Original Resear	Volume - 11 Issue - 02 February - 2021 PRINT ISSN No. 2249 - 555X DOI : 10.36106/ijar Surgery EVALUATION OF CLINICAL DATA IN PATIENTS THAT UNDERWENT DIFFERENT SURGICAL TREATMENTS FOR SPONTANEOUS PNEUMOTHORAX
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ABSTRACT Introduction: Spontaneous pneumothorax (SPT) is surgically treated with two different techniques: Video Assisted Thoracoscopy (VATS) or open thoracotomy (OT). Despite the different invasiveness of the techniques, literature gives controversial results in correlation of the techniques to the clinical outcomes (like length of hospital stay (LOHS), recurrences of the pneumothorax, duration, collection of the drains and etc). The aim of our study was to analyze perioperative clinical features in patients that underwent SPT treatment surgically.

Materials and methods: prospectively, we evaluated data of patients treated for SPT in two-year period at the University clinic for thoracic surgery in Skopje. Patients were divided into VATS group and OT group, according to the surgical technique used for treatment. In both groups we analyzed demographical, laboratory data, duration of the chest drains presence, early inflammatory markers and total LOHS. Patients with recurrent pneumothorax, older than 70 years with severe cardiological impairment were excluded.

Results: The study included 42 patients, 23 patients (54.8%) underwent VATS treatment and 19 patients (45.2%) underwent OT. In both groups more patients were male. VATS group of patients showed nonsignificant difference in postoperative laboratory and inflammatory findings, non-significantly lower presence of the drains in terms of days, significantly lower drain fluid collections for the first 3 days and significantly shorter LOHS compared to the OT group.

Conclusion: Our study has showed that patients treated for spontaneous pneumothorax with VATS have shorter length of hospital stay, shorter chest drain presence and overall show better outcome.

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KEYWORDS: VATS, spontaneous pneumothorax, open thoracotomy, LOHS

INTRODUCTION

Spontaneous pneumothorax (SPT) in non-malignant states is one of the most frequent pleural diseases diagnoses. In patients with emphysematous lung disease or large bullae it is a common finding and many of them are referred to thoracic surgery. The overall incidence of SPT is reported higher in man with 7.7 and 1.5 cases per 100 000 patients in woman [1].

Conservative treatments for the SPT, that include observations, chest tube, needle aspiration has shown not so effective results especially in terms of recurrences and has not been established as methods for reexpansion of the affected lung. Over this, surgical treatment with open thoracotomy (OT) has been used with great results in the last century [2,3].

Enthought, the surgical treatment of SPT goes back to history in the 1937, when the first thoracoscopy and bulla extraction was done, today a lot of questions stay open whether this technique or novel extremely advanced techniques and technologies like Video Assisted Thoracoscopy (VATS) show advantages in treatment of the SPT [4,5,6].

Most of the surgeons nowadays support the novel VATS techniques as efficient and safe procedure for most of the thoracic procedures when the treatment of SPT is discussed in correlation to lower pulmonary complications, better and faster patient outcome, quicker recovery, earlier mobilization, less opioid usage and overall shorter length of hospital stay (LOHS)[5,6].

However, the perfection of the former sentence is not established as an evidence-based medicine so far. Contrary to this some authors strongly argue that conservative treatment or OT is recommended for uncomplicated first time or recurrent pneumothorax or different pleural diseases [6].

So far, no consensus is established of preferring one technique over other technique in patients with first time SPT. This is due to many factors and controversial reports in correspondence to different outcome measurements as well as different methodological approaches. In 2010th British Thoracic Society relisted recommendation that weighted decision for the treatment of SPT should be done giving some priorities to the VATS (in terms of better tolerating from the patients) over OT but when the risk of higher recurrences rate is calculated [1].

