

Perioperative risk factors for pulmonary complications after non-cardiac surgery

Surbhi Gupta, Roshan Joseph Fernandes, Joseph Sushil Rao¹, Radhika Dhanpal²

Departments of Anesthesiology and ¹Surgical Oncology, St. John's Medical College and Hospital, ²Department of Anesthesiology, Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, Karnataka, India

Abstract

Background and Aims: Postoperative pulmonary complications (PPCs) lead to increased morbidity, mortality, length of hospital stay, and cost to the patient. This study was conducted to determine the risk factors and assess the incidence of PPC after non-cardiac surgery.

Material and Methods: This prospective, observational study was conducted on 1,170 patients undergoing non-cardiac surgery. Details of patient, surgical, and anesthetic factors were collected and patients were followed up for the entire duration of hospital stay for the occurrence of PPC. Assess Respiratory Risk in Surgical Patients in Catalonia (ARISCAT) score and the length of hospital stay was noted for all the patients. Regression analysis was used to find the risk factors associated with development of respiratory complications.

Results: The incidence of PPC was found to be 59 in 1,170 patients (5%) in our hospital. Multivariate analysis revealed that patients with intermediate and high risk ARISCAT scoring had higher odds of developing PPC. Higher age (>50 years), positive cough test, presence of nasogastric tube, and intraoperative pulmonary complications were identified as independent risk factors associated with the occurrence of PPC.

Conclusion: We found 5% incidence of PPC in our study. Recognition of the delineated risk factors and routine use of ARISCAT score for preoperative assessment may help identify patients at a higher risk of developing postoperative pulmonary complications.

Keywords: Complications, postoperative, prevention, pulmonary, risk factors

Introduction

Postoperative pulmonary complications (PPCs) constitute one of the commonest complications following anesthesia and surgery. They prolong hospital stay and add to the healthcare burden.^[1-5] Incidence of PPC varying from 2 to 40% has been reported in literature.^[6-8]

Recognition of perioperative modifiable and non-modifiable patient, anesthetic and surgical factors can help identify

patients at risk of developing PPC. Appropriate perioperative strategies can then be undertaken to minimize occurrence of pulmonary complications.

The present study was done to evaluate the incidence of PPC after non-cardiac surgery in our hospital and to determine the related perioperative risk factors. The secondary objective was to identify the independent risk factors associated with PPC.

We chose to check the predictive value of the ARISCAT score for PPC in our population. ARISCAT scoring is based on

Address for correspondence: Dr. Surbhi Gupta,
Department of Anesthesiology, St. John's Medical College and Hospital, Sarjapur Road, Koramangala, Bengaluru - 560 034, Karnataka, India.
E-mail: surbhi_pg@yahoo.com

Access this article online	
Quick Response Code:	Website: www.joacp.org
	DOI: 10.4103/joacp.JOACP_54_19

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How to cite this article: Gupta S, Fernandes RJ, Rao JS, Dhanpal R. Perioperative risk factors for pulmonary complications after non-cardiac surgery. *J Anaesthesiol Clin Pharmacol* 2020;36:88-93.

Submitted: 24-Feb-2019 **Revised:** 14-Aug-2019 **Accepted:** 13-Sep-2019
Published: 18-Feb-2020

seven easily measurable variables.^[9] It utilizes simple variables obtained from the history and physical examination of the patient which can predict risk of pulmonary complications and does not involve any intervention which would add to the cost of healthcare for the patient.

Material and Methods

This prospective, observational study was conducted in a tertiary care teaching hospital over a period of 10 months. After obtaining approval from the ethical committee and written informed consent, 1,170 patients greater than 18 years undergoing non-cardiac surgery under general anesthesia, neuraxial block, or regional anesthesia were included. This study was registered retrospectively with Clinical Trials Registry of India (CTRI/2018/02/012124).

Pregnant patients, or those with preoperatively intubated trachea, and procedures done under local anesthesia alone were excluded. Also, patients undergoing procedures related to a surgical complication, transplantation procedures, outpatient procedures (hospital stay of <24 h) were not included.

