Journal of Cardiothoracic Surgery

RESEARCH

Open Access

Clinical significance of postoperative thrombocytosis after vats lobectomy for NSCLC

Beatrice Leonardi[1*], Giovanni Natale[1], Salvatore Ferraioli[1], Francesco Leone[1], Mario Grande[1], Maria Antonietta Puca[1], Anna Rainone[1], Gaetana Messina[1], Antonello Sica[2] and Alfonso Fiorelli[1]

Abstract

Objectives Thrombocytosis is a clinical condition generally associated with poor prognosis in patients with cancer. Thrombocytosis may be present after lung cancer resection, but the clinical significance of thrombocytosis remains unclear. Herein, we evaluated whether postoperative thrombocytosis was a negative prognostic factor in patients undergoing thoracoscopic lobectomy for lung cancer.

Methods It was a retrospective monocentric study including consecutive patients undergoing thoracoscopic lobectomy for lung cancer from January 2020 to January 2023. The outcome of patients with postoperative thrombocytosis (defined as platelet count ≥ 450 × 10^9/L at 24 h after the surgery and confirmed at postoperative day 7) was compared with a control group. Postoperative morbidity, mortality, and survival were compared between the two groups to define whether thrombocytosis negatively affected outcomes.

Results Our study population included 183 patients; of these, 22 (12%) presented postoperative thrombocytosis: 9 (5%) mild thrombocytosis (451–700 × 10^9/L), 10 (5%) moderate thrombocytosis (701–900 × 10^9/L), and 3 (2%) severe thrombocytosis (901–1000 × 10^9/L). No significant differences were found regarding postoperative morbidity ($p = 0.92$), mortality ($p = 0.53$), overall survival ($p = 0.45$), and disease-free survival ($p = 0.60$) between the two study groups. Thrombocytosis was associated with higher rate of atelectasis (36% vs. 6%, $p < 0.001$) and residual pleural effusion (31% vs. 8%, $p = 0.0008$). Thrombocytosis group was administered low-dose acetylsalicylic acid for 10 days and no thrombotic events were observed. In all cases the platelet count returned to be within normal value at postoperative day 30.

Conclusions Postoperative thrombocytosis seems to be a transient condition due to an inflammatory state and it does not affect the surgical outcome and survival after thoracoscopic lobectomy.

Keywords Lobectomy, Thrombocytosis, Lung cancer, Thoracoscopy

*Correspondence:
Beatrice Leonardi
beatrice.leonardi@unicampania.it
[1]Thoracic Surgery Unit, University of Campania "Luigi Vanvitelli" Università degli Studi della Campania "Luigi Vanvitelli", Via Pansini, 5, Naples I-80138, Italy
[2]Department of Precision Medicine, University of Campania "Luigi Vanvitelli", Naples 80138, Italy

Introduction

Lung cancer is the most common cancer and the leading cause of cancer deaths worldwide [1, 2]. Non-small-cell lung cancer (NSCLC) accounts for 80% of all cases. Surgical resection remains the only treatment with curative intent for early-stage lung cancer [3].

Many studies have shown that thrombocytosis, defined as platelet count ≥ 450 × 10^9/L, plays a role in cancer genesis and development. Increasing evidence has indicated that platelet count correlates with prognosis in various malignancies, such as lung, renal, gastric, colorectal, and hepatocellular cancer and pre-treatment thrombocytosis is considered a poor prognostic factor in NSCLC [4, 5]. Thrombocytosis may be occasionally observed in patients undergoing lung cancer resection with normal pre-operative platelet count, but its clinical significance and management remains unclear. Given the undefined role of postoperative thrombocytosis in patients with NSCLC, a focus on this specific clinical condition could help the physician understand if the patient is undergoing a para-physiological condition or if concern regarding the oncological prognosis should be raised.

Herein, we evaluated whether postoperative thrombocytosis after video-assisted thoracoscopic (VATS) lobectomy affects the surgical outcome and/or prognosis in patients undergoing surgical resection for NSCLC.

Materials and methods

Study design

This was a retrospective monocentric study conducted at the Thoracic Surgery Unit of Campania "Vanvitelli", Naples, Italy. The clinical data of consecutive patients undergoing lobectomy for lung cancer from January 2020 to January 2023 were evaluated. The data of patients (i) undergoing lobectomy for lung cancer; (ii) with complete data and (iii) with follow-up for at least 3 months were included in the analysis. We excluded the data of patients: (i) undergoing lung resection different from lobectomy (i.e. wedge resection, segmentectomy, bilobectomy and pneumonectomy); (ii) with incomplete pre and postoperative data, to minimize the amount of missing data; and (iii) with pre-existing haematological conditions. Patients undergoing resection different from lobectomy were excluded to have a homogeneous sample, as a more extended resection could be associated with different surgical and oncological outcomes, as well as a sub-lobar resection. Furthermore, pre-existing haematological conditions could constitute a confounding factor to assess any association between postoperative thrombocytosis and surgical/oncological variables. The CONSORT flow diagram showing the process of assessing the eligibility is reported in Fig. 1.

The patients were divided in two groups based on whether they had postoperative thrombocytosis (Thrombocytosis group), or not (Control group). The inter group

