Impact of video-assisted thoracic surgery approach on postoperative mortality after lobectomy in octogenarians

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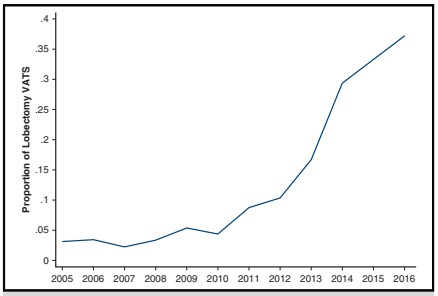
ABSTRACT

Objective: The number of octogenarians who present with localized lung cancer eligible for surgical resection is increasing. Video-assisted thoracic surgery lobectomy has been widely accepted, but the potential benefit in octogenarians is not well established, especially for postoperative mortality. This study aimed to assess the impact of a video-assisted thoracic surgery approach on postoperative mortality after lobectomy for lung cancer in octogenarians.

Methods: From January 2005 to December 2016, all patients aged more than 80 years who received lobectomy treatment for lung cancer were retrieved from the French Administrative Database. The end point was 30-day postoperative death. A propensity score was generated with 16 pretreatment variables and used to create balanced groups with matching (578 matches 1:1). Results are reported as odds ratios and 95% confidence intervals.

Results: Of the 75,892 patients operated for lobectomy during this period, 3560 were octogenarians. Video-assisted thoracic surgery was performed in 16.7% (n = 597) of cases, and thoracotomy was performed in 83.23% (n = 2963) of cases. From 2005 to 2016, the number of patients aged more than 80 years who were operated for lung cancer increased from 160 to 456 patients per year, and the proportion of lobectomy performed by video-assisted thoracic surgery increased as well (from 3.13% to 37.28%). Unmatched postoperative mortality was 3.85% (n = 23) for video-assisted thoracic surgery versus 7.9% (n = 234) for thoracotomy ($P < .0001$). Matched postoperative mortality was significantly lower in the video-assisted thoracic surgery approach with an odds ratio of 0.51 (95% confidence interval, 0.27-0.96; $P = .038$).

Conclusions: Video-assisted thoracic surgery was significantly associated with reduced postoperative mortality compared with open thoracotomy after lobectomy for lung cancer in octogenarians. (J Thorac Cardiovasc Surg 2019;■:1-8)



Increase in the rate of lobectomies performed by VATS in French octogenarians.

Central Message

More and more octogenarians are fit for surgical management of localized LC. VATS techniques significantly reduce postoperative mortality after lobectomy in this population.

Perspective

The life expectancy of octogenarians in western countries is approximately 10 years. A minimally invasive approach such as VATS lobectomy is a surgical management option with acceptable postoperative mortality that should be offered to octogenarians with localized LC.

See Commentary on page XXX.

THOR

Lung cancer (LC) is the fourth most common type of cancer, with estimations of more than 234,030 new cases in 2018. It is the leading cause of cancer death with approximately 154,050 cases per year, which represents 25% of all cancer deaths in the United States.[1] LC is diagnosed at a median age of 70 years in the Western world, and the probability of developing LC after 70 years of age is approximately 6.1% for men and 4.8% for women.[1,2] According

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Abbreviations and Acronyms
CCI = Charlson Comorbidity Index
LC = lung cancer
OT = open thoracotomy
PS = propensity score
VATS = video-assisted thoracic surgery

to the statistical analysis issued by the US Department of Health and Human Services in 2015, the life expectancy of octogenarians is increasing, and the total population of octogenarians will increase by 50% to 70% in Europe and the United States over the next 20 years.[3] As a result, thoracic surgeons are increasingly faced with elderly patients, particularly octogenarians, with localized LC for whom surgical management is a subject of debate. At present, lobectomy remains the best treatment for localized LC.[4] When video-assisted thoracic surgery (VATS) is used, there is a significant benefits in terms of postoperative pain, respiratory complications, and length of hospital stay after lobectomy.[5-8]

Since the 1990s, many publications have highlighted the feasibility of LC surgery in octogenarians and the importance of establishing a precise preoperative evaluation of cardiopulmonary function in these patients.[9] In 2011, Rivera and colleagues[10] described the specificities for surgical management of octogenarians using data from Epithor (French clinical database).

