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ORIGINAL RESEARCH

Postoperative pulmonary complications in adult surgical patients in low- to middle-income countries: a systematic review and meta-analysis

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Background: After surgery, patients are at risk of developing postoperative pulmonary complications (PPCs). Our current understanding of PPCs is based on data from high-income countries (HICs).

Methods: A systematic review and meta-analysis was conducted to evaluate the incidence of PPCs in adult postsurgical patients from low- to middle-income countries (LMICs). The protocol was registered on the PROSPERO database (CRD42020212932). The search strategy was performed in 2021 on several electronic databases. Studies were assessed for risk of bias with the modified Newcastle-Ottawa Scale. Forest plots of the event rate for the incidence of PPCs and factors associated with PPCs were created.

Results: The search strategy identified 1 052 records. Fifteen studies were included in the final review (total of 4 873 participants). Five studies were of high methodological quality. The overall pooled event rate for the incidence of PPCs was 22.4% (95% confidence interval (CI), 15.76–30.78%). In-hospital mortality in patients who developed PPCs was 33.1%. PPCs were identified as a risk factor for in-hospital mortality (odds ratio (OR) 18.2, CI 11.01–30.09). Insufficient outcome data were available to determine the association of PPCs between elective versus emergency surgery, and cardiothoracic versus non-cardiothoracic surgery. Advanced age was associated with the development of PPCs (MD 4.7, 95% CI 0.63–8.7). Male sex was associated with the development of PPCs (OR 1.5, 95% CI 1.17–2.02). PPCs were associated with increased length of hospital stay (mean difference (MD) 6.5, 95% CI 4.04–8.96).

Conclusion: The incidence of PPCs was 22.4% following surgery in adult patients in LMICs and was influenced by differences in the definitions of PPCs used. PPCs were identified as a risk factor for in-hospital mortality. Data on the type of surgery and patient characteristics were poorly reported. Further research on PPCs in LMICs is needed to provide granular data for future use.

Keywords: pulmonary complications, outcomes, mortality, low- to middle-income

Introduction

Postoperative pulmonary complications (PPCs) are common following surgery and include respiratory infection, respiratory failure, pleural effusion, atelectasis, pneumothorax, bronchospasm and aspiration pneumonitis.[1] Depending on the definitions used to describe PPCs, the incidence of PPCs ranges from 1–23%.[2-9] In 2015, the European Perioperative Clinical Outcome (EPCO) definitions for PPCs were published and subsequently used by some researchers.[1] The Standardized Endpoints for Perioperative Medicine Core Outcome Measures in Perioperative and Anaesthetic Care (StEP-COMPAC) group performed a systematic review as part of their initiative. By means of a Delphi consensus method, definitions were created for pulmonary complications that are more precise and easier to apply. Exclusions were made for pulmonary embolism, pleural effusions, cardiogenic pulmonary oedema, pneumothorax and bronchospasm due to a lack of common biological pathophysiological mechanisms.[10] The use of different definitions of PPCs in clinical trials makes it difficult to compare the results of different studies.

Multiple risk factors for PPCs have been described and include patient characteristics, and surgical and anaesthetic risk factors. Cardiothoracic surgery is considered to have an increased risk for the development of PPCs. A cohort by Jenson and Yang[11] demonstrated that PPCs occurred in 99.4% of coronary artery bypass graft surgery patients. Ball et al.[12] recently reported the incidence of PPCs in patients undergoing cardiac surgery to be 39%. In a study by Davies et al.[13] in non-cardiothoracic surgery, the occurrence of PPCs was 12.5% in elective cases and 5.8% after major abdominal surgery. Neck, upper abdominal, major vascular, abdominal aorta aneurism repair, neurosurgery and thoracic surgery have been identified as risk factors for PPCs.[14,15] Emergency surgery increases the risk for the development of PPCs.[14,16,17] The risk has been reported to be increased six-fold in some studies.[14] Patients with an American Society of Anesthesiologists (ASA) physical status classification of II or higher are at an increased risk for the development of PPCs.[13,14,17-19] Patients with advanced age have associated comorbidities that could influence the risk for PPCs.[13,14,18,19] Smetana et al.[16] and Smetana[17] demonstrated that advanced age is a risk factor for the development of PPCs even when it was adjusted for existing comorbidities.

PPCs are linked to increased morbidity, mortality and length of hospital stay (LOS).[20,21] Between 14% and 30% of patients with a PPC will die within 30 days of major surgery, compared to 0.2–3%

without a PPC.[14] In a multicentre study by Fernandez-Bustamante et al.[21] in non-cardiothoracic surgery, the development of early mortality was significantly increased in patients who had one or more PPCs, even if it was mild. Length of stay is increased by six days in patients with at least one PPC. Furthermore, PPCs are linked to increased patient care costs and an increase in the number of intensive care unit (ICU) admissions.[21]

