

Predictors of postoperative complication and prolonged intensive care unit stay after complete pericardiectomy in tuberculous constrictive pericarditis

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Abstract

Purpose

The risk factors of postoperative outcomes after pericardiectomy in tuberculous constrictive pericarditis have still been unclear. This study aimed to investigate the predictors of postoperative complication and prolonged intensive care unit (ICU) stay in the patients with tuberculous constrictive pericarditis undergoing pericardiectomy.

Methods

A total of 88 patients with tuberculous constrictive pericarditis undergoing pericardiectomy were retrospectively enrolled. Logistic regression and Cox regression analysis were performed to identify the predictors of postoperative complication and prolonged ICU stay, respectively.

Results

All patients underwent complete pericardiectomy and 35 (39.8%) had postoperative complications with no mortality within 30 days after surgery. Postoperative complication delayed postoperative ICU stay ($P < 0.001$), duration of chest drainage ($P < 0.001$) and postoperative hospital stay ($P < 0.001$). Preoperative NYHA functional class ($P = 0.004$, OR 4.051, 95%CI 1.558–10.533) and preoperative central venous pressure (CVP) ($P = 0.031$, OR 1.151, 95%CI 1.013–1.309) were independent risk factors of postoperative complication. Postoperative complication ($P < 0.001$, HR 4.132, 95%CI 2.217–7.692) was the independent risk factor for prolonged ICU stay.

Conclusion

Complete pericardiectomy was associated with high risk of postoperative complication in tuberculous constrictive pericarditis. Poor preoperative NYHA functional class and high preoperative CVP were shown to predict postoperative complication which was the predictor of prolonged ICU stay.

Introduction

Tuberculosis is one of the globally significant infectious diseases with a high incidence and is the leading cause of infection related deaths, especially in developing countries^[1]. In the low and middle income areas, tuberculosis is the most common cause of constrictive pericarditis with the reported incidence range from 23–91%^[2, 3]. Surgical intervention has been recommended if there has been persistent clinical evidence of pericardial constriction after anti-tuberculous drug therapy^[4]. Pericardiectomy is the standard surgical method for constrictive pericarditis^[5]. In spite of its satisfactory effect in relieving pericardial

constriction, pericardiectomy is accompanied by the high risk of postoperative complication and in-hospital mortality^[6-8].

In current clinical practice, the extent of decortication is varied according to the experience of surgeons and the surgical difficulty. However, complete pericardiectomy has been reported to be superior to partial pericardiectomy in the improvement of hemodynamics and associated with better prognosis^[9, 10], while the factors influencing the outcomes after complete pericardiectomy still remain unclear, especially in tuberculous constrictive pericarditis. This study aimed to identify the determinants of postoperative complication and prolonged intensive care unit (ICU) stay after complete pericardiectomy in tuberculous constrictive pericarditis.

Methods

Patients selection

We retrospectively reviewed the records of all patients who was diagnosed as tuberculous constrictive pericarditis in our department from August 2012 to August 2019. The patients undergoing pericardiectomy were included in this study. The diagnosis of tuberculous constrictive pericarditis was based on bacteriological detection, nucleic acid detection and pathological examination. Finally, a total of 88 patients were enrolled and their clinical characteristics were collected from the hospital electronic medical records system. The study protocol was approved by the Institutional Review Board of Hangzhou Red Cross Hospital.

Perioperative process

Preoperative preparations included routine blood test, cardiopulmonary function assessment and imaging examination. The evaluation of pericardium mainly depended on cardiac ultrasound and contrast-enhanced computed tomography. Percutaneous internal jugular vein puncture and catheterization were performed preoperatively to measure the central venous pressure (CVP).

All patients underwent general anesthesia and were placed in horizontal position. Median sternotomy was routinely performed in all cases without the use but with the preparation of cardiopulmonary bypass. The extent of complete pericardiectomy was defined as the resection of anterolateral pericardium between the two phrenic nerves including the pericardium lying on the ventricles, the basal pericardium over the diaphragmatic surface, the pericardium on the great arteries and the pericardium from superior vena cava-right atrium junction to inferior vena cava-right atrium junction^[7, 11]. Other less extent was regarded as partial pericardiectomy. Prior closing, the cavity was rinsed by hydrogen peroxide and normal saline repeatedly. One drainage tube was placed in the mediastinum and two tubes were placed in the left and right chest cavity respectively at the end of surgery. The tube was removed when it was clearly confirmed no air leak and the volume of drainage was less than 100 mL/day. All patients were routinely admitted to ICU after surgery and transferred to the normal ward when the condition was steady.

