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REVIEW ARTICLE





Complications of robot-assisted thymectomy: A single-arm meta-analysis and systematic review

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Abstract

Background: Recently, thymectomy using minimally invasive approaches has been increasing with the development of robotic video-assisted thoracoscopic surgery (R-VATS). Although multimodal approach is effective for robot assisted thymectomy, it is necessary to determine the approach (left, right or subxiphoid) associated with the least complications.

Methods: An electronic retrieval from PubMed, Embase, Web of Science, GreyNet International and The Cochrane Library. The single-arm meta-analysis was performed to compare the rate of complications of right- and left-side approaches by R-VATS.

Results: A total of 21 studies including 930 patients were identified. The pooled incidence of total complications was 12.2% (confidence interval: 10.0%-14.8%) for all studies. The overall complication rate was 17.3% for the right-side compared with 7.4% for the left side (P < 0.001, odds ratio = 2.484, 1.601-3.852). The pooled incidence of air leak was significantly higher for the right versus left side (5.1% vs. 1.2%, respectively; p = 0.004). The incidence of atrial fibrillation was higher for the right-side compared with the left-side approach (4% vs. 1.2%, respectively; p = 0.004). The open conversion rate was significantly higher for the right versus the left-side (6.5% vs. 2.9%, respectively; p = 0.004). However, there was no significant difference in the pooled incidence of pleural effusion and thoracic duct fistula when comparing the right- and left-side approaches. In subgroup analysis, in the left approach, the incidence of overall complications (28.6% vs. 5.5%, respectively; p = 0.002) and pleural effusion (14.3% vs. 1%, respectively; p = 0.002) was higher for the 'Old Age' group compared with the 'Youth' group; However, In the subgroup analysis of gender, there was no significant difference in the incidence of complications after thymectomy.

Conclusion: Robotic video-assisted thoracoscopic surgery can be performed on the left- and right-sides; however, complications are minimal with the left-side

The authors Jia-Xin Xu, Kai Qian and Yi Deng contributed equally to this work.

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approach. These data demonstrate that the incidence of overall complications, atrial fibrillation, open conversion ratios, and air leak rate of left-side R-VATS thymectomy are lower than those of right-side. Further subgroup analysis showed that the incidence of postoperative complications was higher in the older group.

KEYWORDS

complication, meta-analysis, thoracoscopic, thymectomy

1 | INTRODUCTION

Thymectomy is the main treatment for thymic diseases and patients with myasthenia gravis (MG).¹ The traditional thymectomy approach is through a median sternotomy or via traditional video-assisted thoracoscopic surgery (VATS).² The performance of minimally invasive thymectomy has been increasing recently with the development of robotic VATS (R-VATS).³ Although the overall results of multimodal approaches, including left side, right side and sub-xiphoid, are useful to patients, the outcomes of robot-assisted thymectomy with different modes are different. The purpose of the current study is to analyse and discuss the clinical presentation, diagnostic procedures and the surgical techniques associated with thymectomy. Post-operative complications and results are also considered until July 2018.

2 | MATERIAL AND METHODS

PubMed, Embase, Web of Science, GreyNet International (http:// www.greynet.org/) and The Cochrane Library were searched for articles published until July 2018. Articles on thymectomy for special diseases, such as MG, thymic cyst, thymus hyperplasia and anterior mediastinal tumour, were also manually retrieved. To increase sensitivity, the search strategy used both MeSH terms and free-text words. To maximise search sensitivity, no filters or limits on language were applied (the retrieval process is shown in Figure 1).

2.1 | Search strategy and election of the studies

The inclusion criteria were as follows: (1) articles investigating the use of robot-assisted thymectomy; (2) studies reporting information regarding periprocedural complications. The exclusion criteria were as follows: (1) repeat articles, letters, editorials, expert opinions, case reports; (2) studies without usable data; (3) the articles published in languages other than English.

2.2 | Data extraction

Two investigators independently extracted data from eligible studies; disagreements were resolved by discussion with a third investigator. For each study, the following information was recorded: necessary information (e.g., first author, year of publication), research characteristics (e.g., randomised controlled trial (RCT), case report, letter, course of treatment) and study subject characteristics (e.g., disease type, number, gender, age, risk rating, surgical paths of the thymectomy, complications and the incidence of complications).