All patients received routine preoperative, intraoperative, and postoperative care. All patients who were recruited for the study were followed up by daily visits to the respective wards for the entire duration of hospital stay till discharge. A structured questionnaire on patient, anesthetic and surgical factors was filled perioperatively by the investigators. Routine preoperative assessment was conducted and data regarding age, gender, height, weight, pre-existing comorbidities, American Society of Anesthesiologists (ASA status), smoking history, respiratory infection in the last 1 month, patient's oxygen saturation on room air, and hemoglobin concentration was collected. A thorough evaluation of the respiratory system was undertaken and cough test was carried out for all patients where the patient was asked to take a deep breath and cough once and recurrent coughing implied a positive cough test.

Data recorded on the surgical procedure included the type of anesthesia, site and duration of surgery, elective/emergency surgery, intraoperative blood transfusion, and any intraoperative respiratory complication (laryngospasm, bronchospasm, pulmonary edema, desaturation below SpO₂ of 95%, high airway pressures, presence of endobronchial secretions). Postoperative presence of nasogastric (NG) tube was also noted.

ARISCAT score was calculated for each patient which was based on seven independent risk factors for PPC: preoperative arterial oxygen saturation, acute respiratory infection during the previous month, age of the patient,

preoperative hemoglobin levels, site of surgery, duration of surgery, and emergency surgery [Table 1].

PPCs were identified based on routine clinical diagnosis. Patients who were found to have respiratory symptoms were subjected to chest X-ray and other relevant investigations [Table 2]. Length of hospital stay was also noted for all the patients. Data was then tabulated on an excel sheet.

Table 1: The ARISCAT score

Predictor	Risk score
Age: ≤50 yrs	0
Age: 51-80 yrs	3
Age: > 80 yrs	16
Preoperative SpO ₂ : ≥96%	0
Preoperative SpO ₂ : 91-95%	8
Preoperative SpO ₂ : ≤ 90%	24
Respiratory infection in past 1 month: No	0
Respiratory infection in past 1 month: Yes	17
Preoperative Hemoglobin<10 gm/dl: No	0
Preoperative Hemoglobin<10 gm/dl: Yes	11
Peripheral incision	0
Upper abdominal incision	15
Intrathoracic incision	24
Surgery duration <2 h	0
Surgery duration=2-3 h	16
Surgery >3 h	23
Emergency procedure: No	0
Emergency procedure: Yes	8

Low risk: <26, Intermediate risk: 26-44, High risk: ≥45

Table 2: Definition of Postoperative pulmonary complications

Complication	Definition
Respiratory failure	Postoperative PaO ₂ <60 mmHg on room air, a ratio of PaO ₂ to inspired oxygen fraction <300, or arterial oxyhemoglobin saturation measured with pulse oximetry <90% and requiring oxygen therapy
Respiratory infection/ Pneumonia	Treatment with antibiotics for a respiratory infection, plus at least one of the following criteria - New or changed sputum, New or changed lung opacities on a clinically indicated chest radiograph, Temperature >38.3°C, Leukocyte count >12,000/mm ³
Pleural effusion	Chest radiograph demonstrating blunting of the costophrenic angle, loss of the sharp silhouette of the ipsilateral hemidiaphragm (in upright position), evidence of displacement of adjacent anatomical structures, or (in supine position) a hazy opacity in one hemithorax with preserved vascular shadows
Atelectasis	Suggested by lung opacification with shift of the mediastinum, hilum, or hemidiaphragm toward the affected area, and compensatory overinflation in the adjacent nonatelectatic lung
Pneumothorax	Air in the pleural space with no vascular bed surrounding the visceral pleura on chest radiograph
Bronchospasm	Newly detected expiratory wheezing treated with bronchodilators
Aspiration pneumonitis	Respiratory failure after the inhalation of regurgitated gastric contents

Statistical analysis

Based on a study by Canet *et al.*, to observe a 5% proportion of pulmonary complications among patients who have undergone surgery with 25% relative precision and 95% confidence interval, the number required to be studied was estimated to be 1,170 subjects.^[9]

In order to assess the factors associated with presence of PPC, for every case, three controls were randomly chosen in a ratio of 1 case to 3 controls.