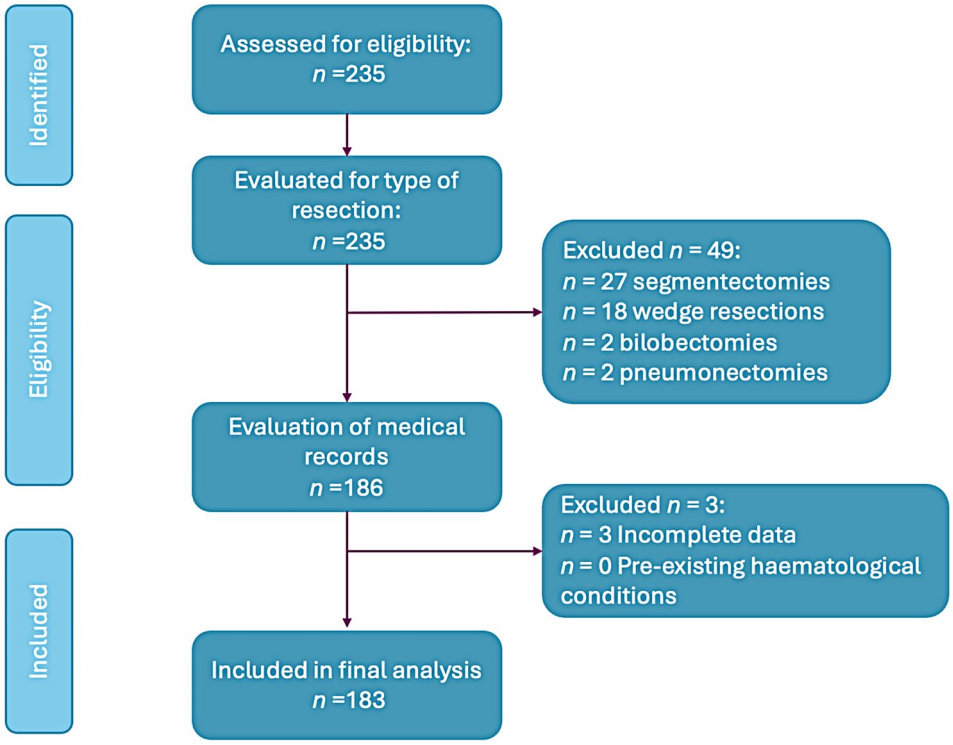

Fig. 1 CONSORT flow diagram of the study

differences regarding postoperative morbidity, mortality and survival were statistically compared to define whether thrombocytosis negatively affected outcomes and survival (endpoints of the study).

The Institutional Review Boards of the University of Campania "Luigi Vanvitelli" waived the need for ethical approval due to the retrospective nature of the study since there was no modification to the standard of care for the patients. In all cases, informed written consent was obtained from the patients for the treatment and for the anonymous use and publication of their data for scientific purposes. All procedures were performed in accordance with international guidelines; with the Helsinki Declaration of 1975, revised in 1983; and the rules of the Italian laws of privacy.

Study population

We recorded the following data for each patient: age, sex, symptoms, comorbidities, respiratory function data, histology and tumor stage based on 8th edition of TNM stage. Operative time (minutes), blood loss (mL), chest drainage output (mL), length of chest drainage (days), length of hospital stay (LHOS, days), laboratory data, postoperative complications, 90-day mortality were also recorded. Recurrence and time of recurrence were recorded. Overall survival (OS) and disease-free survival (DFS) were also measured from the date of surgery until death or recurrence, respectively.

Blood markers

Thrombocytosis was defined as platelet count $\geq 450 \times 10\text{^}9/L$ first detected with routine blood test 24 h after the surgery and confirmed at postoperative day 7. Thrombocytosis was classified in mild ($451–700 \times 10\text{^}9/L$), moderate ($701–900 \times 10\text{^}9/L$), severe ($901–1000 \times 10\text{^}9/L$) or extreme ($>1000 \times 10\text{^}9/L$), following a classification previously adopted in literature [6]. Additionally, we evaluated the following blood inflammatory biomarkers: neutrophil/lymphocyte ratio (NLR), lymphocyte/monocyte ratio (LMR), platelet/lymphocyte ratio (PLR), systemic pan-immune-inflammation index (SII) [7–10].

In patients with post-operative thrombocytosis, platelet count and the other inflammatory markers were evaluated weekly until 30 post-operative day.

Surgical procedure

All the patients underwent pulmonary lobectomy with systematic ilo-mediastinal lymphadenectomy through a standard anterior thoracoscopic triportal approach. The procedures were carried out under general anaesthesia with selective intubation. A single 28Fr drainage tube was placed in the pleural cavity at the end of the procedure and removed when the amount of fluid drained was less than 250 mL in 24 h, in absence of air leaks.

Statistical analysis

Data were expressed as mean ± Standard Deviation (SD) for continuous variables and as absolute number and percentage for categorical variables. Differences between groups were evaluated using Chi-squared test for categorical variables and with Student´s T-test for continuous variables. The correlation between thrombocytosis and the other inflammatory markers were calculated by Pearson correlation coefficient. The OS and DFS were evaluated by Kaplan-Meier method and the log-rank test was used to calculate the difference between two study groups. Univariable and multivariable analysis were used to identify independent risk factors for postoperative complications (dependent variable). A p-value less than 0.05 was considered statistically significant. MedCalc statistical software (Version 12.3, Broekstraat 52; Mariakerke, Belgium) was used for this analysis.

Results

During the study period, 235 patients underwent lung resection for NSCLC. Out of these, 52 patients were excluded from the study due to resections different from lobectomy ($n=49$), and missing data ($n=3$). Thus, our study population included 183 patients; of these, 22 (12%) presented postoperative thrombocytosis: 9 (5%) mild, 10 (5%) moderate, and 3 (2%) severe thrombocytosis (Table 1). There were no cases of extreme thrombocytosis.

No significant differences were found between two study groups regarding pre-operative data, histology, and tumor stage, as summarized in Table 1.

Surgical outcome

Perioperative outcomes were summarized in Table 2. Operative time ($p=0.56$), blood loss ($p=0.41$), transfusion rate ($p=0.7$), conversion rate ($p=0.73$), chest drainage output ($p=0.25$), length of chest drainage ($p=0.35$) and LHOS ($p=0.32$) were similar between two study groups without significant difference.

Thrombocytosis compared to control group was associated with a higher rate of residual pleural effusion (31% vs. 8%, $p=0.0008$), and atelectasis that needed bronchoscopic aspiration (36% vs. 6%, $p<0.001$). However, no significant difference was found regarding the overall complications rate between two study groups. Multivariable analysis showed that only COPD was an independent prognostic factor for complications (Table 3).