From the increase in mortality and LOS associated with PPCs, it is easy to understand the importance of preventing and prognosticating PPCs. A meta-analysis was published in 2020 describing the evidence for perioperative interventions for the prevention of PPCs.[22] They identified seven interventions that could reduce the development of PPCs:[22] enhanced recovery pathways, prophylactic mucolytics, postoperative continuous positive airway pressure (CPAP), lung protective ventilation intraoperatively, prophylactic respiratory physiotherapy, epidural analgesia and goal-directed haemodynamic therapy. The quality of evidence for determining the effectiveness of these interventions was low to moderate.[22] The Student Audit and Research in Surgery (STARSurg) collaborative and the Trials and Audit in Surgery by Medical Students in Australia and New Zealand (TASMAN) collaborative evaluated by means of a systematic review prognostic risk models for the prediction of PPCs specifically in patients undergoing major abdominal surgery. Data were collected to validate six eligible models in the international external validation cohort study. The Assess Respiratory Risk in Surgical Patients in Catalonia (ARISCAT) score was identified as the superior model for discrimination with the area under the receiver operating characteristic curve of 0.70 and a 95% confidence interval of 0.68 to 0.71.[23] However, with the development of consensus definitions from the StEP-COMPAC group, novel risk models will need to be developed.

The current evidence base describing PPCs has largely been obtained from high-income countries (HICs). Healthcare systems in low- to middle-income countries (LMICs; see definition in Supplementary Table I) have more vulnerable drug policies and supply systems. There is also inadequate technical guidance, programme management and supervision. Other factors that influence the healthcare systems of LMICs are the lack of equipment and infrastructure, and poor accessibility to health services.[24,25] This may affect the incidence of PPCs and the severity of subsequent complications in patients treated in LMICs. Communicable, maternal, perinatal and nutritional conditions are a major burden on low-income countries, and this is exacerbated by the HIV/AIDS pandemic.[26] The significance of PPCs in laparotomies and abdominal cancer surgeries are important factors in LMICs. Fragmentation of care and the lack of primary care assistance leads to patients being operated on in advanced stages of disease.[27-29] With these facts in mind, one can expect that the incidence of PPCs in LMICs will be higher than those in HICs.

The aim of this systematic review was to establish and outline the incidence of PPCs in adult surgical patients in LMICs with a view to identifying risk factors and to quantify outcomes such as mortality and length of stay (in hospital and ICU). This information could generate research opportunities to guide future clinical practice and healthcare policymaking in patients at risk of developing PPCs in LMICs.

The specific objectives or questions that this review aims to address are the following:

- What is the incidence of PPCs and the association between PPC and perioperative mortality in low- to middle-income countries?
- How does the PPC rate compare between elective and emergency surgery in LMICs?
- How does the PPC rate compare between cardiothoracic and non-cardiothoracic surgery in LMICs?
- What is the associated PPC rate according to age in LMICs?
- What is the associated PPC rate according to sex in LMICs?
- How does the development of PPCs influence the length of hospital or ICU stay?

Methods

Review question

The PICO (population, intervention, control, outcome) principle was used to formulate the review question. The population was defined as adult (≥ 18 years) surgical patients undergoing anaesthesia in LMICs (as defined by the World Bank – Supplementary Table I) and included all procedures conducted under general, regional or local anaesthesia. The intervention and comparison sections were not applicable. The outcome of the review was the incidence of PPCs and associated mortality. We included observational studies and randomised controlled trials.

Protocol and registration

The protocol adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines[30] (PRISMA checklist – Supplementary Table II) and was registered with PROSPERO (CRD42020212932). The study was approved by the Health Science Research Ethics Committee (HSREC) of the University of the Free State in Bloemfontein, South Africa (ethics number UFS-HSD2020/1486/2710).

Eligibility criteria

We included studies of adult (older than 18 years) postoperative patients reporting the incidence of PPCs and associated mortality. Surgical procedures conducted under general, regional or local anaesthesia were all included. We also included both randomised controlled trials and observational studies. Studies that were not from low- or middle-income countries as defined by the World Bank (refer to Supplementary Table I), duplicate studies, studies not in English, studies in which insufficient data points had been reported, reviews and trial registrations were all excluded.

Information sources, searches and study selection

Searches were conducted using terms based on concepts from the research question. A detailed example of the search is shown in the Supplementary Table III. No restriction was placed on when studies were published. Search strategies were, however, limited to the title of search results. The search strategy was applied in the following databases: MEDLINE (PubMed), CINAHL (via EBSCOhost), Scopus (including Embase), Web of Science (all databases), Cochrane Central Register of Controlled Trials and Proquest.

Data collection process

The search results of each database were exported to a reference management tool (Zotero Version 5.0; Corporation for Digital Scholarship; Vienna, VA, USA). Duplicates were removed using the built-in function of the reference management tool. The remaining results were extracted into two identical Microsoft® Excel v 365 (Microsoft Corp.; Redmond, WA, USA) spreadsheets. Each spreadsheet contained columns for the title, author, journal and citation information as well as the full abstract for each identified article. Every article was assigned a record number by the reference management tool by which it could be identified. All abstracts in the spreadsheet were screened by two independent researchers (authors EE and ET) according to the predefined eligibility criteria as set out above. Discrepancies were reviewed and resolved by a third independent researcher (author RR).

Studies in which PPCs were not explicitly defined were excluded. Similar to the abstracts, the full-text publications of the remaining eligible studies were reviewed by the two independent researchers. Discrepancies were reviewed and resolved by the third independent researcher. Data were extracted into a standardised form by the two independent researchers and compared for accuracy. Any inconsistencies were resolved by the third independent researcher.

