Risk Factors Affecting the Survival of Patients With Pericardial Effusion Submitted to Subxiphoid Pericardiostomy*

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Study objectives: Surgical subxiphoid drainage of the pericardial cavity has been established as a safe and effective method of treatment of pericardial effusion; however, the risk factors affecting survival of these patients have not been clarified. The aim of this study was to investigate the risk factors affecting the short-term and long-term survival of patients with pericardial effusion submitted to subxiphoid pericardiostomy.

Design: Retrospective study.

Patients: The records of all patients who underwent subxiphoid pericardiostomy for treatment of pericardial effusion from January 1991 to December 2001 were reviewed. According to underlying pathology the patients were classified into four groups: (1) hematologic malignancies (n = 17); (2) other malignant diseases (n = 29); (3) AIDS (n = 5); and (4) other benign diseases (n = 53). Multivariate Cox regression analysis was used to test the relationship of short-term and long-term survival to age, sex, cardiac tamponade, pericardial malignant invasion, postoperative low cardiac output syndrome (PLCOS), and underlying pathology.

Results: There were 104 patients (59 men) with a mean age of 53.6 years (range, 13 to 85 years). Follow-up was complete in 99 patients (95.2%) for a mean of 23.9 months (range, 0 to 92 months). Overall 30-day mortality was 16.3%, while operation-related mortality was 4.8%. The underlying disease was the main risk factor for short-term and long-term survival (p < 0.00001), while PLCOS was a major predictor of early mortality (p = 0.029). Patients with AIDS showed the worst prognosis. On the contrary, patients with hematologic malignancies presented significantly longer survival compared to all other patients with malignant diseases (p < 0.05).

Conclusions: The underlying disease was the main risk factor for short-term and long-term survival, while PLCOS was a major predictor of early mortality. The prognosis of AIDS patients with pericardial effusion was grave; therefore, surgical intervention in such patients should be reevaluated. Patients with hematologic malignancies had significantly longer survival compared to all other patients with malignant diseases.

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Key words: AIDS; hematologic malignancy; low cardiac output syndrome; pericardial effusion; risk factors

Abbreviation: PLCOS = postoperative low cardiac output syndrome

Surgical subxiphoid drainage of the pericardial cavity is a widely applied treatment of recurrent pericardial effusion and pericardial tamponade. The terms pericardial window or pericardiostomy have also been used to describe similar techniques with the same objectives: determination of the cause of pericardial effusion, decompression of pericardial cavity, and prevention of recurrence with minimal risk and discomfort to the patient; however, the risk factors that determine the short-term and long-term survival of...
these patients have not been clarified. The aim of this study was to investigate the risk factors affecting the short-term and long-term survival of patients with pericardial effusion submitted to subxiphoid pericardiotomy.

Materials and Methods

Patients

From January 1, 1991, to December 31, 2001, 104 consecutive patients with symptomatic pericardial effusion were operated on by one surgeon in our hospital. There were 45 female patients (43.3%) and 59 male patients (age range, 13 to 85 years; mean, 53.6 years). The clinical histories of all patients were reviewed retrospectively, and the preoperative echocardiographic findings as well as the results of bacteriologic, cytologic, and histologic examinations, and patient outcomes were examined. Sixty-one patients (58.7%) had a specific underlying pathology or a relevant clinical history; including malignant disease of a known origin (n = 38), chronic renal failure (n = 12), AIDS (n = 5), connective tissue disease (n = 3), recent cardiac surgery (n = 2), and myocardiopathy (n = 1). According to the final diagnosis, the patients were classified into four groups: (1) hematologic malignancies (n = 17); (2) other malignant diseases (n = 29); (3) AIDS (n = 5); and (4) other benign diseases (n = 53).

Surgical Technique

The surgical technique utilized was similar to that outlined by Fontenelle and colleagues in 1970.1 No local anesthetics were used before or during the operation. In all patients, the procedure was performed under general endotracheal anesthesia after the patient was draped and the surgical team was prepared to commence the operation. For induction to anesthesia, fentanyl, etomidate, and rocuronium or cis-atracurium were administered. Maintenance of anesthesia was obtained by isoflurane or sevoflurane and mixture of oxygen/air supplemented by fentanyl as needed. The xiphoideal process was excised. A piece of pericardium of approximately 2 cm by 5 cm was removed from the lower portion of the anterior surface of the pericardium. The usual duration of the operation was 35 to 50 min.

Follow-up

Follow-up was obtained by telephone call up to March 2002. If a patient had died, the information regarding the cause of death and the possibility of recurrence was obtained by contact with the family doctor. Five patients (4.8%) were unavailable for follow-up and the possibility of recurrence was obtained by contact with the family doctor. Five patients (4.8%) were unavailable for follow-up immediately after hospital discharge. The remainder were followed up for a mean of 23.9 months.

Statistical Methods

Survival curves were plotted by the Kaplan-Meier method. Statistical differences in survival were determined by the log-rank test. Multivariate Cox regression analysis was used to test the relationship of short-term and long-term postoperative survival to age, sex, cardiac tamponade, postoperative low cardiac output syndrome (PLCOS), and underlying pathology. Statistical differences were considered significant if the p value was ≤ 0.05.