However, the available data regarding the results of LC surgery in octogenarians are based on small sample sizes, especially as regards the benefit of VATS on postoperative mortality,[9,11-17] making it difficult to draw conclusions about the benefit of VATS in this particular population. The aim of this study was to assess the impact of a VATS approach compared with open thoracotomy (OT) for lobectomy in octogenarians by using the French national administrative database. This database collects data from all hospitals in France performing lobectomy for LC and is more representative than data collected from specialized centers alone. A propensity score (PS) matching analysis was used to yield a more powerful and comprehensive comparison of postoperative mortality.

MATERIALS AND METHODS

Data Source and Study Population

All data for patients who underwent pulmonary resection for LC in France from January 2005 to December 2016 were collected from the national administrative database. This database, the Programme de Médicalisation des Systèmes d'Information, was inspired by the US Medicare system. The reliability and validity of Programme de Médicalisation des Systèmes d'Information data have been assessed.[18] Routinely collected medical information includes the principal diagnosis, secondary diagnoses, and procedures performed. Diagnoses identified during the hospital stay are coded according to the International Classification of Diseases, Tenth Revision.[19] We selected patients in whom a diagnosis of primary LC was coded as the principal discharge diagnosis (all Codes C34). Procedures are coded according to the Classification Commune des Actes Médicaux. For all patients, LC was proven by pathology analyses according to the 2004 World Health Organization classification of LC.[20] Surgery-related variables included the surgical technique: thoracotomy or VATS. The video of the VATS technique is available as Video 1.

Patients' Characteristics

Baseline demographics included age and gender. We included the following comorbidities that were available from the national administrative database: pulmonary disease (chronic bronchitis, emphysema), heart disease (coronary artery disease, cardiac arrhythmia, congestive heart failure, valvular heart disease, pulmonary artery hypertension, pulmonary embolism), peripheral vascular disease, alcoholism, liver disease, cerebrovascular events, neurologic disorders (hemiplegia or paraplegia), dementia, diabetes mellitus without complications, diabetes mellitus with complications, kidney disease, coagulopathy, leukemia, lymphoma, ulcer disease, history of malignant disease, obesity, and other therapies (preoperative chemotherapy, steroids). We also calculated a modified Charlson Comorbidity Index (CCI) as a marker of comorbidity.[21]

Outcome Measurements

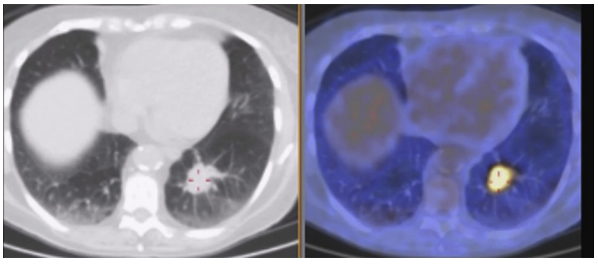
Postoperative mortality was defined as any patient who died in hospital (including transferred patients) within the first 30 days after the operation and those who died later during the same hospitalization.

Variables Used for Propensity Score Analysis

Variables used to estimate the PS were age, sex, comorbidities (pulmonary disease, heart disease, peripheral vascular disease, neurologic diseases, liver disease, kidney disease, coagulopathy, hematologic disease, infectious disease, and metabolic disease), other treatment, modified CCI score, type of medical center, hospital volume, and year of surgery.

