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Perioperative outcomes in redo VATS for pulmonary ipsilateral malignancy: A single center experience

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ABSTRACT

Background: The role of video-assisted thoracoscopic surgery for oncological major pulmonary resections is now well established; however, the literature within pulmonary re-operations is still limited. The purpose of this study is to evaluate the safety and efficacy of redo thoracoscopic resections for ipsilateral pulmonary malignancy.
Methods: Data from patients undergoing video-assisted thoracoscopic surgery at the Unit of Thoracic Surgery of Padua were analyzed, comparing the results between the first and second ipsilateral surgery. The retrospective study included patients who underwent 2 thoracoscopic surgeries for oncological reasons between 2015 and 2022. The variables considered included patients' baseline characteristics, pre, intra, and postoperative data.
Results: The study enrolled 51 patients undergoing ipsilateral thoracoscopic re-operation. The statistical analysis showed that surgical time (95min *vs* 115min; $p = 0.009$), the presence of intrapleural adhesions at second surgery (30 % *vs* 76 %; $p < 0.001$), overall pleural fluid output (200 *vs* 560 ml; $p = 0.003$), time with pleural drainage (2 *vs* 3 days; $p = 0.027$), air leaks duration time ($p = 0.004$) and post-operative day of discharge (3 *vs* 4 days; $p = 0.043$) were significantly higher in the re-operation group.
No statistical differences were observed between the 2 groups respect to R0 resection rate (90.2 % *vs* 89.1 %; p=>0.9) and complications (5.8 % *vs* 15.6 %; $p = 0.11$).
The conversion rate to open surgery was 11.8 %.
Conclusion: Although some differences emerged between the first and second intervention, they had minimal impact on the clinical course of the patients.
Therefore, thoracoscopic surgery has been shown to be safe and effective in re-operations with satisfying peri-operative outcomes. To achieve such results, these procedures should be reserved for experienced surgeons.

1. Introduction

Video-Assisted Thoracoscopic Surgery (VATS) represents nowadays the gold standard for the treatment of most intrathoracic malignancies [1–4]. Indeed, VATS is associated with a reduction of post-operative pain and length of stay and with a less rate of post-operative complications, whilst respecting oncological dogmas [5]. Even if the role of VATS has been widely accepted in standard situations, one big issue still in debate is how to approach a second ipsilateral thoracic surgery. Indeed, redo VATS intervention is sometimes considered a relative contraindication because of its more complexity and technically demanding procedure [6]. Conversely, some recent studies demonstrated that redo VATS is a valid alternative to thoracotomy and is associated with fewer peri-operative complications and a shorter hospital stay [7–10].

The main objective of this study is to evaluate the safety and feasibility of VATS re-interventions for oncological reasons in terms of perioperative and postoperative complications, analyzing the first and the second VATS surgery.

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2. Materials and methods

In this study We retrospectively reviewed a total of 51 patients that underwent redo VATS at the Thoracic Surgery Unit of Padua University Hospital between January 2015 and December 2022. This study received the approval by the Institutional Review Board of Padua University Hospital (340n/AO/23).

We included all patients that underwent ipsilateral VATS surgery conducted for a primary or secondary intrathoracic tumor with both surgeries performed via VATS approach. Conversion to thoracotomy for the second surgery didn't represent an exclusion criterion. Backwards, exclusion criteria were conversion to thoracotomy required for the first VATS surgery and surgery performed for non-neoplastic reasons.

General variables included: gender, age, months between the 1st and 2nd surgery patient pulmonary and general comorbidities (calculated by Charlson Comorbidity Index), history of smoke and eventual pre-operative oncological therapies. The comparison between the first and second procedure was performed by analyzing the following variables: age at the different procedure, type of surgery (wedge resection, segmentectomy, lobectomy, hilo-mediastinal lymphadenectomy), duration of intervention, presence of adherences, conversion rate of the 2nd surgery, liquid and air leakage from the pleural drainage, day with pleural drainage, post-operative day of discharge, ICU length of stay, histological features, radical resection (R0 or R1) and length of surgical margins. Moreover, we analyzed post-operative outcomes in terms of development of complications (prolonged air leaks, pneumonia, hemothorax, empyema, bronchopleural fistula) day of chest-tube removal and day of discharge.

