Perioperative Improvements for Changing the Non-small Cell Lung Cancer Surgical Approach

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Abstract

Background

Video-assisted thoracic surgery (VATS) procedures for non-small cell lung cancer (NSCLC) have steadily increased and become the gold standard, but the prognostic advantage compared to thoracotomy has not been elucidated. This study retrospectively evaluated perioperative characteristics of VATS for NSCLC over time.

Methods

We collected the clinical data of 760 patients with NSCLC who underwent pulmonary resection over the last decade, classifying patients into early (2011–2015) and late (2016–2020) periods. Changes in NSCLC patient characteristics, surgical approaches, perioperative factors, postoperative morbidities, and prognoses were analyzed.

Results

Patients in the late period were older ($p = 0.01$), had more comorbidities ($p = 0.01$), and had earlier-stage cancer ($p < 0.01$) than those in the early period. The late period had significantly fewer operative procedures for lobectomy or more ($p < 0.01$), open thoracotomies ($p < 0.01$), postoperative ($p = 0.02$) and severe morbidities ($p < 0.01$), and a significantly shorter postoperative hospital stay than the early period. Operative procedures of lobectomy or more ($p < 0.01$) were significant risk factors for postoperative morbidity, and being in the early period ($p < 0.01$) and operative procedures of lobectomy or more ($p < 0.01$) were significant risk factors for severe postoperative morbidities. The overall survival prognosis significantly differed between the groups ($p = 0.02$), but progression-free survival did not ($p = 0.89$).

Conclusion

The incidence of postoperative morbidities decreased over time in older patients and patients with more comorbidities. The prognosis of patients with NSCLC did not change with increasing VATS or sublobar resection.

Trial registration:

The Institutional Review Board of Kanazawa Medical University approved the protocol of this retrospective study (approval number: I392), and written informed consent was obtained from all patients.

Introduction

Since the development of endoscopic surgery, minimally invasive surgery (MIS) has become a viable treatment option for several cancers [1–4]. MIS leads to fewer postoperative complications and a shorter

hospital stay, which are advantageous. Video-assisted thoracic surgery (VATS) for non-small cell lung cancer (NSCLC) was implemented in 1992. Since then, VATS procedures for NSCLC have steadily increased and have become the gold standard [5]. Moreover, the VATS procedure (an MIS) is associated a lower incidence of postoperative complications, a shorter hospital stay, less intraoperative blood loss, and less chest tube drainage compared with thoracotomy [6–8]. Some studies reported better prognosis after VATS than after thoracotomy [7, 9], but others indicated that survival was comparable [10, 11].

Thus, in this study, we retrospectively evaluated changes in NSCLC patient characteristics, the surgical approach, perioperative factors, and postoperative morbidities to elucidate the prognoses following VATS over the last decade.

Material And Methods

Patients

We enrolled NSCLC patients who underwent pulmonary resection at Kanazawa Medical University between 2011 and 2020. The cases were divided into early (2011–2015) and late (2016–2020) periods based on the date of surgery.

We collected data on clinical factors, including sex, age, comorbidities, smoking history, carcinoembryonic antigen (CEA) levels, respiratory function, pathological findings, stage, and histology. Smoking history was assessed using the Brinkman Index (BI), calculated by multiplying the number of cigarettes smoked per day by the number of years the subject had been smoking [12]. We also collected comorbidity data, including information on interstitial pneumonia, asthma, diabetes mellitus, chronic obstructive pulmonary disease, chronic renal failure, autoimmune disease, ischemic heart disease, arrhythmia, and malignant disease. The comorbidities were evaluated using the Charlson Comorbidity Index (CCI) [13]. Respiratory function parameters, such as the percent-predicted vital capacity and the forced expiratory volume in 1 second as a percentage of the forced vital capacity (FEV_1%), were also collected.

Operative factors

The operative approaches were classified into four categories: VATS (the surgery was performed only for monitoring, and the wound length was less than 8 cm), hybrid VATS (H-VATS; the surgery was combined with direct vision without rib spreading, and the wound length was > 8 cm), robot-assisted thoracic surgery, and thoracotomy. Further, the operative procedures were classified into eight categories: partial resection, segmentectomy, lobectomy, sleeve lobectomy, lobectomy combined with segmentectomy, lobectomy combined with chest wall resection, bilobectomy, and pneumonectomy.

Postoperative complications

Postoperative complications were categorized into five grades based on the Clavien-Dindo classification system, established in 1992 [14]. This system is a simple and feasible way to grade all types of

postoperative complications [15]. In 2004, modifications allowed for the grading of life-threatening complications and long-term disability caused by complications [16]. This revised version has five defined severity grades with subgrades (grades I, II, IIIa, IIIb, IVa, IVb, and V), and the suffix “d” (for “disability”) denotes any postoperative impairment. The modified version of the Clavien-Dindo classification system is widely used in clinical practice.