Table 1 Characteristics of study population

Variables	Total (*n* = 183)	Thrombocytosis group (*n* = 22)	Control group (*n* = 161)	*p*-Value
Age (years), M ± SD	66.7 ± 8.3	65.2 ± 8.2	66.9 ± 8.4	0.19
Gender (male), *n* (%)	106 (58)	15 (68)	91 (56)	0.29
Smokers, *n* (%)	83 (45)	13 (59)	70 (44)	0.16
Former smokers, *n* (%)	71 (39)	6 (27)	65 (40)	0.23
BMI (Kg/m^2), M ± SD	27.2 ± 4.3	26.5 ± 3.8	27.4 ± 4.3	0.11
ASA score ≥ 3	65 (35)	7 (31)	58 (36)	0.32
Comorbidities, *n* (%)				
Diabetes	34 (19)	2 (9)	32 (20)	0.22
COPD	53 (29)	8 (36)	45 (28)	0.41
Hypertension	130 (71)	17 (77)	113 (70)	0.49
Coronary artery disease	32 (17)	3 (14)	29 (18)	0.61
History of cancer	59 (32)	4 (18)	55 (34)	0.13
Preoperative FEV1%, M ± SD	94.1 ± 18	89.9 ± 12	94.6 ± 20	0.14
Preoperative DLCO%, M ± SD	87.3 ± 19	88.9 ± 20	87.0 ± 18.6	0.36
Mild thrombocytosis, *n* (%)	9 (5)	9 (41)	0	/
Moderate thrombocytosis, *n* (%)	10 (5)	10 (45)	0	/
Severe thrombocytosis, *n* (%)	3 (2)	3 (14)	0	/
Histology, *n* (%)				
Adenocarcinoma	120 (65)	12 (54)	108 (67)	0.24
Squamous cell carcinoma	35 (19)	7 (32)	28 (17)	0.1
Typical carcinoid	6 (4)	1 (5)	5 (3)	0.72
Atypical carcinoid	6 (4)	0	6 (4)	0.85
Other	16 (8)	2 (9)	14 (9)	0.95
Lobectomy type, *n* (%)				
RUL	58 (32)	8 (36)	50 (31)	0.61
RML	13 (7)	0	13 (8)	0.55
RLL	40 (22)	6 (27)	34 (21)	0.51
LUL	34 (18)	6 (27)	28 (17)	0.26
LLL	38 (21)	2 (9)	36 (22)	0.19
Pathological stage, *n* (%)				
IA	78 (43)	11 (50)	67 (42)	0.45
IB	29 (16)	3 (14)	26 (16)	0.76
IIA	5 (3)	1 (5)	4 (2)	0.57
IIB	22 (12)	4 (18)	18 (11)	0.34
IIIA	23 (13)	2 (9)	21 (13)	0.59

BMI: body mass index. ASA: American Society of Anesthesiologists. COPD: chronic obstructive pulmonary disease. FEV1: forced expiratory volume in 1 s. DLCO: diffusing capacity of the lung for carbon monoxide. RUL: right upper lobectomy. RML: right middle lobectomy. RLL: right lower lobectomy. LUL: left upper lobectomy. LLL: left lower lobectomy

Correlation between thrombocytosis and other inflammatory markers

Preoperative and postoperative laboratory data were reported in Table 4. Thrombocytosis group compared to control group presented higher value of SII (2155 ± 1244 vs. 643 ± 200, $p = 0.0004$); of PLR (312 ± 139 vs. 134 ± 64, $p = 0.0028$); of NLR (4.6 ± 1.2 vs. 2.6 ± 0.8; $p = 0.93$), and lower value of LMR (3.4 ± 1.1vs. 5.8 ± 0.5; $p = 0.000046$). Additionally, Pearson correlation coefficient (Fig. 2) found a moderate positive correlation between platelet count and SII (r(181) = 0.50, $p = 0.0001$, Fig. 2/A); a positive correlation between platelet count and PLR (r(181) = 0.22, $p = 0.002$, Fig. 2/B); a moderate positive correlation between platelet count and NLR (r (181) = 0.46, $p < 0.0001$, Fig. 2/C), and a negative correlation between platelet count and LMR (r (181) = -0.23, $p = 0.0014$, Fig. 2/D).

All the patients with thrombocytosis received weekly hematologic evaluation and were treated with low-dose acetylsalicylic acid. In all cases the platelet count (Supplementary Fig. 1) and all inflammatory markers (Fig. 3) returned to be within normal values at postoperative day 30. No thrombotic events or other complications were observed during the follow-up.

Table 2 Surgical outcome comparison

Variables	Total (*n* = 183)	Thrombocytosis group (*n* = 22)	Control group (*n* = 161)	*p*-value
Operative time (minutes), M ± SD	169 ± 46	166 ± 43	170 ± 47	0.35
Chest drainage (mL/day), M ± SD	142 ± 60	146 ± 63	140 ± 70	0.25
Chest tube duration (days), M ± SD	6 ± 4	6 ± 4	5 ± 4	0.35
Blood loss (mL), M ± SD	282 ± 55	280 ± 50	285 ± 61	0.41
Transfusion, *n* (%)	21 (11)	2 (9)	19 (11)	0.70
Conversion, *n* (%)	20 (10)	2 (9)	18 (10)	0.73
LHOS (days), M ± SD	7.2 ± 4.0	7.6 ± 3.5	6.8 ± 3.4	0.32
Complications, n (%): Patients with any complication Minor complications (grade I-II*) Major complications (grade III-IV*)	65 (35) 51 (28) 14 (7)	8 (36) 7 (32) 1 (5)	57 (35) 44 (27) 13 (8)	0.92 0.65 0.55
Bronchoscopy for atelectasis, *n* (%)	18 (10)	8 (36)	10 (6)	< 0.001
Residual pleural effusion, *n* (%)	20 (11)	7 (31)	13 (8)	0.00081
90 – day mortality, *n* (%)	3 (2)	0	3 (2)	0.53
OS (months), M ± SD	14 ± 11	15 ± 4	14.5 ± 5	0.45
DFS (months), M ± SD	13 ± 10	15 ± 11	13 ± 10	0.60

LHOS: Length of hospital stay. OS: Overall survival. DFS: Disease free survival

*According to the Systematic Classification of Morbidity and Mortality After Thoracic Surgery (Seely AJE et al.)

