

Perioperative Outcomes in Patients with Type I Pulmonary Arterial Hypertension Undergoing Elective Non-Cardiac Surgery: A Retrospective Case Series from a National Reference Center

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Abstract

Background: Idiopathic pulmonary arterial hypertension (IPAH), a subtype of World Health Organization (WHO) Group I pulmonary hypertension (PH), is characterized by elevated pulmonary vascular resistance (PVR) and right ventricular (RV) dysfunction in the absence of an identifiable cause¹. Patients with IPAH are considered at high perioperative risk, but outcome data in this population remain limited².

Methods: We conducted a retrospective case series including 36 adult IPAH patients under follow-up at a Belgian national reference center. These patients underwent 61 elective non-cardiac procedures between 1992 and 2023. Diagnosis was confirmed by right heart catheterization (RHC)³. Preoperative cardiac index (CI) was categorized into high, intermediate, or low risk using European Society of Cardiology (ESC) and European Respiratory Society (ERS) 2022 criteria⁴. The primary outcome was 30-day all-cause mortality. Secondary outcomes included 90-day mortality, unplanned intensive care unit (ICU) admission, and prolonged hospitalization. Associations with baseline hemodynamic parameters were explored descriptively.

Results: Thirty-day mortality was 1.6% (1/61); 90-day mortality was 4.9% (3/61). Descriptive analysis showed that all deaths occurred in patients with low CI and elevated PVR⁵. Unplanned ICU admission occurred in 6.6% (4/61), and prolonged hospitalization in 18.0% (11/61). No statistically significant associations were found between baseline hemodynamics and adverse outcomes.

Conclusion: Despite modern disease-targeted therapies, patients with IPAH remain vulnerable to perioperative complications and delayed mortality⁶. Adverse events occurred predominantly in patients with high-risk hemodynamic profiles or procedures performed in non-expert centers⁷. Structured preoperative risk stratification and referral to experienced centers may improve perioperative outcomes in this population.

Ethical approval: Ethics Committee Research UZ/KU Leuven (S64278; Chair: Prof. Dr. L. Helsen; 18/12/2023).

Keywords: Idiopathic Pulmonary Arterial Hypertension, Perioperative Outcomes, Elective Surgery, Intensive Care, Cardiac Index, Case Series.

Introduction

Pulmonary arterial hypertension (PAH) is a rare but severe condition classified under Group I of the WHO pulmonary hypertension framework. It

is characterized by progressive pulmonary vascular remodeling, elevated PVR, and increased RV afterload, leading to RV dysfunction and ultimately right heart failure¹. IPAH is a distinct subtype defined by the absence of identifiable etiologic

Previous Presentation: None.

Ethics Approval: This study was approved by the Ethics Committee of University Hospitals Leuven (Herestraat 49, 3000 Leuven, Belgium). Protocol number: S67433. Approved by: Prof. Dr. Sabine D. Allard. Date of approval: 10 October 2023.

Patient Consent: Due to the retrospective nature of the study, the requirement for written informed consent was waived by the Ethics Committee.

factors and represents a diagnostic and therapeutic challenge due to its insidious progression and systemic impact⁸.

Despite substantial advances in targeted therapies, such as endothelin receptor antagonists (ERA), phosphodiesterase type 5 inhibitors (PDE5i), prostacyclin analogs (PCA), and soluble guanylate cyclase stimulators (sGC), patients with IPAH remain at high risk for perioperative complications⁶. Anesthesia, mechanical ventilation, volume shifts, and surgical stress may precipitate acute RV failure in these patients, particularly those with limited cardiopulmonary reserve⁶. The ESC and ERS guidelines recommend that patients with PAH undergo surgery in expert centers with multidisciplinary experience in perioperative hemodynamic management⁴.

Available data on perioperative risk in PAH are limited and heterogeneous². Most studies have included mixed PH populations, emergency procedures, or patients lacking complete hemodynamic profiling⁹. IPAH-specific data remain scarce¹⁰. Moreover, there is insufficient evidence on whether baseline hemodynamic parameters, such as mean pulmonary artery pressure (mPAP), PVR, or cardiac output (CO), predict adverse perioperative outcomes in elective surgery. This gap limits the development of structured risk stratification models for this high-risk population⁵.