Therefore, the aim of our study was to analyze and compare several important perioperative clinical data and complications in patients that underwent these two different surgical techniques for spontaneous pneumothorax treatment. The primary outcome was comparing the recurrence rate and length of hospital stay (LOHS). The secondary outcomes were to evaluate and compare level of postoperative complications, drain presence (in terms of days) as well as postoperative inflammatory and laboratory findings in respect to the techniques used.

MATHERIALAND METHOD

The prospective clinical study was conducted for two-year period at the University Clinic of Thoracic and Vascular surgery in Skopje. The study was conducted after the approval of the ethic committee of the clinic.

Inclusion, exclusion criteria and stratification of the patients:

The study included patients surgically treated for first time SPT with emphysematous lung disease, previously treated with pleural drainage and in whom (per guidelines) [1] air leak persisted for one week after the pleural drainage, [7] without known malignancies. Patients older than 70, younger than 18 years, patients with BMI>30, patients with cardiological impairment (EF<50%), as well as patients that were not willing to be in the study were excluded from the study. Aditionaly patients in whom conversion from VATS to conventional thoracotomy was needed were excluded.

In this period, 72 consecutive patients were admitted to the clinic for the first-time treatment of spontaneous pneumothorax. Out of them30 patients were excluded and 42 patients were left for analyzes. Patients were divided into one of the two group depending on what surgical technique was used for treatment. Group OT (n=19) included patient in whom open thoracotomy was used while in the group VATS (n =23) video assisted thoracotomy was used.

Analyzes.

Analyses were done similar to our previous pilot study published in

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2017[7]. For all patients analyzes and comparation of the demographic characteristics: (age, gender), clinical data (side of the SPT, comorbidities, laboratory findings (1 and 3^{st} day) and duration of the surgery were done. For both groups we analyzed postoperative complications: ICU admission, postoperative bleeding, drain presence (in terms of days), drain collection (amount of volume in ml on the first and the third postoperative day), length of hospital stay(LOHS-defined as length from admitting to the clinic till discharge) and late recurrence of the pneumothorax (defined as pneumothorax on the same side that was operated after 3 month period). We analyzed and compared the early inflammatory laboratory markers (CRP, leucocytes and albumin) and laboratory findings for erythrocytes and thrombocytes on the 3^{st} postoperative day.

Surgical procedure choice.

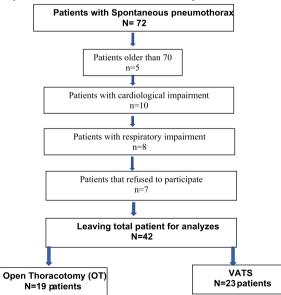
In all patients preoperatively conventional x-ray and computed tomography (CT scan 2-5 mm intervals) for confirming the underlying disease was done. Which surgical procedure was done was based on the size, site, degree of the collapsed lung and desmoplastic range evaluation. General anesthesia with double lumen tube was used in all patients. Patients were placed in lateral decubitus position (contralateral hemitorax on the surgical table) and after finishing of either of the procedures chest drains were placed. Open thoracotomy technique was done via 15-25 cm incision when rib spreader was applied. For the VATS technique: The video equipment was positioned on the affected hemithorax of the patient through incision up to 5 cm at the 7th intercostal space and additional two ports were applied in the mid axillary line at the 5th intercostal space.

Statistics:

Analysis of mean parameters and standard deviation in both groups and between the groups was done with parametrical (paired and unpaired t-test) depending on the distribution. In all patients we analyzed and compared. For the comparation of the duration of the intervention, LOHS, structure of the drain presence, structure of the laboratory findings (erythrocytes, leucocytes, platelets, CRP, albumin and total proteins) between the groups we obtained data either symmetric or if it is asymmetric. For symmetry testing in these variables we used help of characterized histograms for each group separately as box & wisker diagrams and done Mann Whitney U test.

RESULTS

We analyzed data from total of 42 patents where 54.9 % went VATS treatment while 45% underwent Open Thoracotomy (OT) treatment for spontaneous pneumothorax. 30 patients were excluded from the study due to the exclusion criteria. Flowchart is presented below.



