Mediterranean Journal of Hematology and Infectious Diseases

Original Article

Safety of Bronchoalveolar Lavage in Hematological Patients with Thrombocytopenia. A Retrospective Cohort Study

Ivan Gur*[1], Roei Tounek*[2], Yaniv Dotan[1,2], Elite Vainer Evgrafov[1,2], Stav Rakedzon[1] and Eyal Fuchs[1,2].

[1] Rambam Medical Center, Haifa, Israel.
[2] The Ruth and Bruce Rappaport Faculty of Medicine, Technion Israel Institute of Technology, Haifa, Israel.
* The authors equally contributed to the work.

Competing interests: The authors declare no conflict of Interest.

Abstract. ***Background*: Hospitalized hematological patients often require bronchoalveolar lavage (BAL). Scarce evidence exists regarding the potential risks in patients with very severe thrombocytopenia (VST).**
***Methods*: This retrospective-cohort study included adult hematological in-patients with VST, defined as platelets<20x10^3/µL, undergoing BAL during 2012-2021. Mechanically ventilated patients or those with known active bleeding were excluded. Primary outcomes included major bleeding halting the BAL or deemed significant by the treating physician, need for any respiratory support other than low flow O2, or death within 24 hours. Any other bleedings were recorded as secondary outcomes.**
***Results*: Of the 507 patients included in the final analysis, the 281 patients with VST had lower hemoglobin (Md=0.3, *p=0.003*), longer prothrombin-time (Md=0.7s, *p=0.025*), higher chances of preprocedural platelet transfusion (RR 3.68, 95%CI[2.86,4.73]), and only one primary-outcome event (death of septic shock 21h postprocedurally) - compared with 3 (1.3%) events (two bleedings halting procedure and one need for non-invasive-ventilation) in patients with platelets ≥20x10^3/µL (*p=0.219*). The risk of minor spontaneously resolved bleeding was higher (RR=3.217, 95% CI [0.919,11.262]) in patients with VST (4.3% vs 1.3%, *p=0.051*). No association was found between the complications recorded and preprocedural platelets, age, aPTT, P.T., hematological status, or platelet transfusion.**
***Conclusions*: This data suggests BAL to be safe even when platelet counts are <20x10^3/µL.**

Keywords: Bronchoalveolar Lavage (BAL); Thrombocytopenia; Hematological patients; BAL complications.

Citation: Gur I., Tounek R., Dotan Y., Evgrafov E.V., Rakedzon S., Fuchs E. Safety of bronchoalveolar lavage in hematological patients with thrombocytopenia. A retrospective cohort study. Mediterr J Hematol Infect Dis 2024, 16(1): e2024006, DOI: http://dx.doi.org/10.4084/MJHID.2024.006

Published: January 01, 2024 **Received: September 11, 2023** **Accepted: December 12, 2023**

Correspondence to: Ivan GUR, MD, MPH, MHA. Department of Internal Medicine C, Rambam Medical Center, 4 HaAlia Street, Haifa 3109601, Israel. Tel: (+972)-4-777-2661, Fax: (+972)-542-555-655. E-mail: I_GUR@rambam.health.gov.il

Introduction. Patients with hematological malignancies are at increased risk of opportunistic pulmonary infections.[1] Flexible bronchoscopy-facilitated bronchoalveolar lavage (BAL) is important in this population's diagnosis and therapy guidance.[2] Coincidentally, thrombocytopenia is a common occurrence in this population. Thrombocytopenia, combined with other comorbidities and hemostatic dysfunction, is a common concern when considering BAL's safety and cost-benefit ratios in hematological

patients.[3] This is particularly true in patients with platelet counts below $50x10^3/\mu L$, prompting most providers to consider prophylactic platelet transfusions (particularly in very low platelet counts below $10x10^3/\mu L$) in an attempt to mitigate the risk of periprocedural complications.[4]

Nonetheless, there are no universally accepted platelet count thresholds for BAL or the decision to transfuse periprocedurally. Previous observational studies have described vanishingly low complication rates above $20x10^3/\mu L$[5] or even $10x10^3/\mu L$.[6,7] Current accepted guidelines, based on low-level observational data, agree on the general safety of BAL when the platelet count is above $20x10^3/\mu L$.[8,9]

In this study, we aimed to describe the incidence of various periprocedural complications of BAL in hospitalized hematological patients with significant thrombocytopenia, assessing potential predictors of increased risk, in an attempt to assess the safety of this invasive and yet essential procedure in such a frail population.