Descriptive statistics were reported using mean and standard deviation for the continuous variables and number and percentages for the categorical variables. The incidence of PPC was reported using proportion and percentages. Association between clinical and demographic variables with the presence of PPC was assessed using Chi-square test. Independent *t*-test was used to compare the means between patients with PPC and patients without PPC.

Multivariate logistic regression was performed as model 1 and model 2 to assess the factors associated with the presence of PPC. In model 1, ARISCAT score was adjusted for age alone. In model 2, variables that were significant in univariate analysis were subjected for multivariate analysis except ARISCAT score. In multivariate analysis, variable selection was performed with backward elimination method. *P* value less than 0.05 was considered statistically significant. Analysis was done using SPSS software version 23.0.

Results

Fifty-nine PPCs (5.04%) were recorded in the study population of 1,170 patients. 48 patients had postoperative pulmonary infection (81.3% of cases), three had aspiration pneumonitis (5.1%), three had atelectasis (5.1%), three had bronchospasm (5.1%), one had pulmonary embolism (1.7%), and one patient had pleural effusion (1.7%). The median length of hospital stay in patients who developed PPC was significantly prolonged [10, (6--14) days] as compared to patients without a PPC [4 (2-7) days] (*P* < 0.001).

Univariate analysis showed that patients aged >50 years, ASA status >II, anemia (hemoglobin <10 g/dl), SpO₂ <96%, preoperative respiratory symptoms, and positive cough test had a significantly higher incidence of PPC. Surgical and anesthetic risk factors which showed significant association with the occurrence of PPC were general anesthesia, emergency surgery, upper abdominal incision, duration of surgery greater than 3 h, presence of postoperative NG tube, intraoperative blood transfusion, intraoperative pulmonary complications, and high ARISCAT score [Table 3].

Gender, respiratory infection in the last 1 month, and smoking were not associated with a higher incidence of PPC.

Multivariate analysis revealed that in model 1 higher ARISCAT score was significantly associated with PPC after adjusting for age. Patients who had intermediate risk ARISCAT score had 4.5 (95% CI [confidence interval] 2.2--9.1) times higher risk of getting PPC and patients with high risk ARISCAT score had 17.7 (95% CI 4.6-68.6) times higher risk of getting PPC than patients with low risk ARISCAT score.

In model 2, patients with age greater than 50 years had 3.1 times increased odds of developing respiratory illness. Positive cough test (adjusted odds ratio, AOR-2.3), presence of postoperative NG tube (AOR-4.86), and intraoperative pulmonary complications (AOR-7.01) were independent factors associated with the occurrence of postoperative respiratory illness [Table 4].

Discussion

PPCs adversely affect patient outcome after surgery.^[6] A wide variation in PPC incidence (2--40%) has been reported in literature which may be due to differences in the population, race, geographical areas, healthcare setup, disease spectrum, procedures studied, and prospective or retrospective nature of the study. We found a 5% incidence of PPCs in patients undergoing non-cardiac surgery. This incidence was similar to two European studies, the ARISCAT and the Prospective Evaluation of a Risk Score for Postoperative Pulmonary Complications in Europe (PERISCOPE) which found PPC rates of 5% and 7.9% in patients undergoing non-cardiac surgery, respectively.^[9,10] Recognition of the incidence of respiratory complications is therefore important to understand the implications of PPC.

Various risk indices have been proposed in order to predict risk of PPC but these may not be applicable to every population.^[9,12] We calculated the ARISCAT score for our patients and found that patients with low risk scores had fewer PPC than patients with intermediate and high risk scores. In a study done on patients undergoing renal transplantation, ARISCAT score was found to be a better modality for predicting PPC than ASA classification.^[13] ARISCAT score is based on seven easily measurable variables and hence can be easily incorporated during preoperative evaluation of patients.^[9]

Similar to other studies we found higher age to be an independent risk factor for PPC.^[14-17] Qaseem *et al.*