The objective of this study was to characterize perioperative outcomes in a well-defined cohort of adult patients with confirmed IPAH undergoing elective non-cardiac surgery. We also describe preoperative hemodynamic indices and explore their descriptive associations with postoperative events. By providing a focused analysis of this rare patient group, we aim to inform clinical decision-making and support future investigations on perioperative risk modification in IPAH.

Methods

Study Design and Patient Population

This retrospective case series included adult patients with IPAH, a subtype of WHO Group I PH, under regular follow-up at University Hospitals Leuven, one of two national PAH reference centers in Belgium¹. Patients who underwent elective non-cardiac surgical procedures between January 1992 and June 2023 were included. IPAH diagnosis was established by RHC, defined at the time of diagnosis by a mPAP ≥ 25 mmHg and pulmonary artery wedge pressure (PAWP) ≤ 15 mmHg at rest, in accordance with prevailing guidelines during the study period³. Although recent guidelines have lowered the diagnostic mPAP threshold to >20

mmHg (ESC/ERS 2022), this updated criterion was not applied retrospectively in the present study⁴. Two patients with borderline mPAP values were retained due to consistent hemodynamic documentation and PAH-specific treatment initiated by specialized centers; this is addressed in the limitations.

Patients were excluded if they had WHO Group II–V PH, underwent emergency procedures without completed preoperative RHC, or had previously undergone lung or heart transplantation. Of 182 screened patients, 146 were excluded based on predefined criteria, resulting in 36 patients and 61 procedures included in the final analysis.

Ethical Approval

The study was approved by the Ethics Committee Research UZ/KU Leuven (S64278; Chair: Prof. Dr. L. Helsen; 18/12/2023). Due to the retrospective design and anonymized data collection, informed consent was waived.

Data Collection

Collected variables included demographic characteristics (age, sex, body mass index), comorbidities, and preoperative New York Heart Association (NYHA) functional class where available. Most patients received PAH-targeted combination therapy.

Hemodynamic data were extracted from preoperative RHC reports and included mPAP, PVR, CO and CI. Because diagnosis of IPAH required documented RHC at baseline, preoperative hemodynamic parameters (mPAP, PVR, CO, and CI) were extracted from the most recent catheterization prior to surgery³. These data were available for the majority of the 61 procedures, with missing values in 3 to 5 cases per parameter; pairwise deletion was applied where applicable.

CI was categorized into low (<2.0 L/min/m²), intermediate (2.0–2.4), and high (≥ 2.5) risk groups according to ESC/ERS 2022 guidelines⁴. Six-minute walk distance (6MWD) and cardiopulmonary exercise testing (VO₂ max) were not systematically performed within 6 months before or after surgery in any patient and were therefore excluded⁵. Their omission avoided bias from outdated or inconsistently documented measurements. CI, available for all patients, served as the primary functional indicator⁵. Postoperative hemodynamic values were available in a minority of cases and are reported descriptively.

Surgical procedures were classified by anatomical region (e.g., abdominal, urological, vascular). Both anesthetic technique (general, regional, or combined) and surgical center type

(secondary, tertiary, or quaternary/cardiac) were systematically documented for all cases.

ICU admissions were classified as planned if scheduled preoperatively; all others were labeled unplanned. Hospital and ICU lengths of stay were recorded. Prolonged hospitalization was defined pragmatically based on deviation from the expected postoperative course, typically related to increased oxygen demand or unplanned ICU admission¹¹.

Data were retrieved through electronic patient record review using the KWS and COZO platforms, allowing access to both institutional and external surgical records. All data were collected and reviewed manually from the institutional electronic health records system and surgical databases.

Outcome Measures

The primary outcome was 30-day all-cause mortality. Secondary outcomes included 90-day all-cause mortality, unplanned ICU admission, prolonged hospitalization, and occurrence of major perioperative complications (acute right heart failure, arrhythmias, respiratory failure, or reintervention within 90 days). Outcomes were summarized descriptively. No formal adjustment for confounding was performed due to sample size limitations and the descriptive nature of the study.

Statistical Analysis

Continuous variables were summarized using medians and interquartile ranges (IQR). Categorical variables were presented as counts and percentages. Differences between groups were explored using Mann–Whitney U tests or Fisher’s exact tests, depending on variable type and sample size. Logistic regression was limited to three pre-specified exploratory covariates: mPAP, PVR, and unplanned ICU admission. No multivariable

modeling was performed. Missing data were handled using pairwise deletion. All statistical analyses followed institutional standards using SPSS (version 29.0).