Methods. This retrospective cohort study was conducted in Rambam Health Care Campus (RMC), a tertiary 1000-bed medical center, the largest medical center in northern Israel. The Electronic Health Registry (EHR) files of all patients undergoing BAL between January 1, 2012, and December 31, 2021, were reviewed.

The study included all adult patients (18 years or older) undergoing BAL while hospitalized in our hematology ward with a platelet count below $50x10^3/\mu L$ 24 hours before the procedure. Exclusion criteria were: 1) Active hemoptysis, epistaxis, or known upper gastrointestinal bleeding in the 24 hours prior to the bronchoalveolar lavage and 2) BAL performed while the patient is mechanically ventilated.

Physician's notes, admission and discharge reports, imaging interpretations, and background diagnoses were manually and individually reviewed for each patient in this study. Additional demographic, clinical, and laboratory data, including date of birth, vital signs, and laboratory results upon presentation, were mined using the MD-Clone® interface (version 4.25 or older). Machine-mined data was assessed for accuracy and relevance by the investigator reviewing the EHR.

The primary outcome was any major complication in the 24 hours after the initiation of BAL, including any of the following: 1) clinically significant major bleeding, either resulting in the premature termination of the BAL and / or necessitating packed red blood cells transfusion peri procedurally and / or deemed by any of the treating physicians as potentially life-threatening; 2) The need for ventilatory support other than low flow conventional supplementary oxygen therapy (COT), including high flow (>10 L/min) oxygen therapy or any positive pressure ventilation (both invasive and noninvasive) or 3) death from any cause. The secondary outcomes were defined as any non-major bleeding within the first 24 hours post-procedurally, including self-limiting bleeding visualized during bronchoscopy and any epistaxis, whether said bleeding resolved spontaneously, or hemostatic measures (such as nasal packing, intraluminal epinephrine, tranexamic acid or cold saline injections) were required. Additional secondary outcomes included a decrease of ≥5 mmHg in mean arterial pressure (MAP) in the lowest measurement 24 hours post-BAL (compared with MAP measured immediately prior to BAL); an increase of ≥10 beats per minute (bpm) in heart rate (similarly defined as the highest resting heart rate documented in the 24 hours after bronchoscopy minus the heart rate immediately before bronchoscopy), a decrease of ≥1 mg/dL in hemoglobin (similarly defined) and a decrease of ≥5% capillary hemoglobin saturation (SpO2) as measured by pulse oximetry within 24 hours (similarly defined). In addition, we recorded the diagnostic yield of the BAL, i.e., whether any pathogens were recovered and the type of infectious syndrome (e.g., invasive pulmonary aspergillosis, bacterial pneumonia, or atypical infection such as legionellosis) supported by the BAL results.

Per institutional protocols, BAL was performed transnasally unless technically infeasible, in which case the transoral approach was implemented. This study was reviewed and approved by the RMC institutional ethics committee (RMB-22-0017).

Statistical Analysis. Standard descriptive statistics were used to summarize population characteristics. We used a chi-square test for categorical variables, a Mann-Witney U test for nonparametric variables, and a student's unpaired t-test for normally distributed continuous variables. Tukey's correction was applied when applicable to adjust for multiple comparisons. Categorical variables were described using proportions and percentages, nonparametric variables with median and interquartile range (IQR), and normally distributed continuous variables as mean with standard deviation (S.D.).

Multivariate logistic regression modeling was performed using Pearl and Reed's method. We used the Pearson correlation coefficient to determine possible correlations between independent variables; only variables that were not co-related (Pv>0.1 on univariate analysis) were included in the model. A 2-sided Pv<0.05 was considered statistically significant for all tests. All calculations were performed using PASW software version 29.0 (IBM, Chicago, IL).

