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AWAKE OR INTUBATED SURGERY IN DIAGNOSIS FOR INTERSTITIAL LUNG DISEASES? A PROSPECTIVE STUDY

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KEYWORDS:

Awake Surgery; Video-assisted thoracic surgery; Interstitial lung disease; Lung biopsy; Morbidity.

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ABSTRACT

BACKGROUND

Risks associated with Video-Assisted Surgical Lung Biopsy (VASLB) for interstitial lung disease (ILD) with endotracheal intubation and mechanical ventilation are not nil. Awake Video-Assisted Surgical Lung Biopsy (Awake-VASLB) has been proposed as a method to obtain a precise diagnosis in several different thoracic diseases.

OBJECTIVES

To compare clinical outcomes of Awake-VASLB and Intubated-VASLB in patients with suspected ILDs.

METHODS

From June 2016 to February 2020, all patients submitted to elective VASLB for suspected ILD were included. Differences in outcomes between Awake-VASLB and Intubated-VASLB were assessed through univariable, multivariable-adjusted, and a propensity score-matched (PS) analysis.

MEASUREMENTS AND MAIN RESULTS

Awake-VASLB was performed in 66 out of 100 patients, while 34 underwent Intubated-VASLB. The Awake- VASLB resulted in a lower postoperative morbidity (OR 0.025; CI95% 0.001, 0.35; P= 0.006), a less unexpected Intensive Care Unit (ICU) admission, a less need for rescue therapy for pain, a reduced surgical and anaesthesiologic time, a reduced chest drain duration, a lower postoperative length of stay.

CONCLUSION

Awake-VASLB in patients affected by ILD is feasible and seems safer than Intubated-VASLB.

INTRODUCTION

Interstitial lung diseases (ILDs) include a number of pulmonary diseases, either restricted to lungs or characterized by a pulmonary involvement of a systemic disease. They are grouped together because of similar clinical, radiographic, physiologic, or pathologic features and are classified as idiopathic or secondary (related to a known aetiology). Among the idiopathic ILDs, the most frequent and severe is the Idiopathic Pulmonary Fibrosis (IPF).[1] It follows that IPF should be confirmed or excluded in all subjects presenting with unexplained progressive dyspnoea, chronic cough, and/or Velcro-like crackles at chest examination, especially if aged 65 or more. Moreover, early and accurate diagnosis of IPF is advisable because its natural history, treatment options, and prognosis greatly differs even in the context of ILDs. In particular, anti-fibrotic drugs have proved most effective especially in IPF and in a subgroup of other ILDs with a clear demonstrated progressive fibrosing pattern[2,3]; early application of appropriate treatment reduces either disease progression or even allowing a better quality of life.[4,5] In other simple words: an early and highly confident diagnosis is always the key of good clinical practice. In the meantime, a particular attention must be paid in optimising the risk benefit ration of the diagnostic procedures employed

The diagnosis of IPF could be obtained in a majority of cases with High-Resolution CT scan (HRCT) evidence of definite Usual interstitial pneumonia (UIP) pattern [1,6]. Alternatively, the results of clinical evaluation, laboratory tests, imaging, pulmonary function test are often discussed in a multidisciplinary team (MDT) setting, eventually deciding whether surgical biopsy is deemed necessary or not.

Histologic diagnosis can be obtained by transbronchial biopsy, trans-bronchial cryobiopsy, or surgical lung biopsy (SLB), either through thoracotomy or by Video-Assisted Surgical Lung Biopsy (VASLB). The American Thoracic Society (ATS) clinical practice guidelines suggest the use of SLB in patients with newly detected ILD of unknown cause, clinically suspected of having IPF and displaying an HRCT pattern of probable UIP, indeterminate for UIP, or an alternative diagnosis.[1]

There is increasing awareness that a considerable proportion of histologic confirmed UIP had a previous HRCT pattern of “inconsistent UIP” and “alternative diagnosis”.