Severe morbidity was defined according to the Society of Thoracic Surgeons General Thoracic Database [17, 18], and included respiratory failure, interstitial pneumonia, tracheobronchial fistula, pulmonary thromboembolism, pneumonia, redo surgery, myocardial infarction, arrhythmia requiring therapy, renal failure, postoperative bleeding, and chylothorax. Further, we added air leakage requiring therapy, atelectasis, and cerebral infarction as postoperative morbidities.

Statistical analyses

Pearson’s chi-squared test of independence was used to compare the frequencies of the variables. Risk factors related to postoperative complications were analyzed using logistic regression analysis. Significant factors in the univariate analysis were included in the multivariate analysis. The cumulative survival rates were calculated using the Kaplan–Meier method, and survival curves were compared using the log-rank test. All statistical analyses were two-sided, and statistical significance was set at $p < 0.05$. Statistical analyses were conducted using the JMP software (version 13.2; SAS Institute Inc., Cary, NC, USA).

This study followed the principles of the Declaration of Helsinki. The Institutional Review Board of Kanazawa Medical University approved the protocol (approval number: I392), and written informed consent was obtained from all patients.

Results

Patient characteristics

We enrolled 760 patients; Table 1 presents their clinicopathological characteristics. Age ($p = 0.01$), CCI ($p = 0.01$), lymphatic invasion ($p < 0.01$), vascular invasion ($p < 0.01$), and the pathological stage ($p < 0.01$) significantly differed between the early and late periods. Patients in the late period were older, had more comorbidities, and had earlier-stage disease than those in the early period.

Table 1
Differences of patient characteristics between 2011–2015 and 2016–2020

	2011–2015 (n = 254)	2016–2020 (n = 506)	*p*
Gender (M/F)	160 (63.0%) / 94 (37%)	306 (60.5%) / 200 (39.5%)	0.50
Age	69.1 (33–84)	70.9 (22–92)	0.01
IP	7 (2.7%)	16 (3.2%)	0.75
Asthma	11 (4.3%)	14 (2.8%)	0.25
DM	29 (11.4%)	89 (17.6%)	0.02
COPD	16 (6.3%)	28 (5.5%)	0.66
CRF	1 (0.4%)	9 (1.8%)	0.11
Autoimmune	4 (1.6%)	12 (2.4%)	0.47
IHD or arrhythmia	19 (7.5%)	59 (11.7%)	0.07
Malignant disease	35 (13.8%)	113 (22.3%)	< 0.01
CCI (0 / 1 / 2 / 3 / 4 / 5 / 6)	155 / 57 / 34 / 8 / 0 / 0 / 0	259 / 100 / 107 / 31 / 7 / 1 / 1	0.01
CCI > 2	8 (3.1%)	40 (7.9%)	0.01
Brinkman index	600 (0-2800)	510 (0-3600)	0.72
%VC	99.2 (65.5-164.1)	100.3 (53.4-177.7)	0.24
FEV1%	73.6 (32.1–99.2)	73.2 (30.5–99.4)	0.43
CEA	3.7 (0.6-163.5)	3.5 (0.5-142.6)	0.07
Histology (Ad/Sq/AdSq/LCNEC/Pleo/Large/Carci)	185/57/5//5/1/0/1	391/85/5/13/6/3/3	0.26
Ly	108 (42.5%)	137 (27.1%)	< 0.01
V	133 (52.3%)	193 (38.1%)	< 0.01

IP; interstitial pneumonia, DM; diabetes mellitus, COPD; chronic obstructive pulmonary disease, CRF; chronic renal failure, IHD; ischemic heart disease, CCI; Charlson comorbidity index, VC; vital capacity, FEV_1%; forced expiratory volume % in one second, CEA; carcinoembryonic antigen, Ad;

adenocarcinoma, Sq; squamous cell carcinoma, AdSq; adenosquamous cell carcinoma, LCNEC; large cell neuroendocrine cell carcinoma, Pleo; pleomorphic cell carcinoma, Large; large cell carcinoma, Carci; carcinoid, Ly; lymphatic invasion, V; vascular invasion, G; grade of differentiation, pStage; pathological stage.

