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Original Article

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Evaluation of the effects of preoxygenation with different oxygen concentrations during spontaneous breathing before anesthesia induction using lung ultrasonography

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ABSTRACT

Aims: To compare lung aeration loss after preoxygenation with 80% or 100% fraction of inspired oxygen (FiO_2) during spontaneous breathing before induction of general anesthesia using the modified lung ultrasound score (MLUS).

Methods: Fifty-four ASA I–II adults aged 18–65 years without known pulmonary disease were randomized before elective surgery to three-minute spontaneous-breathing preoxygenation with 80% FiO_2 (group E) or 100% FiO_2 (group H). After four post-randomization exclusions, 50 patients were included in the analysis (25 per group). Lung ultrasonography was performed in 12 thoracic regions before and after preoxygenation by an investigator blinded to group allocation. Total MLUS scores, peripheral oxygen saturation, end-tidal oxygen (EtO_2), and ultrasound assessment duration were recorded.

Results: Demographic and clinical characteristics were similar between groups. Post-preoxygenation EtO_2 was higher in group H than in group E ($p<0.001$). Total MLUS scores increased from baseline in both groups ($p<0.001$ for both). The proportion of patients with a post-preoxygenation total MLUS score >0 was 76% in group E and 92% in group H ($p=0.247$). However, the post-preoxygenation total MLUS score was higher in group H than in group E [5.0 (0.0-11.0) vs 3.0 (0.0-6.0); $p=0.002$]. Exploratory regional analyses showed a between-group difference in post-preoxygenation MLUS scores in the combined lateral region (unadjusted $p=0.001$).

Conclusion: Preoxygenation during spontaneous breathing increased total MLUS scores with both 80% and 100% FiO_2. Although 100% FiO_2 achieved higher EtO_2, it was associated with higher total MLUS scores than 80% FiO_2; the clinical implications of this sonographic difference remain uncertain.

Keywords: Pulmonary atelectasis, ultrasonography, anesthesia, oxygen, oxygen inhalation therapy

INTRODUCTION

Atelectasis is defined as impaired gas exchange in an affected lung region resulting from complete or partial collapse of the lung.[1] It may occur in up to 90% of patients undergoing general anesthesia and is among the most common perioperative pulmonary problems.[2] Atelectasis may be associated with impaired oxygenation, decreased lung compliance, ventilation-perfusion mismatch, and hypoxemia. During general anesthesia, decreased muscle tone and cranial displacement of the diaphragm reduce functional residual capacity. Airway closure, particularly in dependent lung regions, and absorption of distal alveolar gas into the blood contribute to the development of absorption atelectasis. A high fraction of inspired oxygen (FiO_2) may accentuate this process by accelerating alveolar nitrogen washout.[3]

Preoxygenation is performed before induction of general anesthesia to increase body oxygen stores, reduce the risk of hypoxemia, and prolong the safe apnea time. The American Society of Anesthesiologists (ASA) difficult airway management guidelines recommend preoxygenation before airway interventions.[4] However, high oxygen concentrations may increase absorption atelectasis; therefore, an appropriate balance should be maintained between adequate oxygen reserve and preservation of lung aeration.[5]

Lung ultrasonography is a bedside, repeatable imaging method that does not involve ionizing radiation. The modified lung ultrasound score (MLUS) allows perioperative aeration loss to be monitored by including small subpleural

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consolidations in addition to B-lines and consolidations.[6] This study aimed to compare sonographic changes consistent with atelectasis using MLUS in patients preoxygenated with 80% or 100% FiO_2 during spontaneous breathing before induction of general anesthesia.

METHODS

Ethics

This study was conducted with the approval of the Clinical Researches Ethics Committee No. 1 of Ankara Etlik City Hospital (Date: 22.03.2023, Decision No: AESH-EK1-2023-001). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Written informed consent was obtained from all individual participants prior to their inclusion in the study.

Study Design

This study was designed as a randomized, prospective, observer-blinded, parallel-group clinical study. The study was registered at ClinicalTrials.gov under the registration number NCT05850988. The study was conducted between April and May 2023 in accordance with the Good Clinical Practice principles. After patients were informed about the aim, method, potential benefits, and risks of the study, written informed consent was obtained from all participants.

Participants and Randomization

Between April and May 2023, 70 patients scheduled for elective surgery under general anesthesia in the operating room of Ankara Etlik City Hospital were assessed for eligibility. Sixteen patients who met the exclusion criteria were not included. Fifty-four patients who met the inclusion criteria were randomized in a 1:1 ratio to group E (preoxygenation with 80% FiO_2) or group H (preoxygenation with 100% FiO_2) using a randomization table generated with MedCalc 20.218. In group H, 2 patients were excluded because of face-mask intolerance during preoxygenation. In group E, 1 patient was excluded because baseline ultrasonography showed pleural effusion and parenchymal changes suggestive of lung contusion, and 1 patient was excluded because splenomegaly causing marked left hemidiaphragm elevation was detected. Thus, four patients were excluded after randomization for the reasons described above. The analysis population comprised the remaining 50 patients (25 in each group), who completed the assigned preoxygenation procedure and both baseline and post-preoxygenation lung ultrasonography assessments (Figure 1).

Patients aged 18-65 years, with ASA physical status I-II, and scheduled for elective surgery under general anesthesia were included. Patients with known obstructive or restrictive pulmonary disease; a history of pulmonary infection, surgery, or multiple trauma within the previous three months; a BMI of 30 or higher; pregnancy; diaphragmatic hernia; a diagnosis of gastroesophageal reflux disease; or current smoking were excluded because these factors predispose patients to atelectasis and other pulmonary complications.

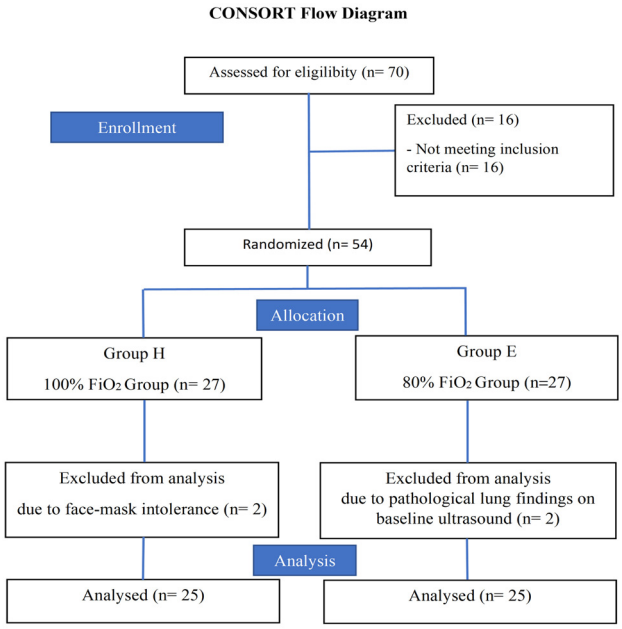

Figure 1. CONSORT flow diagram showing participant assessment, randomization, allocation, exclusions after allocation, and inclusion in the final analysis
CONSORT: Consolidated Standards of Reporting Trials; FiO_2: Fraction of inspired oxygen

Preoxygenation and Lung Ultrasonography Procedures

In the preoperative assessment room, patients underwent lung ultrasonography for baseline MLUS assessment before preoxygenation. The modified lung ultrasound scoring system described by Monastesse et al.[6] was used for MLUS assessment. The thorax was divided into 12 regions using the midsternal, anterior axillary, and posterior axillary lines as reference lines. Regions 1, 2, 3, and 4 were grouped as anterior; regions 5, 6, 7, and 8 as lateral; and regions 9, 10, 11, and 12 as posterior (Figure 2). Each region was scored from 0 to 3 according to the MLUS system, and the sum of scores from the 12 regions was recorded as the total MLUS score (Figure 3). The scoring criteria for each MLUS grade are presented in Supplementary Table.

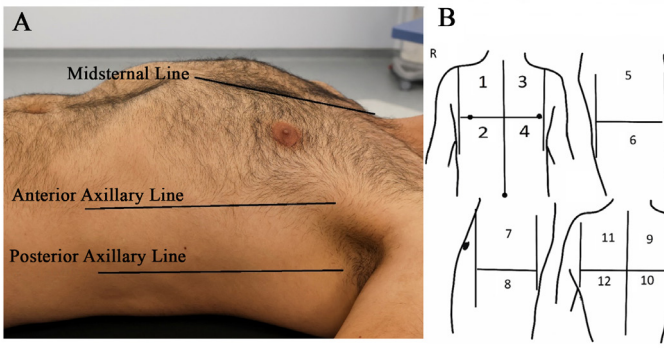

Figure 2. Schematic representation of the 12 thoracic regions assessed by lung ultrasonography. (A) Anatomical reference lines used to divide the thorax into anterior, lateral, and posterior regions: the midsternal line, anterior axillary line, and posterior axillary line. (B) Numbering of the 12 thoracic regions evaluated in the study. Each hemithorax was divided into anterior, lateral, and posterior regions, and each region was further subdivided into upper and lower zones

Lung ultrasonography was performed in B-mode using a Logiq P9 ultrasound system (GE Healthcare, USA) and a 2-9 MHz convex probe. MLUS values, ASA physical status,

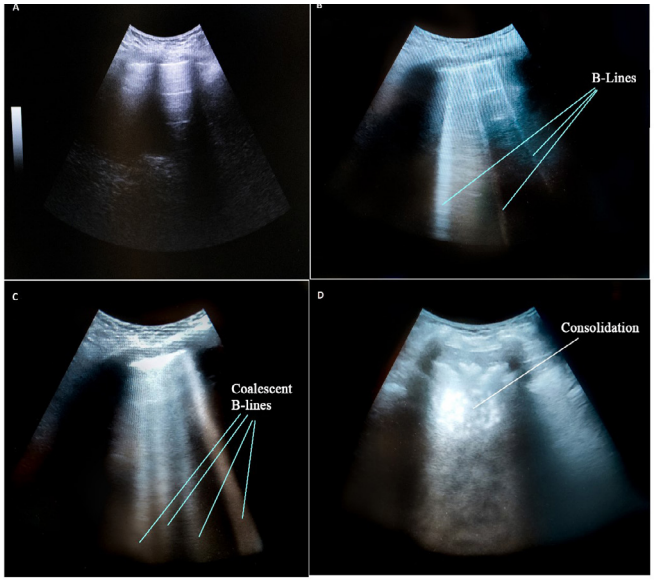

Figure 3. Representative lung ultrasonography images according to the modified lung ultrasound score. (A) Score 0: normal lung pattern with 0-2 B-lines. (B) Score 1: three or more B-lines or one or more subpleural consolidations separated by a normal pleural line. (C) Score 2: multiple coalescent B-lines or multiple small subpleural consolidations associated with a thickened or irregular pleural line. (D) Score 3: consolidation or subpleural consolidation larger than 1×2 cm

Supplementary Table. Modified lung ultrasound scoring system

MLUS score	Ultrasonographic findings
0	Normal lung pattern with 0-2 B-lines
1	Three or more B-lines or one or more subpleural consolidations separated by a normal pleural line
2	Multiple coalescent B-lines or multiple small subpleural consolidations associated with a thickened or irregular pleural line
3	Consolidation or subpleural consolidation larger than 1×2 cm

MLUS: Modified lung ultrasound score

comorbidities, age, gender, height, and body weight were recorded on the case report form. No patient received premedication.

After baseline MLUS assessment, patients were transferred to the operating room. Standard monitoring, including SpO_2, noninvasive blood pressure, and electrocardiography, was applied to all patients. On the Dräger Primus® anesthesia machine with integrated anesthetic gas monitoring, the FiO_2 value was set according to the patient's randomized group. Fresh gas flow was set at 5 L/min, and the APL valve was set to the spontaneous breathing position. The FiO_2 was set according to the randomized group, and the FiO_2 display on the anesthesia machine was covered with opaque paper before preoxygenation. The investigator performing lung ultrasonography remained blinded to group allocation until completion of the second ultrasound assessment.

FiO_2 was set to 80% in group E and 100% in group H. Patients were preoxygenated for three minutes in the supine position during spontaneous breathing using a leak-free face mask selected according to facial structure and connected to the Y-piece of the circle breathing system of the anesthesia machine.[7] Face-mask fit was assessed based on appropriate $EtCO_2$ values and capnogram pattern, with no visible leak around the mask.

At the end of the three-minute preoxygenation period, a second lung ultrasonography assessment was performed while patients were still breathing spontaneously, and MLUS values were recorded. During assessment of the posterior quadrants, patients were asked to turn slightly from the supine position. After completion of ultrasonography, EtO_2 and SpO_2 values at the end of preoxygenation and the time required to assess all 12 thoracic regions were recorded.

After study measurements were completed, general anesthesia induction was performed according to the preference of the anesthesiologist responsible for the case. Patients were intubated with an endotracheal tube to secure the airway during surgery. Intraoperatively, patients were ventilated with a tidal volume of 6-8 ml/kg according to ideal body weight, a respiratory rate of 10-14 breaths/min, and 5-8 cm H_2O positive end-expiratory pressure. In patients with findings consistent with atelectasis on MLUS assessment before or after preoxygenation, an alveolar recruitment maneuver was performed after completion of study measurements using sustained insufflation at 30 cm H_2O for 30 seconds.

Outcome Measures

The primary outcome was the comparison of post-preoxygenation total MLUS score between group E and group H. Secondary outcome measures were the within-group change in total MLUS score from baseline to after preoxygenation, the proportion of patients with a total MLUS score >0, regional MLUS scores in the 12 thoracic regions, MLUS scores for the anterior, lateral, and posterior regions, SpO_2 values before and after preoxygenation, EtO_2 at the end of preoxygenation, and the time required for ultrasonographic assessment of the 12 thoracic regions.

Statistical Analysis

Sample size was calculated using OpenEpi based on data reported in previous literature.[8] With a two-sided alpha level of 0.05, 80% power, and a 1:1 allocation ratio, the minimum required sample size was 44 patients (22 per group) using the Fleiss method with continuity correction. To compensate for possible exclusions, 50 patients were planned for inclusion in the study.

The analyses were restricted to the 50 evaluable participants (25 in each group) who completed the assigned preoxygenation procedure and both baseline and post-preoxygenation lung ultrasonography assessments. Four of the 54 randomized patients were excluded from the analyses for the reasons described in the Participants and Randomization section. Therefore, an intention-to-treat analysis was not performed. Statistical analyses were performed using IBM Statistical Package for the Social Sciences (SPSS) version 21.0. Categorical variables are presented as number (n) and percentage (%). The normality of continuous variables was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests, and homogeneity of variance was assessed using Levene's test.

Continuous variables that were normally distributed and met parametric assumptions are presented as mean±standard

deviation (mean±SD), and between-group comparisons were performed using Student's t-test. Non-normally distributed continuous variables and ordinal data are presented as median (minimum-maximum); between-group comparisons were performed using the Mann-Whitney U (MWU) test, and within-group repeated measurements were compared using the Wilcoxon signed-rank test.

Categorical variables were compared between groups using the Pearson Chi-square test, and Fisher's exact test was used when the expected cell count was insufficient. Fisher's exact test was also used for comparisons in which total MLUS score was classified as =0 or >0. Regional MLUS comparisons were exploratory; their p-values were not adjusted for multiple comparisons and were interpreted descriptively. For nonregional analyses, a p-value <0.05 was considered statistically significant.

RESULTS

Between April and May 2023, 70 patients scheduled for elective surgery under general anesthesia were assessed for eligibility, and 54 were randomized (27 to each group). Following four exclusions after randomization, 50 patients were included in the final analysis (25 in each group; Figure 1). Of these patients, 27 (54%) were male and 23 (46%) were female. Patients were analyzed in two groups: group E (preoxygenation with 80% FiO_2, n=25) and group H (preoxygenation with 100% FiO_2, n=25).