Undeniably, Video-Assisted Surgical Lung Biopsy (VASLB) with endotracheal intubation and mechanical ventilation is associated with a risk of mortality and morbidity that is far from nil.[7,8] Nevertheless, in recent years VASLB approach performed in awake subjects under loco-regional anaesthesia (Awake-VASLB) has been suggested as an effective method to obtain a highly confident diagnosis in several different thoracic diseases.[9]

Being post-anaesthesia burden not negligible, especially in fragile patients, there is clear evidence in the literature that avoidance of neuromuscular blocking agents (NMBA)[10], intra- and postoperative strong opioids[11], injurious mechanical ventilation[12,13,14] could improve outcomes.

The objective of the present study was to compare clinical outcomes of Awake-VASLB and Intubated-VASLB in patients undergoing surgical lung biopsy for suspected ILDs.

METHODS

All patients undergoing elective pulmonary biopsy via VATS for suspected ILD in the Department of Thoracic Surgery of the ‘Città Della Salute e Della Scienza’ University Hospital in Torino (Italy) between June 2016 to February 2020 were enrolled. The decision to approach the procedure using Intubated-VASLB or Awake-VASLB followed a multidisciplinary discussion including thoracic Surgeon, anaesthesiologist, and pulmonologist. Exclusion criteria was the precognition of difficult endotracheal intubation.

The study protocol was approved by local Institutional Review Boards.

Awake-VASLB Anaesthesia Management

Local anaesthesia was induced in all cases with aerosolized Lidocaine 10ml (20mg/ml). Sedation from 2 to 3 on Ramsey Scale was obtained through a Target Controlled Infusion of Propofol (mean target 0,8 microg/ml) and Remifentanil 0.05mcg/kg/min. Oxygen was administered through an air-entrainment mask (SpO_2 target >92%). Arterial pressure was invasively monitored in all cases.

Locoregional anaesthesia was achieved through epidural catheter or local injection of lidocaine 2% 20ml performed by the surgeon under direct vision supplemented, when needed, with subsequent bolus of 10ml of local anaesthetic. After the collapse of the lung on the surgical side induced by artificial pneumothorax, the inhaled oxygen concentration was set to maintain SpO2>90%.

Intubated-VASLB Anaesthesia *Management*

Following intravenous Remifentanil 0.05-0.15ug/kg/min Ideal body weight (IBW), Propofol 1.5-2mg/kg recommended body weight (RBW) and Rocuronium 0.6-1.2mg/kg adjusted body weight (ABW) double-lumen tracheal tube was inserted under direct laryngoscope use as soon as train-of-four (TOF) = 0. Breathing parameters on Draeger Zeus anaesthesia machine were settled as tidal volume (VT) 6~8ml/kg IBV during dual lung ventilation and VT 4~6ml/kg IBW and RR 12~14 times/min during one-lung ventilation, respiration rate (RR) according to arterial blood gas (ABG) or $EtCO_2$, in volume-controlled ventilation (VCV) mode. PEEP was always set at 5 cmH_2O. Arterial pressure was invasively monitored in all cases. Anaesthesia was maintained through inhaled Desflurane 0.8~1.3 times minimum alveolar concentration (MAC), Remifentanil 0.05~0.15, and Rocuronium according to neuro-muscular monitoring (moderate block). Sugammadex was routinely given for antagonization.

Post-operative Management

In both groups, lung recruitment manoeuvres were performed according to Tusman protocol.[15] After the procedure, patients were discharged to the ward with a standardized therapy consisting of Acetaminophen 1 gr EV every 8 hours. Rescue therapy for pain (e.g. ketorolac, parecoxib, or tramadol, as appropriate) was administrated in the case patients complained a pain grade 3 or more according to the numeric rating scale (NRS). Chest X-ray was routinely performed on post-operative day 1 and after chest drain removal. Chest drain removal included favourable chest X-

Ray, no air-leak for at least 24 h, overall fluid output not higher than 250 mL/day, and drained fluid neither chylous nor haemorrhagic.[16]

Patients' discharge was planned for the day after chest tube removal if no clinical or radiological contraindications were observed.