Results

Patient Characteristics

Of the 182 patients initially screened, 146 were excluded due to duplication (n = 22), absence of surgery (n = 98), missing anesthesia records (n = 3), or a history of lung or heart transplantation (n = 7). An additional 16 were excluded due to incomplete documentation or emergency surgery without preoperative PAH-specific hemodynamic evaluation. The final cohort included 36 patients who underwent 61 elective non-cardiac surgical procedures between 1992 and 2023.

The median age at surgery was 66 years (IQR 41–74), and 62.3% of procedures were performed in male patients. Documented comorbidities included systemic hypertension, obesity, chronic obstructive pulmonary disease (COPD), and chronic kidney disease (CKD).

At the time of surgery, 80.3% of procedures were performed in patients receiving PAH-targeted therapy. The most frequently used agents included PDE5i (60.7%), ERA (59.0%), sGC (19.7%), and PCA (13.1%). These treatments were administered either as monotherapy or in combination⁶. Anticoagulant therapy was prescribed in 70.5% of procedures. Long-term oxygen therapy was documented in 9.8%¹¹. The proportions of patients receiving PAH-specific monotherapy, combination therapy, or no therapy are shown in Table I. NYHA functional class was available in 56 of the 61 procedures. Of these, 59.6% were classified as NYHA I–II, 33.3% as NYHA III, and 7.0%

Table I. — Preoperative PAH-targeted therapies and additional medications. Reports the proportion of patients receiving PAH-specific monotherapy or combination therapy at the time of surgery. Also includes the use of anticoagulants and long-term oxygen therapy.

Demographics		mean	median	
Number of patients	36			100%
Number of interventions	61			100%
Age (years)	61	54.33	66	
Sex (% male)	36			62.3%
NYHA classification				
NYHA I–II	34			59.65%
NYHA III	19			33.33%
NYHA IV	4			7.02%
Abbreviations: VKA = vitamin K antagonist; NOAC = non-vitamin K oral anticoagulant; LMWH = low molecular weight heparin; PDE5i = phosphodiesterase type 5 inhibitor; ERA = endothelin receptor antagonist; PCA = prostacyclin analog; NO = nitric oxide; sGC = soluble guanylate cyclase.				

as NYHA IV. In five procedures (8.2%), NYHA classification was not recorded. These omissions were primarily due to incomplete documentation or procedures performed at external surgical sites without standardized preoperative functional assessment.

Hemodynamic Data

Preoperative pulmonary hemodynamic parameters were available for all patients. The mPAP was 58.0 ± 22.6 mmHg, with a range of 17 to 90 mmHg. The mean preoperative CO was 5.3 ± 1.4 L/min (range: 2.6–7.3), and the mean PVR was 8.4 ± 3.0 Wood units (range: 5.2–16.6).

Postoperative hemodynamic measurements were available in a limited number of patients. Among those, mPAP increased to a mean of 63.6 ± 19.0 mmHg (range: 37–88), and CO decreased slightly to 5.2 ± 1.5 L/min (range: 3.5–8.8). Due to incomplete documentation and heterogeneous timing of these assessments, postoperative values were excluded from formal group comparisons.

CI was calculated for all patients and categorized according to ESC/ERS 2022 risk criteria⁴. Based on this classification, 44.3% of procedures were performed in patients with low-risk CI values (≥ 2.5 L/min/m²), 27.9% in intermediate-risk (2.0–2.4), and 27.9% in high-risk (< 2.0). CI

served as the principal marker of functional status, given the absence of systematic 6MWD or VO₂ max measurements within six months before or after surgery⁵. The distribution of preoperative hemodynamic values, including mPAP, PVR, CO, and CI, is summarized in Table II.

RV dysfunction was commonly documented on preoperative imaging, with findings ranging from mild dilation and preserved systolic function to severe enlargement with impaired contractility. Postoperative RV function was assessed in a minority of cases and was not included in the comparative analysis due to limited availability and inconsistent reporting.

Perioperative Outcomes

The 30-day all-cause mortality rate was 1.6% (1/61 procedures), and the 90-day mortality rate was 4.9% (3/61)⁹. The 30-day death occurred following surgery at a secondary care center⁷. All 90-day deaths were observed in patients with elevated preoperative PVR and mPAP compared to the overall cohort⁵.

