. After PSM, the rate of postoperative chylothorax after thoracoscopic esophagectomy was significantly lower in the MRTD group (0.8%) than in the non-MRTD group (6.3%) ($p = 0.036$).

Factors predictive of chylothorax before PSM

Table 4 shows the results of the multivariate logistic regression analysis performed to identify the risk factors for chylothorax in 389 patients unadjusted for propensity scores. The analysis identified that the performance/nonperformance of preoperative MRTD and the presence/absence of preoperative treatment were significant risk factors for the development of chylothorax.

Factors predictive of chylothorax after PSM

Table 5 shows the results of the multivariate logistic regression analysis performed to identify the risk factors for chylothorax in the 256 patients adjusted by propensity scores. This analysis also identified that performance/nonperformance of preoperative MRTD and the presence/absence of preoperative treatment were independent risk factors for the development of chylothorax, as in the unmatched patient cohorts.

Evaluation of TD morphology using the Tokai classification

An anatomical evaluation was performed in the 228 patients who underwent MRTD prior to thoracoscopic esophagectomy at our hospital between April 2014 and September 2018. Thirty-seven of the 228 patients (16.2%) had anatomical abnormalities according to the Tokai classification. Among the abnormalities, abnormal divergence (13 patients, 5.7%), window formation (8 patients, 3.5%), and flow into the right clavicular vein (7 patients, 3.0%) were common. In addition, regarding the incidence of chylothorax according to the presence/absence of morphological abnormalities of the TD, the incidence was significantly higher in the patients with branching abnormalities (Table 6).

Table 2 Background date of clinicopathological features in MRTD group and non-MRTD group

Variables	Unmatched group [$N=389$]		p value	Matched group [$N=256$]		p value
	MRTD [$n=228$] (%)	Non-MRTD [$n=161$] (%)		MRTD [$n=128$] (%)	Non-MRTD [$n=128$] (%)	
Age (mean ± SD)	67.3 ± 0.6	65.6 ± 0.7	0.074	65.7 ± 0.8	65.8 ± 0.8	0.950
Sex						
Male	196 (86.0)	136 (84.5)	0.681	112 (87.5)	109 (85.2)	0.585
Female	32 (14.0)	25 (15.5)		16 (12.5)	19 (14.8)	
Location of tumor						
Upper	32 (14.0)	18 (11.2)	0.396	20 (15.6)	12 (9.4)	0.101
Middle	119 (52.2)	95 (59.0)		63 (49.2)	79 (61.7)	
Lower	77 (33.8)	48 (29.8)		45 (35.2)	37 (28.9)	
Preoperative therapy						
Yes	112 (49.1)	32 (19.9)	< 0.001	34 (26.6)	34 (26.6)	1.000
NAC	107 (95.5)	34 (97.1)		30 (88.2)	33 (97.1)	
CRT	5 (4.5)	1 (2.9)	< 0.001	4 (11.8)	1 (2.9)	0.380
No	116 (50.9)	129 (80.1)		94 (73.4)	94 (73.4)	
Resection TD						
Yes	139 (61.0)	66 (41.0)	< 0.001	65 (50.8)	53 (41.4)	0.132
Operative time for thoracic procedure (min)	228.7 ± 50.2	244.1 ± 62.4	0.007	229.9 ± 51.7	241.9 ± 59.5	0.093
Blood loss for thoracic procedure (mL)	50.8 ± 96.4	49.3 ± 8.7	0.773	50.8 ± 96.4	49.3 ± 8.7	0.911
Pathological T						
0	29 (12.7)	26 (16.2)	0.212	17 (13.3)	18 (14.1)	0.184
1	72 (31.6)	54 (33.5)		36 (28.1)	41 (32.0)	
2	26 (11.4)	24 (14.9)		15 (11.7)	23 (18.0)	
3	97 (42.5)	57 (35.4)		57 (44.5)	46 (35.9)	
4	4 (1.8)	0 (0.0)		3 (2.3)	0 (0.0)	
Pathological N						
Negative	101 (44.3)	83 (51.6)	0.158	51 (39.8)	65 (50.8)	0.079
Positive	127 (55.7)	78 (48.5)		77 (60.2)	63 (49.2)	
Pathological stage						
0	21 (9.2)	25 (15.5)	0.092	12 (9.4)	18 (14.1)	0.726
I	45 (19.7)	37 (23.0)		21 (16.4)	27 (21.1)	
II	59 (25.9)	26 (16.2)		34 (26.6)	24 (18.8)	
III	78 (34.2)	53 (32.9)		43 (33.6)	42 (32.8)	
IV	25 (11.0)	20 (12.4)		18 (14.1)	17 (13.3)	