Results. Of 720 adult (age 18 or older) hematological patients undergoing BAL while hospitalized during the study period, only 553 (76.8) had a platelet count below $50x10^3/\mu L$. Nine (1.6%) patients were excluded due to

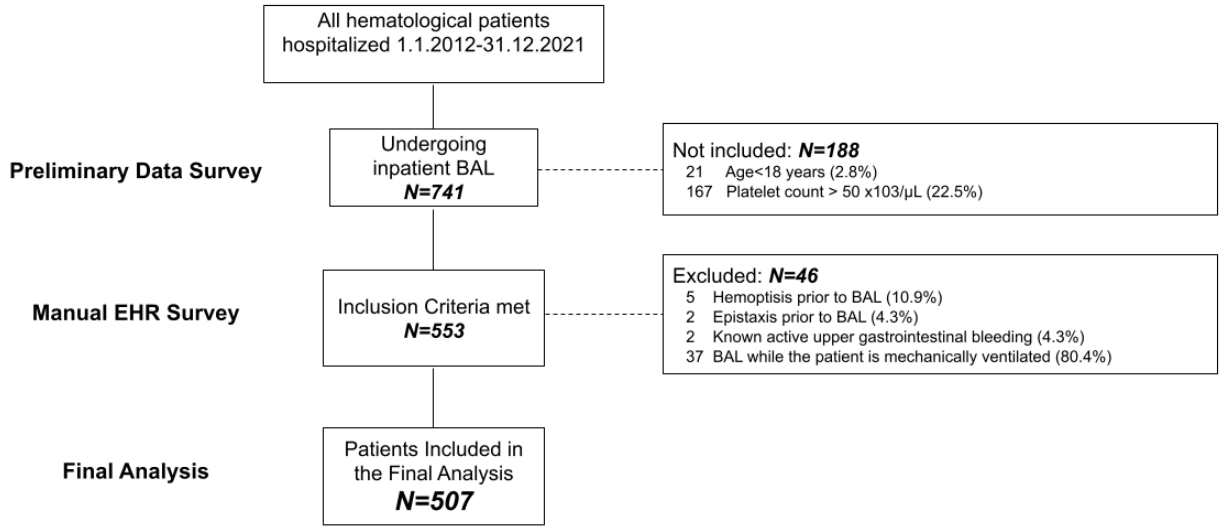

Figure 1. Study Design. The study phases are presented in accordance with the CONSORT guidelines. **Abbreviations:** EHR - electronic healthcare registry, BAL - Bronchoalveolar Lavage.

active hemoptysis, epistaxis, or upper gastrointestinal bleeding in the 24 hours prior to bronchoscopy, and 37 (6.7%) patients were mechanically ventilated while undergoing BAL. A Consolidated Standards of Reporting Trials (CONSORT) diagram summarizing the data mining and filtering process is presented in **Figure 1**.

Of the 507 patients included in the final analysis, 281 (55.4%) had a platelet count below $20x10^3/\mu L$, and 210 (41.4%) were females. The mean age was 55.3 years (median 59, Sd 15.1), and the mean platelet count was $20.4x10^3/\mu L$ (median 18, Sd 12). Regarding the background hematological diagnosis, the most common diagnosis was acute myeloid leukemia, affecting 264 (52.1%) of patients. Overall, 324 (63.9%) had acute leukemia, 6 (1.2%) chronic leukemia, 11 (2.1%) indolent lymphomas, 66 (13%) other lymphomas, 46 (9.1%) multiple myeloma, 40 (7.9%) myelodysplastic syndrome, 10 (1.9%) myeloproliferative disorders, and 7 (1.4%) aplastic anemia. Only the rates of myelodysplastic syndrome were significantly (p=0.017) associated with higher platelet counts.

When examining the bloodwork and vital signs obtained on the morning of the procedure, mean hemoglobin concentration was 0.3mg/dL lower (p=0.003), and mean prothrombin time 0.7 seconds longer in patients with platelet counts below $20x10^3/\mu L$. The mean activated partial thromboplastin time was 29.9 seconds (Sd 5.5), heart rate 89.4 bpm (18.3), SpO2 95.8% (Sd 3.4) or mean arterial pressure 82.4 mmHg (Sd 10.4) with no significant association with platelet count. There was no significant difference between patients with platelet counts below and above $20x10^3/\mu L$ in any of the other baseline characteristics examined, with the notable exception of the rates of periprocedural platelet transfusion occurring in four times as many patients with platelet counts below $20x10^3/\mu L$ ($p<0.001$). These data are summarized in **Table 1**.

Clinically significant bleeding (2 patients, 0.9%) and need for ventilatory support with noninvasive bilevel positive pressure (one patient, 0.4%) occurred exclusively in patients with platelet counts above $20x10^3/\mu L$, and the only primary outcome to have been recorded in the $<20x10^3/\mu L$ group was one account of death due to cardiovascular collapse in a patient with severe septic shock and multiorgan failure (manifested prior to bronchoscopy) 21 hours after BAL (p=0.219 for the composite of primary outcomes).

