Incidence and risk factors of postpericardiotomy syndrome requiring medical attention: The Finland postpericardiotomy syndrome study

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Objectives: Postpericardiotomy syndrome is a well-known complication after cardiac surgery. Nevertheless, little is known about the incidence and predictors of postpericardiotomy syndrome requiring medical attention or hospitalization in a contemporary set of patients undergoing isolated coronary bypass.

Methods: This retrospective analysis included 688 patients from 2008 to 2010. The median follow-up time was 5.3 [4.5-6.0] years.

Results: The incidence of postpericardiotomy syndrome was 61 of 688 patients (8.9%), and the median time to diagnosis was 21 [11-52] days, but only 13 patients (22%) required pleural drainage and 3 patients (4.9%) required pericardiocentesis. Patients with postpericardiotomy syndrome more often had 1 or more red blood cell units transfused (61% vs 43%, $P = .008$) after surgery and less often had diabetes (12% vs 31% $P = .002$) or metformin medication (3.3% vs 20%, $P = .001$) compared with those without postpericardiotomy syndrome. In multivariable Cox regression model, renal insufficiency and 1 or more red blood cell units transfused remained as independent predictors of postpericardiotomy syndrome and diabetes remained as a protective factor. Incidence of recurrences was high (38%), and increasing body mass index was the only predictor of relapse.

Conclusions: The incidence of symptomatic postpericardiotomy syndrome leading to medical care contact was markedly lower compared with that reported in older clinical studies. Postpericardiotomy syndrome was associated with the use of red blood cell units and was less common in patients with medically treated diabetes. (J Thorac Cardiovasc Surg 2015;149:1324-9)

Postpericardiotomy syndrome (PPS) is a common complication after cardiac surgery. It may lead to prolonged hospital stay, readmissions, and invasive interventions including pericardial or pleural drainage, but the majority of cases have a benign course with mild fever and self-limiting pericardial and pleural effusions. In the literature, the incidence of PPS varies from 10% to 40%,[1-10] and differences in definitions, patient populations, and postdischarge follow-up likely explain this variability and discrepancy. Although recent randomized

clinical trials, the COlchicine for Prevention of the Postpericardiotomy Syndrome and Postoperative Atrial Fibrillation 1 and 2, reported 21% to 29% incidences of PPS at 3 to 12 months follow-up, little is known about the incidence and predictors of PPS requiring medical attention or hospitalization because of symptoms related to PPS in clinical practice.

In this retrospective "real world" study, we sought to assess the incidence and predictors of PPS requiring medical attention as defined by hospital stay prolongation, readmission, or medical therapy for its treatment.

MATERIAL AND METHODS

This study is part of a wider protocol in progress to assess thrombotic and bleeding complications of cardiac procedures in Western Finland.[11-13] Follow-up data were retrieved retrospectively up to 24 months from the surgery from the catchment areas of the Turku University Hospital, the Turku City Hospital, and the Satakunta Central Hospital, Finland. The overall patient population included a consecutive series of 699 patients who underwent isolated coronary artery bypass grafting (CABG) at Turku University Hospital, Finland, from 2008 to 2010. Follow-up data were complete for 688 patients. Hospital records and death certificates from the Statistics Finland were used to acquire data on the mode and date of death. The study protocol was approved by the Ethics Committees of participating hospitals.

Definition of Postpericardiotomy Syndrome and Relapse

PPS was defined by the presence of at least 2 of the following criteria: fever without alternative causes, pleuritic chest pain, friction rub, evidence of new

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Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CI = confidence interval
HR = hazard ratio
NSAID = nonsteroidal anti-inflammatory drug
PPS = postpericardiotomy syndrome

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or worsening pleural effusion, and evidence of new or worsening pericardial effusion.[14] Relapse was defined by worsening of pericardial or pleural effusion while on medication or after withdrawal of medication.