Data items

Data regarding the definitions of PPCs, the incidence of PPCs, mortality, sex, age, elective versus emergency surgery, cardiothoracic versus non-cardiothoracic surgery, LOS, and length of ICU stay were extracted. It was decided to extract data that are frequently and consistently reported in studies evaluating PPCs. Common variables identified for the prediction of PPCs include the type of surgery, the patient's age and whether the procedure was listed as an emergency as proven by STARSurg collaborative study.[23] Outcome data that would indicate the magnitude of associated effects of PPCs (such as mortality, LOS) have also been reported consistently.

Outcomes

The primary outcome was the incidence of PPCs and the association between PPCs and mortality in LMICs. Secondary outcomes were to compare the incidence of PPCs between elective versus emergency surgery, and cardiothoracic versus non-cardiothoracic surgery in LMICs, and to evaluate the association between sex and age with PPCs. The LOS associated with the development of PPCs was also evaluated.

Risk of bias assessment

Included articles were assessed for risk of bias by using a modified Newcastle-Ottawa Scale (NOS) (see Supplementary Table IV).[31] This quality assessment was done by two independent researchers on the data extraction forms. Any discrepancies were resolved by the third researcher.

Summary measures and synthesis of results

A minimum of three studies reporting outcome data was set as the criterion for data synthesis. SAS v 9.3 (SAS Institute Inc.; Cary, NC, USA) was used for the statistical analysis.

The meta-analysis included the calculation of pooled odds ratios (OR), 95% confidence intervals (CI) and mean differences (MD). The event rate for the incidence of PPCs of each included study was calculated and a pooled overall event rate of the incidence of PPCs was calculated. Individual forest plots of all the factors associated with PPCs were created.

Heterogeneity between studies was assessed using an X^2 test and an I^2 test. A p-value of < 0.10 and an I^2 of $> 25\%$ indicated heterogeneity requiring a random effect model. If no heterogeneity was found, a fixed effect model was used. Mean differences and interquartile ranges (IQRs) were converted to medians, as proposed by Luo et al.,[32] and estimated standard deviations (SDs), as proposed by Wan et al.,[33] were used for inverse variance analysis. We performed a sensitivity analysis of patients undergoing abdominal surgery to explore sources of heterogeneity. Funnel plots were used to evaluate the risk of publication bias.

Results

Study selection

The search strategy identified 1 052 records (Supplementary Figure 1). Of these, 445 duplicates were removed and the remaining 607 records were individually reviewed by two independent researchers. Six articles were further excluded due to unavailability of an English-language abstract, while two articles were retracted and not included. Full-text publications of 91 articles were sought and reviewed. After the full-text review, 15 studies published between 2004 and 2021 (Table I) met the inclusion criteria. The calculated Cohen's kappa for the level of agreement after full-text review between researchers EE and ET was 0.98, indicating excellent agreement.

Study characteristics of included studies

The 15 studies that were included represented a total of 4 837 patients. The studies had relatively small sample sizes, with seven (46.7%) of the studies reporting results on sample sizes of less than 200 patients.[34-40] The average sample size of the studies was 322.5 patients, ranging from 35[34] to 1 170[41] patients in two separate Indian studies. Ten out of the 15 studies

Table I: Characteristics of studies included describing the country, sample size, patients' age, study type, title of publication, type of surgery, risk factors and mortality, and number of cases of postoperative pulmonary complications

Reference First author (year)	Country (region)	Sample size (n)	Patients' age (years)*	Study type	Title of publication	Urgency of surgery and operative speciality	Risk factors associated with PPCs identified	Mortality rate with PPC (%)	Postoperative pulmonary complications: *n* (%)
Chai (2021)[45]	China	445	71 (IQR 65–91)	Retrospective	Identification of the risk factors of postoperative pulmonary complications in elderly patients undergoing elective colorectal surgery.	Elective, colorectal	Older age ASA > II Basic lung disease Hypertension Myocardial ischaemia Preoperative haemoglobin < 100 g/L Albumin < 35 g/L Laparotomy versus laparoscopic Blood transfusion	Not reported	Number of patients with PPCs 49 (11.0%)
Charokar (2020)[34]	India	35	42.03 (SD ± 21.83)	Prospective	Evaluation of postoperative pulmonary complications after emergency abdominal surgery – a prospective study.	Emergency, abdominal	Age > 45 years Smoking Underlying lung disease Duration of surgery Socio-economic status	5.7 (in hospital)	Number of patients with PPCs 8 (51.4%) Pneumonia 9 (25.7%) Acute respiratory failure 4 (11.4%) Pleural effusion 2 (5.7%) Pulmonary oedema 2 (5.7%) Atelectasis 1 (2.8%)
De Ávila (2017)[42]	Brazil	314	46.61 (SD ± 15.98)	Prospective	Incidence and risk factors for postoperative pulmonary complications in patients undergoing thoracic and abdominal surgeries.	Urgency not stated, thoracic, abdominal	Diabetes Previous lung disease Video surgery Hospitalisation for more than 5 days Surgical size Duration of surgery more than 3 hours Presence of neoplasm COPD	1.9 (in hospital)	Number of patients with PPCs 36 (11.5%) Respiratory failure 29 (9.2%) Pleural effusions 4 (1.3%) Pneumonia 4 (1.3%) Prolonged mechanical ventilation 3 (1%) Bronchospasm 2 (0.6%) Tracheobronchitis 2 (0.6%) Pulmonary oedema 2 (0.6%) Pneumothorax 1 (0.3%) Atelectasis 1 (0.3%) Pulmonary embolism 1 (0.3) Prolonged intubation 3 (1%)
Gülsen (2020)[35]	Turkey	124	56.72 (SD ± 14.85)	Prospective	Comparison of postoperative pulmonary complication indices in elective abdominal surgery patients.	Elective, abdominal	ASA > III CPRI with score 3 or more RFI score of 4 and above Pneumonia risk index score 3 or above Higher Shapiro risk index score	Not reported	Number of patients with PPCs 5 (52.4%) Pleural effusion 23 (18.5%) Atelectasis 12 (9.7%) Prolonged mechanical ventilation 11 (8.9%) Respiratory failure 7 (5.6%) Bronchospasm 5 (4.0%) Pneumonia 4 (3.2%) ARDS 2 (1.6%) Reintubation 1 (0.8%)
Gupta (2020)[41]	India	1 170	≥ 18	Prospective	Perioperative risk factors for pulmonary complications after non-cardiac surgery.	Elective and emergency, multi-specialty non-cardiac surgery	Higher ARISCAT score Older age Positive cough test Postoperative nasogastric tube Intraoperative pulmonary complications ASA status > II Haemoglobin levels < 10 g/dL Preoperative saturation on room air < 95 %	Not reported	Number of patients with PPCs 9 (5.0%) Postoperative pulmonary infection 48 (4.1%) Aspiration pneumonitis 3 (0.2%) Atelectasis 3 (0.2%) Bronchospasm 3 (0.2%) Pulmonary embolism 1 (0.1%) Pleural effusion 1 (0.1%)