2.3 | Quality control

All included studies were single-arm studies; thus the Newcastle-Ottawa Scale was used to assess quality. Assessment scores of 0-3, 4-6 and 7-9 indicated poor, fair and good studies, respectively. Discrepancies were resolved by consensus.

2.4 | Publication bias

Because more than 10 studies were included in each approach group, funnel plots were used to detect publication bias. Publication bias was analysed using Egger's linear regression test, which measures funnel plot symmetry.

2.5 | Statistical analysis

All statistical analyses were performed using Comprehensive Metaanalysis (Version 2). The results are expressed as incidences and 95% CIs. A fixed-effects model was used to perform the statistical analyses, and a chi-squared test and l^2 statistic were used to assess the inter-study heterogeneity. $l^2 > 50\%$ indicates statistical heterogeneity.

3 | RESULTS

3.1 | Search results

The initial search resulted in a total of 123 articles: 74 from PubMed, 41 from Embase and 8 from GreyNet International Of these, 64 duplicates were filtered out, and 32 articles were excluded after browsing through titles and abstracts. The remaining 27 studies were subjected to the full-text screening process, and an additional six **FIGURE 1** Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) chart showing the flow of publications via the review process



studies were eliminated based on the inclusion and exclusion criteria. A total of 21 articles were identified for further analysis (Figure 1).

3.1.1 | Quality assessment of included studies

Of the 21 articles, 6 were single-arm studies, 1 was a RCT and 14 were retrospective studies. Levels of evidence for the majority of studies were III (n = 8) and IV (n = 13). The quality index score ranged from 13 to 20, with an average score of 16.5 and a standard deviation of 1.9. A higher-quality study was defined as 19–20, a moderate-quality study as 16–18 and a poor-quality study as 13–15. There were 2 higher-quality studies, 13 moderate-quality studies and 6 poor-quality studies.

3.2 | Postoperative complications of robot-assisted thymectomy via right-side and left-side approaches

3.2.1 | Overall complications

Complications occurred in 55 out of 350 patients who underwent surgery via the right-side approach and in 37 out of 580 patients who underwent surgery via the left-side approach. The pooled incidence of total complications was 12.2% (confidence interval [CI]: 10.0%-14.8%) for all studies. The pooled incidence of total complications was 17.3% (CI: 13.5%-20.0%) for the right-side approach and 7.4%

(CI: 5.4%–10.1%) for the left-side approach. A statistically significant difference in total complications between the two groups (P < 0.001, odds ratio [OR] = 2.484, 1.601–3.852) was exhibited. There was moderate heterogeneity in the right-side group (Q = 15.13, $I^2 = 40.53\%$) and no evident heterogeneity in the left-side group (Q = 16.08, $I^2 = 37.82\%$) (Figure 2).

3.2.2 | Pleural effusion

Pleural effusion was reported in two right-side approach studies (380 patients) and six left-side approach studies (580 patients). The pooled incidence of pleural effusion was 2.5% (CI: 1.5%-4.0%) for all studies. The pooled complication rate was 1.9% (CI: 0.9%-4.1%) for the right-side approach group and 2.9% (CI: 1.6%-5.5%) for the left-side approach group. There was no significant difference in pleural effusion between the two groups (p = 0.490, OR = 0.506, 0.102-2.522). There was no heterogeneity in the right-side group (Q = 0.89, $l^2 = 0\%$) and the left-side group (Q = 12.72, $l^2 = 21.36\%$) (Figure 3).

3.2.3 | Air leak

Air leak was reported in six right-side approach studies (380 patients) and in no left-side approach studies (580 patients). The pooled incidence of air leak was 2.9% (CI: 1.8%–4.8%) for all studies. The pooled incidence of air leak was 5.1% (CI: 2.7%–9.4%) for right-side



FIGURE 2 Forest plots of the incidence of overall complications. There was statistical difference between right side and left side (P < 0.001, OR = 2.484, 1.601–3.852)

approach and 1.2% (CI: 0.5%–2.7%) for left-side approach. The rightside group had a significantly higher incidence of air leak than the left-side group (p = 0.004, OR = 20.15, 1.131–359). No substantial heterogeneity was found in the right-side (Q = 10.91, $l^2 = 18.11\%$) and the left-side groups (Q = 2.79, $l^2 = 0\%$) (Figure 4).

