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Incidence and Outcomes of Pneumonia after Isolated Off-Pump Coronary Artery Bypass Grafting

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ABSTRACT

Background: Pneumonia is a major complication of cardiac surgery, with cardiopulmonary bypass considered one of the causes of pulmonary dysfunction. The incidence of pneumonia has decreased with improved surgical techniques and postoperative management; however, the incidence and outcome of pneumonia after off-pump coronary artery bypass grafting (OPCAB) are largely unknown.

Methods: We retrospectively reviewed the records of 719 patients who underwent isolated OPCAB between September 2004 and June 2008. Pneumonia was confirmed with a chest radiograph or by computed tomography. We compared preoperative and postoperative variables for patients with and without pneumonia, and for patients with postoperative pneumonia who died from pneumonia and those who survived.

Results: We identified 11 patients (1.5%) as having pneumonia after OPCAB. The most frequently observed organism in patients with postoperative pneumonia was *Klebsiella*. There were no significant differences between patients with pneumonia and those without pneumonia with respect to age (75.5 ± 7.1 years versus 67.8 ± 10.0 years; $P = .0724$), prior myocardial infarction (72.7% versus 47.5%; $P = .0792$), or postoperative intubation time (16.2 ± 15.1 hours versus 10.2 ± 16.0 hours; $P = .2781$). The operative mortality rate (within 30 days) was significantly higher in patients with pneumonia (36.4% versus 0%; $P < .0001$).

Conclusion: The incidence of pneumonia after OPCAB is low, although pneumonia remains one of most devastating complications after OPCAB.

INTRODUCTION

Despite recent advances in anesthesia, surgical techniques, and postoperative management, pneumonia remains one of the major complications of cardiac surgery. Cardiopulmonary bypass is considered one of the causes of pulmonary dysfunction [Asimakopoulos 1999], potentially via mechanisms such as failure of the lung's antibacterial defense mechanism, ischemia/reperfusion injury, and endothelial damage [Carrel 2001]. One may speculate that eliminating cardiopulmonary bypass would decrease the rate of pneumonia after coronary artery bypass grafting. In support of this hypothesis, differences in pulmonary function have been reported between coronary artery bypass grafting (CABG) with cardiopulmonary bypass and operations without it [Montes 2004; Staton 2005]. Staton et al [2005] reported that off-pump CABG (OPCAB) yielded better gas exchange and earlier extubation compared than CABG with cardiopulmonary bypass; however, the incidence and outcome of pneumonia after OPCAB are largely unknown [Cheng 2005]. Thus, the aim of the present study was to identify the incidence and outcome of pneumonia after OPCAB and to determine the predictors affecting outcome in patients with pneumonia.

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PATIENTS AND METHODS

Patient Population

Between September 2004 and June 2008, 719 patients underwent isolated OPCAB at the Sakakibara Heart Institute. Table 1 summarizes the preoperative characteristics of all of the patients. Perioperative antibiotic prophylaxis was administered with ampicillin-sulbactam (1.5 g intravenously), starting 30 minutes before skin incision and continuing for 48 hours postoperatively at a dose of 1.5 g every 12 hours. In cases of contraindication for β-lactams, vancomycin (1 g intravenously) was used for prophylaxis. Pneumonia was confirmed by the following: (1) a chest radiography or computed tomography scan that showed new infiltrates, consolidation, or cavitation; (2) a fever exceeding 38°C; and/or (3) positive-testing cultures of sputum, transtracheal fluid, or blood. Even though no bacteria were cultured, pneumonia was considered probable if clinical and radiologic improvement was achieved after administration of antibiotics. When the organism was identified, antibiotics were changed according to the antibiotics-sensitivity test.

Our strategy for isolated CABG was targeted toward obtaining complete myocardial revascularization with an off-pump technique whenever feasible. The operation technique for OPCAB has been described previously [Fukui 2007]. We bypassed all significantly diseased coronary vessels (a reduction in diameter of at least 50%) larger than 1 mm in diameter. When necessary, concomitant long segmental reconstruction (length ≥2.0 cm) of the left anterior descending artery with or without endarterectomy was performed in patients with a diffusely diseased left anterior descending artery [Fukui 2005]. Deep pericardial stay sutures were not used, and a commercially available heart positioner and stabilizer were applied in

Table 1. Preoperative Characteristics of Patients with and without Pneumonia after Off-Pump Coronary Artery Bypass Grafting*

