

Predictors of postoperative pulmonary complications after liver resection: Results from a tertiary care intensive care unit

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Abstract

Background: Postoperative pulmonary complication (PPC) is a serious complication after liver surgery and is a major cause of mortality and morbidity in the intensive care unit (ICU). Therefore, the early identification of risk factors of PPCs may help to reduce the adverse outcomes. **Objective:** The aim of this retrospective study was to determine the predictors of PPCs in patients undergoing hepatic resection. **Design:** Retrospective, observational. **Methods:** The patients admitted after hepatic resection in the gastrosurgical ICU of our institute between October 2009 and June 2013 was identified. The ICU charts were retrieved from the database to identify patients who developed PPCs. A comparison of risk factors was made between the patients who developed PPC (PPC group) against the patients who did not (no-PPC group). **Results:** Of 117 patients with hepatic resection, 28 patients developed PPCs. Among these, pneumonia accounted for 12 (42.8%) followed by atelectasis in 8 (28.5%) and pleural effusion in 3 (10.7%). Among the patients developing PPCs, 16 patients were over a 70-year-old (57.1%), 21 patients were smokers (75%) and 8 patients (28.5%) had chronic obstructive pulmonary disease (COPD). The requirement for blood transfusion and duration of mechanical ventilation were greater in the patients developing PPC (2000 ± 340 vs. 1000 ± 210 ml; 10 ± 4.5 vs. 3 ± 1.3 days). **Conclusion:** Old age, chronic smoking, COPD, increased blood product transfusion, increased duration of mechanical ventilation and increased length of ICU stay increased the relative risk of PPC, presence of diabetes and occurrence of surgical complications (leak, dehiscence, etc.) were independent predictive variables for the development of PPC.

Keywords: Hepatic resection, postoperative pulmonary complications, posthepatic resection complications

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Introduction

Hepatic resection is the treatment of choice for various primary and secondary liver malignancies and is a potentially curative option in many situations.^[1,2] The advancements in surgical and anesthetic techniques coupled with better intensive care facilities have produced improved outcome after hepatic resection over

the past few decades.^[2,3] Despite this, hepatic resection remains a complex procedure with important risks of perioperative mortality and morbidity.^[4,5]

Postoperative pulmonary complications (PPCs) have been defined as “any pulmonary abnormality occurring in the postoperative period that produces identifiable disease or dysfunction that is clinically significant and adversely affects clinical course.”^[6] PPC are a major cause of morbidity and mortality in the postoperative period after hepatic resection and include pulmonary atelectasis, pleural effusion, pulmonary edema, and pneumonia.^[7,8] The incidence of PPC is variable, but may be as high as 63.6-86.7% after orthotopic liver transplantation.^[9] The

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progression from certain PPCs viz. pneumonia to acute lung injury (ALI) is often rapid and is associated with high mortality and limited treatment options.^[10]

Methods

This study is a retrospective analysis of 117 patients admitted in the gastro surgical intensive care unit (ICU) of our institute between October 2009 and June 2013, where hepatic resection was performed, either for a primary or a secondary liver tumor. Sample size calculation was not done because *post-hoc* power analysis in the setting of negative trials ($P < 0.05$) in a retrospective study produces a low *post-hoc* power result, which can be misinterpreted as the trial having inadequate power.

All cases were analyzed in terms of etiology, Child-Turcotte-Pugh score, American Society of Anesthesiology status, presence of comorbid diseases, extent of hepatic resection, duration of surgery, duration and need for mechanical ventilation, blood and blood product transfusion, requirement of inotropes and vasopressors, electrolyte abnormalities, coagulopathy, other surgical complications (leak, wound dehiscence, etc.), and the mortality.

A comparison was made between the patients who developed PPCs against those who did not.

The following operational definitions of PPC were chosen for the purpose of the study [Table 1].