Unplanned ICU admission occurred in 4 procedures (6.6%), all prompted by hemodynamic instability or respiratory deterioration. These cases were associated with poorer clinical outcomes, including prolonged hospitalization and increased

Table II. — Patient demographics and baseline clinical characteristics.

Summarizes sex, age at time of surgery (median, IQR), NYHA functional class, and distribution of comorbidities. NYHA classification was not available in all cases due to missing documentation in historical records.

	n	Percentage
Anticoagulation at intervention		
VKA	18	29,5%
NOAC	3	4,9%
Low-dose acetylsalicylic acid	15	24,6%
LMWH	4	6,6%
Combination	3	4,9%
None	18	29,5%
PH drugs pre-intervention		
Monotherapy		
PDE5i	4	6,6%
ERA	9	14,8%
PCA	1	1,6%
NO-inhalation	1	1,6%
sGC stimulator	0	0%
None	12	19,67%
No PAH-specific therapy	9	14,8%
Combination therapy		
Any combination	37	60,7%
Use of PAH therapies in combination		
Uses PDE5i in combination with other	37	60,7%
Uses ERA in combination with other	36	59,0%
Uses sGC stimulator in combination with other	12	19,7
Uses PCA in combination with other	8	13,1%
Oxygen therapy at intervention	6	9,83%

mortality⁵. In contrast, 6 procedures (9.8%) included a planned postoperative ICU stay. ICU admission status was typically documented in preoperative planning records, although anticipated ICU duration was rarely specified. The length of ICU stay varied substantially across patients.

Prolonged hospitalization occurred in 11 procedures (18.0%) and was most often related to increased postoperative oxygen requirements or complications necessitating unplanned ICU admission¹¹. The median additional length of stay was two days. No specific preoperative variable showed a statistically significant association with prolonged hospitalization or unplanned ICU admission.

Associations with Outcomes

Univariate analyses revealed a non-significant trend toward increased perioperative mortality in patients with elevated mPAP (≥ 60 mmHg) and PVR (>700 dyn·s/cm⁵), although neither reached statistical significance (mPAP: $p = 0.09$; PVR: $p = 0.12$)⁵. Similarly, patients experiencing unplanned ICU admission or prolonged hospitalization had numerically higher preoperative mPAP and PVR, and lower Co, compared to the remainder of the cohort⁵. Group comparisons for continuous

variables were performed using the Mann–Whitney U test; categorical variables were compared using Fisher’s exact test. These parameters are summarized in Figure 1 and Table III.

Patients with adverse outcomes, defined as unplanned ICU admission or 90-day mortality, demonstrated a lower median cardiac index and higher PVR at baseline⁵. CI <2.0 L/min/m² was more frequently observed in these individuals (42.9% vs. 25.0% in those without adverse events), although the difference was not statistically significant ($p = 0.11$)⁴. Similarly, PVR >800 dyn·s/cm⁵ was observed in 71.4% of those with adverse outcomes versus 47.7% in the remaining cohort ($p = 0.13$)⁴. No meaningful association was identified between prolonged hospitalization and any individual hemodynamic variable when assessed independently.

A limited univariate logistic regression analysis was performed to explore associations between selected baseline variables and the composite endpoint of 90-day mortality or unplanned ICU admission. Covariates were restricted to mPAP, PVR, and unplanned ICU admission due to the small number of outcome events ($n = 4$), precluding multivariable adjustment. No individual variable reached statistical significance (all $p > 0.05$), though unplanned ICU admission was associated

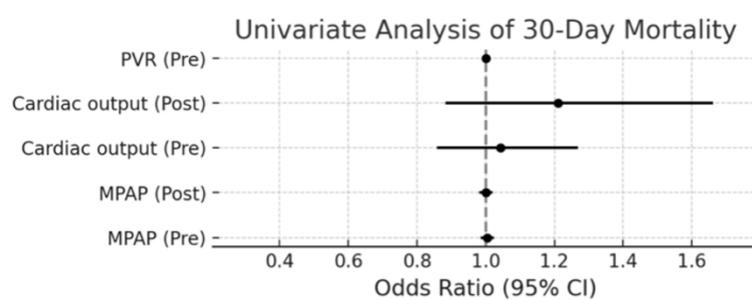


Fig. 1 — Forest plot showing univariate logistic regression analysis of 30-day mortality. Odds ratios with 95% confidence intervals (CI) are shown for mPAP, PVR, and CO.

