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Research Article

Comparative Study For The Effectiveness Of VATS Wedge Resection For Peripheral Pulmonary Nodules Using Clamp And Saw Technique Augmented By Tissue Sealants.

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Abstract

Introduction: The video-assisted thoracoscopic surgery (VATS) has become progressively popular as a minimally invasive method for pulmonary resection surgery [1]. As a result, multiple technologies have been developed parallel to this technique to overcome the limitations for limited access and reduce the postoperative air leak. This included the wide use of staplers because of their convenience and quickness. However, using staplers are not devoid of complication. The purpose of the current study is to evaluate the effectiveness of VATS wedge resection using non-crushing clamp and continuous absorbable sutures augmented by tissue sealants for resection of peripheral pulmonary nodules and spotlights on the technical aspects to enhance safety and efficacy.

Patient and methods: We conducted retrospective observational comparative study on a cohort of patients who underwent wedge resection using VATS for solitary or multiple peripheral pulmonary nodules. Patients were divided into two main groups. Group A included patients who had VATS wedge resection using staplers' technique. Group B included patients who had VATS wedge resection with clamp and saw technique.

Results: A total of 134 patients were included. 75 patients were excluded since they did not meet the selection criteria. The remaining 59 patients were divided between the two groups. Group A included 27 while Group B included 32 patients. There were 33 males (55.9%) and 26 females (44.1%). There were no significant differences in patient characteristics between both groups. Lung nodules had a mean maximal transverse diameter of 22.1±7.2 mm (range 14.9–29.3 mm). The mean distance from the pleura to superficial nodule margins was 12.0±3.1 mm (range: 8.9–25.1 mm). Univariate regression analysis was conducted on patients' characteristics, nodule size and depth, comorbidities included smoking history and preoperative FEV1, and resection technique used. The results showed that neither of the variables was risk factor for development of the complications. However, the multivariate Logistic regression analysis of the results showed that stapler use in deeper nodules were among the influencing factor of postoperative complication ($P < 0.05$). This variable along with the other variables with $P < 0.2$ in univariate regression were further included in multivariate logistic regression. The final results demonstrated nodule depth (OR 4.07, 95% CI 2.05–14.66, P = 0.0.31) and stapler use (OR 2.17, 95% CI 2.11–7.13, P = 0.043) were risk factors for postoperative complications.

Conclusion: in clinical practice, it is necessary to choose the appropriate treatment according to the patients' individual situation. The clamp and saw technique augmented by surgical sealants for wedge resection of peripheral pulmonary nodule would be a substitute for staplers with similar air leak incidence, durations and severity.

Keywords: Clamp and saw technique, wedge resection, VATS wedge resection.

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INTRODUCTION

The video-assisted thoracoscopic surgery (VATS) has become progressively popular as a minimally invasive method for pulmonary resection surgery [1]. As a result, multiple technologies have been developed parallel to this technique to overcome the limitations for limited access and reduce the postoperative air leak. This included the wide use of staplers in the modern thoracic surgery era. The advantage of using the staplers lies in its convenience and quickness [2].

The combination of VATS approach using staplers has been widely used for wedge resection of solitary pulmonary nodules. However, the strong compression from the stapler entails the risk of recruitment difficulties for lung tissues near the cutting edge. The limitation in angles which became prominent if the uniport thoracoscopic surgery is being performed. This may result in insufficient incision margins and excessive use of multiple staplers and rise in the cost. Additionally, it has been found that parenchymal tissue thickening, and granuloma grow along the stapler resection and concerns for recurrence. Moreover, with increased cost and reporting stapler lines as obvious sources of air leaks after pulmonary resections would lead to investigating various techniques [3,4,5,6]. Some studies have suggested alternative methods such as energy devices, laser or thermal ablation, and ligation [3,7,8]. Traditionally, the clamp and saw technique was widely used before the introduction of various staplers for tissue sealing.

The purpose of the current study is to evaluate the effectiveness of VATS wedge resection using non-crushing clamp and continuous absorbable sutures augmented by tissue sealants for resection of peripheral pulmonary nodules and spotlights on the technical aspects to enhance safety and efficacy.

