Original Article

Risk factors and prognosis of critically ill cancer patients with postoperative acute respiratory insufficiency

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BACKGROUND: This study aimed to investigate the risk factors and outcome of critically ill cancer patients with postoperative acute respiratory insufficiency.

METHODS: The data of 190 critically ill cancer patients with postoperative acute respiratory insufficiency were retrospectively reviewed. The data of 321 patients with no acute respiratory insufficiency as controls were also collected. Clinical variables of the first 24 hours after admission to intensive care unit were collected, including age, sex, comorbid disease, type of surgery, admission type, presence of shock, presence of acute kidney injury, presence of acute lung injury/acute respiratory distress syndrome, acute physiologic and chronic health evaluation (APACHE II) score, sepsis-related organ failure assessment (SOFA), and $\text{PaO}_2/\text{FiO}_2$ ratio. Duration of mechanical ventilation, length of intensive care unit stay, intensive care unit death, length of hospitalization, hospital death and one-year survival were calculated.

RESULTS: The incidence of acute respiratory insufficiency was 37.2% (190/321). Multivariate logistic analysis showed a history of chronic obstructive pulmonary diseases ($P=0.001$), surgery-related infection ($P=0.004$), hypo-volemic shock ($P<0.001$), and emergency surgery ($P=0.018$), were independent risk factors of postoperative acute respiratory insufficiency. Compared with the patients without acute respiratory insufficiency, the patients with acute respiratory insufficiency had a prolonged length of intensive care unit stay ($P<0.001$), a prolonged length of hospitalization ($P=0.006$), increased intensive care unit mortality ($P=0.001$), and hospital mortality ($P<0.001$). Septic shock was shown to be the only independent prognostic factor of intensive care unit death for the patients with acute respiratory insufficiency ($P=0.029$, RR: 8.522, 95%CI: 1.243–58.437, B=2.143, SE=0.982, Wald=4.758). Compared with the patients without acute respiratory insufficiency, those with acute respiratory insufficiency had a shortened one-year survival rate (78.7% vs. 97.1%, $P<0.001$).

CONCLUSION: A history of chronic obstructive pulmonary diseases, surgery-related infection, hypovolemic shock and emergency surgery were risk factors of critically ill cancer patients with postoperative acute respiratory insufficiency. Septic shock was the only independent prognostic factor of intensive care unit death in patients with acute respiratory insufficiency. Compared with patients without acute respiratory insufficiency, those with acute respiratory insufficiency had adverse short-term outcome and a decreased one-year survival rate.

KEY WORDS: Acute respiratory insufficiency; Risk factors; Prognosis; Critical illness; Postoperative care; Septic shock; Chronic obstructive pulmonary disease; Survival

World J Emerg Med 2013;4(1):43–47

DOI: 10.5847/wjem.j.issn.1920-8642.2013.01.008

INTRODUCTION

Acute respiratory insufficiency (RI) occurs frequently after major operations with an incidence of 3% to 27.4%.^[1–4] It is associated with increased hospital mortality, increased

costs, and a decreased long-term survival rate.^[4–5] Studies on the risk factors and outcomes of acute RI focused on patients with hematologic malignancies or solid tumors who received non-operative treatment. However, there were

few studies on the risk factors and prognosis of critically ill cancer patients receiving mechanical ventilation owing to acute RI after surgery. Therefore, the present study was to determine the risk factors and prognostic factors of acute RI in critically ill cancer patients after surgery. One-year survival of this cohort was also studied.

METHODS

Patients' data

This retrospective case-control study was conducted on the data from the intensive care unit (ICU), Cancer Institute, Chinese Academy of Medical Sciences, China. The ICU is a 10-bed surgical unit. Acute RI was defined as pulmonary insufficiency requiring intubation and ventilation for a period of ≥ 24 hours. Informed consent was waived owing to the observational nature of this study.

The following data of the patients, who received mechanical ventilation within the first 24 hours between November 2008 and October 2009, were prospectively collected and retrospectively analyzed. These data included age, gender, comorbidities (including coronary heart diseases, diabetic mellitus and chronic obstructive pulmonary diseases), procedures performed (including lobectomy, pneumonectomy, pulmonary wedge resection, esophagectomy, upper abdomen surgery, lower abdomen surgery, head and neck surgery, and neurosurgery), type of admission (elective or emergent), presence of sepsis (including surgery related infection, pulmonary infection and blood stream infection), presence of acute kidney injury, presence of shock (hypovolemic or septic), presence of acute lung injury/acute respiratory distress syndrome (ALI/ARDS), acute physiology and chronic health evaluation II (APACHE II) score, sequential organ failure assessment (SOFA) and $\text{PaO}_2/\text{FiO}_2$ ratio. Duration of ventilation, length of ICU stay, ICU mortality, length of hospitalization and hospital mortality were also collected. Patients who stayed in ICU less than 24 hours were excluded from this study.