Table 3 Univariable and multivariable analysis for peri-operative complications (dependent variable)

Variables	Univariable		Multivariable	
	Odds Ratio	*p*-value	Odds Ratio	*p*-value
Age (> 70)	0.96 (CI: 0.90–1.02)	0.20	-	-
Gender	0.70 (CI: 0.23–2.10)	0.53	-	-
Smoking status	0.87 (CI: 0.29–2.63)	0.81	-	-
COPD	3.02 (CI: 1.00-9.12)	0.049*	3.40 (CI 1.52–8.35)	0.022
Diabetes	1.21 (CI: 0.31–4.61)	0.77	-	-
Thrombocytosis	0.54 (CI 0.06–4.35)	0.53	-	-
ASA ≥ 3	0.70 (CI: 0.21–2.35)	0.56	-	-
FEV1 < 70%	1.24 (CI 0.25–5.95)	0.79	-	-
History of cancer	1.12 (CI: 0.35–3.50)	0.84	-	-

COPD: chronic obstructive pulmonary disease. ASA: American Society of Anesthesiologists. CI: confidence interval

Recurrence and survival

The median follow-up was 15 months. Overall survival ($p = 0.45$), disease-free survival ($p = 0.60$) and 90-day mortality ($p = 0.53$) were similar between the two groups. Kaplan-Meier survival curves are reported in Fig. 4. Log-rank test showed no significant difference between the two groups regarding overall survival ($p = 0.35$) and disease-free survival ($p = 0.15$) Fig. 4.

Discussion

Thrombocytosis is a poor prognostic factor in neoplastic patients [11]. The association between thrombocytosis and cancer is well defined despite the mechanism remains unclear. A role is attributed to epithelial mesenchymal transformation of tumor cells promoted by platelets through secretion of transforming growth factor-β [12]. On the other hand, some support that a proangiogenic role of activated platelets favours tumor diffusion [13, 14]. Preoperative thrombocytosis is suspected to have a role in metastatic diffusion as activated platelets facilitate hematological diffusion of tumor cells, shielding them from immune destruction. Even though the relation between preoperative thrombocytosis and tumor prognosis is yet not clearly defined, preoperative thrombocytosis is considered a marker of cancer aggressivity.

Nevertheless, thrombocytosis may occur after lung cancer resection, but the clinical significance is still unexplored. Postoperative thrombocytosis has been observed and studied after colorectal oncological surgery [15] and urological surgery [16]. Hemorrhage, urosepsis and thromboembolism were the most common complications recorded in patients with thrombocytosis after urological surgery, while median overall survival resulted worse in patient with thrombocytosis after colorectal surgery. No studies, before the present, evaluated whether postoperative thrombocytosis after lung cancer resection is a poor prognostic factor for surgical outcome and survival.

First, postoperative thrombocytosis did not negatively affect post-operative surgical outcome. No significant differences between the two study groups were found regarding the complications rate. These results were confirmed by multivariable analysis that identified only COPD as an independent prognostic factor for complications. The distribution of COPD was homogeneous between the two study groups, and COPD is known to be a risk factor for postoperative complications in patients undergoing VATS lobectomy for lung cancer [17]. Thus, our data showed no significant association between COPD and thrombocytosis. However, since the small sample size of our study population and the lack of data from literature, we are unable to provide any definitive conclusion about this issue that should be investigated in further studies.

In thrombocytosis group, a significant increase of residual pleural effusion and atelectasis was found compared to control group, requiring more often bronchoscopic aspiration. Pleural effusion has been associated with pleural and local inflammation [18–20], that may be a predisposing factors for thrombocytosis in this cohort of patients. This hypothesis is supported by the

Table 4 Laboratory data and inflammatory biomarkers

Variables	Total (*n* = 183)	Thrombocytosis (*n* = 22)	No thrombocytosis (*n* = 161)	*p*-Value
Preoperative laboratory data, (M ± SD):	7750 ± 2238	8020 ± 2711	7720 ± 2173	0.15
• White blood cells (/uL)	13.96 ± 1.8	13.1 ± 2.2	13.9 ± 1.8	0.18
• Hemoglobin (g/dL)	241 ± 58	297 ± 108	232 ± 59	0.000017
• Platelet count (x10^3/uL)	6.9 ± 0.71	6.8 ± 0.65	7 ± 0.71	0.45
• Total protein (g/dL)				
Postoperative laboratory data (day 7), (M ± SD):	8720 ± 2200	1050 ± 2033	8200 ± 1500	0.17
• White blood cells (/uL)	11.9 ± 1.7	10.8 ± 1.3	11.7 ± 1.5	0.34
• Hemoglobin (g/dL)	300 ± 179	690 ± 153	250 ± 72	< 0.00001
• Platelet count (x10^3/uL)	6.8 ± 0.81	6.6 ± 0.75	6.9 ± 0.53	0.82
• Total protein (g/dL)				
SII, (cutoff < 1266) (M ± SD)	763 ± 502	2155 ± 1244	643 ± 200	0.0004
PLR, (cutoff < 200) (M ± SD)	156 ± 89	312 ± 139	134 ± 64	0.0028
NLR, (cutoff < 4) (M ± SD)	2.8 ± 1.7	4.6 ± 1.2	2.6 ± 0.8	0.93
LMR, (cutoff ≥ 4) (M ± SD)	5.5 ± 2.4	3.4 ± 1.1	5.8 ± 2.4	0.000046
Postoperative day 30 data, (M ± SD):				
Platelet count (x10^3/uL)	/	350 ± 62	/	/
SII, (cutoff < 1266) (M ± SD)	/	710 ± 97	/	/
PLR, (cutoff < 200) (M ± SD)	/	152 ± 34	/	/
NLR, (cutoff < 4) (M ± SD)	/	2.86 ± 0.9	/	/
LMR, (cutoff ≥ 4) (M ± SD)	/	5.75 ± 2.13	/	/

SII: systemic pan-immune-inflammation index. PLR: platelet/lymphocyte ratio. NLR: neutrophil/lymphocyte ratio. LMR: lymphocyte/monocyte ratio

significant correlation observed between platelet count and other inflammatory markers in thrombocytosis group. Atelectasis and residual pleural effusion are common complications after VATS lobectomy, which should be addressed to prevent hypoxemia and infections. Breathing exercises, physical therapy, and bronchoscopy, are key elements in the management of these complications. It is important to correlate to clinical signs and general condition to exclude any underlying conditions (e.g. infection, pulmonary embolism, etc.) [21].