PATIENT AND METHODS

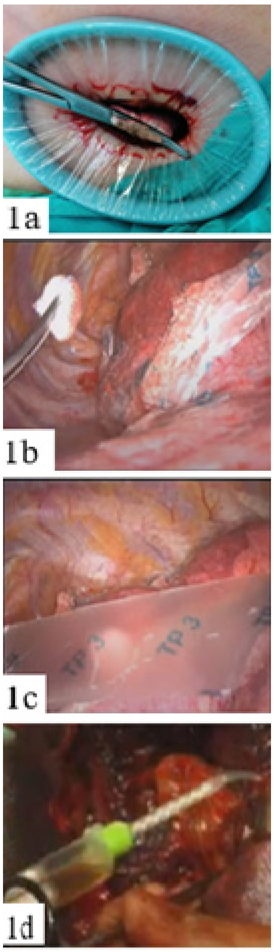
We conducted retrospective observational comparative study on a cohort of patients who underwent wedge resection using VATS for solitary or multiple peripheral pulmonary nodules. Patients were divided into two main groups. Group A included patients who had VATS wedge resection using staplers' technique. Group B included patients who had VATS wedge resection with clamp and saw technique. The exclusion criteria were preoperative bullous disease identified on chest CT or severe emphysema as evidenced by FEV1, and previous history of lung cancer treatment. Intraoperatively, should a conversion to standard thoracotomy incision were required for completion of the procedure, patients were also excluded.

Surgical procedures

The same anesthetic and analgesic strategies were used for all patients. All patients had double-lumen tube intubation as a routine anesthetic intubation under general anesthesia. No local or epidural anesthesia adjunct techniques were used. Uni-portal VATS was performed by a single 3-4 cm mini-thoracotomy incision done between the mid and anterior axillary lines in the fourth intercostal space for pulmonary nodules in the upper lobe or fifth intercostal space for pulmonary disease in the middle, Ligula or lower lobes. Deflation of the ipsilateral lung was done just before entering the thoracic cavity. An Alexis soft tissue retractor was inserted, and a 5 mm telescope was introduced into the chest cavity for assessment and exploration on the lung surface. Three-stage lung mobilization were performed by dividing adhesions of the lung surface to surrounding structures, dividing the inferior pulmonary ligament, and dividing the hilar pleural reflections anteriorly and posteriorly. Following this three-stage mobilization, pulling the lung parenchyma by Doval non-crushing clamp and gently palpating the whole deflated lung parenchyma were achieved. Once locate the pulmonary nodule in question, the Doval clamp readjusted and relocated just across the nodule onto the normal lung tissue and pull it just outside or at the level of the incision.

In the stapler technique, the wedge was resected using an endoscopic linear cutter stapler. In the clamp and saw technique, the non-crashing clamp was applied and slowly closed with 2 cm safety margin to cross the parenchymal tissue, a second crossing clamp can be adjusted if needed (**Figure 1a**). The lung was sutured using a two-layer closure with 4-0 Vicryle sutures rounded needle. The first layer was a continuous running (transverse mattress) suture. This was followed by shaving the pulmonary wedge containing the lesion. We prefer to do the first layer on clamp and before resection to avoid slipping off the tissue after resection. After removing the clamp, a continuous second layer of over running sutures were performed and additional pledgeted sutures were placed as required. The lung was brought back to the thoracic cavity hung lightly by the suture ends. Before inflation, additional measurements were taken to augment the suture line. Firstly, thin strips of fibrillar and surgical Tissue Patch 3™ has been used as an adjunctive treatment in control and prevention of air leak in all cases with clamp and saw. We used a longitudinal thin strip of Fibrillar and the 50 mm width tissue patches on top of the suture line, the length was adjusted according to the area of the wedge resected. We apply it while the lung is collapsed and wait 5 minutes before inflating the lung to test for the air leak. This 5-minute period would allow activation of the Tissue Bond to form cross-links at proteins that are present at the site of application (**Figure1b &1c**). Secondly, Flow seal has been added on top of external edges of the patches to support adhesions between the patch and lung tissue as required (**Figure1d**).

