Original Article

Use of the anatomical formulae for predicted postoperative (PPO) evaluation overestimates the loss of FEV1 and DLCO after minimally invasive lung resections

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Background: Pulmonary function assessment is mandatory before oncological lung resection surgery. To do so, subjects undergo a pulmonary function test (PFT) and the calculation of predicted postoperative (PPO) values to estimate the residual lung function after surgery. The aim of this study is to evaluate the use of anatomical formulae in estimating postoperative pulmonary function in patients undergoing minimally invasive surgery (MIS).

Methods: This is a retrospective study. Patients affected by lung cancer who underwent pulmonary lobectomy or segmentectomy with MIS or thoracotomy approach at our center from June 2020 to May 2021 were considered. Exclusion criteria were: subjects who underwent atypical pulmonary resection surgery or pneumonectomy; and patients who underwent adjuvant therapy (chemotherapy or immunotherapy). PFT data measured before and 1 year after surgery were collected. In particular, postoperative PFT data, especially forced expiratory volume in the first second (FEV1) and diffusing capacity for carbon monoxide (DLCO), and PPO values calculated by the anatomical formulae were compared. Secondary endpoints were: analysis of the postoperative pulmonary function in patients who underwent lung resection with the standard approach (thoracotomy) and evaluation of the anatomical formulae accuracy in subjects operated through thoracotomy.

Results: The sample consisted of 48 patients operated on MIS (video-assisted thoracoscopic surgery and robotic-assisted thoracoscopic surgery) and 20 subjects who underwent thoracotomy for stage I–IIA and I–IIB lung cancer in both groups. The anatomical formula seemed to underestimate the postoperative FEV1% by 8.65% [interquartile range (IQR), 0.5–17.28%; P<0.001]. Furthermore, when comparing postoperative $PPO_{DLCO\%}$ and post-operative DLCO%, a significant difference was shown with an underestimation of the actual postoperative value of 2.78% (IQR, −3.63% to 10.47%; P=0.045).

Conclusions: Our results confirmed that the anatomical formulae currently used to predict postoperative pulmonary function are reliable in the case of the standard approach (thoracotomy), while they tend to overestimate the loss of FEV1 and DLCO in the postoperative period in patients who were operated on MIS, thus excluding some subjects from the operation.

Keywords: Lung function; spirometry; lobectomy; video-assisted thoracoscopic surgery (VATS); robotic-assisted thoracoscopic surgery (RATS)

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Introduction

The standard of care for stage I and stage II non-small cell lung cancer (NSCLC) is surgical resection. Although the appropriate surgical procedure is anatomical resection, the extent of the resection (segmentectomy or lobectomy) depends on the site and size of the tumor (1).

The decision to take the patient to the operating room depends on a comprehensive assessment which includes their preoperative functional respiratory, cardiac, and anesthesia assessment.

As far as pulmonary function is concerned, the first step in studying a patient candidate for thoracic surgery is performing a pulmonary function test (PFT) to assess the forced expiratory volume in the first second (FEV1) and diffusing capacity for carbon monoxide (DLCO) values. If both values exceed 80% of the predicted, defining a low surgical risk, surgery can proceed without further pulmonary function analysis. Conversely, the patient should undergo additional assessments in cases where FEV1 and DLCO are <80% [e.g., predicted postoperative (PPO) pulmonary function and further tests if needed, such as low-technology exercise tests, perfusion lung scintigraphy, and cardiopulmonary exercise testing] (2).

The first method for ascertaining that a patient may be a candidate for major lung resection is the calculation of postoperative predictors such as PPO_{FEV1} and PPO_{DLCO}. The resected lung volume is a theoretical determinant of postoperative respiratory function; this can be obtained using the anatomical or scintigraphic formula. Indeed, PPO values are influenced by several factors, such as the surgical technique used (minimally invasive or traditional), the lobe resected (upper or lower), and concomitant lung diseases (3).

Various formulas can estimate these values, although the anatomical is the most widely used (3). The postoperative predicted FEV1 and DLCO consider preoperative PFT values and the amount of lung parenchyma resected during surgery. In particular, PPO_{FEV1} is regarded as a significant predictor of the amount of resectable parenchyma and postoperative risks and complications (4-6).