	2011–2015 (n = 254)	2016–2020 (n = 506)	*p*
G (1/2/3/4)	91/117/39/7	167/263/58/18	0.27
pStage (0 / 1a / 1b / 2a / 2b / 3a / 3b / 4 / y1a / y2a)	0 / 117 / 64 / 0 / 21 / 23 / 25 / 1 / 1 / 0 / 1 / 1	45 / 303 / 62 / 1 / 17 / 42 / 26 / 3 / 3 / 2 / 4/0	< 0.01
pStage 0-I	181 (71.3%)	411 (81.2%)	< 0.01

IP; interstitial pneumonia, DM; diabetes mellitus, COPD; chronic obstructive pulmonary disease, CRF; chronic renal failure, IHD; ischemic heart disease, CCI; Charlson comorbidity index, VC; vital capacity, FEV_1%; forced expiratory volume % in one second, CEA; carcinoembryonic antigen, Ad; adenocarcinoma, Sq; squamous cell carcinoma, AdSq; adenosquamous cell carcinoma, LCNEC; large cell neuroendocrine cell carcinoma, Pleo; pleomorphic cell carcinoma, Large; large cell carcinoma, Carci; carcinoid, Ly; lymphatic invasion, V; vascular invasion, G; grade of differentiation, pStage; pathological stage.

Operative factors and postoperative morbidity

Table 2 details the operative factors and postoperative morbidity rates. In the late period, there were significantly fewer operative procedures of lobectomy or more ($p < 0.01$) and open thoracotomy or H-VATS ($p < 0.01$) than in the early period. Further, the operation time ($p < 0.01$) and wound length ($p < 0.01$) were significantly shorter in the late period than in the early period. The late period also had significantly fewer overall postoperative morbidities ($p = 0.02$), postoperative morbidities classified as Clavian-Dindo grades > 2 ($p = 0.02$), and severe morbidities ($p < 0.01$) than the early period, and the postoperative hospital stay was significantly shorter ($p < 0.01$) in the late period than that in the early period.

Table 2
Differences of perioperative factors between 2011–2015 and 2016–2020

	2011–2015 (n = 254)	2016–2020 (n = 506)	*p*
Lobectomy or more	213 (83.8%)	313 (61.8%)	< 0.01
Operation time	229 (78-1149)	140 (27–456)	< 0.01
Wound length	7 (3–30)	5 (3–36)	< 0.01
Open or Hybrid VATS	221 (87.0%)	223 (44.1%)	< 0.01
Approach (R / V / H / O)	0 / 33 / 187 / 34	12 / 271 / 184 / 39	< 0.01
Operative procedure (Part/Seg/Lob/SL/LS/CW/BL/Pneu)	36/5/192/0/1/3/8/9	127/66/290/6/2/6/2/7	< 0.01
Leak	29(11.4%)	73 (14.4%)	0.25
Atelectasis or pneumonia	15 (5.9%)	17 (3.3%)	0.09
Arrhythmia	26 (10.2%)	16 (3.2%)	< 0.01
Cerebral infarction	2 (0.8%)	3 (0.6%)	0.75
Severe morbidity	37 (14.6%)	28 (5.5%)	< 0.01
Morbidity	80 (31.5%)	120 (23.7%)	0.02
C-D (0 / 1 / 2 / 3a / 3b)	174 / 1 / 34 / 41/4	386 / 0 / 40 / 79 / 1	< 0.01
C-D ≥ 2	79 (31.1%)	120 (23.7%)	0.02
Postop-hospital stay	15 (5–89)	8 (3–71)	< 0.01

IP; interstitial pneumonia, DM; diabetes mellitus, COPD; chronic obstructive pulmonary disease, CRF; chronic renal failure, IHD; ischemic heart disease, CCI; Charlson comorbidity index, VC; vital capacity, FEV_1%; forced expiratory volume % in one second, CEA; carcinoembryonic antigen, Ad; adenocarcinoma, Sq; squamous cell carcinoma, AdSq; adenosquamous cell carcinoma, LCNEC; large cell neuroendocrine cell carcinoma, Pleo; pleomorphic cell carcinoma, Large; large cell carcinoma, Carci; carcinoid, Ly; lymphatic invasion, V; vascular invasion, G; grade of differentiation, pStage; pathological stage, R; robotic-assisted thoracic surgery, V; video-assisted thoracic surgery, H; hybrid video-assisted thoracic surgery, O; open thoracotomy, Part; partial resection, Seg; segmentectomy, Lob; lobectomy, SL; sleeve lobectomy, LS; lobectomy combined with segmentectomy, CW; lobectomy combined with chest wall resection, BL; bi-lobectomy, Pneu; pneumonectomy,C-D; Clavian-Dindo classification.