Data were described using absolute numbers and percentages for categorical data and median and interquartile range (I–III quartile) for continuous data. Comparisons were performed with McNemar's test for categorical variables and with the Wilcoxon signed rank test for continuous ones. Benjamini & Hochberg's correction for multiple testing was applied when comparing outcome variables. Univariable gamma and logistic regression were built to estimate the effect of multiple independent variables on continuous and discrete outcomes, respectively. The outcomes considered were pleural adherences, complications, and days of air and liquid leaks from the chest drainage in the second surgical procedure. Results were provided as average marginal effect (AME) for continuous outcomes, odds ratio (OR) for categorical ones and 95 % confidence interval (CI). For all analyses, a 2-sided $p < 0.05$ was significant. Statistical analyses were performed using the R System version 4.2.1 and packages "Gtsummary" [11] and "margins".

3. Results

3.1. Study population

51 patients were enrolled in this study, including 25 females (49.0 %) and 26 males (51.0 %). Pulmonary comorbidities were found in 16/51 (31.4 %) patients: the most frequent represented by chronic obstructive pulmonary disease, observed in 5/51 (9.8 %). The age-adjusted Charlson Comorbidity Index demonstrated a median of 6 (IQR_{1-3} 5–7). When analyzing the smoking habit, we found 14/51 (27.4 %) non-smoking patients, 24/51 (47.1 %) active smokers and 13/51 (25.5 %) former smokers, with a median Pack/Years in the smoking population of 38 (IQR_{1-3} 19–54). Regarding the therapeutic strategy related to the first malignancy, 29/51 (56.9 %) patients underwent surgery alone, 15/51 (29.4 %) surgery and chemotherapy, 2/51 (3.9 %) surgery and radiotherapy and 5/51 (9.8 %) surgery and chemo-radiotherapy, independently from them being neoadjuvant or adjuvant. 4 senior surgeons (S·N., F.R., A.D.A., M.S.), with more than a decade of experience as first surgeons and at least 300 major pulmonary VATS resections, performed all the redo cases. Regarding the surgical indication for the redo procedure, 25/51 (49.0 %) patients underwent completion resection for the same relapsing neoplasm, 15/51 (29.4 %) patients underwent double surgery for metastasectomy, 8/51 (15.7 %) patients underwent lymphadenectomy, and 2/51 (3.9 %) patients underwent resection for 2 different lung tumors. The conversion rate to open surgery was 11.8 %.

Table .1 resumes data on the characteristics of the study population.

3.2. First-second procedure comparison

The median age at first surgery was 63 years (IQR_{1-3} 54–70) as at second intervention was 65 (IQR_{1-3} 58–71), with an expected statistical difference observed ($p < 0.001$).

The most common surgical procedure in the first intervention was non-anatomic parenchymal resection, completed in 24/51 (47.0 %) patients, while in the second surgery wedge resections were performed in 16/51 (31.4 %) patients (Fig. 1). Pulmonary anatomic resections were practiced in 21/51 (41.2 %) patients in the first series and in 31/51 (60.8 %) in the second. The data obtained through histological examination of the operative pieces are summarized in Table .2, together with the comparison of the population who underwent the 2 different surgical procedures. The size of the pathologic T was significantly greater in the first surgery ($p = 0.018$), with a median of 16 mm (IQR_{1-3} 11–28) and of 14 mm in the re-VATS group (IQR_{1-3} 5–23). The most frequent diagnosis in both interventions was lung adenocarcinoma, in 27/51 (52.9 %) patients in the first intervention and in 20/51 (39.2 %) patients in the second, followed by lung metastasis in 16/51 (31.4 %) patients in both the first and second surgery. Surgical margins were not statistically different between the two procedures, with a median of 7 mm in the first procedure (IQR_{1-3} 2–15 mm) and of 5 mm in the second (IQR_{1-3} 3–15

Table 1
General characteristics of the population.