Flowchart of inclusion in the study

Demographic data between the groups was homogenic. Age difference was not significantly different between the groups. More patients were male 78.9% vs 73.9% in both of the groups. Same number of patients were smokers in the groups. Most common comorbidities found were diabetes mellitus (present in 21.3% vs 26.1%) and hypertension (in

31.5% vs 34.8%) in respect to the groups. Demographic and clinical data are shown in the Table 1.

Table 1. Pati	ients demogr	aphic and	basic clinical	data

	OT	VATS	Significance
	N=19	N=23	
Male/Female (n)	15/4	17/6	NS
Mean age (Mean+ Sd)	40.5 +10.4	41.4+11.9	NS
Right/left side(n)	11//8	13/10	NS
Smokers(n)	13	13	NS
Diabetes Melitus (n)	4	6	NS
Hypertension (n)	6	8	NS
Erythrocytes (mean + sd)	4.5+15.4	4.5 + 0.3	NS
Leucocytes (mean + sd)	12.2+3.1	12.02 ± 4.4	NS
Thrombocytes (mean + sd)	270+78.1	260+67.2	NS

OT- Open Thoracotomy; VATS- Video Assisted Thoracoscopy; n= number; NS-Not Significant; sd-standard deviation

Right side pneumothorax was surgically treated in 57.9% of the patients in the OT group and in 56.5% in the VATS group. Basic laboratory data for erythrocytes, leucocytes and thrombocytes count were insignificantly different between the groups.

The duration of surgery was not statistically significant between the both groups for p=0.19 according to the Mann Whitney U test (Table 2).

Table 2. Duration of surgery between the groups	
Mann-Whitney U Test (OT.VATS) By variable OT_V	ATS

Duration 242, 352, 106, -1, 0, -1, 0, 16 18 of 5000 5000 5000 29387 19571 29884 1939 19		Sum -	Rank Sum - VATS	Z	p- level	Z - adjuste d		d		2* 1sided exact p
surgery 0 99	of						1939		18	0, 198455

Drain collection in terms of ml, for the day 1 and day 3 day was not significantly different between the groups for p=0.7 and p=0.3. LOHS was significantly different between the groups (for p=0.04).

Table.3. LOHS

Mann-Whitney U Test (OT.VATS) By variable OT_VATS Marked tests are significant at p <,05000										
	Sum	Rank Sum - VATS		Z	p- level	Z - adjusted				2*1sided - exact p
LOHS	357,5 000				0,050 243	1,967671	0,04 9107	16	20	0,049370

Two patients (0.38%) from the OT group were admitted to the ICU (one of them needed prolonged mechanical ventilation for 24 hours) while in the VATS group none of the patients were admitted to the ICU. No statistically significant differences were found between the groups for the laboratory features postoperatively (erythrocytes, leucocytes, platelets) as well as the early inflammatory markers as CRP and albumin. Table 4.

Table 4. Clinical	characteristics	between the groups
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Parameter	OT(N=19)	VATS(N=23)
Perioperative bleeding N/%	1(0.09%)	/
Drains presence in days (mean	5.4 <u>+</u> 2.8	5.2 <u>+</u> 3.2
+sd)	4.1 <u>+</u> 0.5	4.3 <u>+</u> 3.2
Erythrocytes (mean +sd)	15.4 <u>+</u> 3.5	14.8 <u>+</u> 3.1
Leucocytes (mean +sd)	292.2 <u>+</u> 122	260.8 <u>+</u> 130
Platelets (mean +sd)	10.4 <u>+</u> 5.5	10.01 <u>+</u> 6.4
CRP (mean +sd)	4(0.76%)	3(0.69%)
Late recurrence N/%		

In both groups no major complications and mortality occurred.

DISCUSSION

The treatment of the SPT can incorporate different and many modalities but for none of them consensus is present (8-12).