Definition

Sepsis was defined using the definitions established by the Chinese Society of Critical Care Medicine, the Chinese Medical Association as the presence of clinical signs of systemic inflammatory response syndrome (SIRS) associated with infection confirmed by culture. SIRS was defined as the presence of two or more of the following: temperature greater than 38°C or less than 35°C , heart rate greater than 90 bpm, respiratory rate greater than 20 bpm or $\text{PaCO}_2 < 32$ mmHg, white blood cell count greater than $12 \times 10^9/\text{L}$ or less than $4.0 \times 10^9/\text{L}$ or relative count of immature cells greater than 10% of

total leukocytes.^[6] Shock was defined as systolic blood pressure < 90 mmHg or 40 mmHg lower than basic blood pressure for more than one hour or in need of vasoactive drugs.^[2] Acute kidney injury was defined as absolute rise in serum creatinine of ≥ 0.3 mg/dL (≥ 26.4 $\mu\text{mol/L}$), increase in serum creatinine of $\geq 50\%$, reduction in urine output, defined as < 0.5 mL/kg per hour for more than 6 hours.^[7] ALI/ARDS was defined according to the 2006 Guidelines of Diagnosis and Treatment established by the Chinese Society of Critical Care Medicine, the Chinese Medical Association.^[8] APACHE II score was computed based on several measurements (age, physiologic status and underlying health) as an integer score from 0 to 59, higher scores correspond to more severe disease and a higher risk of death.^[9] SOFA score was based on six different scores, one each for the respiratory, cardiovascular, hepatic, coagulation, renal and neurological systems, extent of a patient's organ function or rate of failure as one to four.^[10] Overall survival was defined as the time from the ICU admission to death from any cause during an one-year follow up. Type of acute RI was classified according to the definition of Kress et al.^[11]

Statistical analysis

The SPSS software package 13.0 for Windows was used for statistical analysis. Data were presented as mean $\pm$ SD or median (25%–75% interquartile range) for continuous variables, and percentages for dichotomous variables. Continuous variables were analyzed using Student's *t* test, and categorical variables were analyzed using the Chi-square test. The survival was estimated by the Kaplan-Meier method, and the survival rate was compared using the log-rank test. A *P* value < 0.05 was considered statistically significant.

RESULTS

A total of 190 patients developed RI. In the same period, 321 patients did not develop RI, with an incidence of 37.2%. Primary cancers included lung cancer, esophageal cancer, cancer of esophagogastric junction, abdominal cancer, gynecological cancer, urinary cancer, cancer of the head and neck, and intracranial cancer.

Univariate analysis of risk factors of respiratory insufficiency

Compared with patients without RI, patients with RI had more pneumonectomies, more infections, more shocks, more acute kidney injuries and more emergency surgeries. More patients had a history of COPD (Table 1). Multivariate analysis demonstrated four independent risk

factors for RI: a history of COPD, surgery-related infection, hypovolemic shock and emergency surgery (Table 2).

Short-term outcomes of patients with RI

Compared with patients without RI, those with acute respiratory insufficiency had a prolonged length of intensive care unit stay, a prolonged length of hospitalization, an increased intensive care unit mortality rate, and a hospital mortality rate (Table 3). Of the 190 patients with RI, 14 died in ICU. Of the 14 patients, 11 died from septic shock, 1 from neurological disease, and 2 from respiratory failure. Therefore, the ICU mortality rate was 7.4% (14/190). Other two patients died from septic shock in a surgical ward after being transferred from ICU, with a hospital mortality rate of 8.4% (16/190).

Prognosis of patients with respiratory insufficiency

Univariate analysis showed that emergency admission, shock at admission, higher APACHE II score, high SOFA score, high non-pulmonary SOFA score, and presence of ALI/ARDS were associated with ICU death in patients with acute RI (Table 4). Multivariate analysis demonstrated that septic shock was the only independent prognostic factor of intensive care unit death in patients with acute RI ($P=0.029$, RR: 8.522, 95%CI: 1.243–58.437, B=2.143, SE=0.982, Wald=4.758).