Statistical analysis

The Statistical Software Package for the Social Sciences (SPSS, version 16.0, IL, Chicago) was used for the analysis of data. Summary descriptive statistics, including frequencies, means, and standard deviations, were computed for the preoperative variables. Fourteen preoperative and demographic risk factors [Table 2] were dichotomized (absent or present), and cut-off points for continuous variables (e.g. age, type of resection, body mass index, preoperative hemoglobin, prothrombin time, etc.) were chosen on the basis of the literature and were examined to determine the best association of PPCs with the Fisher exact test. The variables with a $P \leq 0.05$ in the univariate analysis were entered into a reverse stepwise multivariate model to test for independence. The significance level was set at 5% in the multivariate analysis. The statistical analysis was performed using Fishers exact test. Relative risks were calculated to measure the degree of association. Separate multiple logistic regression models were developed to determine the effects of the perioperative and ICU events that had a significant association with PPCs.

Results

A total of 28 out of 117 (23.9%) patients had PPCs.

The incidence of various PPC's is shown in Table 2. The most common PPC was pneumonia followed by atelectasis and pleural effusion.

The demographic characteristics of patients with and without PPC are shown in Table 3. It was seen that age over 70 years, history of smoking and presence of chronic obstructive pulmonary disease (COPD) carried a greater relative risk for PPC.

The perioperative variables in the two groups are shown in Table 4. It was seen that greater blood and blood product transfusion was associated with a greater risk of PPC. The risk was also higher with a greater duration of mechanical ventilation and increased length of ICU stay. The mortality was not different in the two groups.

Table 5 shows the predictive variables for PPCs. Logistic regression analyses were used to identify factors predictive of PPCs. It was seen that advanced age (>70 years), history of smoking, presence of diabetes,

Table 1: Operational definitions of the various lung conditions

Pathology	Definition
Atelectasis	Lung opacification with a shift of the mediastinum, hilum or hemidiaphragm toward the affected area, and compensatory overinflation in the adjacent nonatelectatic lung
Pleural effusion	Chest X-ray 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 a hazy opacity in one hemithorax with preserved vascular shadows
Pulmonary edema	Any abnormal accumulation of fluid in the extravascular compartment of the lung as evidenced in chest X-ray
Pneumonia	When a patient received antibiotics for a suspected respiratory infection and met at least one of the following criteria: New or changed sputum, new or changed lung opacities, fever, leukocyte count > 12,000/cu mm
ARDS	Acute, diffuse, inflammatory lung injury leading to increased pulmonary vascular permeability with hypoxemia and bilateral radiographic opacities, associated with increased venous admixture, increased physiological dead space and decreased lung compliance

ARDS: Adult respiratory distress syndrome

Table 2: Incidence of pulmonary complications

Complication	Number (%)
Atelectasis	8 (28.5)
Pleural effusion	3 (10.7)
Pulmonary edema	2 (7.14)
Pneumonia	12 (42.8)
ARDS	3 (10.7)

ARDS: Adult respiratory distress syndrome

occurrence of surgical complications (leak, dehiscence, etc.), and blood transfusion were independently associated with a greater risk of PPC.

Discussion

Postoperative pulmonary complications account for a substantial proportion of risk related to critical care and is a major cause of mortality, morbidity, and longer ICU stay. About 23% incidence of PPCs that we observed in this broad, homogeneous surgical population falls within the range reported in the literature.^[11-13]

Pneumonia was the most common pulmonary complication in our study. It has been reported that pneumonia usually tends to occur within first 5 postoperative days and presents with fever, leukocytosis, increased secretions, and pulmonary infiltrates on chest radiographs.^[14] Patients develop hypoxemia

and eventually respiratory distress. Postoperative pneumonia should be suspected in the presence of fever, leukocytosis, and development of new pulmonary infiltrates on chest radiographs.

Atelectasis was the next common PPC found in our study. Postoperative atelectasis is usually caused by decreased compliance of lung tissue, impaired regional ventilation, retained airway secretions, and postoperative pain that interferes with spontaneous deep breathing and coughing.^[15] After major hepatic resections right sub-diaphragmatic collections and postoperative pain are the major causes. Atelectasis can be reduced by early mobilization, incentive spirometry, aggressive chest physiotherapy and good postoperative analgesia.