We present a study where we evaluate and compare perioperative clinical features and complication analyzes in patients with spontaneous pneumothorax treated by two different techniques (OT vs VATS). Firstly, we have to mention that literature which have evaluated some similar data is scattered, limited to small single center studies and furthermore the results are controversial. In 2017^{th} a meta analyses has been done that included almost 7000 patients in order to give preference of one surgical technique over other and the result have confirmed the clinicians and researchers do not have enough disease or performance based knowledge to confirm which technic is superior in correlation to different outcomes (13).

In the last decades VATS have mainly changed the approach to treatment of the SPT. Even though this is preferable technique for most of the surgeons some societies and researchers (An American Collage of Chest Physicians Delphi Consensus) (6) do not advocate it as a technique of choice for first time SPT. On the other hand, other societies do agree that surgical treatment is needed when persistent air leak after one week of drainage is present in first time SPT, radiologically confirmed. In our study decision for surgical treatment of the SPT was done based on this, according to the British Thoracic Society Pleural Disease Guideline released in 2010(1).

As for our study,19 patients underwent OT while 23 underwent VATS treatment and decision for what type of treatment was made upon surgent decision and expertise.

In our study more patients with SPT were male, that is corresponding to the fact of the global incidence knowledge (1). Duration of surgery was not statistically different between the both techniques which was to our surprise, due to the fact that VATS is basically quicker procedure (less invasive, no thoracotomy and shorter time needed for closure) (8,12). Additionally, in our previous pilot study (done on 24 patients in total) similarly we have not found difference in the duration of the surgery as in the present study (7). Contrary to our studies, the study of Weisberg D and Rafaely Y. (1199 patients included) (14) as well as the study of Mouroux J et al. (15) (100 patients included) confirmed shorter time of surgery in VATS. In our studies we measured surgery time from the start of anesthesia to extubating which is methodologically different approach to their studies. However, authors do agree that the duration of the VATS procedure is corelated to the surgeon experience and routine as well as to the number of bullas ligated (which in current study we did not evaluated) (14,15).

Another point of evaluation in current study is the amount of drain collection on the first and on the third day in respect to the both techniques. Mainly drain volume amount depends on the type of the surgery, irrigation as well as the tissue trauma and other factors (4,10). In our study no difference was found in the drain collection volume between the both groups. In the former our study as well as other studies patients that underwent OT had significantly larger drain volume collection in total for the first 3 days (7,14). The differences in the studies results need larger evaluation, but to our modest opinion are due to the fact that in the former studies the drain collection for the three days was calculated in total, while in our current study we have evaluated the drain volume amount on the first and on the third day separately, which in terms of statistics do change the structure of the results.

Jakupi N et al. (7) have concluded that in patients that undergo OT, chest drains stay longer in terms of days when compared to the patients in whom VATS is done. Unlike the citated study in the present study (chest drain presence was on average 5.4 vs 5.2 days) and similar to Mouroux J. et al. (15) and Li WW et al. (16) studies, no statistically significant difference was found for the drain presence between the groups. Similar to us, Guiseppe C. and the coworkers report drain presence longer than 4 days, but differently to our methodology they have used talc powdering in the VATS patients (17).

Shorter persistence of chest drains to mean of 1.9 ± 1.01 days was mentioned in the study of Galbis Caravajal JV. et al. They evaluated the complications after VATS in 107(83 with SPT) consecutive patients with primary and secondary pneumothorax (18). Even though they did not methodologically work and compared their results to patients with OT, they certainly report very short time of drain presence in compare to our results. In here we have to take into consideration the different methodological approach in both studies.

Overall, guidelines and literature on the management of pneumothorax, report different recurrence rates. Lower recurrence rates (0-7%) are reported after open thoracotomy compared to the higher recurrence rates after VATS (2-14% on average 5 %) (1,6).