Postoperative complications were defined as the comorbidities that occurred after surgery but did not exist before.

Statistical analysis

The enrolled patients were divided into two groups according to the advent of postoperative complication or not. The measurement data and numeration data of two groups were statistically analyzed with t test and χ^2 test respectively. If the P value of any clinical characteristics was < 0.1 , multivariate analysis was performed for those characteristics by the binary logistic regression to identify the factors predicting postoperative complication. Univariate and multivariate Cox regression analysis were performed to identify the independent risk factors of prolonged ICU stay. The length of ICU stay was compared between the patients with postoperative complication and those without postoperative complication by the Kaplan-Meier method and the log-rank test to further analyzed the association between the length of ICU stay and postoperative complication. All the above analysis was conducted by SPSS software (version 24.0, IBM SPSS Inc. United States). Statistical significance was set at P value < 0.05 (All P values presented were 2-sided).

Results

Postoperative complication and outcomes

We identified 88 patients with tuberculous constrictive pericarditis over the 7-year time period and all of them underwent complete pericardiectomy without the use of cardiopulmonary bypass. A total of 35 patients (39.8%) suffered postoperative complication which were listed in Table 1. Among these patients, the majority of cases (N = 23, 65.7%) had hypoalbuminemia. Low cardiac output occurred in 11 patients (31.4%), followed by pulmonary infection (N = 7, 20.0%). Arrhythmia occurred in 3 patients (8.6%) and incision infection in 2 (5.7%). Hypohepatia was detected in 2 patients (5.7%) as well as hypokalemia (N = 2, 5.7%). Pulmonary embolism occurred in 1 patient (2.9%). It should be noted that 16 patients (45.7%) suffered two or more postoperative complications.

Table 1
Postoperative complication after pericardiectomy in study patients

Complication	N = 35
Hypoalbuminemia*	23 (65.7%)
Low cardiac output	11 (31.4%)
Pneumonia	7 (20.0%)
Atrial fibrillation	3 (8.6%)
Wound infection	2 (5.7%)
Liver dysfunction	2 (5.7%)
Hypokalemia	2 (5.7%)
Pulmonary embolism	1 (2.9%)
Values presented as N (percentage).	
There were 16 patients suffering two or more postoperative complications.	
* Hypoalbuminemia was defined as the level of albumin lower than 30 g/L.	

The short term outcomes of postoperative complication were showed in Table 2. The patients with postoperative complication had longer postoperative ICU stay ($P < 0.001$) and postoperative hospital stay ($P < 0.001$) than those without postoperative complication. The duration of chest drainage was also delayed in the postoperative complication group ($P < 0.001$), while postoperative NYHA functional class of patients with postoperative complication was similar to that of those without postoperative complication ($P = 0.085$). It was notable that there was no mortality within 30 days after surgery.

Table 2
Outcomes of study patients stratified by postoperative complication status

Variables	Postoperative complication		P value
	Yes (N = 35)	No (N = 53)	
Postoperative ICU stay, days	4.8 ± 2.4	2.1 ± 1.1	< 0.001
Duration of chest drainage, days	17.3 ± 8.3	9.2 ± 2.9	< 0.001
Postoperative hospital stay, days	24.0 ± 10.1	14.1 ± 3.4	< 0.001
Postoperative NYHA functional class			0.085
□	20 (57.1%)	42 (79.2%)	
□	14 (40.0%)	10 (18.9%)	
□	1 (2.9%)	1 (1.9%)	
Mortality within 30 days	0 (0.0%)	0 (0.0%)	/
Values presented as mean ± standard deviation for continuous variables and N (percentage) for categorical variables.			
ICU, intensive care unit; NYHA, New York Heart Association			

Risk factors of postoperative complication

A total of 35 (39.8%) and 53 (60.2%) patients were assigned to the postoperative complication group and the no postoperative complication group, respectively. Table 3 showed the relationship between postoperative complication and various perioperative characteristics. Statistical differences were observed in terms of symptom duration (P = 0.014), preoperative NYHA functional class (P = 0.019), pulse rate (P = 0.009), preoperative CVP (P = 0.041), pleural effusion (P = 0.035) and serum sodium (P = 0.038) between two groups.