The anatomical formulae for calculating PPO_{FEV1} and PPO_{DLCO} are $PPO_{FEV1} = preoperative\ FEV1 \times (1 - a/b)$ and $PPO_{DLCO} = preoperative\ DLCO \times (1 - a/b)$, where a is the number of lung segments to be removed, and *b* is the total number of lung segments, i.e., 19.

Our objective for this study is to assess the accuracy of the anatomical formulae in estimating pulmonary functionality in patients undergoing anatomical pulmonary resection through minimally invasive surgery (MIS) (*Figure 1*). We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-447/rc).

Highlight box

Key findings

- The anatomical formulae currently used to predict postoperative pulmonary function overestimate the loss of forced expiratory volume in the first second (FEV1) and diffusing capacity for carbon monoxide (DLCO) in the postoperative period in patients operated on minimally invasive surgery, potentially excluding good candidates from operation.

What is known and what is new?

- Surgery is the gold standard for I–IIA and I–IIB stage non-small cell lung cancer, and patients must be studied carefully preoperatively.
- The anatomical formulae currently used in calculating the postoperative predicted FEV1 and DLCO should consider the surgical approach since this formula tends to deviate more from the actual postoperative pulmonary function test data when patients are operated on minimally invasive technique.

What is the implication, and what should change now?

- The anatomical formulae tend to overestimate the loss of FEV1 and DLCO (as well as FEV1% and DLCO%) in the postoperative period in the case of the minimally invasive approach, potentially excluding good candidates from surgery. A revision of the formula should be carried out considering the type of surgical approach intended for the specific patient.

Methods

This is a retrospective study that has been conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by AOU Maggiore della Carità di Novara Institutional Review Board (IRB approval No. 974, CE /20, 15/10/2021) and informed consent was taken from all the patients. Patients affected by stage I–IIA to I–IIB lung cancer undergoing pulmonary lobectomy and segmentectomy through MIS [video-assisted thoracoscopic surgery (VATS) and robotic-assisted thoracoscopic surgery (RATS)] or open approach (thoracotomy) from June 2020 to May 2021 at Ospedale Maggiore della Carità di Novara (Novara, Italy) were considered in our study. We have applied the following exclusion criteria: subjects younger than 18 years of age; patients older than 18 years of age who underwent atypical pulmonary resection surgery or pneumonectomy; and subjects who underwent adjuvant

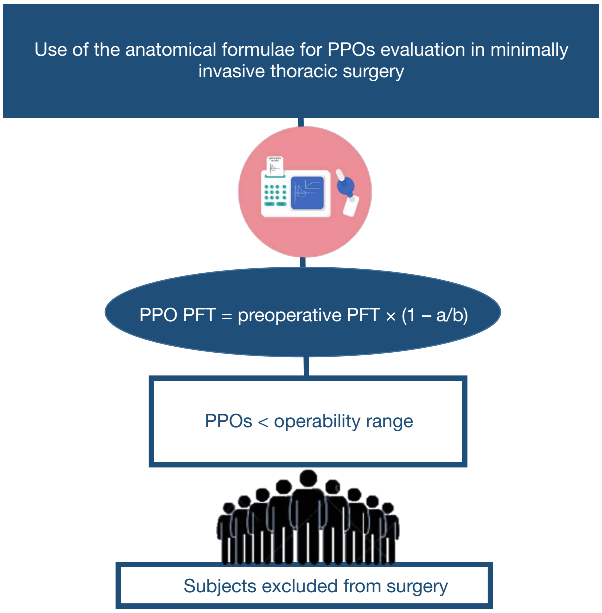

Figure 1 Operability evaluation flowchart. PPO, predicted postoperative; PFT, pulmonary function test.

therapy (chemotherapy or immunotherapy). Patients were contacted one year after surgery and invited to perform a PFT consisting of basal and post-bronchodilation spirometry (using salbutamol, 400 µg), DLCO assessment, and plethysmography. At this stage, patients signed informed written consent to be enrolled in the study.