Mainly, researchers agree that the increased recurrence rates in VATS may be as a result of incomplete and inadequate exposure of the chest cavity which leads to unadjusted detections of the changes (8,9).

If we go back in the literature reports for recurrence rate, we can find studies that had higher recurrence rate (20-25%) after VATS when compared to OT and advocate this to the learning curve of the technique (19, 20, 21). In our study late recurrence was found in 0.76% in open thoracotomy group compared to 0.69% in VATS group. Even though our results are not statistically significant we cannot forget that in our study there was a different number of patients for the groups. We have to point out that we are center that is relatively novel in the usage of VATS, therefore we found these results very important to us. Furthermore differences in the results may be due to the definition of the late recurrence rate only after 3^{rd} , 6^{th} month and not like most studies that incorporate recurrence rates after 3^{rd} , 6^{th} month, one to 5 years (21, 22, 8).

Contrary to this, in the study of Bilgi Z. and Batirel HF, authors have confirmed that there is no correlation of learning curve to the adverse events in patients undergoing much major surgery in VATS compared to OT (resection of cT2 non-small cell lung cancer) (23) which opens a door to further discussions. However, all former studies (21,8, 23) and this study are different in several aspects so direct comparation cannot be done.

Guiseppe C. *at al.* reported a recurrence rate of 1.9% of the patients that is more similar to our data but in their study, they have corelated recurrence rate to the smokers and non-smokers patients (17). More studies refer tobacco smoking and cannabis usage as factors that increase at the same time the occurrence of SPT as well as the recurrence rates after surgical treatments in patients without previous parenchymal disease (24, 25). The fact that our study included patients with emphysematic lungs, we consider that small percent of recurrences as personal achievement. However, in our study in both groups, same number of patients were smokers (13 pts) and furthermore we have not done structured correlation of the smokers or non-smokers to the recurrence rate so direct comparation with the citated studies is not possible.

Olavarrieta Lucena RJ et al. (26) have conducted a similar to our study for 100 consecutive patients with primary pneumothorax that underwent surgical treatment and were examining the expectations and satisfaction of the patients in regard the surgical techniques. His study results confirmed that more preferable technique for the patient is VATS in correspondence to overall satisfaction and LOHS. For their study patient in the OT group stayed on average 12 days in the hospital while in the VATS group 3.2 days. Our results in the current study show significantly shorter LOHS for the VATS group. The study of Torresini G. and coauthors (27) was interested in whether VATS is justified in primary SPT and justified VATS with smaller recurrence rate and economic benefit when compared to conservative treatment. However, on average LOHS for conservative treatment group in their study was 12 days and for the VATS was 6 days. Similarly, to our current study in the pilot study of Jakupi N.et al.(7) LOHS was on average 14.3 vs 10.2 in respect to the groups. From clinical point of view, it seems absolutely logical that the LOHS will be shorter in less invasive techniques than in major surgery regardless the surgeon experience and learning curve.

The fact that the VATS is less invasive technique it leads to confirmation that the inflammatory response to this technique should be lower. This has been seen and proven by lower levels of cytokine response during VATS when compared to more profound suppression in lymphocytes and natural killer cells in standard thoracotomy (28,29). However, for our study early inflammatory markers such as CRP, leucocytes and albumin levels postoperatively did not show significant difference between the groups. As researchers and clinicians, we cannot find any significant logical explanation for this structure of the results just assume several hypotheses. Firstly- that maybe larger sample of patients is needed , secondly- more specific inflammatory response markers should be advocated and last but not least we have to consider that the results for inflammations markers in the former studies were studied in patients with malignancies which by itself is an inflammation trigger.

CONCLUSION

Treating spontaneous pneumothorax with the VATS technique

maintains a curve of decreasing the LOHS and better postoperative management. VATS technique should be proposed as a treatment of choice in the cases of spontaneous pneumothorax, but larger studies are needed. Our study does not perfectly clearly solve the controversies of the still going questions, but it opens door for further randomized studies.