One-year survival rate of patients with acute respiratory insufficiency

The Kaplan-Meier method showed that patients with acute RI had a decreased one-year survival rate

Table 1. Univariate analysis of predictors of respiratory insufficiency

Clinical variables	ARI (n=190)	No-ARI (n=321)	t/χ^2 value	P value
Age (yr)	63.26±12.66	65.64±11.44	1.791	0.074
Sex (male)	124 (65.3)	204 (63.6)	0.152	0.704
Coronary heart disease (%)	26 (13.7)	60 (18.7)	2.138	0.178
Diabetic mellitus (%)	22 (11.6)	37 (11.5)	0.000	0.986
COPD (%)	14 (7.4)	4 (1.2)	13.164	0.001
Procedures performed				
Pneumonectomy (%)	11 (5.8)	6 (1.9)	5.704	0.022
Lobectomy (%)	32 (16.8)	5 (15.6)	0.142	0.710
Pulmonary wedge resection (%)	15 (7.9)	24 (7.5)	0.030	0.865
Esophagectomy (%)	50 (26.3)	65 (20.2)	2.519	0.125
Upper abdomen surgery (%)	25 (13.2)	57 (17.8)	1.874	0.212
Lower abdomen surgery (%)	39 (20.5)	79 (24.6)	1.121	0.329
Head and neck surgery (%)	13 (6.8)	40 (12.5)	4.054	0.051
Neurosurgery (%)	6 (3.2)	0 (0)	10.257	0.003
Sepsis				
Pulmonary infection (%)	23 (12.1)	0 (0)	40.689	<0.001
Surgery-related infection (%)	27 (14.2)	5 (1.6)	35.522	<0.001
Blood stream infection (%)	3 (1.6)	0 (0)	5.098	0.024
Acute kidney injury (%)	12 (6.3)	4 (1.2)	10.114	0.003
Shock				
Hypovolemic shock (%)	30 (15.8)	8 (2.5)	30.659	<0.001
Septic shock (%)	14 (7.4)	0 (0)	24.319	<0.001
Admission				
Elective (%)	104 (54.7)	278 (86.6)	64.228	<0.001
Emergent (%)	86 (45.3)	43 (13.4)		

ARI: acute respiratory insufficiency; COPD: chronic obstructive pulmonary disease.

Table 2. Multivariate analysis of predictors of respiratory insufficiency

Clinical variables	B	S.E.	Wald	RR (95%CI)	P value
COPD	2.004	0.597	11.268	7.416 (2.302–23.890)	0.001
Surgery-related infection	1.597	0.562	8.078	4.939 (1.642–14.857)	0.004
Hypovolemic shock	1.664	0.462	12.990	5.283 (2.137–13.061)	<0.001
Emergent admission	0.654	0.275	5.644	1.923 (1.121–3.297)	0.018

COPD: chronic obstructive pulmonary disease.

Table 3. Short-term outcomes of patients with acute respiratory insufficiency

Clinical variables	ARI (n=190)	No-ARI (n=321)	t/χ^2 value	P value
ICU length of stay (d)	3 (2–6)	2 (1–3)	–6.493	<0.001
ICU mortality (%)	14 (7.4)	4 (1.2)	13.164	0.001
Length of hospitalization (d)	23 (18–31)	20 (15–25)	–2.378	0.006
In-hospital mortality (%)	16 (8.4)	5 (1.6)	14.267	<0.001

ARI: acute respiratory insufficiency; ICU: intensive care unit.

Table 4. Univariate analysis of intensive care unit death of patients with acute respiratory insufficiency

Clinical variables	Survival (n=176)	Death (n=14)	t/χ^2 value	P value
Age (yr)	63.52±12.81	65.07±10.99	-0.441	0.660
Sex (male)	115 (65.3)	9 (64.3)	0.011	0.936
Coronary heart disease (%)	25 (14.2)	1 (7.1)	0.310	0.697
Diabetic mellitus (%)	20 (11.4)	2 (14.3)	0.324	0.668
COPD (%)	13 (7.4)	1 (7.1)	0.017	0.973
Admission			15.490	<0.001
Elective (%)	103 (58.5)	1 (7.1)		
Emergency (%)	73 (41.5)	13 (92.9)		
Sepsis				
Pulmonary infection (%)	19 (10.8)	4 (28.6)	5.425	0.072
Surgery-related infection (%)	23 (13.1)	4 (28.6)	1.223	0.118
Blood stream infection (%)	2 (1.1)	1 (7.1)	3.760	0.206
Acute kidney injury (%)	10 (5.7)	2 (14.3)	2.319	0.217
Shock				
Hypovolemic shock (%)	24 (13.6)	6 (42.9)	11.275	0.011
Septic shock (%)	9 (5.1)	5 (35.7)	22.076	0.001
APACHE II score	11 (8.0–14.0)	15.0 (13.0–33.5)	-3.059	0.012
SOFA score	2.0 (1.0–3.0)	7.0 (5.0–9.0)	-4.301	0.001
Non-pulmonary SOFA score	0 (0–1.0)	6.0 (2.0–6.5)	-4.208	0.001
PaO ₂ /FiO ₂ ratio	207 (136–329)	274 (108–403)	-0.084	0.704
Duration of ventilation (d)	2.0 (1.0–4.0)	5.0 (2.0–17.5)	-2.108	0.070
ALI/ARDS (%)	25 (14.2)	5 (35.7)	6.451	0.050

