Outcomes After Noncardiac Surgery For Patients With Pulmonary Hypertension: A Historical Cohort Study

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Abstract

Abstract Background: Pulmonary hypertension (PH) is a significant preoperative risk factor. We aimed to determine predictors of perioperative morbidity and mortality after noncardiac surgery for patients with precapillary PH. Methods: We conducted a retrospective cohort study of adults with pulmonary hypertension having surgery at a single large medical referral center. The PH and surgical databases were reviewed from 2010 to 2017. Patients were excluded if PH was attributable to left-sided heart disease or they had undergone cardiac or transplant operations. To assess whether PH-specific diagnostic or cardiopulmonary testing parameters were predictive of perioperative complications, analyses were performed using generalized estimating equations. Results: Of 196 patients with PH undergoing noncardiac operations, 53 (27%) experienced 1 or more complications, including 5 deaths (3%) within 30 days. After adjustment for age and PH type, there were more complications in those undergoing moderate-to-high vs low-risk procedures (odds ratio [OR], 4.17 [95% CI, 2.07 to 8.40]; P<0.001). After adjustment for age, surgical risk, and PH type, the risk for complications was higher for patients with worse functional status (OR, 2.39 [95% CI, 1.19 to 4.78]; P=0.01 for class 3/4 vs class 1/2) and elevated serum N-terminal fragment of the prohormone brain natriuretic peptide (NT-proBNP) (OR, 2.28 [95% CI, 1.05 to 4.96]; P=0.04 for ≥300 vs. <300 pg/mL). From an analysis that included covariates for age, surgical risk, and functional status, elevated serum NT-proBNP levels remained associated with increased risk (OR, 2.23 [95% CI, 1.05 to 4.76]; P=0.04). Conclusions: Patients with PH undergoing noncardiac surgery with general anesthesia have a high frequency of perioperative complications. Specific clinical (functional status), diagnostic (serum NT-proBNP), and intraoperative factors (higher-risk surgery) are predictive of worse outcomes.

Background

Patients with pulmonary hypertension (PH) are at increased risk for perioperative morbidity and mortality [1-3], and PH is an independent risk factor for complications after noncardiac surgery [4]. Besides the intrinsic, complex cardiopulmonary pathologic conditions associated with PH, numerous comorbid conditions can substantially contribute to adverse outcomes [5]. These systemic conditions, together with pathology related to PH, may predispose patients to complications such as acute right ventricular failure, dysrhythmias, coronary ischemia, respiratory failure, and stroke [1, 2, 6].

A substantial morbidity can occur after cardiopulmonary operations in patients with PH [1, 2, 7-10]. However, few studies have analyzed the relationship between clinical presentation of PH and outcomes after noncardiac surgery [6, 11]. Likewise, whether specific patient and disease characteristics predict perioperative outcomes for these patients is not well known. Our primary aim was to evaluate morbidity and mortality in a contemporary cohort of adult patients with PH undergoing noncardiac surgery and to explore the association between clinical and diagnostic parameters and morbidity and mortality.

Methods

This study conformed to the requirements of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement, it was approved by the Mayo Clinic Institutional Review Board (**IRB #:** 15-009560). The study is approved by the expedited review procedures (45 CFR 46.110, item 5) on December 28, 2015. All included patients gave consent to be included in the study.

Study Population

Patients with PH, 18 years and older, were identified from the Mayo Clinic Pulmonary Hypertension database with rationale that patients in registry have complete and detailed assessments of their PH. These patients were cross-referenced with those in the anesthesia electronic database to identify all patients who had undergone noncardiac, nontransplant operations with general anesthesia between February 10, 2010, and December 8, 2017.

This study included patients with groups 1, 3, or 4 PH. Because of fundamental differences in pathophysiologic changes, including in right ventricular afterload in postcapillary PH, patients with established group 2 PH (pulmonary venous hypertension) were not included [12]. Patients were categorized into group 1 (pulmonary arterial hypertension), group 3 (PH due to lung diseases or hypoxia, or both), or group 4 (chronic thromboembolic PH), according to the Nice PH classification criteria [13]. World Health Organization (WHO) classifications were used to describe the functional classes of disease [14, 15]: class I, no physical activity limitation; class II, slight limitation but comfortable at rest; class III, marked limitation of physical activity but comfortable at rest; less than ordinary physical activity causes dyspnea, fatigue, chest pain, or near syncope; and class IV, patients are unable to carry out any physical activity without symptoms.