General features of the population	
Population number	N = 51[a]
Sex	
Males	25 (49.0 %)
Females	26 (51.0 %)
Month between 1st and 2nd surgery	15 (4.3)
≤ 12 months	24 (47.1 %)
> 12 months	27 (52.9 %)
Charlson Comorbidity Index	6.00 (5.00, 7.00)
Pulmonary Comorbidity	
Absent	35 (68.6 %)
Present	16 (31.4 %)
Type of Pulmonary Comorbidity	
None	35 (68.6 %)
COPD	5 (9.8 %)
Asthma	2 (3.9 %)
Emphysema	2 (3.9 %)
Tuberculosis	1 (1.9 %)
Previous pneumonia	2 (3.9 %)
Others	4 (7.8 %)
Smoke	
Non smoker	14 (27.4 %)
Former	13 (25.5 %)
Actual smoker	24 (47.1 %)
Pack/years	38 (19.5–54.0)
Therapies related to 1st surgery	
None	29 (56.9 %)
Chemotherapy	15 (29.4 %)
Radiotherapy	2 (3.9 %)
Chemo/radiotherapy	5 (9.8 %)
Type of redo VATS	
Completion	25 (49.0 %)
Metastasectomy	15 (29.4 %)
Lymphadenectomy	8 (15.7 %)
Other tumor	2 (3.9 %)
Other reason	1 (1.9 %)
RedoVATS conversion to open surgery	
No	45 (88.2 %)
Yes	6 (11.8 %)

[a] n (%); Median (IQR).

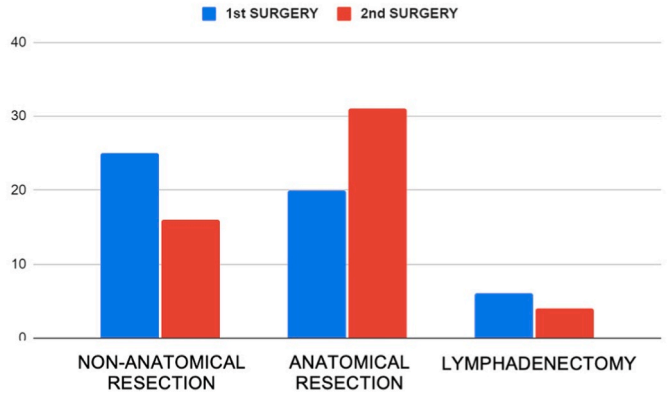

Fig. 1. Different type of surgery in relation to the 1st and 2nd VATS.

mm). An R0 radical resection was found in 37/41 (90.2 %) patients for the first operation and in 41/46 (89.1 %) in the second. On the other hand, an R1 microscopically invaded resected margin was obtained in 4/41 (9.8 %) cases and 5/46 (10.9 %) respectively. The median duration of surgery was significantly longer in re-VATS (115 min, $IQR_{1\text{-}3}$ 90–152), compared with the first surgery (95 min, $IQR_{1\text{-}3}$ 58–122) with a p-value of 0.009. In addition, a statistical significance was also found concerning presence of more pleural adhesions in reoperations ($p < 0.001$). In fact, in the first intervention they were absent in 35/51 (68.6 %) patients and present in 15/51 (29.4 %); in the second intervention, however, we didn't find any in 12/51 (23.5 %) patients and they were present in 39/51 (76.5 %) of them. Total liquid leaks from chest drainage were compared between the two procedures, and their level was statistically higher in the second intervention (200 ml vs 560 ml; $p = 0.003$). Same results were found for duration of days with chest drainage (2 days vs 3 days; $p = 0.027$) and duration of air leaks from the pleural drainage ($p = 0.004$). The length of stay in the ICU (1 day for both the surgeries, $p = 0.3$) and complications, which occurred in 3/51 (5.9 %) patients in the first surgery and in 8/51 (15.6 %) in the second were not different between the two procedures. Specific complications are summarized in Table 2.

The median length of in-hospital stay was also higher in the second intervention (4 days, $IQR_{1\text{-}3}$ 3–7 days), compared with the first (3 days, $IQR_{1\text{-}3}$ 3–5 days), with a p-value of $p = 0.043$.

4. Discussion

4.1. General considerations

Even if VATS represents the gold standard to address most oncological lung resections, the same cannot be said for re-interventions [6]. Indeed, especially in the past, there was a kind of a taboo that a previous surgical intervention was a contraindication to a thoracoscopic redo surgery, particularly because of the technical difficulties related to the possible formation of pleural adhesions and the presence of scarring tissue derived from the previous surgery (Fig. 2) [6,12].