[a]Date expressed as mean ± SD

TD thoracic duct

Table 3 Comparison of postoperative chylothorax incidence using PSM in groups examined with or without MRTD

Variables	Unmatched group [$N=389$]		p value	Matched group [$N=256$]		p value
	MRTD [$n=228$] (%)	Non-MRTD [$n=161$] (%)		MRTD [$n=128$] (%)	Non-MRTD [$n=128$] (%)	
Chylothorax	3 (1.3)	9 (5.6)	0.033	1 (0.8)	8 (6.3)	0.036

Table 4 Potential risk factors of Chylothorax (Clavien–Dindo Grade2 ≦) for Unmatched group [$N=389$]

Variables	Univariate analysis		p value	Multivariate analysis		p value
	OR	95% CI		OR	95% CI	
Sex						
Male	1.92	0.24–15.2	0.537			
Age, years						
70≦	0.96	0.30–3.07	0.943			
Location of tumor						
Upper third	0.61	0.08–4.82	0.638			
MRTD						
Present	0.23	0.05–0.85	0.027	0.10	0.03–0.40	0.001
Preoperative therapy						
present	8.76	1.89–40.6	0.006	17.5	3.59–85.3	< 0.001
Operative time for thoracic procedure (min)						
235≦	2.38	0.63–8.95	0.184			
Blood loss for thoracic procedure (mL)						
42≦	3.39	0.43–26.69	0.216			
Pathological T						
2≦	1.23	0.38–3.93	0.732			
Pathological N						
positive	1.83	0.54–6.17	0.332			
Pathological Stage						
3≦	2.51	0.74–8.50	0.138			
Resection TD						
Resected	1.83	0.54–6.17	0.332			
Metastasis of LN around TD						
Positive	5.62	0.62–50.7	0.124			
Invasion to TD						
Positive	6.76	0.73–62.9	0.093			

TD Thoracic Duct, *LN* Lymph Node, *MRTD* Magnetic Resonance Thoracic Ductography

Variation of the TD according to the MRTD and the intraoperative findings

In our series, 37 patients (16.2%) were preoperatively diagnosed as having anatomical variations of the TD by the Tokai classification and 40 patients (17.5%) were diagnosed as having variations of the TD according to the intraoperative findings, respectively. The findings of preoperative MRTD in the 10 patients who were diagnosed as having abnormal variations of the TD according to the intraoperative findings were as follows: Normal: 4 patients, 1.8%; Window formation: 3 patients, 1.3%; Interruption: 2 patients, 0.9%; Poor image: 1 patient, 0.4% (Table 7).

Discussion

This study showed that preoperative examination of the TD anatomy by MRTD, paying particular attention to the presence of anatomical abnormalities, may contribute to the prevention of postoperative chylothorax.

In the present study, the incidence of chylothorax was lower in the MRTD group, presumably because the presence/absence of anatomical abnormalities of the TD could be determined preoperatively. While 16.2% of the patients were considered to have an abnormal variation of the TD according to the MRTD, 17.5% of patients were diagnosed as having an abnormal variation of the TD according to the intraoperative findings. The reason for the failure of MRTD to reveal the abnormal branch of the TD, which was discovered intraoperatively, is that MRTD imaging is affected by the beating of the aorta and air artifacts in the lungs, which can lead to poor visualization. The Tokai classification is similar to the Adachi classification with respect to the anatomy and openings of the main TDs; however, it differs from the latter in that it also includes branching abnormalities of the TD in the thoracic cavity; therefore, while 94.7% of the patients were considered to have normal TD anatomy according to the Adachi classification, only 83.8% were considered to have normal TD anatomy according to the Tokai classification. In our study, all patients with chylothorax presented with

Table 5 Potential risk factors of Chylothorax (Clavien–Dindo Grade2 ≦)for Matched group [$N=256$]