Statistical Analysis

To determine the independent factors of in-hospital death, we first performed univariate analysis with the chi-square test for binary and categoric variables and a *t* test for continuous variables. The PS is the conditional probability of assignment to a particular treatment given a vector of observed covariates.[22] PS matching was used to balance the distributions of measured potentially confounding covariates for patients treated by VATS or OT. A mirrored histogram was used to measure the discriminatory ability of the PS matching. Matching used a search algorithm to find a set of weights for each covariate so that optimal balance is achieved after matching.[23] We used 1:1 matching without replacement in descending order with a caliper of 0.01. We evaluated PS matching by its ability to balance the measured covariates between VATS and OT by reducing the standardized



VIDEO 1. VATS left lower lobectomy for pulmonary adenocarcinoma. Video available at: http://www.jtcvs.org.

difference,[24] which is the difference between sample means in the VATS and OT groups divided by the standard deviation in the treatment group overall.[23] For postoperative mortality, a logistic regression model was used to generate odds ratios, *P* values, and confidence intervals. STATA 14 statistical software (StataCorp, LP, College Station, Tex) and R statistical software, for which we used Harrell's Design library (http://www.r-project.org), were used for the analyses.

RESULTS

Study Cohort

Of the 75,892 patients who underwent lobectomy from January 2005 to December 2016, 3560 were octogenarians. Lobectomy was performed by VATS in 597 patients (16.77%), and OT was performed in 2963 patients (83.23%). There was a continuous increase in the number of patients aged more than 80 years who were operated for LC over the study period, going from 160 patients in 2005 to 456 patients in 2016 (Figure 1). Moreover, there was a progressive increase in the proportion of VATS lobectomies, from 3.13% in 2005 to 37.28% in 2016 (Figure 2).

Unmatched patient demographics and hospital characteristics are presented in Table 1. In the OT group, there was a significantly greater proportion of men and younger patients. They also tended to have a history of pulmonary, heart, and vascular disease, with a CCI score of 3 or greater and other treatment, but a lower likelihood of liver disease (Table 1). VATS was performed in all health center types, but significantly more often in centers that saw more than 21 lobectomies per year (Table 1).

The characteristics of the matched groups are outlined in Table 2. In the matched samples, 578 patients were balanced in each group, and none of the patient characteristics are significantly different for the 2 groups (Table 2).

Propensity Score Estimation

The mirrored histogram shows the well-balanced distribution of the covariates after PS matching (Figure 3). The median distribution of standardized biases was 0.022 for the matching approach (Table 2). The standardized difference never reached the value of 10% (Table 2), which shows that the covariates of 2 groups were well balanced by matching.[25]

Postoperative Mortality

Unmatched crude postoperative mortality was 3.85% (n = 23) for VATS versus 7.9% (n = 234) for OT ($P < .0001$). After matching, postoperative mortality was 3.46% (n = 20) for VATS versus 6.57% (n = 238) for OT. Over the time period, matched-adjusted postoperative mortality significantly decreased ($P = .04$) (Figure 4). Matched postoperative mortality was significantly lower in the VATS sample with an odds ratio of 0.51 (95% confidence interval, 0.27-0.96; $P = .038$).

DISCUSSION

In 2015, LC was the second leading cause of death after heart disease in the American population of octogenarians and the leading cause of death by cancer, with approximately 40,000 attributed deaths in 2015.[1] However, it has been noted that age had a stronger impact than comorbidities on the probability of being offered surgical treatment.