Statistical Analysis

Baseline patient characteristics are summarized by the mean and standard deviation (SD) or number and percentages as appropriate. Between-group differences were evaluated by t-test (continuous variables) or $\chi 2$ test or Fisher's exact test (categorical variables) as appropriate.

Being the aim of the study to have at least 90% power to detect a decrease of the 90% post-operative complication incidence after VASLB reported in the literature (25%),[17,18] a sample size of at least 99 patients (enrolment ratio 2:1) was computed (significance level of 0.05). The secondary outcome were chest drain duration, unexpected Intensive Care Unit admission (defined as a non-scheduled admission at ICU after surgical procedure), reintervention, post-operative death, (i.e. at 30 days from surgery), rescue therapy administration for pain, hospital length of stay, number of biopsies achieved, surgical and anaesthesiologic time.

Univariable and multivariable-adjusted logistic regression models were used to evaluate categorical outcomes, while different continuous outcomes were compared by means of the unpaired Wilcoxon-Mann-Whitney test.

The variables in the adjusted models were age, gender, smoking habit, body mass index (BMI), American Society of Anaesthesiologists (ASA) physical status classification, pre-operative corticosteroid therapy, pre-operative O_2 therapy, and pathological diagnosis of UIP.

Differences in outcomes between the two surgical approaches were also assessed using a propensity score-matched (PS) analysis using genetic method. PS was estimated using a priori selected variables that have been associated with Awake-VASLB: age, gender, smoking habit, BMI, ASA, pre-operative corticosteroid therapy, pre-operative O_2 therapy. After the matching, outcomes were evaluated with the same methods described above.

All statistical tests were two-sided and P values of 0.05 or less were considered statistically significant. Data analysis was performed using Stata software version 15.1 (Stata- Corp, College Station, Texas), R software version 3.5.1 (R Foundation for Statistical Computing, HTTP: //www.r-project.org/).

RESULTS

Awake-VASLB was performed in 66 (66.0%) out of 100 patients who underwent surgical lung biopsy for suspected ILD, while 34 (34.0%) were submitted to Intubated-VASLB. Most patients were male (62.0 %) and the mean age at the time of surgery was 60.7 years (SD ± 15.4). The UIP pattern was the most observed at histology (30.0 %), followed by hypersensitivity pneumonitis -HP- (19.0%), Non-specific Interstitial Pneumonia -NSIP- (16.0%-) and Sarcoidosis (8.0%) (Table 1). The majority of operations were performed via bi-port VATS (55 – 55%), followed by single-port VATS (35 – 35%), and three-port VATS (10 – 10%). Mean surgical time was 51 minutes (SD ± 37), mean anaesthesiologic time was 51 minutes (SD ± 35), the mean number of biopsies obtained during surgery was 2.5 (SD ± 0.7), mean chest drain duration 2.7 days (SD ± 3.5) and mean postoperative length of stay 4.3 days (SD ± 5.8). No cases of conversion from Awake-VASB to Intubated-VASLB was observed. Sixteen (16.0 %) patients need rescue therapy for pain. In the whole cohort, 9 (10.0 %) major complication, 5 (5.0 %) unexpected admissions to ICU, 2 (2.0 %) reinterventions and 1 (1.0 %) post-operative death were observed.