Table I: Continued

Reference First author (year)	Country (region)	Sample size (n)	Patients' age (years)*	Study type	Title of publication	Urgency of surgery and operative speciality	Risk factors associated with PPCs identified	Mortality rate with PPC (%)	Postoperative pulmonary complications: *n* (%)
Hooda (2019)[48]	India	288	36.7 (SD ± 12.6)	Retrospective	Incidence and predictors of postoperative pulmonary complications in patients undergoing craniotomy and excision of posterior fossa tumour.	Elective, neurosurgery	Postoperative blood transfusion LCN palsy Prolonged ICU stay Massive blood transfusion ASA class III Need for tracheostomy	4.2 (in hospital)	Number of patients with PPCs 35 (12.1%) Atelectasis 9 (3.1%) Pneumonia 6 (2.1%) Tracheobronchitis 6 (2.1%) Weaning failure/reintubation 9 (3.1%) Pneumothorax 2 (0.7%) ARDS/respiratory failure 3 (1.0%)
Jing (2018)[46]	China	453	56 (IQR 43–70)	Retrospective	Incidence and risk factors of postoperative pulmonary complications after thoracic surgery for early non-small cell lung cancer.	Urgency not stated, thoracic, oncological	Advanced age History of smoking History of COPD History of CKD History of liver disease Massive blood loss Oliguria Accumulation of lactate	0.8 (in hospital)	Number of patients with PPCs 102 (22.5%) Pulmonary oedema 42 (9.3%) Atelectasis 32 (7.1%) Pneumonia 19 (4.2%) ARDS 8 (1.8%) Respiratory failure 1 (0.2%)
Kanat (2007)[36]	Turkey	60	55 (SD ± 16)	Prospective	Risk factors for postoperative pulmonary complications in upper abdominal surgery.	Elective, upper abdominal	Preoperative respiratory symptoms Abnormal FEV1/FVC		Number of patients with PPCs 35 (58.3%) Pneumonia 9 (15%) Pneumonitis 9 (15%) Atelectasis 8 (13.3%) Bronchitis 7 (11.7%) Pulmonary embolism 1 (1.7%) Acute respiratory failure 1 (1.7%)
Kodra (2016)[43]	Albania	450	59.85 (SD ± 13.64)	Prospective cohort	Risk factors for postoperative pulmonary complications after abdominal surgery.	Elective and emergency, abdominal	Age 65 years and older Duration of operation 2.5 hours or more History of previous pulmonary disease ASA class higher than II	13.3 (in hospital)	Number of patients with PPCs 123 (27.3%)
Kumar (2018)[37]	India	150	52.76 (SD ± 14.35)	Prospective	Predictors and outcomes of postoperative pulmonary complications following abdominal surgery in a South Indian population.	Elective and emergency, abdominal.	Emergency surgery Cardiac comorbidity	Not reported	Number of patients with PPCs 24 (16%)
Özdī lekcan (2004)[38]	Turkey	95	60.7 (SD ± 13.0)	Prospective	Risk factors associated with postoperative pulmonary complications following oncological surgery.	Elective, abdominal, genitourinary, head-and-neck	Duration of anaesthesia per hour Abdominal incision FEV1 < 50 %	Not reported	Number of patients with PPCs 38 (40%) Atelectasis 13 (13.7%) Bronchospasm 13 (13.7%) Pneumonia 11 (11.6%) Effusion 8 (8.4%) Respiratory failure 5 (5.3%) Thromboembolism 2 (2.1%)
Pramanik (2020)[39]	India	70	63 (IQR 57–68)	Retrospective	Postoperative pulmonary complications in robot-assisted uro-oncological surgeries: our experience in a tertiary cancer care centre.	Elective, robot-assisted, uro-oncological	Could not identify due to small sample size.	Not reported	Number of patients with PPCs 3 (4.3%)