Association of patient characteristics and operative factor with postoperative and severe morbidity

Table 3 presents the relationships between patient characteristics or operative factors and the postoperative morbidity or severe morbidity incidence rates. Postoperative morbidities were significantly higher in the early period ($p = 0.02$) and in males ($p < 0.01$) and for patients with asthma ($p < 0.01$), a BI of > 600 ($p < 0.01$), a FEV_1% of < 70 ($p < 0.01$), and those undergoing lobectomy ($p < 0.01$). Severe postoperative morbidities were significantly higher in the early period ($p < 0.01$) and in males ($p < 0.01$) and for patients with a CEA level of > 5 ng/mL ($p = 0.01$) and for those undergoing lobectomy ($p < 0.01$).

Table 3
Relationship between patient characteristics or operative factors and incident rate of postoperative morbidity or severe morbidity

	Morbidity (%)	*p*	Severe morbidity (%)	*p*
Period (2011–2015/2016–2020)	31.1 / 23.7	0.02	14.5 / 5.5	< 0.01
Gender (male / female)	31.9 / 17.0	< 0.01	10.7 / 5.1	< 0.01
Age (≧ 75 / <75)	27.4 / 25.7	0.62	7.3 / 9.0	0.43
IP (present / absent)	13.0 / 26.6	0.14	13.0 / 8.4	0.43
Asthma (present /absent)	52.0 / 25.3	< 0.01	12.0 / 8.4	0.53
DM (present / absent)	26.2 / 26.1	0.98	5.9 / 9.0	0.26
COPD (present / absent)	34.1 / 25.7	0.21	13.6 / 8.2	0.21
CRF (present / absent)	50.0 / 25.8	0.08	10.0 / 8.5	0.86
Autoimmune (present / absent)	12.5 / 26.5	0.20	6.2 / 8.6	0.73
IHD or arrhythmia (present / absent)	28.2 / 23.3	0.66	7.7 / 8.6	0.77
Malignant (present / absent)	20.9 / 27.4	0.10	6.1 / 9.1	0.23
BI (> 600 / ≤600)	31.4 / 21.0	< 0.01	10.5 / 6.5	0.04
%VC (< 80 / ≥80)	35.1 / 25.4	0.11	10.5 / 8.4	0.57
FEV1% (< 70 / ≥70)	33.7 / 21.8	< 0.01	11.1 / 7.0	0.05
CEA (> 5 / ≤5)	28.8 / 24.9	0.24	12.2 / 6.8	0.01
Operative procedure (Lob or more/ Seg or Part)	31.3 / 14.5	< 0.01	11.4 / 2.1	< 0.01
Operative approach (RATS or VATS / H-VATS or Open)	26.9 / 25.6	0.70	6.6 / 9.9	0.11
Pathology (SQ / Others)	26.7 / 26.0	0.86	11.9 / 7.7	0.10
pStage (0-I / others)	26.0 / 26.8	0.84	7.7 / 11.3	0.14

IP; interstitial pneumonia, DM; diabetes mellitus, COPD; chronic obstructive pulmonary disease, CRF; chronic renal failure, IHD; ischemic heart disease, BI; Brinkmann index, VC; vital capacity, FEV_1%; forced expiratory volume % in one second, CEA; carcinoembryonic antigen, Lob; lobectomy, Seg; segmentectomy, Part; partial resection, RATS; robotic-assisted thoracic surgery, VATS; video-assisted thoracic surgery, H-VATS; hybrid video-assisted thoracic surgery, Open; open thoracotomy, SQ; squamous cell carcinoma, pStage; pathological stage.

Multivariate analysis results

Table 4 presents the multivariate analysis results of the postoperative morbidity risk factors. Male sex (odds ratio [OR] 2.360, 95% confidence interval [CI] 1.467–3.798, $p < 0.02$), asthma (OR 3.481, 95% CI 1.462–8.288, $p < 0.02$), FEV_1% <70 (OR 1.596, 95% CI 1.103–2.308, $p = 0.01$), and operative procedure of lobectomy or more were significant risk factors for postoperative morbidity ($p < 0.01$). Furthermore, the early period (OR 2.246, 95% CI 1.320–3.823, $p < 0.01$), male sex (OR 2.269, 95% CI 1.235–4.171, $p < 0.01$), CEA level > 5 ng/mL (OR 1.859, 95% CI 1.094–3.158, $p = 0.02$), and the lobectomy procedure (OR 5.008, 95% CI 1.954–12.834, $p < 0.01$) were significant risk factors for postoperative severe morbidities (Table 5).