Second, postoperative thrombocytosis was not a poor prognostic factor. Indeed, no significant difference in terms of recurrence and overall survival was found between the two study groups. A correlation between pretreatment thrombocytosis and unfavorable lung cancer prognosis has been reported in recent meta- analysis and systematic reviews [1, 22], while some suggest that a high platelet count is not an independent prognostic factor for survival [23, 24]. In fact, thrombocytosis role in lung cancer is yet not clear as the prognostic value of thrombocytosis could not be confirmed by all studies.

In our study, postoperative thrombocytosis was not associated with survival and recurrence. Patients with postoperative thrombocytosis presented a normal preoperative platelet count, therefore platelet formation mechanism could be considered a reactive process. This finding is supported by the parallel inflammatory biomarkers and platelet count normalization at postoperative day 30. We think that the differences between our findings and the studies supporting a negative prognostic value of thrombocytosis in NSCLC resides in the diverse circumstance of thrombocytosis occurrence. Most of the studies that have found an association between thrombocytosis and a worse prognosis refer to preoperative or pre-treatment thrombocytosis [1, 5, 8, 25]. Other studies found a correlation between thrombocytosis and poor survival in cohorts of patients with advanced metastatic NSCLC treated with chemo-immunotherapy [26, 27].

To our knowledge, only a paper from Maràz et al. explicitly included patients with postoperative thrombocytosis [28], reporting that perioperative thrombocytosis in patients undergoing lung cancer surgery should be considered as an independent prognostic factor of poor survival. However, their research is based on the assessment of platelet count higher than 400×10^3/uL just before surgery and on postoperative day 1 and 7. One study that analyzed postoperative thrombocytosis in colorectal surgery for cancer [15] found that both preoperative and postoperative thrombocytosis are predictive for worse survival. Nevertheless, postoperative thrombocytosis in this study was measured at postoperative day 30, with the intent of excluding the inflammatory effects of the surgery. In our study, we included only patients with resectable NSCLC and postoperative thrombocytosis, that was in all cases transient, being absent before surgery and with return to normal platelet values within postoperative day 30.

Third, our results highlighted that postoperative transient thrombocytosis is a phenomenon related to an inflammatory reactive condition, that can be easily managed by the physician without influencing the patient recovery after thoracic surgery. Treatment with low-dose