Table 3: Univariate analysis to find the factors associated with PPC

Variables	Coding	Control n-177	Cases n-59	P*
Gender	Male	106 (75.2%)	35 (24.8%)	0.939
	Female	71 (74.7%)	24 (25.3%)	
American Society of Anesthesiologists (ASA) status	I	88 (49.7%)	18 (30.5%)	0.002
	II	76 (42.9%)	27 (45.8%)	
	III	12 (6.8%)	12 (20.3%)	
	IV	1 (0.6%)	2 (3.4%)	
Hemoglobin (gm/dl)	<10	17 (54.8%)	14 (45.2%)	0.006
	>10	158 (77.8%)	45 (22.2%)	
Preoperative SpO ₂ on room air (%)	>96%	168 (79.6%)	43 (20.4%)	<
	<96%	9 (36.0%)	16 (64.0%)	
Cough test	+ve	6 (37.5%)	10 (62.5%)	0.001
	-ve	171 (77.7%)	49 (22.3%)	
Type of Surgery	Elective	161 (83.4%)	32 (16.6%)	<
	Emergency	16 (37.2%)	27 (62.8%)	
Type of Anaesthesia	General Anesthesia	119 (69.6%)	52 (30.4%)	0.005
	Neuraxial Block only	47 (92.2%)	4 (7.8%)	
	Regional Anesthesia only (peripheral nerve blocks)	9 (75.0%)	3 (25.0%)	
Duration of surgery (h)	< 3	81 (85.3%)	14 (14.7%)	0.003
	> 3	96 (68.1%)	45 (31.9%)	
Site of Surgical incision	Upper abdominal	12 (46.2%)	14 (53.8%)	<0.001
	Lower abdominal/peripheral	164 (78.5%)	45 (21.5%)	
Postoperative nasogastric tube	Yes	2 (18.2%)	9 (81.8%)	<0.001
	No	170 (77.3%)	50 (22.7%)	
Intraoperative blood transfusion	Yes	6 (46.2%)	7 (53.8%)	0.022
	No	169 (76.5%)	52 (23.5%)	
Intraoperative pulmonary complications	Yes	1 (11.1%)	8 (88.9%)	<0.001
	No	174 (77.3%)	51 (22.7%)	
Age	<50 years	124 (81.0%)	29 (19.0%)	0.004
	>50 years	53 (63.9%)	30 (36.1%)	
Smoking	Never	133 (76.9%)	40 (23.1%)	0.413
	Former	26 (66.7%)	13 (33.3%)	
	Current	18 (75.0%)	6 (25.0%)	
Preoperative respiratory symptoms	Present	2 (22.2%)	7 (77.8)	<0.001
	Absent	172 (76.8)	52 (23.2)	
ARISCAT Score	0	10 (100)	0 (0)	<0.001
	<26	139 (83.2)	28 (16.8)	
	26-44	25 (54.3)	21 (45.7)	
	>45	2 (23.1)	10 (76.9)	

P < 0.05 is considered statistically significant

Table 4: Multivariate analysis to find the factors associated with PPC

Variables	P	Adjusted OR	95% CI	
			LL	UL
ARISCAT	<0.0001	3.17	2.13	4.71
Age	0.005	3.09	1.404	6.825
Cough test	0.04	2.39	1.01	5.68
Postoperative nasogastric tube	0.002	4.86	1.77	13.36
Intraoperative pulmonary complications	0.03	7.01	1.15	43.17

OR : Odds ratio; CI : Confidence interval

reported that the odds ratio of developing PPC was 2.09 (95% CI, 1.70--2.58) for patients 60--69 years of age and

3.04 (95% CI, 2.11--4.39) for those 70--79 years of age compared with younger patients.^[18] Age related deterioration of pulmonary function and increased work of breathing due to reduced lung elasticity, decreased alveolar surface area, and increased dead space leads to ventilation--perfusion mismatch in the elderly and can predispose to the development of PPC.^[8]

Like other studies, we found an increased incidence of PPC in patients with ASA status > II, hemoglobin levels < 10 gm/dl, and preoperative SpO₂ on room air < 95%. Though these factors were not found to be significant on multivariate analysis, anemia and low oxygenation of arterial blood can cause tissue

hypoxia and increase the risk of infection by affecting the immune system.^[9,15,19,20]

Studies have shown that patients with intraoperative respiratory complications had greater incidence of postoperative complications.^[21,22] A positive cough test was found to be independent risk factors for PPC. Cough test is a simple bedside test which can be easily included in the preoperative clinical evaluation of patients.^[14] A positive cough test may indicate persisting respiratory tract infection which makes a patient susceptible to PPC.^[14,17] It may be advisable to delay elective surgery in such patients till the respiratory infection is eliminated.^[23]

