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Pulmonary complications after non-cardiac surgeries: temporal patterns and risk factors

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Abstract

Background: Postoperative complications are the primary determinants of survival following major surgery. We aimed to characterize the early perioperative risk factors for postoperative pulmonary complications (POPCs) in patients undergoing major non-cardiac surgeries.

Methods: This study utilized a multicenter prospective observational cohort design. Adult patients undergoing non-cardiac surgeries and admitted to 21 Brazilian ICUs were screened for inclusion in the study. POPCs were defined as the presence of acute pulmonary oedema, nosocomial pneumonia, and extubation failure in the postoperative period.

Results: Of the 581 patients enrolled, 110 (19%) had at least one POPC, of whom 5% had acute pulmonary oedema, 10% extubation failure while 10% had pneumonia. Most cases of pulmonary oedema occurred in the first week after surgery, while pneumonia was more frequently a later occurrence. The mortality rate was significantly higher in the group with POPCs compared to the group of patients without POPCs (62% vs. 11%, RR: 5.1, 95% CI: 4.23–7.69; $P < 0.001$). A low functional capacity (RR: 4.6, 95% CI: 2.1–10.0), major surgery (RR: 3.6, 95% CI: 1.2–10.7), preoperative hemodynamic instability (RR: 3.4, 95% CI: 1.1–10.6), alcoholism (RR: 3.3, 95% CI: 1.0–10.7), unplanned surgery (RR: 2.3, 95% CI: 1.0–5.2), the SOFA score (RR: 1.1, 95% CI: 1.0–1.2), and increased central venous pressure (RR: 1.1, 95% CI: 1.0–1.1) were independent predictors of POPCs.

Conclusions: Pulmonary complications are common in intensive care units after major non-cardiac surgeries. Awareness of the risk factors for POPCs may help multidisciplinary teams develop strategies to prevent these complications.

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Key words: pulmonary complications, postoperative; pneumonia; pulmonary oedema; extubation failure

Pulmonary complications frequently occur after major surgeries, leading to increases in the time spent in the intensive care unit (ICU), length of hospital stay, morbidity and mortality, and a substantial increase in the costs and use of health care resources [1, 2]. Complications occurring within 30 days are the main

predictors of survival after major surgery with a quarter of deaths that occur in the first six postoperative days following surgery being related to respiratory complications [3, 4].

Postoperative pulmonary complications (POPCs) may include atelectasis, bronchospasm, tracheobronchitis, pneumonia, pulmonary embolism, pneumothorax, acute pulmonary oedema, and acute respiratory failure. The pathogenesis of POPCs depends on patient-related risk factors, the type of surgery performed and anaesthetic technique, including mechanical ventilation and second hit factors [3]. Because events in the postoperative period are more important than preoperative patient risk factors in determining survival [4], the identification of risk factors for serious POPCs is critical to the development of strategies for prevention, early diagnosis and treatment. This study aimed to investigate risk factors for early POPCs in patients admitted to an ICU following major non-cardiac surgery.

METHODS

This study was a multicenter prospective observational cohort study involving 21 Brazilian intensive care units (ICUs) from 18 hospitals. Recruitment both of participant hospitals and patients into the study was by open invitation through individual contacts. Other related studies describing this recruitment process have been published elsewhere [3]. The Research and Ethics Committee approved the study, while the need for informed consent was waived due to its observational nature.

All adult patients who underwent non-cardiac, elective, or emergency surgeries and admitted to a participating ICUs within 24 hours were screened for inclusion in the study. Exclusion criteria were trauma, cardiac, neurological, gynaecologic, obstetric and palliative surgeries.

Data were collected on age, gender, smoking habits (active last year), alcohol abuse, chronic obstructive pulmonary disease (COPD), and the presence of malignant disease. Low functional capacity was defined as the inability to climb two flights of stairs in a subjective evaluation [5]. Hemodynamic instability before surgery was considered in the presence of hypotension leading to fluid administration and/or the use of a vasopressor. Heart rate (HR), central venous pressure (CVP) and the most abnormal values of laboratory tests collected (blood gas analysis, serum lactate, and blood cell count) over the first 24 hours after ICU admission were recorded. An electronic case report form in a dedicated server was used to gather data, while two authors carefully checked the variables. We considered unplanned surgeries as admission after urgent (within 48 of referral) or emergent (immediately after referral/consultation) surgeries. The following procedures were considered major surgeries: laparotomy, enterectomy, cholecystectomy with choledochostomy, vascular surgery, major amputation, any aortic procedure, abdominoperineal resection of the rectum, pancreatectomy, esophagectomy, and hepatectomy.