The incidence of non-major bleeding was higher (13 (4.6%) vs 4(1.8%)) in patients with platelets below $20x10^3/\mu L$ (RR 2.614, 95% CI [0.864,7.906]), a trend that approached statistical significance (p=0.076). Further analysis demonstrated spontaneously resolved minor bleeds to be responsible for this trend (RR 3.217, 95% CI [0.919,11.262]), with a virtual similar rate of one patient (0.4%) requiring nasal packing with topical tranexamic acid in both groups. A decrease in mean arterial pressure (169 patients, 33%), SpO2 (40 patients, 7.9%), hemoglobin (61 (12%)) or an increase in heart rate (94 (18%)) as defined in the secondary outcomes section above was similar between groups, as presented in **Table 2**.

When examining the microbiological diagnostic significance of these BAL samples, overall diagnostic yield and the types and counts of major pathogens recovered did not differ significantly between groups. These findings are presented in **Figure 2**.

To further illuminate the potential association between the degree of pre-procedural thrombocytopenia and potential patient-specific confounders, three multivariate logistic regression models were constructed, predicting major complications (as defined by the primary outcome), any bleeding or a composite of all recorded complications (both primary and secondary

Table 1. Study patients characteristics.

	PLT ≥ 20 x10^3/µL N=226	PLT < 20 x10^3/µL N=281	P-value
Female (%)	98 (43.4%)	112 (39.9%)	0.426
Age (Sd)	55.1 (15.7)	55.5 (14.7)	0.740
Primary hematological diagnosis (%):			
Acute Myeloid Leukemia	109 (48.2%)	155 (55.2%)	0.121
Acute Lymphocytic Leukemia	25 (11.1%)	35 (12.5%)	0.629
Aplastic Anemia	2 (0.9%)	5 (1.8%)	0.391
Chronic Myeloid Leukemia	1 (0.4%)	2 (0.7%)	0.694
Chronic Lymphocytic Leukemia	2 (0.9%)	1 (0.4%)	0.440
Diffuse Large B-cell lymphoma	19 (8.4%)	16 (5.7%)	0.231
Hodgkin's Lymphoma	8 (3.5%)	9 (3.2%)	0.834
Follicular Lymphoma	1 (0.4%)	2 (0.7%)	0.694
Marginal Cell Lymphoma	5 (2.2%)	2 (0.7%)	0.150
T-Cell Lymphoma	4 (1.8%)	8 (2.8%)	0.428
Myelodysplastic Syndrome	**25 (11.1%)**	**15 (5.3%)**	**0.017**
MyeloFibrosis	1 (0.4%)	6 (2.1%)	0.104
Multiple Myeloma	23 (10.2%)	23 (8.2%)	0.438
Laboratory results and vital signs on the morning before bronchoscopy (Sd):			
Hemoglobin (mg/dL)	**8.2 (1.1)**	**7.9 (1.1)**	**0.003**
Platelets (1000/µL)	31.5 (9)	11.6 (4.4)	n/a
activated Partial Thromboplastin Time (s)	29.3 (4.5)	30.3 (5.2)	0.089
Prothrombin Time (s)	**12.9 (1.9)**	**13.6 (2.3)**	**0.025**
Heart Rate (beats/min)	88.5 (17.4)	91.2 (17.3)	0.094
Pulse-oximetry saturation (%)	95.9 (3.2)	95.6 (3.4)	0.418
Mean arterial pressure (mmHg)	87.19 (18.3)	88.48 (19)	0.471
Prior Hematopoietic Stem-Cell Transplant	102 (45.1%)	117 (41.6%)	0.430
of which autologous	45 (19.9%)	46 (16.4%)	0.564
Platelets transfused peri procedurally	**50 (22.1%)**	**229 (81.5%)**	**<0.001**
Body Mass Index (kg/m^2)	29 (5.75)	29.6 (6.23)	0.240

Abbreviations: PLT - Platelets count, Sd - standard deviation.