Data Retrieval

Medical, surgical, and anesthesia records were electronically abstracted using previously described proprietary software [16, 17]. Information unavailable electronically was abstracted manually by two authors (AD and MS).

Comorbid Disease

The burden of comorbid diseases was determined from the components of the Charlson comorbidity index [18] (individual components are listed in Table 1). Relevant preoperative medications were also recorded (Table 1).

Clinical Testing Parameters

Severity of PH was also assessed from clinical testing. The results of the closest test obtained prior to surgery were considered. The results of the 6-minute walk test were dichotomized (≥330 vs. <330 meters). N-terminal fragment of the prohormone brain natriuretic peptide (NT-proBNP) is a biochemical marker used in risk stratification of patients with congestive heart failure [19]. NT-proBNP was dichotomized using a cut point of <300 pg/mL which has been shown to have a 99% negative predictive value for excluding acute congestive heart failure, although this diagnostic utility is hampered by impaired renal function.[20] Spirometry results were considered abnormal when the forced expiratory volume in the first second of expiration (FEV_1) was <80% of predicted, the forced vital capacity <70% of predicted, and/or diffusing capacity ≤80% of predicted. Transthoracic 2-dimensional echocardiography (2DE) results included ejection fraction, diastolic dysfunction, right ventricular (RV) enlargement or hypertrophy, estimated RV systolic pressure (RVSP), and RVSP as a ratio of systemic systolic blood pressure (RVSP/SBP). PH was considered moderate if the RVSP/SBP was <0.66 or severe if the RVSP/SBP was ≥0.66. We also report tricuspid annular plane systolic excursion (TAPSE), a parameter of RV systolic function, which is used as a prognostic factor in PH [21, 22]. Patients were divided into higher risk (TAPSE <18 mm), and lower risk (TAPSE ≥18mm) [22, 23]. Another indicator of RV systolic dysfunction is RV peak systolic strain, with the following reported reference ranges: normal/mild reduction, ≥ -20%, moderately abnormal, -15% to -19%; and severe, 0% to -14%.[23, 24] 6) Information gathered from right-sided heart catheterization were mean pulmonary artery pressure (mean PAP), from which PH was graded as mild (25 to 40 mm Hg), moderate (41 to 55 mm Hg), or severe (>55 mm Hg), and right atrial pressure with values <10 mm Hg considered as mild to moderate PH; and ≥10 mm Hg, severe PH.

Anesthesia and Surgical Characteristics

Procedures were categorized as low-risk, and intermediate to high risk operations (Table 3). We reviewed the duration of surgery, anesthetic agents used, and vasoactive pharmacologic treatments.

Outcome Measures

In addition to 30-day mortality, we considered in-hospital complications, specifically, major cardiovascular, pulmonary, neurologic, and renal complications (increased postoperative serum creatinine within 48 hours of ≥0.3 mg/dL from the preoperative value [25] or increased serum creatinine >1.3 mg/dL after surgery). We also considered all surgical complications (bleeding, newly developed coagulopathy, and reoperation for any reason); or other complications primarily related to existing pathology at the time of surgery (e.g., postoperative sepsis or septic shock in a patient undergoing surgery for gangrenous gallbladder).

Statistical Analyses

Patient and procedural characteristics were summarized for all qualifying operations using count and percentage for nominal or dichotomous variables and mean (SD) or median and interquartile range (IQR) for continuous variables. Perioperative complications were categorized as cardiovascular, pulmonary, neurologic, renal, and other. To assess whether PH-specific diagnostic or cardiopulmonary testing parameters were predictive of perioperative complications, a series of analyses were performed. Since some individuals underwent multiple surgeries during the study period these analyses were performed using generalized estimating equations (GEE). For these models, the dependent variable was any complication or death within 30 days. The GEE analyses were performed with a logit link function using robust standard error estimates. For each diagnostic and testing parameter, patients were grouped using predetermined categories. Each characteristic was assessed by univariate analysis and also after adjusting for age, surgical risk (low vs intermediate/high), and WHO group (PH 1 vs 3 vs 4). Because impaired renal function may hamper NT-proBNP diagnostic utility, we excluded patients with serum creatinine levels >2 mg/dL from the analysis of NT-proBNP. Findings from all analyses were summarized using odds ratios (OR) and corresponding 95% CI. In all cases, $P<.05$ was used to denote statistical significance. Analyses were performed with the R statistical package (The R Foundation) [26].