The pleural effusion occurring in a few patients may be due to surgical manipulation, which disappeared within a few days. The occurrence of pulmonary edema was related to transfusion-related ALI or overzealous fluid administration causing increased permeability across alveolar capillary membrane. They resolved spontaneously within a short period of time with no longterm sequelae. The same complications have been reported in a few other studies.^[16,17]

Our study found that age greater than 70 years, history of smoking and presence of COPD were significantly associated with an increased risk of PPC among the demographic and preoperative characteristics. Iwamoto *et al.* conducted a retrospective study of 4380 patients undergoing thoracic, abdominal or neurosurgery under

Table 3: Comparison of Demographic & clinical profile

	PPC (n=28, 23.9%)	No PPC (n=89, 76.1%)	P value	Relative risk	95% CI
Age > 70 years (%)	16 (57.1)	12 (13.4)	0.003*	3.06	0.76-2.19
BMI > 28 (%)	6 (21.4)	21 (23.5)	0.87	1.21	0.88-2.56
Male (%)	18 (64.2)	54 (60.6)	0.56	0.67	1.26-3.64
ASA class > 3 (%)	5 (17.8)	14 (15.7)	0.17	1.05	1.44-4.18
Smoker (%)	21 (75.0)	54 (60.6)	0.04*	2.06	0.88-2.74
Diabetes (%)	11 (39.2)	39 (43.8)	0.32	0.89	1.27-3.29
COPD (%)	8 (28.5)	11 (12.3)	0.03*	2.48	0.92-1.84
Coronary artery disease (%)	5 (17.8)	17 (19.1)	0.16	1.32	1.46-3.76
Hypertension (%)	9 (32.1)	25 (28.0)	0.3	0.97	1.66-3.24
Kidney disease (%)	3 (10.7)	10 (11.2)	0.53	0.88	1.48-3.08
Alcoholic cirrhosis (%)	16 (57.1)	59 (66.2)	0.09	1.24	0.78-2.56
Child-Turcotte-Pugh score A (%)	4 (14.2)	13 (14.6)	0.22	0.92	1.44-2.84
Type of resection					
< 3 segments	22 (78.5)	69 (77.5)	0.43	0.98	1.08-3.67
> 3 segments	6 (21.4)	20 (22.4)	0.29	1.04	1.24-3.12
Indication for surgery					
Benign	3 (10.7)	7 (7.8)	0.56	1.32	0.67-1.35
Malignant	25 (89.2)	82 (92.1)	0.27	0.96	1.56-2.69

PPC: Postoperative pulmonary complication; CI: Confidence interval; BMI: Body mass index; ASA=American Society of Anesthesiologists, COPD: Chronic obstructive pulmonary disease

Table 4: Comparison of the perioperative characteristics

	PPC group (n=28)	Non-PPC group (n=89)	P value	Relative risk	95% CI
Preoperative hemoglobin (mean±SD) (%)	10.4±8.1	11.0±3.7	0.68	0.86	1.23-3.46
Preoperative Prothrombin time (mean±SD) (s)	14.3±2.5	15.1±2.4	0.48	1.06	1.48-4.67
Duration of surgery (mean±SD) (min)	250±67	227±39	0.1	1.12	0.95-2.26
Blood transfusion requirements (mean±SD) (ml)	2000±340	1000±210	0.03*	2.76	0.84-1.86
Inotrope and vasopressor requirement (n) (%)	17 (60.7)	54 (60.6)	0.9	0.89	1.21-3.79
Duration of mechanical ventilation (mean±SD) (days)	10±4.5	3±1.3	0.02*	1.7	0.92-1.39
Surgical complications (leak, dehiscence etc.,) (n) (%)	6 (21.4)	21 (23.5)	0.61	1.09	0.87-2.24
Length of ICU stay (mean±SD) (days)	14±8	6±1.5	0.04*	2.58	1.24-3.82
Mortality (n) (%)	2 (7.1)	5 (5.6)	0.68	0.92	1.06-2.48