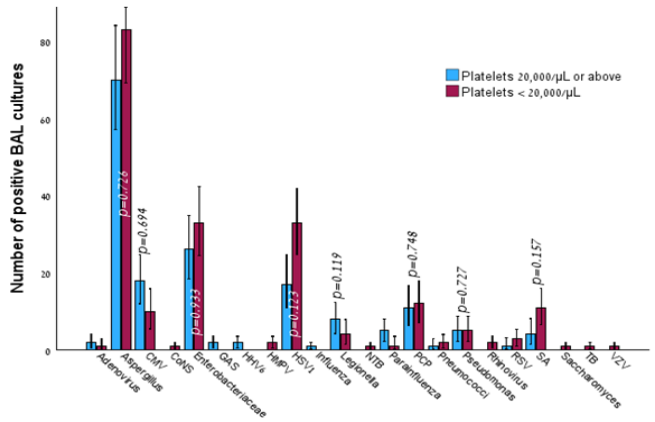

Figure 2. Diagnostic Yield of Bronchoalveolar Lavage. Positive results of BAL microbiology, either by means or direct culture or nucleic acid amplification. **Abbreviations**: CMV - cytomegalovirus, GAS - group A streptococci, HHV6 - human herpesvirus 6, HMPV - human metapneumovirus, HSV - herpes simplex virus, NTB - nontuberculous mycobacteria, PCP - pneumocystis Jirovecii pneumonia, RSV - respiratory syncytial virus, S.A. - Staphylococcus aureus, T.B. - Mycobacterium tuberculosis, VZV - varicella-zoster virus.

outcomes). A trend towards increased risk of any bleeding was observed with preprocedural platelet transfusion (aRR 3.55, 95% CI [0.83,15.18]), although this finding did not reach the accepted level of statistical significance (p=0.087). Age, activated partial thromboplastin time, prothrombin time, preprocedural hemoglobin concentration or platelet count, gender, the presence of acute leukemia, or history of hematopoietic stem-cell transplant did not significantly predict the development of major complications, any bleeding, or any of the recorded complications, as detailed in **Table 3**.

Discussion. This study suggests a very low incidence (0.8%) of serious periprocedural complications when performing BAL in hematological patients, even in the presence of VST. Both cases of major bleeding (British Thoracic Society grade 3[10] for the twain) were recorded in patients with higher platelet counts. While the reported

Table 2. Primary and secondary outcomes.

	PLT ≥ 20 x10^3/μL *N=226*		PLT < 20 x10^3/μL *N=281*		P-value
Primary outcome	3	1.3%	1	0.4%	0.219
Clinically significant bleeding	2	0.9%	0	0.0%	
Ventilatory support needed	1	0.4%	0	0.0%	
Death from any cause	0	0.0%	1	0.4%	
Secondary outcomes					
Non-major bleeding	4	1.8%	13	4.6%	0.076
Of which spontaneously resolved	**3**	**1.3%**	**12**	**4.3%**	**0.051**
Needed a minor intervention (nasal packing, topical tranexamic acid, or cold-water injection)	1	0.4%	1	0.4%	0.877
MAP decrease ≥ 5 mmHg	70	31.0%	99	35.2%	0.312
HR increase ≥ 10 bpm	47	20.8%	47	16.7%	0.241
Hemoglobin decrease ≥ 1 mm/dL	25	11.1%	36	12.8%	0.547
SpO2 decrease ≥ 5 %	19	8.4%	21	7.5%	0.698
Composite secondary outcomes	128	56.6%	168	59.8%	0.475

Abbreviations: PLT - Platelets count, MAP - mean arterial pressure, H.R. - heart rate; SpO2 - pulse oximetry hemoglobin saturation.

Table 3. Multivariate Logistic Regression. Multivariate logistic regression models predict the primary outcome (major bleeding, need for ventilatory support or death), any bleeding, or any outcome (a composite of all primary and secondary outcomes).