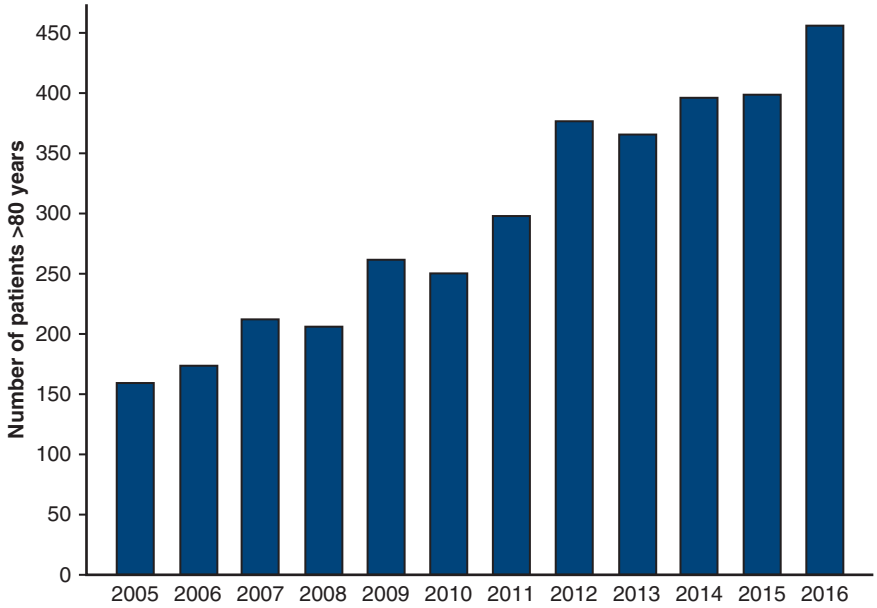


FIGURE 1. Number of patients aged more than 80 years treated by lobectomy each year from 2005 to 2016. The adhesion of the thoracic surgeons to the VATS program is highlighted by the increasing number of patients who were operated with the VATS approach for lobectomy.

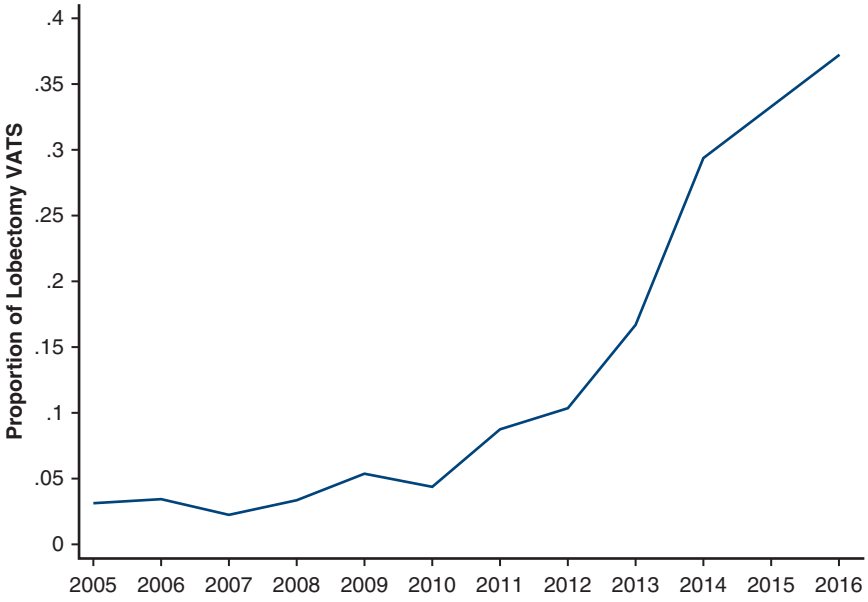


FIGURE 2. Proportion of octogenarians undergoing lobectomy with the VATS technique each year from 2005 to 2016, highlighting the growth of the VATS program for lobectomy in France. *VATS*, Video-assisted thoracic surgery.