There were no significant differences between group E and group H in age (34.2±12.2 years vs 34.6±12.1 years; p=0.917) or BMI (24.9±3.1 kg/m² vs 25.0±3.4 kg/m²; p=0.904). The groups were also similar in terms of gender, presence of comorbidity, ASA class, and BMI category (p>0.05 for all comparisons) (Table 1).

Table 1. Comparison of demographic and clinical characteristics between groups

	Group E (n=25)	Group H (n=25)	p
Age, years	34.2±12.2	34.6±12.1	0.917
Body weight, kg	70.0±13.0	71.7±11.4	0.614
Height, m	1.7±0.1	1.7±0.1	0.437
BMI, kg/m²	24.9±3.1	25.0±3.4	0.904
Gender (male/female), n (%)	14 (56.0)/11 (44.0)	13 (52.0)/12 (48.0)	0.777
Comorbidity, n (%)	5 (20.0)	6 (24.0)	0.733
ASA (I/II), n (%)	20 (80.0)/5 (20.0)	19 (76.0)/6 (24.0)	0.733
Overweight, n (%)	12 (48.0)	13 (52.0)	0.777

Data are presented as mean±standard deviation or n (%). Student's t-test was used for between-group comparisons of continuous variables, and Pearson Chi-square test was used for comparisons of categorical variables. p<0.05 was considered statistically significant. Normal BMI was defined as 18.5–24.9 kg/m² and overweight as 25.0–29.9 kg/m². BMI: Body-mass index, ASA: American Society of Anesthesiologists, kg: kilograms; m: meters, kg/m²: Kilograms per square meter

Post-preoxygenation EtO_2 was 67.0 (51.0-81.0) in group E and 77.0 (64.0-95.0) in group H and was significantly higher in group H (p<0.001). The lung ultrasonography assessment duration was 316.0 (240.0-380.0) seconds in group E and 311.0 (267.0-381.0) seconds in group H, with no significant difference between groups (p=0.994) (Table 2).

Table 2. Comparison of EtO_2 and assessment duration between groups

	Group E (n=25)	Group H (n=25)	p
EtO_2, %	67.0 (51.0–81.0)	77.0 (64.0–95.0)	<0.001
Duration, s	316.0 (240.0–380.0)	311.0 (267.0–381.0)	0.994

Data are presented as median (minimum–maximum). The Mann–Whitney U test was used for between-group comparison. p<0.05 was considered statistically significant. EtO_2: End-tidal oxygen, FiO_2: Fraction of inspired oxygen, s: Seconds

In both groups, post-preoxygenation SpO_2 values increased significantly compared with baseline values (p<0.001 for both groups). The initial SpO_2 value was 99.0 (96.0-100.0) in group E and 98.0 (96.0-100.0) in group H, with no significant difference between groups (p=0.937). Post-preoxygenation SpO_2 was 100.0 (99.0-100.0) in both groups, and no significant difference was observed between groups (p=0.556) (Table 3).

Table 3. Between-group and within-group comparison of SpO_2 values

	Group E (n=25)	Group H (n=25)	p
Initial SpO_2, %	99.0 (96.0–100.0)	98.0 (96.0–100.0)	0.937
Final SpO_2, %	100.0 (99.0–100.0)	100.0 (99.0–100.0)	0.556
Within-group p	<0.001	<0.001	

Data are presented as median (minimum–maximum). The Mann–Whitney U test was used for between-group comparisons, and the Wilcoxon signed-rank test was used for within-group comparison of initial and final measurements. p<0.05 was considered statistically significant. SpO_2: Peripheral oxygen saturation, FiO_2: Fraction of inspired oxygen

At baseline assessment, the total MLUS score was 0 in 22 patients (88%) in group E and in 22 patients (88%) in group H, and the distribution of patients with a total MLUS score =0 and >0 was similar between groups (p=0.999). After preoxygenation, the number of patients with a total MLUS score >0 was 19 (76%) in group E and 23 (92%) in group H. Although this proportion was higher in group H, the difference between groups was not statistically significant (p=0.247) (Table 4).

Table 4. Between-group comparison of MLUS scores classified as 0 and greater than 0

	Group E (n=25)	Group H (n=25)	p
Baseline total MLUS score =0, n (%)	22 (88.0)	22 (88.0)	0.999
Baseline total MLUS score >0, n (%)	3 (12.0)	3 (12.0)	
Post-preoxygenation total MLUS score =0, n (%)	6 (24.0)	2 (8.0)	0.247
Post-preoxygenation total MLUS score >0, n (%)	19 (76.0)	23 (92.0)	

Data are presented as n (%). At each assessment time point, the total MLUS score was classified into two categories: MLUS score =0 and MLUS score >0. Between-group comparisons were performed using Fisher's exact test based on 2×2 contingency tables constructed for each assessment time point. Therefore, p-values do not refer to a single row or a single category, but to the overall distribution of the two categories at the corresponding assessment time point. The baseline p-value compares the distribution of patients with a total MLUS score =0 and >0 between group E and group H; the post-preoxygenation p-value compares the distribution of patients with a total MLUS score =0 and >0 between group E and group H. p<0.05 was considered statistically significant. MLUS: Modified lung ultrasound score

Baseline total MLUS scores were 0.0 (0.0-2.0) in group E and 0.0 (0.0-3.0) in group H, with no significant difference between groups (p=0.986). Post-preoxygenation total MLUS scores increased significantly from baseline in both groups (p<0.001 for both groups). The post-preoxygenation total MLUS score was 3.0 (0.0-6.0) in group E and 5.0 (0.0-11.0) in group H and was significantly higher in Group H (p=0.002) (Table 5).

Although the proportion of patients with a post-preoxygenation total MLUS score >0 was higher in group H,

Table 5. Within-group and between-group comparison of baseline and post-preoxygenation total MLUS scores

	Group E (n=25)	Group H (n=25)	Between-group p
Baseline total MLUS score	0.0 (0.0–2.0)	0.0 (0.0–3.0)	0.986
Post-preoxygenation total MLUS score	3.0 (0.0–6.0)	5.0 (0.0–11.0)	0.002
Within-group p	<0.001	<0.001	

MLUS scores are presented as median (minimum–maximum). Between-group p-values refer to the comparison of total MLUS scores between group E and group H at the corresponding assessment time point and were calculated using the Mann–Whitney U test. Within-group p-values refer to the paired comparison of baseline and post-preoxygenation total MLUS scores within the same group and were calculated using the Wilcoxon signed-rank test. A higher MLUS score indicates more pronounced loss of lung aeration. p<0.05 was considered statistically significant. MLUS: Modified lung ultrasound score

this difference was not statistically significant. However, the significantly higher total MLUS score in group H indicates that preoxygenation with 100% FiO_2 was associated with higher total MLUS scores.

When baseline MLUS scores were compared across the 12 defined thoracic regions, no statistically significant differences were found between group E and group H in any region (p>0.05 for all comparisons). In the exploratory post-preoxygenation analyses, nominal between-group differences in MLUS score distributions were observed in regions 5, 6, 7, 8, 9, 10, and 12 (all p<0.05; Table 6). Although these findings suggest regional differences in sonographic lung aeration loss between the groups, no adjustment for multiple comparisons was performed; therefore, the regional results should be interpreted cautiously.

Baseline MLUS scores in the anterior, lateral, and posterior regions were similar between group E and group H (p>0.05 for all comparisons). Following preoxygenation, the median MLUS score in the lateral region was higher in group H than in group E (2.00 vs. 0.00; nominal p=0.001), whereas the between-group comparisons in the anterior and posterior regions yielded p-values of 0.394 and 0.059, respectively (Table 7). Within-group comparisons yielded nominal p-values below 0.05 for the lateral and posterior regions in group E and for all three regions in group H. As no adjustment for multiple comparisons was performed, these regional findings are exploratory and should be interpreted cautiously.

DISCUSSION

The main finding of this study was that three minutes of preoxygenation during spontaneous breathing increased lung aeration loss in both the 80% and 100% FiO_2 groups, and that the post-preoxygenation total MLUS score was higher in the 100% FiO_2 group. In contrast, the difference between groups in the proportion of patients with an MLUS score greater than zero was not statistically significant. Accordingly, the between-group difference in total MLUS score should be interpreted as a difference in sonographic lung aeration loss rather than evidence of clinically significant atelectasis or improved postoperative pulmonary outcomes, which were not assessed in this study.

Table 6. Between-group comparison of baseline and post-preoxygenation MLUS scores according to the assessed region

	Baseline MLUS			Post-preoxygenation MLUS		
	Group E (n=25)	Group H (n=25)	p	Group E (n=25)	Group H (n=25)	p
	Median (min–max)	Median (min–max)		Median (min–max)	Median (min–max)	
1	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.999	0.00 (0.00–0.00)	0.00 (0.00–1.00)	0.153
2	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.999	0.00 (0.00–1.00)	0.00 (0.00–1.00)	0.999
3	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.999	0.00 (0.00–0.00)	0.00 (0.00–1.00)	0.317
4	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.999	0.00 (0.00–1.00)	0.00 (0.00–1.00)	0.641
5	0.00 (0.00–1.00)	0.00 (0.00–0.00)	0.317	0.00 (0.00–2.00)	0.00 (0.00–1.00)	0.019*
6	0.00 (0.00–0.00)	0.00 (0.00–1.00)	0.153	0.00 (0.00–1.00)	1.00 (0.00–2.00)	0.004*
7	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.999	0.00 (0.00–1.00)	0.00 (0.00–1.00)	0.018*
8	0.00 (0.00–0.00)	0.00 (0.00–1.00)	0.317	0.00 (0.00–1.00)	1.00 (0.00–1.00)	0.043*
9	0.00 (0.00–1.00)	0.00 (0.00–0.00)	0.317	0.00 (0.00–2.00)	1.00 (0.00–2.00)	0.016*
10	0.00 (0.00–1.00)	0.00 (0.00–1.00)	0.999	1.00 (0.00–2.00)	1.00 (0.00–2.00)	0.049*
11	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.999	0.00 (0.00–1.00)	0.00 (0.00–1.00)	0.139
12	0.00 (0.00–1.00)	0.00 (0.00–1.00)	0.999	1.00 (0.00–1.00)	1.00 (0.00–2.00)	0.013*

Data are presented as median (minimum–maximum). Between-group comparisons were performed using the Mann–Whitney U test for each assessed region. p-values indicate the comparison of score distributions between group E and group H in the corresponding region. Regional comparisons were evaluated descriptively. * indicates a nominal p-value <0.05 (uncorrected for multiple comparisons). No adjustment for multiple comparisons was performed. Therefore, regional analyses should be interpreted as exploratory, and the reported p-values should be interpreted cautiously. FiO_2: fraction of inspired oxygen; MLUS: Modified lung ultrasound score, Min: Minimum, Max: Maximum

Table 7. Within-group and between-group comparison of baseline and post-preoxygenation MLUS scores according to predefined regions

	Group E (n=25)			Group H (n=25)			Between p	
	Baseline	Post	Within p	Baseline	Post	Within p	Baseline	Post
Anterior	0.00 (0.00–0.00)	0.00 (0.00–1.00)	0.083	0.00 (0.00–0.00)	0.00 (0.00–2.00)	0.038*	0.999	0.394
Lateral	0.00 (0.00–1.00)	0.00 (0.00–3.00)	0.007*	0.00 (0.00–2.00)	2.00 (0.00–5.00)	<0.001*	0.540	0.001*
Posterior	0.00 (0.00–2.00)	2.00 (0.00–4.00)	<0.001*	0.00 (0.00–1.00)	3.00 (0.00–5.00)	<0.001*	0.967	0.059

MLUS scores are presented as median (minimum–maximum). Within p-values refer to within-group comparisons between baseline and post-preoxygenation MLUS scores and were calculated using the Wilcoxon signed-rank test. Between p-values refer to between-group comparisons of score distributions between group E and group H at the corresponding assessment time point and were calculated using the Mann–Whitney U test. * indicates a nominal p-value <0.05 (uncorrected for multiple comparisons). No adjustment for multiple comparisons was performed. Therefore, regional analyses should be interpreted as exploratory, and the reported p-values should be interpreted cautiously. MLUS: Modified lung ultrasound score

Lung ultrasonography is a rapid, radiation-free method that allows bedside assessment of perioperative atelectasis. In a pediatric study comparing lung ultrasonography with magnetic resonance imaging, lung ultrasonography showed 88% sensitivity and 89% specificity for anesthesia-induced atelectasis.[9] Similarly, high diagnostic performance has been reported in an adult study comparing lung ultrasonography with computed tomography.[10] The MLUS system used in the present study includes small subpleural consolidations and is therefore suitable for monitoring limited aeration changes that occur after a short intervention such as preoxygenation.[6] However, the relationship between score changes and clinical outcomes was not evaluated in this study.

High oxygen concentrations have previously been shown to increase perioperative atelectasis. Edmark et al.[11] compared preoxygenation with 60%, 80%, and 100% oxygen and found more atelectasis in the 100% oxygen group. In a randomized study of infants, preservation of spontaneous breathing was associated with less atelectasis than manual positive-pressure ventilation.[8] Clinical studies examining different FiO_2 levels have reported that a higher FiO_2 may be associated with atelectasis or sonographic aeration loss, while the clinical effects of perioperative high FiO_2 have also been evaluated in systematic reviews.[12-14] Our findings are consistent with these studies in that MLUS scores were higher after preoxygenation with 100% FiO_2.

A distinctive feature of our study is that all ultrasonography measurements were completed before premedication, anesthesia induction, neuromuscular blockade, intubation, and mechanical ventilation. Therefore, the observed changes are related to the preoxygenation period independently of the effects of surgery, positioning, controlled ventilation, or anesthetic drugs. Nevertheless, the increase in MLUS in both groups suggests that preservation of spontaneous breathing does not completely prevent early aeration loss associated with high oxygen concentrations. The lower MLUS values observed in our study compared with those reported during general anesthesia, surgery, or the postoperative period may also be explained by this early assessment time point.[6,15]

When the regional distribution of sonographic lung aeration loss was evaluated, exploratory within-group analyses yielded nominal p-values below 0.05 for the lateral and posterior regions in the 80% FiO_2 group and for the anterior, lateral, and posterior regions in the 100% FiO_2 group. In the post-preoxygenation between-group comparisons, a nominal difference was observed in the lateral region ($p=0.001$), but not in the anterior or posterior regions ($p=0.394$ and $p=0.059$, respectively). Previous computed tomography and ultrasonography studies have shown that anesthesia-related atelectasis is concentrated particularly in dependent posterior lung regions.[8,11,15,16] However, the within-group findings do not establish a broader anatomical distribution of lung aeration loss in the 100% FiO_2 group. As no adjustment for multiple comparisons was performed, these regional findings should be interpreted cautiously.

At the end of the three-minute preoxygenation period, EtO_2 was higher in the 100% FiO_2 group; however, median EtO_2 values in both groups remained below the 90% target commonly used as an indicator of adequate denitrogenation.[17] Previous studies have also reported that some patients do not reach target EtO_2 levels with standard preoxygenation methods.[18] Although face-mask fit was confirmed by capnography and visual assessment of mask leak in our study, the fixed three-minute duration, individual respiratory characteristics, and anatomical differences may have affected achievement of the target value. The median EtO_2 values below 90% suggest that complete denitrogenation may not have been achieved in either group under the study protocol. Although 80% FiO_2 was associated with lower post-preoxygenation MLUS scores, our data do not establish whether this approach provides an oxygen reserve or safe apnea time comparable to that achieved with 100% FiO_2. This uncertainty is particularly relevant to patients with anticipated difficult airways, in whom the potential benefit of lower sonographic aeration loss must be weighed against the need to establish an adequate oxygen reserve before anesthesia induction.