3.2.4 | Thoracic duct fistula

Thoracic duct fistula was reported in no right-side approach studies (380 patients) and in four left-side approach studies (580 patients). The pooled incidence of thoracic duct fistula was 1.7% (Cl: 1.0%–2.9%) for all studies. The pooled incidence of thoracic duct fistula was 1.8% (Cl: 0.7%–4.2%) for right-side approach and 1.6% (Cl: 0.8%–3.3%) for left-side approach (p = 0.157, OR = 0.168, 0.009–3.138) with no significant difference between the two groups. There was no heterogeneity between studies in the right-side group (Q = 2.06, $l^2 = 0\%$) and the left-side group (Q = 3.86, $l^2 = 0\%$) (Figure 5).

3.2.5 | Atrial fibrillation

Atrial fibrillation was reported in six right-side approach studies (380 patients) and one in left-side approach studies (580 patients). The pooled incidence of atrial fibrillation was 2.5% (CI: 1.5%-4.1%) for all

studies. The pooled incidence of atrial fibrillation was 4.0% (CI: 2.1%– 7.7%) for right side and 1.2% (CI: 0.5%–2.7%) for left side. The incidence of atrial fibrillation in the right-side group was significantly higher than in the left-side group (p = 0.004, OR = 20.15, 1.131– 359). No substantial heterogeneity was found in the right- (Q = 7.50, $l^2 = 0\%$) and left-side groups (Q = 2.78, $l^2 = 0\%$) (Figure 6).

3.2.6 | Open conversion

Open conversion was reported in six right-side approach studies (380 patients) and in seven left-side approach studies (580 patients). The pooled incidence of open conversion was 4.8% (CI: 3.30%-6.90%) for all studies. The pooled incidence of open conversion was 6.5% (CI: 4.1%-10.1%) for right-side and 2.9% (CI: 1.5%-5.3%) for left-side. The incidence of open conversion was significantly higher in the right-side than in the left-side group (p = 0.004, OR = 3.598, 1.466-8.833). No substantial heterogeneity was found in the right- (Q = 10.25, $l^2 = 12.16\%$) and left-side groups (Q = 12.27, $l^2 = 18.49\%$) (Figure 7).

3.2.7 Sensitivity analysis and publication bias

Because more than 10 studies were included in each approach group, funnel plots were used to estimate the sensitivity and publication

Meta Analysis

Group by	Study name	<u>Comparison</u>		Statistic	cs for ea	ch study				Event ra	te and 95	i% CI	
Comparison			Event rate	Lower limit	Upper limit	Z-Value p	-Value						
L	Mussi, 2012	L	0.143	0.036	0.427	-2.346	0.019	- T	I			-1	Ĩ
L	RUCKERT ., 2008	L	0.005	0.000	0.078	-3.704	0.000				.		
L	Tomulescu, 2009	L	0.022	0.001	0.268	-2.662	0.008						
L	Melfi,2012	L	0.051	0.013	0.183	-4.019	0.000						
L	Freeman,2011	L	0.007	0.000	0.097	-3.536	0.000				.		
L	Marulli, 2013	L	0.005	0.000	0.074	-3.741	0.000				.		
L	Rea, 2006	L	0.015	0.001	0.196	-2.951	0.003						
L	Fleck, 2009	L	0.026	0.002	0.310	-2.519	0.012				-	-	
L	Rea, 2011	L	0.005	0.000	0.074	-3.741	0.000				.		
L	Marina, 2017	L	0.056	0.008	0.307	-2.753	0.006					-	
L	Ricciardi, 2016	L	0.015	0.002	0.100	-4.143	0.000				-		
L			0.029	0.016	0.055	-10.490	0.000				•		
R	Keijzers, 2015	R	0.016	0.004	0.062	-5.778	0.000				É		
R	Wilshire, 2016	R	0.021	0.001	0.259	-2.694	0.007						
R	Augustin, 2007	R	0.015	0.001	0.201	-2.929	0.003						
R	Jun, 2014	R	0.009	0.001	0.127	-3.315	0.001				-		
R	Castle, 2008	R	0.019	0.001	0.236	-2.781	0.005						
R	Goldstein, 2010	R	0.019	0.001	0.236	-2.781	0.005						
R	Cerfolio, 2011	R	0.028	0.002	0.322	-2.479	0.013					-	
R	Hsin,2011	R	0.038	0.002	0.403	-2.232	0.026					_	
R	Savitt, 2004	R	0.033	0.002	0.366	-2.341	0.019					-	
R	Kneuertz, 2017	R	0.024	0.001	0.287	-2.594	0.009					-	
R			0.019	0.009	0.041	-9.906	0.000				+		
		-						-1.00	-0.5	50	0.00	0.50	1.00
								F	Propor	rtion	of ple	ural ef	ffusion