Figure 1. 1a, clamp applied across the parenchymal tissue. 1b & 1c, strips of fibrillar and surgical Tissue Patch 3™ has been used as an adjunctive. 1d, Flow seal applied on top of external edges of the patches to support adhesions between the patch and lung tissue as required.



Intraoperative test for air leak

We test the air leak from the treated lung by visual inspection of any visceral pleural tears and bubble test after immersion the lung into saline within the thoracic cavity.

Drain insertion and closure

After confirmation of the absence of air leak, a small chest tube (16 or 18 Fr) or hemovac drain (12 Fr, 400 ml) was inserted through the same incision used for VATS and connected to a single-chamber water-sealed bottle or small auto suction Redivac bottle. Followed by closure of the incision in layers.

Postoperative care

patients were admitted to the recovery bay for few hours after surgery and chest radiography was performed to confirm lung inflation and drain positions. On postoperative day one, fully inflated lungs with no pleural effusion or pneumothorax was to be confirmed by repeat Xray and the drain was removed if no air leak and drainage volume of <150 ml. The absence of air leak was confirmed clinically by the simple air bubble test from the underwater seal or suction seal test (SST) from the Redivac bottle hub.

Operative morbidity and mortality

Operative morbidity or mortality was considered as occurring within 30 days after the operation.

Statistical analysis

Data was collected and analyzed using IBM SPSS 19.0 software package (IBM, Armonk, NY, USA). For quantitative data, the distribution morphology and homogeneity of variance were verified. If the data were normally distributed, the student's t-test was compared and represented by the mean □} standard deviation (mean □} SD); otherwise, median (interquartile spacing) [M (IQR)], the Mann–Whitney U test was applied. Categorical data was compared using the chi-square ($\chi 2$) test or Wilcoxon rank-sum test. Association data were analysed using odds ratio (OR) and 95% confidence interval (CI) analysis. The logistic regression model of stepwise regression was used for univariate and multivariate analysis, and variables with $P < 0.2$ in univariate analysis were included in multivariate analysis. P -value < 0.05 was considered statistically significant.

RESULTS

A total of 134 patients underwent wedge resection using VATS. 75 patients were excluded since they did not meet the selection criteria. These patients were: 40 patients subsequently diagnosed with primary lung cancer and completion lobectomy was done in the same session, 28 patients had pulmonary bullae identified on preoperative chest CT scans or severe emphysema with FEV1 < 60% of the predicted, and 7 patients converted to thoracotomy. The remaining 59 patients were divided into two groups. Group A included 27 patients who underwent wedge resection using stapler and Group B included 32 patients who underwent wedge resection using the clamp and saw technique. There were 33 males (55.9%) and 26 females (44.1%). The ratio of male to female patients was 1.26:1 (33:26). The mean age was 53.7 with a range from 43 to 82 years. Lung nodules had a mean maximal transverse diameter of 22.1 ± 7.2 mm (range 14.9–29.3 mm). The mean distance from the pleura to superficial nodule margins was 12.0 ± 3.1 mm (range: 8.9–25.1 mm). In group A, 20 patients were found having smoking history (74.1 %) with mean FEV1 of 2.78 ± 0.76 litters and 85.9 ± 13.0 % of the predicted. In group A, 21 patients smoked with no statistically significant difference in the mean FEV1. The demographics, clinical characteristics, preoperative lung function, and radiological and surgical data of the patients are demonstrated in **Table 1**. There were no significant differences in patient characteristics between both groups (P > 0.05, **Table 1**).

Table 1. Patients' characteristics and comparison of the two groups.

Factors	Group A	Group B	P-value
Age (years)			
• Median	53.7	51.5	0.122
• Range	43-82	37-79	
Gender			
• Men	16 (59.3%)	17 (53.1%)	0.636
• Women	11 (40.7%)	15 (46.9%)	0.179
Smoking history	20 (74.1 %)	21 (65.6%)	0.483
FEV1, liter, (mean±SD)	2.78 ± 0.76	2.74 ± 0.69	0.543
FEV1, % of predicted (mean±SD)	85.9 ± 13.0	82.4± 19.7	0.777

* FEV1, Forced expiratory volume in the first second. SD, standard deviation.