However, more recent literature has made encouraging contributions regarding the role of thoracoscopy in re-interventions [7–10,13]. In 2020, Sun et al. demonstrated that redo VATS are feasible and safe for major lung resections by publishing a series of 14 thoracoscopic re-interventions, in which only 1 was converted to thoracotomy [9]. Chen et al. compared 36 redo VATS with 28 re-thoracotomies, showing excellent results for the redo VATS group, which was characterized by fewer days of hospitalization (11.0 *vs* 20.4) and fewer complications (16.7 % *vs* 39.3 %) than the re-thoracotomy group [10]. Fabian et al. in a case series of 41 patients undergoing redo VATS for malignancy showed good results in terms of perioperative outcomes also for those patients (6/41) with a first thoracotomy operation [8]. These promising data were also confirmed in this work.

Table 2
Comparison between 1st and 2nd surgery.

Comparison between 1st and 2nd surgeries				
Variable	N°	1st procedure[a]	2nd procedure[a]	p-value[b]
Age (years)	**51**	63 (54, 70)	65 (58, 71)	**<0.001**
Tumor dimension (mm)	**51**	16 (11, 28)	14 (5, 23)	**0.018**
Side	**51**			0.4
Right		31 (60.8 %)	31 (60.8 %)	
Left		20 (39.2 %)	20 (39.2 %)	
Type of Surgery	**51**			0.5
Wedge resection		24 (47.0 %)	16 (31.4 %)	
Segmentectomy		5 (9.8 %)	7 (13.7 %)	
Lobectomy		16 (31.4 %)	24 (47.1 %)	
Lymphadenectomy		6 (11.8 %)	4 (7.8 %)	
Parenchymal resection		**45**	**47**	0.2
Non anatomical		24 (53.3 %)	16 (34.0 %)	
Anatomical		21 (46.6 %)	31 (66.0 %)	
Diagnosis	**51**			NA
Lung adenocarcinoma		27 (52.9 %)	20 (39.2 %)	
Metastasis		16 (31.4 %)	16 (31.3 %)	
Lung adenosquamosus carcinoma		1 (2 %)	0 (0 %)	
Lung neuroendocrine tumor		3 (5.9 %)	3 (5.9 %)	
Lung squamocellular tumor		4 (7.8 %)	6 (11.8 %)	
Results of tumorectomy		0 (0 %)	4 (7.8 %)	
Lung other tumor		0 (0 %)	2 (4.0 %)	
Staging	**51**			
No evidence of disease		0 (0 %)	12 (23.5 %)	
Stage I		22 (43.1 %)	8 (15.7 %)	
Stage II		9 (17.6 %)	9 (17.6 %)	
Stage III		3 (5.9 %)	6 (11.8 %)	
Stage IV		1 (2.0 %)	0 (0 %)	
Metastatic		16 (31.4 %)	16 (31.4 %)	
R° 2nd surgery		**41**	**46**	>0.9
0		37 (90.2 %)	41 (89.1 %)	
1		4 (9.8 %)	5 (10.9 %)	
Margins (mm)	**31**	7 (2, 15)	5 (3, 15)	0.8
Time (min)		95 (58, 122)	115 (90, 152)	**0.009**
Pleural Adhesions				**<0.001**
Absent		35 (68.6 %)	12 (23.5 %)	
Present		15 (29.4 %)	39 (76.5 %)	
Liquid leakage (ml)		200 (100, 665)	560 (280, 1542)	**0.003**
Day with pleural drainage		2.0 (1.0, 3.0)	3.0 (2.0, 6.0)	**0.027**
Day with air leaks		0.0 (0.0, 0.5)	0.0 (0.0, 2.5)	**0.004**
ICU length of stay (day)		1.0 (1.0, 1.0)	1.0 (1.0, 1.0)	0.3
Complications				0.11
Absent		48 (94.1 %)	43 (84.2 %)	
Present		3 (5.9 %)	8 (15.8 %)	
Type of complication				
Prolonged air leaks (>5 days)		3 (5.9 %)	6 (11.8 %)	
Hemothorax + Pneumonia			1 (2 %)	
Pulmonary embolism			1 (2 %)	
POD Discharge		3.0 (3.0, 5.0)	4.0 (3.0, 7.0)	**0.043**

[a] Median (IQR); n (%).
[b] Wilcoxon signed rank test with continuity correction; McNemar's Chi-squared test with continuity correction; Benjamin & Hochberg correction for multiple testing.