Limitations

This study has several limitations. The sample size was limited, and patients with obesity, smoking, known lung disease, or other pulmonary risk factors were excluded; therefore, the findings cannot be generalized to high-risk groups. Ultrasonography was performed only before and immediately after preoxygenation, and changes during general anesthesia and the postoperative period, as well as pulmonary complications, were not evaluated. Safe apnea time and peri-induction hypoxemia were not assessed; therefore, the lower MLUS scores observed with 80% FiO_2 cannot establish an oxygen reserve or clinical safety comparable to that achieved with 100% FiO_2. MLUS assessment was performed using a single imaging method, and a reference method such as computed tomography was not used. In addition, lung ultrasonography is operator-dependent, and interobserver agreement was not assessed in this study. Regional MLUS analyses were exploratory, and no adjustment for multiple comparisons was performed; therefore, these findings should be interpreted cautiously. The results should be confirmed in studies with larger sample sizes, different risk groups, and postoperative clinical outcomes.

CONCLUSION

Three minutes of preoxygenation during spontaneous breathing was associated with an increase in total MLUS score with both 80% and 100% FiO_2. Although the 100% FiO_2 group had higher EtO_2 and higher post-preoxygenation total MLUS scores than the 80% FiO_2 group, the clinical implications of these sonographic differences remain uncertain. Larger studies evaluating the effects of lower FiO_2 during preoxygenation on oxygen reserve, sonographic aeration loss, and postoperative clinical outcomes in low-risk elective surgical patients are needed.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was conducted with the approval of the Clinical Researches Ethics Committee No. 1 of Ankara Etlik City Hospital (Date: 22.03.2023, Decision No: AESH-EK1-2023-001).

Informed Consent

Written informed consent was obtained from all individual participants prior to their inclusion in the study. Participants were fully informed about the study's aims, procedures, potential risks and benefits, and their rights-including the right to withdraw at any time without consequence. All participants voluntarily signed a written informed consent form.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

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Author Contributions

Concept: AM; Design: DÖ; Control: DÖ; Resources: AM; Materials: AM; Data Collection and/or Processing: AM; Analysis and/or Interpretation: DÖ; Literature Review: AM; Article Writing: AM; Critical Review: All Authors.

Editor Note

Derya Özkan is a member of the Editorial Board of this journal. She was not involved in the editor assignment, reviewer selection, peer review process, or editorial decision for this manuscript. The peer review process was managed independently by another editor.

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Medical device related pressure injuries as an issue of increasing awareness in intensive care units: a bibliometric analysis of global trends

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ABSTRACT

Aims: Medical device related pressure injuries (MDRPI) are a patient safety issue that is gaining increasing recognition and attention, particularly in intensive care units (ICUs). This study aims to identify research trends related to MDRPI and to map the scientific collaboration network.

Methods: A bibliometric analysis was conducted on September 21, 2026, using the Web of Science (WoS) Core Collection as the database. Publications classified as articles and review articles from the period 2010-2026 were included. Publication characteristics, authors, institutions, journals, research areas, and citations were analyzed. The VOSviewer analysis network was used to visualize keyword co-occurrence, co-authorship, and journal analyses.

Results: A total of 308 publications meeting the criteria were included in the study. The highest number of publications was recorded in 2021 (n=43, 13.96%). The publications received a total of 5488 citations, and the h index was 38. The USA leads in publication output with 67 publications (21.75%). Among WoS categories, nursing stood out with 51.62%; Amit Gefen was the most productive author with 17 publications, and the International Wound Journal ranked first among journals with 36 publications. Keyword analysis revealed seven thematic clusters, with pressure injury and medical device related pressure injury serving as the central themes.

Conclusion: MDRPI is a topic that has gained increased awareness, particularly following the COVID-19 pandemic. Studies focused on intensive care and prevention protocols will become the focal point for the development of algorithms. Multicenter, interdisciplinary studies will guide the establishment of standards for MDRPI prevention and management.

Keywords: Pressure ulcer, intensive care units, bibliometrics, patient safety, nursing

INTRODUCTION

Medical device related pressure injuries (MDRPI) have become an increasingly prominent issue in intensive care units (ICUs) in recent years, posing a threat to patient care and safety.[1] ICUs are settings where patients with various life threatening critical illnesses particularly respiratory failure and hemodynamic instability are monitored and treated. While advancements in medical technology, the development of new medical devices, and the enhancement of intensive care capabilities and monitoring standards are crucial for patient management, they also give rise to certain medical issues and complications. Although medical devices such as endotracheal tubes, central venous catheters, non invasive ventilation masks, arterial monitoring lines, nasogastric tubes, urinary catheters, orthoses, and compression stockings are indispensable components of intensive care, their extensive use has increased the incidence of device related pressure injuries.[2-4]

Pressure injuries generally refer to tissue damage resulting from prolonged pressure on the skin and subcutaneous tissues, typically over bony prominences. While these injuries usually arise from immobility and external pressure, MDRPI occurs as a result of direct contact between the mucosa or skin and the shape and rigidity of a device, leading to localized edema and perfusion impairment.[5,6] ICU patients are at risk for MDRPI development due to factors such as

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sedation or altered states of consciousness and alertness, immunosuppression, malnutrition, the need for vasopressors, tissue and extremity edema, and hypoperfusion.[7]

Beyond merely being a source of pain and an aesthetic concern for patients, MDRPI presents clinicians with risks such as increased infection rates, a greater need for mechanical ventilation and vasopressors, prolonged ICU and hospital stays, and elevated morbidity and mortality rates.[5,8] Consequently, the preventability of MDRPI has become a significant indicator regarding both patient safety and the delivery of optimal, high quality healthcare services.

The recent increase in academic publications concerning MDRPI particularly following the COVID-19 pandemic highlights the importance of nursing care and wound management.[9] Growing awareness and research activity create a need to investigate global trends in MDRPI, document the evolution of patient management innovations, foster international collaborations, and identify the researchers and research efforts focused on this subject.

While MDRPI are of particular concern in ICUs due to factors such as critical illness, immobilization, the widespread use of invasive medical devices, and the administration of sedation they are not limited to patients in intensive care. Patients in other settings, including acute care units, dermatology wards, physical therapy and rehabilitation departments, and wound care units, may also be at risk of developing MDRPI if medical devices are used in their care. Consequently, a thorough examination of the scientific literature on MDRPI requires the review and analysis of research conducted across various clinical settings, rather than focusing solely on publications centered on intensive care.

Bibliometric analysis is a research approach that aims to evaluate the scientific output, development trends, and intellectual structure of a specific research field through the quantitative examination of bibliographic data from scientific publications. It enables the study of performance metrics such as publication counts and citation indicators as well as patterns of collaboration among authors, institutions, and countries, the relationships between keywords, and the distribution of research themes. Consequently, it is used to assess interdisciplinary connections and identify focal topics for future research.[10,11]

Accordingly, the aim of this study is to present a detailed bibliometric analysis of MDRPI publications indexed in the Web of Science (WoS) Core Collection; to identify the institutions, authors, and research areas concentrating on this topic; to visualize scientific network maps; and to provide guidance for future research themes.

METHODS

Ethics

This bibliometric analysis is based solely on publicly available data from the WoS Core Collection. The study did not involve patient data, human participants, or animal experiments; therefore, ethics committee approval and informed consent were not required. The study was conducted in accordance with ethical rules and principles.

Data Source Selection and Search Method

The WoS Core Collection database was utilized for this bibliometric analysis. It was selected as the sole, objective database due to its provision of comprehensive author and citation data, detailed publication indexing, and adherence to high scientific standards regarding publication quality. This approach prevented the duplication of records from multiple databases and avoided complications arising from inconsistent data formats. Furthermore, it ensured standardization in citation mapping; this not only provided a citation architecture compatible with VOSviewer but also facilitated appropriate mapping for the bibliometric analysis.

An advanced search mode and the "Topic" (TS) field were utilized for the search. Searches were conducted across titles, abstracts, keyword plus, and author keywords. To verify the relevance of the records retrieved from the search to the MDRPI, the titles and abstracts of the publications were evaluated; in cases where relevance was unclear, the full texts were examined. Publications directly related to the MDRPI were included in the study. The logical operator "OR" was employed to ensure comprehensive coverage of the literature and to avoid missing any relevant publications. The search query was structured as follows: TS=("medical device related pressure injuries" OR "medical device related pressure ulcers" OR "medical device related pressure injury" OR "medical device related pressure ulcer" OR "device related pressure ulcer" OR "device related pressure ulcers" OR "device related pressure injuries" OR "device related pressure injury" OR "MDRPI" OR "MDRPU").

The literature search was conducted on September 21, 2026. No language restrictions were applied; publications in all languages were included in the study. Studies classified as articles and review articles were included, whereas other types of publications and retracted articles were excluded. Publications indexed in the Science Citation Index Expanded (SCIE) and Emerging Sources Citation Index (ESCI) within the WoS database were included. No time restrictions were applied, with the aim of including publications from all time periods.

Data Analysis and Analysis Tools

The scanned publications were examined under the subheadings of publication years, document types, researcher profiles, authors, WoS categories, WoS indices, affiliations, departmental affiliations, publication titles, languages, countries, publishers, author keywords, and research areas. Additionally, citation counts for the publications were analyzed by year. This analysis determined the total number of publications and total citations, as well as the average number of citations per publication and the h index. The h index was defined as the highest number h such that there are h publications, each having received at least h citations.

Visualization, Mapping, and Network Analysis

VOSviewer (version 1.6.20, Leiden University, Netherlands) was used to visualize and map the data obtained in the study. In this context, analyses regarding author co-authorship, co-occurrence of words or citations, author keyword linkages,

country and institution density maps and connections were visualized.[12] The full counting method was applied to all networks, while link strength was normalized using the association strength method. For the author level co-authorship analysis, a threshold of at least three publications per author was applied; for the keyword co-occurrence analysis, a minimum of five occurrences was required for each author keyword. Data were extracted from the WoS database in the full record and cited references format as tab delimited files and subsequently processed using Python (v3.12) and Microsoft Excel to generate descriptive statistics and visual charts.

RESULTS

A total of 308 publications meeting the criteria were analyzed in this study. Although there were no time restrictions, the earliest publication identified was from 2010; consequently, the study analyzed publications from the period of 2010-2026. While there was only one publication in 2010, the highest number of publications (43; 13.96%) appeared in 2021. Of the publications, 263 (85.39%) were research articles, and 45 (14.61%) were review articles. Regarding language, 307 (99.675%) publications were in English, while only one (0.325%) was in Korean. Of all publications, 272 (88.31%) were indexed in the Science Citation Index Expanded (SCI-E), and 36 (11.69%) were indexed in the Emerging Sources Citation Index (ESCI). An analysis of the countries of origin revealed the top five to be the United States of America (USA), the People's Republic of China, Turkiye, Australia, and Israel, in that order. The USA accounted for the highest number of publications (67; 21.75%), followed by the People's Republic of China (62 publications) and Turkiye (41 publications). An examination of WoS categories showed that more than half of the publications (159; 51.62%) fell within the field of nursing. This was followed by dermatology (39.61%), surgery (22.72%), and critical care medicine (8.76%). The general distribution characteristics of the publications are presented in Table 1.

Table 1. General characteristics of the publications

Characteristics	n (%)
Total number of publications	308 (100)
Publication years	
2026*	39 (12.66)
2025	41 (13.31)
2024	38 (12.34)
2023	37 (12.01)
2022	28 (9.09)
2021	43 (13.96)
2020	27 (8.77)
2019	18 (5.84)
2018	11 (3.57)
2017	11 (3.57)
2016	4 (1.30)
2015	4 (1.30)
2014	3 (0.97)
2013	1 (0.32)
2012	2 (0.65)
2010	1 (0.32)
Document types	
Article	263 (85.39)
Review article	45 (14.61)
Web of Science Index	
SCI-E	272 (88.31)
ESCI	36 (11.69)
Languages	
English	307 (99.675)
Korean	1 (0.325)
Countries (top 5)	
USA	67 (21.75)
People's Republic of China	62 (20.13)
Turkiye	41 (13.31)
Australia	26 (8.44)
Israel	21 (6.81)
Web of science categories (top 5)	
Nursing	159 (51.62)
Dermatology	122 (39.61)
Surgery	70 (22.72)
Critical care medicine	27 (8.76)
Medicine general internal	18 (5.84)

*Data for the year 2026 covers publications indexed in the WoS Core Collection database up to September 21, 2026. Therefore, this should be taken into account when making comparisons with previous years. SCI-E: Science Citation Index Expanded, ESCI: Emerging Sources Citation Index, USA: United States of America

Annual Publication Distributions and Citation Relationship

A literature review revealed that while the first publication concerning MDRPI appeared in 2010, the annual number of publications did not exceed five until 2017. Double digit figures were reached in 2017 with 11 publications, and the upward trend continued, and peaked in 2021 with 43 publications. This was followed by 41 publications in 2025, while 2026 ranks third with 39 publications, despite the year not yet having concluded (Table 1). The number of publications for 2026 reflects records indexed up to September 21, 2026 the date the database search was conducted and therefore represents data for an incomplete calendar year.

A total of 2187 publications cited these 308 papers; excluding self citations, this figure stands at 1909. The total number of citations received by these papers is 5488, or 3282 when self citations are excluded. The average number of citations per publication is 17.82, and the h index is 38. Similar to publication counts, citation numbers have also risen, particularly since 2018; the highest citation count 953 was recorded for 2026 on the day of the search, even though the year is still ongoing. This was followed by 2024 with 883 citations and 2025 with 852 citations. A significant increase in both publication and citation numbers is evident, particularly over the last five years; the relationship between citation counts and publication numbers over the years is illustrated in Figure 1.

Most Cited Publications

The most highly cited publication is the article titled "Medical device related pressure ulcers in hospitalized patients" published by Black et al.[6] in the International Wound Journal in 2010. This publication holds the distinction of being the first to meet the screening criteria for MDRPI while also

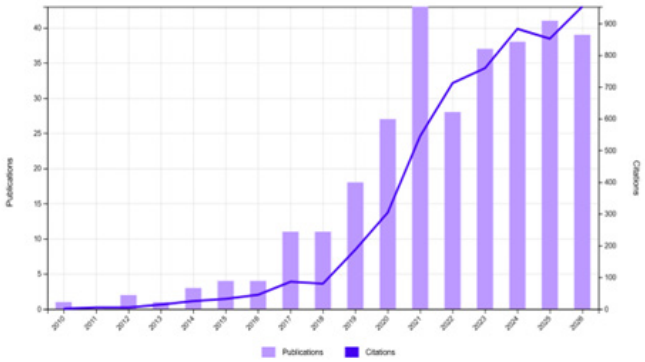

Figure 1. Relationship between publication and citation counts over the years. (Data for the year 2026 reflects records indexed up to September 21, 2026; the data for this year pertains to an incomplete calendar year)

being the most cited, with 271 citations. Ranking second is the study titled "Pressure Injury" published by Hajhosseini et al.[5] in the Annals of Surgery in 2020, with 204 citations. Following in the ranking is the study titled "Medical device-related pressure ulcers: A systematic review and meta-analysis" published by Jackson et al.[13] in the International Journal of Nursing Studies in 2019, with 180 citations. The top 10 most cited articles are presented in Table 2.