Based on data available from the patients' anaesthetic records and ICU admission the Physiological and Operative Severity Score for the enumeration of Mortality and Morbidity (POSSUM) was calculated. Acute Physiology and Chronic Health Disease Classification System II (APACHE II), Multiple Organ Dysfunction System (MODS), and Sequential Organ Failure Assessment (SOFA) scores were also calculated from data recorded within 24 hours after ICU admission.

POPCs were considered to be the presence of one or more of the following conditions: pulmonary oedema (cardiogenic and non-cardiogenic), nosocomial pneumonia, and extubation failure, in the postoperative period following major surgery. Acute pulmonary oedema was defined as the presence or evidence of fluid accumulation, and was determined by radiological signs of vascular congestion and or pulmonary oedema characterized by widespread patchy alveolar infiltrates in both lungs and clinical signs or symptoms of pulmonary oedema. Nosocomial pneumonia was defined according to the guidelines from the Centers for Disease Control and Prevention (CDC) as pneumonia that occurs after 48 hours after admission using radiological, microbiological, and clinical criteria [6]. Extubation failure was defined as the failure to extubate within 24 hours or reintubation within 72 hours. The patients were followed up for outcome data until death, hospital discharge, or for a maximum of 90 days.

STATISTICAL ANALYSIS

Categorical data were analyzed as frequencies and compared using Pearson's Chi-square tests or Fisher's exact tests. Continuous variables are presented as means ± SDs and were compared using Student's *t*-test. To identify independent predictors for POPCs, we performed a logistic regression analysis. Variables considered for the regression analysis included the following: age; gender; type of admission; type of surgery; severe malnutrition; diabetes; arrhythmias; compensated and decompensated heart failure; arterial hypertension; unstable angina; severe

valvulopathy; low functional capacity; history of previous cerebral vascular accident (CVA); history of acute myocardial ischemia (AMI); alcoholism; liver failure (Child-Pugh C); chronic renal failure requiring renal replacement therapy (RRT); smoking habit (active last year); COPD; previous or scheduled vascular surgery; SOFA score; haemodynamic instability before surgery; duration of surgery; intraoperative crystalloids; CVP; HR; haematocrit level; serum lactate concentrate; body temperature; and blood pH. The collinearity between variables was excluded before modelling. Covariates were selected and entered in the model if they attained a *P*-value < 0.2 in a univariate analysis. A *P*-value ≤ 0.05 was considered statistically significant. The CVP and SOFA scores were assessed by the area under receiver operating characteristic (ROC) curves.

RESULTS

A total of 885 patients were screened, of whom 304 were excluded (neurosurgery, 127; heart surgery, 51; palliative surgery, 35; gynaecologic surgery, 6; trauma surgery, 32; incomplete data, 48; unneeded ICU admission, 5). The demographic and baseline characteristics of the 581 patients included in the study are shown in Table 1. The mean age was 62.2 ± 15.9 years, while 55% of patients were male. The most frequent pre-existing condition was arterial hypertension (60%), followed by diabetes (22.5%). The mortality rate was significantly higher in the group with POPCs (61.8%) compared to the group of patients without POPCs (10.8%) (RR 5.71, 95% CI 4.23–7.69; $P < 0.001$).

Of the 581 patients enrolled, 110 (19%) had at least one POPC. A total of 27 patients (5%) had acute pulmonary oedema, 59 patients (10%) had extubation failure and 59 (10%) had pneumonia. A total of 71 patients (12%) had one complication, 31 (5%) had two while 4 patients (0.7%) had three complications. POPCs were more prevalent after unplanned admission (61%) and gastrointestinal (43%) than after vascular (9%), thoracic (3%) or orthopaedic surgeries (3%) (Fig. 1). Figure 2 shows the temporal patterns of the postoperative pulmonary complications. Most of the cases of pulmonary oedema occurred in the first seven days after ICU admission (70%), while pneumonia was more frequent after one week of admission.