Table 4
Risk factors of morbidity

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*p*	OR	95%CI	*p*
Period (2011–2015/2016–2020)	1.452	1.038–2.030	0.02	1.211	0.848–1.730	0.29
Gender (male / female)	2.293	1.598–3.291	< 0.01	2.360	1.467–3.798	< 0.01
Age (≥ 75 / <75)	1.091	0.765–1.555	0.628			
IP (present / absent)	0.414	0.121–1.408	0.15			
Asthma (present /absent)	3.197	1.433–7.130	< 0.01	3.481	1.462–8.288	< 0.01
DM (present / absent)	1.002	0.643–1.570	0.98			
COPD (present / absent)	1.495	0.784–2.851	0.22			
CRF (present / absent)	2.865	0.820-10.006	0.09			
Autoimmune (present / absent)	0.396	0.089–1.760	0.22			
IHD or arrhythmia (present / absent)	1.120	0.665–1.889	0.66			
Malignant (present / absent)	0.700	0.453–1.080	0.10			
BI (> 600 / ≤600)	1.722	1.240–2.391	< 0.01	0.901	0.579–1.401	0.64
%VC (< 80 / ≥80)	1.582	0.895–2.797	0.11			
FEV1% (< 70 / ≥70)	1.819	1.309–2.529	< 0.01	1.596	1.103–2.308	0.01
CEA (> 5 / ≤5)	1.223	0.870–1.719	0.24			

IP; interstitial pneumonia, DM; diabetes mellitus, COPD; chronic obstructive pulmonary disease, CRF; chronic renal failure, IHD; ischemic heart disease, BI; Brinkmann index, VC; vital capacity, FEV_1%; forced expiratory volume % in one second, CEA; carcinoembryonic antigen, Lob; lobectomy, Seg; segmentectomy, Part; partial resection, RATS; robotic-assisted thoracic surgery, VATS; video-assisted thoracic surgery, H-VATS; hybrid video-assisted thoracic surgery, Open; open thoracotomy, SQ; squamous cell carcinoma, pStage; pathological stage.

	Univariate analysis			Multivariate analysis		
Operative procedure (Lob or more/ Seg or Part)	2.688	1.788–4.041	< 0.01	2.745	1.792–4.206	< 0.01
Operative approach (RATS or VATS / H-VATS or Open)	1.065	0.767–1.477	0.70			
Pathology (SQ / Others)	1.037	0.686–1.566	0.86			
pStage (0-I / others)	0.961	0.652–1.416	0.84			

IP; interstitial pneumonia, DM; diabetes mellitus, COPD; chronic obstructive pulmonary disease, CRF; chronic renal failure, IHD; ischemic heart disease, BI; Brinkmann index, VC; vital capacity, FEV_1%; forced expiratory volume % in one second, CEA; carcinoembryonic antigen, Lob; lobectomy, Seg; segmentectomy, Part; partial resection, RATS; robotic-assisted thoracic surgery, VATS; video-assisted thoracic surgery, H-VATS; hybrid video-assisted thoracic surgery, Open; open thoracotomy, SQ; squamous cell carcinoma, pStage; pathological stage.

Table 5
Risk factors of severe morbidity

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*p*	OR	95%CI	*p*
Period (2011–2015/2016–2020)	2.910	1.736–4.878	< 0.01	2.246	1.320–3.823	< 0.01
Gender (male / female)	2.235	1.231–4.059	< 0.01	2.269	1.235–4.171	< 0.01
Age (≥ 75 / <75)	0.791	0.439–1.424	0.43			
IP (present / absent)	1.633	0.472–5.649	0.43			
Asthma (present /absent)	1.480	0.430–5.084	0.53			
DM (present / absent)	0.634	0.282–1.427	0.27			
COPD (present / absent)	1.758	0.713–4.330	0.21			
CRF (present / absent)	1.190	0.148–9.550	0.86			
Autoimmune (present / absent)	0.708	0.092–5.449	0.74			
IHD or arrhythmia (present / absent)	0.879	0.366–2.109	0.77			
Malignant (present / absent)	0.642	0.310–1.331	0.23			
BI (> 600 / ≤600)	1.680	0.997–2.830	0.05			
%VC (< 80 / ≥80)	1.284	0.528–3.117	0.58			
FEV1% (< 70 / ≥70)	1.643	0.985–2.739	0.05			
CEA (> 5 / ≤5)	1.900	1.137–3.176	0.01	1.859	1.094–3.158	0.02

IP; interstitial pneumonia, DM; diabetes mellitus, COPD; chronic obstructive pulmonary disease, CRF; chronic renal failure, IHD; ischemic heart disease, BI; Brinkmann index, VC; vital capacity, FEV_1%; forced expiratory volume % in one second, CEA; carcinoembryonic antigen, Lob; lobectomy, Seg; segmentectomy, Part; partial resection, RATS; robotic-assisted thoracic surgery, VATS; video-assisted thoracic surgery, H-VATS; hybrid video-assisted thoracic surgery, Open; open thoracotomy, SQ; squamous cell carcinoma, pStage; pathological stage.