At the univariable analysis (Figure 1 and Figure 2), the Awake-VASLB group showed a significant lower post-operative morbidity rate (2 vs 7 – 3.0% vs 20.6%) (OR 0.12; CI95% 0.024, 0.62; P= 0.011). Moreover, patients submitted to Awake-VASLB showed less unexpected admission to ICU (1 vs 4; 1.5% vs 11.8%; OR 0.12, CI95% 0.012 , 1.08 , P= 0.058), less need of a rescue therapy for pain (6 vs 10; 9.1% vs 29.4%; OR 0.24, CI95% 0.079, 0.73; P= 0.012), a reduced surgical time (38 minutes vs 77 minutes, P <0.0001), a reduced anaesthesiologic time (97 vs 132 minutes, P <0.0001), a reduced chest drain duration (2.3 vs 3.5 days, P= 0.015) and a less mean postoperative length of stay (3.1 vs 6.7, P= 0.0002). The unexpected admissions to ICU were imputable to pneumonia (2 case Intubated-VASLB group), Type 1 Respiratory Failure (1 case Intubated-VASLB group), Type 2 Respiratory Failure (1 case Intubated-VASLB group), failure of epidural analgesia, and poor pain control immediately after the procedure (1 case - Awake-VASLB group). Patients submitted to Awake-VASLB had an increased number of biopsies obtained during the surgical procedure (2.6 vs 2.1, P <0.0001). No case of reintervention or post-operative death was observed in the Awake-VASLB group, while 1 (2.9%) reintervention and 1 (2.9%) post-operative death were observed in the Intubated-VASLB group.

At the multivariable analyses (Figure 1 and Figure 2), the Awake-VASLB resulted to be an independent protective factor for post-operative morbidity rate (OR 0.025; CI95% 0.001, 0.35; P= 0.006), unexpected admission to ICU (OR 0.042; CI95% 0.002, 0.70; P= 0.027). A slight reduction[19] of the need for a rescue therapy for pain was also observed (OR 0.30; CI95% 0.088,1.00; P= 0.050).

Propensity Score-Matched Analysis

Propensity score matching was used to create a cohort of 94 patients. The two groups resulted in well-matched regarding demographic and clinicopathological characteristics (Table 2).

After matching (Figure 1 and Figure 2), the Awake-VASLB group resulted associated with a lower post-operative morbidity rate than the Intubated-VASLB group (OR 0.11; CI95% 0.022 , 0.61; P= 0.011), a less unexpected admission to ICU (OR 0.092; CI95% 0.009 , 0.87; P= 0.037), a reduced need for a rescue therapy for pain (OR 0.25, CI95% 0.07 , 0.81; P= 0.021), a reduced surgical (P= 0.002) and anaesthesiologic time (P= 0.0001), a reduced chest drain duration (P= 0.008), a lower post-operative length of stay (P= 0.0006), and an increased number of biopsies obtained during surgery (P= 0.0011).

DISCUSSION

Surgical lung biopsy is still considered the standard approach when a confident diagnosis of UIP cannot be obtained by imaging features and after a multidisciplinary team (MDT) discussion, as is still endorsed by the last evidence-based international guidelines.[1]

Nevertheless, surgical lung biopsy, including the use of Intubated-VASLB, is affected by elevated morbidity (up to 30%) and mortality rate (up to 4%), difficult to accept in routine clinical practice for a pure diagnostic scope[20]. On the contrary transbronchial cryobiopsy is generally a safer procedure showing lower morbidity (pneumothorax rate 9.8%; severe bleeding rate 0.3%, moderate bleeding rate 8.7%) and mortality rate (0.3-0.5%)[21]. Even considered its lesser diagnostic efficacy in ILDs compared to surgical lung biopsy, the use of transbronchial cryobiopsy for this purpose has gained increasing attention, mostly because of its safety compared to the high morbidity and mortality risk associated to traditional Intubated-VASLB[21]. Moreover, its attractiveness resides in its easy applicability to most of thoracic endoscopy facilities, especially compared to the strong anaesthesiologic and operative room expertise that are considered essential for successful application of Awake-VASLB.

The present prospective study evidenced that Awake-VASLB: 1) presents a consistent reduction of post-operative morbidities; 2) determines a reliable decrease of both post-operative mortality and reintervention rates, and also a reduction of the use of rescue therapy for pain; 3) allows to save hospital resources in terms of post-operative drainage time, as well in term of hospital length of stay, and minimize the use of unplanned ICU admissions; 4) provides at least the same amount of lung tissue biopsies than Intubated-VASLB.