Table 3
The analysis of perioperative characteristics predicting postoperative complication

Variables	Postoperative complication		P value	Multivariate analysis		
	Yes (N = 35)	No (N = 53)		OR	95%CI	P value
Sex	29 (82.9%)	39 (73.6%)	0.310			
Male	6 (17.1%)	14 (26.4%)				
Female						
Age, years	56.6 ± 18.4	52.7 ± 15.2	0.288			
Symptom duration, months	2.1 ± 2.1	3.8 ± 4.1	0.014	1.160	0.909–1.480	0.233
Preoperative NYHA functional class			0.019	4.051	1.558–10.533	0.004
0	0 (0.0%)	7 (13.2%)				
1	9 (25.7%)	20 (37.7%)				
2	22 (62.9%)	25 (47.2%)				
3	4 (11.4%)	1 (1.9%)				
Hypertension	5 (14.3%)	9 (17.0%)	0.735			
Diabetes	2 (5.7%)	3 (5.7%)	0.991			
Arrhythmia	8 (22.9%)	6 (11.3%)	0.148			
Body weight, kg	57.0 ± 8.9	60.4 ± 11.6	0.140			
SBP, mmHg	113.8 ± 14.0	116.7 ± 16.0	0.386			
DBP, mmHg	79.3 ± 12.0	79.1 ± 12.3	0.914			
Pulse rate (beats/min)	108.0 ± 15.5	99.0 ± 15.4	0.009	1.026	0.982–1.073	0.253
Preoperative CVP, cmH ₂ O	27.9 ± 5.8	25.2 ± 5.3	0.041	1.151	1.013–1.309	0.031

Values presented as N (percentage) for categorical variables and mean ± standard deviation for continuous variables.

OR, odds ratio; CI, confidence interval; NYHA, New York Heart Association; SBP, systolic blood pressure; DBP, diastolic blood pressure; CVP, central venous pressure; LVEF, left ventricular ejection fraction (measured on echocardiogram); CRP, C-reactive protein; ESR, erythrocyte sedimentation rate

Variables	Postoperative complication		P value	Multivariate analysis		
	Yes (N = 35)	No (N = 53)		OR	95%CI	P value
Pleural effusion	2 (5.7%)	8 (15.1%)	0.035	6.057	0.675–54.367	0.108
Unilateral	33 (94.3%)	39 (73.6%)				
Bilateral						
Ascites	20 (57.1%)	27 (50.9%)	0.568			
Pericardial effusion	27 (77.1%)	41 (77.4%)	0.981			
Pericardial calcification	10 (28.6%)	12 (22.6%)	0.530			
Pericardial thickness, mm	11.2 ± 2.9	9.8 ± 3.4	0.055	1.126	0.902–1.406	0.293
LVEF, %	58.5 ± 6.9	58.9 ± 7.1	0.759			
Hepatomegaly	1 (2.9%)	1 (1.9%)	0.767			
Hemoglobin, g/dl	124.9 ± 15.0	121.1 ± 14.8	0.248			
CRP, mg/L	23.9 ± 20.1	23.6 ± 30.8	0.956			
ESR, mm/h	27.7 ± 18.3	27.8 ± 27.9	0.995			
Albumin, g/L	31.6 ± 4.1	33.3 ± 5.1	0.087	1.011	0.852–1.201	0.898
Serum sodium, mmol/L	136.7 ± 3.1	138.2 ± 3.5	0.038	1.098	0.887–1.360	0.390
Serum potassium, mmol/L	4.0 ± 0.5	3.9 ± 0.5	0.466			
Serum creatinine, µmol/L	84.4 ± 16.8	79.8 ± 12.4	0.144			
Operative duration, min	249.5 ± 45.6	233.3 ± 64.9	0.202			
Blood loss, ml	199.7 ± 163.9	166.0 ± 86.5	0.212			
Intraoperative fluid infusion, ml	1842.9 ± 446.9	1779.3 ± 526.6	0.558			

Values presented as N (percentage) for categorical variables and mean ± standard deviation for continuous variables.

OR, odds ratio; CI, confidence interval; NYHA, New York Heart Association; SBP, systolic blood pressure; DBP, diastolic blood pressure; CVP, central venous pressure; LVEF, left ventricular ejection fraction (measured on echocardiogram); CRP, C-reactive protein; ESR, erythrocyte sedimentation rate

Variables	Postoperative complication		P value	Multivariate analysis		
	Yes (N = 35)	No (N = 53)		OR	95%CI	P value
Postoperative CVP, cmH ₂ O	15.0 ± 6.6	13.6 ± 5.2	0.315			
Values presented as N (percentage) for categorical variables and mean ± standard deviation for continuous variables.						
OR, odds ratio; CI, confidence interval; NYHA, New York Heart Association; SBP, systolic blood pressure; DBP, diastolic blood pressure; CVP, central venous pressure; LVEF, left ventricular ejection fraction (measured on echocardiogram); CRP, C-reactive protein; ESR, erythrocyte sedimentation rate						