FIGURE 3 Forest plots of the incidence of pleural effusion. There was no statistical difference between right side and left side (p = 0.490, OR = 0.506, 0.102–2.522)

Meta Analysis

Group by	Study name	Comparison		Statisti	cs for ea	ach study			Even	t rate and 9	5% CI	
Comparison			Event rate	Lower limit	Upper limit	Z-Value	p-Value					
L	Mussi, 2012	L	0.033	0.002	0.366	-2.341	0.019	1		- -	- 1	1
L	RUCKERT -, 2008	L	0.005	0.000	0.078	-3.704	0.000					
L	Tomulescu, 2009	L	0.022	0.001	0.268	-2.662	0.008			₽	-	
L	Melfi,2012	L	0.013	0.001	0.171	-3.070	0.002			-		
L	Freeman,2011	L	0.007	0.000	0.097	-3.536	0.000			-		
L	Marulli, 2013	L	0.005	0.000	0.074	-3.741	0.000					
L	Rea, 2006	L	0.015	0.001	0.196	-2.951	0.003			—		
L	Fleck, 2009	L	0.026	0.002	0.310	-2.519	0.012			- -	-	
L	Rea, 2011	L	0.005	0.000	0.074	-3.741	0.000					
L	Marina, 2017	L	0.026	0.002	0.310	-2.519	0.012			₽	-	
L	Ricciardi, 2016	L	0.007	0.000	0.108	-3.445	0.001			-		
L			0.012	0.005	0.027	-10.329	0.000	_				
R	Keijzers, 2015	R	0.004	0.000	0.060	-3.899	0.000					
R	Wilshire, 2016	R	0.130	0.043	0.335	-3.064	0.002				- 1	
R	Augustin, 2007	R	0.015	0.001	0.201	-2.929	0.003			-		
R	Jun, 2014	R	0.009	0.001	0.127	-3.315	0.001			* -		
R	Castle, 2008	R	0.038	0.005	0.228	-3.156	0.002					
R	Goldstein, 2010	R	0.019	0.001	0.236	-2.781	0.005					
R	Cerfolio, 2011	R	0.118	0.030	0.368	-2.677	0.007				_	
R	Hsin,2011	R	0.038	0.002	0.403	-2.232	0.026			⊨	— I	
R	Savitt, 2004	R	0.033	0.002	0.366	-2.341	0.019			⊨	- 1	
R	Kneuertz, 2017	R	0.024	0.001	0.287	-2.594	0.009			-	-	
R		_	0.051	0.027	0.094	-8.674	0.000			♦		
		-						-1.00	-0.50	0.00	0.50	1.00
									pr	oportic	on of air	r leak