Guiding Publications and Authors

Among the most prolific authors, Amit Gefen[9] holds the undisputed top spot with 17 publications. Gefen[9] is followed by Fiona Coyer with 7 publications, while three authors Ayişe Karadağ, Ann-Marie Nie, and Münevver Sönmez rank consecutively with six publications each, securing significant positions in the MDRPI research literature. Consequently, reflecting Amit Gefen's background as a biomedical engineer, Tel Aviv University's Iby and Aladar Fleischman Faculty of Engineering emerged as the institution with the highest number of publications. This was followed by the Queensland University of Technology's Faculty of Health, associated with Fiona Coyer. Koç University School of Nursing ranks third among institutions, corresponding to the third place ranking of its faculty member, Ayişe Karadağ. These findings align with the country level analysis, in which Turkiye, Australia, and Israel appear among the top five nations. Furthermore, an analysis of the journals reveals that the International Wound Journal published the highest number of articles on MDRPI, with 36 publications (11.68% of the total). The Journal of Tissue Viability ranked second with 33 publications, followed by Advances in Skin & Wound Care in third place with 21 publications. Overall, the publication activities of these journals appear consistent with the characteristics and general nature of both the subject matter and the field of study; journals specializing in wound care, nursing, and critical care were notably preferred. Table 3 lists the top ten authors and the top ten journals by publication volume, while Figure 2 presents the VOSviewer co-authorship network map at the author level. The relationships and clusters among the journals are visualized in Figure 3. A bibliographic coupling analysis was conducted to evaluate the bibliometric relationships among journals. In this analysis, nodes represent journals, while the connections between them represent bibliometric relationships based on bibliographic coupling. The visualization of the network has enabled the assessment of the relationships between journals and the publication patterns within the research field.

Keyword Co-occurrence Analysis

Keyword co-occurrence mapping in VOSviewer (minimum: 5 occurrences) revealed seven main thematic clusters (Figure 4). The size of the circles indicates the frequency of the term in the literature, while the lines between the circles represent the intensity of co-occurrence within the same studies. The largest circle at the center of the network represents "pressure injury". Different colors represent groups of terms that are frequently associated with one another. The yellow cluster forms the core of the subject matter, comprising terms such as "pressure injury", "medical device related pressure injury", "intensive care", "nursing", "prevention", and "risk factor". It focuses primarily on pressure injuries and MDRPI in ICUs, as well as the practices and approaches of nurses and other healthcare professionals regarding this issue. While the purple cluster groups assessments concerning pediatric and neonatal patient populations, the red cluster reflects the intersection of MDRPI

Table 2. The top 10 most cited publications on medical device related pressure injuries

Rank	Authors (year)	Title	Journal	Citations
1	Black et al. (2010)[6]	Medical device related pressure ulcers in hospitalized patients	Int Wound J	271
2	Hajhosseini et al. (2020)[5]	Pressure Injury	Ann Surg	204
3	Jackson et al. (2019)[13]	Medical device-related pressure ulcers: a systematic review and meta-analysis	Int J Nurs Stud	180
4	Kayser et al. (2018)[14]	Prevalence and analysis of medical device-related pressure injuries: results from the international pressure ulcer prevalence survey	Adv Skin Wound Care	143
5	Gefen and Ousey. (2020)[9]	Update to device-related pressure ulcers: SECURE prevention. COVID-19, face masks and skin damage	J Wound Care	113
6	Coyer et al. (2014)[3]	A prospective window into medical device-related pressure ulcers in intensive care	Int Wound J	113
7	Barakat-Johnson et al. (2019)[15]	The incidence and prevalence of medical device-related pressure ulcers in intensive care: a systematic review	J Wound Care	108
8	Alshahrani et al. (2021)[16]	Nursing interventions for pressure injury prevention among critically ill patients: a systematic review	J Clin Nurs	102
9	Jiang et al. (2020)[17]	The prevalence, characteristics, and prevention status of skin injury caused by personal protective equipment among medical staff in fighting COVID-19: a multicenter, cross-sectional study	Adv Wound Care (New Rochelle)	98
10	Barakat-Johnson et al. (2017)[18]	Medical device-related pressure injuries: an exploratory descriptive study in an acute tertiary hospital in Australia	J Tissue Viability	97

SECURE: Skin/tissue, education, champion/collaborate, understanding, report, evaluate

Table 3. Guiding journals and authors

Rank	Authors (top 10)	Publications n (%)	Rank	Journal (top 10)	Publications n (%)
1	Gefen, Amit	17 (5.51)	1	International Wound Journal	36 (11.68)
2	Coyer, Fiona	7 (2.27)	2	Journal of Tissue Viability	33 (10.71)
3	Karadağ, Ayişe	6 (1.94)	3	Advances in Skin Wound Care	21 (6.81)
4	Nie, Ann-Marie	6 (1.94)	4	Journal of Wound Ostomy and Continence Nursing	18 (5.84)
5	Sönmez, Münevver	6 (1.94)	5	Journal of Clinical Nursing	15 (4.87)
6	Erbay Dallı, Öznur	5 (1.62)	6	Journal of Wound Care	11 (3.57)
7	Worsley, Peter	5 (1.62)	7	Intensive and Critical Care Nursing	10 (3.24)
8	Bahar, Arzu	4 (1.29)	8	Wound Management Prevention	10 (3.24)
9	Bai, Yuxuan	4 (1.29)	9	Nursing in Critical Care	6 (1.94)
10	Barakat-Johnson, Michelle	4 (1.29)	10	Frontiers in Medicine	5 (1.62)

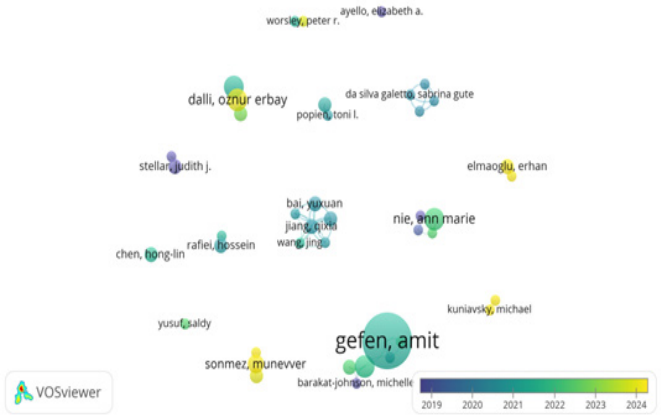

Figure 2. VOSviewer co-authorship network map at the author level. Each circle represents a single author, and the size of the circle corresponds to the number of publications. The connecting lines between the circles reflect the strength of collaboration. The map indicates that the authors work in small, isolated groups rather than within a large, unified network
VOSviewer: Visualization of similarities viewer

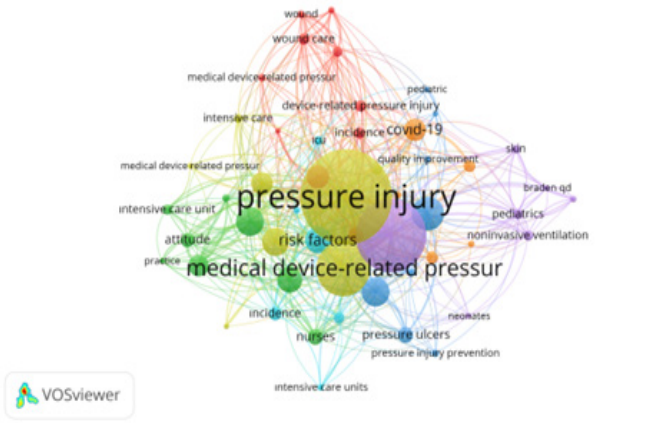

Figure 4. VOSviewer keyword co-occurrence network map. While the size of the circles reflects keyword frequency, the connecting lines indicate the strength of the co-occurrence between the words
VOSviewer: Visualization of similarities viewer



Figure 3. VOSviewer network map showing bibliographic coupling relationships between journals. While each circle represents a journal, the size of the circle and the text indicates the respective journal's weight within the dataset
VOSviewer: Visualization of similarities viewer

and wound care management. The orange cluster highlights studies examining the relationship between MDRPI and the increased use of medical devices during the COVID-19 pandemic. Furthermore, while the green cluster highlights the attitudes and practices of healthcare professionals in ICUs regarding the use of protective equipment and devices, the blue cluster focuses on sensitive patient groups such as pediatric patients and encompasses prevention strategies. The turquoise cluster, meanwhile, prioritizes incidence reporting specifically within the context of intensive care.

DISCUSSION

This study presents a comprehensive bibliometric analysis based on a detailed examination of the literature regarding MDRPI within the WoS Core Collection. By evaluating 308 publications indexed between 2010 and 2026 that met the study criteria, the research outlines the evolution and current distribution of MDRPI related literature while identifying indicators of future trends. Through a systematic and holistic analysis of influential authors, collaboration networks, institutions, and key research themes, the study highlights the enrichment of the literature and emphasizes the importance of raising awareness across the disciplines of dermatology, intensive care, nursing, and wound care.

The study reveals that while the first publication in the field of MDRPI appeared in 2010 with fewer than five publications released up to 2017 there was a marked upward trend, peaking at 43 publications in 2021.[6] The increase in publications during this period is noteworthy because it coincides temporally with the COVID-19 pandemic. While the increase in publications seems to align with the period when the pandemic affected intensive care monitoring and significantly altered the use of medical devices, a direct causal relationship

cannot be established. The pandemic may have made the clinical significance of MDRPI and other pressure injuries more visible, highlighting the need for careful monitoring and preventive measures in critical care settings.[19] The global deployment of invasive and non invasive mechanical ventilation systems, the widespread adoption of high flow oxygen therapy, and the prolonged use of oxygen masks and endotracheal tubes during the pandemic had adverse effects on skin integrity. In addition to the prolonged use of medical devices, prone positioning and immobility posed significant challenges regarding both pressure injuries and MDRPI.[20,21] In this context, the annual publication trend observed in the research confirms that MDRPI gained greater visibility in the medical literature during and after the COVID-19 pandemic. Furthermore, publications related to COVID-19 by Gefen and Ousey[9] and Jiang et al.[17] hold a significant place in the MDRPI literature due to their high citation counts and align with the findings of this study.

Supporting this perspective from a different angle, two separate studies published in 2019 one by Jackson et al.[13] and another by Barakat-Johnson et al.[15] conducted prior to the COVID-19 pandemic noted that MDRPI incidence and prevalence rates vary significantly and exhibit high heterogeneity. In their review, which focused specifically on intensive care patients, Barakat-Johnson et al.[15] highlighted that although MDRPI is a clinically significant issue, a lack of standardization persists regarding staging, definition, data collection, and reporting methods. Both studies emphasized the need for future research to better elucidate the subject and underscored the necessity of standardized data collection and processing. In this context, this bibliometric analysis can contribute to addressing this gap in the literature by mapping existing publications, identifying interrelationships, and highlighting key areas of interest and emerging trends. Consequently, the increase in publications observed over the years can be interpreted not merely as a rise in the disease burden, but rather as a reflection of improved problem definition, heightened clinician awareness, and the issue's growing prominence within the literature.

While this analysis reveals a significant increase in the number of publications particularly after 2018 substantial growth in citation counts has also been observed. A total of 5488 citations were recorded for the 308 publications identified during the search period, and the h index was determined to be 38. These results indicate that the subject has become a focal point of research interest, evidenced by the rise in both publication and citation numbers. The study by Black et al.[6] played a pioneering role; not only was it the first study identified in the search, but with 271 citations, it also underscored the fact that MDRPI is a distinct entity separate from conventional pressure injuries. Although it may appear to have a citation advantage over more recent publications, it should be recognized as a cornerstone of the MDRPI literature and a valuable resource when outlining the key aspects of the topic. Additionally, studies conducted by Jackson et al.[13] and Kayser et al.[14] stand out due to their high citation rates; both studies are significant in the context of international prevalence research. It has been highlighted that priorities for MDRPI research include epidemiological characterization, prevalence studies, and the synthesis of medical literature. In addition to the objective of determining prevalence, Coyer et al.[3] evaluated MDRPI in intensive care patients regarding its prevalence, anatomical location, etiology, and severity. Similarly, in a highly cited review focused on the intensive care setting, Barakat-Johnson et al.[15] noted that this issue is significant and warrants close attention within that environment. In their study, Black et al.[6] identified patients with edema or at risk of developing it, those with impalpable arterial pulses, and immobile patients unable to alert nurses to pain or compression caused by a device as being at risk for MDRPI, while emphasizing the importance of quality nursing care. Therefore, concepts such as nursing, intensive care, and wound care are not merely keywords but fundamental concepts regarding MDRPI.

Regarding the geographical distribution of publications, the United States, the People's Republic of China, Turkiye, Australia, and Israel constitute the top five countries. Research output is concentrated in specific nations, indicating that MDRPI research clusters around particular groups and academic centers. The United States naturally leads in these publications, supported by its robust and consistent infrastructure in nursing, patient safety, and wound care. The People's Republic of China remains a leading nation in publication output, driven by its scientific research capacity in recent years. Turkiye's position in third place is noteworthy, reflecting significant research activity in intensive care, wound management, and nursing services. It is evident that awareness of MDRPI is growing particularly in Turkiye and other nations alongside increasing efforts to establish and improve clinical practice standards. An analysis of the authors reveals that researchers such as Ayişe Karadağ and Münevver Sönmez are among the most prolific, with a specific focus on nursing and the MDRPI field. Similarly, Amit Gefen leads the list with 17 publications, having made the most significant contribution to the literature by synthesizing his work in biomedical engineering with the field of MDRPI. These findings demonstrate that MDRPI research lends itself to a multidisciplinary approach, with the fields of nursing and biomedical engineering playing a major role in raising awareness. Consequently, the works of these authors serve as valuable guides for future researchers.

However, it is also necessary to note the following: although the authors have produced numerous significant publications, an examination of VOSviewer co-authorship analyses reveals that they tend to work within small, isolated groups rather than engaging in collaborative, joint, and organized publishing efforts. This situation may well motivate future researchers in this field and pave the way for multicenter, international, and large scale collaborative studies.

When the WoS categories of the studies included in the bibliometric analysis were examined, more than half of the publications fell within the nursing field, followed by dermatology at 39.61%. While this was an expected finding, it illustrates that research on MDRPI primarily focuses on skin integrity, wound assessment, care processes, and nursing monitoring. Given that MDRPI is associated not only with device related factors but also with issues such as vasopressor use, the need for mechanical ventilation, edema, immobility, and prone positioning in intensive care patients, the field of

critical care medicine currently representing 8.76% of the studies may attract greater research interest in the future.[22] The journal analysis aligns with these findings; while a multidisciplinary structure is maintained, journals focused on nursing, wound care and management, tissue and skin integrity, and intensive care predominate. Given the multidisciplinary nature of the subject, while this study considers ICUs as settings of high clinical significance for the prevention and management of MDRPI, the bibliometric analysis is not limited solely to ICU patients. The analysis also encompasses publications related to MDRPI conducted in various other clinical settings, provided they meet the established search strategy and inclusion criteria. Consequently, the findings reflect the overall scientific structure of the MDRPI literature rather than representing publication trends specific exclusively to intensive care. An examination of the inter journal relationship network reveals strong citation and content linkages between journals focused on wound management and care and those dedicated to critical care nursing. This research focus can serve as a guide and provide direction for new researchers in the field.

In the keyword co-occurrence analysis, the term "pressure injury" sits at the center of the network. Terms such as "medical device related pressure injury", "intensive care", "nursing", "prevention", and "risk factor" are clustered together, indicating that the primary research focus lies in the development of risk assessment and prevention algorithms for intensive care patients.[23] The VOSviewer analysis reflects a vision centered on taking necessary preventive measures before a wound develops, rather than treating it after it has occurred. Given the existence of distinct thematic clusters, future research may take shape around various topics; while intensive care and risk factors will remain high priority and relevant, studies may also concentrate or specialize in areas such as vulnerable patient groups, device management and wound care, and the COVID-19 pandemic.