In this study, administration of general anesthesia as against regional (peripheral nerve block) or neuraxial block alone, longer surgical duration, surgeries involving upper abdominal incisions, and emergency surgeries were associated with an increased incidence of PPC. Increased risk of PPC with every additional minute of operating time has been reported.^[6] Alternative anesthetic (regional or neuraxial anesthesia rather than general anesthesia) and modified surgical techniques (minimally invasive surgical procedures instead of open surgeries and limiting the duration of surgery) should be considered in high risk patients.^[24-26]

The presence of NG tube postoperatively has been described as a risk factor for PPC.^[4,14,27] NG tube leads to ineffective coughing, retention of secretions, and atelectasis.^[4] It can cause incompetency of the lower esophageal sphincter leading to silent aspiration and pneumonia. A systematic review reported that patients with selective use of NG after laparotomy had a lower rate of pneumonia and atelectasis as compared to patients in whom NG was kept till return of gastrointestinal motility.^[28] Hence its judicious and selective use is recommended.^[14]

We did not find a correlation between smoking and PPC. This is at variation to the correlation observed in other studies.^[29] This may be attributed to the fact that 40% of our study population were females who may not smoke or may not disclose their true smoking status.

In this study, patients with PPC had a greater length of hospital stay as compared to patients without PPC. Increased length of hospital stay increases the cost of healthcare and also causes physical and emotional discomfort to the patient.^[4,7,14]

Identification of risk factors is helpful in predicting postoperative outcome of patients. The patient and surgeon should be informed about the increased risk of PPC associated with the presence of non-modifiable risk factors like higher age.

Modifiable factors like respiratory infection should be treated preoperatively and routine use of NG should be discouraged.

Conclusion

We found 5% incidence of PPC in our study. Recognition of the delineated risk factors and routine use of ARISCAT score for preoperative assessment may help identify patients at a higher risk of developing postoperative pulmonary complications.

Limitation

One limitation of the study was that we did not evaluate the risk factors of PPC for each type of surgery individually.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Acknowledgements

We would like to thank Mrs. Sumithra Selvam for helping out with the statistical analysis of the data.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest

References

1. Smetana GW, Lawrence VA, Cornell JE. Preoperative pulmonary risk stratification for noncardiothoracic surgery: Systematic review for the American College of Physicians. *Ann Intern Med* 2006;144:581-95.
2. Davies OJ, Husain T, Stephens RC. Postoperative pulmonary complications following non-cardiothoracic surgery. *BJA Educ* 2017;17:295-300.
3. Miskovic A, Lumb AB. Postoperative pulmonary complications. *Br J Anaesth* 2017;118:317-34.
4. Mitchell CK, Smoger SH, Pfeifer MP, Vogel RL, Pandit MK, Donnelly PJ, *et al.* Multivariate analysis of factors associated with post-operative pulmonary complications following general elective surgery. *Arch Surg* 1998;133:194-8.
5. Inokuchi M, Kojima K, Kato K, Sugita H, Sugihara K. Risk factors for post-operative pulmonary complications after gastrectomy for gastric cancer. *Surg Infect* 2014;15:314-21.
6. Patel K, Hadian F, Ali A, Broadley G, Evans K, Horder C, *et al.* Postoperative pulmonary complications following major elective abdominal surgery: A cohort study. *Perioper Med (Lond)* 2016;5:10.