A common point among the various studies published on the subject and supported by our group too, is certainly represented by the fact that redo surgeries are often complex and technically demanding procedures for which a great deal of surgical experience and technical skill is required. Indeed, we believe that redo surgery is strongly surgeon dependent, and this is why these procedures, in our center, are entrusted only to senior surgeons. They carry out daily thoracoscopic procedures, from basic pulmonary resections to complex broncho-vascular reconstructions, so that they can deal promptly with possible complications. They are hence prepared to intervene in any circumstance either mini-invasively or to convert to open thoracotomy when judged safer; these are some of the characteristics that a surgeon engaged in this type of surgery should possess.

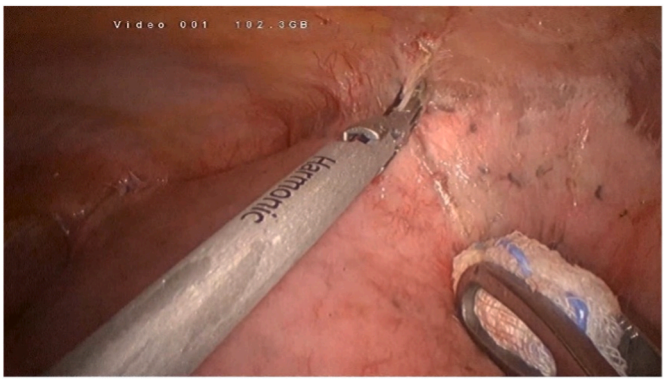

Fig. 2. Adhesiolysis in a left upper lobectomy in a redo VATS.

4.2. Study population

About the study population, with 51 patients, this paper includes one of the largest case series published of patients undergoing redo VATS for pulmonary malignancy, either primary or secondary tumors. The gender distribution of the population was homogeneous with 49 % of males and 51 % of females with a median age in line with other studies in the literature. More than half of the patients did not receive any further treatment other than surgery for the first malignancy; these other treatments were collected to see if they could in any way affect the main intra- and postoperative outcomes of the second surgery, although nothing statistically significant emerged. Regarding the indications for the redo VATS, more than 50 % of the patients underwent second surgery for local recurrence or completion resection for primary lung cancer, and this figure is also in line with other studies in the literature.

4.3. Comparison between the 1st and 2nd surgery

Comparison between the first and second surgeries showed that the only variables for which a statistical significance was observed were: surgical time, presence of pleural adhesions, fluid and air leakage from chest drain, and in-hospital length of stay.

In this case series a statistically significant difference of 20 min was observed between the first and second surgery; the only study in literature that provided a comparison of operating time between the first and second procedure was published by Fabian et al., in which a difference of 40 min, albeit not statistically significant, was observed [8]. However, this finding could be explained by the different type of surgery. Indeed, in this study, the most common procedures of the first surgery were non-anatomical resections (53.3 %), while for the redo VATS were anatomical parenchymal resections (66.0 %). Obviously, another possible interpretation of the longer surgical time during the reoperations is the time required to perform the dissection of pleural adhesions, since it was found a statistically significant difference in the presence of pleural adhesions, which were greater in the redo VATS. In any case, an average increased time of 20 min seems to be reasonable for a thoracoscopic redo surgery without affecting the judgement about its feasibility and safety.

The presence of pleuro-parenchymal adhesions is generally associated with an increased technical difficulty of the surgery and an increased conversion rate. In this case series, the presence of adhesions represented the main reason for conversion to thoracotomy and was observed in 4 out of 6 cases. This aspect is also confirmed by the study of Hamaji et al. which shows that the conversion rate of re-VATS was lower if the patient had a previous thoracoscopic procedure (10 %) compared with an open procedure (50 %), which is characterized by an increased postoperative adhesion [7].