Results

During the study period, 131 individuals with PH underwent 196 operations that met study criteria. Of these, 89 individuals underwent 1 operation; 29 underwent 2 operations; 7 underwent 3 operations; 2 underwent 4 operations; and 4 underwent 5 operations. Baseline patient data for the 196 surgeries are summarized in Table 1. The mean (SD) patient age was 59.0 (14.9) years. The comorbidity burden and use of vasoactive medications was high, as would be expected for this patient population. The diagnostic and hemodynamic variables for PH are summarized in Table 2. Of the 196 patients, 144 (74%) had group 1 PH; 27 (14%), group 3 PH; and 25 (13%), group 4 PH. The WHO functional classification was class I/II for 115 (59%) patients and class III/IV for 81 (41%). NT-proBNP levels were available before the surgical procedure for 144 patients and were elevated (≥300 pg/mL) for 79 (55%) patients. Other echocardiographic and right-sided heart catheterization parameters were similarly reflective of a mix of patients with various stages of PH (Table 2). Procedural characteristics are described in Table 3. There were 108 (55%) low-risk and 88 (45%) intermediate or high-risk operations. Most (98.5%) operations were

performed using general anesthesia with volatile agents. Pulmonary vasodilators were used during 165 (84%) cases, and vasopressor infusions were used during 161 (82%) cases (Table 3).

Fifty-three patients (27%) had 1 or more perioperative complications (Table 4). Among these patients were 32 (16%) who had major cardiovascular complications, including 2 patients (1%) who had cardiac arrest; 28 (14%) had severe pulmonary complications; and 23 (12%) had other complications.

From analyses adjusting for patient age and WHO PH group, the rate of complications was higher for patients who underwent intermediate/high vs low-risk procedures (OR, 4.17 [95% CI, 2.07 to 8.40]; $P<0.001$). Results from analyses assessing whether other preoperative diagnostic and hemodynamic variables were associated with postoperative complications are presented in Table 5. After adjusting for age, surgical risk, and type of PH, the risk for complications was found to be higher for patients with worse WHO functional class (OR, 2.39 [95% CI, 1.19 to 4.78]; $P=0.01$ for class III/IV vs class I/II) and elevated NT-proBNP serum levels (OR, 2.28 [95% CI, 1.05 to 4.96]; $P=0.04$ for ≥300 pg/mL vs <300 pg/mL). No other echocardiographic or right-sided heart catheterization parameters were found to be significantly associated with complications. To assess whether elevated serum NT-proBNP level was independently predictive of complications after adjusting for functional class, an analysis was performed that included covariates for age, surgical risk, and WHO PH functional class. From this analysis, elevated NT-proBNP serum level was still found to be associated with an increased risk for complications (OR, 2.23 [95% CI, 1.05 to 4.76]; $P=.04$).

Emergency Procedures

A total of 13/196 (6.6%) procedures were emergent. Of these, 8 (62%) were associated with perioperative complications, and 2 (15%) patients died. In the nonemergency group, there were 183 procedures with 45 (25%) complications, including 3 (2%) that resulted in the patient's death. The difference in the rate of complications between emergent vs nonemergent procedures was significant ($P=0.008$). From an analysis that included only nonemergency surgery and that was adjusted for age, surgical risk, and type of PH, the risk for complications was shown to be higher for patients with worse WHO functional class (OR, 2.72 [95% CI, 1.28 to 5.78]; $P=0.009$ for class III/IV vs class I/II).

30-Day Mortality

Five patients (3%), 4 females and 1 male, age range between 43 and 65 years, died within 30 postoperative days (Table 6). The limited number of deaths in our series precluded performing analyses to assess predictors of mortality.