Table I: Continued

Reference First author (year)	Country (region)	Sample size (n)	Patients' age (years)*	Study type	Title of publication	Urgency of surgery and operative speciality	Risk factors associated with PPCs identified	Mortality rate with PPC (%)	Postoperative pulmonary complications: *n* (%)
Sogame (2008)[44]	Brazil	236	42 (SD ± 14)	Prospective cohort	Incidence and risk factors for postoperative pulmonary complications in elective intracranial surgery.	Elective, neurosurgery	Type of surgery performed Duration of mechanical ventilation for more than 48 hours Length of ICU stay more than 3 days Postoperative lower level of consciousness Duration of surgery 300 minutes or more Presence of chronic lung disease	8.9 (in hospital)	Number of patients with PPCs 76 (32.2%) Atelectasis 5 (2.11%) Bronchospasm 19 (8.0%) Tracheobronchitis 32 (13.6%) Pneumonia 20 (8.5%)
Vasu (2019)[40]	India	155	≥ 18	Prospective	Perioperative factors influencing the incidence of postoperative pulmonary complications in patients undergoing head-and-neck versus abdominal surgeries and their outcome.	Elective, head-and-neck, abdominal	Abdominal surgery Increase duration of perioperative mechanical ventilation	9.0 (in hospital	Number of patients with PPCs 52 (33.54%)
Wang (2017)[47]	China	828	64.5 (SD ± 10.3)	Retrospective cohort	The long-term impact of postoperative pulmonary complications after video-assisted thoracic surgery lobectomy for lung cancer.	Elective, video-assisted thoracic surgery, oncological	Increased age Male sex Higher ASA grade	Not reported	Number of patients with PPCs 139 (16.78%) Pneumonia 37 (4.5%) Respiratory failure 7 (0.8%) Pleural effusion 28 (3.4%) Atelectasis 12 (1.4%) Pneumothorax 7 (0.8%) Prolonged air leak 66 (8.0%) Chylothorax 16 (1.9%) Subcutaneous emphysema 14 (1.7%) Haemothorax 3 (0.4%) Empyema 1 (0.1%) Bronchial pleural fistula 4 (0.5%) ARDS 2 (0.2%) Idiopathic pulmonary interstitial fibrosis 1 (0.1%)

ARDS – acute respiratory distress syndrome, ARISCAT – Assess Respiratory Risk in Surgical Patients in Catalonia Score, ASA – American Society of Anesthesiologists physical status classification system, CI – confidence interval, CKD – chronic kidney disease, COPD – chronic obstructive pulmonary disease, CPRI – Epstein's cardiopulmonary risk index, FEV1 – forced expiratory volume in one second, FVC – forced vital capacity, ICU – intensive care unit, LCN – lower cranial nerve, OR – odds ratio, PPC – postoperative pulmonary complication, RFI – respiratory failure index
*Reported as median and standard deviation (SD) or mean and interquartile range (IQR). Where age was not reported, it is indicated that the participants were older than 18 years of age.

were prospective observational studies.[34-38,40-44] Countries of origin of these studies included Albania,[43] Brazil,[42,44] China,[45-47] India[34,37,39-41,48] and Turkey.[35,36,38] The characteristics of the studies, outcomes and the patients' age distribution per study are shown in Table I. The different definitions used in these studies to define PPCs are summarised in the Supplementary Table V.

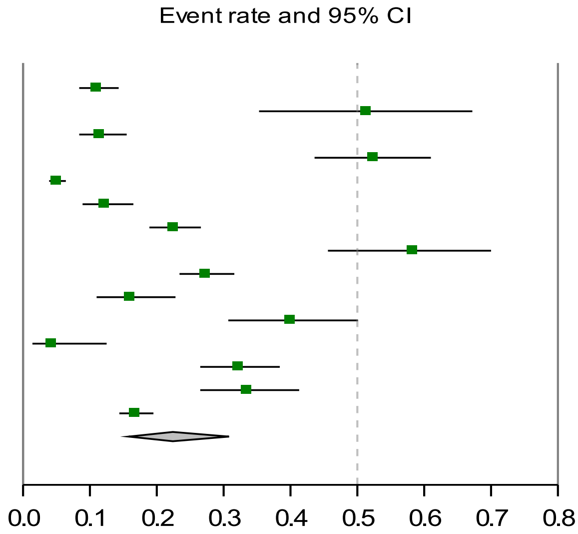
Risk of bias within and across studies

Risk of bias assessment was determined by using the modified NOS[31] (Supplementary Table VI). A maximum of nine stars can be awarded in total. With regard to the categories selection and outcome, five studies received four stars[34-36,41,48] and 10 studies received three stars.[34-36,39,41,43,44,46-48] No stars were awarded to any of the studies for the comparability category. None of the 15 studies controlled for interventions or comorbidity risk factors. Five studies were considered to be of high-quality (received seven or more stars)[34-36,41,48] and 10 of low-quality.[37-40,42-47]