Indeed, elderly patients without significant comorbidities were less likely to be recommended surgery compared with younger patients with significant comorbidities.[26]

In 2015, an 80-year-old French man was expected to live for an additional 8.6 years and a French woman for 10.8 more years. As a result, radical management for localized LC should be considered a treatment option.[3]

Since the end of the 1990s, surgeons have revolutionized the surgical management of the elderly. In parallel, research has highlighted the predictable changes in pulmonary physiology occurring with surgery and anesthesia and developed existing knowledge of the factors associated with postsurgical complications. Lobectomy reduces lung capacity, increases diaphragm dysfunction, and impairs gas exchange, cough, and mucociliary clearance, leading to the development of postoperative complications particularly in patients with chronic obstructive pulmonary disorder and the elderly.[9]

In the last decade, significant advances in anesthesia and surgery techniques have led to an increase in the number of elderly patients who are offered surgery, which can be seen in our study. Indeed, the appeal of VATS for lobectomy has been widely acknowledged by thoracic surgeons. In 2016, our data reveal that VATS was used on approximately 40% of octogenarians undergoing lobectomy. The sweeping use of VATS for lobectomy in France slightly exceeds the proportion of VATS lobectomy reported by Abdelsattar and colleagues[27] from the US National Cancer database (30.5%), but is lower than the 63% reported in the Society of Thoracic Surgeons database.[28] This upwards trend could be explained by the reports of decreased postoperative complications and the benefits for patients with a history of pulmonary disease, like those seen in our study.[29]

Postoperative Mortality

The impact of VATS lobectomy on postoperative mortality is not yet well established. There have been reported decreases in postoperative mortality in standard populations of patients with LC who are operated with the VATS technique. The studies in question took patient records from 3 large databases (1 clinical database [European Society of Thoracic Surgery] and 2 administrative databases [SEER database and Nationwide Inpatient Sample database]) and used PS matching analyses.[30-32] However, several other studies (meta-analysis or from the French National Epithor database) did not report a difference between VATS and OT techniques in a general population with localized LC.[5-8,33] A recent article from the American College of Surgeons National Surgical Quality Improvement Program reported less postoperative mortality after VATS in patients aged less than 75 years, but not for patients aged 75 to 80 years.[34] Moreover, recent results from large randomized controlled trials comparing VATS with OT for lobectomy found no difference in postoperative mortality.[35] The mean age in these studies ranges from 58 to 75 years.

The patients in our population were all aged more than 80 years, with a crude postoperative mortality of 3.85% after VATS and 7.9% after OT. Few articles have been published regarding postoperative mortality after lobectomy in octogenarians. Studies that have included a series of more than 100 patients report postlobectomy mortality

TABLE 1. Patients aged more than 80 years: Unmatched baseline characteristics

	VATS (n = 597)	OT (n = 2963)	*P* value
Demographics			
Gender			.001
Male	380 (63.65%)	2083 (77.05%)	
Female	217 (36.35%)	880 (22.95%)	
Age (y)	82.25 ± 2.12	82.07 ± 2.08	.05
History			
Pulmonary disease	170 (14.7%)	983 (33.2%)	.025
Heart disease	139 (13.5%)	892 (30.1%)	.001
Peripheral vascular disease	46 (7.7%)	369 (12.4%)	.001
Liver disease	6 (1%)	9 (0.3%)	.016
Neurologic disease	25 (4.1%)	177 (6%)	.085
Kidney disease	28 (4.7%)	149 (5%)	.728
Anemia	66 (11%)	296 (10%)	.432
Hematologic disease	18 (3%)	128 (4.3%)	.142
Infectious disease	6 (1%)	33 (1.1%)	.816
Metabolic disease	225 (37.7%)	1180 (39.8%)	.330
Other treatment	57 (9.5%)	417 (14%)	.003
Modified CCI score			.003
0	247 (41.4%)	1011 (34.1%)	
1	76 (12.7%)	359 (12.1%)	
2	55 (9.2%)	357 (12%)	
≥3	219 (36.7%)	1236 (41.7%)	
Hospital characteristics			
Type			.895
Nonteaching	57 (9.5%)	300 (10.1%)	
Private	307 (51.5%)	1526 (51.5%)	
Teaching	233 (39%)	1137 (38.4%)	
Volume (procedures/y)			.0001
<4	1 (0.1%)	24 (0.8%)	
4-21	23 (3.9%)	270 (9.1%)	
>21	573 (96%)	2669 (90.1%)	