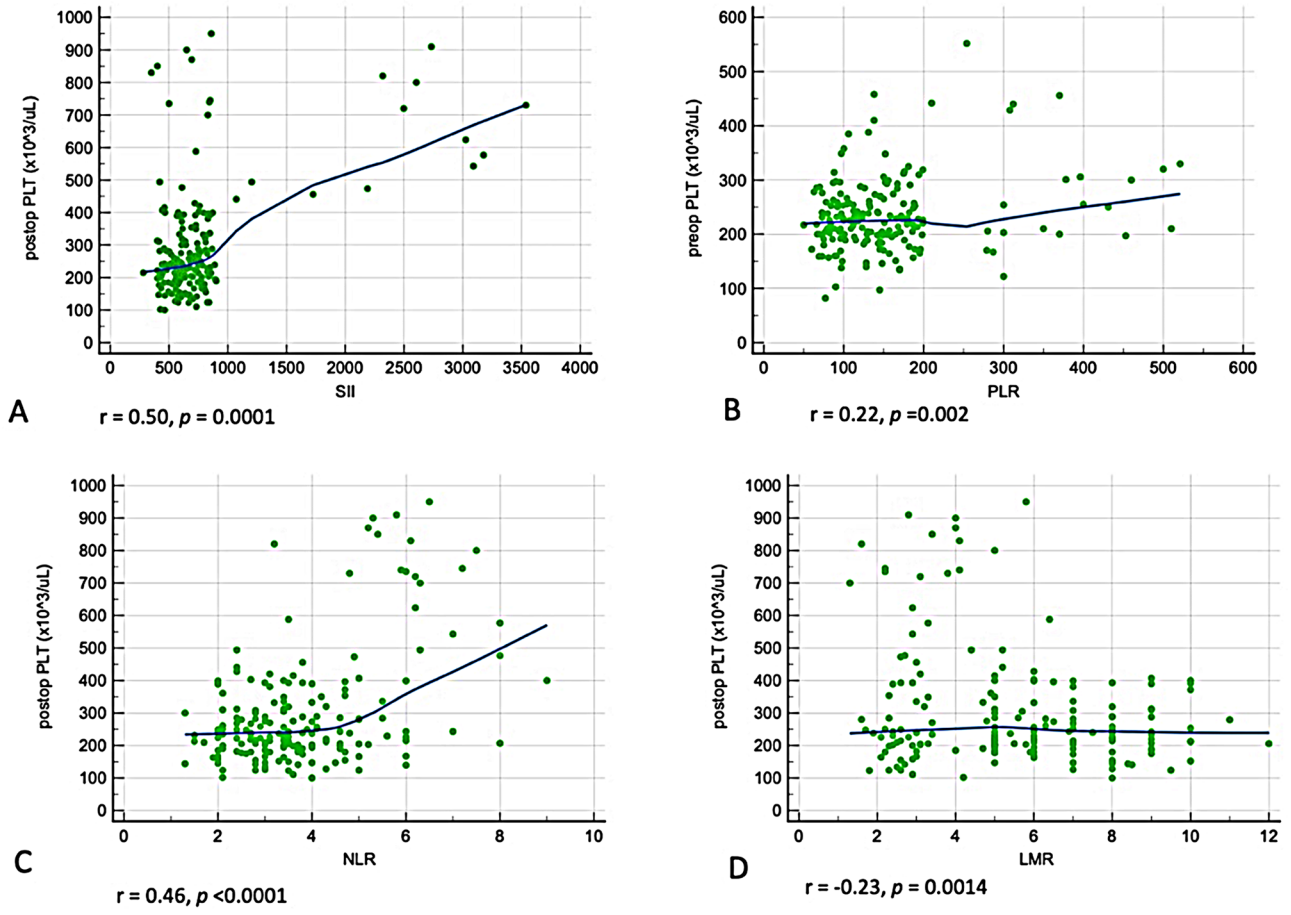

Fig. 2 Pearson Correlation coefficient between thrombocytosis and inflammatory biomarkers. (**A**): Moderate positive correlation between platelet count and SII (r(181) = 0.50, $p = 0.0001$); (**B**): Positive correlation between platelet count and PLR (r(181) = 0.22, $p = 0.002$); (**C**): Moderate positive correlation between platelet count and NLR (r (181) = 0.46, $p < 0.0001$); (**D**): Negative correlation between platelet count and LMR (r (181) = -0.23, $p = 0.0014$) LMR

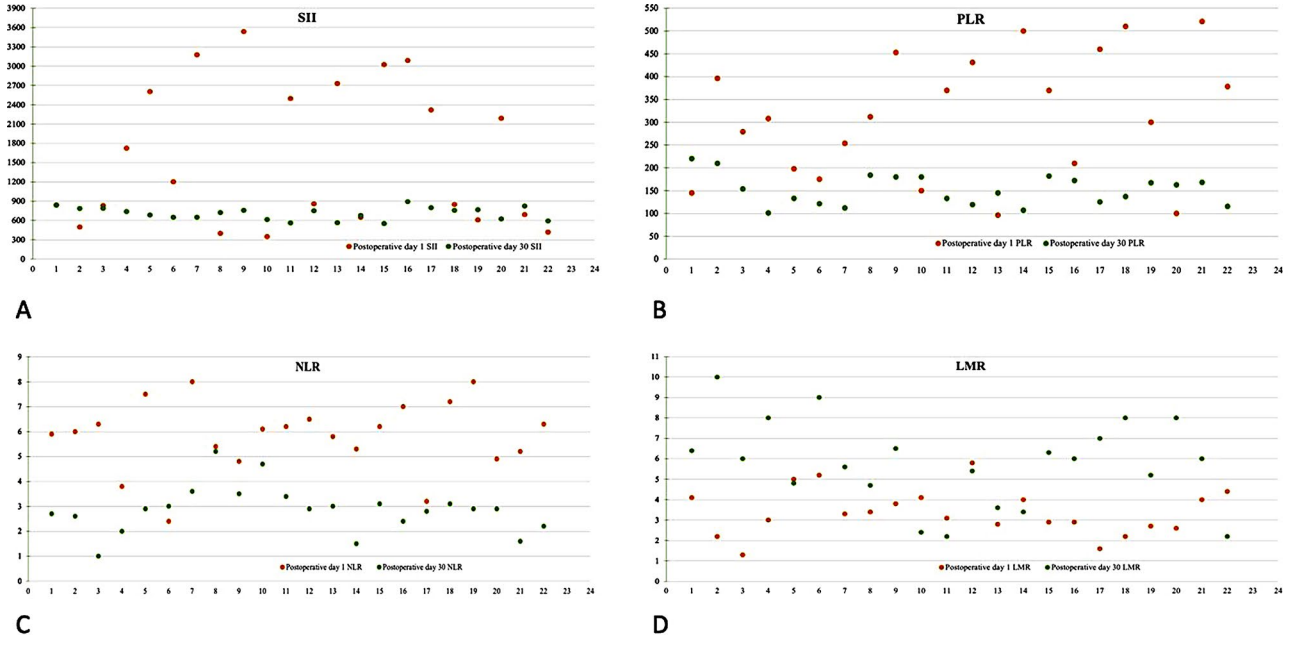

Fig. 3 Inflammatory biomarkers distribution in Thrombocytosis group at 1 and 30 postoperative days. (**A**): SII; (**B**): PLR; (**C**): NLR; (**D**): LMR

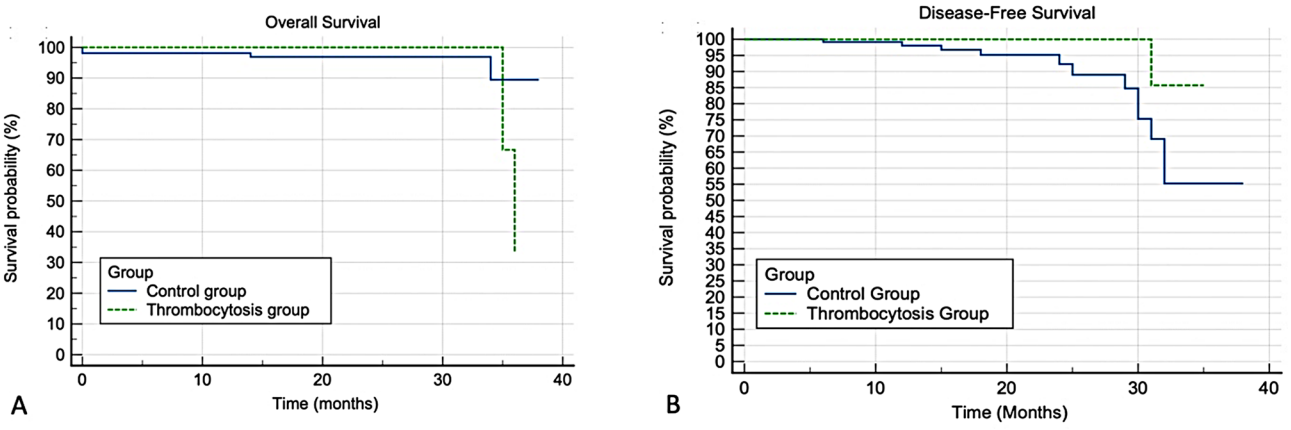

Fig. 4 Kaplan-Meier curves. (**A**): Overall survival; **(B)**: Disease-free survival

acetylsalicylic acid is generally used to prevent thrombotic events in essential thrombocytosis [29, 30], but we considered its use in reactive thrombocytosis with prophylactic intent. Mohamud et al. [31] did not treat postoperative thrombocytosis but observed a higher rate of complications in the thrombocytosis group. In our study, the platelet count returned to normal within 30-day postoperative, along with inflammatory biomarkers descent. The relationship between thrombocytosis and atelectasis/residual pleural effusion should be better investigated, as it could offer some perspective about platelet role in the mechanisms of postoperative recovery and of injury-induced inflammatory response [32, 33].