Variables	Univariate analysis		p value	Multivariate analysis		p value
	OR	95% CI		OR	95% CI	
Sex						
Male	1.28	0.15–10.5	0.820			
Age, years						
70≦	0.74	0.18–3.00	0.668			
Location of tumor						
Upper third	0.87	0.10–7.20	0.898			
MRTD						
Present	0.12	0.01–0.96	0.046	0.11	0.01–0.97	0.047
Preoperative therapy						
Present	24.9	3.06–203	0.003	18.9	2.22–161	0.007
Operative time for thoracic procedure (min)						
235≦	2.33	0.46–11.75	0.293			
Blood loss for thoracic procedure (mL)						
42≦	2.21	0.26–18.33	0.451			
Pathological T						
2≦	2.81	0.57–13.8	0.203			
Pathological N						
Positive	6.97	0.86–56.6	0.069			
Pathological stage						
3≦	9.64	1.19–78.3	0.034	5.34	0.61–46.8	0.130
Resection TD						
Resected	2.22	0.54–9.09	0.266			
Metastasis of LN around TD						
Positive	7.59	0.76–75.9	0.084			
Invasion to TD						
Positive	10.1	0.95–108	0.055			

TD Thoracic Duct, *LN* Lymph Node, *MRTD* Magnetic Resonance Thoracic Ductography

Table 6 MRTD findings

	$n=228$ (%)	Chylothorax $n=3$	p value
Normal	191 (83.8%)	0 (0%)	
Abnormal	37 (16.2%)	3 (100%)	0.004
Abnormal divergence	13 (5.7%)	1 (33.3%)	
Window formation	8 (3.5%)		
Stitch formation	2 (0.9%)		
Knob formation	1 (0.4%)		
Flow into right clavicular vein	7 (3.0%)	1 (33.3%)	
Interruption	4 (1.8%)		
Poor image	1 (0.4%)	1 (33.3%)	
False negative	1 (0.4%)		

Table 7 The results of MRTD and intraoperative findings of TD

$n=228$ (%)	MRTD	Intraoperative findings
Normal	191 (83.8%)	188 (82.5%)
Abnormal	37 (16.2%)	40 (17.5%)
Abnormal divergence	13 (5.7%)	23 (10.0%)
Window formation	8 (3.5%)	5 (2.2%)
Stitch formation	2 (0.9%)	2 (0.9%)
Knob formation	1 (0.4%)	1 (0.4%)
Flow into right clavicular vein	7 (3.1%)	7 (3.1%)
Interruption	4 (1.8%)	2 (0.9%)
Poor image	1 (0.4%)	0 (0.0%)
False negative	1 (0.4%)	0 (0.0%)

abnormal branching of TD. Furthermore, the method of TD treatment in the thoracic cavity is important in MIE. For example, for branching abnormalities of the TD that can be pointed out by MRTD, it should be considered to prioritize clipping over sealing. We believe that preoperative MRTD is extremely useful for delineating any anatomical abnormalities.

The risk of postoperative chylothorax was reported to be elevated in patients undergoing combined resection of the TD [9]. One of the possible reasons for this is the failure to recognize an abnormal branching pattern of the TD

during the surgery. In the present study, a TD draining into the right venous angle was identified in 7 of the 228 patients (3.0%). Such patients could have bilateral TDs, and the risk of chylothorax may remain high after the usual TD treatment, because of a remaining left TD. On the other hand, preoperative MRTD enables detection of branching to the left TD, which cannot be recognized intraoperatively by the usual right thoracic cavity approach. In our present study, the presence/absence of combined resection of the TD was not identified as a risk factor for postoperative development of chylothorax.

Furthermore, Gupta et al. [17] reported an increased incidence of postoperative chylothorax in patients with squamous cell carcinoma of the thoracic esophagus who had received preoperative chemoradiotherapy. The authors speculated that radiation-induced cell signaling could activate the surrounding tissue, making it difficult to separate the surrounding tissue from the esophagus intraoperatively and thereby increasing the risk of developing chylothorax. In addition, Congdon et al. [18] reported that chylothorax can be caused by damage to the lymphatic system caused by radiotherapy. They reported that preoperative radiotherapy may damage the local lymphatic system in the mediastinum, resulting in delayed wound healing of the stump of the thin lymphatic vessel after intraoperative manipulation and increasing the risk of developing postoperative chylothorax. On the other hand, some authors have also reported that preoperative chemoradiotherapy is not associated with an increased in the incidence of postoperative chylothorax [19, 20]. Yang et al. [21] reported that in patients with locally advanced esophageal squamous cell carcinoma, the incidence of chylothorax was similar between the groups that received and did not receive preoperative chemoradiotherapy. Although previous reports have shown a higher incidence of chylothorax associated with NACRT, in this study, we did not find any case of chylothorax in the group that received NACRT. Therefore, it was not possible to compare the risk of chylothorax between the patient groups treated by NAC and NACRT. In the present study, multivariate analysis identified the presence/absence of preoperative treatment as an independent risk factor for the development of chylothorax.