Valuable data for the evaluation included FEV1, FEV1%, DLCO, DLCO%, forced vital capacity (FVC), and FVC%. In addition, residual volume (RV) and total lung capacity (TLC) values were collected. Pain was evaluated one year after surgery during PFT follow-up; subjects were asked to define their grade of pain according to the Numeric Rating Scale (NRS-11). Histological diagnoses were also collected.

Objectives of the study

The primary endpoint of the study was to evaluate the differences between actual and PPO values calculated with the anatomical formulae previously illustrated. The same formulae were also used to calculate the predicted PPO% values. The postoperative predicted values obtained were compared with the actual postoperative values measured one year after surgery. The aim was to assess how reliable the anatomical formulae were in estimating postoperative PFT values in subjects who underwent anatomical pulmonary resection with MIS, in particular VATS and RATS.

Secondary endpoints were: analysis of the postoperative pulmonary function in patients who underwent lung resection with the standard approach (thoracotomy) and evaluation of the anatomical formulae accuracy in subjects operated through thoracotomy.

Statistical analysis

Demographic and clinical characteristics were summarized using descriptive statistics. In particular, absolute frequencies and percentages were used for qualitative variables. At the same time, arithmetic means, and standard deviation constituted the summary indices for quantitative variables in the Gaussian distribution and median and interquartile range in the non-Gaussian distribution of variables. The difference in respiratory function parameters was assessed using a non-parametric Mann-Whitney test.

A P value of less than 0.05 was considered statistically significant. Statistical analyses were conducted with STATA v. 16 software.

Results

The sample consisted of 68 patients affected by stage I–IIA and I–IIB lung cancer, especially pulmonary adenocarcinoma. Patients' pre- and post-operative characteristics are presented in *Table 1*, while PFT data are summarized in *Table 2*. Forty-eight subjects were operated on through MIS (MIS group): 7 patients underwent RATS and 41 subjects underwent VATS. While 20 patients underwent lung resection through thoracotomy (Open group); in particular, 13 patients underwent conversion to an open approach due to: vessel injury (n=5), benign adenopathy (n=4), and perivascular fibrosis (n=4); 7 subjects underwent pulmonary open lobectomy because of the dimension of the tumor >5 but <7 cm. RATS was performed with the Da Vinci Xi robot, using 4 robotic arms; while, VATS was performed with a different number of ports, according to the anatomy of the patient and the location of the tumor. Patients' surgery characteristics are presented in *Table 3*.

Comparison of postoperative PFT data and PPO values in the MIS group

When comparing PPO_{FEV1} and postoperative FEV1 (*Table 4*), we highlighted a statistically significant difference; in particular, the anatomical formula tended to underestimate

Table 1 Patients' pre- and post-operative characteristics

Variables	MIS group (n=48)	Open group (n=20)
Sex: male	25 (52.08)	12 (60.00)
Age at surgery, years	70.47±8.03	68.15±9.04
Smoking history		
Active smoker	6 (12.50)	2 (10.00)
Former smoker	26 (54.17)	10 (50.00)
Non-smoker	16 (33.33)	8 (40.00)
COPD	5 (10.42)	2 (10.00)
Histology		
Adenocarcinoma	34 (70.83)	15 (75.00)
Squamous cell carcinoma	9 (18.75)	4 (20.00)
Carcinoid	5 (10.42)	1 (5.00)
Lung cancer stage		
IA	33 (68.75)	3 (15.00)
IB	11 (22.92)	2 (10.00)
IIA	1 (2.08)	8 (40.00)
IIB	3 (6.25)	7 (35.00)
Pain at follow-up (1 year)		
No pain	42 (87.50)	16 (80.00)
Mild pain	5 (10.42)	3 (15.00)
Moderate pain	1 (2.08)	1 (5.00)
Severe pain	0	0
Post-operative complications		
Atrial fibrillation	0	2 (10.00)
Prolonged air leak (>5 days)	5 (10.42)	1 (5.00)
Persistent pleural space	2 (4.17)	1 (5.00)
Length of hospital stay, days	7.97 [5.75–8]	8.45 [7–9]
Chest tube, days	4.31 [2–4]	4.89 [3–4.5]

Data are presented as mean ± standard deviation, median [interquartile range] or n (%). MIS, minimally invasive surgery; COPD, chronic obstructive pulmonary disease.

the observed postoperative FEV1 value by 0.19 L (IQR, −0.01 to 0.37 L; P<0.001) in subjects who underwent anatomical lung resection with MIS. Similarly, we found a significant difference when comparing $PPO_{FEV1\%}$ and measured postoperative FEV1%. The anatomical formula underestimated the actual postoperative FEV1% by 8.65% (IQR, 0.5–17.28%; P<0.001).