Multivariate logistic analysis was further performed for the characteristics whose P values were < 0.1 to identify the risk factors of postoperative complication. As shown in Table 3, symptom duration, pulse rate, pleural effusion, pericardial thickness, albumin and serum sodium were not statistically associated with postoperative complication. The results revealed that preoperative NYHA functional class (P = 0.004, OR 4.051, 95%CI 1.558–10.533) and preoperative CVP (P = 0.031, OR 1.151, 95%CI 1.013–1.309) were independent risk factors of postoperative complication.

Factors associated with length of ICU stay

The relationships between the perioperative factors and the length of ICU stay were analyzed with Cox regression model. Univariate Cox regression analysis showed that the length of ICU stay was significantly associated with age (P = 0.040), preoperative NYHA functional class (P = 0.042) and postoperative complications (P < 0.001). Additional multivariate Cox regression analysis further proved that postoperative complication was the independent risk factor for prolonged ICU stay (P < 0.001, HR 4.132, 95%CI 2.217–7.692; Table 4). Kaplan–Meier curves comparing the length of ICU stay after surgery for the patients with and without postoperative complication were shown in Fig. 1. The log-rank test showed that the patients with postoperative complication had longer ICU stay than those without postoperative complication (P < 0.001).

Table 4
Cox regression analysis of factors associated with the length of ICU stay

Variables	Univariate Analysis			Multivariate Analysis		
	P value	HR	95% CI	P value	HR	95% CI
Sex	0.639	1.139	0.662–1.957			
Age	0.040	1.014	1.001–1.027	0.559	1.004	0.990–1.019
Symptom duration	0.333	1.031	0.969–1.096			
Preoperative NYHA functional class	0.042	1.408	1.013–1.957	0.470	1.134	0.806–1.595
Hypertension	0.242	1.449	0.778–2.703			
Diabetes	0.481	1.387	0.558–3.448			
Arrhythmia	0.533	1.209	0.665–2.199			
Body weight	0.800	1.003	0.983–1.022			
SBP	0.424	1.007	0.990–1.024			
DBP	0.364	1.009	0.989–1.030			
Pulse rate	0.742	1.003	0.987–1.018			
Preoperative CVP	0.509	1.016	0.969–1.065			
Pleural effusion	0.255	1.285	0.834–1.980			
Ascites	0.164	1.380	0.877–2.171			
Pericardial effusion	0.953	1.016	0.599–1.724			

HR, hazard ratio; CI, confidence interval; NYHA, New York Heart Association; SBP, systolic blood pressure; DBP, diastolic blood pressure; CVP, central venous pressure; LVEF, left ventricular ejection fraction (measured on echocardiogram); CRP, C-reactive protein; ESR, erythrocyte sedimentation rate

Variables	Univariate Analysis			Multivariate Analysis		
	P value	HR	95% CI	P value	HR	95% CI
Pericardial calcification	0.897	1.034	0.620–1.727			
Pericardial thickness	0.807	1.009	0.938–1.085			
LVEF	0.534	1.012	0.975–1.051			
Hepatomegaly	0.482	2.043	0.280–14.927			
Hemoglobin	0.657	1.004	0.987–1.020			
CRP	0.481	1.005	0.992–1.017			
ESR	0.979	1.000	0.989–1.011			
Albumin	0.537	1.016	0.966–1.068			
Serum sodium	0.473	1.025	0.957–1.098			
Serum potassium	0.410	1.223	0.757–1.977			
Serum creatinine	0.542	1.005	0.989–1.021			
Operative duration	0.519	1.001	0.997–1.006			
Blood loss	0.145	1.001	1.000–1.003			
Intraoperative fluid infusion	0.642	1.000	1.000–1.001			
Postoperative CVP	0.480	1.016	0.972–1.063			
Postoperative complication	< 0.001	4.505	2.494–8.130	< 0.001	4.132	2.217–7.692

HR, hazard ratio; CI, confidence interval; NYHA, New York Heart Association; SBP, systolic blood pressure; DBP, diastolic blood pressure; CVP, central venous pressure; LVEF, left ventricular ejection fraction (measured on echocardiogram); CRP, C-reactive protein; ESR, erythrocyte sedimentation rate