	All (n = 719)	Pneumonia (n = 11)	No Pneumonia (n = 708)	*P*
Age, y	67.9 ± 10.0	75.5 ± 7.1	67.8 ± 10.0	.0724
Female sex, n	136 (18.9%)	0	136 (19.2%)	.1365
Body surface area, m^2	1.7 ± 0.2	1.6 ± 0.2	1.7 ± 0.2	.8218
Unstable angina, n	239 (33.2%)	6 (54.5%)	233 (32.9%)	.2272
CCS class	2.3 ± 0.9	2.5 ± 1.2	2.3 ± 0.9	.5705
Ejection fraction, %	55.7 ± 12.3	51.6 ± 13.9	55.8 ± 12.3	.3236
No. of diseased vessels	2.8 ± 0.5	2.7 ± 0.5	2.8 ± 0.5	.9129
Left main disease, n	251 (34.9%)	3 (27.3%)	248 (35.0%)	.5565
Creatinine, mg/dL	1.2 ± 1.3	1.0 ± 0.2	1.2 ± 1.3	.6421
Congestive heart failure, n	106 (14.7%)	3 (27.3%)	103 (14.5%)	.3996
Prior myocardial infarction, n	344 (47.8%)	8 (72.7%)	336 (47.5%)	.0792
Hypertension, n	463 (64.4%)	4 (36.4%)	459 (64.8%)	.1278
Diabetes mellitus, n	334 (46.5%)	3 (27.3%)	331 (46.8%)	.1548
Insulin, n	75 (10.4%)	2 (18.2%)	73 (10.3%)	.3613
Hyperlipidemia, n	431 (59.9%)	2 (18.2%)	429 (60.6%)	.0167
Smoking, n	429 (59.7%)	7 (63.6%)	422 (59.6%)	.7705
Previous stroke, n	85 (11.8%)	2 (18.2%)	83 (11.7%)	.6427
Peripheral vascular disease, n	60 (8.3%)	2 (18.2%)	58 (8.2%)	.2643
COPD, n	28 (3.9%)	1 (9.1%)	27 (3.8%)	.3815
More than trivial MR, n	70 (9.7%)	3 (27.3%)	67 (9.5%)	.1026
Nonelective surgery, n	95 (13.2%)	2 (18.2%)	93 (13.1%)	.6652
Previous PCI, n	209 (29.1%)	5 (45.5%)	204 (28.8%)	.3448
Redo, n	13 (1.8%)	0	13 (1.8%)	>.9999

*Data are presented as the mean ± SD where indicated. CCS indicates Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; MR, mitral regurgitation; PCI, percutaneous coronary intervention.

all cases. The apical suction device was applied to minimize the need for fluid loading during posterior/lateral anastomoses. Postoperative antacids were routinely administered to all patients. Preoperative, intraoperative, and postoperative variables were evaluated for the patients with and those without pneumonia. All data were reviewed retrospectively. The study protocol was approved by our Institutional Review Committee, and the board chairperson waived the need for patient consent.

Nonelective operations included both emergency and urgent cases. Operative death was defined as death occurring within 30 days of the surgery. Low-output syndrome was defined as the need for adrenaline or >5 μg/kg per minute of dopamine or dobutamine. Perioperative myocardial infarction was defined as the presence of new Q waves in an electrocardiogram or a peak creatine kinase isoenzyme MB level of >10% of the total creatine kinase. Respiratory failure was defined as a requirement for prolonged ventilation (>48 hours) or the presence of pneumonia. A postoperative cerebrovascular accident was defined as the occurrence of new stroke or intracranial bleeding, which was confirmed by computed tomography. In patients with preoperative stroke, postoperative stroke was defined as a worsening of the neurologic deficit with new radiologic findings.

Statistical Analysis

All statistical analyses were performed with the StatView 5.0 software package (SAS Institute, Cary, NC, USA). Continuous variables are reported as the mean ± SD. Continuous variables were compared with the Student *t* test, and discrete variables were compared with the χ^2 test or the Fisher exact test. Differences were considered statistically significant at *P* levels <.05.