	Univariate analysis			Multivariate analysis		
Operative procedure (Lob or more/ Seg or Part)	5.896	2.336–14.885	< 0.01	5.008	1.954–12.834	< 0.01
Operative approach (RATS or VATS / H-VATS or Open)	0.647	0.376–1.111	0.11			
Pathology (SQ / Others)	1.615	0.898–2.901	0.10			
pStage (0-I / others)	0.660	0.375–1.161	0.15			

IP; interstitial pneumonia, DM; diabetes mellitus, COPD; chronic obstructive pulmonary disease, CRF; chronic renal failure, IHD; ischemic heart disease, BI; Brinkmann index, VC; vital capacity, FEV_1%; forced expiratory volume % in one second, CEA; carcinoembryonic antigen, Lob; lobectomy, Seg; segmentectomy, Part; partial resection, RATS; robotic-assisted thoracic surgery, VATS; video-assisted thoracic surgery, H-VATS; hybrid video-assisted thoracic surgery, Open; open thoracotomy, SQ; squamous cell carcinoma, pStage; pathological stage.

Survival analysis

Figure 1 illustrates relapse-free survival (RFS); there were no prognostic differences between the early and late periods (p = 0.89) in this regard. Figure 2 details overall survival (OS), and the prognoses in this case significantly differed between the early and late periods (p = 0.02).

Discussion

This study retrospectively evaluated changes in NSCLC patient characteristics, surgical approaches, perioperative factors (including postoperative morbidities), and prognoses over the last decade. Several factors, such as age, comorbidity, smoking history, the operative approach, and the procedure type, have been reported as postoperative morbidity risk factors in NSCLC patients who underwent pulmonary resection [19–24]. Another study reported that similar factors, such as sex, asthma, FEV_1%, and the procedure type, were significant risk factors for postoperative morbidity [25]. Our study supported these results as well; sex asthma, FEV_1%, and the procedure type were significant risk factors for postoperative morbidity. Further, the early period, sex, the CEA level, and operative procedure type were significant risk factors for severe postoperative morbidity.

The reported advantages of VATS (a MIS) are reduced pain, fewer postoperative morbidities, and a shorter length of hospital stay [6, 26–28]. As the VATS approach for NSCLC patients has become more widely accepted, predictions indicate that the number of patients eligible for surgery has also increased. In our study, older patients and those with more comorbidities were included in the late period, when the VATS approach was more common. Despite a decreased incidence of postoperative morbidities in the late period, the operative approach, including the VATS approach, was not a significant risk factor for

postoperative morbidity. We hypothesize that an increase in operative procedures less invasive than a lobectomy caused a decrease in postoperative morbidities.

Some reports have demonstrated that VATS has a prognostic advantage over thoracotomy, while others indicated no long-term survival advantage [7, 9–11]. Our previous study demonstrated that RFS and OS were better for patients receiving VATS than for those receiving a thoracotomy; another multivariate analysis of RFS and OS also confirmed the superiority of VATS [29]. In this study, the OS in the late period (with increased VATS) was better than that in the early period. Therefore, we suspect that OS improved because, in recent years, NSCLC prognosis has improved and patient bias influenced the prognosis in favor of the late period [30]. In this study, RFS did not differ between the early and late periods, despite an increase in VATS and other less invasive procedures in the late period. One study reported a higher local recurrence rate for patients receiving VATS than for those receiving thoracotomy [7], but others indicated that RFS for VATS and thoracotomy were comparable, supporting our results [11, 29]. Since the RFS did not differ between sublobar resection and lobectomy for patients with early-stage NSCLC [31], the VATS approach or sublobar resection as an MIS might become suitable indications for select patients.

This study has several limitations. Its design was retrospective, possibly resulting in unobserved confounding factors and selection bias. Further, this study was performed at a single institution.

Conclusions

This study evaluated the changes in NSCLC patient characteristics, surgical approaches, and perioperative factors over the last decade. In recent years, the patients were older and had more comorbidities, but the postoperative morbidity incidence decreased owing to an increase in sublobar resection. The prognosis of patients with NSCLC did not change in this study. Therefore, the VATS approach or sublobar resection as an MIS might become suitable indications for select patients.