In light of all these analyses, MDRPI is a preventable patient safety issue. Both device related and patient related factors can play a role in its development. Factors such as hypoperfusion, the need for vasopressor agents, and edema can reduce tissue resilience, leading to varying degrees and locations of injury across different patients. Given that any medical device can potentially be the culprit, determining which patients and under what medical conditions are at higher risk for MDRPI will serve as a key starting point for future research. This is particularly relevant to intensive care practice. Each patient must be reevaluated daily regarding their general condition, level of consciousness, mobility, device dependency, and sedation status. Consequently, the importance of nursing care, knowledge, and patient management is undeniable. Training programs, informational initiatives, and strategic guidelines regarding nursing care in this area must be adopted and implemented.[24] Algorithms should be developed to prevent the occurrence of MDRPI. Practices such as individualized repositioning, frequent and early mobilization, moisture control, the use of thin dressings, and pressure relieving maneuvers must be adopted.[25,26]

MDRPI is a field of research in which the risks associated with medical devices used in various clinical settings as well as strategies for their prevention are gaining increasing importance. However, examining publication counts alone is insufficient to fully explain the structure of scientific output in this field, the collaborations among researchers, or the relationships between prominent themes. Bibliometric analysis and network visualization methods can contribute to a systematic examination of these relationships and provide an overview of the research landscape. Bibliometric analyses are used to reveal how scientific interest in specific diseases or clinical issues evolves over time, and to identify influential publications and research groups within the field.[27,28]

Although MDRPI has gained increasing visibility in the literature in recent years, it cannot be said to rest on a fully homogeneous foundation. Heterogeneous results may still arise due to factors such as a lack of clarity regarding incidence and prevalence rates, variations in patient populations and timing of assessments, and differences in device categories. As demonstrated by this bibliometric analysis, despite the rising number of publications over the years, a unified approach to data analysis remains elusive. Future prospective, multicenter, and comprehensive studies will provide greater clarity regarding the standardized definition, staging, and device classification of MDRPI, as well as its relationship with patient outcomes. ICUs could serve as the focal point for future research. Studies should adopt a multidisciplinary approach incorporating diverse stakeholders such as nurses, intensive care specialists, and biomedical engineers to pave the way for preventive and protective interventions. Furthermore, the early identification of high risk patients could be a key objective for the future. Accordingly, this bibliometric analysis aimed to chart a roadmap for future research by examining past studies on MDRPI and identifying areas of interest, trending topics, temporal changes, the boundaries of the research field, and key contributors shaping the literature.

Limitations

The study has certain limitations that should be noted. The bibliometric analysis was conducted using only the WoS Core Collection database; although a single database was selected to ensure data standardization and prevent duplicate entries, publications indexed in PubMed, Scopus, or other databases may have been excluded. Furthermore, the study included only articles and review articles, potentially limiting the representation of contributions from other publication types such as conference papers and book chapters. There were no language or date restrictions. The literature search was conducted as of September 2026; consequently, citation and publication counts by the end of 2026 may be higher, which could alter the ranking and priority of certain data. While bibliometric analyses examine various relationships and Networks primarily based on publication and citation counts they may not reflect the clinical quality or methodological differences of the studies.

CONCLUSION

Awareness and visibility regarding the subject of MDRPI have continued to increase in recent years. MDRPI represents a significant patient safety concern that reflects the quality of patient care. Although the field has historically evolved

around wound care, pressure injuries, and the fundamentals of nursing, future focus may shift toward areas such as intensive care, critical care, prevention protocols, and smart medical devices. In this context, intensive care based studies will not only address research gaps but also contribute to the standardization of definitions and reporting systems by fostering data homogenization. Collaborative, multicenter studies involving various institutions and countries rather than isolated, fragmented efforts will strengthen the global advancement of this field. Collaborative action among diverse disciplines including intensive care physicians, nurses, physiotherapists, and biomedical engineers will be crucial for the early recognition of MDRPI and the development of personalized risk assessments and prevention policies.

ETHICAL DECLARATIONS

Ethics Committee Approval

As this study is a bibliometric analysis based on data extracted from the Web of Science Core Collection, it did not involve human participants, patient data, or animal experiments; therefore, ethics committee approval was not required.

Informed Consent

This bibliometric study used only publicly available data and did not involve human subjects or personal information; therefore, informed consent was not required.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The author declares no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

The author is solely responsible for the conception, data collection, analysis, and writing of this manuscript.

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Integrated Pulmonary Index in pediatric sedation for bronchoscopy, a prospective cohort study

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ABSTRACT

Aims: To compare periprocedural Integrated Pulmonary Index (IPI) values in pediatric patients undergoing bronchoscopy under propofol- or ketamine-based sedation, and to evaluate associated physiological parameters, recovery time, and procedural satisfaction.

Methods: In this prospective cohort study, 60 children aged 1 month to 18 years undergoing elective diagnostic bronchoscopy were included. Patients received either propofol (group P) or ketamine (group K) at the discretion of the attending anesthetist. All patients received midazolam and remifentanil, and respiratory parameters were continuously monitored using an IPI monitor. End-tidal carbon dioxide ($ETCO_2$), respiratory rate (RR), peripheral oxygen saturation (SpO_2), pulse rate (PR), and IPI values were recorded at 3-minute intervals. Primary outcome was mean periprocedural IPI. Secondary outcomes included recovery time, airway interventions, bronchoscopist and anesthetist satisfactions.

Results: There was no statistically significant difference in mean IPI values between the groups (4.4±1.6 vs 4.5±1.1 in group P and group K, respectively; p=0.909). Group K had significantly lower RR and higher PR than group P (p=0.023 and p<0.001, respectively). Bag-mask ventilation was required more frequently in group K (p=0.029), and recovery time was significantly longer (p<0.001). Satisfaction scores did not differ significantly between groups. $ETCO_2$, RR, SpO_2, and PR differed significantly across low (1–3), medium (4–6), and high (7–10) IPI categories (all p<0.001).

Conclusion: Propofol and ketamine provided comparable periprocedural IPI values during pediatric diagnostic bronchoscopy despite differences in respiratory and cardiovascular profiles and recovery characteristics. IPI demonstrated consistent associations with standard physiological respiratory parameters and may provide a useful integrated measure for detecting changes in respiratory status during pediatric sedation.

Keywords: Child, ketamine, monitoring; physiologic, procedural sedation, propofol

INTRODUCTION

Respiratory depression and airway obstruction are the primary causes of morbidity and mortality during pediatric sedation.[1,2] While diagnostic bronchoscopy is essential for assessing airway pathologies, it is an invasive procedure that necessitates various sedo-analgesia methods to minimize anxiety and pain. Current clinical practice guidelines emphasize the continuous monitoring of a patient's hemodynamic and ventilatory status, as well as their state of consciousness, to facilitate the early recognition of adverse outcomes.[2]

Pulse oximetry remains the standard of care for detecting hypoxemia, yet it has significant limitations, including a delayed display of arterial deoxygenation and a lack of real-time information regarding ventilation. In the presence of supplemental oxygen, significant alveolar hypoventilation may go undetected by pulse oximetry alone.[3] In contrast, capnography has been found superior in detecting hypoventilation and airway obstruction, frequently identifying disordered respiration before the onset of measurable hypoxia. Guidelines now suggest that

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capnography should be used routinely, especially during deep sedation where verbal communication is interrupted.[4–6]

The Integrated Pulmonary Index (IPI) is a tool designed to simplify the assessment of respiratory status by utilizing a fuzzy logic mathematical model algorithm. It integrates four key physiological parameters—end-tidal carbon dioxide ($ETCO_2$), respiratory rate (RR), peripheral oxygen saturation (SpO_2), and pulse rate (PR)—into a single numerical value ranging from 1 to 10. An IPI score of 10 represents optimal status, while a score of 1–2 indicates the need for immediate emergency intervention (**Supplementary Table 1**). Studies have shown that IPI scores correlate well with clinical assessments, making the monitor a practical adjunct for clinicians in non-operating room settings.[1]

Supplementary Table 1. Patient status definition according to different IPI scores

IPI	Patient status
1	Requires immediate intervention
2	Requires immediate intervention
3	Requires intervention
4	Requires intervention
5	Requires attention and may require intervention
6	Requires attention and may require intervention
7	Close to normal range; requires attention
8	Within normal range
9	Within normal range
10	Normal

IPI: Integrated Pulmonary Index

Propofol and ketamine are frequently used agents for pediatric endoscopy and bronchoscopy. Propofol is favored for its rapid onset and short half-life, which provides quick recovery; however, it is associated with a risk of dose-dependent respiratory depression, apnea, and hemodynamic instability. Ketamine, a dissociative anesthetic, generally preserves airway muscle tone and protective reflexes, causing less respiratory and hemodynamic suppression, though it may result in increased oral secretions and a prolonged recovery period.[7]

Despite the widespread use of these agents, their individual effects on IPI values in the pediatric population remain understudied. This prospective cohort study aimed to investigate and compare the periprocedural IPI values in pediatric patients sedated with either propofol or ketamine during diagnostic bronchoscopy. The primary outcome measure was average periprocedural IPI values. The secondary outcome measures were recovery time, bronchoscopist and anesthetist satisfactions. We hypothesized that patients sedated with ketamine would maintain higher IPI values due to the drug's more favorable respiratory profile.

METHODS

This study received approval from the Marmara University Faculty of Medicine Clinical Researches Ethics Committee (Date: 07.05.2021, Decision No: 09.2021.497) and was registered at ClinicalTrials.gov (No: NCT05137587). Pediatric patients who underwent elective bronchoscopy under sedation at our institution between September 2022 and February 2023 were enrolled in the study. Written informed consent was obtained from the patients' parents or legal guardians prior to participation. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients older than 1 month and younger than 18 years of age with an American Society of Anesthesiologists Physical Status Classification (ASA) score of I–III were included in the study. Patients were excluded if participation was declined by their guardians, if they had an ASA physical status of IV or higher, if they were not suitable candidates for non-operating room anesthesia, or if they had a known allergy to any of the sedative drugs used. In addition, patients who developed any of the following conditions after enrollment were excluded from further analysis: anaphylactic reactions related to the administered drugs, respiratory failure requiring endotracheal intubation, hemodynamic instability, or major bronchoscopy-related complications.

Participants were allocated into two groups according to the sedative agent administered. In the first group (group P), sedation was achieved using propofol, whereas ketamine was used in the second group (group K). No randomization was performed and the choice of the sedative agent was left to the discretion of the primary anesthetist. Patients were unaware of the group allocation and were blinded to the study design. The anesthetist responsible for drug administration and data collection was the same for all procedures and was not blinded. However, the pediatric bronchoscopist performing the bronchoscopy procedure was blinded to group allocation.

Upon arrival in the procedure room, routine monitoring was initiated, including pulse oximetry (SpO_2), three-lead electrocardiography (ECG), and non-invasive blood pressure (NIBP) monitoring. After peripheral intravenous access was obtained, a balanced crystalloid solution was infused at a rate of 10 ml/kg/h. Sedation and anxiolysis were initiated with intravenous midazolam at a dose of 0.05 mg/kg. For respiratory monitoring, a specialized nasal cannula (Smart CapnoLine Plus; Oridion Medical, Needham, MA, USA) capable of measuring IPI was placed and connected to a monitor (Capnostream 20; Oridion Medical, Needham, MA, USA). Oxygen was administered at a rate of 2 L/min through the nasal cannula.

After confirmation that the bronchoscopy team was ready, remifentanil 0.5 µg/kg IV was administered. The patient was then positioned supine. Subsequently, propofol 0.5 mg/kg IV was administered in group P and ketamine 0.5 mg/kg IV in group K. When a sedation depth corresponding to a score of 5 or 6 on the Ramsay Sedation Scale (minimal or no response to glabellar tapping) was achieved, the patient was handed over to the bronchoscopy team to begin the procedure. Additional doses of remifentanil (0.5 µg/kg IV), propofol (0.5 mg/kg IV for group P), or ketamine (0.5 mg/kg IV for group K) were administered when necessary according to the anesthetist's clinical judgment.

All study data were recorded by the anesthetist performing the sedation. Demographic and anthropometric characteristics,

ASA physical status, drug doses administered, and procedure and recovery durations were documented. $ETCO_2$, RR, SpO_2, and PR values were recorded at three-minute intervals beginning from the induction of anesthesia.

The primary outcome of the study was the mean IPI value. Secondary outcomes included recovery time as well as bronchoscopist and anesthetist satisfactions. Satisfaction levels were evaluated using a Likert scale ranging from 1 to 10. The number of jaw-thrust maneuvers and bag-valve-mask assisted ventilations applied during the procedure were also documented. Furthermore, correlations between IPI values and $ETCO_2$, RR, SpO_2, and PR were analyzed. IPI values were categorized into three groups: Low IPI (1-3), Medium IPI (4-6), and High IPI (7-10). The $ETCO_2$, RR, SpO_2, and PR measurements were compared among these categories.

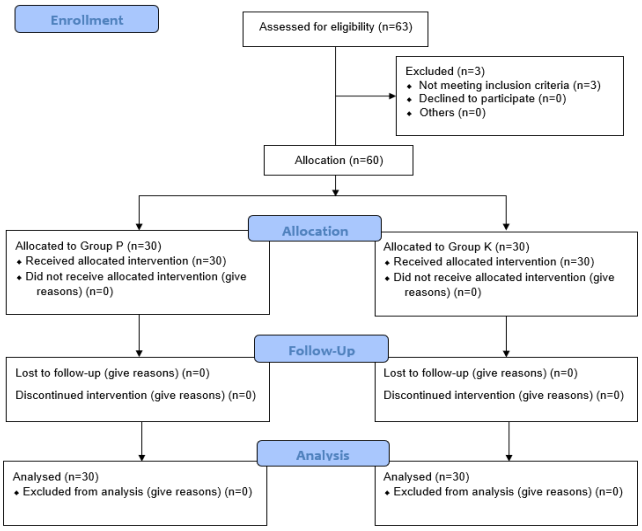

Figure 1. Study flow diagram

Statistical Analysis

The data were analyzed using jamovi statistical software (Version 2.3). Categorical variables were presented as frequencies and percentages, whereas continuous variables were expressed as mean±standard deviation for normally distributed data and median with interquartile range for non-normally distributed data. Normality was assessed using the Shapiro-Wilk test and histogram inspection. The Chi-squared or Fisher's exact test was used for the analysis of categorical variables. Continuous variables were analyzed using Student's or Welch's t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. Comparisons of $ETCO_2$, RR, SpO_2, and PR values across IPI score categories were performed using the Kruskal-Wallis test, followed by pairwise comparisons with the Dwass-Steel-Critchlow-Fligner (DSCF) test. Independent variables in the study included age, gender, height, body weight, procedure duration, midazolam dose, remifentanil dose, sedative drug group, ASA score, intervention type, and the number of bag-valve-mask maneuvers. Dependent variables consisted of $ETCO_2$, RR, SpO_2, PR, IPI scores, and IPI score categories. Power analysis was conducted using G*Power (version 3.1). Based on the primary outcome (IPI score), assuming an alpha error of 5%, a study power of 80%, and an effect size of 0.75 derived from preliminary measurements obtained from eight patients, the required sample size was calculated as 58. A total of 60 patients in two groups was decided to be recruited.

RESULTS

Among the 63 patients assessed for eligibility, 60 were ultimately included in the final analysis. The study flow diagram is shown in Figure 1. Of the included participants, 33 (55%) were male. The median age of the cohort was 9 years (25th-75th percentiles: 3-13.5). The demographic and clinical characteristics of the patients are summarized in Table 1.

Patients in group P had significantly greater age, height, and body weight compared with those in group K (p=0.020, p=0.038, and p=0.030, respectively; Mann-Whitney U test). No significant differences were observed between the groups regarding gender distribution and ASA physical status. Doses of midazolam and remifentanil administered per kilogram basis were significantly higher in group K (p values 0.023 and 0.043, respectively). There was no statistically significant difference in mean IPI values between the groups (4.4±1.6 in group P vs 4.5±1.1 in group K; median difference -0.04, 95% CI: -0.73 to 0.66, p=0.909, Welch's t-test).