RESULTS

Eleven patients (1.7%) were identified as having pneumonia after OPCAB. Table 1 summarizes the preoperative data for the patients with and without postoperative pneumonia. The incidence of hyperlipidemia was significantly lower in patients with pneumonia than in those without pneumonia (18.2% versus 60.6%, respectively; *P* = .0167), and slight but insignificant differences in age (75.5 ± 7.1 years versus 67.8

Table 2. Operative and Postoperative Characteristics of Patients with and without Pneumonia after Off-Pump Coronary Artery Bypass Grafting*

	All (n = 719)	Pneumonia (n = 11)	No Pneumonia (n = 708)	*P*
No. of anastomoses/patient	4.1 ± 1.3	3.8 ± 1.0	4.1 ± 1.3	.5208
Long segment reconstruction of LAD, n	272 (37.8%)	3 (27.3%)	269 (38.0%)	.5476
Use of left internal thoracic artery, n	708 (98.5%)	11 (100%)	697 (98.4%)	>.9999
Use of right internal thoracic artery, n	637 (88.6%)	10 (90.9%)	627 (88.6%)	>.9999
Operation time, min	272.2 ± 61.8	258.6 ± 52.2	272.4 ± 62.0	.6093
Transfusion, n	259 (36.0%)	5 (45.5%)	254 (35.9%)	.7642
Intubation, h	10.3 ± 16.0	16.2 ± 15.1	10.2 ± 16.0	.2781
Intensive care unit stay, d	2.2 ± 9.5	26.4 ± 61.7	1.9 ± 5.3	<.0001
In-hospital stay, d	17.2 ± 11.1	30.0 ± 24.4	17.0 ± 10.7	<.0001
Operative death (within 30 days), n	4 (0.6%)	4 (36.4%)	0	<.0001
Reexploration due to bleeding, n	6 (0.8%)	0	6 (0.8%)	>.9999
Low-output syndrome, n	15 (2.1%)	2 (18.2%)	13 (1.8%)	.0238
Perioperative myocardial infarction, n	11 (1.5%)	0	11 (1.6%)	>.9999
Severe ventricular arrhythmia, n	5 (0.7%)	0	5 (0.7%)	>.9999
Atrial fibrillation, n	194 (27.0%)	5 (45.5%)	189 (26.7%)	.0963
Hemodialysis requirement, n	16 (2.2%)	4 (36.4%)	12 (1.7%)	<.0001
Stroke, n	11 (1.5%)	1 (9.1%)	10 (1.4%)	.1701
Mediastinitis, n	10 (1.4%)	0	10 (1.4%)	.1558

*Data are presented as the mean ± SD where indicated. LAD indicates left anterior descending artery.

± 10.0 years, respectively; $P = .0724$) and prior myocardial infarction rate (72.7% versus 47.5%, respectively; $P = .0792$) were noted. Table 2 summarizes the operative and postoperative results. The mean numbers of anastomoses per patient for patients with pneumonia and those without pneumonia were not different ($P = .5208$). Furthermore, the 2 groups did not differ with regard to a requirement for the internal thoracic artery ($P > .9999$). The rate of operative mortality (within 30 days) was significantly higher in patients with pneumonia than in those without it (36.4% versus 0%; $P < .0001$). Although the patients with pneumonia did not differ from those without it with respect to intubation time (16.2 ± 15.1 hours versus 10.2 ± 16.0 hours, respectively; $P = .2781$), intensive care unit stays were significantly longer for patients with pneumonia than in those without it (26.4 ± 61.7 days versus 1.9 ± 5.3 days; $P < .0001$). Furthermore, patients with pneumonia had a significantly higher incidence of low-output syndrome (18.2% versus 1.8%; $P = .0238$) and a significantly greater postoperative requirement for hemodialysis (36.4% versus 1.7%; $P < .0001$) than those without pneumonia.

Table 3 summarizes the details of the patients with postoperative pneumonia. The diagnosis of pneumonia was confirmed at postoperative day 6.5 ± 4.8. All patients had clinical findings of fever exceeding 38°C. New infiltrates and consolidation were apparent in the chest radiographs of 90.1% (10/11) of the patients. Computed tomography was used to diagnose pneumonia in 45.5% (5/11) of the patients. The most frequently observed organism was *Klebsiella* (5 patients). There were 4 deaths (36.4%) among the patients with pneumonia, with the cause of death being respiratory failure due to pneumonia in all patients. When preoperative and postoperative variables of the deceased and surviving patients were compared, only the incidence of left main disease was significantly higher in the deceased patients ($P = .0242$) in a univariate analysis (Table 3).

DISCUSSION

The present study demonstrated that although the rate of pneumonia after OPCAB was low (1.5%), it remained a devastating complication after OPCAB because of its high mortality rate (36.4%). In general, the incidence of pneumonia after CABG has been reported to be 3.8% to 9.9% [Gaynes 1991; Carrel 2001; Cheng 2005]; however, there have been few reports on the incidence and outcome of postoperative pneumonia after OPCAB.