Patients with POPCs had significantly higher POSSUM scores (43.7 ± 10.8 vs. 34.1 ± 9.7, $P < 0.001$), APACHE II scores (17.6 ± 6.3 vs. 13.6 ± 6.2, $P < 0.001$) and SOFA scores (6.9 ± 4.4 vs. 4.5 ± 3.7, $P < 0.001$) than patients without POPCs upon ICU admission (Table 1). Despite similar durations of surgery, the total volume of crystalloids administered intraoperatively was significantly higher in patients with POPCs than in those without POPCs ($P < 0.001$) (Table 2). Patients with POPCs had significantly higher levels of HR and CVP in the first 24 hours after ICU admission ($P < 0.001$ for both groups) in comparison to patients without POPCs.

A low functional capacity (RR: 4.6, 95% CI: 2.1–10.0), major surgery (RR: 3.6, 95% CI: 1.2–10.7), preoperative hemodynamic instability (RR: 3.4, 95% CI: 1.1–10.6), alcoholism (RR: 3.3, 95% CI: 1.0–10.7), unplanned surgery (RR: 2.3, 95% CI: 1.0–5.2), SOFA score (RR: 1.1, 95% CI: 1.0–1.2), and increased CVP (RR: 1.1, 95% CI: 1.0–1.1) were independent predictors of POPCs (Table 3) (Final model Goodness-of-Fit Test: DF 285; Chi-square 297,9; $P = 0.959$; 95% CI: 0.68–0.95). The areas under the curve (AUC) for model discrimination were 0.67 for CVP (cut-off value: 14 mm Hg; sensitivity: 58.7%; specificity: 67.7%) and 0.66 for the SOFA score (cut-off value: 6; sensitivity: 50.5%; specificity: 75.7%). ROC analysis revealed moderate utility for both curves in discriminating those who will have POPCs.

DISCUSSION

We found a high incidence of POPCs (19%) associated with a significant mortality rate (62%) in non-cardiac surgeries. Pulmonary oedema was present in 5% of patients, extubation failure was present in 10% of patients, while pneumonia was present in 10% of patients. Low functional capacity, preoperative haemodynamic instability, major surgery, unplanned surgery, alcoholism, SOFA score, and high CVP were independent predictors of POPCs.

Due to the lack of definitions, studies on POPCs are difficult to interpret and are typically not comparable. The incidence of respiratory complications varies between different studies depending on the definitions used and the populations studied. Attempts have been made to implement standard definitions and outcome measures [7]. In a large retrospective study of patients undergoing hip fracture surgical repair, 19% of patients had complications, of whom 2.6% had POPCs [8]. After abdominal surgery, the incidence of POPCs increases substantially [9]. Patel *et al.* [10] reported an 11.9% incidence of POPCs following elective major abdominal surgery.

Both pneumonia and pulmonary oedema are complications known to increase both the costs of, and the demand for health care resources, in addition to prolonging the length of stay, potentially impacting the likelihood of mortality. The incidence of pneumonia ranges between 2% and 19% following major abdominal surgery, with rates as high as 22.7% after

Table 1. Characteristics of the study group upon admission to the ICU and outcomes