LIMIITATONS AND FUTURE RECCOMAENDATIONS

Overall our study has several limitations. The number of participants is small, the stratification of patients was according to surgical performance prefeasibility and it is a single center study. There are differences in the number of the groups 19 vs 23 patients and the surgery was done by several different surgeons. The data analyses and variables that we measured should be expanded to longer postoperative follow up as well as more clinical features and complications should be included in the study. This may lead to future recommendation.

Apart for these limitations, we have to say that the study has benefits. Firstly, VATS is a method that is not very long time used in our country, to our knowledge we are the only center that has reported similar study. The aims of the study are perfect in terms of solving to so far neverending story of which surgical technique is more preferable.

CONFLICT OF INTEREST: Denied

REFERENCES

- MacDuff A, Arnold A, Harvey J, Management of spontaneous pneumothorax: British 1. thoracic Society Pleural Disease Guidelines 2010. Torax 2010;65 Suppl2: ii18-31 2
- Sahn SA, Heffner JE. Primary care: spontaneous pneumotorax. N Eng J Med 2000;34(2):868-874. 3.
- Lui HP, Yim APC, Izzat MB, Lin PJ, Chang CH. Thoracoscopic surgery for spontaneous pneumotorax. World J Surg. 1999;23(11):1133-6.
- Braimbirdge MV. Thoracoscopy: a historical perspective. In: Yim APC, Hazelrigg SR, Izzat MB. Eds. Minimal access cardiothoracic surgery. Philadelphia: WB 4. Saunders, 1999.
- 5 Cardillo G, Facciolo F, Giunti R, Gasparri R, Lopergolo M, Orsetti R, et al. Videothoracoscopic treatment of primary spontaneous pneumothorax: a 6 year experience. Ann Thorac Surg 2000;69: 357-62. Bauman MH, Strange C, Heffner JE, Light R, Kirby JT, Klein J, Luketich JD, Panacek
- 6. EA, Sahn SA. Management of Spontaneous Pneumothorax. An American College of Chest Physicians Delphi Consensus Statement. Chest 2001;11(2):590-602.
- Jakupi N, Spirovski Z, Dzikovski I, Kokareva A, Maric N, Nikolov S, Vela I, Jordanov 7. D, Stevic M, Jovanovski-Srceva M. Pneumothorax treatment in patients with emphysematous lung disease with two different surgical techniques. Evaluation of complications, risks and benefits. Macedonian Journal of Anesth 2017;3:27-33. Doi: 616.25-003.219:616.712-089.87.
- Noppen M, Alexander P, Driesen P, et al. Manual aspiration versus chest tube drainage in 8. first episodes of primary spontaneous pneumothorax: a multicenter, prospective, randomized pilot study. Am J Respir Crit Care Med 2002;165:1240-4.
- Tschopp JM. Bintcliffe O.,Astoul P,Canalis E, Dreisen P,Janssen J. ERS task force statements:Diagnosis and treatment of primary spontaneus pneumothorac. The 9
- Europian Respiratory Journal.2015;46(2):321-35. Foroulis CN. Surgery for primary spontaneous pneumotorax. Journal of Thoracic Disease.2016;8(12):1743-1745 10
- Wong A,Galiabovich E,Bhagwat K. Management of primary spontaneous pneumotorax: A review.AZN Journal of surgery 2018; h t t p : / / d o i . w i l e y . 11. com/10/1111/ans/14713
- 12. Ashby M, Haug G, Mulcahy P, Odgen KJ, Jensen O, Walters JA. Conservative versus interventional management for primary spontaneous pneumothorax in adults. Cohhrane Database Syst Rev.2014;18(12):CD01565. doi: 10.1002/14651858.CD010565.pub2.