Discussion

Constrictive pericarditis is an uncommon but potentially life-threatening disease with various causes. Because of the inflammatory disorder and fibrosis, pericardium becomes inelastic gradually and then inhibits the cardiac filling. This process leads to the diastolic heart failure in the end with unfavorable clinical outcome^[12]. Early surgical intervention was reported to play a positive role in reducing mortality rate^[13, 14], but the diagnosis seems to be challenging in the early stage. The detection of constrictive pericarditis often relies on the typical clinical symptoms such as dyspnea and clinical signs such as jugular vein distention. Imaging examinations such as chest CT and cardiac MRI are important in the identification of pericardial effusion, calcification and thickening^[12, 14, 15]. Meticulous echocardiographic examination is also valuable in the assessment of pericardial condition. Invasive haemodynamic catheterization and pressure measurement were of great significance in the diagnostic confirmation and the evaluation of the constrictive extent^[16].

The definitive treatment for constrictive pericarditis is surgical pericardiectomy^[17]. The surgical methods are classified as complete pericardiectomy and partial pericardiectomy according to the extent of pericardial resection. Complete pericardiectomy has been proven to be not only associated with lower perioperative mortality^[9] but also confer significant long-term survival benefit and clinical functional improvement^[10, 18]. Generally, pericardiectomy can be performed through either median sternotomy or left anterolateral thoracotomy, while median sternotomy provides adequate exposure of the right atrium, right ventricle and the vena cava, thus enabling extensive pericardial resection^[19].

Despite the undoubtable effectiveness in treating constrictive pericarditis, pericardiectomy is accompanied with high risk of postoperative complication and mortality. An American nationwide outcomes study revealed that the in-hospital complication and mortality rates after pericardiectomy were approximately 48% and 8%, respectively^[8]. Also, Tokuda, Y. and his colleagues conducted a nationwide study on the outcome of pericardiectomy for constrictive pericarditis in Japan which showed the operative mortality was 10% and the major morbidity such as bleeding requiring reoperation was 15%^[6]. In the respect of long-term outcome, Busch, C. et al. reviewed 97 consecutive patients undergoing surgery for constrictive pericarditis and reported that 1-year and 5-year survival rates were 66.5% and 51.6%, respectively^[20]. Another retrospective study including 98 cases showed 1-year, 5-year, and 10-year survival rates were 82.5%, 64.3%, and 49.2%, respectively^[21]. Although there are many researches about the surgical treatment for constrictive pericarditis in developed countries, the studies on tuberculous constrictive pericarditis have been limited in recent years due to the decreased incidence of tuberculosis worldwide. However, tuberculosis still remains the major etiology of constrictive pericarditis in developing countries.

We have analyzed the short-term outcome of the patients with tuberculous constrictive pericarditis undergoing complete pericardiectomy over 7 years in our department. Although nearly 40% of patients in our study suffering postoperative complication, there was no mortality within 30 days after surgery. Hypoalbuminemia was the major postoperative complication possibly because of the negative nitrogen balance after surgery. The incidence of low cardiac output was also high enough to warrant attention,

because it was proven to be the major contributor to in-hospital death in other studies^[3, 22, 23]. In our study, postoperative complication was seemed to be associated with symptom duration, preoperative NYHA functional class, pulse rate, preoperative CVP, pleural effusion and serum sodium, while multivariate analysis eventually proved that poor preoperative NYHA functional class and high preoperative CVP were independent risk factors of postoperative complication, which might provide a valuable reference for preoperative preparation and risk evaluation. We also found postoperative complication significantly delayed the postoperative ICU stay, duration of chest drainage and postoperative hospital stay. Additionally, postoperative complication was the independent risk factor for prolonged ICU stay. It should be emphasized that all patients undergoing complete pericardiectomy in our department were not routinely performed cardiopulmonary bypass, which was also proven to be safe in other studies^[24, 25].

There are several limitations in this study. First, this is a single-center retrospective research that inevitably has the selection bias. Secondly, some important data such as duration of anti-tuberculosis medication and body mass index (BMI) are missing due to the retrospective design. Finally, survival outcome includes only the mortality within 30 days after surgery. Long-term outcome is required to be analyzed in the future.

Conclusions

Our study showed that although effective at improving cardiac function of tuberculous constrictive pericarditis, complete pericardiectomy was associated with high risk of postoperative complication. Poor preoperative NYHA functional class and high preoperative CVP were shown to predict postoperative complication which was the predictor of prolonged ICU stay. Our study has illustrated the need for early surgical intervention before the symptoms deteriorate to poor NYHA class or diastolic heart failure.