Discussion

Among patients with different types of PH undergoing noncardiac surgery, 27% had at least 1 major complication, and 3% died within 30 days. In addition to high risk surgery, independent predictors for postoperative complications were WHO functional class III/IV, elevated serum levels of NT-proBNP.

Perioperative Morbidity and Mortality

Information regarding perioperative morbidity and mortality of patients with PH undergoing noncardiac surgery is scarce. In our earlier report [6], which used a similar study design, we reported a 42% complication rate for PH

patients who underwent noncardiac surgery between 1991 and 2003. In the present study the rate of perioperative complications between 2010 and 2017 is lower, 27%. Compared with our earlier study,[6] the present cohort included a higher proportion of patients with advanced stages of PH (41% of patients were in WHO functional class III/IV in the present study vs 27% of patients in the earlier study[6] who were in New York Heart Association functional class III and IV). At the same time, in the present study, 45% of patients underwent high-risk procedures compared with 79% in the earlier study [6]. PH functional class and exposure to higher-risk procedures are the 2 main determinates of surgical outcomes in patients with PH, and because these risks were divergently distributed between the 2 study epochs, it is difficult to comment as to whether the decreased rate of complications in the present study was related to advances in management over the decades or to an imbalance of risk factors between the 2 cohorts.

Perioperative mortality for patients with PH is difficult to compare across studies because of methodologic differences. For patients with PH, 30-day mortality in our institution from 1991 to 2003 was 7% [6], and from 2010 to 2017, it was 3% (Table 6). Other reported mortality rates for PH after noncardiac surgery were 18% between 1996-2002 [27], 7% between 2000-2007 [28], and 4% between 2007 and 2010 (15% for emergency and 2% for nonemergency procedures) [11].

Predictors of Morbidity

Price et al. [28] reported that risk factors for perioperative complications in patients with PH undergoing noncardiac surgery were greater for emergency, major, and longer surgery. In the present study, we confirmed that the acuity of surgery is an important predictor of morbidity, and patients undergoing intermediate/major operations had 4.2 times increased likelihood for experiencing a perioperative complication than patients undergoing minor procedures. Furthermore, patients in functional class III/IV had a 2.4 times higher likelihood of experiencing a complication than patients in class I/II. This mirrors our earlier finding that New York Heart Association class ≥II in patients with PH was associated with an odds ratio of 2.9 for development of postoperative complications [6]. Finally, in the present study, only 13 patients underwent an emergency operation, and they had higher complication (62%) and mortality (15%) rates than patients undergoing nonemergency procedures.

NT-proBNP is released from ventricular myocytes in response to mechanical stretching related to increased ventricular pressure or volume overload and has been used as a surrogate marker for ventricular failure [29]. In our study, an elevated NT-proBNP level was a predictor of perioperative complications. Specifically, an NT-proBNP serum level ≥300 ng/mL was associated with 2.2-fold higher odds for developing a complication even after we adjusted for age, type of surgery, and WHO functional class.

Different functional tests, echocardiographic variables, and cardiac catheterization parameters were formerly used to predict long-term outcomes for nonsurgical patients with PH [22, 30, 31]. For example, Miyamoto et al. [31] demonstrated that the 6-minute walk test was predictive of mortality for patients with primary PH during a mean follow-up period of 21 months. Forfia et al. [22] showed TAPSE to be a good long-term predictor of mortality for patients with PH. Several studies showed that abnormal 6-minute walk and 2DE parameters were predictive of increased perioperative morbidity and mortality [11, 32]. For example, TAPSE <18 mm was found to be an independent predictor of intraoperative cardiopulmonary resuscitation and death in patients undergoing emergent pulmonary embolectomy [21]. In our study, none of the selected parameters derived from the pulmonary and cardiac tests was found to be a statistically significant predictor of perioperative morbidity, which is similar to findings from our previous study [6]. However, it is noteworthy that for pulmonary function tests, echocardiography,

and right-sided heart catheterization variables (RV enlargement, RVSP/SBP ratio, RV strain, TAPSE), the point estimates are directionally consistent with the premise that worse PH stage may be associated with a higher likelihood for perioperative complications. Since these measurements were not available for all patients the statistical power for these analyses was limited. Therefore, the results for these parameters should not be interpreted as evidence of no association.