VATS, Video-assisted thoracic surgery; *OT*, open thoracotomy; *CCI*, Charlson Comorbidity Index.

rates ranging from 2% to 6%.[15-17] The higher rate of postoperative mortality in our study could be due to several factors. First, approximately 40% of patients had a CCI score 3 or greater even after matching, including at least a history of pulmonary with cardiac disease and a metabolic dysfunction, which has been correlated to a relative risk of death after 80 years of age of 12.76 by Charlson and colleagues.[21] A recent article by Eguchi and colleagues,[36] dealing with the cause of death after lobectomy for stage I LC, showed that 30- and 90-day mortality were caused by cardiopulmonary complications, and that low predictive postoperative diffusing capacity of the lung for carbon monoxide was an independent predictor of 1-year mortality and noncancer-specific mortality.[36] Therefore, they also highlighted that noncancer-specific mortality was higher than cancer-specific mortality in patients aged more than 75 years until 2.5 years after surgery.[36]

So, the mechanism to obtain a lower postoperative mortality with the VATS approach seems to be linked to better postoperative pulmonary function, especially in octogenarians. Detillon and Veen[17] recently highlighted percentage of predicted forced expiratory volume in 1 second to be an independent factor of postoperative mortality in individuals aged more than 80 years. The postoperative recovery of forced expiratory volume in 1 second has been shown to be faster in patients who undergo minimally invasive anatomic lung resection compared with OT.[37] The benefit of the VATS approach seems to disappear after 3 months, and, at that point, loss of pulmonary function is equivalent for VATS and OT.[38]

Second, our study was conducted using the French administrative database, which includes all centers performing LC surgery in France whatever the type and the volume of activity. This could explain the higher postoperative mortality compared with other publications whose data were restricted to teaching hospitals or a group of centers with a significant volume of thoracic surgery.[11-16]

PS matching was used to balance covariates, and consequently the 2 groups were comparable in terms of preoperative comorbidities and hospital characteristics. Therefore, we were able to assess the impact of the chosen technique on postoperative mortality. Potential explanations for the lower postoperative mortality in the VATS group could be attributed to lower postoperative pain and to a de facto lower incidence of respiratory complications, as previously described.[5-8] However, octogenarians are a singular population, in whom the weight of preoperative comorbidities, especially histories of cardiac and pulmonary disease, is a major source of postoperative complications and postoperative mortality.

Only 1 set of recommendations for the management of elderly patients with LC has been published in the last years. However, these guidelines focus on surgery in the elderly, who are generally aged 70 to 80 years, and are based on small retrospective studies. No randomized control trials have been conducted on an elderly population whatever the treatment, and, as previously reported, the elderly are frequently underrepresented in clinical trials evaluating new cancer treatments or surgical techniques.[39]

Study Strengths and Limitations

We recognize that there are limitations to our study. Given our reliance on International Classification of Diseases, Tenth Revision codes for the selection of patients and the ascertainment of outcomes, there was a potential for misclassification or underdetection-related biases, especially for comorbidities. Coding practices vary significantly among institutions. Nevertheless, coding quality is checked by medical information professionals in each hospital to correct diagnoses and increase the number of recorded comorbidities. No details were available for certain center

TABLE 2. Patients' baseline characteristics in matched data with standardized difference