In general, the operation time was slightly shorter in Group A than B. Mean duration in group A was 60.9±14 minutes and in Group B was 70.4±10 minutes. This difference was not statistically significant (p=0.115). 5 patients (8.47%) had 2 wedges in the same session, 3 patients in group A (11.1%) and 2 in group B (6.25%). The remaining 54 patients (91.5%) had single wedge resection. The localization of lobe involved was shown in **Table 2**.

Table 2. Operative and Hospitalization data and comparison of the two groups.

Factors	Group A	Group B	P-value
Mean operative duration (minutes)	60.9±14	70.4±10	0.115
Location of the wedge			
• Upper lobe	15 (55.6%)	18 (56.2%)	0.897
• Middle lobe/lingula	3(11.1%)	3 (9.3%)	0.688
• Lower lobe	9(33.3%)	11 ((34.3%)	0.71
Mean drainage volume on D0 (ml)	95 ± (75)	102 ± (50)	0.888
Total postoperative drainage volume (ml)	129± (500)	577.5 ± (266)	0.265
Postoperative chest tube retention duration (days)	1.89	1.87	0.224
Postoperative hospital stays (days)	1.90	1.93	0.118
Number of staplers used (per patient)	3.15	0	< 0.05
Surgical expenses (Euro)	1187.55	431	< 0.05

During the postoperative period, there were no significant differences in drainage volume on the first postoperative day, total postoperative drainage volume, postoperative chest tube retention duration, and postoperative hospital stay between the two groups (P > 0.05). There was a statistically significant reduction in the overall cost of surgical treatment for individual patients with the clamp and saw technique (P < 0.05, Table 2). Mean postoperative stay was quite similar in both groups of 1.90 and 1.89 days. There was no major cardiovascular, or cerebral perioperative morbidity (i.e. up to 30 days post-surgery). However, in the stapler group A, 7 patients (25.9%) had atelectasis 2 of them (7.4%) developed pneumonia and treated with oral antibiotic for 5 days. 9 patients (33.3%) had grade I air leak that last for one day. In group B, 3 patients (9.3%) had atelectasis, one of them developed pneumonia (3.1%) and treated in the same way as other group. 11 patients noted to have grade 1 air leak for one day after procedure (3.1%). The difference between both groups was statistically insignificant **Table 3**. No suction was applied to these leaks in both groups as we believe it prolongs the leak and delays the fistula healing.

Table 3. Postoperative complications after VATS wedge resections.

Complications	Group A	Group B	P-value
Atelectasis	7 (25.9%)	3 (9.3%)	0.291
Pulmonary infection	2 (7.4%)	1 (3.1%)	0.840
Air Leak (grade I)	9 (33.3%)	11 (34.4%)	0.877
Air leak duration	1 (day)	1 (day)	0.257
Air space	3 (11.1%)	2 (6.2%)	0.061
Wound infection	1 (3.7%)	0	0.193

In both groups, Patients with grade I air leak had it for a median duration of 1 day. The postoperative drainage time, hospital stay was not affected. The median hospital stays for group A and B were 1.90 and 1.93 respectively. The total air leak duration and postoperative drainage time, and length of hospital stay, in day, were not statistically significant between both groups (p=0.257, p=0.224, and p=0.118, respectively) Tables 2 &3. After drain removal, small apical space less than 2 cm was noticed in chest radiograph in 5 patients, 3 in group A (11.1%) and 2 in group B (6.2%) (p=0.061). They were asymptomatic and neither of them needed intervention as they were managed conservatively. During follow-up, all pneumothoraxes were resolved by the next outpatient clinic appointment. No patient needed re-admission within one month after discharge.