7. Kodra N, Shpata V, Ohri I. Risk factors for postoperative pulmonary complications after abdominal surgery. *Open Access Maced J Med Sci* 2016;4:259-63.
8. Avila AC, Fenili R. Incidence and risk factors for postoperative pulmonary complications in patients undergoing thoracic and abdominal surgeries. *Rev Col Bras Cir* 2017;44:284-92.
9. Canet J, Gallart L, Gomar C, Paluzie G, Vallès J, Castillo J, *et al.* Prediction of postoperative pulmonary complications in a population-based surgical cohort. *Anesthesiology* 2010;113:1338-50.
10. Mazo V, Sabaté S, Canet J, Gallart L, de Abreu MG, Belda J, *et al.* Prospective external validation of a predictive score for postoperative pulmonary complications. *Anesthesiology* 2014;121:219-31.
11. Arozullah AM, Khuri SF, Henderson WG, Daley J, Participants in the National Veterans Affairs Surgical Quality Improvement Program. Development and validation of a multifactorial risk index for predicting postoperative pneumonia after major non-cardiac surgery. *Ann Intern Med* 2001;135:847-57.
12. Gupta H, Gupta PK, Schuller D, Fang X, Miller WJ, Modrykamien A, *et al.* Development and validation of a risk calculator for predicting postoperative pneumonia. *Mayo Clin Proc* 2013;88:1241-9.
13. Kupeli E, Er Dedekarginoglu B, Ulubay G, Oner Eyuboglu F, Haberal M. American Society of anesthesiologists classification versus ARISCAT risk index: Predicting pulmonary complications following renal transplant. *Exp Clin Transplant* 2017;15:208-13.
14. McAlister FA, Bertsch K, Man J, Bradley J, Jacka M. Incidence of and risk factors for pulmonary complications after nonthoracic surgery. *Am J Respir Crit Care Med* 2005;171:514-7.
15. Fernandez-Bustamante A, Frenzl G, Sprung J, Kor DJ, Subramaniam B, Martinez Ruiz R, *et al.* Postoperative pulmonary complications, early mortality, and hospital stay following noncardiothoracic Surgery: A multicenter study by the perioperative research network investigators. *JAMA Surg* 2017;152:157-66.
16. Verma S, Bhardwaj A, Patil SM. Study of post-operative pulmonary complications in patients of emergency abdominal surgeries. *Int Surg J* 2018;5:3057-65.
17. Sin DD. Postoperative pulmonary complications: What every general practitioner ought to know. *BCM J* 2008;50:152-4.
18. Qaseem A, Snow V, Fitterman N, Hornbake R, Lawrence VA, Smetana GW, *et al.* Risk assessment for and strategies to reduce perioperative pulmonary complications for patients undergoing noncardiothoracic surgery: A guideline from the American College of Physicians. *Ann Intern Med* 2006;144:575-80.
19. Hall JC, Tarala RA, Hall JL, Mander J. A multivariate analysis of the risk of pulmonary complications after laparotomy. *Chest* 1991;99:923-7.
20. Denu ZA, Yasin MO, Melekie TB, Berhe A. Postoperative pulmonary complications and associated factors among surgical patients. *J Anesth Clin Res* 2015;6:554.
21. Kumar L, Satheesan KN, Rajan S, Vasu BK, Paul J. Predictors and outcomes of postoperative pulmonary complications following abdominal surgery in a South Indian population. *Anesth Essays Res* 2018;12:199-205.
22. Parameswara G. Anesthetic concerns in patients with hyper-reactive airways. *Karnataka Anesthesia J* 2015;1:8-16.
23. Rudra A, Das S. Postoperative pulmonary complications. *Indian J Anaesth* 2006;50:89-98.
24. Kelkar KV. Post-operative pulmonary complications after non-cardiothoracic surgery. *Indian J Anaesth* 2015;59:599-605.
25. Saraswat V. Effects of anaesthesia techniques and drugs on pulmonary function. *Indian J Anaesth* 2015;59:557-64.
26. Pöpping DM, Elia N, Marret E, Remy C, Tramèr MR. Protective effects of epidural analgesia on pulmonary complications after abdominal and thoracic surgery: A meta-analysis. *Arch Surg* 2008;143:990-9.
27. Fisher BW, Majumdar SR, McAlister FA. Predicting pulmonary complications after nonthoracic surgery: A systematic review of blinded studies. *Am J Med* 2002;112:219-25.
28. Nelson R, Tse B, Edwards S. Systematic review of prophylactic nasogastric decompression after abdominal operations. *Br J Surg* 2005;92:673-80.
29. Agostini P, Cieslik H, Rathinam S, Bishay E, Kalkat MS, Rajesh PB, *et al.* Postoperative pulmonary complications following thoracic surgery: Are there any modifiable risk factors? *Thorax* 2010;65:815-8.