Abbreviations

MIS; minimally invasive surgery, VATS; video-assisted thoracic surgery, NSCLC; non-small cell lung cancer, CEA; carcinoembryonic antigen, BI; Brinkman index, COPD; chronic obstructive pulmonary disease, IP; interstitial pneumonia, CCI; Charlson comorbidity index, %VC; percent-predicted vital capacity, FEV_1%; forced expiratory volume in 1 s as a percentage of forced vital capacity, H-VATS; hybrid VATS, RATS; robot-assisted thoracic surgery,OR; odds ratio, CI; confidence interval, RFS; relapse free survival, OS; overall survival.

Declarations

Ethics approval and consent to participate

The present study was conducted in accordance with the amended Declaration of Helsinki. The Institutional Review Boards of Kanazawa Medical University approved the protocol (approval number:

I392), and written informed consent was obtained from all of the patients.

Consent to publish

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to [our institutional restrictions e.g. them containing information that could compromise research participant privacy/consent], but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

N. M. performed the research, collected and analyzed the data and wrote the paper. M.I., S. I., A.Y., and Y.I. contributed to sample collection. H. U. contributed to supervision of this study and revision of the manuscript. All authors have read and approved the manuscript, and ensure that this is the case.

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Competing interests

The authors declare that they have no competing interests.

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Figures

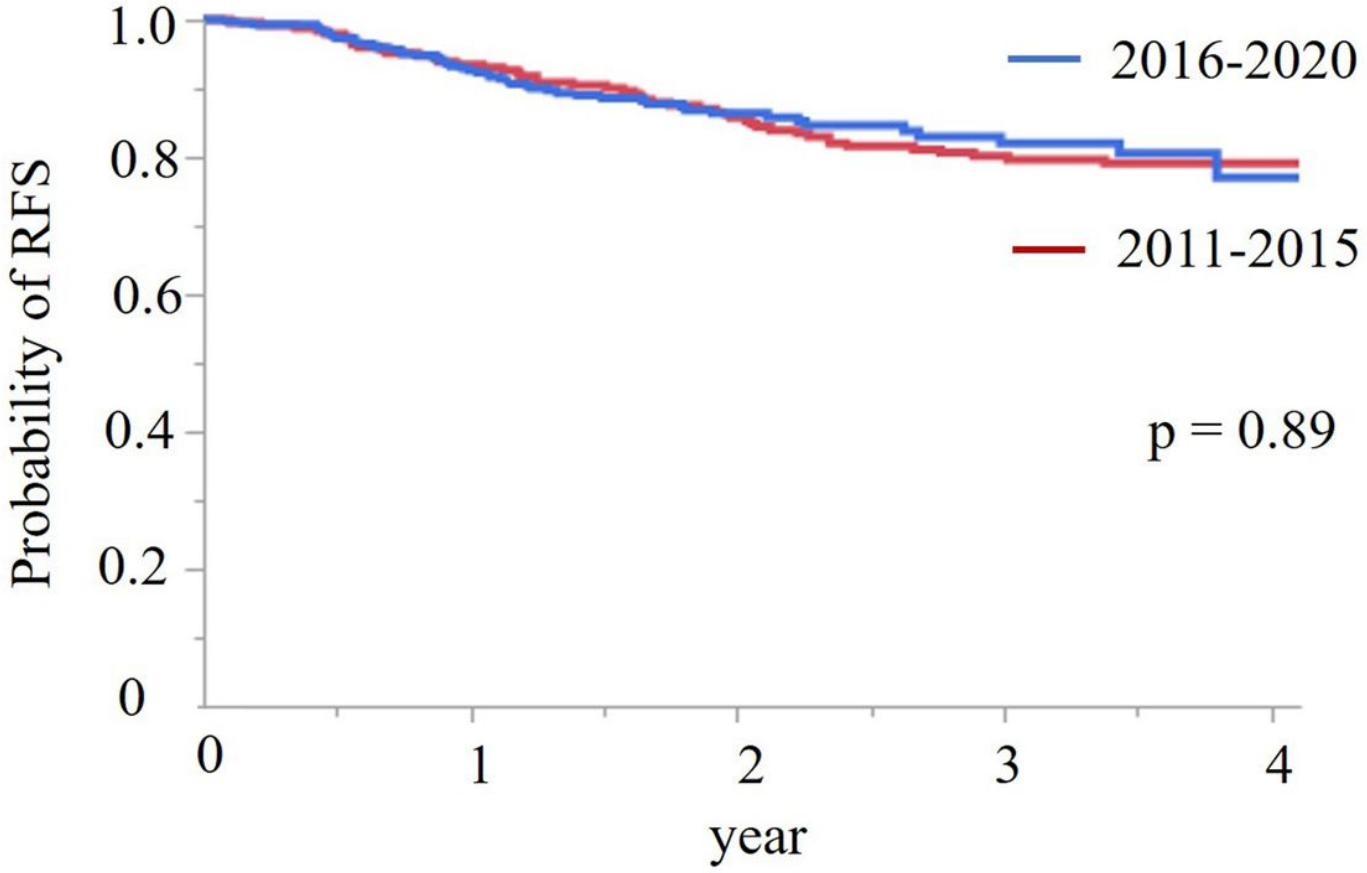

Figure 1

Relapse free survival

There was not significant difference between preceding period and late period (p=0.89)