Atropine administration was significantly more frequent in group K (p<0.001, Chi-squared test). The number of jaw-thrust maneuvers did not differ significantly between the groups (p=0.181, Mann-Whitney U test). However, the number of bag-mask ventilations was higher in group K (p=0.029, Mann-Whitney U test). Although procedure duration was comparable between the groups, recovery time was significantly longer in group K (p<0.001, Mann-Whitney U test). Bronchoscopist and anesthetist satisfaction scores were also similar between the groups.

Regarding physiological parameters, the average SpO_2 and $ETCO_2$ values were comparable between the groups. PR was significantly higher in group K than in group P (p<0.001, Welch's t-test), whereas RR was significantly lower in group K compared with group P (p=0.023, Mann-Whitney U test).

Descriptive statistics of the IPI values together with their associated physiological parameters are presented in Figure 2 and Supplementary Table 2. The comparison of physiological parameters ($ETCO_2$, RR, SpO_2, and PR) among the low, medium, and high IPI categories is shown in Table 2. Significant differences were identified among the three IPI groups for $ETCO_2$, RR, SpO_2, and PR (p<0.001, Kruskal-Wallis test). Pairwise comparisons demonstrated that $ETCO_2$ values in the medium IPI group were significantly higher than those in both the low and high IPI groups (p<0.001 and p=0.004, DSCF test). RR differed significantly among all three IPI groups (p<0.001, DSCF test). Similarly, SpO_2 values were significantly different across the three groups (p<0.001, DSCF test). In addition, PR values in the low IPI group were significantly higher than those observed in the medium and high IPI groups (p=0.042 and p<0.001, DSCF test).

No complications directly related to the bronchoscopy procedure were observed in any of the patients.

Table 1. Demographic and clinical characteristics of patients

		Group P (n=30)	Group K (n=30)	p
Age (years)		12 (5.5-15.8)	5 (2-11.5)	0.020*[m]
Gender	Female	16 (53.3)	11 (36.7)	0.194[c]
	Male	14 (46.7)	19 (63.3)	
Height (cm)		150 (112.5-160)	118 (100-147.5)	0.038*[m]
Body weight (kg)		43 (21.5-50)	21.5 (11.3-43.5)	0.030*[m]
BMI (kg/m^2)		18.8±4.6	17.8±5.0	0.511[t]
ASA	I	11 (36.7)	12 (40)	0.580[f]
	II	14 (46.7)	16 (53.3)	
	III	5 (16.7)	2 (6.7)	
Midazolam amount (mg/kg)		0.04 (0.04-0.05)	0.05 (0.04-0.05)	0.023*[m]
Remifentanil amount (µg/kg)		0.94 (0.67-1.00)	1.11 (0.85-1.48)	0.043*[m]
Propofol/ketamine amount (mg/kg)		2.04 (1.94-2.85)	1.86 (1.00-2.00)	NA
IPI		4.4±1.6	4.5±1.1	0.909[w]
Atropine use		9 (30)	24 (80)	<0.001*[c]
Jaw-thrust maneuver (number)		1 (0-2) (0-3)	1 (1-2.8) (0-5)	0.181[m]
	0	10 (33.3)	6 (20)	0.493[c]
	1	9 (30)	10 (33.3)	
	≥2	11 (36.7)	14 (46.7)	
Bag mask ventilation (number)		0 (0-0)	0 (0-1)	0.029*[m]
	0	27 (90)	20 (66.7)	NA
	1	2 (6.7)	6 (20)	
	≥2	1 (3.3)	4 (13.3)	
Procedure duration (min)		10 (7.3-11)	9.5 (8-13)	0.583[m]
Recovery duration (min)		10 (8-12.8)	19.5 (15-25)	<0.001*[m]
Bronchoscopist satisfaction (1–10-point Likert scale)		10.0 (10-10)	10.0 (8.3-10)	0.126[m]
	≤6	1	2	NA
	7-9	3	7	
	10	26	21	
Anesthetist satisfaction (1–10-point Likert Scale)		9 (7.3-10)	7 (5-10)	0.074[m]
	≤6	3	12	NA
	7-9	18	9	
	10	9	9	
SpO_2 (%)		89.7 (84.8-93)	88.4 (80.6-93.2)	0.460[m]
PR (beats/min)		123.9±23.2	145.7±15.7	<0.001*[w]
RR (breaths/min)		14.1 (11.6-18)	11.6 (8.8-15.7)	0.023*[m]
$ETCO_2$ (mmHg)		38.9±9.6	36.8±9.1	0.391[t]

Continuous variables are given as median (25th–75th percentiles) or mean±standard deviation. Categorical variables are given as number (percentage). For jaw-thrust maneuvers minimum-maximum values are given in the separate parentheses as well. group P, propofol group; group K, ketamine group; [c]Chi-squared test; [f]Fisher's exact test; [m]Mann-Whitney U test; [t]Student's t test; [w]Welch's t test; NA, not assessed. *p<0.05. BMI: Body-mass index, ASA: American Society of Anesthesiologists physical status, IPI: Integrated Pulmonary Index, SpO_2: Peripheral oxygen saturation (%), PR: Pulse rate (beats/min), RR: Respiratory rate (breaths/min), $ETCO_2$: End-tidal carbon dioxide (mmHg), min: Minute

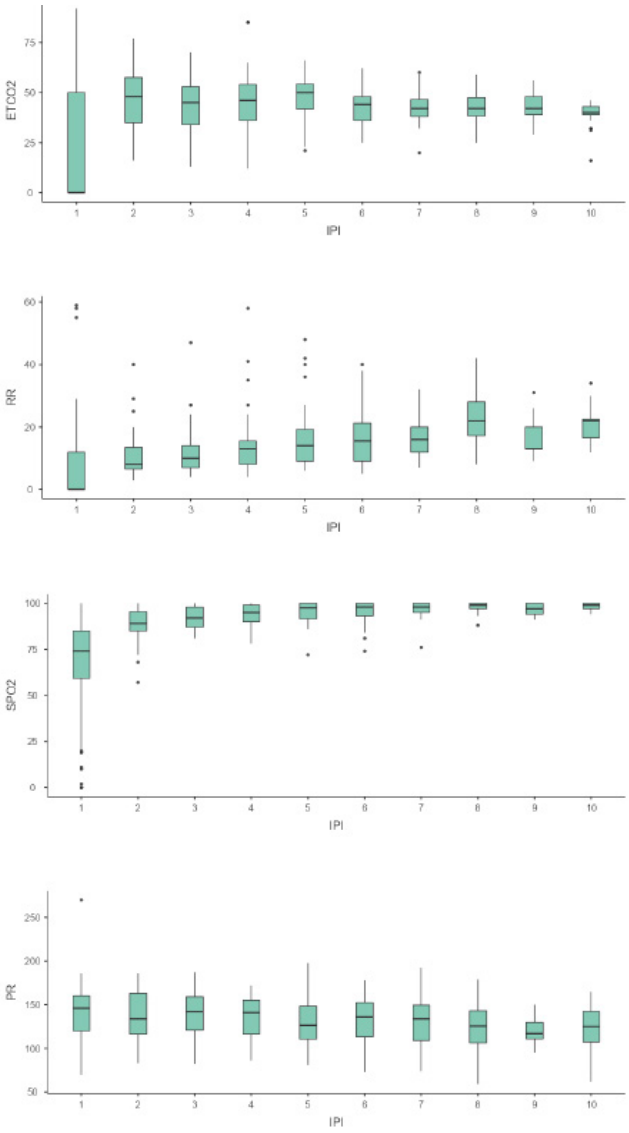

Figure 2. Distribution of physiological variables with different IPI values

Please note that IPI is determined by the combination of all the four parameters using the fuzzy logic principle (see text). IPI: Integrated Pulmonary Index, $ETCO_2$: End-tidal carbon dioxide, RR: Respiratory rate, SpO_2: Peripheral oxygen saturation, PR: Pulse rate

DISCUSSION

The primary finding of this prospective cohort study was that pediatric patients undergoing diagnostic bronchoscopy exhibited comparable periprocedural IPI scores when sedated with either propofol or ketamine. Specifically, the average IPI scores were 4.4±1.6 in the propofol group and 4.5±1.1 in the ketamine group. These results suggest that while the two agents possess distinct pharmacological profiles, they provide a similar level of respiratory status during invasive airway procedures when managed by a dedicated anesthesia team. Interestingly, the average IPI values in our study were lower than those reported in recent pediatric gastrointestinal endoscopy literature, such as the median values of 6.3–6.8 observed by Abdullayev et al.[1] This discrepancy likely reflects the more stimulating and invasive nature of bronchoscopy, which involves direct manipulation of the airway and a higher inherent risk of respiratory interference.[8]

Although IPI scores were similar, significant physiological differences were observed between the groups. The RR was significantly lower in the ketamine group compared to the propofol group, while the PR was significantly higher in the ketamine group. The higher PR in group K is consistent with ketamine's known sympathomimetic effects, which typically result in increased heart rate and blood pressure. Conversely, propofol is often associated with dose-dependent respiratory depression and hemodynamic instability, including bradycardia and hypotension.[9]

Supplementary Table 2. Distribution of physiological variables with different IPI values

IPI	Number of measurements	$ETCO_2$ (mmHg)	RR (breaths/min)	SpO_2 (%)	PR (beats/min)
1	126	0 (0–50)	0 (0–12)	74 (59.25–85)	146 (120–160)
2	35	48 (35–57.5)	8 (6.5–13.5)	89 (85–95.5)	134 (116.5–163)
3	49	45 (34–53)	10 (7–14)	92 (87–98)	142 (121–159)
4	31	46 (36–54)	13 (8–15.5)	95 (90–99)	141 (116.5–155)
5	36	50 (41.75–54.3)	14 (9–19.3)	97.5 (91.5–100)	126.5 (110.75–148.5)
6	48	44 (36–48)	15.5 (9–21.3)	98 (93–100)	136 (113.25–152.5)
7	39	42 (38–46.5)	16 (12–20)	98 (95–100)	134 (109–149.5)
8	54	42 (38.25–47.5)	22 (17.25–28)	99 (97–100)	125.5 (106.5–143.3)
9	9	42 (39–48)	13 (13–20)	97 (94–100)	117 (111–130)
10	31	40 (39–43)	22 (16.5–22.5)	99 (97–100)	125 (107.5–142.5)
Total	458	42 (32–50)	13 (7–20)	94.5 (85–99)	137 (114–155)

Variables are given as median (25th–75th percentiles). IPI: Integrated Pulmonary Index, ETCO2: End-tidal carbon dioxide, RR: Respiratory rate, SpO2: Peripheral oxygen saturation; PR: Pulse rate.

Table 2. Distribution of physiological parameters according to low, medium, and high IPI groups

	Low IPI (1-3) (n=210)	Medium IPI (4-6) (n=115)	High IPI (7-10) (n=133)	p
$ETCO_2$ (mmHg)	36.5 (0-52)	46 (37.5-52.5)[a]	41 (38-46)	<0.001*
RR (breaths/min)	7 (0-13)[b]	14 (9-19.5)[b]	20 (14-24)[b]	<0.001*
SpO_2 (%)	84 (70-92)[c]	97 (92-100)[c]	99 (97-100)[c]	<0.001*
PR (beats/min)	143 (119-160)[d]	137 (114-154)	126 (106-146)	<0.001*

Variables are given as median (25th–75th percentiles). *p<0.05. Kruskal-Wallis test was used. [a]Significant difference compared to the low and high IPI groups (p<0.001 and 0.004, respectively, Dwass-Steel-Critchlow-Fligner (DSCF) test). [b]Significant difference between all the IPI groups (p<0.001, DSCF test). [c]Significant difference between all the IPI groups (p≤0.001, DSCF test). [d]Significant difference compared to the medium and high IPI groups (p=0.042 and<0.001, respectively, DSCF test). IPI: Integrated Pulmonary Index, $ETCO_2$: End-tidal carbon dioxide, mmHg: Millimeters of mercury, RR: Respiratory rate, SpO_2: Peripheral oxygen saturation, PR: Pulse rate, Min: Minute

Even though the midazolam and remifentanil doses administered per kilogram basis were statistically different between the groups, being higher in group K, this difference was too low to have clinical significance.

A notable clinical finding was that bag-mask ventilation was required significantly more often in the ketamine group. While ketamine is generally recognized for preserving spontaneous respiration and protective airway reflexes, it can also cause increased oral secretions and, in rare instances, laryngospasm.[10,11] These factors can compromise the airway even if the patient's drive to breathe remains intact, necessitating assisted ventilation to restore normoventilation. In our study, this was further evidenced by the significantly higher use of atropine in the ketamine group, likely administered to manage secretions or potential bradyarrhythmias, though the latter is less common with ketamine.[12,13] As the PR is one of the four parameters incorporated into the IPI calculation, administration of ketamine might have influenced the composite IPI score. Interpretation of IPI in patients in whom ketamine was administered as part of the regimen should be made in this context.

Our results showed that recovery time was significantly longer in the ketamine group compared to the propofol group, which aligns with established pharmacological data. Propofol is favored for its rapid onset and short half-life, leading to quick awakening and shorter recovery periods. Ketamine, despite its benefits in preserving hemodynamics, is associated with a more prolonged recovery and the potential for unpleasant emergence reactions. Despite the differences in recovery dynamics and the need for more frequent airway interventions in the ketamine group, bronchoscopist satisfaction scores were comparable between the two groups. This indicates that both agents provide adequate procedural conditions for diagnostic bronchoscopy.[9] Even though not statistically significant, a trend towards lower satisfaction scores were noted in the ketamine group. This might have been attributed to increased secretions, as noted by higher rate of atropine administration, and bag-mask ventilation need in this group. As this was not the primary endpoint of the study, this needs further investigation.

The study demonstrated a strong and consistent correlation between IPI scores and standard physiological parameters ($ETCO_2$, RR, SpO_2, and PR). IPI can be a simplified and practical tool for real-time respiratory monitoring in the pediatric population. Our analysis showed that low IPI scores (1–3 points) were significantly associated with the lowest values for RR and SpO_2. Interestingly, the PR was significantly higher in the low IPI group compared to the medium and high groups, likely reflecting a compensatory tachycardic response to respiratory distress or the inherent "fuzzy logic" algorithm of the IPI monitor which incorporates PR into its calculation.[2,14,15]

Pairwise comparisons using the DSCF test revealed that $ETCO_2$ was significantly higher in the medium IPI group compared to both the low and high groups. High $ETCO_2$ is often a sign of hypoventilation or hypercapnia during sedation, which would naturally lower the IPI score from 'normal' (8–10) to 'requires attention' (4–7).[1,2,13] However, the very low $ETCO_2$ values observed in the low IPI group (1–3) likely indicate apnea or complete airway obstruction, where CO2 fails to reach the sampling line entirely. These findings support previous research suggesting that IPI monitoring is superior to pulse oximetry alone because it captures ventilatory changes—such as apnea or hypopnea—long before measurable desaturation occurs.