Limitations

Our study has inherent limitations related to its retrospective design. Both known and unknown confounding variables may have been present and thus not accounted for in the analyses. We have identified variables associated with morbidity; however, we cannot conclude causality. In this study we included a wide variety of surgical procedures, which implies vastly different surgical acuities. Due to the limited overall sample-size, we cannot perform analyses which adjust for specific surgery types.

Conclusions

In conclusion, patients with PH undergoing noncardiac surgery under general anesthesia had a high frequency of perioperative complications. The main predictors of perioperative morbidity included poor baseline functional status, increased serum NT-proBNP, and higher-risk operations.

Abbreviations

2DE, 2-dimensional echocardiography

FEV_1, forced expiratory volume in the first second of expiration

GEE, generalized estimating equation

IQR, interquartile range

NT-proBNP, N-terminal fragment of the prohormone brain natriuretic peptide

OR, odds ratio

PAP, pulmonary artery pressure

PH, pulmonary hypertension

RV, right ventricular

RVSP, right ventricular systolic pressure

SBP, systemic systolic blood pressure

TAPSE, tricuspid annular plane systolic excursion

WHO, World Health Organization

Declarations

Ethics approval and consent to participate.

Study was approved by the Mayo Clinic Institutional Review Board (**IRB #:** 15-009560). The study is approved by the expedited review procedures (45 CFR 46.110, item 5) on December 28, 2015. All included patients gave consent to be included in the study.

Consent for publication: Not applicable

Availability of data and materials: The datasets generated and analysed during the current study are available from the corresponding author on reasonable request. Juraj Sprung and Darrell Schroeder have full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Competing interests: T.N.W. consults with Medtronic PLC and serves as the PRODIGY trial chairman of the Clinical Events Committee. T.N.W. has received an unrestricted investigator-initiated grant from Merck & Co and research equipment from Respiratory Motion Inc. J.S. expert panelist on Lung Protective Ventilation Forum sponsored by GE-Healthcare. All other authors have nothing to declare.

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Authors' contributions: A.D. and M.S: contributed substantially to the conception/design of the study; data acquisition; drafting of the manuscript; approved the final version of the manuscript. G.C.K., R.P.F., H.M.D., T, N.W, and D.P.M. contributed substantially to interpretation of data for the work; approved the final version of the manuscript. D.R.S. and M.Q.J. conducted: data analysis; interpretation of data; approved the final version of the manuscript. M.Q.J.: data analysis; interpretation of data; final approval of the manuscript. T.N.W.: substantial contributions to the design of the study; interpretation of data; final approval of the manuscript. J.S.: conception/manuscript design; interpretation of data; data analyses; writing the final manuscript version; approval of the final version of the manuscript.

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Tables

Table 1. Demographic characteristics, comorbid conditions, and preoperative treatments

Characteristic	Summary Statistics (N=196)
Age, y, mean (SD)	59.0 (14.9)
Women	150 (77%)
Body mass index, kg/m^2, mean (SD)	29.6 (8.1)
ASA physical status	
III	154 (79%)
IV	42 (21%)
Charlson comorbidity index, median (IQR)	2 [1-4]
Chronic obstructive pulmonary disease	52 (27%)
Obstructive sleep apnea	77 (39%)
History of pulmonary thromboembolism	35 (18%)
Congestive heart failure	34 (17%)
Systemic hypertension	91 (46%)
Coronary artery disease	31 (16%)
History of or current atrial fibrillation	26 (13%)
History of deep venous thrombosis	22 (11%)
History of cerebrovascular disease	18 (9%)
Liver disease	23 (12%)
Renal disease, creatinine ≥1.4 mg/mL	25 (13%)
Connective tissue disease	34 (17%)
Diabetes mellitus	42 (21%)
Hematologic malignancy	6 (3%)
Preoperative anemia[a]	89 (45%)
Home medications	
Home oxygen use	17 (9%)
Diuretics	102 (52%)
b-adrenergic blockers	57 (29%)
ACEI/ARB	51 (26%)
Calcium channel blockers	43 (22%)
Anticoagulants (other than aspirin)	78 (40%)

Digoxin	35 (18%)
Steroids	40 (20%)
PDE_5 inhibitors and GC stimulators	99 (51%)
Prostaglandin analogs	2 (1%)
Endothelin receptor antagonists	75 (38%)

Abbreviations: ACEI/ARB, angiotensin-converting-enzyme inhibitors/angiotensin II receptor blockers; ASA, American Society of Anesthesiologists; GC, guanylate cyclase; PDE_5, phosphodiesterase type 5.