Finally, when comparing postoperative $PPO_{DLCO\%}$ and DLCO%, a significant difference was shown with an underestimation of the actual postoperative value of 2.78% (IQR, −3.63% to 10.47%; P=0.045).

Comparison of preoperative and postoperative PFTs data: Open vs. MIS

Statistical analysis showed a better recovery of respiratory function for the MIS group compared with the thoracotomy approach (*Table 5*). For FEV1, the change at 1 year was −0.32 L (IQR, −0.63 to −0.22 L) for the Open group and −0.22 L (IQR, −0.38 to 0.01 L) for the MIS group, with P=0.01. Similarly, a 1-year difference of −11% (IQR, −18.5% to −7%) for the Open group and −7% (IQR, −12.5% to 2.5%) for the MIS group was shown for FEV1%, with P=0.01. A statistically significant difference was also observed for FVC and FVC% values. Specifically, the change in FVC at 1 year was −0.32 L (IQR, −0.56 to 0.04 L) for the Open group and −0.06 L (IQR, −0.3 to 0.17 L) for the MIS group, with P=0.049. Consequently, the mean FVC% loss was −8% (IQR, −14% to 3.5%) in the Open group and −0.5% (IQR, −7.5% to 6.5%) in the MIS group, with P=0.03. For all other PFT values analyzed, no statistically significant difference was found.

Comparison of postoperative PFT data and PPO values in the Open group

The comparison between measured postoperative FEV1 and PPO_{FEV1} showed no significant differences (P=0.06) (*Table 4*). Similarly, the same analyses were performed for postoperative DLCO and PPO_{DLCO}, as well as postoperative DLCO% and $PPO_{DLCO\%}$, without proving any statistical differences. However, when comparing $PPO_{FEV1\%}$ and postoperative FEV1%, a statistical difference was found since the anatomical formula underestimated the actual postoperative FEV1% by 3.26% (P=0.03).

Discussion

In our study, the actual postoperative values of FEV1, FEV1%, DLCO, and DLCO% measured 1 year after surgery were compared with the predicted values of PPO_{FEV1}, $PPO_{FEV1\%}$, PPO_{DLCO}, and $PPO_{DLCO\%}$ calculated using the anatomical formula. The anatomical formula overestimates the loss of PFT values in the case of the

Table 2 Preoperative and postoperative PFT data

PFT values	MIS preoperative PFT	MIS postoperative PFT	Open preoperative PFT	Open postoperative PFT
FEV1 (L)	2.24 [1.95–2.52]	2.07 [1.76–2.42]	2.46 [2.01–2.77]	2.03 [1.54–2.33]
FEV1%	85.5 [73.5–103]	82.08 [68.75–95.75]	90.45 [80.75–106]	75.3 [62–87.5]
FVC (L)	3.11 [2.6–3.57]	3.07 [2.44–3.68]	3.22 [2.65–3.80]	2.91 [2.39–3.42]
FVC%	91.5 [83–104]	92.39 [82.75–106]	90.04 [83–100]	82.55 [75.5–89.25]
DLCO (mL/min/mmHg)	17.26 [14.24–20.78]	14.6 [11.84–17.06]	17.73 [14.21–21.10]	13.57 [11.41–16.08]
DLCO%	73 [62–85.5]	63.64 [53–74.50]	74.6 [65.5–83]	56.75 [49.75–68.75]
TLC (L)	5.88 [4.72–6.85]	5.83 [4.62–6.59]	5.79 [4.86–6.24]	5.81 [4.38–5.83]
RV (L)	2.55 [2–3.6]	2.39 [1.77–2.62]	2.61 [1.96–2.77]	2.29 [1.7–2.51]

Data are presented as median [interquartile range]. PFT, pulmonary function test; MIS, minimally invasive surgery; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; DLCO, diffusing capacity of the lungs for carbon monoxide; TLC, total lung capacity; RV, residual volume.

minimally invasive technique for $PPO_{FEV1\%}$, where there was an overestimation of the loss of 8.65% (P<0.001). On the other hand, this difference was much less pronounced in the case of the thoracotomy technique, where the formulae seemed to be more reliable in predicting postoperative pulmonary function.