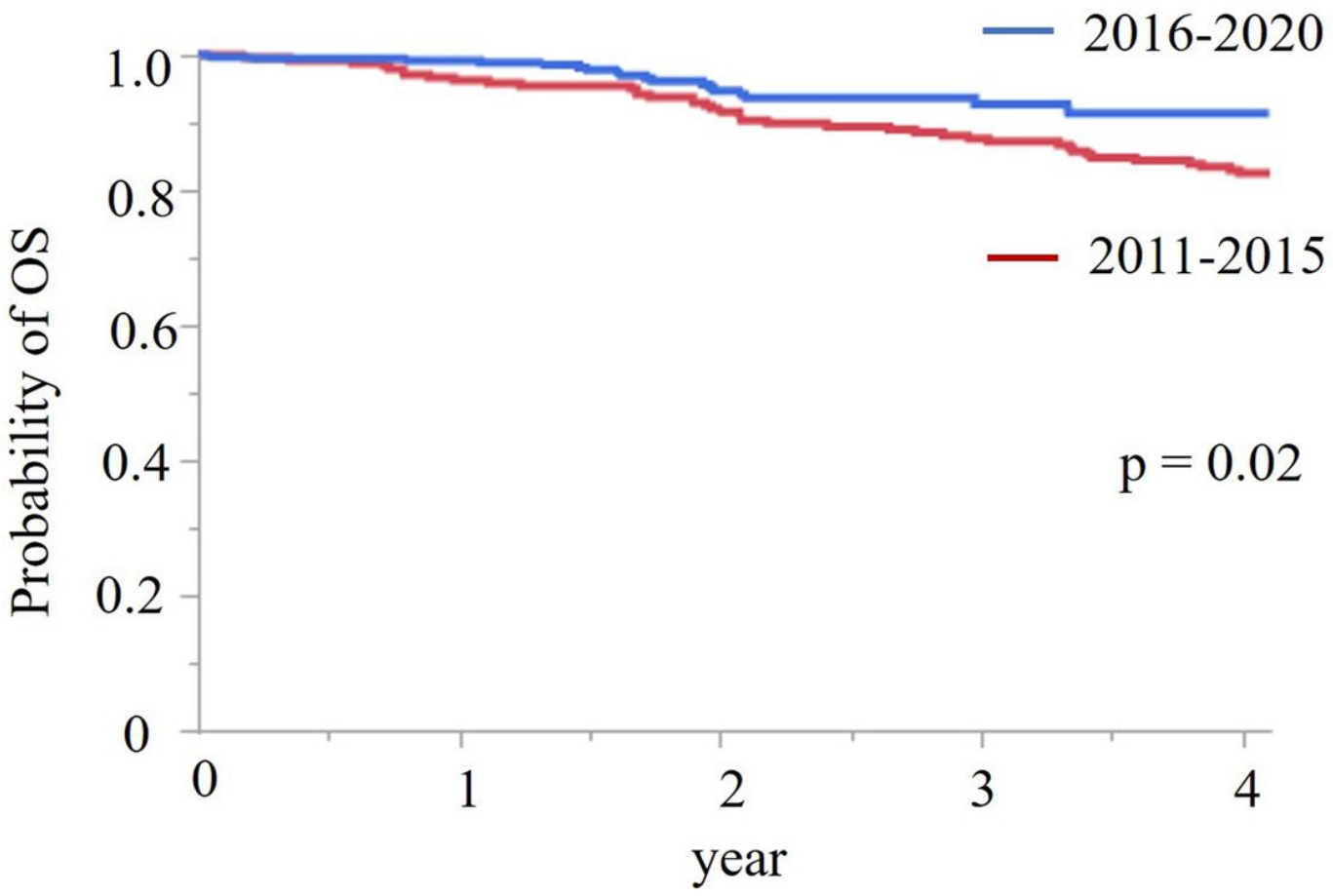

Figure 2

Overall survival

Overall survival of late period was significantly better than that of preceding period (p=0.02)