PPC: Postoperative pulmonary complication; ICU: Intensive care unit; SD: Standard deviation; CI: Confidence interval

Table 5: Results of the multiple logistic regression analysis

Variable	P value	OR	95% CI
Age > 70 years	0.01	2.13	1.04-1.06
Smoking	0.002	3.97	0.9-1.67
Diabetes	0.04	1.71	0.87-1.04
Surgical complications	0.03	1.62	1.05-1.18
Blood transfusion	0.008	2.76	0.96-1.27

OR: Odds ratio; CI: Confidence interval

general anesthesia and reported that elderly patients aged 65 years or older who underwent thoracic surgery had the highest incidence of pneumonia.^[18] However, elderly patients did not show a higher mortality than the younger patients. Another meta-analysis of 11 trials and comprising 5186 patients found an increased incidence of postoperative mortality and pneumonia after pancreaticoduodenectomy in elderly patients over 75 years of age. Another study reported that patients over 80 years of age with a preoperative severe liver dysfunction showed postoperative mortality of 57%, and all of these patients developed postoperative complications and therefore recommended against resection for these patients.^[19]

The effect of smoking on postoperative pneumonia has been reported from a retrospective cohort analysis of 393,794 patients where a dose-dependent increase in pulmonary complications based on pack-year exposure with greater than 20 pack years led to a significant increase in smoking-related surgical complications.^[20] Our findings are also in conformity with another study, which regarded elderly patients with a history of heavy smoking and poor pulmonary function as a high-risk group for developing pneumonia in esophagus surgery.^[21]

In prospective data of 468,795 patients from the national surgical quality improvement program database, patients with COPD undergoing surgery had an increased morbidity, mortality, and length of stay.^[22] It was seen that patients who developed postoperative pneumonia did not differ from those with no pneumonia after the operation except for a history of COPD, which was found in 38.5% of those with postoperative pneumonia compared with 20% of patients with no pneumonia.^[23]

Our study has also found that blood and blood product transfusion is associated with an increased risk of PPC. Vamvakas *et al.* have reported an association between the length of storage of transfused red blood cells and the development of postoperative pneumonia in patients undergoing coronary artery bypass surgery.^[24] The possible cause of such a complication has been attributed to transfusion related immunomodulation as a consequence of allogenic blood transfusion. Allogenic transfusion increase humoral immunity and decrease cell-mediated immunity. The mechanism of allogenic transfusion-induced immunomodulation may involve altered cytokine regulation with a shift toward a type-2 (Th2) immune response. However, the same authors were not able to detect any relationship

between exposure to allogenic plasma and the risk of postoperative pneumonia.^[25]

Our study has found an increased risk of PPCs with increased duration of mechanical ventilation and ICU length of stay. This has also been reported by Shander *et al.* who found that the most practicable marker identifying patients at highest risk for PPCs is the need for postoperative mechanical ventilation of a cumulative duration of more than 48 h.^[26]

Generally speaking, PPCs lead to increased mortality. However, in our study, PPC was not a risk factor for mortality through logistic regression analysis. However, further large multicenter studies are required to clarify this point.

The primary limitation of this study is its retrospective and observational nature, limiting generalization of its results. This can both underestimate and overestimate the results of the conclusions. Another limitation of this study is the lack of detailed respiratory function data. PaO₂ was measured routinely in the perioperative period, but forced expiratory volume in 1 s and forced vital capacity were not routinely measured after surgery. Moreover, some patients had acute kidney injury combined with multiple organ dysfunction syndrome, low cardiac output, endotoxemia, hypervolemia, hyperkalemia, and acidosis. This had a negative impact on respiratory function, causing prolonged mechanical ventilation, and increased incidence of PPC.

Conclusion

Older age, chronic smoking, COPD, increased blood product transfusion, increased duration of mechanical ventilation, and increased length of ICU stay were six independent risk factors for PPC after hepatic resection. In addition, diabetes and occurrence of surgical complications (leak, wound dehiscence, etc.) were independent predictive variables for PPC.

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