Abbreviations

CVP, central venous pressure; ICU, intensive care unit; CT, computed tomography; MRI, magnetic resonance imaging; NYHA, New York Heart Association; OR, odds ratio; CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HR, hazard ratio; CI, confidence interval

Declarations

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Author Contributions

Drs. Likui Fang and Bo Ye contributed to the conception and design of the work. Drs. Likui Fang and Wuchen Zhao contributed to data analysis and editing the manuscript. Drs. Likui Fang, Guocan Yu and Jinpeng Huang contributed to data acquisition, statistical analysis and interpretation of the data. Drs. Guocan Yu and Bo Ye contributed to the revision of the manuscript. All authors have approved the final draft of the manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study protocol was approved by the Institutional Review Board of Hangzhou Red Cross Hospital.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

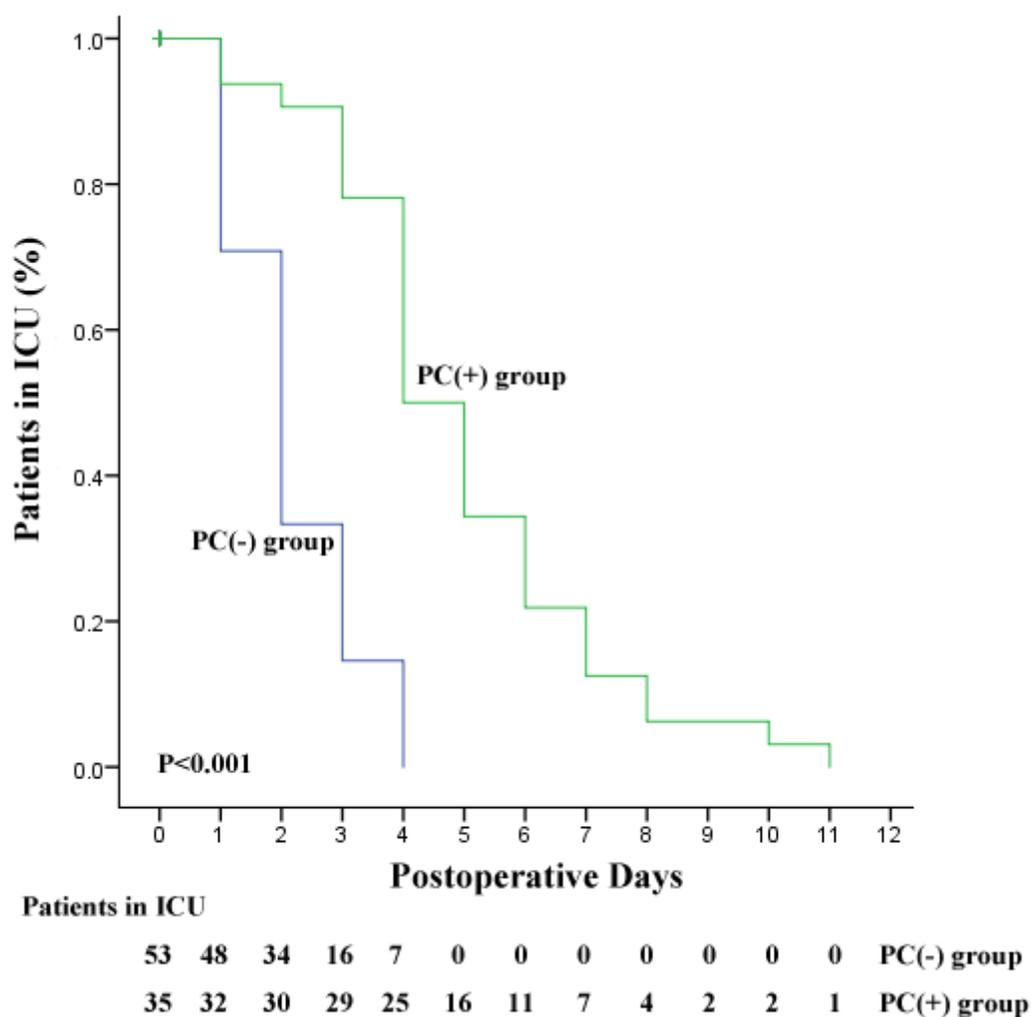


Figure 1

Kaplan–Meier curves comparing the length of ICU stay after surgery for the patients with and without postoperative complications. PC(+) group, the postoperative complication group; PC(-) group, the no postoperative complication group.