As a result, subjects may be excluded from surgery (pulmonary lobectomy or segmentectomy), even if that surgery is performed with a minimally invasive technique, such as VATS or RATS. Baser *et al.* reported that 37% of surgically treatable lung cancer patients are excluded from surgery due to reduced preoperative lung function (7).

Recently, Shibazaki *et al.* demonstrated that the measured postoperative FEV1 values were significantly higher than the PPO_{FEV1} values calculated by the subsegmental method. Shibazaki's group showed that the postoperative FEV1 tended to improve over 3 and then 12 months after surgery; in particular, the measured postoperative FEV1 was 8% higher at 3 months and 13% higher at 12 months after surgery than the PPO_{FEV1} calculated with the anatomical formula. Hypothetically, this recorded difference could be due to improved surgical techniques and the introduction of the minimally invasive procedure (8). In 2007, Brunelli *et al.* conducted a large-sample prospective study (>200 subjects) showing that actual respiratory function reaches predicted values (PPO) within 1 month after surgery, further improving 3 months later (9). Consequently, Shibazaki's and Brunelli's studies agree with our study's comparison of actual postoperative values with postoperative predicted values calculated with the anatomical formula.

MIS superiority in pulmonary function recovery has been acknowledged many times. This difference may be due precisely to the low degree of invasiveness of the VATS and RATS techniques since minimally invasive operations produce very little damage to the intercostal muscles and nerves, thus leading to a lower incidence of morbidity and pleural adhesion. Our study recorded an 11% loss of FEV1% in patients operated with the traditional technique versus a 7% loss in patients managed with the minimally invasive procedure. Similarly, an 8% loss of FVC% was shown in the Open group versus 0.5% in the MIS group.

Nakata *et al.* compared pre and postoperative PFT data from patients who underwent minimally invasive lobectomy with those who underwent open lobectomy. In this case, no significant differences in the recovery of respiratory function 1 year after surgery were found; however, it is possible that no differences were found because of the small number of patients analyzed in the sample (n=21) (10). Other studies have compared the loss of FEV1 and FVC between VATS/RATS and open in the postoperative time; most of these studies, however, analyzed differences in the immediate postoperative period or at 3–6 months, whereas there are currently few data at 1 year after surgery. Kaseda *et al.* (2000) evaluated FEV1% and FVC% 3 months after surgery; in this case, a loss of FEV1% of 15% was demonstrated in VATS-operated patients compared with 29% in anterolateral thoracotomy-operated patients. Similarly, a 3-month loss of 15% FVC% was shown in patients with the minimally invasive technique compared with a loss of 23% in patients operated via an open approach (11). Therefore, the two techniques had no significant difference regarding the change in static lung volumes (such as RV and

Table 3 Patients' surgical characteristics

Characteristics	MIS patients (n=48)	Open patients (n=20)
VATS, n (%)	41 (85.42)	
Uniportal	17 (41.46)	
Two-port	17 (41.46)	
Three-port	7 (17.07)	
RATS (Da Vinci Xi), n (%)	7 (14.58)	
Lobectomy, n (%)	30 (62.50)	18 (90.00)
RUL	12 (40.00)	4 (22.22)
ML	8 (26.67)	2 (11.11)
RLL	2 (6.67)	2 (11.11)
LUL	4 (13.33)	6 (33.33)
LLL	4 (13.33)	2 (11.11)
Bilobectomy		2 (11.11)
Segmentectomy, n (%)	18 (37.50)	2 (10.00)
Culmen	6 (33.33)	1 (50.00)
Lingula	2 (11.11)	
S1 right	2 (11.11)	
S2 right	1 (5.56)	1 (50.00)
S3 right	2 (11.11)	
S6 right	1 (5.56)	
S6 left	1 (5.56)	
S8 right	1 (5.56)	
S7–10 right	1 (5.56)	
S10 left	1 (5.56)	

VATS, video-assisted thoracoscopic surgery; RATS, robot-assisted thoracoscopic surgery; MIS, minimally invasive surgery; RUL, right upper lobe; ML, medium lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe.