- Sudduth CL, Shinnick JK, Geng Z, McCracken CE, Clifton MS, Raval MV. Optimal 13 surgical technique in spontaneous pneumothorax: a systematic review and meta-analysis. Journal of surgical research. 2017;2010: 32-46
- Weisberg D, Rafaely Pneumothorax: experience with 1,199 patients. Chest 2000;11(17):1279-1285. 14
- Mouroux J.Elkaim D, Padovani B, et al.Video-assisted thoracoscopic treatment of spontaneous pneumothorax: Technique and results of one hundred cases. J Thorac 15. Cardiovasc Surg 1996;112:385-91.
- Li WW. lee Rl, lee Tw at al. The impact of thoracic surgical access on early shoulder 16 Europhysics and the impact of undate surgery versus post lateral thoracotomy. Eur.J.Cardiothorac Surg 2003;23(3):390-6 Giuseppe C., Oliver JB., Francesco C., Luigi C., Marco Di M., Brennan CK.,Nick AM.
- 17. Primary spontaneous pneumothorax: a cohort study of VATS with talc poudrage . Thorax 2016;71:847–853. doi:10.1136/thoraxjnl-2015-207976 Galbis Caravajal JV. Maťé Madueño JJ. Benlloch Carrión S. Baschwitz Gómez B,
- 18 Rodriguez Paniagua JM.Video-assisted thoracoscopic surgery in the treatment of pneumothorax: 107 consecutive procedures. Arch Bronconeumol 2003;39(7):310-3 Cole FH, Khandekar A, Maxwell JM, Pate JW, Walker WA. Video assisted thoracic
- 19. surgery:primary therapy for spontaneous pneumothorax. AnnThorac Surg 1995;60;931-
- 3. Guerin JC, Vanderschueren RGJRA. Traitment des pneumothorax recidivants par application de colle de fibrine sous endoscopie.Rev Mal Resp 1989;6:443-5. Sedrakyan A, van der Meulen J, Lewsey J, et al. Video assisted thoracic surgery for another service and the recent provide a service of randomised 20.
- 21. treatment of pneumothorax and lung resections: systematic review of randomised
- clinical trials. BMJ 2004;329:1008 Chen JS, Chan WK, Tsai KT, et al. Simple aspiration and drainage and intrapleural 22. minocycline pleurodesis versus simple aspiration and drainage for the initial treatment of primary spontaneous pneumothorax: an open-label, parallel-group, prospective, randomised, controlled trial. Lancet 2013;381:1277–82.
- 23. Bilgi Z, Batirel HF, YildizeliB, Bostanci K, Lacin T, Yuksel M. No adverse outcome of video -assisted thoracoscopic surgery resection of cT2 non-small cell lung cancer during the learning curve. The Korean Journal of Thoracic and Cardiovascular Surgery 2017;50(4):275-280.
- Cheng YL, Huang TW, Lin CK et al. The impact of smoking in primary spontaneous pneumothorax. J Thorac Cardiovasc Surgery.2009;131:192-195. 24

- Johnson MK, Smith RP, Morrison D et al. Large bullae in marijuana smokers. Thorax.2000;55:340-342. 25 Olavarrieta Lucena RJ, Coronel P. Expectations and patient satisfaction related to the use of thoracotomy and video-assisted thoracoscopic surgery for treating recurrence of 26
- spontaneous primary pneumothorax. J Bras Pneumol. 2009;35(2):122-128. Torresini G, Vaccarili M, Divisi D, Crisci R. Is Video-assisted thoracic surgery justified
- 27 at first spontaneous pneumothorax? European Journal of Cardio-thoracic Surgery. 2001; 20.42-45
- 28 Yim APC, Wan S, Lee TW et al. VATS lobectomy reduces cytokine response compared
- In the Conventional surgery. Ann. Thoras Surg 2000;70:243-247. Ng CSH, Lee TW, Wan S et al. Thoracotomy is associated with significantly more profound suppression of lymphocytes and natural killer cells than video-assisted 29. thoracic surgery following major lung resection for cancer. J Invest Surg.2005; 18:81-