In contrast to our data, some studies have reported that the incidences of respiratory complications were not different for patients with and without cardiopulmonary bypass [Montes 2004; Staton 2005]. For instance, Montes et al [2004] reported no difference in the PaO_2/FiO_2 ratio. In that study, however, the mean patient age was low, and patients with significantly impaired pulmonary function were excluded. Staton et al [2001] reported no differences in chest radiographs, spirometry, and rates of death, pneumonia, pleural effusion, or pulmonary edema; however, in that study, OPCAB yielded

Table 3. Preoperative and Operative Characteristics of the Deceased and the Surviving Patients with Pneumonia after Off-Pump Coronary Artery Bypass Grafting*

	Pneumonia (n = 11)	Death (n = 4)	Survival (n = 7)	*P*
Age, y	75.5 ± 7.1	77.5 ± 8.2	68.9 ± 11.4	.2181
Body surface area, m^2	1.6 ± 0.2	1.6 ± 0.2	1.7 ± 0.1	.1171
Unstable angina, n	6 (54.5%)	2 (50.0%)	3 (42.9%)	>.9999
CCS class	2.5 ± 1.2	2.5 ± 1.7	2.1 ± 0.3	.6315
Ejection fraction, %	51.6 ± 13.9	49.5 ± 18.2	54.3 ± 12.3	.6127
No. of diseased vessels	2.7 ± 0.5	2.5 ± 0.6	2.9 ± 0.4	.2413
Left main disease, n	3 (27.3%)	3 (75.0%)	0	.0242
Creatinine, mg/dL	1.0 ± 0.2	1.0 ± 0.2	0.9 ± 0.1	.5281
Congestive heart failure, n	3 (27.3%)	1 (25.0%)	1 (14.3%)	>.9999
Prior myocardial infarction, n	8 (72.7%)	2 (50.0%)	6 (85.7%)	.4909
Hypertension, n	4 (36.4%)	1 (25.0%)	3 (42.9%)	>.9999
Diabetes mellitus, n	3 (27.3%)	1 (25.0%)	2 (28.6%)	>.9999
Insulin, n	2 (18.2%)	1 (25.0%)	1 (14.3%)	>.9999
Hyperlipidemia, n	2 (18.2%)	1 (25.0%)	1 (14.3%)	>.9999
Smoking, n	7 (63.6%)	2 (50.0%)	5 (71.4%)	.5758
Previous stroke, n	2 (18.2%)	0	2 (28.6%)	.4909
Peripheral vascular disease, n	2 (18.2%)	1 (25.0%)	1 (14.3%)	>.9999
COPD, n	1 (9.1%)	0	1 (14.3%)	>.9999
More than trivial MR, n	3 (27.3%)	1 (25.0%)	2 (28.6%)	>.9999
Nonelective surgery, n	2 (18.2%)	2 (50.0%)	0	.1091
Previous PCI, n	5 (45.5%)	2 (50.0%)	3 (42.9%)	>.9999
No. of anastomoses/patient	3.8 ± 1.0	3.3 ± 1.0	4.0 ± 0.8	.2004
Long segment reconstruction of LAD, n	3 (27.3%)	2 (50.0%)	1 (14.3%)	.4909
Use of left internal thoracic artery, n	11 (100%)	4 (100%)	7 (100%)	>.9999
Use of right internal thoracic artery, n	10 (90.9%)	3 (75.0%)	7 (100%)	.3636
Operation time, min	258.6 ± 52.2	231.3 ± 59.6	285.4 ± 42.7	.1114
Transfusion, n	5 (45.5%)	2 (50.0%)	2 (28.6%)	.5758

*Data are presented as the mean ± SD where indicated. CCS indicates Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; MR, mitral regurgitation; PCI, percutaneous coronary intervention; LAD, left anterior descending artery.

better gas exchange and earlier extubation than CABG with cardiopulmonary bypass. On the other hand, a metaanalysis revealed the incidence of pneumonia after OPCAB to be 4.6%, and OPCAB significantly reduced postoperative respiratory infections compared with conventional CABG (odds ratio, 0.41; 95% confidence interval, 0.23-0.74) [Cheng 2005]. In that study, the reduction in rates of respiratory infection, as well as other complications, was suggested as evidence that exposure to cardiopulmonary bypass pump induces a systemic inflammatory response that may predispose patients to increased myocardial irritability, platelet dysfunction, respiratory failure, and immune dysfunction [Menasché 2001; Laffey 2002]. Cardiopulmonary bypass was also suggested to lead to an activation of complement, monocytes, macrophages, platelets, and endothelial cells that correlated with pulmonary dysfunction [Asimakopoulos 1999]. Thus, these data suggest that elimination of cardiopulmonary bypass may preserve pulmonary function and avoid pulmonary infection.