Univariate regression analysis was conducted on patients' characteristics, nodule size and depth, comorbidities included smoking history and preoperative FEV1, and resection technique used. The results showed that neither of the variables was risk factor for development of the complications. These results are displayed in **Table 4**. However, the multivariate Logistic regression analysis of the results showed that stapler use in deeper nodules were among the influencing factor of postoperative complication (P < 0.05). This variable along with the other variables with P < 0.2 in univariate regression were further included in multivariate logistic regression. The final results demonstrated nodule depth (OR 4.07, 95% CI 2.05–14.66, P = 0.0.31) and stapler use (OR 2.17, 95% CI 2.11–7.13, P = 0.043) were risk factors for postoperative complications.

Table 4. Univariate and multivariate logistic regression of postoperative complications.

Factors	OR (95%CI)	P-value
Univariate Logistic Regression		
Age	1.02 (0.98–1.06)	0.285
Gender	0.91 (0.37–2.25)	0.832
BMI	1.00 (0.95–1.05)	0.887
Smoking history	3.29 (0.94–11.44)	0.061
Comorbidities	0.456 (0.15–1.38)	0.165
Nodule size (mm)	1.11 (0.98–1.27)	0.106
Nodule location and depth	2.60 (1.05–6.44)	0.097
Preoperative FEV1%	1.02 (0.99–1.05)	0.194
Stapler use	3.19 (2.41–9.16)	0.180
Clamp, Saw, Sealant use	2.13 (0.79–3.76)	0.118
Multivariate Logistic Regression		
Age	1.49 (0.88–1.27)	0.687
gender	0.78 (0.29–2.42)	0.818
BMI	0.89 (0.95–1.61)	0.117
Smoking history	5.08 (1.05–24.56)	0.073
Comorbidities	0.28 (0.08–1.04)	0.057
Nodule size (mm)	1.14 (0.98–1.33)	0.091
Nodule location and depth	4.07 (2.05–14.66)	0.031
Preoperative FEV1%	1.02 (0.98–1.06)	0.257
Stapler use	2.17 (2.11–7.13)	0.043
Clamp, Saw, Sealant use	1.01 (0.97–1.05)	0.692

DISCUSSION

There has been a significant increase in the number of non-anatomical lung resection surgeries for solitary pulmonary nodules due to accessibility to well established lung cancer screening programs. This has put a burden on developing health systems with resource depletion and increased cost of treatment [9].

Alveolar air leak has considered to be the most important complication following lung resection and is the leading cause for postoperative negative impacts if remain prolonged [10]. The impacts of prolonged air leaks would negatively affect the patients' recovery. This raises the overall pulmonary and cardiac morbidity, increases risk of postoperative empyema, prolongs the chest drainage time, prolongs the hospital stay, and finally the treatment cost increases by 15 % for any air leak and 35% for prolonged air leak [11,12,13]. We believe that the best treatment for air-leak complications is by prevention. Various methods are described to prevent air-leak after lung resection surgery. These included modified surgical techniques and use of different sealant agents.

The local pulmonary related risk factors for prolonged or significant air leak following pulmonary resection include advanced emphysema, dissection of adhesions, excessive manipulation of the lung, incomplete interlobar fissures, and creation of new fissures. Other general major factors that caused pulmonary air leaks include uncontrolled diabetes mellitus, and hypoalbuminemia [13]. In our current study, we adopted fissure-less surgery protocols and have chosen peripherally located pulmonary nodules to avoid creation of new fissures and excessive manipulation of the lung. No major comorbidities that could interfere with the general healing process in our selected cohort of patients.

We noticed various technique were described to reduce the leak from the staples lines such as buttressing the staple lines with pericardial strips. This obviously increased the cost of treatment and did not significantly reduce the postoperative air leak [6,14]. Miller et al. did a prospective randomized multicentre trial on 80 patients undergone lobectomy or segmentectomy. They assigned the patients either to receive buttressing with bovine pericardial strips or standard treatment. Despite a trend towards shorter air leak time was found, they could not note advantage of buttressing technique regarding drainage time and length of hospital stay [14].