Group by	Study name	<u>Comparison</u>		Statistic	s for ea	ch study				Event ra	ate and S	95% CI	
Comparison			Event rate	Lower limit	Upper limit	Z-Value p	-Value						
L	Mussi, 2012	L	0.033	0.002	0.366	-2.341	0.019	1	1		-	- 1	1
L	RUCKERT ., 2008	L	0.005	0.000	0.078	-3.704	0.000				* -		
L	Tomulescu, 2009	L	0.045	0.006	0.261	-2.975	0.003					- 1	
L	Melfi,2012	L	0.013	0.001	0.171	-3.070	0.002						
L	Freeman,2011	L	0.007	0.000	0.097	-3.536	0.000				* -		
L	Marulli, 2013	L	0.010	0.001	0.068	-4.572	0.000						
L	Rea, 2006	L	0.030	0.004	0.186	-3.413	0.001						
L	Fleck, 2009	L	0.026	0.002	0.310	-2.519	0.012					_	
L	Rea, 2011	L	0.010	0.001	0.068	-4.572	0.000						
L	Marina, 2017	L	0.026	0.002	0.310	-2.519	0.012				-	-	
L	Ricciardi, 2016	L	0.007	0.000	0.108	-3.445	0.001				-		
L			0.016	0.008	0.033	-11.142	0.000				•		
R	Keijzers, 2015	R	0.004	0.000	0.060	-3.899	0.000						
R	Wilshire, 2016	R	0.021	0.001	0.259	-2.694	0.007					- 1	
R	Augustin, 2007	R	0.015	0.001	0.201	-2.929	0.003						
R	Jun, 2014	R	0.009	0.001	0.127	-3.315	0.001						
R	Castle, 2008	R	0.019	0.001	0.236	-2.781	0.005				-	-	
R	Goldstein, 2010	R	0.019	0.001	0.236	-2.781	0.005				-	-	
R	Cerfolio, 2011	R	0.028	0.002	0.322	-2.479	0.013					-	
R	Hsin,2011	R	0.038	0.002	0.403	-2.232	0.026					_	
R	Savitt, 2004	R	0.033	0.002	0.366	-2.341	0.019				-	- 1	
R	Kneuertz, 2017	R	0.024	0.001	0.287	-2.594	0.009				-	-	
R			0.018	0.007	0.042	-8.876	0.000				•		1
								-1.00	-0.5	50	0.00	0.50	1.00
								Pro	nortic	on of	thors	icic due	t fictula
								110	point	n or	more	iore duc	/ instand

FIGURE 5 Forest plots of the incidence of thoracic duct fistula. There was no statistical difference between right side and left side (p = 0.157, OR = 0.168, 0.009–3.138)

Meta Analysis

Group by	Study name	Comparison		Statisti	cs for each s	study			ļ	Event rate	and 95%	CI	
Comparison			Event rate	Lower limit	Upper limit Z-Va	alue p-\	/alue						
L	Mussi, 2012	L	0.033	0.002	0.366 -2.	.341	0.019	- I			 		
L	RUCKERT ", 2008	L	0.005	0.000	0.078 -3.	.704	0.000			I			
L	Tomulescu, 2009	L	0.022	0.001	0.268 -2.	.662	0.008						
L	Melfi,2012	L	0.013	0.001	0.171 -3.	.070	0.002			1	—		
L	Freeman,2011	L	0.007	0.000	0.097 -3.	.536	0.000				-		
L	Marulli, 2013	L	0.005	0.000	0.074 -3.	.741	0.000						
L	Rea, 2006	L	0.015	0.001	0.196 -2.	.951	0.003						
L	Fleck, 2009	L	0.026	0.002	0.310 -2.	.519	0.012						
L	Rea, 2011	L	0.005	0.000	0.074 -3.	.741	0.000			1			
L	Marina, 2017	L	0.026	0.002	0.310 -2.	.519	0.012						
L	Ricciardi, 2016	L	0.007	0.000	0.108 -3.	.445	0.001			1	-		
L		_	0.012	0.005	0.027 -10.	.329	0.000						
R	Keijzers, 2015	R	0.004	0.000	0.060 -3.	.899	0.000	-			É.		
R	Wilshire, 2016	R	0.043	0.006	0.252 -3.	.023	0.003						
R	Augustin, 2007	R	0.015	0.001	0.201 -2.	.929	0.003			1			
R	Jun, 2014	R	0.009	0.001	0.127 -3.	.315	0.001			1	-		
R	Castle, 2008	R	0.038	0.005	0.228 -3.	.156	0.002						
R	Goldstein, 2010	R	0.019	0.001	0.236 -2.	.781	0.005			1	<u> </u>		
R	Cerfolio, 2011	R	0.118	0.030	0.368 -2.	.677	0.007						
R	Hsin,2011	R	0.038	0.002	0.403 -2.	.232	0.026					-	
R	Savitt, 2004	R	0.071	0.010	0.370 -2.	.472	0.013						
R	Kneuertz, 2017	R	0.050	0.007	0.282 -2.	.870	0.004						
R			0.040	0.021	0.077 -8.	.978	0.000				•		
								-1.00	-0.5	0 0.	.00	0.50	1.00
									Propo	rtion o	of atri	al fib	rillation