Thrombocytosis should be differentiated according to its onset and duration: a transient postoperative thrombocytosis is more likely to be an inflammatory phenomenon without significant influence on the patient's prognosis, while persistent preoperative or pre-treatment thrombocytosis is commonly related to a worse oncological prognosis, as it relates with advanced stages of NSCLC. In the postoperative period, a finding of thrombocytosis should not scare the surgeon with a certainty of a worse prognosis, but it should be considered in the context of the patient's clinical evolution.

The main limitations of our study were the retrospective nature, the absence of randomization, the small cohort of patients and the relatively short follow-up (median 15 months). For these reasons our findings must be investigated with further larger and prospective studies.

Conclusions

Postoperative thrombocytosis seems to be a transient condition due to an inflammatory state and it does not seem to affect the surgical outcome and survival after thoracoscopic lobectomy for lung cancer. Prophylactic treatment with low-dose acetylsalicylic acid may be considered to prevent thrombotic events. Our preliminary results should be corroborated by larger, prospective studies.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13019-024-03032-y.

Supplementary Material 1

Acknowledgements

None.

Author contributions

Conceptualization: B.L. and A.F. Data curation: B.L. and S.F Methodology: G.N. and F.L; Investigation: M.G and M.A.P., Formal analysis: A.R and F.L. Resources: A.S and A.R. Writing – original draft: B.L. and G.N., Writing – review and editing: A.F., M.G. Visualization: B.L. S.F and A.F. Supervision: G.M.

Funding

Funded by the European Union - Next Generation EU - PNRR M6C2 Investimento 2.1 "Valorizzazione e potenziamento della ricerca biomedica del SSN" - Grant n. PNRR-TR1-2023-12377418 – CUP Master: G85E23000410007 – CUP UO: I65E2400070006.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The Institutional Review Boards of the University of Campania "Luigi Vanvitelli" waived the need for ethical approval due to the retrospective nature of the study since there was no modification to the standard of care for the patients. In all cases, informed written consent was obtained from the patients for the treatment and for the anonymous use and publication of their data for scientific purposes. All procedures were performed in accordance with international guidelines; with the Helsinki Declaration of 1975, revised in 1983; and the rules of the Italian laws of privacy.

Consent for publication

All patients signed an informed consent for the anonymous publications of their data for scientific purposes.

Competing interests

The authors declare no competing interests.