In addition to that, The STS guidelines [15] on the intraoperative and postoperative management of alveolar air leaks recommend buttressing staple lines in performing non-anatomic pulmonary resections in patients with moderate to severe pulmonary emphysema (FEV1 <60% predicted) to prevent postoperative air leaks. In patients with emphysema less than moderate the use of buttressed staples is not well established and should be avoided given the increased costs of treatment [6,15]. Since the mean FEV1 in the stapler group A was 80.5±21.6, and the overall mean FEV1 for both groups were 81.6± 20.3, We strongly believe that the severity of emphysema in the selected patient was less than moderate and buttressing the stapler lines was not indicated Using stapler resection to the parenchymal tissue causes tissue thickening along the surgical margin. Sun B et al defined the time course and radiographic characteristics of such thickening and to determine their association with possible recurrence. The authors found that stapling across lung parenchyma has led to tissue granulation in 96.2% (75 patients) in their 78 sample of patient who underwent limited resection for non-small cell lung cancer. These granulations were linear in 32.0% (n = 24), focal along the pleura, hilum, or parenchyma in 24.0% (n = 18), and nodular in 44.0% (n = 33). This granulation could be confused in follow up scans as a concern for recurrence. Sun B et al, suggested a characteristics and initial size of granulation tissue for prediction of recurrence versus normal healing process [5]. We strongly believe that preserving surgical margin is a significant concern and the use of surgical staplers in pulmonary nodules should be carefully planned. Despite certain limitations, wedge resection with a clamp and suturing by absorbable sutures may overcome these challenges.

There has been variable feasibility of the routine clinical use of sealants products after lung resections in significant number of randomized and nonrandomized studies over the recent years. Different sealing material has been studied and each of these products has its specific properties and indication fields [6]. In a systemic review of literature [16], the authors concluded that surgical sealants reduce postoperative air leaks and time to chest drain removal, but this reduction is not always associated with a reduction in length of postoperative hospital stay. This Cochrane databases review included randomized controlled clinical trials in which standard closure techniques plus a sealant were compared with the same intervention with no use of any sealant in patients undergoing elective pulmonary resection. Sixteen trials with a total of 1,642 randomized patients were included. Six trials were able to demonstrate a significant reduction of postoperative air leaks using sealants and three trials showed a significant reduction in time to chest drain removal in the treatment group. In two trials the percentage of patients with PAL was significantly smaller and in three trials a statistically significant was found with the intraoperative use of sealants.

Up to date the indications for the use of surgical sealants are controversial. In contrast, we routinely used sealant agents to group B with the tissue patch and flow seal since the clamp and saw technique in the recent trend for non-anatomical pulmonary resection have not been tested in the standard closure techniques into those randomised trials. We augmented the suture line by a piece of Tissue Patch and Flow seal. Tissue Patch is a synthetic sealant [17], which has self-adhesive characteristics through the bio adhesive polymer component. Once activated, it forms cross-links at proteins that are present at the site of application. This patch is largely absorbed within 70 days.

The clamp and saw technique widely used before the introduction of various staplers for tissue sealing. Adjunct this with tissue sealants as described, there were no statistical differences in short-term outcomes of duration of air leakage, time for chest drain removal, length of hospital stays or the need for a second drainage method between patients undergoing wedge resection with a clamp and those undergoing stapler application. Using non crushing clamp helped to avoid the prolonged atelectasis to the remaining parenchymal tissue. Bring the tissue at the level of incision facilitated hemostatic and secured two rows of running sutures. By using absorbable sutured covered by a patch of absorbable sealant material to decrease tissue reaction at the suture line.

LIMITATIONS

This study was conducted on patients with less than moderate emphysema, the results and conclusion cannot be automatically applied on more severe disease without further investigations and research. Performing wedge resection with a non-crush clamp can be challenging in cases where the nodule is deep, the base of the bulla is wide in patients with bullous disease, or multiple metastatic nodules in different lobes.

CONCLUSION

The authors of this article recommend that, in clinical practice, it is necessary to choose the appropriate treatment according to the patients' individual situation. The clamp and saw technique augmented by surgical sealants for wedge resection of peripheral pulmonary nodule would be a substitute for staplers with similar air leak incidence, durations and severity. In addition, it can be better for the adjacent lung tissue that will have better recruitment and plasticity and associated with fewer postoperative atelectasis and pulmonary infection.

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