Table III. — Perioperative outcomes following 61 elective non-cardiac procedures in 36 patients with idiopathic pulmonary arterial hypertension (IPAH).

Reports 30-day and 90-day all-cause mortality, planned versus unplanned ICU admissions, and the number of procedures associated with prolonged hospitalization. Prolonged hospitalization was pragmatically defined as deviation from expected postoperative recovery, typically involving increased oxygen demand or unplanned ICU transfer.

Mortality	Number of procedures	% of total procedures (n=61)
30-day all-cause mortality	1	1.6%
90-day all-cause mortality	3	4.9%
ICU admission		
Unplanned ICU admission	4	6.6%
Planned ICU admission	6	9.8%
No ICU admission	51	83.6%
Prolonged stay	8	13.1%

with an odds ratio (OR) of 4.1 [95% CI: 0.8–21.3] for 90-day mortality⁶.

These findings highlight a consistent numerical trend toward increased risk in patients with elevated preoperative hemodynamic burden, though limited by sample size and statistical power⁵. These parameters are summarized in Figure 1. Figure 2 displays the unadjusted odds ratios with 95% confidence intervals for selected covariates. The figure confirms that none of the tested covariates were statistically associated with 90-day mortality.

Discussion

This retrospective case series highlights the persistent perioperative risk despite advances in targeted medical therapies in patients with IPAH undergoing elective non-cardiac surgery⁶. While the observed 30-day mortality rate of 1.6% is lower than historically reported rates of 4–7% in similar populations, this increased to 4.9% at 90 days, which reflects the continued postoperative risks and highlights the need for structured longitudinal care and follow-up⁹.

Unplanned ICU admissions occurred more frequently in patients with prolonged hospitalization and 90-day mortality, although no variable reached statistical significance in regression analysis⁶. This observation is consistent with previous reports describing acute postoperative deterioration in IPAH patients undergoing elective non-cardiac surgery¹⁰. Patients requiring unplanned ICU admission had numerically higher mPAP and PVR and lower CO at baseline, although these

differences did not reach statistical significance⁵. The co-occurrence of unplanned ICU admission and elevated preoperative hemodynamic burden underscores the potential importance of anticipatory planning, multidisciplinary involvement, and early postoperative surveillance in this high-risk group⁷.

Elevated preoperative PVR and mPAP, as well as lower CO, were more common in patients with adverse outcomes including unplanned ICU admission, prolonged hospitalization, or 90-day mortality, although none of these differences reached statistical significance, likely due to the limited sample size⁴. These parameters may warrant further investigation in prospective studies aimed at improving preoperative risk assessment in IPAH patients⁵. No statistically significant association was observed between specific preoperative hemodynamic thresholds and prolonged hospitalization when assessed independently. This may reflect the complex, multifactorial nature of prolonged recovery in IPAH patients, which is often influenced by comorbidities, institutional protocols, or postoperative complications not solely driven by preoperative physiology¹¹.

The single 30-day death occurred following surgery at a secondary care center. While this may raise concern, the small sample size and observational design preclude any causal inference regarding institutional effect. This may reflect differences in perioperative protocols or available expertise rather than inherent institutional capacity. Nonetheless, this observation may support the rationale for referring IPAH patients to experienced centers with specialized anesthetic and postoperative care

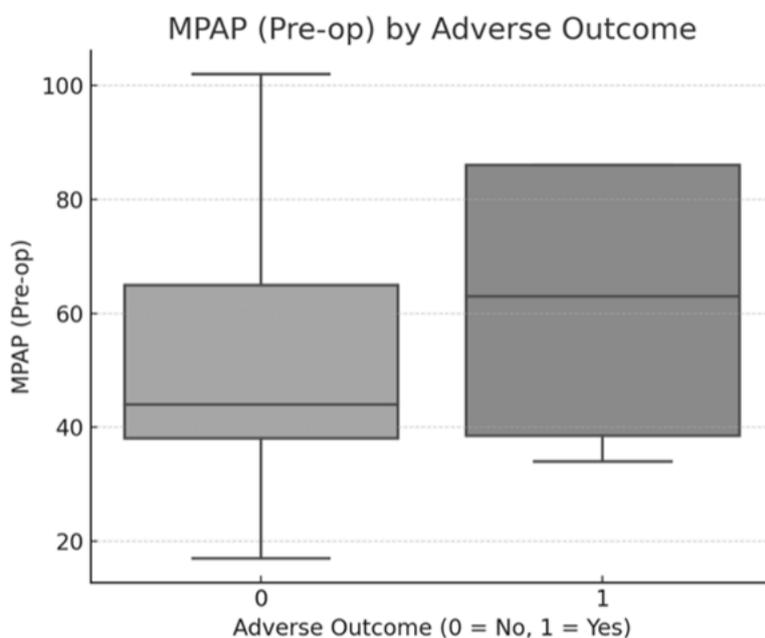


Fig. 2 — Boxplot of preoperative mPAP in patients with and without adverse outcomes. Adverse outcome: unplanned ICU admission or 90-day mortality. Whiskers denote 1.5× IQR.