	All patients (n = 581)	POPC — no (n = 471)	POPC — yes (n = 110)	*P*-value
Age (years)	62.2 ± 15.9	61.4 ± 17.1	65.9 ± 15.6	0.015
Gender (M) (%)	317 (55)	250 (43)	67 (61)	0.166
APACHE II	14.4 ± 6.4	13.6 ± 6.2	17.6 ± 6.3	< 0.001
SOFA score	5.0 ± 3.9	4.5 ± 3.7	6.9 ± 4.4	< 0.001
POSSUM	35.9 ± 10.6	34.1 ± 9.7	43.7 ±10.8	< 0.001
Baselines conditions (%)				
Arterial hypertension	382 (70)	298 (63)	47 (43)	< 0.001
Diabetes mellitus	120 (22)	89 (19)	31 (28)	0.041
Smoking habit	117 (22)	86 (18)	31 (28)	0.028
COPD	85 (16)	61 (13)	24 (22)	0.026
Previous AMI	52 (9.9)	44 (9.3)	8 (7.2)	0.610
Alcoholism	39 (7.4)	24 (5)	15 (14)	0.002
Previous CVA	37 (7.0)	25 (5.3)	12 (11)	0.051
Liver failure	31 (5.9)	25 (5.3)	6 (5.4)	0.846
Heart failure (NYHA I–II)	29 (5.6)	17 (3.6)	12 (11)	0.003
Heart failure (NYHA III–IV)	12 (2.3)	6 (1.2)	6 (5.4)	0.014
Chronic renal failure (need for RRT)	11 (2.1)	8 (1.6)	3 (2.7)	0.702
Neoplastic disease	186 (32)	159 (32)	37 (34)	0,685
Surgical procedures (%)				
Unplanned admission	170 (29)	104 (22)	67 (61)	< 0.001
Gastrointestinal	259 (45)	212 (45)	47 (43)	0.741
Vascular	135 (23)	125 (27)	10 (9)	< 0.001
Exploratory Laparotomy	44 (8)	36 (8)	8 (7)	0.954
Thoracic	27 (5)	24 (5)	3 (3)	0.259
Orthopedic	39 (7)	36 (8)	3 (3)	0.101
Outcomes				
Sepsis	135 (23)	106 (23)	29 (26)	0.695
Mechanical ventilation	156 (27)	120 (25)	36 (33)	0.157
ICU LOS, days	5 [2–14]	5 [2–14]	6 [2–20]	0.146
Hospital LOS, days	10 [4–20]	10 [4–19]	10 [4–28]	0.105
Mortality rate (%)	119 (20)	51 (11)	68 (62)	< 0.001

POPC — postoperative pulmonary complications; COPD — chronic obstructive pulmonary disease; AMI — acute myocardial infarction; CVA — cerebral vascular accident; APACHE II — Acute Physiologic Chronic Health Evaluation; SOFA — Sequential Organ Failure Assessment; LOS — length-of-stay; IQ — interquartile range. Results are presented as number (%), median [Interquartis range] or mean ± standard deviation

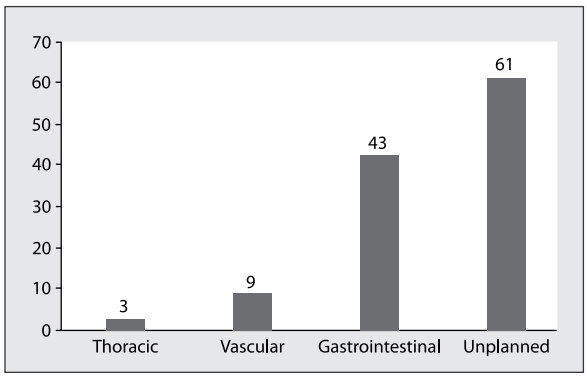

Figure 1. Prevalence of postoperative pulmonary complications according to the type of surgery

liver transplantation [2, 11, 12]. Furthermore, 2.4% of patients presented with acute pulmonary oedema following pneumonectomy, while 7% presented with acute pulmonary oedema following liver transplantation [11, 12].

Postoperative respiratory failure is possibly the most devastating of all complications and a cause of high postoperative mortality. Depending on the definition used and characteristics of the patients studied, associated mortality rates can exceed 25% [1]. One large nested case-control study reported that 5.4% of patients developed postoperative respiratory failure, defined as the need for mechanical ventilation

for greater than 48 hours postoperatively, or the need for reinstitution of mechanical or non-invasive ventilation after extubation, with non-hydrostatic pulmonary oedema being the most common cause [13].

Our study showed a 5.7-fold increase in the risk of dying in patients with POPCs compared to those without complications. A study conducted on 105,951 surgical patients reported that the occurrence of any 30-day complication significantly impacted patient outcomes and reduced median patient survival by 69%. Furthermore, this same study found that the occurrence of pulmonary complications reduced the median 30-day survival rate by 87% [4].