TLC). Still, there was an appreciable difference in dynamic lung volumes, such as FEV1, FEV1%, FVC, and FVC%. Several studies have shown that posterolateral thoracotomy was associated with reduced respiratory excursion in the postoperative period, thus leading to a transient extrapulmonary restrictive syndrome (12,13).

Strengths and limitations

This single-center study includes a few patients. Nevertheless, the results are promising. We aim to further expand the sample, eventually creating a multicenter study to revise the anatomical formulae and adjust it to the minimally invasive thoracic surgery.

Table 4 Comparison of postoperative PFT data and PPO values in MIS and Open patients

PFT values	Median (IQR)	P value
FEV1 (L)		
Open	0.06 (–0.00 to 0.21)	0.06
MIS	0.19 (–0.01 to 0.37)	<0.001
FEV1%		
Open	3.26 (0.60 to 10.5)	0.03
MIS	8.65 (0.5 to 17.28)	<0.001
DLCO		
Open	0.44 (–1.61 to 2.03)	0.86
MIS	0.63 (–0.97 to 2.64)	0.09
DLCO%		
Open	2.31 (–5.15 to 9.07)	0.75
MIS	2.78 (–3.63 to 10.47)	0.045

PPO, predicted postoperative; PFT, pulmonary function test; MIS, minimally invasive surgery; FEV1, forced expiratory volume in 1 second; DLCO, diffusing capacity of the lungs for carbon monoxide; IQR, interquartile range.

Table 5 Comparison of preoperative and postoperative PFT data: Open *vs.* MIS

PFT values	Open group	MIS group	P value
FEV1 (L)	–0.32 (–0.63 to –0.22)	–0.22 (–0.38 to 0.01)	0.01
FEV1%	–11 (–18.5 to –7)	–7 (–12.5 to 2.5)	0.01
FVC (L)	–0.32 (–0.56 to 0.04)	–0.06 (–0.3 to 0.17)	0.049
FVC%	–8 (–14 to 3.5)	–0.5 (–7.5 to 6.5)	0.03
DLCO (mL/min/mmHg)	–2.67 (–6.17 to –0.71)	–2.01 (–3.96 to –0.3)	0.20
DLCO%	–11 (–25.5 to –3)	–6 (–14 to –1)	0.15
TLC (L)	–0.57 (–0.77 to 0.04)	–0.25 (–0.8 to 0.17)	0.65
RV (L)	–0.39 (–0.66 to –0.02)	–0.32 (–0.78 to 0.01)	0.82

Data are presented as median (interquartile range). PFT, pulmonary function test; MIS, minimally invasive surgery; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; DLCO, diffusing capacity of the lungs for carbon monoxide; TLC, total lung capacity; RV, residual volume.

Implications and actions needed

Our study demonstrates a poor prediction of postoperative functional values in case patients were operated on with MIS. Therefore, it would be useful to expand our sample to review and modify the anatomical formulae for calculating PPOs according to the intended surgical approach for that specific patient.

Conclusions

Our study demonstrates how the anatomical formula tends to overestimate the loss of FEV1 and DLCO (as well as FEV1% and DLCO%) in the postoperative period in the case of a minimally invasive approach (VATS or RATS), thus excluding some subjects from surgery. The same formulae seem to be much more reliable in the case of the open approach. Further efforts will be needed to see if the results of this study are also applicable to a large scale of patients, eventually modifying the formulae currently used.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-447/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-447/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-447/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by AOU Maggiore della Carità di Novara Institutional Review Board (IRB approval No. 974, CE/20, 15/10/2021) and informed consent was taken from all the patients.

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