Another possible benefit of OPCAB in reducing pulmonary complications is the prevention of excess fluid balance. Staton et al [2005] reported that OPCAB was associated with a greater reduction in postoperative respiratory compliance associated with increased fluid administration and rotation of the heart into the right chest to perform posterior/lateral grafts, compared with CABG with cardiopulmonary bypass. In that study, however, suction-based apical cardiac-positioning devices were not routinely used. We have always adopted the apical suction device for use with the heart stabilizer, because it minimizes the need for fluid loading during posterior/lateral anastomoses. We believe that an appropriate fluid balance

decreases secretion by the respiratory tract and, consequently, may reduce the incidence of pneumonia after OPCAB.

Several risk factors for pulmonary complications after CABG have been described. For instance, a history of chronic obstructive pulmonary disease, receiving a gastric acid inhibitor, and days on ventilation before diagnosis of pneumonia have been identified as independent risk factors for pneumonia [Gaynes 1991], and preoperative smoking, a preoperative positive tracheal aspirate, low cardiac output, and transfusion of >4 units of concentrated red cells were reported as independent predictors of early postoperative pneumonia [Carrel 2001]. More recently, diabetes has also been identified as a risk factor for pulmonary complications, with patients with undiagnosed and insulin-treated diabetes having a higher incidence of reintubation and a prolonged ventilation time [Lauraschkat 2008]. In this study, a reduced forced expiratory volume in 1 second and forced vital capacity, specific neurologic and neuromuscular dysfunction, and extensive pulmonary edema and alveolar protein accumulation were suggested to contribute to a worse outcome in diabetic patients. In the present study, we could not identify diabetes as a risk factor for pneumonia after OPCAB. This result may be because we did not include all patients with pulmonary complications, such as reintubation and prolonged ventilation time. Furthermore, we could not identify any independent risk factors for postoperative pneumonia except a low incidence of hyperlipidemia in patients with postoperative pneumonia.

In a previous study, the majority of organisms isolated in patients with postoperative pneumonia were found to be gram-negative bacilli [Gaynes 1991]. Similarly, in the present study we identified gram-negative bacilli, particularly *Klebsiella pneumoniae*, as the most frequently observed organisms. These data contrast with a study showing that gram-positive cocci were the organisms most often isolated [Carrel 2001]. In general, because we identified a gram-negative bacillus as the most frequently identified organism, we used carbapenem or cephalosporin of second or third generation. In the present study, pneumonia was confirmed with several findings (clinical findings, a chest radiograph, computed tomography scan, and positive cultures of sputum or blood), and the regimen of antibiotic treatment was chosen according to the results of the antibiotics-sensitivity test. Although culturing oral contaminants is possible unless the samples were obtained via bronchoscopy or in intubated patients, we collected sputum cultures several times to decrease contamination error; we also examined blood cultures.

The mortality rate of the patients with postoperative pneumonia in the present study was extremely high (36.4%); previous reports of mortality rates in such patients have ranged from 3.4% to 26.6% [Carrel 2001; Gaynes 1991]. Patients with postoperative pneumonia in our study were older, however, and more of these patients had a higher rate of prior myocardial infarction than the patients without postoperative pneumonia. Furthermore, patients who had postoperative pneumonia had a high rate of low-output syndrome (18.2%) and a requirement for hemodialysis (36.4%). These comorbidities may have led to the high mortality rate we observed in the patients with postoperative pneumonia. Although we identified left main disease as the only independent predictor of mortality in patients with pneumonia (P = .0242), the relevance of this finding is difficult to explain. The small number of patients may have distorted the incidence of mortality in patients with postoperative pneumonia, which along with the retrospective observational design, are potential limitations of the present study.

Finally, although the Society of Thoracic Surgeons Practice Guideline [Edwards 2006] suggests that antibiotic prophylaxis of a 48-hour duration is effective, such an antibiotic regimen may be excessive and may increase the possibility of developing pulmonary complications. Furthermore, the mean length of hospital stay was relatively long in the present study (17.2 ± 11.1 days), because early postoperative angiography was performed during the same hospitalization (>7 days after surgery).

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