Results of individual studies and synthesis of results

Incidence of PPCs and associated mortality. The overall pooled event rate for the incidence of PPCs was 22.4% (95% CI 15.76–30.78%) with significant heterogeneity between studies. The potential for publication bias was assessed as high (funnel plot, Supplementary Figure 2). A representation of PPC incidence in the form of the overall event rate (OER) is shown in Figure 1. Three studies had an OER for PPCs above 50%, which were studies with small sample sizes of surgical patients after abdominal surgery.[34-36] The lowest and highest OER for PPCs were 4.3% (95% CI 1.39–12.46%)[39] and 58.3% (95% CI 45.59–70.05%),[36] respectively. Pulmonary oedema had the highest incidence of PPCs at 5.7% (*n* = 46 out of 802 patients). Of the 46 patients who developed pulmonary oedema, 42 (91.3%) patients were reported from one study.[46] The second most common PPC was pneumonia with an incidence of 4.6% (*n* = 167 out of 3 603 patients). Seven studies reported on mortality associated with PPCs.[34,40,42-44,46,48] The follow-up of mortality outcome reported

Study	Event rate	Lower limit	Upper limit	Total	Weight
Chai, 2021	0.110	0.084	0.143	49/445	6.9%
Charokar, 2020	0.514	0.353	0.672	18/35	6.1%
de Ávila, 2017	0.115	0.084	0.155	36/314	6.8%
Gülsen, 2020	0.524	0.436	0.610	65/124	6.8%
Gupta, 2020	0.050	0.039	0.064	59/1170	7%
Hooda, 2019	0.122	0.089	0.165	35/288	6.8%
Jing, 2018	0.225	0.189	0.266	102/453	7%
Kanat, 2007	0.583	0.456	0.700	35/60	6.5%
Kodra, 2016	0.273	0.234	0.316	123/450	7%
Kumar, 2018	0.160	0.110	0.228	24/150	6.7%
Özdi̇lekcan, 2004	0.400	0.307	0.501	38/95	6.7%
Pramanik, 2020	0.043	0.014	0.125	3/70	4.7%
Sogame, 2008	0.322	0.265	0.384	76/236	6.9%
Vasu, 2019	0.335	0.265	0.413	52/155	6.9%
Wang, 2017	0.168	0.144	0.195	139/828	7.1%
Total (95% CI)	**0.224**	**0.158**	**0.308**		**100%**



Heterogeneity: Tau ^{2} = 0.68; Q= 402, df = 14 (P < 0.0001); I^2= 97%

Figure 1: Meta-analysis of overall event rate for postoperative pulmonary complications in postoperative patients from low- to middle-income countries
CI – confidence interval

Study	PPCs Events	PPCs Total	Non PPCs Events	Non PPCs Total	Weight	Odds Ratio M-H, fixed, 95% CI
Charokar, 2020	2	18	0	17	5.8%	5.30 [0.24, 118.89]
de Ávila, 2017	6	36	1	278	2.5%	55.40 [6.45, 475.72]
Kodra, 2016	60	123	18	327	66%	16.35 [9.04, 29.56]
Sogame, 2008	21	76	2	160	12.2%	30.16 [6.85, 132.84]
Vasu, 2019	12	52	2	103	13.5%	15.15 [3.24, 70.74]
Total (95% CI)	**101**	**305**	**23**	**885**	**100%**	**18.20 [11.01, 30.09]**

Heterogeneity: Chi^2 = 2.26, df= 4 (P = 0.69); I^2 = 0%
Test for overall effect: Z = 11.32 (P < 0.00001)

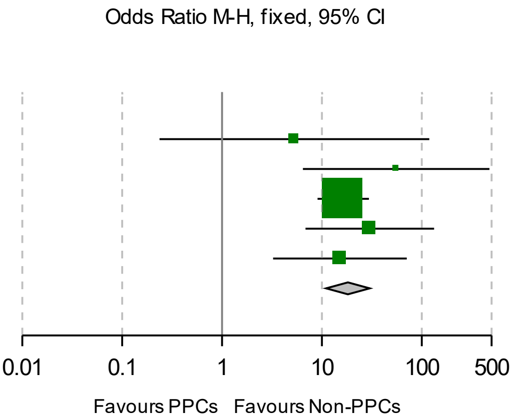


Figure 2: Meta-analysis of in-hospital mortality associated with postoperative pulmonary complications for adult surgical patients in low- to middle-income countries
PPCs – postoperative pulmonary complications, M-H – Mantel-Haenszel, CI – confidence interval

in the studies varied. PPCs were identified as a risk factor for in-hospital mortality (OR 18.20, 95% CI 11.01–30.09), as illustrated in Figure 2.[34,40,42-44] The potential for publication bias was assessed as high (funnel plot, Supplementary Figure 3).

Comparing the incidence of PPCs in elective versus emergency surgery and cardiothoracic versus non-cardiothoracic surgery. A meta-analysis of these types of surgery could not be conducted due to insufficient data. Only one study reported the incidence of PPCs in both elective and emergency surgery, which was 12.1% (*n* = 16/132) and 44.4% (*n* = 8/18), respectively.[37] PPCs in cardiothoracic versus non-cardiothoracic surgery could not be compared due to a lack of data.

