

Risk factors and prognosis of postpericardiotomy syndrome in patients undergoing valve surgery

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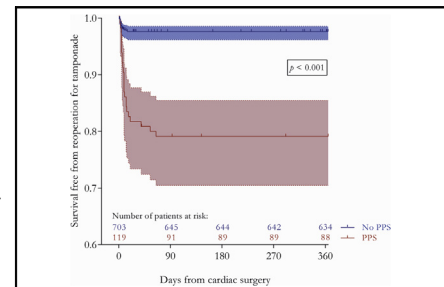
ABSTRACT

Objective: The study aim was to investigate the long-term prognosis and risk factors of postpericardiotomy syndrome (PPS).

Methods: We performed a single-center cohort study in 822 patients undergoing nonemergent valve surgery. Risk factors of PPS were evaluated using multivariable logistic regression analysis. We also compared the incidence of reoperation for tamponade at 1 year between patients with and without PPS. Main secondary outcomes were hospital stay and mortality.

Results: Of the 822 patients, 119 (14.5%) developed PPS. A higher body mass index (odds ratio (OR) per point increase, 0.94; 95% confidence interval (CI), 0.89-0.99) was associated with a lower risk of PPS, whereas preoperative treatment for pulmonary disease without corticosteroids (OR, 2.55; 95% CI, 1.25-5.20) was associated with a higher risk of PPS. The incidence of reoperation for tamponade at 1 year in PPS versus no PPS was 20.9% versus 2.5% (OR, 15.49; 95% CI, 7.14-33.58). One-year mortality in PPS versus no PPS was 4.2% versus 5.5% (OR, 0.68; 95% CI, 0.22-2.08). Median hospital stay was 13 days (interquartile range, 9-18 days) versus 11 days (interquartile range, 8-15 days) ($P = .001$), respectively.

Conclusions: Despite longer hospital stays and more short-term reoperations for tamponade, patients with PPS had an excellent 1-year prognosis. (J Thorac Cardiovasc Surg 2016; ■:1-8)



Survival free from reoperation for tamponade in patients with postpericardiotomy syndrome (PPS) versus no PPS.

Central Message

Despite a 10-fold higher risk of short-term reoperation for tamponade, the 1-year prognosis of patients with PPS is excellent.

Perspective

PPS is an important complication of cardiac surgery, leading to a 10-fold higher risk of reoperation for tamponade within 2 months after surgery, and despite a higher rethoracotomy risk, PPS patients have an excellent 1-year prognosis, leading us to conclude that preventing PPS might be worthwhile, in particular for patient comfort and cost-effectiveness. Therefore it is important to study risk factors of PPS.

Postpericardiotomy Syndrome (PPS) is a common complication of cardiac surgery.¹ The syndrome is associated with early postoperative problems such as prolonged hospital stay and cardiac tamponade.^{2,3} The long-term prognosis of PPS has not been studied extensively. PPS is thought to be related to inflammation and autoimmune phenomena in response to surgical trauma and use of cardiopulmonary bypass.^{1,4} In a subanalysis of the

Dexamethasone for Cardiac Surgery (DECS) trial,⁵ we found no protective effect of 1.0 mg/kg dexamethasone on the incidence of PPS.⁶ In the present study, we investigated the short-term (1 month) and long-term (1 year) prognosis of PPS. Furthermore, we searched for risk factors of PPS, to better identify patients who are at risk of PPS and to be more alert on adverse events in these patients.

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This trial is registered with ClinicalTrials.gov (No. NCT00293592).

*The members of the Dexamethasone for Cardiac Surgery Study Group are listed in Appendix E1.

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Abbreviations and Acronyms

AF	= atrial fibrillation
BMI	= body mass index
CABG	= coronary artery bypass grafting
DECS	= Dexamethasone for Cardiac Surgery trial
IL	= interleukin
LMWH	= low molecular weight heparin
PPS	= postpericardiotomy syndrome

Scanning this QR code will take you to a video and Appendix for the article.

MATERIALS AND METHODS**Study Design and Population**

The study population consisted of 822 patients enrolled in the DECS trial. The DECS trial was a double blind, randomized, placebo-controlled trial investigating the effect of an intraoperative dose of 1 mg/kg dexamethasone on a composite end point of death, myocardial infarction, stroke, renal failure, or respiratory failure, in 4494 adult patients undergoing cardiac surgery.⁵ The population of the present study consists of a subgroup of 822 patients undergoing valve surgery at a single center (University Medical Center Utrecht, Utrecht, the Netherlands) and who were included in the earlier published DECS PPS substudy.⁶ In the DECS PPS substudy, 852 DECS patients initially underwent valve surgery. Thirty patients (3.5%) were excluded because no postoperative echocardiography was available ($n = 20$) or other follow-up data needed to establish the diagnosis of PPS were missing ($n = 10$). The remaining 822 patients were included for data analyses. The study consisted of patients undergoing valve surgery only because of the availability of routine surveillance echocardiography, usually on postoperative days 4 to 6.