Diabetes was defined as diabetes requiring medical treatment, pulmonary disease was defined as a lung disease requiring long-term use of bronchodilators or steroids, and stroke was defined as a new neurologic deficit after surgery and lasting more than 24 hours accompanied by new structural changes in computed tomography or magnetic resonance imaging or otherwise verified by clinical assessment. Extracardiac arteriopathy was defined as 1 or more of the following: claudication, carotid occlusion or greater than 50% stenosis, and previous or planned intervention on the abdominal aorta, limb arteries, or carotid arteries. Recent acute myocardial infarction was defined as an acute myocardial infarction less than 3 months before CABG. Urgent operation was defined as an operation during the same in-hospital stay, and emergency operation was defined as an operation before the next working day or within a few hours after angiography. Positive x-ray was defined by new or worsening pleural effusion or new or worsening cardiac silhouette enlargement. Positive electrocardiogram was defined by widespread ST elevations. Postoperative bleeding was defined as bleeding measured in the intensive care unit on the morning of the first postoperative day. Surgical bleeding was defined as a significant bleeding from any anastomosis, graft, or vessel in the surgical field (pericardial artery, thoracic vessels, Keynes veins). The classification of "normal," "abnormal," and "major" use of red blood cell units, fresh-frozen plasma cell units, and platelet units was based on the classification of a wider study in which the patient population of the present study was included.[15]

Statistical Analysis

Statistical analysis was performed using SPSS statistical software (version 22, IBM SPSS Inc, Armonk, NY). Continuous variables were reported as the mean ± standard deviation if they were normally distributed and as median [25th, 75th percentiles] if they were skewed. Data were tested for normality assumption using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Categoric variables were described with absolute and relative (percentage) frequencies. Chi-square test, Mann–Whitney test, and Cox regression were used for univariable analysis. The Kaplan–Meier method was used to present survival curves. Multivariable analysis was performed using the Cox regression method by including variables of relevance. Variables with a P value less than .10 in the univariable analysis were entered in the multivariable analysis.

RESULTS
Incidence of Postpericardiotomy Syndrome

The median follow-up time was 5.3 ± 1.0 years. Altogether, 61 of 688 patients (8.9%) undergoing CABG had PPS leading to delayed hospital discharge, readmission, or medical therapy due to symptoms. The mean latency between operation and hospital admission to PPS was 21 (11-52) days [range, 3-140 days]. Freedom from PPS in patients undergoing isolated CABG is detailed in

Figure 1. Pleuritic chest pain, dyspnea, and fever occurred in 20%, 44%, and 41% of patients with PPS, respectively. Abnormal C-reactive protein values were found in 84%, abnormal erythrocyte sedimentation rate was found in 90%, pericardial effusion was found in 93%, positive chest x-ray was found in 93%, friction rub was found in 6.9%, and positive electrocardiogram was found in 45% of patients with PPS.

The baseline characteristics and operative data in patients with and without PPS are detailed in Table 1. No differences in the baseline characteristics were detected except that patients with PPS significantly less often had diabetes and were less often taking metformin. Postoperative characteristics in patients with and without PPS are detailed in Table 2. Red blood cell units were significantly more often transfused in the PPS group, and they had a nonsignificant trend toward more postoperative bleeding.

Pleural puncture was performed in 13 patients (22%) with PPS, and pericardiocentesis was performed in 3 patients (4.9%) with PPS. One patient had PPS leading to clinical cardiac tamponade. No differences in the mortality rates were detected.

Predictors of Postpericardiotomy Syndrome and Relapse

Cox regression univariable model identified the following variables as predictors of PPS: 1 or more red blood cell units used (hazard ratio [HR], 2.1; 95% confidence interval [CI], 1.3-3.5; $P = .005$) and abnormal use of red blood cell units (HR, 1.9; 95% CI, 1.1-3.4; $P = .016$). Diabetes (HR, 0.31; 95% CI, 0.14-0.69; $P = .004$) and metformin (HR, 0.14; 95% CI, 0.034-0.58; $P = .006$) were protective factors. The variables with a P value less than .10 were entered in the multivariable Cox regression analysis. Metformin was excluded because of its association with diabetes, and abnormal use of red blood cell units was excluded because of its association with the use of 1 or more red blood cell units. In multivariable analysis, 1 or more red blood cell units used (HR, 1.9; 95% CI, 1.1-3.2; $P = .017$) and decreasing estimated glomerular filtration rate using the Modification of Diet in Renal Disease formula (HR, 0.99; 95% CI, 0.98-1.0; $P = .078$) remained as independent predictors of PPS. Diabetes (HR, 0.32; 95% CI, 0.15-0.71; $P = .005$) remained an independent protective factor.

Overall, 23 of 61 patients (38%) with PPS had a relapse as defined by worsening of pericardial or pleural effusion while on medication or after withdrawal of medication. The baseline characteristics, operative data, symptoms, and clinical findings of patients with relapsed PPS versus patients with nonrelapsed PPS are detailed in Table 3. Patients with relapsed PPS were more obese. The outcome events of relapsed PPS versus nonrelapsed PPS are detailed in Table 4. Patients with relapsed PPS had significantly