Any thoracic surgical procedure in ILD patients represents a challenge for thoracic surgeons and anesthesiologist[22]. Nevertheless, the thoracic surgery domain is incessantly developing, and anaesthesiologists and thoracic surgeons should maintain a continued focus on minimizing procedure-related morbidity and, at the same time, maximizing therapeutic and diagnostic benefits in such frequently fragile patients (e.g. age, type of disease, frequent comorbidities). In this context, Awake-VASLB has been recently proposed for surgical lung biopsy (SLB) in suspected ILDs. [23]

Undoubtedly, feasibility and patients' safety are major issues in ILD patients referred for SLB. In particular, the reported morbidity and mortality rate could follow respiratory dysfunction induced by mechanical ventilation (barotrauma). This has been clearly reported in the literature. [10,12,13,14] In particular, muscle relaxants are known to produce adverse respiratory effects by residual muscle block, including weakness of upper airway muscles, airway obstruction, and diaphragmatic dysfunctions[10]. Consequently, a surgical approach based on spontaneous ventilation avoiding the use of neuromuscular blocking agents is expected to reduce intraoperative lung injury and, therefore, to be associated with less postoperative adverse events, representing a valid strategy in high-risk ILD patients. Indeed, our study seems to confirm that patients undergoing Awake-VASLB were found to be associated with a remarkable reduction of postoperative morbidity and mortality (Odds Ratio for postoperative complications in VASLB: 8.1, P= 0.011). Remarkably, we also observed a decrease in anaesthesiologic time and unanticipated use of ICU postoperatively. This is also in line with a more favourable postoperative period characterized by a reduction of thoracic drain maintenance and post-postoperative length of stay. These results are consistent with current literature reporting about the use of concerning Awake in the context of other thoracic disease[24] and the observed rate of complication is not dissimilar to that reported for cryobiopsy performed in expert centers.[21]

The MDT (that usually comprises clinicians, thoracic radiologists, and thoracic pathologists) is considered the best way to manage the diagnostic pathway as well as other aspects of management of patients affected by an ILD[26,27]. Moreover, an acceptable risk-benefit ratio should be considered as a guide during the multidisciplinary discussion (including thoracic surgeons) for the choice of either the Awake-VASLB or the intubated surgery. Indeed, the decrease of the risk-benefit balance together with an enhanced diagnostic yield represents the goal to be reached in each patient, taking into account the disease severity per se, the patient comorbidity, and the possible deadly outcome of potential acute exacerbations related to the intubated procedure. Consequently, in our Institution, throughout the MDT discussion, a careful evaluation of the risk-benefit ratio tailoring the technique for every single patient was carried out. Interestingly, we observed is a trend towards lower DLCO in the Awake-VASLB group. Actually, this data could suggest that in our cohort patients with more severe ILD more likely underwent awake surgery in order to minimize the risk of possible complications and, in particular, acute exacerbations.

One of the major concerns of the diagnostic procedure in ILD is to obtain sufficient material for an accurate diagnosis. In our study, we observed a slightly increased number of biopsies performed in the Awake-VASLB group. A possible explanation could be related to the surgeon's preference to perform an “extra biopsy”, influenced by the awake patient setting, and to be sure to obtain sufficient material for diagnosis. However, in both groups, the mean number of biopsies performed was according to most recent guidelines (i.e. at least 2 biopsies), and the difference observed (i.e. 0.5 biopsies in favour of Awake-VASLB) was in our opinion not of clinical or practical relevance. On the other hand, is important to note that our study demonstrated that the Awake-VASLB procedure did not imply an inferior number of biopsies achieved, as compared to Intubated-VASLB.

Almost certainly, patients undergoing thoracic surgery could experience postoperative pain, even if submitted to minimally invasive thoracic surgery (e.g. VATS). On the other hand, intraoperative and post-operative use of opioids could be related to impaired recovery and readmission after hospital discharge[11]. In recent years chronic opioid use and addiction have emerged as a public concern, even if more perceived in the USA than in Europe. Even if a correct therapeutic approach to acute pain relief certainly plays a major role in this context [28], the use of spontaneous ventilation in the Awake-VASLB group led to a significant reduction in rescue therapy administration. Nevertheless, further studies are needed to better define the advantage of spontaneous ventilation surgery on pain control.