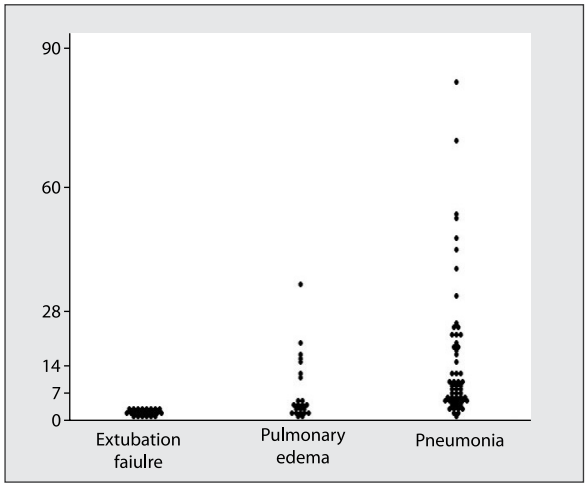

Figure 2. Temporal patterns of postoperative pulmonary complications

A previous study identified six indicators as independent risk factors for the development of POPCs following abdominal surgery, namely: an age greater than 60 years; impaired preoperative cognitive function; a recent smoking history; a body mass index greater than 27; a history of neoplastic disease; and either upper abdominal or both upper/lower abdominal incision sites [14]. Additionally, the PERISCOPE study group reported that emergency surgery, preoperative respiratory symptoms, chronic liver disease, congestive heart failure, open intrathoracic or upper abdominal surgery, and surgical procedures lasting at least two hours were independent risk factors for POPCs [15]. Interestingly, in our study, age was not an independent predictor, whereas low functional capacity led to an almost 5-fold increase in the risk for POPCs. We also found that the type of admission (unplanned), alcoholism, haemodynamic instability before surgery and type of surgery (major) were independent predictors of POPCs, with emergency surgery having more than twice the risk of complications in comparison to elective surgeries.

Alcohol abuse is known to be related to the risk of nosocomial infections with alcoholics being two to three times more likely to have an increased rate of postoperative complications than non-alcoholics. Alcohol abuse is associated with greater levels of ex-

Table 2. Intraoperative and postoperative measurements in patients with and without postoperative pulmonary complications

	POPC — no (n = 471)	POPC — yes (n = 110)	*P*-value
Intra-operative			
Lenght of surgery (hours)	4.1 ± 2.1	4.2 ± 2.5	0.763
Crystalloids (mL)	818 [570–1200]	1000 [667–1500]	0.011
Colloids (mL)	500 [500–1000]	500 [500–1000]	0.730
Red blood cells (Units)	2 [1–3]	2 [2–3]	0.59
ICU admission			
pH	7.31 ± 0.08	7.25 ± 0.11	< 0.001
Heart rate, bpm	100 ± 21	111 ± 25	< 0.001
Higher CVP (mm Hg)	11.3 ± 7.2	15.9 ± 8.4	< 0.001
Lower CVP (mm Hg)	6.4 ± 4.8	10.1 ± 7.0	< 0.001
PaO_2 (mm Hg)	101 ± 49	108 ± 69	< 0.001
$PaCO_2$ (mm Hg)	41 ± 27	41 ± 10	0.735
Hematocrit (%)	31 ± 7.3	30 ± 6.1	< 0.001
Lactate (mEq L^{-1})	3.6 ± 6.2	3.6 ± 3.0	< 0.001
Lower temperature (ºC)	35.5 ± 0.8	35.4 ± 0.9	0.735

POPC — postoperative pulmonary complications; CVP — central venous pressure; PaO_2 — partial pressure of oxygen; $PaCO_2$ — partial pressure of carbon dioxide; ICU — intensive care unit. Results are presented as Median [IQ range] or mean ± standard deviation

Table 3. Independent predictors of postoperative pulmonary complications (POPC)