Results

The final etiologic diagnoses of pericardial effusion in all patients are presented in Table 1; in patients with two or more pathologic conditions, only the main cause of the pericardial effusion was included. The overall 30-day mortality, including the in-hospital mortality, was 16.3% (n = 17), ranging among the four groups: 23.5% in patients with hematologic malignancies (group 1), 31% in patients with other malignancies (group 2), 20% in patients with AIDS (group 3), and 5.7% in patients with benign diseases (group 4). The 30-day mortality of all patients with underlying malignant diseases (groups 1 and 2) was 28.3%, differing statistically compared to that of patients of group 4 (p < 0.001). Twelve of the 17 early postoperative deaths were due to the underlying disease. The remaining five deaths (4.8%) resulted from complications related to the surgical procedure itself: four patients died of PLCOS and one patient died from cardiac arrest during induction to general anesthesia. Major postoperative complications were noticed in 14 patients (13.5%). Five patients (4.8%) had low cardiac output syndrome (Table 2), and four of them died. Nine patients presented transient arrhythmias, and one of them died.

The mean survival time was 20.4 months for patients with hematologic malignancies, 4.9 months for patients with other malignancies, 2.4 months for patients with AIDS, and 38.9 months for patients with benign diseases. One-year, 3-year, and 5-year survival rates were 47.1%, 29.4%, and 29.4%, respectively, for patients with hematologic malignancies, and 77.1%, 75%, and 72.9% for patients with benign diseases. For patients with other malignancies, 1-year survival was 13.8%. Twenty-seven of 29 patients (93.1%) of this group died within 16 months.

Table 1—Etiologic Diagnosis of Pericardial Effusion

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Patients, No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant diseases</td>
<td>46</td>
<td>44.2</td>
</tr>
<tr>
<td>Hematologic malignancies</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Lung cancer</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Cancer of undetermined origin</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Breast cancer</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Other*</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>104</td>
<td>100</td>
</tr>
</tbody>
</table>

*One each with melanoma, mesothelioma, oropharyngeal cancer, and primary mediastinal germ cell tumor.
after the operation. At the time of writing, two end-stage patients are still alive 18 months and 25 months, respectively, after the operation. All patients with AIDS died within 5 months after the operation (Fig 1). The underlying disease was the cause of all late deaths. Long-term survival differed significantly between patients with benign diseases and those with malignant diseases ($p < 0.0001$) or with AIDS ($p < 0.0001$). Among the patients with malignant diseases, patients with hematologic malignancies presented significantly higher survival rates in comparison to those with other malignancies ($p < 0.05$).

Of the 46 patients with underlying malignancies, only 31 patients were proved by cytologic and histologic examination to have malignant invasion of the pericardium: 47.1% in patients with hematologic malignancy and 79.3% in patients with other malignant diseases. There was no statistical significance in the cumulative survival curves between the patients with histologically or cytologically proved malignant pericardial invasion and patients without confirmed pericardial invasion by the underlying malignant disease.

Recurrent pericardial effusion requiring further surgical intervention occurred in two patients (2%).

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### Table 2—Characteristics of Patients With PLCOS

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Gender</th>
<th>Age, yr</th>
<th>Main Underlying Disease</th>
<th>Cardiac Tamponade</th>
<th>Malignant Pericardial Invasion</th>
<th>Predisposing Factor(s) to PLCOS</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Female</td>
<td>37</td>
<td>Non-Hodgkin lymphoma</td>
<td>Yes</td>
<td>No</td>
<td>Chemotherapy, previous mediastinal radiotherapy, right pleural effusion</td>
<td>Death</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>69</td>
<td>Nonspecific pericarditis</td>
<td>Yes</td>
<td>No</td>
<td>None</td>
<td>Survival</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>67</td>
<td>Breast cancer</td>
<td>Yes</td>
<td>Yes</td>
<td>Chemotherapy</td>
<td>Death</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>31</td>
<td>AIDS</td>
<td>Yes</td>
<td>No</td>
<td>Myocardiopathy</td>
<td>Death</td>
</tr>
<tr>
<td>5</td>
<td>Male</td>
<td>70</td>
<td>Mesothelioma</td>
<td>Yes</td>
<td>Yes</td>
<td>None</td>
<td>Death</td>
</tr>
</tbody>
</table>

**Figure 1.** Kaplan-Meier survival curves.
Etiologic diagnosis of pericardial effusion in both patients was “idiopathic pericarditis.” One patient had recurrent cardiac tamponade and died 3 months after the operation. The other patient had recurrent pericardial effusion and underwent pericardectomy 2 months after pericardiostomy. There was no recurrence of pericardial effusion in patients either with malignant diseases (patients of group 1 and 2) or with AIDS.