	Primary Outcome				Any Bleeding				Any Outcome			
	aRR	95% CI		p	aRR	95% CI		p	aRR	95% CI		p
Age (years)	1.035	[0.969,	1.106]	0.308	1.015	[0.983,	1.049]	0.351	0.996	[0.983,	1.008]	0.494
aPTT (s)	0.889	[0.749,	1.055]	0.176	0.991	[0.911,	1.077]	0.826	1.038	[0.988,	1.088]	0.228
PT (s)	1.185	[0.702,	2.000]	0.525	0.907	[0.742,	1.109]	0.343	0.995	[0.915,	1.081]	0.898
Preprocedural H.B. (mg/dL)	1.468	[0.499,	4.315]	0.486	1.496	[0.905,	2.475]	0.116	0.69	[0.572,	1.832]	0.391
Platelets (1000/μL)	0.955	[0.868,	1.050]	0.342	0.992	[0.938,	1.050]	0.791	1.002	[0.982,	1.022]	0.848
Gender (female)	0.674	[0.088,	5.174]	0.704	0.584	[0.223,	1.527]	0.273	1.04	[0.717,	1.510]	0.835
Any acute leukemia	0.14	[0.011,	1.851]	0.136	0.494	[0.171,	1.426]	0.192	1.283	[0.839,	1.962]	0.251
HSCT	1.882	[0.170,	20.85]	0.607	0.924	[0.319,	2.676]	0.883	1.303	[0.856,	1.983]	0.217
Preprocedural platelet transfusion	2.246	[0.158,	31.95]	0.550	3.554	[0.832,	15.18]	0.087	1.183	[0.736,	1.904]	0.488

Abbreviations: PLT - Platelets count, MAP - mean arterial pressure, H.R. - heart rate; SpO2 - pulse oximetry hemoglobin saturation.

rates of bronchoscopy complications range between 1 percent to 12%, various retrospective studies have demonstrated the incidence of serious complications (i.e., major bleeding halting procedure, need for ventilatory support or death) to be consistently in the range of 0.7-0.9%.[4,6,7,11-13] Interestingly, the rates of both serious complications in general and major bleeding, in particular, are similar when examining large cohorts of BAL in the general population and in patients with various degrees of thrombocytopenia, which could serve as a weak, albeit ecological, corroboration to the lack of a direct link between platelet counts and major complications in bronchoscopy.[6,11,14]

The rates of non-major bleeding were higher in severely thrombocytopenic patients, approaching significance only due to very minor, spontaneously resolving bleeding. Echoed in some previous reports[4,7,12] and considerably lower than others,[11] this observation is consistent with our understanding of platelet function in primary hemostasis. Namely, superficial bleeding (e.g., petechiae and purpura) is the major clinical manifestation of isolated thrombocytopenia.[15]

The trend towards increased risk of any bleeding with platelet transfusion represents correlation rather than causation. When adjusted for other observed confounders, such as hemoglobin concentration and hematological history, our data showed no clear signal toward the direct benefit of platelet transfusion in preventing BAL complications. Previous attempts to establish a safety threshold of 30x10^3/μL or even 10x10^3/μL were hampered by their retrospective nature and high prevalence of platelet transfusions in the control group.[6,7] Our study demonstrates the very strong predilection of clinicians to administer platelet

transfusion below the currently set threshold of $20x10^3/\mu L$, which is based on a very low level of evidence.[8]

More interestingly, there was no significant association between platelet count or coagulation studies and any of the BAL complications examined. Coherent with the limited role of the coagulation cascade in minor superficial injuries, this observation is also consistent with the mounting evidence of these limited coagulation studies' very low predictive ability in predicting bleeding risk.[16]

To our knowledge, this is the only study focused exclusively on BAL by primary design. We attribute the relatively low incidence of bleeding of all varieties observed in the study to mild tissue derangement when bronchoscopy is confined to visualization and BAL.[17] The shorter duration, low energy, smaller bore diameters, and minimal tissue disruption could all explain the general safety of this procedure, even in the sickest of patients.[18] This is particularly important given the recent departure from tissue sampling to diagnose infectious diseases. Particularly, most recent guidelines[8,19] have accepted BAL-based testing, such as galactomannan, as a preferable alternative to diagnosing invasive pulmonary aspergillosis - by far the most prevalent diagnosis resulting from bronchoscopy in our sample.[20]

Of note, examining the BAL aspirate most often yielded a diagnosis of Invasive Pulmonary Aspergillosis, followed by gram-negative *Enterobacteriaceae*, Herpes Simplex Virus, Cytomegalovirus, and *Pneumocystis jirovecii*. These rates and relative incidence are similar to previously reported cross-sectional studies of diagnostic BAL in hematological patients.[21] While the degree of thrombocytopenia seems to correlate with bone marrow dysfunction (as evidenced by the high correlation with white and red blood cell counts), the microbiological yield is similar when compared to patients without severe thrombocytopenia (and by conjecture, probably a lesser degree of myelosuppression). Actually, the underlying hematological disease, rather than peripheral counts themselves, can explain the majority of immune dysfunction and resultant, rather opportunistic infectious profile.[1] Alternatively, patient selection (i.e., those who undergo BAL are those manifesting clinical characteristics of opportunistic infections) and characteristics (prolonged hospitalization, exposure to multiple antimicrobial agents, etc.), rather than the degree of pancytopenia, may be the main mechanism explaining BAL microbiology.