	VATS (n = 578)	OT (n = 578)	*P* value	Standardized difference
Demographics				
Gender				−0.022
Male	366 (63.32%)	375 (64.88%)	.713	
Female	212 (36.68%)	203 (35.12%)		
Age (y)	82.25	82.26	.924	−0.06
History				
Pulmonary disease	166 (28.72%)	161 (27.85%)	.794	−0.015
Heart disease	136 (23.53%)	147 (25.43%)	.495	0.039
Peripheral vascular disease	45 (7.79%)	48 (8.30%)	.746	0.017
Liver disease	3 (0.52%)	3 (0.52%)	1	0
Neurologic disease	25 (4.33%)	20 (3.46%)	.448	−0.039
Kidney disease	28 (4.84%)	26 (4.50%)	.781	−0.016
Anemia	64 (11.07%)	56 (9.69%)	.441	−0.045
Hematologic disease	18 (3.11%)	12 (2.08%)	.267	−0.055
Infectious disease	6 (1.04%)	2 (0.35%)	.256	−0.051
Metabolic disease	222 (38.41%)	237 (41%)	.435	0.046
Other treatment	56 (9.69%)	53 (9.17%)	.689	−0.021
Modified CCI score 0				
1	70 (12.11%)	72 (12.46%)	1	0
2	55 (9.52%)	49 (8.48%)	.538	−0.034
≥3	216 (37.37%)	233 (40.31%)	.305	0.06
Hospital characteristics				
Type				
Nonteaching	55 (9.5%)	56 (9.6%)		
Private	302 (52.25%)	299 (51.8%)	.860	−0.01
Teaching	221 (38.25%)	223 (38.6%)	.904	0.04
Volume (procedures/y)	142.22 ± 5.96	134.55 ± 7.21	.412	−0.047
Overall PS				
Mean				0.027
Median				0.022

A standardized difference greater than 0.1 (10%) signified a meaningful imbalance in a given variable between treatment groups. *VATS*, Video-assisted thoracic surgery; *OT*, open thoracotomy; *CCI*, Charlson Comorbidity Index; *PS*, propensity score.

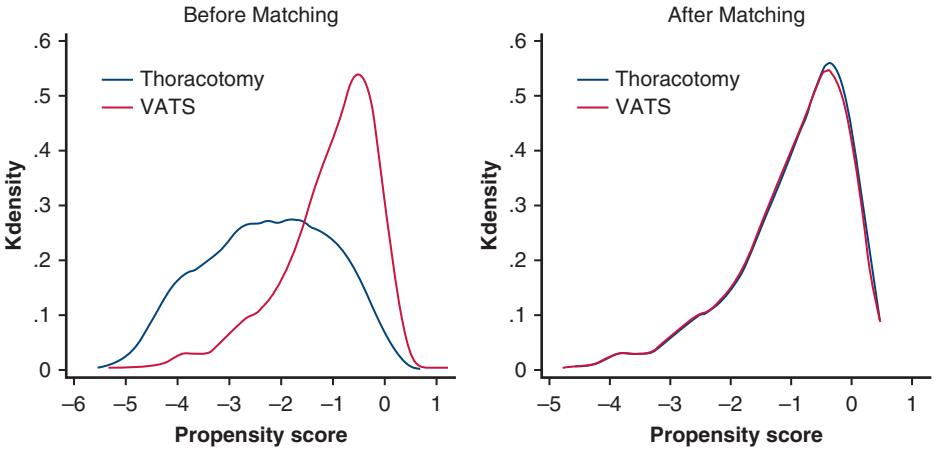


FIGURE 3. PS matching in each group of patients who underwent thoracotomy or VATS lobectomy. Each line represents the number of patients with the same PS in both groups. After matching, the lines are stackable; therefore, covariates are well balanced and the groups comparable. *VATS*, Video-assisted thoracic surgery.