[a] Anemia was defined as hemoglobin ≤13 mg/dL for men and ≤12 mg/dL for women.

Table 2. Diagnostic and hemodynamic variables

Characteristic	N	No. (%)
WHO group	196	
1		144 (74%)
3		27 (14%)
4		25 (13%)
WHO functional classification	196	
Class I/II		115 (59%)
Class III/IV		81 (41%)
6-minute walk distance, m	114	-
Mildly impaired ≥330		81 (71%)
Severely impaired <330		33 (29%)
NT-proBNP, serum, pg/mL	144	-
Normal/mild increase <300		65 (45%)
Severe increase ≥300		79 (55%)
Diffusing capacity, %	138	-
Normal ≥80		24 (17%)
Abnormal <80		114 (83%)
Pulmonary function tests[a]	155	
Normal		32 (21%)
Abnormal		123 (79%)
Ejection fraction, %[b]	193	-
Normal ≥50		189 (98%)
Abnormal <50		4 (2%)
Diastolic dysfunction[b]	196	80 (41%)
RV enlargement[b]	192	163 (85%)
RVSP, mm Hg[b]	188	-
Normal ≤50		56 (30%)
Abnormal >50		132 (70%)
RVSP/SBP ratio, %[b]	187	-
Normal <66		146 (78%)
Abnormal ≥66		41 (22%)
TAPSE, mm[b]	151	-

Normal <18		31 (21%)
Abnormal ≥18		120 (80%)
RV strain, %[b]	116	–
Normal/mild reduction, ≥ -20		80 (69%)
Moderately abnormal, -15 to -19		20 (17%)
Severely abnormal, 0 to -14		16 (14%)
PAP, mean, mm Hg[c]	149	–
Mild increase, <40		64 (43%)
Moderate increase, 41 to 55		56 (38%)
Severe increase, >55		29 (20%)
RA pressure, mm Hg[c]	190	
Mild increase, ≤10		146 (77%)
Severe increase, >10		44 (23%)

Abbreviations: NT-proBNP, N-terminal fragment of the prohormone brain natriuretic peptide; PAP, pulmonary artery pressure; RA; right atrial; RV, right ventricular; RVSP, right ventricular systolic pressure; SBP, systemic systolic blood pressure; TAPSE, tricuspid annular plane systolic excursion; WHO, World Health Organization.

[a] Pulmonary function tests considered abnormal at a forced expiratory volume in the first second of expiration at <80% or forced vital capacity <70%.

[b] Echo-derived parameters.

[c] Cardiac catheterization–derived parameters.

Table 3. Intraoperative variables for 196 patients with pulmonary hypertension undergoing a surgical procedure with general anesthesia

Characteristic	No. (%)
Type of surgery[a]	
Low risk	108 (55%)
Intermediate/high risk	88 (45%)
Duration of surgery, minutes, median (IQR)	84 [50-134]
Type of anesthesia	
All intravenous	3 (2%)
Volatile (isoflurane/sevoflurane/desflurane)	193 (99%)
Emergency procedure	13 (7%)
Monitoring	108 (55%)
Arterial line	107 (55%)
Central line	11 (6%)
Pulmonary artery catheter	11 (6%)
Transesophageal echocardiography	1 (<1%)
Intraoperative drugs and fluids	
Pulmonary vasodilators	165 (84%)
Prostaglandins	13 (7%)
Vasopressor infusions	161 (82%)
b-adrenergic blockers	8 (4%)
Crystalloids/colloids, liters, median (IQR)	1.1 [0.7-1.7]
Packed red blood cells	18 (9%)
Other blood products[b]	9 (5%)

[a] Low-risk (tumor ablation, colonoscopy, procedures in interventional radiology and breast, dermatologic, otorhinolaryngologic, gynecologic, neurologic, plastic/reconstructive, and urologic) operations; and intermediate to high risk (major abdominal, gastrointestinal, orthopedic, thoracic, and vascular) operations.