In addition to this finding, a statistically significant difference was observed between the presence of adhesions between the first and second surgery, which, however, did not appear to be related to the type of parenchymal resection. This contrasts with the findings of Fabian and colleagues, for which adhesions appeared to be greater in anatomic resection redo surgery following a previous parenchymal anatomical resection [8]. Playing a major role, especially with a view to redo surgery, potential factors predicting the presence of adhesions at the time of 2nd surgery have been analyzed; it was found that being an active smoker is associated with a 5-fold increased risk, as well as an interval time greater than 12 months between the first and the second operation (**Suppl.1**). Particularly, the correlation between being an active smoker and the presence of pleuro-parenchymal adhesions, to our knowlwdge, is not described in literature; however, this is an interesting feature, and we think that smoking, with its pro-inflammatory action may somehow exacerbate the postoperative inflammatory state underlying formation of the adhesions.

A significant difference in air leaks and in total liquid leakages collected from the pleural drainage was also observed: they were higher in the redo VATS group ($p = 0.004$, $p = 0.027$). This could be related to the greater presence of adhesions and to the need for adhesiolysis in the second surgery or to the increased complexity of the redo surgery (66.0 % vs. 34.0 % of anatomical resection in the redo group), but both hypotheses do not reach statistical significance. Undoubtedly, tissues that have already been surgically manipulated are, by definition, more fragile, and probably characterized by a greater local inflammatory response following redo surgery; this might be an aspect to be considered in relation to the data presented above and for which future studies are required. However, the worst results of the redo surgery related to air leaks and liquid leaks, in addition to a higher complications rate (15.8 % for redo VATS *vs* 5.9 % for first surgery), entail an average hospital stay of only one day longer, with minimal impact on the patient (3 days *vs* 2 days of pleural drainage for redo VATS group).

While the differences between the 2 surgeries showed limited impact on patients, it should be emphasized that for other perioperative outcomes analyzed, no significant differences were observed. Notably, no differences were observed in margins and R0 resection rate, and this prove the effectiveness of VATS even for redo surgery. Moreover, the conversion rate at 11.8 % is also absolutely in line with the literature and even overlaps with studies that report it as similar for first surgeries [7–10]. In our center the overall conversion rate is about 6 %; even though the conversion rate in the reintervention cohort is almost twice as much, this data is to be considered acceptable due to the challenging issues related to a reoperation.

Obviously, these results should also be evaluated considering the limitations of this study (retrospective and monocentric) and it is hoped that new prospective and multicenter studies could start soon to improve the general knowledge about this topic.

5. Conclusion

In conclusion, this study confirms that VATS is feasible, safe, and effective even in redo surgery, with satisfying intraoperative and postoperative outcomes. To achieve good results, these procedures should be reserved for experienced surgeons.

Surgical time, presence of pleural adhesions, fluid and air leakage from chest drain and in-hospital length of stay where higher in the redo group; however, they had minimal impact on the clinical course of the patients with no differences concerning surgical complications between the two groups.

In the light of the above, therefore, a first VATS surgery does not itself represent a contraindication to a redo VATS surgery.

Consent to publication

The patients signed informed consent for their participation in the study. This study received the approval by the Local Institutional Review Board (340n/AO/23).

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Credit statement

Vincenzo Verzeletti: Conceptualization; Data curation; Investigation; Methodology; Roles/Writing - original draft.

Alberto Busetto: Conceptualization; Data curation; Investigation; Methodology; Roles/Writing - original draft.

Patrizia Bartolotta: Conceptualization; Data curation; Investigation; Methodology; Roles/Writing - original draft.

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Samuele Nicotra: Conceptualization; Data curation; Investigation; Methodology; Roles/Writing - original draft.

Marco Schiavon: Conceptualization; Data curation; Investigation; Methodology; Roles/Writing - original draft.

Eleonora Faccioli: Supervision; Validation; Visualization; Writing - review & editing.

Giovanni Maria Comacchio: Supervision; Validation; Visualization; Writing - review & editing.

Andrea Dell'Amore: Conceptualization; Project administration; Supervision; Validation; Visualization; Writing - review & editing.

Federico Rea: Conceptualization; Project administration; Supervision; Validation; Visualization; Writing - review & editing.

Disclosure

The authors have no disclosure.

Declaration of competing interest

None.

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