Limitations. This study has several important limitations. Firstly, the retrospective design inherently raises the risk of biases, particularly since no randomization was performed and no strict protocol detailing the use of platelet transfusion was followed. Secondly, despite extensive and decade-long data collection in one of our nation's largest hematological referral centers, the incidence of significant adverse outcomes (defined in this study as primary outcomes) or any bleeding complication was low. The rare event limits our ability to fully appreciate the potentially rare complications of BAL in thrombocytopenic patients.

Conclusions. This observational study showed no increased risk of major or minor complications in patients with severe thrombocytopenia due to bronchoalveolar lavage. Consistent with previous reported evidence, our data suggests BAL to be generally safe in hematological patients, irrespective of platelet count. Additionally, prospectively randomized studies are needed to validate the safe platelet count threshold prior to BAL further and elucidate the clinical yield of periprocedural platelet transfusion.

References:

1. Bitterman R, Hardak E, Raines M, Stern A, Zuckerman T, Ofran Y, et al. Baseline Chest Computed Tomography for Early Diagnosis of Invasive Pulmonary Aspergillosis in Hemato-oncological Patients: A Prospective Cohort Study. Clin Infect Dis. 2019 October 30;69(10):1805-8. https://doi.org/10.1093/cid/ciz194 PMid:30855077
2. Kim SW, Rhee CK, Kang HS, Lee HY, Kang JY, Kim SJ, et al. Diagnostic value of bronchoscopy in patients with hematologic malignancy and pulmonary infiltrates. Ann Hematol. 2015 Jan;94(1):153-9. https://doi.org/10.1007/s00277-014-2172-3 PMid:25062720
3. Choo R, Naser NSH, Nadkarni NV, Anantham D. Utility of bronchoalveolar lavage in the management of immunocompromised patients presenting with lung infiltrates. BMC Pulm Med. 2019 February 26;19(1):51. https://doi.org/10.1186/s12890-019-0801-2 PMid:30808314 PMCid:PMC6390608
4. Uruga H, Sato T, Nishida A, Uchida N, Tsuji M, Moriguchi S, et al. Safety of bronchoscopy in patients with malignant hematologic disorders. BMC Pulm Med. 2020 September 11;20(1):243. https://doi.org/10.1186/s12890-020-01283-8 PMid:32917185 PMCid:PMC7488692
5. Kaur R, Alolaiwat AA, Ritz E, Mokhlesi B, Vines DL. A new index, Respiratory Insufficiency index and Modified Early Warning Scores predict extubation failure. Can J Respir Ther. 2023 May 18;59:117-22. https://doi.org/10.29390/cjrt-2023-003 PMid:37214344 PMCid:PMC10194084
6. Facciolongo N, Patelli M, Gasparini S, Lazzari Agli L, Salio M, Simonassi C, et al. Incidence of complications in bronchoscopy. Multicentre prospective study of 20,986 bronchoscopies. Monaldi Arch Chest Dis. 2009 Mar;71(1):8-14. https://doi.org/10.4081/monaldi.2009.370 PMid:19522159
7. Faiz SA, Jimenez CA, Fellman BM, Huk T, Jazbeh S, Haque SA, et al. Incidence of bleeding complications with flexible bronchoscopy in cancer patients with thrombocytopenia. J Bronchology Interv Pulmonol. 2019 Oct;26(4):280-6. https://doi.org/10.1097/LBR.0000000000000590 PMid:30973520 PMCid:PMC6768748
8. Du Rand IA, Blaikley J, Booton R, Chaudhuri N, Gupta V, Khalid S, et al. British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults: accredited by NICE. Thorax. 2013 Aug;68 Suppl 1:i1-44. https://doi.org/10.1136/thoraxjnl-2013-203618 PMid:23860341