Predictors	Coeficient	SE	OR	CI 95%	*P*-value
Low functional capacity	1.524	0.399	4.6	2.1–10.0	< 0.001
Alcoholism	1.204	0.594	3.3	1.0–10.7	0.040
Hemodynamic instability	1.239	0.572	3.4	1.1–10.6	0.030
Type of surgery	1.286	0.552	3.6	1.2–10.7	0.020
Unplanned surgery	0.839	0.415	2.3	1.0–5.2	0.043
SOFA score	0.106	0.048	1.1	1.0–1.2	0.026
High CVP	0.080	0.024	1.1	1.0–1.1	0.001

SOFA — Sequential Organ Failure Assessment; CVP — central venous pressure; SE — standard error; OR — odds ratio; CI — confidence interval

travascular lung water (EVLW) and a trend toward slower resolution of oedema in patients who develop acute respiratory distress syndrome (ARDS) [16].

Despite similar durations of surgery, patients with POPCs received more fluids intraoperatively and had significantly higher levels of CVP in the first 24 hours following the operation. Indeed, increases in CVP were predictive of POPCs in our study.

The areas under the curve (AUC) for model discrimination were 0.67 for CVP (cut-off value: 14 mm Hg; sensitivity: 58.7%; specificity: 67.7%) and 0.66 for SOFA score (cut-off value: 6; sensitivity: 50.5%; specificity: 75.7%).

Increases in the extra-vascular lung water (EVLW) and positive fluid balances have been associated with complications and death in critically ill patients [17, 18]. POPCs were more likely to occur after elective high-risk surgeries in patients receiving large amounts of fluids and transfusions [19]. More attention should be given to the detrimental impact of liberal fluid therapy in terms of POPCs, especially in subjects with elevated CVP at baseline. Pulmonary oedema after surgery may be the consequence of fluid overload, cardiac dysfunction or both. The driving pressure that determines venous return is the mean circulatory filling pressure (MCFP) while venous return is determined by the gradient between MCFP and CVP [17]. An increase in the CVP or a fall in the MCFP will impede venous return, reduce stroke volume and cardiac output. A high CVP transmitted backwards will increase venous pressure with profound effects on microcirculatory flow and organ function. Furthermore, increased filling pressures and a positive fluid balance increase EVLW impairing gas exchange, lung compliance and increasing work of breathing.

Early changes in organ function are strongly associated with outcomes in the ICU [20]. The Sequential Organ Failure Assessment (SOFA) score is a tool developed to quantitatively describe the time course of organ dysfunction [14]. A previous study found that the SOFA score was an independent predictor of developing early acute respiratory failure in a heterogeneous population of critically ill patients [21]. Our data suggest that a 10% increase in the risk of POPCs is likely for each unit increase in the SOFA score at ICU admission.

Our study has several limitations. Firstly, we chose to include only pneumonia, pulmonary oedema and extubation failure as pulmonary complications. Other minor complications such as pleural effusion and atelectasis were not registered in our casuistic study as we considered that interobserver variability in the radiologic diagnosis would be very likely in the diagnosis of these conditions. Secondly, the level of severity of the event was not incorporated. Thirdly, differentiation between cardiogenic and non-cardiogenic pulmonary oedema was not possible. Transpulmonary thermodilution has emerged as the technique allowing clinicians to estimate the volume of lung oedema at the bedside and differentiate pulmonary oedema from those with cardiac origin and from those due to increased vascular permeability. However, very few centres had this technology available.

The primary strengths of our study were the homogeneous population of high-risk surgical patients admitted into ICUs from different regions of the country included in the cohort, and its prospective nature. In addition, the purpose of the original study was to evaluate the epidemiology and outcomes with a defined panel of complications.

Events in the postoperative period are more important than preoperative patient risk factors in determining survival after major surgery [4]. In addition, surgical complications are expensive for patients, hospitals, and taxpayers. An emphasis on identifying risk factors will therefore help multidisciplinary teams develop strategies in order to prevent complications.

CONCLUSION

POPCs, such as pulmonary oedema, and particularly, extubation failure and pneumonia, were frequent after non-cardiac surgeries and were linked to higher mortality rates. Low functional capacity, major surgery, preoperative hemodynamic instability, alcoholism, unplanned surgery, the SOFA score, and increased central venous pressure are independently associated with POPCs.

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