Patient characteristics and their association with PPCs. Sufficient data were available to perform a meta-analysis of age[35-39] and sex[35-38,43,45] associated with PPCs. Advanced age (MD 4.7, 95% CI 0.63–8.7) was associated with PPCs. Heterogeneity was observed in these estimates (Supplementary Figure 4). Male sex was associated with the development of PPCs (OR 1.53, 95% CI 1.17–2.02) with no heterogeneity among the studies included (Supplementary Figure 5).

Length of hospital stay and length of ICU stay associated with PPCs. Supplementary Figure 6 shows that PPCs were associated with increased LOS[34,37,41,43,48] (MD 6.5, 95% CI 4.04–8.96). A meta-analysis of length of ICU stay could not be performed because data associated with PPCs and ICU admission were reported in only two studies.[37,48]

Sensitivity analysis. Studies that reported outcome data for patients undergoing abdominal surgeries were included in a sensitivity analysis to explore sources of heterogeneity and enable a more uniform analysis for PPCs.[34-37,40,43,45] The total sample size for these studies included 1 342 patients. The analysis found a higher overall PPC event rate of 35.1% (Supplementary Figure 7), significantly higher than the initial analysis with reduced heterogeneity (I^2 of 6.89%). There was little impact on the other outcomes, as most of the studies included in the sensitivity analysis dominated the main analysis (Supplementary Figures 8–11). This could be because the studies reporting other types of surgeries did not report the needed outcome data to be included in the initial analysis. The meta-analysis for PPCs associated with age in the sensitivity analysis continued to demonstrate high heterogeneity. For mortality outcome, the heterogeneity was unchanged, and the overall estimated effect remained high.

Discussion

This systematic review of adult surgical patients in LMICs has found a high incidence of PPCs. Different definitions were used to define PPCs, which influenced the true incidence of PPCs (see Supplementary Table V). The estimated pooled incidence was 22.4%. PPCs were associated with an increase in the LOS. In our review, the overall in-hospital PPC-associated mortality was 33.1% (*n* = 101/305). Advanced age and male sex were associated with the development of PPCs. No comparison of elective versus emergency surgery and the development of PPCs could be made due to insufficient outcome data reported in the studies. This was also true when comparing cardiothoracic versus non-cardiothoracic surgery.

Strengths and weaknesses of this review

The strength of this review lies in its standardised and robust methodology (PRISMA guidelines).[30] Two independent researchers screened abstracts and full texts, performed data extraction and risk of bias assessment. A third independent researcher was responsible for resolving any discrepancies. No limitation was set on the date of publication, and multiple relevant databases were used to conduct the search strategy.

The weakness of this systematic review, however, is that different PPC definitions were used in the included studies, consequently affecting the true incidence of PPCs. The total sample size was small and may not reflect the true characteristics of the intended study population. After reviewing the full texts of 607 articles, only 15 studies were included in the final systematic review. Search strategies were limited to include the title of search results. Most of the studies excluded from data synthesis for the outcome of morality did not specifically report mortality in patients with or without PPCs, and in many cases the follow-up period for mortality was not indicated. Two multicentre studies were excluded due to a lack of usable data points.

The review is dominated by studies from India, China and Turkey, and might not reflect representative data of studies conducted in other LMICs. The full text of 16 articles could not be obtained. The corresponding authors of these articles were contacted at the time of full-text screening (1 March 2022), but no response was received at the time of finalising this manuscript. The library services of the University of the Free State also could not retrieve the full-text articles. Our review has been limited by the large between-study heterogeneity in the calculation of estimates and by the inclusion of only studies published in the English language. The heterogeneity in our study could be explained by differences in baseline disease severity, comorbidities, differences in the anaesthetic and surgical management, and the different types of surgical populations (abdominal versus other types of surgery). None of the 15 studies controlled for interventions or comorbidity risk factors.

Strengths and weaknesses in relation to other studies

We could identify no previously published systematic reviews or meta-analyses on PPCs in LMICs and could, therefore, not perform any comparisons. Furthermore, none of the 15 studies included in the review was derived from research conducted in any country on the African continent, obviously emphasising the necessity for African-based research. Our study highlighted the need for further research in this area and strengthens the evidence that PPCs are common and associated with increased mortality and an increased LOS.

Comparison with evidence from high-income countries

The incidence of PPCs from studies performed in HICs demonstrated notable variation. An incidence of 14.4% was found in a systematic review and meta-analysis performed by Odor et al.[22] that included 21 940 patients. Their analysis included patients undergoing various types of procedures, predominantly abdominal, vascular and thoracic surgery.[22] A systematic review of PPCs after non-cardiac surgery that included predominantly studies related to abdominal surgery, reported an incidence of 2–19% among the included studies.[49] The systematic review by the STARSurg and TASMAN Collaborative that evaluated prognostic risk models for PPCs, demonstrated an incidence of 0.2–24.6% in patients undergoing major abdominal surgery.[23]

In our analysis, we found a high incidence of PPCs that corresponded to the upper end of the reported incidence of PPCs in HICs. If we considered the incidence of PPCs in the subgroup of our patients that underwent abdominal surgery, the incidence was 31.5%, which was notably higher than reported in HICs. Between 14% and 30% of patients with a PPC will die within 30 days of major surgery.[14] The duration of follow-up for mortality outcome in our included studies varied. In this study, PPCs were associated with increased mortality with an odds ratio of 18.20 (95% CI 11.01–30.09).