9. Mohan A, Madan K, Hadda V, Tiwari P, Mittal S, Guleria R, et al. Guidelines for diagnostic flexible bronchoscopy in adults: Joint Indian Chest Society/National College of chest physicians (I)/Indian association for bronchology recommendations. Lung India. 2019 Jul;36(Supplement):S37-89.
10. Folch EE, Mahajan AK, Oberg CL, Maldonado F, Toloza E, Krimsky WS, et al. Standardized definitions of bleeding after transbronchial lung biopsy: A delphi consensus statement from the nashville working group. Chest. 2020 Jul;158(1):393-400. https://doi.org/10.1016/j.chest.2020.01.036 PMid:32067944 PMCid:PMC7403751
11. Bo L, Shi L, Jin F, Li C. The hemorrhage risk of patients undergoing bronchoscopic examinations or treatments. Am J Transl Res. 2021 August 15;13(8):9175-81.
12. Cefalo M, Puxeddu E, Sarmati L, Paterno G, Fontana C, Nasso D, et al. Diagnostic performance and safety of bronchoalveolar lavage in thrombocytopenic haematological patients for invasive fungal infections diagnosis: A monocentric, retrospective experience. Mediterr J Hematol Infect Dis. 2019 November 1;11(1):e2019065. https://doi.org/10.4084/mjhid.2019.065 PMid:31700590 PMCid:PMC6827601
13. Jacomelli M, Margotto SS, Demarzo SE, Scordamaglio PR, Cardoso PFG, Palomino ALM, et al. Early complications in flexible bronchoscopy at a university hospital. J Bras Pneumol. 2020 Jun 1;46(4):e20180125. https://doi.org/10.36416/1806-3756/e20180125 PMid:32490906 PMCid:PMC7567622
14. Nandagopal L, Veeraputhiran M, Jain T, Soubani AO, Schiffer CA. Bronchoscopy can be done safely in patients with thrombocytopenia. Transfusion. 2016 Feb;56(2):344-8. https://doi.org/10.1111/trf.13348 PMid:26446048
15. Schiffer CA, Bohlke K, Delaney M, Hume H, Magdalinski AJ, McCullough JJ, et al. Platelet transfusion for patients with cancer: american society of clinical oncology clinical practice guideline update. J Clin Oncol. 2018 Jan 20;36(3):283-99. https://doi.org/10.1200/JCO.2017.76.1734 PMid:29182495
16. Shi Y, Zhang G, Ma C, Xu J, Xu K, Zhang W, et al. Machine learning algorithms to predict intraoperative hemorrhage in surgical patients: a modeling study of real-world data in Shanghai, China. BMC Med Inform Decis Mak. 2023 Aug 10;23(1):156. https://doi.org/10.1186/s12911-023-02253-w PMid:37563676 PMCid:PMC10416513
17. Zhou G-W, Zhang W, Dong Y-C, Huang H-D, Hu C, Sun J, et al. Flexible bronchoscopy-induced massive bleeding: A 12-year multicentre retrospective cohort study. Respirology. 2016 Jul;21(5):927-31. https://doi.org/10.1111/resp.12784 PMid:27061330
18. Costa A da S, Scordamaglio PR, Suzuki I, Palomino ALM, Jacomelli M. Indications, clinical outcomes and complications of 1,949 flexible bronchoscopies. Einstein (Sao Paulo). 2018 Nov 8;16(4):eAO4380. https://doi.org/10.31744/einstein_journal/2018AO4380 PMid:30427487 PMCid:PMC6223942
19. Hardak E, Fuchs E, Leskes H, Geffen Y, Zuckerman T, Oren I. Diagnostic role of polymerase chain reaction in bronchoalveolar lavage fluid for invasive pulmonary aspergillosis in immunocompromised patients - A retrospective cohort study. Int J Infect Dis. 2019 Jun;83:20-5. https://doi.org/10.1016/j.ijid.2019.03.025 PMid:30926540
20. Shimoda M, Tanaka Y, Morimoto K, Abe T, Asaga R, Nakajima K, et al. Analysis of predicted factors for bronchoalveolar lavage recovery failure: An observational study. PLoS ONE. 2022 Sep 30;17(9):e0275377. https://doi.org/10.1371/journal.pone.0275377 PMid:36178919 PMCid:PMC9524652
21. Gur I, Giladi A, Isenberg YN, Neuberger A, Stern A. COVID-19 in Patients with Hematologic Malignancies: Clinical Manifestations, Persistence, and Immune Response. Acta Haematol. 2022 Mar 2;145(3):297-309. https://doi.org/10.1159/000523872 PMid:35235928 PMCid:PMC9254311