FIGURE 6 Forest plots of the incidence of atrial fibrillation. The right-side group had a significantly higher incidence than the left-side group (p = 0.004, OR = 20.15, 1.131-359)

Meta Analysis

Group by	Study name	<u>Comparison</u>		Statistic	cs for each	n study			Event r	ate and 95	<u>% CI</u>	
Comparison			Event rate	Lower limit	Upper limit Z-V	Value p	Value					
L	Mussi, 2012	Ĺ	0.143	0.036	0.427 -	2.346	0.019	1	1]	-1	1
L	RUCKERT -, 2008	L	0.011	0.001	0.071 -	4.519	0.000					
L	Tomulescu, 2009	L	0.022	0.001	0.268 -	2.662	0.008			—		
L	Melfi,2012	L	0.051	0.013	0.183 -	4.019	0.000			-		
L	Freeman,2011	L	0.013	0.002	0.089 -	4.275	0.000					
L	Marulli, 2013	L	0.005	0.000	0.074 -	3.741	0.000			Ē.		
L	Rea, 2006	L	0.015	0.001	0.196 -	2.951	0.003					
L	Fleck, 2009	Ĺ	0.056	0.008	0.307 -	2.753	0.006				.	
L	Rea, 2011	L	0.005	0.000	0.074 -	3.741	0.000			.		
L	Marina, 2017	L	0.026	0.002	0.310 -	2.519	0.012				.	
L	Ricciardi, 2016	L	0.007	0.000	0.108 -	3.445	0.001			-		
L			0.029	0.015	0.053 -1	0.848	0.000			•		
R	Keijzers, 2015	R	0.040	0.017	0.093 -	6.963	0.000					
R	Wilshire, 2016	R	0.043	0.006	0.252 -	3.023	0.003					
R	Augustin, 2007	R	0.031	0.004	0.191 -	3.380	0.001					
R	Jun, 2014	R	0.009	0.001	0.127 -	3.315	0.001					
R	Castle, 2008	R	0.038	0.005	0.228 -	3.156	0.002					
R	Goldstein, 2010	R	0.154	0.059	0.345 -	3.136	0.002				-	
R	Cerfolio, 2011	R	0.028	0.002	0.322 -	2.479	0.013				-	
R	Hsin,2011	R	0.038	0.002	0.403 -	2.232	0.026				-	
R	Savitt, 2004	R	0.071	0.010	0.370 -	2.472	0.013				-	
R	Kneuertz, 2017	R	0.150	0.049	0.376 -	2.770	0.006			-	-	
R			0.065	0.041	0.101 -1	0.700	0.000			•		
								-1.00	-0.50	0.00	0.50	1.00
								Pro	portion	of ope	en con	version

FIGURE 7 Forest plots of the incidence of open conversion. The right-side group had a significantly higher incidence than the left-side group (p = 0.004, OR = 3.598, 1.466-8.833)

ΤA	A E	3 L	Е	1	The	results	of	the	Egger	test
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Item	SD	95% lower limited	95% upper limited	p-value
Overall complications of all studies	1.10	-3.33	1.268	0.36
Overall complications of the right-side group	1.30	-2.93	3.07	0.96
Overall complications of the left-side group	1.61	-3.91	3.38	0.87

Note: SD, standard error.

bias. All funnel plots were symmetric around the mean effect; the Egger test confirmed that there was no bias (P > 0.05) (Table 1). Funnel plots of the total complication rate are depicted in Figure 8. Analysis of sensitivity and examination of publication bias confirmed the reliability of the meta-analysis results.