Older age was identified in HICs as a risk factor for the development of PPCs. A systematic review for the American College of Physicians demonstrated an odds ratio of 2.09 (CI 1.65–2.64) in patients 60–69 years old, and an odds ratio of 3.04 (CI 2.11–4.39) in patients 70–79 years of age for the development of PPCs.[16] Similarly, we identified age as a risk factor for the development of PPCs with a higher odds ratio (4.67, CI 0.63–8.7). There was significant heterogeneity in our analysis. Studies from HICs identified male sex as a risk factor for the development of PPCs.[7,50] We also identified male sex as a risk factor for the development of PPCs. Postoperative LOS was prolonged by a median of 10 days in patients with at least one PPC.[51] We observed that PPCs were associated with increased LOS with a mean difference of 6.5 days. The quality of evidence from HICs are mostly obtained from studies of low or moderate quality. The STARSurg Collaborative and TASMAN Collaborative assessed their included studies with the PROBAST (Prediction model Risk Of Bias Assessment Tool) tool and found a high overall risk of bias.[23] Our review was dominated by studies of poor quality similar to those from HICs.

The impact of PPCs in abdominal surgery in patients from LMICs

Surgical patients from LMICs undergoing abdominal surgery are highly vulnerable and need special consideration. This group includes patients undergoing emergency laparotomies and laparotomies for oncological surgery. The GlobalSurg collaborative emphasised a markedly increased risk of morbidity and mortality in patients undergoing emergency abdominal surgery in LMICs compared to HICs, with an adjusted 30-day mortality OR of 2.97 (CI 1.84–4.81).[28] The factors involved are complex. Fragmentation of care, lack of primary health assistance, lack of access to healthcare and other factors all play a role. Patients often present in advanced stages of their disease, further increasing the risk of developing complications.[52,53]

Our results demonstrated a high risk for PPC development in patients undergoing abdominal surgery in LMICs. This is aligned with previous studies reporting increased morbidity in adult surgical patients from LMICs undergoing abdominal surgery. In 2021, a study was published evaluating the global variation in postoperative mortality and complications after cancer surgery. The 30-day postoperative mortality was found to be fourfold higher in countries or settings with limited resources. LMICs lacked postoperative care infrastructure (designated postoperative recovery areas, consistently available critical care facilities and radiological services) and protocolised oncological care pathways.[27] The foundation for improvement in the care of patients in LMICs starts with establishing contextually applicable guidelines that are consistent, evidence-based and patient-centred, and facilitate the delivery of high-quality, equitable perioperative care.[54]

The Enhanced Recovery After Surgery Society published guidelines for perioperative care in elective abdominal and pelvic surgery in LMICs.[55] This guideline, in addition to guidelines such as the ICOUGH (Incentive spirometry, Coughing and deep breathing, Oral care, Understanding, Getting out of bed at least three times daily, and Head-of-bed elevation) programme,[56] could mitigate the development of PPCs in these vulnerable abdominal surgical patients from LMICs. The Preventing Pulmonary Complications in Surgical Patients at Risk of COVID-19 (PROTECT-Surg) trial will possibly provide future data regarding PPCs in LMICs (national clinical trial number: **NCT04386070)**.

Implications for clinicians and future research

To gain insight and compare information regarding PPCs in LMICs, there is a need to conduct large observational studies of high-quality that will provide granular data for further research. To represent the intended study population, studies from LMICs other than China, Turkey, Brazil and India are needed. Different pulmonary diseases should be considered in these different countries, as PPCs associated with underlying pulmonary diseases are more likely to occur, e.g. pulmonary tuberculosis is prevalent in South Africa.[57] Socioeconomic factors should be investigated because economically disadvantaged populations are often more immunocompromised due to malnutrition and HIV infection,[58] which could contribute to the incidence of PPCs.

Respiratory diseases associated with exposure to biomass fuels in more rural populations can influence the incidence of PPCs.[59] By obtaining information about underlying pulmonary diseases and socioeconomic factors, alterations in clinical practice and policymaking can be made to reduce the number of PPCs. Examples include preoperative screening for HIV infection and poor nutrition. Mortality outcome data should be documented and the mortality follow-up period reported. Standardised definitions for PPCs, such as those described by the StEP-

COMPAC group, should be used to render outcome data more comparable.

Conclusion

We conclude that the development of PPCs were common following surgery in adult patients of LMICs. However, the incidence might have been influenced by variations in the definitions of PPCs applied in the studies included in this systematic review. Our review included studies with relatively small sample sizes and of poor methodological quality. PPCs were identified as a risk factor for in-hospital mortality. The type of surgery and patient characteristics data were poorly reported in the studies. Further research regarding PPCs in various surgical populations from LMICs are needed to provide granular data for future use. This will enable changes in clinical practice or quality improvement protocols to reduce the incidence of PPCs.

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Conflict of interest

The authors declare no conflict of interest.

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Ethical approval

This study was approved by the Health Science Research Ethics Committee (HSREC) (ethics number UFS-HSD2020/1486/2710) of the University of the Free State.

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