PPS was diagnosed if 2 out of 5 of the following symptoms were present: pericardial rubbing, fever > 72 hours postoperative, pleuritic chest pain, new significant pleural effusion on chest radiograph (above the highest level of the diaphragm), or significant pericardial effusion (≥ 10 mm). In the main study, all patients provided written informed consent before randomization. The Research Ethics Committee at each participating center approved the protocol, which contained the protocol of the present substudy.

Clinical Outcomes

The primary outcome was the incidence of reoperation for tamponade in patients with and without PPS at 1 year. Reoperation for tamponade was defined as a re sternotomy or subxiphoid incision because of excessive pericardial fluid causing echocardiographic or clinical features of cardiac tamponade.

Long-term secondary outcomes at 1 year were mortality, stroke, myocardial infarction, and readmissions (for any reason). Myocardial infarction was defined according to the criteria of the universal definition of myocardial infarction.⁷ Stroke was defined as a neurologic deficit lasting > 24 hours, with increased invalidity (Rankin scale increase, ≥ 1 point) and signs of a new ischemic cerebral infarction on computed tomography or magnetic resonance imaging scan.

Short-term secondary outcomes were total hospital stay in days and at 1 month the incidences of postoperative atrial fibrillation, reoperation for

tamponade, reoperation for surgical bleeding, and percutaneous pericardial or pleural puncture. Postoperative atrial fibrillation (AF) was defined by the occurrence of any episode of AF postoperatively (during ≥ 10 seconds on a 12-channel electrocardiogram or 3-channel rhythm recording), regardless of a medical history of AF.

Data Collection

Mortality, stroke, and myocardial infarction within 1 year after cardiac surgery and total hospital stay in days were collected prospectively as part of the original DECS trial.

Data concerning postoperative AF, reoperations, and pleural and pericardial puncture were collected by examining all surgical reports, medical records, discharge letters, and postoperative electrocardiograms. Detailed information regarding data collection on postoperative AF and reinterventions can be found in the earlier published DECS postoperative AF study⁸ and the DECS rethoracotomy study.⁹

All participants were followed for 1 year after their initial surgery. In case of a hospital readmission, medical reports were collected retrospectively and assessed by an investigator, who was blinded regarding diagnosis of PPS.

Postoperative Anticoagulant Therapy and Chest Tube Management

The standard postoperative anticoagulation regimen was as follows:

The first moment that drain output was <50 mL in the past hour and <100 mL in the past 3 hours, all patients received low molecular weight heparin (LMWH) 2500 IU subcutaneously. If the patient also underwent a coronary artery bypass grafting (CABG), a single intravenous dose of 450 mg acetylsalicylic acid was added.

On the first postoperative morning, all patients received 2500 IU LMWH subcutaneously and in case of a CABG (or preoperative acetylsalicylic acid use), a daily oral dose of 100 mg acetylsalicylic acid was (re)started.

From the evening of the first postoperative day, daily thrombosis prophylaxis was started: LMWH 2500 IU subcutaneously for patients weighing <80 kg and 5000 IU subcutaneously for patients weighing > 80 kg. Also coumarin therapy was initiated, with target international normalized ratios of 2.5 to 3.5. If the international normalized ratio was > 2.0 , LMWH therapy was stopped. Coumarin therapy was continued for 3 months in patients receiving a bioprosthetic valve or valve repair and lifelong for patients receiving a mechanical valve prosthesis.

Chest tubes were removed if the production was decreasing to <60 mL over the past 3 hours, usually on the first postoperative day.

Statistical Analysis

Continuous variables are expressed as mean \pm standard deviation or as median with interquartile range (IQR), where appropriate. Dichotomous variables are expressed as the number of cases followed by a percentage. We used the Kolmogorov-Smirnov test to determine whether the variables were normally distributed or not. For the comparison of categorical variables we used the χ^2 test or Fisher exact test (in variables with a small sample size) and we calculated odds ratios (ORs) with 95% confidence intervals (CIs). For the comparison of continuous variables we used the Student t test for normally distributed data and the Mann-Whitney U test for data that were not normally distributed.

To identify independent perioperative risk factors of PPS, baseline variables that may clinically be associated with inflammation (age, sex, body mass index [BMI], arterial vascular disease [defined as a medical history of stroke, peripheral artery disease, or significant coronary artery disease], diabetes, treatment for pulmonary disease without corticosteroids, preoperative corticosteroid or aspirin use, intraoperative use of dexamethasone [the DECS trial medication], cardiopulmonary bypass time, units of packed red cells transfused, reoperation for surgical

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