3.2.8 | Subgroup analysis of different age groups

Through the study design, the incidence of postoperative complications in patients of different age groups was analysed in subgroups. According to the age classification standard of the World Health Organization, we defined 60 years old and above as the 'Old Age' group, 45–59 years old as the 'Middle Age' group, 18–44 years old as the 'Youth' group and under 18 years old as the 'Minor' group. One article in the right approach of thymectomy did not provide patient's age information. Finally, 11 left-sided studies (580 patients) and 9 right-sided studies (318 patients) were included in this subgroup analysis; in the left approach, the incidence of overall complications was higher for the 'Old Age' group compared with the 'Youth' group (28.6% vs. 5.5%, respectively; p = 0.002) (Figure 9); in addition, the incidence of pleural effusion was higher for the 'Old Age' group compared with the 'Youth' group (14.3% vs. 1%, respectively; p = 0.002) (Figure 10). In the right approach, the incidence of overall complications was higher for the 'Middle Age' group compared with the 'Youth' group (26.2% vs. 14.9%, respectively; p = 0.034) (Figure 11). In the subgroup analysis of different ages, each study showed low statistical heterogeneity ($l^2 < 50\%$).

3.2.9 | Subgroup analysis of different gender groups

Through the study design, the incidence of postoperative complications in patients of different gender groups was analysed in



FIGURE 8 Funnel plots of standard error by logit event rate. (A) Overall complications of all studies; (B) Overall complications of right-side group; (C) Overall complications of left-side group

subgroups. All articles included in this study were not analysed by different gender group. We defined the studies with a proportion of female patients greater than 2/3 as the 'more women' group, and the studies with a proportion of male patients greater than 2/3 as the

'more man' group. Four left-sided studies (251 patients) and four right-sided studies (183 patients) were included in this subgroup analysis after excluding studies with missing data and similar proportion of men and women; Because the number of articles included

Meta Analysis With Age Subgroup(Left)



FIGURE 9 Forest plots of the incidence of overall complications with left side. There was statistical difference between 'Old Age' group and 'Youth' group (p = 0.002)

was small and the studies of left and right approaches were similar to the total number of patients, we chose not to conduct unilateral analysis. The results showed that there was no significant difference in the incidence of postoperative complications between the two groups (P > 0.05). In the subgroup analysis of different gender, each study showed low statistical heterogeneity ($I^2 < 50\%$).

3.3 | Comment

Thoracoscopic thymectomy can be performed from either the right or the left side, and each approach has its proponents. Xie concluded that unilateral VATS thymectomy is a clinically acceptable procedure and can be safely and effectively performed on either side of the thorax.⁴ Tomulescu et al.⁵ demonstrated similar operative times, hospitalisation lengths and remission rates for right- and left-sided VATS thymectomy. However, Yim et al.⁶ first proposed that a right-sided approach might be more appropriate for VATS. The reasons for this difference were the disease of the thymectomy and the different thymectomy methods.

The Da Vinci system R-VATS is a minimally invasive surgical approach for thymectomy with potentially less morbidity,⁷⁻¹¹ which has better outcomes compared with conventional video-assisted techniques.^{12,13} This is especially true for treating stage III thymomas, were limited by using of VATS.¹⁴ Robotic video-assisted thoracoscopic surgery thymectomy can be categorised as unilateral (right or left), bilateral, subxiphoid and bilateral with cervical incision, and each approach has its proponents. Complications from R-VATS may be different from traditional VATS due to different thoracoscope positioning and skilled cooperation. To the best of our knowledge, this is the first evidence-based medical article on comparing robotic thymectomy approaches.

According to some authors, the left-side approach is safer, and dissection of the soft fatty tissue around the pericardiophrenic angle is more suitable because the superior vena cava lies outside the surgical field.¹⁵ Furthermore, Rückert¹⁶ evaluated cadavers that had unilateral thoracoscopic thymectomy and found that all of the eight specified regions (i.e., thymic lobes, pretracheal fatty tissue, tissue behind phrenic nerve, tissue behind v. anonyma, aorto-pulmonary window, aorto-caval groove, anterior mediastinal fatty tissue and cardio-phrenic angle), with the exception of the aortocaval groove, were better visualised from the left side.