Received: 1 June 2024 / Accepted: 30 August 2024

Published online: 14 September 2024

References

1. Yuan Y, Zhong H, Ye L, Li Q, Fang S, Gu W, Qian Y. Prognostic value of pretreatment platelet counts in lung cancer: a systematic review and meta-analysis. BMC Pulm Med. 2020;20(1):96.
2. Andreetti C, Ibrahim M, Gagliardi A, et al. Adjuvant chemotherapy, extent of resection, and immunoistochemical neuroendocrine markers as prognostic factors of early-stage large-cell neuroendocrine carcinoma. Thorac Cancer. 2022;13(7):900–12.
3. Fiorelli A, Forte S, Natale G, Santini M, Fang W. Handling benign interlobar lymphadenopathy during thoracoscopic lobectomy. Thorac Cancer. 2021;12(9):1489–92.
4. Xia S, Wu W, Yu L, Ma L, Chen S, Wang H. Thrombocytosis predicts poor prognosis of Asian patients with colorectal cancer: a systematic review and meta-analysis. Med (Baltim). 2022;101(35):e30275.
5. Sandfeld-Paulsen B, Aggerholm-Pedersen N, Winther-Larsen A. Pretreatment Platelet Count is a prognostic marker in Lung Cancer: a Danish Registry-based Cohort Study. Clin Lung Cancer. 2023;24(2):175–83.
6. Edahiro Y, Kurokawa Y, Morishita S, Yamamoto T, Araki M, Komatsu N. Causes of thrombocytosis: a single-center Retrospective Study of 1,202 patients. Intern Med. 2022;61(22):3323–8. https://doi.org/10.2169/internalmedicine.9282-21. Epub 2022 Nov 15.
7. Yu Y, Qian L, Cui J. Value of neutrophil-to-lymphocyte ratio for predicting lung cancer prognosis: a meta-analysis of 7,219 patients. Mol Clin Oncol. 2017;7(3):498–506.
8. Lim JU, Yeo CD, Kang HS, Park CK, Kim JS, Kim JW, Kim SJ, Lee SH. Prognostic value of platelet count and lymphocyte to monocyte ratio combination in stage IV non-small cell lung cancer with malignant pleural effusion. PLoS ONE. 2018;13(7):e0200341.
9. Zhou K, Cao J, Lin H, Liang L, Shen Z, Wang L, Peng Z, Mei J. Prognostic role of the platelet to lymphocyte ratio (PLR) in the clinical outcomes of patients with advanced lung cancer receiving immunotherapy: a systematic review and meta-analysis. Front Oncol. 2022;12:962173.
10. Keit E, Coutu B, Zhen W, Zhang C, Lin C, Bennion N, Ganti AK, Ernani V, Baine M. Systemic inflammation is associated with inferior disease control and survival in stage III non-small cell lung cancer. Ann Transl Med. 2021;9(3):227.
11. Ma Y, Li G, Yu M, Sun X, Nian J, Gao Y, Li X, Ding T, Wang X. Prognostic significance of thrombocytosis in lung cancer: a systematic review and meta-analysis. Platelets. 2021;32(7):919–27.
12. Geranpayehvaghei M, Dabirmanesh B, Khaledi M, et al. Cancer-associated-platelet-inspired nanomedicines for cancer therapy. Wiley Interdiscip Rev Nanomed Nanobiotechnol. 2021;13(5):e1702.
13. Wojtukiewicz MZ, Sierko E, Hempel D, Tucker SC, Honn KV. Platelets and cancer angiogenesis nexus. Cancer Metastasis Rev. 2017;36(2):249–62.
14. Messina G, Bove M, Noro A, Opromolla G, Natale G, Leone F, Di Filippo V, Leonardi B, Martone M, Pirozzi M, Caterino M, Facchini S, Zotta A, Vicidomini G, Santini M, Fiorelli A, Corte Carminia D, Ciardiello F, Fasano M. Prediction of preoperative intrathoracic adhesions for ipsilateral reoperations: sliding lung sign. J Cardiothorac Surg. 2022;17(1):103.
15. Josa V, Krzystanek M, Eklund AC, Salamon F, Zarand A, Szallasi Z, Baranyai Z. Relationship of postoperative thrombocytosis and survival of patients with colorectal cancer. Int J Surg. 2015;18:1–6.
16. Milojevic B, Janicic A, Grozdic Milojevic I, et al. Prognostic impact of preoperative thrombocytosis on recurrence-free survival in patients with Upper Tract Urothelial Carcinoma. Ann Surg Oncol. 2024;31(4):2538–44.
17. Holleran TJ, Napolitano MA, Duggan JP, Peters AS, Amdur RL, Antevil JL, Trachiotis GD. Predictors of 30-Day Pulmonary complications after Video-assisted thoracoscopic surgery lobectomy. Thorac Cardiovasc Surg. 2023;71(4):327–35.
18. Rashid A, Zeng C, Motta-Ribeiro G, Dillon ST, Libermann TA, Lessa MA, Bagchi A, Hutchinson J, Vidal Melo MF. Proteomics of lung tissue reveals differences in inflammation and alveolar-capillary barrier response between atelectasis and aerated regions. Sci Rep. 2022;12(1):7065.
19. Fiorelli A, Cascone R, Carlucci A, Natale G, Freda C, Bove M, Messina G, Liguori G, Santini M. Uniportal thoracoscopic surgical management using a suture traction for primary pneumothorax. Asian Cardiovasc Thorac Ann. 2021;29(3):195–202.
20. De Waele M, Agzarian J, Hanna WC, Schieman C, Finley CJ, Macri J, Schneider L, Schnurr T, Farrokhyar F, Radford K, Nair P, Shargall Y. Does the usage of digital chest drainage systems reduce pleural inflammation and volume of pleural effusion following oncologic pulmonary resection? - a prospective randomized trial. J Thorac Dis. 2017;9(6):1598–606.
21. Fiorelli A, Natale G, Freda C, Cascone R, Carlucci A, Costanzo S, Ferrara V, Santini M. Montgomery T-tube for management of tracheomalacia: impact on voice-related quality of life. Clin Respir J. 2020;14(1):40–6.
22. Zhang X, Ran Y. Prognostic role of elevated platelet count in patients with lung cancer: a systematic review and meta-analysis. Int J Clin Exp Med. 2015;8(4):5379–87.
23. Lee S, Eo W, Jeon H, Park S, Chae J. Prognostic significance of host-related biomarkers for survival in patients with Advanced Non-small Cell Lung Cancer. J Cancer. 2017;8(15):2974–83.
24. Liu C, Zhang H, Qi Q, Zhang B, Yue D, Wang C. The preoperative platelet distribution width: a predictive factor of the prognosis in patients with non-small cell lung cancer. Thorac Cancer. 2020;11(4):918–27.
25. Skorek P, Stępień K, Fila M, Hauer J, Kużdżał J. Preoperative thrombocytosis in surgically treated patients with non-small cell lung cancer. Pol Arch Intern Med. 2018;128(9):512–7.
26. Li M, Zhao S, Lopez G, Secor A, Das P, Surya N, Grogan M, Patel S, Chakravarthy K, Miah A, Spakowicz D, Tinoco G, Li Z, Wei L, He K, Bertino E, Alahmadi A, Memmott R, Kaufman J, Shields PG, Carbone DP, Presley CJ, Otterson GA, Owen DH. Mean platelet volume, thrombocytosis, and survival in non-small cell lung cancer patients treated with first-line pembrolizumab alone or with chemotherapy. Cancer Immunol Immunother. 2023;72(7):2067–74.
27. Saha B, Khatun N, Azim N, Islam SA, Proteek MF, Islam MR, Begum FA, Biddut MA, Khan MK, Islam MR. Platelet count as a prognostic factor in Stage IV Non-small Cell Lung Cancer. Mymensingh Med J. 2022;31(4):937–46.
28. Maráz A, Furák J, Varga Z, Kahán Z, Tiszlavicz L, Hideghéty K. Thrombocytosis has a negative prognostic value in lung cancer. Anticancer Res. 2013;33(4):1725–9.
29. Scharf RE. Do we need antiplatelet therapy in thrombocytosis? Contra. Proposal for an individualized risk-adapted treatment. Hamostaseologie. 2016;36(4):241–60.
30. Madaan GB, Jairajpuri ZS, Hajini FF, Jetley S. Postoperative thrombocytosis: an unusual case report. Int J Appl Basic Med Res. 2015 Sep-Dec;5(3):225–7.
31. Mohamud M, Osborne L, Jones HG, Ahmed A, Beynon J, Harris DA, Evans M, Davies M, Khot U, Chandrasekaran TV. Thrombocytosis as a marker for postoperative complications in colorectal surgery. Gastroenterol Res Pract. 2018;2018:1978639.
32. Messina G, Bove M, Natale G, Di Filippo V, Opromolla G, Rainone A, Leonardi B, Martone M, Fiorelli A, Vicidomini G, Santini M, Ronchi A, Massimilla E, Della Corte CM, Pirozzi M, Caterino M, Ciardiello F, Fasano M. Diagnosis of malignant pleural disease: Ultrasound as a detective probe. Thorac Cancer. 2023;14(3):223–30.
33. Chen Y, Zhong H, Zhao Y, Luo X, Gao W. Role of platelet biomarkers in inflammatory response. Biomark Res. 2020;8:28.

Publisher's note