[b] Fresh frozen plasma, platelets, or cryoprecipitate.

Table 4. Major complications and 30-day mortality (N=196)

Complication	No. (%)
Any complication	53 (27%)
Cardiovascular	32 (16%)
Heart failure	6 (3%)
Dysrhythmia/atrial fibrillation	21 (11%)
Hypotension	14 (7%)
Cardiac arrest	2 (1%)
Pulmonary	28 (14%)
Pneumonia	6 (3%)
Other pulmonary[a]	26 (13%)
Neurologic	8 (4%)
Delirium	7 (4%)
Stroke	1 (<1%)
Acute kidney injury/renal failure	10 (5%)
Other	23 (12%)
Shock	5 (3%)
Sepsis	7 (4%)
Bleeding	8 (4%)
Reoperation for any reason	9 (5%)
30-day mortality	5 (3%)

[a] Defined as acute respiratory distress syndrome, pulmonary edema, respiratory failure not accounted for by other listed causes, or pneumothorax.

Table 5. Univariable and multivariate analysis of complications after noncardiac surgery for patients with pulmonary hypert

Characteristic	No.	Complication, No. (%)[b]	Univariate Analysis			Multivariable Analysis		
			OR	(95% CI)	*P* Value	OR	(95% CI)	*P* Value
Age[c]	196		0.94	(0.74 to 1.17)	0.56	0.84	(0.65 to 1.09)	0.19
Type of surgery	196							
Low risk		18 (17%)	Ref					
Intermediate/high risk		35 (40%)	3.30	(1.74 to 6.26)	<0.001	4.17	(2.07 to 8.40)	<0.001
WHO group	196							
1		43 (30%)	Ref					
3		4 (15%)	0.41	(0.16 to 1.07)	0.07	0.38	(0.14 to 1.01)	0.05
4		6 (24%)	0.74	(0.26 to 2.10)	0.57	0.79	(0.30 to 2.08)	0.63
WHO functional classification	196							
Class I/II		24 (21%)	Ref			Ref		
Class III/IV		29 (36%)	2.11	(1.05 to 4.25)	0.04	2.39	(1.19 to 4.78)	0.01
6-Minute walk distance, m	114							
Mildly impaired, ≥330		20 (25%)	Ref			Ref		
Severely impaired, <330		12 (36%)	1.74	(0.69 to 4.41)	0.24	1.02	(0.33 to 3.19)	0.97
NT-proBNP, serum, pg/mL	144							
Normal/mild increase, <300		14 (22%)	Ref			Ref		
Severe increase, ≥300		28 (35%)	2.00	(0.94 to 4.25)	0.07	2.28	(1.05 to 4.96)	0.04
Diffusing capacity, %	138							
Normal, ≥80		2 (8%)	Ref			Ref		

Abnormal, <80		35 (31%)	4.87	(0.70 to 34.13)	0.11	5.27	(0.80 to 34.62)	0.08
Pulmonary function tests[d]	155							
Normal		7 (22%)	Ref			Ref		
Abnormal		35 (29%)	1.42	(0.54 to 3.76)	0.48	1.69	(0.63 to 4.51)	0.30
Diastolic dysfunction[e]	196							
No		33 (28%)	Ref			Ref		
Yes		20 (25%)	0.84	(0.43 to 1.63)	0.60	0.84	(0.40 to 1.78)	0.65
RV enlargement[e]	192							
No		4 (14%)	Ref			Ref		
Yes		48 (29%)	2.61	(0.69 to 9.80)	0.16	2.86	(0.77 to 10.55)	0.12
RVSP, mm Hg[e]	188							
Mild increase, ≤50		13 (23%)	Ref			Ref		
Severe increase, >50		37 (28%)	1.29	(0.60 to 2.78)	0.52	1.53	(0.70 to 93.32)	0.29
RVSP/SBP ratio, %[e]	187							
Mild/Normal, <66		38 (26%)	Ref			Ref		
Severe increase, ≥66		11 (27%)	1.04	(0.45 to 2.43)	0.92	1.20	(0.45 to 3.17)	0.72
TAPSE, mm[e]	151							
Normal, ≥18		29 (24%)	Ref			Ref		
Abnormal, <18		12 (39%)	1.98	(0.80 to 4.89)	0.14	2.10	(0.81 to 5.43)	0.13
RV strain, %[e]	116							
Normal/mild reduction, ≥ -20		15 (19%)	Ref			Ref		
Moderately abnormal, -15 to -19		6 (30%)	1.86	(0.62 to 5.56)	0.27	3.14	(0.90 to 10.96)	0.07