The use of IPI is particularly valuable in non-operating room anesthesia settings, such as bronchoscopy suites, where the risk of cardiopulmonary complications remains a significant concern.[16,17] Current guidelines emphasize that capnography should be used routinely during deep sedation when verbal

communication is interrupted, as pulse oximetry can be a lagging indicator of respiratory failure, especially when supplemental oxygen is provided. In our study, IPI served as an important numerical surrogate that allowed the anesthesia team to identify respiratory trends quickly. Studies by Peveling-Oberhag et al.[4] and others have shown that capnography-based tools can detect respiratory compromise 83–99 seconds earlier than standard monitoring, providing a vital window for intervention.[8,18]

Limitations

Several limitations to this study must be addressed. First, there were significant demographic differences between the groups, as patients in group P were older than those in group K. A significant bias in selecting patients for group K might have contributed, as the drug protocol choice was left to the discretion of the primary anesthetist. Taking into consideration physiological development, patient age is an important factor in the pattern of respiratory depression. Younger age has been identified as a factor associated with lower IPI scores and a higher risk of respiratory complications, which may have confounded the comparison. Further studies in this regard should take this fact into consideration, and homogeneous groups particularly the patient age should be considered. Second, we did not utilize objective measures for sedation depth, such as processed electroencephalography. While clinical scales like the Ramsay Sedation Scale are common, objective monitoring could have ensured greater group homogeneity regarding the level of sedation provided. Future studies in this regard should consider objective monitors of depth of anesthesia, like Bispectral Index. Third, the anesthetist performing the sedation was also responsible for recording the IPI scores, which introduces the possibility of observation bias. Finally, the single-center design may limit the generalizability of these findings to broader pediatric populations.

CONCLUSION

As a result, the IPI can be a valuable monitor for pediatric patients undergoing diagnostic bronchoscopy. Our study demonstrates that propofol and ketamine result in comparable IPI scores, although they exhibit different physiological and recovery profiles. While ketamine resulted in a longer recovery time, it remains a clinically acceptable option with high satisfaction among the medical team. The strong correlation between IPI values and physiological data may provide a comprehensive and accurate summary of a patient's respiratory status. We recommend that clinicians utilize IPI monitoring to enhance patient safety during pediatric sedation, particularly in high-risk airway procedures where early detection of hypoventilation is critical. Future studies should aim for more balanced demographics and the inclusion of objective sedation depth monitoring to further refine these comparisons.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study received approval from the Marmara University Faculty of Medicine Clinical Researches Ethics Committee (Date: 07.05.2021, Decision No: 09.2021.497).

Informed Consent

Informed consent was obtained from a parent or legal guardian. Where appropriate, age-adjusted assent was also obtained from the child. The inclusion of vulnerable populations in this study adhered to national and international ethical guidelines. Extra care was taken to ensure voluntary participation, understanding, and protection of participant dignity and autonomy.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

The authors received no financial support for the conduct or publication of this research.

Author Contributions

Concept: YK, RA; Design: YK, RA; Consultation: YK, RA; Data Collection and/or Processing: YK, RA; Analysis and/or Interpretation: YK, RA; Literature Review: YK, RA; Manuscript Preparation: YK, RA; Critical Review: YK, RA.

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Suspected indirect pesticide exposure associated with multiorgan dysfunction after consumption of wild asparagus: a case report

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ABSTRACT

Indirect poisoning is a rare condition causing multiple organ failure (MOF) of unknown cause. In this study, we aimed to present a rare case of suspected pesticide poisoning due to indirect contamination, a clinically unpredictable condition, in a patient admitted to our intensive care unit with MOF of unknown cause, and to raise awareness among clinicians in this context. A 73-year-old female patient with no known underlying medical condition presented to the emergency department with complaints of weakness and shortness of breath. Following clinical and laboratory evaluation, the patient was admitted to the intensive care unit due to unexplained MOF affecting the respiratory, renal, hepatic, hematological, and cardiac systems. Since a clear etiological cause could not be determined in the initial evaluations, the patient's environmental exposure was investigated, and after further investigation of the anamnesis, it was suspected that there was indirect pesticide exposure, and the patient was successfully treated with supportive treatment guided by the clinical presentation. Indirect pesticide exposure, particularly when it occurs after consuming pesticide-contaminated wild plants, can present clinicians with a rare clinical condition that is easily overlooked but can lead to life-threatening multiple organ failure.

Keywords: Pesticides, multiple organ failure, dietary exposure, intensive care units

INTRODUCTION

Pesticides are a broad group of chemical compounds used to control, remove, or eliminate non-target harmful organisms.[1,2] Acute pesticide poisonings resulting from the widespread use of these substances remain a serious global public health problem and one of the leading causes of emergency room visits.[1] Exposure to toxic agents usually occurs intentionally (for suicidal purposes) or accidentally (occupational or environmental). In intentional ingestions, the active substance can often be clearly identified by the patient or their relatives; however, in accidental exposures, there is generally insufficient and limited data on the type, amount, and duration of exposure to the chemical.[3] In medical literature and clinical practice, the usual scenario is cases that develop through direct contact with the toxic agent. In contrast, identifying contaminations and exposures that occur indirectly is a complex and challenging diagnostic process for clinicians. One of the most critical steps in determining clinical success and prognosis in pesticide poisonings is the specific identification of the chemical agent to which the patient is exposed and the selection of appropriate antidotes or elimination methods. However, acute management of cases suspected of poisoning but where the toxic agent has not yet been clinically or laboratory confirmed presents serious challenges. In cases admitted to intensive care units where poisoning is suspected clinically but the agent cannot be identified, the basic approach is stabilization of the patient's vital functions, resuscitation, and aggressive supportive treatment.[4] In this acute period where the chemical agent cannot be clarified, the "toxidromic approach," focusing on the patient's clinical findings and systemic symptoms, comes to the forefront in the diagnostic and treatment algorithm.[5]

Acute poisonings are clinical conditions that can rapidly progress to multiple organ failure (MOF) and require close invasive monitoring in intensive care settings. The most vital point here is that the clinician should consider the

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possibility of "poisoning" behind the atypical picture that leads the patient to MOF in the early stages. With this case presentation; We aimed to present a rare case of suspected pesticide poisoning due to indirect contamination, a clinically unpredictable condition, in a patient admitted to our intensive care unit with MOF of unknown cause, and to raise awareness among clinicians in this context.

CASE REPORT

A 73-year-old female patient with no known underlying medical conditions presented to the emergency department with complaints of weakness and shortness of breath. Her history revealed that her symptoms began on the day of admission and that she had no prior similar complaints. Her vital signs at admission were: pulse 105 beats/minute, respiratory rate 24/minute, blood pressure 145/75 mmHg, body temperature 36.3°C, and peripheral oxygen saturation (SpO_2) 84%. Physical examination revealed no additional pathological findings except for bilateral decreased lung sounds. Initial laboratory investigations showed. White blood cell count was 7.7×10^3/µL, neutrophil count was 72%, hemoglobin was 12.1 g/dl, hematocrit was 35.6%, platelet count was 88×10^3/µL, glucose was 130 mg/dl, creatinine was 2.77 mg/dl, urea was 61 mg/dl, ALT was 253 U/L, AST was 286 U/L, total bilirubin was 9.2 mg/dl, direct bilirubin was 3.4 mg/dl, albumin was 3.9 g/dl, C-reactive protein (CRP) was 18 mg/L, activated partial thromboplastin time (aPTT) was 42.7 seconds, and high-sensitivity troponin I (hs-Troponin I) was 2406 ng/L. Arterial blood gas analysis in room air showed pH 7.40, PaO_2 51 mmHg, $PaCO_2$ 29.4 mmHg, HCO_3 19.4 mmol/L, oxygen saturation 86%, and lactate 2.8 mmol/L, consistent with hypoxemic respiratory failure.

Abdominal computed tomography revealed no pathological findings. Thoracic computed tomography showed interlobular septal thickening, approximately 2.5 cm pleural effusion in the right hemithorax and approximately 1 cm pleural effusion in the left hemithorax, bilateral atelectatic changes in the basal areas, and peripherally located patchy ground-glass opacities in the upper zones (Figure).

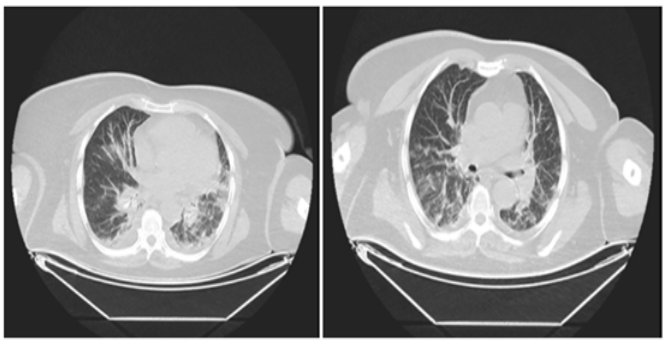

Figure. Thoracic CT scan image of the patient upon admission to the emergency department
CT: Computed tomography

Bedside echocardiographic evaluation revealed a left ventricular ejection fraction of 60%. No left ventricular wall motion abnormality, significant valvular pathology, or significant cardiac dysfunction was detected. Systolic pulmonary artery pressure was measured as 35 mmHg.

The patient was admitted to the intensive care unit due to unexplained multiple organ dysfunction affecting the respiratory, renal, hepatic, hematological, and cardiac systems. Supportive treatment was initiated, and high-flow nasal oxygen therapy was started. Since no clear etiological cause could be identified in the initial assessments, the patient's environmental exposure history was re-examined in detail. It was learned that the patient consumed wild *Asparagus officinalis*, which she had collected from his region (Tosya district, Kastamonu province) and consumed safely for many years, on the day of admission. Furthermore, the patient stated that the agricultural land where the plants were collected had been sprayed with pesticides approximately two days prior to combat harmful insects and weeds, and that rain had occurred in the area after the spraying. Therefore, it was considered that the consumed wild asparagus may have been contaminated with pesticides. The patient stated that she had eaten wild asparagus approximately 8 hours before arriving at the hospital, that she couldn't remember how much she had consumed, and that no one else had eaten the same plant. Considering the patient's history of environmental exposure, clinical presentation with multi-organ involvement, and laboratory findings, a preliminary diagnosis of indirect and suspected pesticide exposure due to consumption of pesticide-contaminated wild asparagus was considered. Sepsis, infection, viral, biliary tract, hematological, ischemic cardiac, and autoimmune causes that could lead to MOF in the patient were ruled out through anamnesis, clinical, laboratory, and radiological examinations. The pesticide agent could not be confirmed due to the inability to perform toxicological analyses to determine the pesticide type at our center. Therefore, the patient received symptomatic and supportive treatment.

During the first 24 hours of intensive care monitoring, the patient developed anuria and her serum creatinine level rose to 4.89 mg/dl, prompting the initiation of intermittent renal replacement therapy. On the seventh day of intensive care treatment, a significant improvement was observed in the patient's respiratory function and liver function tests. The room air SpO_2 value was measured as 93%. In control laboratory investigations; The following values were determined: white blood cell count 8.1×10^3/µL, neutrophil percentage 68%, hemoglobin 12.7 g/dl, hematocrit 36.7%, platelet count 184×10^3/µL, glucose 152 mg/dl, creatinine 3.8 mg/dl, urea 44 mg/dl, ALT 22 U/L, AST 28 U/L, total bilirubin 2.2 mg/dl, direct bilirubin 0.8 mg/dl, albumin 3.6 g/dl, CRP 11 mg/L, aPTT 28.2 seconds, and hs-troponin I 265.3 ng/L. Control arterial blood gas analysis showed pH 7.35, PaO_2 88.2 mmHg, $PaCO_2$ 36.4 mmHg, HCO_3 19.8 mmol/L, oxygen saturation 92%, and lactate 1.2 mmol/L. Although significant improvement was observed in liver and respiratory function, improvement in renal function was delayed, and intermittent renal replacement therapy was continued due to anuria and overload. The patient was transferred to the internal medicine ward on the tenth day of intensive care. On the fifth day of ward observation, spontaneous urine output resumed, and gradual improvement in renal function was observed. The patient's serum creatinine level decreased to 1.45 mg/dl, and on the tenth day of ward observation, the patient was discharged in a clinically stable condition.

DISCUSSION

Pesticide poisoning remains a significant public health problem worldwide, with the vast majority of cases developing as a result of intentional ingestion, occupational exposure, or direct contact with pesticides.[6] In contrast, indirect exposures resulting from the consumption of pesticide-contaminated food are rarer and clinically difficult to recognize. In this case, we share a patient with multiple organ dysfunction resulting from indirect poisoning a difficult-to-predict clinical condition after consuming wild *Asparagus officinalis* collected from a pesticide-treated agricultural area, even though the patient did not have direct contact with the pesticide.

The clinical manifestations of pesticide poisoning show a wide spectrum depending on the class of agent, the dose, the route of exposure, and the individual characteristics of the patient. Although different pesticide groups such as organophosphates, carbamates, pyrethroids, and glyphosate have different toxicity mechanisms, the common end pathway in severe cases is oxidative stress, mitochondrial dysfunction, endothelial damage, and systemic inflammatory response. As a result of these mechanisms, the renal, hepatic, pulmonary, and cardiac systems are affected simultaneously. In our case, there were also findings of multisystemic toxic involvement (acute kidney injury, hepatocellular damage, hypoxemic respiratory failure, thrombocytopenia, and marked troponin elevation), and these findings showed that the patient had this clinical picture as a result of poisoning. Acute kidney injury is one of the most important mortality determinants of pesticide poisoning. Toxic agents can directly cause tubular cell damage, as well as impair kidney function through renal perfusion disorder, oxidative stress, rhabdomyolysis, and microvascular damage.[7] Early initiation of renal replacement therapy, especially in cases presenting with oliguria or anuria, is important for preventing metabolic complications. In our patient, renal replacement therapy was applied due to anuria and progressive creatinine elevation that developed within the first 24 hours, and kidney function recovered later than other organ systems. This situation is consistent with publications showing that renal recovery may be delayed in pesticide-related acute kidney injury.[8]

In this case, the diagnosis causing MOF was made thanks to a detailed environmental exposure history. At the time of admission, the patient herself was unaware of pesticide exposure, and no etiological cause that could explain the multiple organ failure was identified in the initial assessment. Indirect poisoning is a clinical situation that is difficult for clinicians to consider in patients with unexplained multiple organ dysfunction, and a detailed nutritional history, environmental exposure inquiry, and toxidromic approach are critical factors in reaching the diagnosis.[9]

Toxicological analyses to determine pesticide levels or pesticide class cannot be performed at our center. Therefore, the pesticide agent to which the patient was exposed could not be confirmed in the laboratory. The lack of toxicological analysis can be noted as a limitation for our case presentation. The diagnosis of indirect pesticide poisoning due to the patient's consumption of pesticide contaminated wild asparagus was made by evaluating the patient's detailed exposure history, the exclusion of alternative etiologies, the consistency of clinical findings with multisystemic toxicity, and the clinical improvement observed with supportive treatment. In a comprehensive review published in the literature, 63 different outbreaks related to foodborne pesticide exposure were evaluated, and it was stated that most of these events developed as a result of the misuse of pesticides, failure to comply with harvest time, or accidental contamination of food.[10] In our literature search, we did not encounter any cases of indirect poisoning except for the case of Anticholinergic Toxic Syndrome Developed as a Result of Indirect Exposure to Hyoscyamus muticus by Ingesting Locusts, published by Mohammad Halawani in 2025.[11] To our knowledge, our case is; This is the only case of MOF developing after pesticide contamination of wild-collected edible plants. Therefore, this case report makes a significant contribution to the literature by demonstrating that clinicians should consider not only occupational or direct pesticide exposure but also indirect exposure from wild plants collected from agricultural areas in the differential diagnosis. Our case differs from the existing literature in several aspects. First, our patient did not have direct contact with the pesticide; it is a case of indirect pesticide exposure after consuming wild *Asparagus officinalis* collected from a pesticide-treated agricultural area. In the literature, classic cholinergic side effects are seen in pesticide poisoning cases. In our case, initially unexplained hypoxemic respiratory failure, acute renal injury, hepatic dysfunction, etc. The clinical picture was characterized by multiple organ dysfunction accompanied by thrombocytopenia and myocardial damage. This constitutes an atypical clinical presentation that can lead to a delay in diagnosis. With these features, our case demonstrates that a detailed history can be as important as laboratory investigations, especially in emergency department and intensive care unit practice.

