C-Reactive Protein and Fibrinogen as Indicators of Systemic Inflammatory Response in Patients Undergoing VATS and Conventional Pulmonary Lobectomy

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Summary

Introduction. There is still ongoing discussion about superiority of video-assisted thoracoscopic surgery or VATS approach for performing lobectomy over conventional pulmonary lobectomy performed by open thoracotomy for the treatment of non-small cell lung cancer at an early stage.

Aim of the study. This encouraged us to conduct a prospective study for evaluation and comparison of the systemic inflammatory response by using these two approaches.

Materials and methods. We have conducted a prospective study for evaluation of C-reactive protein and Fibrinogen as indicators of systemic inflammatory response during early postoperative course. Surgery was prospectively randomised in two groups: 15 patients underwent VATS lobectomy and 15 patients underwent conventional open lobectomy. Blood samples were taken preoperatively, 24 and 72 hours after operation, on the day of drain removal, and 1 and 9 days after the drain removal.

Results. Surgery caused systemic inflammatory response in both groups. The increase in CRP was notably higher in OL group in all measurements except preoperative ($p < 0.05$). The increase in Fibrinogen concentrations was also higher in OL group but statistical significance ($p < 0.05$) was reached only in day of drain removal.

Conclusions. VATS approach caused reduced systemic inflammatory response compared with conventional open thoracotomy approach and was also associated with lesser postoperative pain as duration of chest drains and total amount of drained effusion is significantly smaller.

Key words: VATS; lobectomy; lung cancer; systemic inflammatory response.

INTRODUCTION

Although first video-assisted dissectional pulmonary lobectomy was performed more than two decades ago (10) and this technique is established as suitable and appropriate for treatment of early stage non-small cell lung cancer (5,6,15,17,20,22,23), there is still ongoing discussion about superiority of this approach over conventional pulmonary lobectomy performed by open thoracotomy approach (1,7,22,24,25).

We started VATS lobectomy in 2006 and observed surgical results and early postoperative outcomes at least equal to open thoracotomy approach in retrospective study we performed (13). This encouraged us to conduct a prospective study for evaluation and comparison of the systemic inflammatory response by using these two approaches.

AIM OF THE STUDY

The aim of our study is to compare systemic inflammatory response in early-stage non small cell lung cancer patients undergoing radical surgical intervention – pulmonary lobectomy with mediastinal nodal dissection by both minimally invasive and conventional approach.

MATERIALS AND METHODS

We have conducted prospective study to evaluate such systemic inflammatory response parameters as C-Reactive Protein (CRP) and Fibrinogen during early postoperative course comparing two approaches – VATS or video-assisted thoracoscopic surgery lobectomy and conventional or open thoracotomy lobectomy. Our study included 30 patients with early-stage (I-II) NSCLC who underwent anatomical resection – pulmonary lobectomy with mediastinal nodal dissection. All patients underwent surgery in the Department of Thoracic Surgery at the Centre of Tuberculosis and Lung Diseases of the Riga East University Hospital between March 2011 and May 2013. Surgery was prospectively randomised in two groups: 15 patients underwent fully thoracoscopic VATS lobectomy without any rib spreading manoeuvre via one utility incision up to 6 cm and 2 additional ports (VATS-L group); 15 patients underwent conventional open lobectomy by lateral thoracotomy approach via incision of 15-25 cm with applying of rib spreader and 1-2 chest drains (OL group). We evaluated patient demographics, tumour histology and stage, type and duration of surgery, as

well as drain management results – duration of chest drain and amount of postoperative pleural effusion. Blood samples were taken for CRP and Fibrinogen analysis in both groups preoperatively, 24 and 72 hours after operation, on the day of drain removal, and 1 and 9 days after the drain removal. For evaluation of data distribution Kolmogorov-Smirnov test and/or diagnostic histograms were used. In each group mean parameters and standard deviations were calculated. In comparison of mean parameters in different time periods in postoperative course in each group and between two groups parametrical (paired and unpaired t-test) or non-parametrical (Wilcoxon or Mann-Witney test) tests were used depending of data distribution.

RESULTS

Patients in both groups had similar demographics as it is shown in Table 1. There was no difference found neither according to patient age, gender, tumour histology and stage nor type of performed lobectomy. Mean age was 58,4 years in VATS-L group and 59,6 years OL group. Adenocarcinoma was most common tumour type in both groups. All types of lobectomies were performed in both groups. Duration of operation was slightly longer in VATS-L group (mean - 141 minutes) compared to OL group (mean - 124 minutes), but difference was not statistically significant.

There were clear advantages in VATS-L group over OL group according to drain management and all these parameters reached statistical significance as it is illustrated in Table No.2. Drains could be removed quicker in VATS-L group on 3,5 (mean) postoperative day versus 4,7 (mean) postoperative day in OL group. Drained volumes of pleural effusion were smaller both in first three postoperative days and in total in VATS-L group (500 ml and 650 ml) in comparison with OL group (1200 ml and 1500 ml) accordingly. Prolonged air-leak more than 7 days were observed in one occasion in each group, no other major complications were observed.