Severely abnormal, 0 to -14		4 (25%)	1.44	(0.40 to 5.26)	0.58	1.90	(0.45 to 8.09)	0.39
Mean PAP, mm Hg[f]	149							
Mild increase, 25 to 40		16 (25%)	Ref			Ref		
Moderate increase, 41 to 55		19 (34%)	1.54	(0.65 to 3.63)	0.32	1.31	(0.56 to 3.08)	0.54
Severe increase, >55		7 (24%)	0.95	(0.36 to 2.57)	0.93	0.74	(0.28 to 1.98)	0.55
RA pressure, mm Hg[f]	190							
Mild/Moderate increase, ≤10		35 (24%)	Ref			Ref		
Severe increase, >10		16 (36%)	1.81	(0.81 to 4.03)	0.15	2.11	(0.96 to 4.64)	0.06

Abbreviations: NT-proBNP, N-terminal fragment of the prohormone brain natriuretic peptide; OR, odds ratio; CI, confidence PAP, pulmonary artery pressure; RA; right atrial; Ref, reference; RV, right ventricular; RVSP, right ventricular systolic press systemic systolic blood pressure; TAPSE, tricuspid annular plane systolic excursion; WHO, World Health Organization.

[a] Results presented are from generalized estimating equations (GEE) predicting complications after surgery. ORs and corre 95% CIs are presented for both univariate and multivariable analyses. For multivariable analyses, each parameter was asse using GEE in a multivariate model that was adjusted for age, type of pulmonary hypertension, and risk of surgery. Results f type of pulmonary hypertension, and type of surgery are reported from the model, which included only these 3 predictors. C indicate increased likelihood of complications.

[b] Complications, No. (%), were calculated based on the number of patients with the complication in a respective category (e low-risk patients had 18 complications for a complication rate of 17%).

[c] ORs correspond to a 10-year increase in age.

[d] Abnormal when a forced expiratory volume in the first second of expiration is <80% or forced vital capacity is <70%.

[e] Echo-derived parameters.

[f] Cardiac catheterization–derived parameters.

Table 6. Demographic and clinical characteristics of the 5 patients who died within 30 days after surgery

Pt.	WHO Functional Class	Surgery Time, min	Mean PAP, mm Hg	RVSP/SBP	Indication for Surgery	Comorbid Conditions at Death	Cause of Death Death (POD)
1	2	98	35	0.46	Craniotomy to evacuate subdural hematoma	Stage 4 CKD, cirrhosis, esophageal varices, sarcoidosis, AF	Acute coagulopathy, chronic subdural hematoma; POD 4
2	2	135	31	0.53	Small bowel obstruction, ileo-ileal bypass	Cirrhosis and hepatic encephalopathy, AF	Sepsis, acute respiratory distress syndrome; POD 10
3	4	45	51	1.09	Placement of bilateral nephrostomy tubes	Chronic debility and paraplegia, urosepsis, pyelonephritis	Severe septic shock; POD 14
4	3	138	51	0.66	Ileus, open abdominal exploration	Stage 3 AKI	Respiratory failure, AKI, discharged to pursue comfort care; POD 15
5	3	18	48	0.69	Insertion of a tunneled dialysis catheter	End-stage liver disease, stage 3 AKI	Cirrhosis, hepatic encephalopathy, sepsis, kidney and respiratory failure. Dismissed for palliative care; POD 20

Abbreviations: AKI, acute kidney injury; AF, atrial fibrillation; CKD, chronic kidney disease; PAP, pulmonary artery pressure; POD, postoperative day (death); Pt, patient; RVSP/SBP, ratio of right ventricular systolic pressure to systemic systolic blood pressure; WHO, World Health Organization.