Three patients who underwent preoperative MRTD developed chylothorax. All 3 patients had received preoperative chemotherapy, and preoperative MRTD had identified an abnormal branching pattern of the TD. Even if the main trunk of the TD was ligated and resected, we believe that chylothorax could still occur if the lymphatic flow into the TD through the abnormal branch is not blocked. The chylothorax, in this case, was thought to be due to the failure of proper manipulation of the abnormal branch draining into the TD, which was difficult to visualize intraoperatively. Furthermore, pretreatment may have affected the TD morphology, as described in the above-mentioned paper, leading to chylothorax in these patients. In the MRTD group, the majority of patients with chylothorax improved with medical treatment, and even in the patient who underwent lymphangiography, it was difficult to identify the location of the TD injury. In the non-MRTD group, embolization by lymphangiography was performed for the chylothorax in three cases, and the procedure indicated leakage from the ligated end of the TD in all three cases. In the three cases of the non-MRTD group that developed chylothorax, the main trunk of the TD was ligated intraoperatively, with double clipping using the Hem-o-lok clip applier. Therefore, we think that the chylothorax was either caused by leakage from an abnormal branch that was unrecognized during the operation or failure of the clip-ligated end of the branch or main trunk of the TD; if the failure is suspected to involve the main trunk, we believe that it is likely to be due to dislodgment of the clip applier postoperatively. Lymphangiography showed leakage from the end of the TD, but it was impossible to judge whether it was from a branch or the main trunk of the TD.

In our study, preoperative MRTD was performed after completion of preoperative treatment; MRTD performed before preoperative treatment may allow the detection of morphological abnormalities of the TD associated with treatment. This would enable accurate intraoperative treatment of the TD in patients who have received preoperative treatment as MRTD performed after treatment poorly visualizes the TD; this may further reduce the incidence of postoperative chylothorax.

Regarding the relationship between the cancer stage and TD treatment, in our hospital, the TD is resected in patients with more advanced disease than stage I cancer. Although some studies have reported cancer metastasis to the lymph nodes around the TD or surrounding tissue in patients undergoing combined resection of the TD, few studies have reported an improved prognosis with combined resection of the TD [22, 23]. In the present study, 139 of the 228 patients (61.0%) who underwent preoperative MRTD underwent combined resection of the TD. Of these patients, 4 (2.9%) had metastases to the lymph nodes around the TD and 4 (2.9%) had cancer invasion of the TD. All the patients with cancer invasion of the TD had an invasion depth of T3, most of them were positive for lymph node metastasis, and 2 of them had branching abnormalities of the TD. These results suggest that the mediastinal lymph nodes may communicate with the TD via a lymphatic network. However, in the present study, we did not investigate the long-term prognosis after resection of the TD, and the clinical significance of dissection needs to be studied in a larger number of cases in the future.

The purpose of this study was to evaluate the prevention of chylothorax after MIE, and this is the first study to show

that morphological evaluation of the TD by preoperative MRTD is useful for reducing the incidence of chylothorax. Abnormal branching of the TD is commonly encountered during esophagectomy, and we demonstrated that preoperative detection of abnormal branching could reduce the risk of intraoperative TD injury.

Limitations

The limitations of our study were its single-center, retrospective design and that a difference in the evaluation periods between the two groups was unavoidable because of the period during which the non-MRTD group was treated was prior to the introduction of MRTD. Therefore, a strict comparison of surgical outcomes between MRTD group and non-MRTD group is difficult.

Conclusions

This study showed that preoperative evaluation of TD anatomy with MRTD prior to MIE contributes to reducing the risk of chylothorax. This result suggests that preoperative detection of the TD abnormalities with MRTD would allow appropriate intraoperative treatment of the TD.

Declarations

Ethical statement All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. This retrospective review was approved by the Institutional Review Board (20R-207).

Conflict of interest The authors declare that have no competing interests.

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