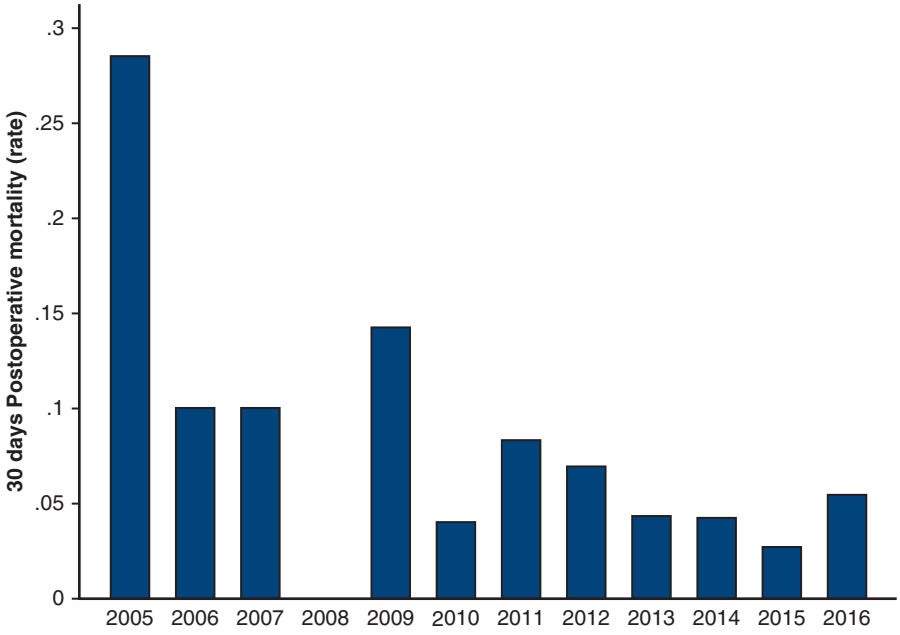


FIGURE 4. Thirty-day postoperative mortality rate for patients aged more than 80 years who underwent lobectomy from 2005 to 2016. As the use of VATS expanded, 30-day postoperative mortality decreased to a rate of approximately 0.5%.

characteristics (number of beds in surgery departments and intensive care units, number of days spent in intensive care, number of nurses and medical practitioners), the organization of the surgery (multidisciplinary team meeting, use of guidelines, surgeon qualifications, surgery performed by residents), or details about preoperative management (chemotherapy) and postoperative outcomes and complications.

The French Administrative database does not record LC information (type of cancer, stage [TNM classification], type of lobe involved), preoperative pulmonary function (preoperative forced expiratory volume, percentage predicted diffusing capacity of lung for carbon monoxide), American Society of Anesthesiologists score, and data for postoperative complications (prolonged air leaks, pneumonia, atelectasis, empyema, hemothorax, arrhythmia, myocardial infarction) and length of hospital stay. No information was available regarding the different types of OT (posterolateral or anterolateral OT, muscle-sparing OT) or the experience of each center in VATS lobectomy before this study.

Analyses using PS methods attempt to emulate randomized comparisons because they allow contrasts between patient groups that are on average similar on all observed confounders; however, unlike the randomized assignment of treatments, the PS typically does not balance covariates that were not observed. Matching reduces the sample size because matches may not be found for some patients. Although we used a PS to create comparable cohorts, we cannot be certain that the PS perfectly neutralized all of the confounding variables. Moreover, it is advisable to underline that PS cannot replace a randomized control trial. In randomized control trials, random allocation of patients to an experimental or a control arm guarantees that treatment allocation is unrelated to measured and unmeasured patient characteristics. It enables researchers to draw unbiased conclusions about a treatment, provided that the number of randomized patients is large enough to minimize random variation. However, in this study the large number of patients in both groups allowed for powerful comparisons. Our analyses were based on data from the French administrative database, which describes clinical practices over several years and includes both teaching and nonteaching hospitals.

CONCLUSIONS

Despite these limits, our study highlights the growing interest of surgical management of LC in octogenarians. Use of the VATS technique led to a significant decrease in postoperative mortality after lobectomy for LC in octogenarians.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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000 Impact of video-assisted thoracic surgery approach on postoperative mortality after lobectomy in octogenarians

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More and more octogenarians are fit for surgical management of localized LC. VATS techniques significantly reduce postoperative mortality after lobectomy in this population.