COPD: chronic obstructive pulmonary disease; APACHE: acute physiology and chronic health evaluation; SOFA: sequential organ failure assessment; ALI/ARDS: acute lung injury/acute respiratory distress syndrome.

Figure 1. One-year survival of patients with or without respiratory insufficiency. **Figure 2.** One-year survival of patients with four types of respiratory insufficiency.

compared with patients without RI (Figure 1). Significant differences in one-year survival were found among four types of RI (78.7% vs. 97.1%, Log-rank test=24.554, $P<0.001$). As shown in Figure 2, patients with type IV RI had the worst survival rate of 21.2%, and those with type III RI had the best survival rate of 94.7%. But there were no significant differences between type I and type II RI (76.6% vs. 73.0%, $P=0.700$).

DISCUSSION

The incidence of RI was reported to be 3% to 27.4%.^[1–4] In this study, the incidence of RI was 37.2%, which was higher than that reported elsewhere. There are two reasons. First, complex procedures such as formerly perceived as high-risk surgery have been increasingly used in the past years. Second, patients who stayed in ICU less than 24

hours were excluded from this study.

In this study, risk factors of RI were found to be a history of COPD, surgery-related infection, hypovolemic shock, and emergency surgery. Indeed, a history of COPD was a risk factor of RI. Johnson et al^[11] reported that a history of COPD increased the risk of RI by 1.517 folds. Wang et al^[3] also found the similar result. In this study, a history of COPD increased the risk of RI by 7.416 folds. Infection is also a risk factor of RI. Vincent et al^[12] reported that the risk for the development of acute respiratory failure in patients who had infection on ICU admission was 2.3 compared with patients who had no infection on ICU admission. Shock is another risk factor of RI. As in shock state, in addition to hypoperfusion of respiratory muscles, pulmonary edema and lactic acidosis result in respiratory distress.^[11] Emergency surgery is a risk factor for RI, which has been validated in most of reports.^[1,4,13] In this study,

patients with RI had a prolonged length of intensive care unit stay, a prolonged length of hospitalization, an increased intensive care unit mortality rate, and a hospital mortality, which are similar to those reported by Franca et al.^[4]

Patients with RI had a decreased one-year survival rate compared with those without RI. Although the precise cause of death was not clear, sequel plays an important role. As previously reported, patients with acute respiratory distress syndrome had a hospital death rate of 48.9%, and an one-year survival rate of 44.9%.^[14] On the other hand, the 2-year survival rate of patients with acute kidney injury varied from 47.9% to 77.7% because of partial or no recovery of kidney function. The 2-year survival rate was significantly lower than that of patients without acute kidney injury.^[15]

Finally, patients with type IV RI had the worst survival, and those with type III RI had the best survival. However, there were no significant differences between type I and type II RI. These results help clinicians predict the long-term outcomes of RI patients according to the pathophysiology of RI. Moreover, the results help clinicians to categorize patients in clinical trials.

Limitations

Our study has several limitations. First, our study was performed in a single medical center confined to surgical patients. Therefore, the result of this study may not be applicable to other medical centers in which trauma and transplantation patients prevail. Second, owing to the retrospective nature of this study, only data of patients who were diagnosed with respiratory insufficiency in the first 24 hours were collected, other diseases such as acute kidney injury and infection may be under-diagnosed.

In conclusion, a history of chronic obstructive pulmonary diseases, surgery-related infection, hypovolemic shock and emergency surgery were risk factors of critically ill cancer patients with postoperative acute respiratory insufficiency. Septic shock was the only independent prognostic factor of intensive care unit death in patients with acute respiratory insufficiency. Compared with patients without acute respiratory insufficiency, those with acute respiratory insufficiency had adverse short-term outcomes and a decreased one-year survival rate.

Funding: None.

Ethical approval: The study was approved by the Ethical Committee of Cancer Hospital (Institute), Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China

Conflicts of interest: The authors declare that there is no conflict of interest.

Contributors: Xing XZ and Sun KL designed the research,

analyzed the data, and wrote the paper. All authors read and approved the final version.

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Received November 3, 2012

Accepted after revision February 1, 2013