protocols, pending confirmation in larger cohorts⁷.

Although ICU length of stay was recorded for all patients, the absence of standardized documentation regarding anticipated ICU duration limited the ability to assess deviations from planned postoperative care. In most cases, the records indicated whether ICU admission was planned or unplanned, but rarely included a predefined expected duration. Furthermore, decisions to extend or abbreviate ICU monitoring were frequently made in real time based on evolving clinical status, and were not systematically recorded in the medical charts. This limitation, inherent to the retrospective design, may have obscured relevant differences in postoperative trajectories and highlights the need for prospective studies with structured perioperative planning and documentation in IPAH patients⁷.

The observed 13.1% rate of prolonged hospitalization was largely attributable to increased oxygen demand, a finding consistent with RV dysfunction and impaired pulmonary reserve seen in IPAH¹¹. While this did not statistically correlate with any specific preoperative variable, its clinical significance remains high, particularly in terms of hospital resource use and discharge planning.

Study Limitations

This study has several limitations. First, the retrospective design limits causal inference and is inherently subject to selection and information bias⁷. Although data collection was systematic, the accuracy of retrospective chart review is constrained by variability in clinical documentation, particularly regarding postoperative course and ICU planning⁷.

Second, the single-center setting in terms of patient follow-up restricts external generalizability. Although patients were consistently followed for their IPAH at University Hospitals Leuven, the diverse range of surgical centers involved means that variations in perioperative protocols and resource availability could have influenced patient outcomes. This variability limits the ability to extrapolate our findings to other healthcare settings or centers without similar expertise in IPAH management⁷.

Third, the relatively small sample size limited statistical power, especially for detecting associations with low-frequency outcomes such as 30-day mortality. Furthermore, the interpretation of 90-day mortality as an extended outcome was complicated due to the limited number of cases. Due to the infrequent occurrence of mortality, time-to-event analysis (e.g., Kaplan–Meier survival analysis) was not feasible. This constrained multivariable analysis to a small set of prespecified covariates, precluding comprehensive adjustment

for confounding factors.

Fourth, perioperative hemodynamic measurements were not uniformly available for all patients. While preoperative data were documented in most cases, postoperative hemodynamics were only available in a subset. This may have introduced bias or misclassification, particularly in assessing trends over time or in relation to outcomes⁷.

Finally, although ICU admission status was often documented, the lack of standardized documentation regarding expected ICU length of stay hindered retrospective evaluation of deviation from planned care⁷. Dynamic in-hospital decisions and undocumented rationale further complicated interpretation of ICU resource use and its impact on outcomes.

Conclusion

Patients with IPAH undergoing elective non-cardiac surgery remain at increased perioperative risk despite advances in disease-specific therapies⁶. In this study, 30-day and 90-day mortality were 1.6% and 4.9%, respectively. Although no preoperative hemodynamic parameter emerged as an independent predictor, patients with elevated pulmonary vascular resistance and mean pulmonary artery pressure had numerically more adverse outcomes⁵.

Unplanned ICU admission occurred more frequently in patients with increased mortality and prolonged hospitalization, suggesting that unexpected postoperative deterioration may contribute to worse outcomes⁶. These findings support the relevance of anticipatory perioperative planning, including preoperative risk stratification, multidisciplinary coordination, and postoperative respiratory monitoring⁷.

The observation that the single 30-day death occurred following surgery at a secondary care center may support referral to expert centers familiar with the disease's hemodynamic complexity, although this finding requires confirmation in larger cohorts⁷. While statistical power was limited due to small sample size, the observed trends suggest clinically relevant vulnerabilities that may inform individualized decision-making in future studies⁵. Larger, prospective multicenter studies are needed to validate these exploratory findings and improve evidence-based perioperative strategies in this population⁷.

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