The right side is preferred by some surgeons because they can clearly identify and use the superior vena cava as a landmark to dissect around the innominate veins. In the bilateral VATS approach, some authors report that a complete excision is more suitable for better visualisation of anatomical structures. Although some studies mentioned postoperative atrial fibrillation after right-side approach thymectomy,¹⁷ the reasons for this are not clear. A probable cause is the high lymph nodes resection rate in the right-side approach, and the right-side surgical approach is more likely to damage the cardiac plexus. In fact, it has been confirmed that conduction from the arrhythmogenic right upper pulmonary vein to the superior vena cava can induce atrial fibrillation.¹⁸ The inadequate surgical extent (residual fatty tissue behind the left brachiocephalic vein, surrounding the left phrenic nerve and in the left pericardiophrenic angle) may account for poorer surgical outcomes after thymectomy,¹⁹ and the risk of rupture pleura when R-VATS were performed from the right side is also increased.

These results need to be interpreted in the context of several limitations. This was a single-arm meta-analysis since there were not enough studies researching the approach in R-VATS. Furthermore, the data in this meta-analysis included all patients who underwent thymectomy but did not differentiate patients by a specific disease.

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Meta Analysis With Age Subgroup(Left)

Group by	Study name	Subgroup within study		Statistic	s for e	ach study		Event rate and 95% CI
Subgroup within study			Event rate	Lower limit	Upper limit	Z-Valuep	-Value	e
old age	Mussi, 2012	old age	0.143	0.036	0.427	-2.346	0.019	9
old age			0.143	0.036	0.427	-2.346	0.019	9
youth	RUCKERT , 200	8youth	0.005	0.000	0.078	-3.704	0.000	0
youth	Freeman,2011	youth	0.007	0.000	0.097	-3.536	0.000	o 📕 🖌
youth	Marulli, 2013	youth	0.005	0.000	0.074	-3.741	0.000	o 📕
youth	Rea, 2006	youth	0.015	0.001	0.196	-2.951	0.003	3
youth	Fleck, 2009	youth	0.026	0.002	0.310	-2.519	0.012	2
youth	Rea, 2011	youth	0.005	0.000	0.074	-3.741	0.000	o 📕
youth	Ricciardi, 2016	youth	0.015	0.002	0.100	-4.143	0.000	o 📕
youth			0.010	0.004	0.025	-9.215	0.000	<u>o</u>
								-1.00 -0.50 0.00 0.50 1.00
								Proportion of pleural effusion

FIGURE 10 Forest plots of the incidence of pleural effusion with left side. There was statistical difference between 'Old Age' group and 'Youth' group (p = 0.002)

Meta Analysis With Age Subgroup(Right)



FIGURE 11 Forest plots of the incidence of pleural effusion with Right side. There was statistical difference between 'Middle Age' group and 'Youth' group (p = 0.034)

By searching the literature, we found that in the study of Hartwich J et al.,²⁰ the incidence of postoperative complications in patients with non-thymoma MG after robot assisted thoracoscopy was 11.11%; Sehitogullari A et al.²¹ reported similar results (9.52%) in patients with thymoma; none of the thymoma patients included in the study had MG. Moreover, in many studies,^{11,22-25} various types of thymic diseases have been discussed together without distinction. Therefore, we have reason to believe that our meta-analysis is scientific. The results of further subgroup analysis showed that age was related to the incidence of postoperative complications after thymectomy, and the incidence of postoperative complications was often higher in the older group. There was no significant difference in gender-related subgroup analysis.

Although initially, thymoma patients treated with R-VATS were analysed, there may be some degree of selection bias among R-VATS patients. Finally, the duration of follow-up for identifying complications was relatively limited given that the majority of papers only reported the early results after R-VATS.

4 | CONCLUSIONS

Robotic video-assisted thoracoscopic surgery can be performed using both the left-side and right-side approaches; however, the left-side approach has fewer complications. These data suggest that the leftside R-VATS thymectomy has fewer overall complications, less atrial fibrillation, lower open conversion ratios and lower incidences of air leaks than right-side procedures. Further subgroup analysis showed that the incidence of postoperative complications was higher in the older group.

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None.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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