Finally, having our results also a positive impact on the optimal management of hospital resources, it follows that the encouraging clinical results so far obtained and the minimal use of hospital resources could, in the next future, facilitate the spreading of Awake-VASLB, even outside high-volume academic centres.

Our study presents several limitations, principally related to the lack of randomization to prevent selection bias[29]. However, the prospective nature of the study consents a real-life adherence, warrant good data reliability, and, therefore, seems to confirm the findings[30]. Moreover, we perform a propensity-matched analysis that was employed in order to minimize the patients' selection bias.

In conclusion, the results obtained from the analysis of our prospective series suggest that Awake-VASLB is feasible and safe in patients affected by ILD significantly reducing post-operative complications, unexpected ICU admission, reintervention, and mortality. Having Awake-VASLB the same diagnostic yield of the Intubated-VASLB we hope that the results so far obtained will lead to more widespread use of Awake-VASLB and stimulate further prospective comparison studies with other procedures presenting similar post-procedural complication rates (as Transbronchial Cryo-biopsy). The emerging evidence regarding the effectiveness of this approach, including the ones obtained in the present study, should be considered in the next guidelines on the management of ILD patients.

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TABLE LEGENDS

TABLE 1. Baseline Characteristics in the overall population.

TABLE 2. Awake-VASLB Versus Intubated-VASLB: Baseline Characteristics Before and After Propensity Score Matching

FIGURE LEGENDS

FIGURE 1. Awake-VASLB Versus Intubated-VASLB: Crude (A), Multivariable-adjusted (B) and Propensity Score Matched (C) analysis for Post-operative morbidity, unexpected admission to ICU, and rescue therapy for pain

FIGURE 2. Awake-VASLB Versus Intubated-VASLB: Box-and-whisker plots illustrate the distribution of anaesthesiologic time (A), chest drain duration (B), and hospital postoperative length of stay (C)

TABLE 1. Baseline Characteristics in the overall population.

Factor	**All** n=100
Surgical Approach, *n (%)*	
Awake	66 (66.0)
Intubated	34 (34.0)
Age (*years*), *mean (SD)*	60.7 (15.4)
Gender *(Male)*, *n (%)*	62 (62.0)
Smoking History, *n (%)*	65 (65.0)
BMI, *mean (SD)*	26.6 (4.7)
ASA*, *n (%)*	
1	2 (2.0)
2	16 (16.0)
3	78 (78.0)
4	4 (4.0)
Corticosteroids Therapy, *n (%)*	12 (12.0)
FEV1 (%), *mean (SD)*	85.8 (22.5)
FVC (%), *mean (SD)*	84.7 (20.5)
DLCO (%), *mean (SD)*	58.7 (15.8)
O2 therapy, *n (%)*	9 (9.0)
UIP^, *n (%)*	30 (30.0)

* American Society of Anesthesiologists (ASA) physical status classification

^Usual Interstitial Pneumonia

TABLE 2. Awake-VASLB Versus Intubated-VASLB: Baseline Characteristics Before and After Propensity Score Matching