Surgery caused systemic inflammatory response as increases in plasma CRP and Fibrinogen concentrations were observed in both groups after surgery. The increase in CRP was notably higher in OL group compared with VATS-L group in all measurements except preoperative (were no statistically significant difference was found) and all reached statistical significance ($p < 0,05$ in all measurements except a day after drain removal where $0,05 < p < 0,1$) as it is illustrated in Graph No.1. In VATS-L group elevation of CRP in postoperative course was slower and reached stable flat-like status before slowing down, whereas in OL group elevation of CRP was much quicker and reached peak in the third postoperative day before dropping back towards preoperative measurement but not reaching it. The increase in Fibrinogen concentrations was also higher in OL group but statistical significance ($p < 0,05$) was reached only in day of drain removal as it is shown in Graph No.2.

DISCUSSION

Currently VATS lobectomy is accepted as feasible and appropriate procedure for selected patients with early-stage non-small cell lung cancer and several large studies have demonstrated that VATS lobectomy is not only safe procedure, but that even provides better functional recovery and oncological efficacy is similar to that what is achieved with conventional thoracotomy (5,10,16,22-24).

VATS approach provide much better results with less pain and quicker recovery to normal activity during early postoperative period compared with conventional open thoracotomy approach (4,7-9,12). But despite that early recovery is fast, there is not so big difference between two approaches according to postoperative pain in later postoperative period starting from three month after surgery. Preservation of lung function is not dependent on surgical approach but rather on the amount of remaining lung (3).

There have been several studies exploring acute phase inflammatory and immunologic response to surgical trauma and cytokine network plays important role, but most of them are devoted to different laparoscopic procedures compared with their counterpart open conventional procedures showing decreased release of cytokines. But few of these studies (2,21,25) confirmed reduced postoperative release of both pro-inflammatory and anti-inflammatory cytokines in VATS lobectomy compared to an open approach.

Other authors also like we experienced some difficulties and limitations in the randomization in presence of the choice of VATS approach, but anyway achieved to form two groups comparable in their demographics as well as in their pathology. They have also understood that not only systemic but also local cytokine responses in pleural cavity and lung tissue may play important role and need to be investigated (25).

There are data available that immunologic response is characterized not only by release of cytokines and inflammatory mediators but also by release of acute phase protein and adverse disturbances in immune cell function. The usage of minimally invasive approach is associated not only with reduced cytokine response but also with reduction of corresponding acute phase protein CRP levels (2,21). Our data also showed slower and less expressed elevation of CRP in early postoperative period when applying VATS approach for performing lobectomy in comparison with conventional open thoracotomy approach.

Other factors predicting postoperative course and pulmonary complications as preoperative serum fibrinogen (14) and lactate dehydrogenase (18,19) levels have been investigated. Our finding of reduced fibrinogen elevation in early postoperative period after VATS lobectomy could also reflect that VATS approach causes less systemic response to surgery compared to open thoracotomy approach.

CONCLUSIONS

Although the clinical significance of this study is not fully elucidated, we have shown that VATS approach causes reduced systemic inflammatory response compared with conventional open approach. This finding may be associated with lesser implications on patient immunological status and tumour immunosurveillance what is extremely important for lung cancer patients. VATS technique was also associated with lesser postoperative pain and local reaction as duration of chest drains and amount of drained postoperative pleural effusion is significantly reduced in comparison with conventional open approach and all this lead to faster recovery in early postoperative period. Elucidation of the mechanisms responsible for these clinical benefits may have strong implications on the future development of lung cancer management strategies.

Conflict of interest: None

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Table 1. Clinical characteristics of patients

	VATS-L group (N=15)	OL group (N=15)
Gender: Male/Female	11/4	9/6
Age (mean±SD)	58,4 ± 10,7	59,6 ± 9,4 ^{NS}
Tumour histology:		
Squamous cell lung cancer	3	5
Adenocarcinoma	10	9
Malignant carcinoid	2	1
Tumour stage:		
T1AN0M0	7	7
T1BN0M0	5	2
T2AN0M0	2	2
T2BN0M0		2
T1AN1M0	1	
T1BN1M0		1
T2BN1M0		1
Type of lobectomy:		
RUL	5	5
RLL	3	2
LUL	2	7
LLL	5	1
Length of operating time in minutes (mean±SD)	141 ± 34	124 ± 21 ^{NS}

^{NS} p > 0,1; RUL – right upper lobectomy; RLL – right lower lobectomy; LUL – left upper lobectomy; LLL – left lower lobectomy

Table 2. Data of drain management

	VATS-L group (N=15)	OL group (N=15)
Drain removal day (mean±SD)	3,5 ± 2,3	4,7 ± 1,5 **
Drained volume in ml until 3 rd POD (mean±SD)	498 ± 206	1178 ± 291 ***
Total drained volume in ml (mean±SD)	644 ± 436	1499 ± 530 ***

** p < 0,05; *** p < 0,001

Graph.1. Dynamics of CRP in plasma (mg/L) during postoperative course

^{NS} p>0,1; * 0,05<p<0,1; ** p<0,05; *** p<0,01; PreOP - preoperative day; POD - postoperative day; DRD - drain removal day

Graph. 2. Dynamics of Fibrinogen in plasma (g/L) during postoperative course

*** p<0,01; PreOP - preoperative day; POD - postoperative day; DRD - drain removal day