CONCLUSION

Indirect pesticide exposure, particularly when occurring after consumption of contaminated wild plants, is a rare clinical condition that can be easily overlooked but can lead to life-threatening multi-organ failure. Clinicians should consider possible indirect toxic exposure and obtain a detailed dietary and environmental history in patients presenting with otherwise unexplained multiorgan dysfunction. Increasing clinical awareness is crucial for the early recognition and appropriate management of similar cases.

ETHICAL DECLARATIONS

Informed Consent

Written informed consent was obtained from the patient included in this report. Signed consent forms are retained by the authors and are available upon request.

Peer Review Process

This report underwent external peer review.

Conflict of Interest

The authors declare no conflicts of interest.

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Author Contributions

Concept: VGS; Design: VGS; Control: VGS, EP; Resources: VGS, ÖT, UD, BTK; Materials: VGS, EP; Data Collection and/ or Processing: VGS, EP; Analysis and/or Interpretation: VGS, ÖT, UD, BTK; Literature Review: VGS; Article Writing: VGS; Critical Review: VGS, ÖT, UD, BTK.

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Anesthetic management of major multivisceral surgery in an anuric hemodialysis-dependent patient: a case report

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ABSTRACT

Patients receiving maintenance hemodialysis for end-stage kidney disease present substantial anesthetic challenges during extensive surgery, particularly when residual urine output is negligible. A 45-year-old female with bilateral atrophic kidneys, dependent on hemodialysis and producing approximately 3–5 ml of urine daily, underwent bilateral nephrectomy, radical cystectomy with urethral resection, total abdominal hysterectomy with bilateral salpingo-oophorectomy, anterior vaginal wall resection, and lymph node dissection. Combined general and epidural anesthesia, invasive hemodynamic monitoring, serial arterial blood gas analyses, individualized crystalloid administration, and titrated norepinephrine support were used. Total surgical blood loss was recorded as 800 ml, while approximately 1,000 ml of 0.9% isotonic crystalloid was administered. Serial intraoperative assessments showed low lactate concentrations and potassium levels within acceptable limits. Norepinephrine, titrated during surgery, was discontinued before extubation; the patient was extubated in the operating room and transferred to the intensive care unit. Maintenance hemodialysis was resumed on postoperative day (POD) 2, and the patient was transferred from intensive care to the surgical ward on POD 3. This case illustrates the importance of physiology-guided, individualized fluid and vasopressor management aimed at maintaining adequate tissue perfusion while avoiding unnecessary fluid loading in an anuric, dialysis-dependent patient.

Keywords: Anuria, renal dialysis, fluid therapy, norepinephrine, analgesia; epidural, nephrectomy

INTRODUCTION

Patients receiving maintenance dialysis have increased perioperative morbidity, and particular attention should be paid to volume status, electrolyte balance, anemia, cardiovascular risk, and altered drug pharmacokinetics.[1,2] Perioperative fluid management is especially challenging in functionally anuric patients because residual renal fluid excretion is absent. At the same time, extensive abdominal and pelvic procedures may be associated with blood loss, vasodilation, and prolonged hemodynamic stress.

Contemporary approaches to perioperative fluid management recommend individualizing treatment according to intravascular volume status, tissue perfusion, comorbidities, and surgical characteristics rather than applying fixed restrictive or liberal fluid regimens.[3,4]

We report the anesthetic management of a functionally anuric patient receiving maintenance hemodialysis who underwent extensive multivisceral surgery, focusing on the balance between limited crystalloid administration and titrated vasopressor support.

CASE REPORT

A 45-year-old female, 160 cm tall, with a recorded body weight of 75 kg and a documented dialysis dry weight of 73 kg, was scheduled for bilateral nephrectomy, radical cystectomy with urethral resection, total abdominal hysterectomy and bilateral salpingo-oophorectomy, anterior vaginal wall resection, and lymph node dissection because of bilateral atrophic kidneys and bladder malignancy.

The patient received maintenance hemodialysis three times weekly. Daily urine output was approximately 3–5 ml, and she was considered functionally anuric. Her medical history included hyperparathyroidism, gout, surgically

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treated spina bifida with residual neurological deficits, and neurogenic bladder. She was classified as American Society of Anesthesiologists (ASA) physical status III.

On the day before surgery, she underwent four hours of heparin-free hemodialysis with a documented ultrafiltration volume of 2,300 ml. Preoperative hemoglobin was 7.8 g/dl, and potassium, sodium, and calcium concentrations were considered acceptable for surgery.

For perioperative monitoring, an arterial catheter was inserted into the left radial artery and a central venous catheter into the right internal jugular vein. A thoracic epidural catheter was placed at the T10 level for perioperative analgesia, and blood products were made available in case transfusion was required.

General anesthesia was induced with intravenous midazolam 1 mg, fentanyl 50 µg, propofol 170 mg, and rocuronium 50 mg. Epidural analgesia was provided using a solution prepared in 100 ml of 0.9% saline containing 0.125% bupivacaine and a total of 200 µg of fentanyl, administered as an initial 3-ml bolus followed by an infusion at 3 ml/h with a 20-minute lockout interval.

Initial arterial blood gas analysis showed pH 7.509, $PaCO_2$ 25.8 mmHg, HCO_3^- 20.1 mmol/L, base excess −2.4 mmol/L, lactate 0.88 mmol/L, potassium 3.49 mmol/L, and ionized calcium 1.18 mmol/L. Minute ventilation was reduced because of respiratory alkalosis.

Serial intraoperative arterial blood gas analyses were performed. At 10:40, pH was 7.44, $PaCO_2$ 28.9 mmHg, HCO_3^- 19.2 mmol/L, potassium 3.95 mmol/L, and lactate 0.80 mmol/L. Thus, the initially marked alkalemia had diminished following adjustment of ventilation. No clinically significant hyperkalemia or rise in lactate was detected on serial measurements.

Bilateral nephrectomy was performed first. Pelvic surgery then proceeded with removal of the bladder and uterus, urethral and anterior vaginal wall resection, and lymph node dissection.

The operation lasted from 08:30 to 14:15 (5 hours 45 minutes). Arterial pressure was monitored continuously and invasively. Hypotension was considered potentially multifactorial, reflecting anesthetic- and epidural-related vasodilation as well as surgical blood loss; the relative contributions could not be objectively distinguished. Rather than administering routine fluid boluses to this functionally anuric patient, the team assessed blood loss, arterial pressure trends, and serial laboratory findings. Norepinephrine was titrated within approximately 0.05–0.1 µg/kg/min according to mean arterial pressure (MAP) and the overall hemodynamic response. The dose was increased toward 0.1 µg/kg/min when MAP fell below approximately 60 mmHg and reduced toward 0.05 µg/kg/min when MAP recovered above this level. This describes the clinical titration approach, not a reconstructed minute-by-minute MAP series.

Approximately 1,000 ml of 0.9% isotonic crystalloid was administered during surgery. Total surgical blood loss was recorded as 800 ml, with the most pronounced bleeding observed during the hysterectomy phase. No packed red blood cells were transfused intraoperatively. Perioperative hemoglobin measurements were 9.5 g/dl at 08:13 (before the recorded surgical start), 9.2 g/dl at 10:41, 9.5 g/dl at 11:26, 9.5 g/dl at 13:21, 8.7 g/dl at 13:52, and 8.4 g/dl at 15:12 (after the recorded surgical end). The discrepancy between the preoperative hemoglobin of 7.8 g/dl and the first perioperative measurement may reflect changes in plasma volume around dialysis and ultrafiltration, although the cause cannot be confirmed from the available records. Transfusion was deferred following repeated assessment of hemoglobin, surgical bleeding, hemodynamic response, and lactate, rather than on the basis of a single hemoglobin threshold.

Toward the end of surgery, arterial blood pressure was 90/52 mmHg while norepinephrine was running at 0.05 µg/kg/min; the corresponding calculated MAP was approximately 65 mmHg. Final arterial blood gas analysis showed pH 7.391, $PaCO_2$ 31.1 mmHg, HCO_3^- 18.4 mmol/L, base excess −5.7 mmol/L, lactate 1.13 mmol/L, potassium 4.06 mmol/L, and ionized calcium 1.11 mmol/L. Persistently low lactate concentrations and acceptable potassium levels on serial intraoperative measurements supported the absence of marked global hypoperfusion or clinically important hyperkalemia.

Norepinephrine was discontinued before emergence. The patient was extubated in the operating room and transferred to the intensive care unit without a requirement for vasopressor support.

The postoperative course was clinically stable without a persistent vasopressor requirement. The early postoperative hemoglobin measurement at 15:12 was 8.4 g/dl. Maintenance hemodialysis was resumed on postoperative day (POD) 2, with an ultrafiltration volume of 2,800 ml. The patient was transferred from the intensive care unit to the surgical ward on POD 3. At that time, lactate was 1.22 mmol/L and potassium was 3.99 mmol/L. Reduced bicarbonate and increased chloride concentrations in the presence of normal lactate were consistent with mild hyperchloremic metabolic acidosis.

The patient subsequently continued her regular three-times-weekly hemodialysis schedule. During the pre-discharge hemodialysis session on POD 11, 3,500 ml was removed by ultrafiltration. She was discharged in clinically stable condition on POD 12.

DISCUSSION

The principal anesthetic challenge in this case was balancing the maintenance of adequate perfusion during extensive surgery against the avoidance of preventable fluid loading in a patient with virtually absent renal fluid clearance.

Although patients with dialysis-dependent kidney failure face increased perioperative risk, evidence specific to many perioperative treatment decisions in this population remains limited.[1,2] Contemporary reviews emphasize individualized assessment of volume status, electrolytes, anemia,

cardiovascular risk, and dialysis timing in patients receiving maintenance hemodialysis.[3]

The 2024 PeriOperative Quality Initiative (POQI) consensus recommends individualizing perioperative fluid therapy according to surgical characteristics, intravascular volume status, and comorbidities.[4] Similarly, the POQI consensus on arterial pressure management recommends treating hypotension according to its likely underlying cause rather than adopting a uniform approach.[5]

This distinction was particularly important in our patient. General anesthesia and epidural sympathetic blockade may contribute to vasodilation, whereas repeated crystalloid boluses in a functionally anuric patient could create a fluid burden that cannot subsequently be eliminated through the kidneys. Accordingly, hypotension was not automatically interpreted as hypovolemia: both vasodilation and blood loss were plausible contributors, and no advanced measure was available to quantify their respective roles. Fluid administration and vasopressor requirements were evaluated in conjunction with clinical and hemodynamic findings.

Nevertheless, the intention was not fluid restriction per se. In the RELIEF trial, a restrictive fluid regimen in patients at increased risk of complications undergoing major abdominal surgery did not improve disability-free survival and was associated with a higher incidence of acute kidney injury.[6] These findings cannot be directly extrapolated to our patient, who was already dialysis-dependent and underwent bilateral nephrectomy. We cite RELIEF only to support the broader principle that arbitrary fluid restriction may be harmful and that maintaining adequate circulating volume and tissue perfusion remains essential.

In our case, approximately 1,000 ml of isotonic crystalloid was administered while norepinephrine was titrated according to hemodynamic response. This should be regarded as an individualized fluid–vasopressor strategy rather than a fixed restrictive fluid protocol.

Serial metabolic measurements were reassuring with regard to global tissue perfusion. Intraoperative lactate remained between 0.80 and 1.13 mmol/L, and no clinically significant hyperkalemia developed. Norepinephrine could be discontinued before emergence. Lactate and potassium levels also remained acceptable on POD 3, when the patient was transferred from intensive care to the ward. Mild metabolic acidosis with hyperchloremia and normal lactate at that time suggested a hyperchloremic component rather than ongoing global hypoperfusion. The influence of crystalloid composition on acid–base balance has also been examined in nonrenal surgical populations.[7] However, causality cannot be established from a single case.

Preoperative hemodialysis was performed one day before surgery. The documented dry weight was 73 kg, and 2,300 ml was removed during the four-hour heparin-free session. These data provide an objective context for the cautious intraoperative fluid strategy, although ultrafiltration volume alone does not establish that the patient was euvolemic at the start of surgery.

Maintenance hemodialysis was resumed on POD 2 with 2,800 ml of ultrafiltration, followed by continuation of the regular dialysis schedule. A large observational cohort study reported a stepwise association between longer intervals from the last hemodialysis session to surgery and increased postoperative mortality.[8] Although the observational design precludes causal inference, these findings support scheduling dialysis close to elective surgery when appropriate.

Preoperative anemia was another important challenge. The 2023 international guidelines from the American Association of Blood Banks (AABB) support restrictive red blood cell transfusion strategies in most hemodynamically stable adults, while emphasizing that transfusion decisions should account for the overall clinical condition rather than hemoglobin concentration alone.[9]

In this case, despite the preoperative hemoglobin of 7.8 g/dl, serial perioperative values ranged from 8.4 to 9.5 g/dl, including an early postoperative value of 8.4 g/dl. The higher initial perioperative concentration could have reflected dialysis-related plasma-volume changes, but this remains unverified. The decision not to administer an intraoperative red blood cell transfusion was individualized on the basis of serial hemoglobin measurements, recorded blood loss, hemodynamic response, low lactate concentrations, and the absence of documented signs of inadequate global perfusion. These observations do not exclude occult hypoperfusion or establish the absence of hypovolemia.

Current POQI guidance describes goal-directed hemodynamic therapy as a protocolized approach involving fluids, vasopressors, and inotropes guided by monitoring and physiological targets.[10] Therefore, it would not be appropriate to describe our management as a formal goal-directed hemodynamic therapy protocol. Instead, we used a pragmatic, patient-specific, physiology-guided approach based on invasive arterial pressure monitoring, serial blood gas measurements, assessment of surgical losses, cautious fluid administration, and titrated norepinephrine.

This report has important limitations inherent to a single case. Advanced cardiac output monitoring or dynamic indices of fluid responsiveness were not used, and perioperative volume status was not quantitatively determined using a dedicated objective method. The timing of the preoperative hemoglobin sample relative to dialysis was not independently verified; therefore, the proposed plasma-volume explanation remains speculative. Although dry weight and ultrafiltration volumes were obtained from dialysis records, these measurements alone cannot establish intraoperative euvolemia. Therefore, the favorable clinical course does not demonstrate superiority of the described fluid–vasopressor strategy or support a fixed fluid or vasopressor regimen for other dialysis-dependent patients.

CONCLUSION

This case demonstrates the feasibility of individualized hemodynamic management in an anuric, hemodialysis-dependent patient undergoing extensive multivisceral surgery. Cautious crystalloid administration, titrated

norepinephrine support, invasive arterial monitoring, and serial metabolic assessments were associated with a stable perioperative course without a marked lactate rise, severe hyperkalemia, or persistent vasopressor requirement.

The key principle is not fluid restriction itself but preservation of adequate tissue perfusion while avoiding unnecessary volume loading. Observations from this single case should not be interpreted as evidence supporting any fixed fluid or vasopressor regimen.

ETHICAL DECLARATIONS

Informed Consent

Written informed consent was obtained from the patient included in this report. Signed consent forms are retained by the authors and are available upon request.

Peer Review Process

This report underwent external peer review.

Conflict of Interest

The authors declare no conflicts of interest.

Financial Disclosure

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Author Contributions

Concept: MSD, ASTY, BAG; Design: MSD, ASTY, BAG; Control/Supervision: MSD, ASTY, BAG; Resources: MSD, ASTY, BAG; Materials/Clinical Case Management: MSD, ASTY, BAG; Data Collection and/or Processing: MSD, ASTY, BAG; Analysis and/or Interpretation: MSD, ASTY, BAG; Literature Review: MSD, ASTY, BAG; Article Writing: MSD, ASTY, BAG; Critical Review: All Authors.

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