	Before Match n= 100			**After Match** n= 94		
	Awake	**Intubated**	**p-value**	**Awake**	**Intubated**	**p-value**
	N= 66	N= 34		N= 66	N= 28	
Age (*years*), *mean (SD)*	60.4 (2.0)	61.4 (13.6)	0.774°	60.4 (2.0)	62.1 (12.5)	0.624°
Gender *(Male), n (%)*	42 (63.6)	20 (58.8)	0.639*	42 (63.6)	16 (57.1)	0.644*
Smoking History, *n (%)*	45 (63.6)	20 (58.8)	0.353*	45 (63.6)	18 (64.2)	0.713*
BMI, *mean (SD)*	26.8 (4.8)	25.9 (4.5)	0.357°	26.8 (4.8)	26.4 (4.6)	0.718°
ASA[§], *n (%)*			0.236*			0.574*
1	1 (1.5)	1 (2.9)		1 (1.5)	1 (3.5)	
2	8 (12.1)	8 (23.5)		8 (12.1)	3 (10.7)	
3	53 (80.3)	25 (73.6)		53 (80.3)	24 (85.7)	
4	4 (6.1)	0 (0)		4 (6.1)		
Corticosteroids Therapy, *n (%)*	6 (9.1)	6 (17.6)	0.212*	6 (9.1)	5 (17.8)	0.294*
FEV1 (%), *mean (SD)*	85.4 (21.8)	86.8 (24.2)	0.775°	85.4 (21.8)	86.1 (24.9)	0.897°
FVC (%), *mean (SD)*	84.1 (20.5)	85.9 (20.7)	0.678°	84.1 (20.5)	85.2 (20.7)	0.812°
DLCO (%), *mean (SD)*	56.4 (16.3)	63.1 (14.1)	0.058°	56.4 (16.3)	61.5 (13.8)	0.164°
O2 therapy, *n (%)*	7 (10.6)	2 (5.9)	0.714	7 (10.6)	2 (7.1)	0.721*
UIP^, *n (%)*	22 (33.3)	8 (23.5)	0.311	22 (33.3)		0.424*

°t-test; * $\chi 2$ test or Fisher's exact test

§ American Society of Anesthesiologists (ASA) physical status classification

^Usual Interstitial Pneumonia

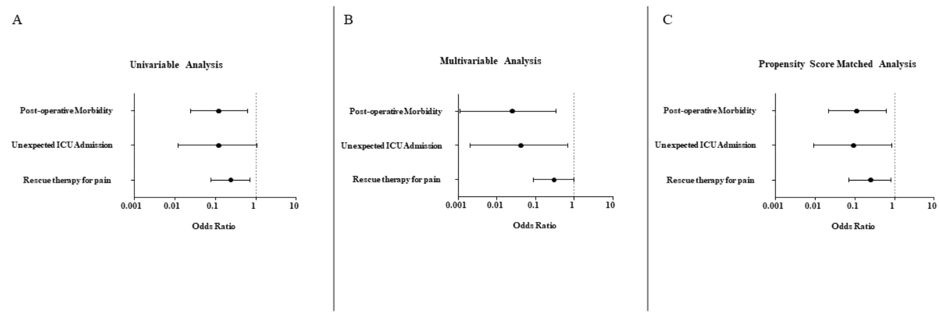

FIGURE 1. Awake-VATS Versus Intubated-VATS: Crude (A), Multivariable-adjusted (B) and Propensity Score Matched (C) analysis for Post-operative morbidity, unexpected admission to ICU, and rescue therapy for pain

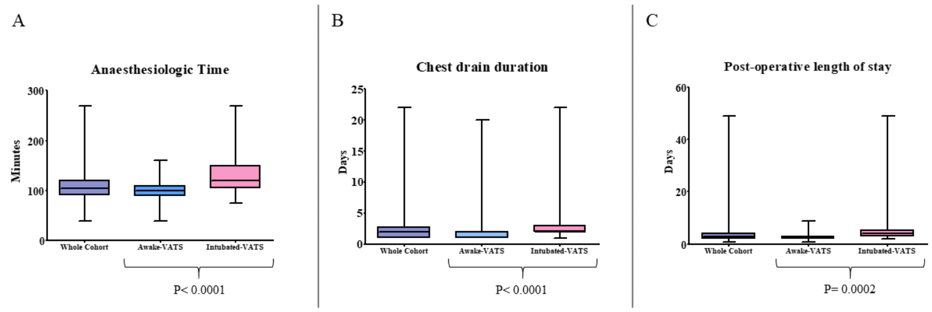

FIGURE 2. Awake-VATS Versus Intubated-VATS: Box-and-whisker plots illustrate the distribution of anaesthesiologic time (A), chest drain duration (B), and hospital postoperative length of stay (C)