The surgical procedure provided evidence of the cause of pericardial effusion in 50 patients (48.1%). In 15 of these patients, the operation established the diagnosis of an unsuspected disease: malignant (n = 8) and benign (n = 7). In 72 patients, the cytologic and histologic analyses were negative, whereas the histologic diagnosis was “nonspecific pericarditis” in 50 patients and “normal pericardium” in 4 patients. Half of these 54 patients had a known history of a benign disease, while the remaining 27 patients did not have a previous history. In these 27 patients, the diagnosis of idiopathic pericarditis was attributed.

Multivariate Cox regression analysis showed that in the entire patient population, age, sex, and cardiac tamponade were not predictors of short-term and long-term survival. Underlying pathology (p < 0.00001) and PLCOS (p = 0.029) were the main risk factors for short-term survival. Underlying pathology was the only predictor of long-term survival (p < 0.00001).

**Discussion**

The vast majority of the studies published in literature2–7 suggest that the subxiphoid pericardios-tomy is an expeditious, easy, and inexpensive procedure, which can be applied to a wide spectrum of pericardial effusions. The technique provides accurate diagnosis and effective, durable treatment with an operation-related mortality ranging between 0% and 5% and a recurrence rate 0 to 9.1%.3–5,8–11 Our results compare with those reported in literature: the operation-related mortality was 4.8% and the recurrence rate of the pericardial effusion was 2%.

The first remarkable observation that comes up from our study is that PLCOS is a major risk factor for short-term mortality. We think that the significance of this factor has not been emphasized enough. We were able to find only two references on this subject,12,13 although scattered deaths directly related to the procedure as a result of paradoxical severe systolic heart dysfunction occurring soon after decompression of pericardial tamponade have been reported.13–15 In our series, five patients (4.8%) acquired this syndrome during the immediate post-operative period and four of them died. The causes of PLCOS complicating the subxiphoid pericardios-tomy are obscure. Several factors have been implicated, such as direct myocardial involvement by tumor, myocardial ischemia during tamponade, myocardial damage from antineoplastic drugs or anesthetic agents,16 stunning and reversible myocardial hibernation and rapid pericardial decompression following tamponade, and occult systolic dysfunction.12,13,17 It seems more plausible that the pathophysiologic mechanism of this early and rapid cardiac failure is the same as that producing the syndrome in up to 28% of patients with chronic constrictive pericarditis subjected to pericardiectomy.18 We suggest that the chronic external support of the heart by the pericardial fluid, when rapidly released, may result to overdilatation of the heart, leading to systolic dysfunction and failure. Whatever the cause of PLCOS might be, the lesson learned from this small series of patients is that thoracic surgeons, as well as anesthesiologists, cardiologists, and intensivists, should be aware of the possibility that patients with even normal-looking myocardium may have transient or even fatal heart failure after relief of a benign or malignant pericardial tamponade. Appropriate monitoring and inotropic support may result in recovery of some of these patients.

It is widely accepted that the underlying disease is the main risk factor for short-term and long-term survival of patients submitted to subxiphoid pericardiostomy,11 which is in accordance with our findings. However, in this series, two pathways with significant, although opposite impact on late survival have emerged: AIDS and hematologic malignancy.

Five patients with AIDS are included in our study. Their mean survival was 2.4 months. All patients died within a 5-month period after the operation because of their disease. In addition, the cytologic and histologic analyses were diagnostic only in one patient with mediastinal lymphoma, who was ineligible for appropriate therapy based on his critical general condition. In the remaining four patients, the operative results did not alter the clinical management. These findings corroborate the clinical observation of Flum and colleagues19 that in patients with AIDS, pericardial drainage has limited diagnostic and therapeutic value. Therefore, we suggest that in AIDS-related pericardial effusion the usefulness of such a surgical intervention is dubious and must be reevaluated.

In contrast to the extremely low survival of patients with AIDS, patients with hematologic malignancies had significantly longer survival compared to all other patients with malignant diseases. Their mean survival time (20.4 months) differed significantly compared to that of patients with other ma-
lignant diseases (4.9 months). We believe that the longer survival of patients with hematologic malignancies is due to better response of these diseases, and particularly lymphomas, to chemotherapy and radiotherapy compared to all other types of malignancies.

However, it seems logical that malignant pericardial invasion indicates more extensive malignant disease and consequently worse prognosis. We found that among 46 patients with different malignant diseases, histologically and/or cytologically proved malignant pericardial invasion was not a predictor of short-term and long-term survival. The data in the literature on this subject are controversial. Some authors agree with our findings, while others suggest that malignant pericardial invasion is a bad prognostic sign. Since the number of patients in our study is small, we think that more extensive studies are required to confirm these findings.

In conclusion, the findings of this study suggest that in patients with pericardial effusion submitted to subxiphoid pericardiostomy, age, sex, and cardiac tamponade were not predictors of short-term and long-term survival. The underlying disease was the main risk factor for short-term and long-term survival, while PLCOS was a major predictor of early mortality. The prognosis of patients with AIDS was grave; therefore, surgical intervention in patients with pericardial effusion associated with AIDS should be reevaluated. Among the limited number of patients with malignant diseases, malignant pericardial invasion was not a predictor of short-term and long-term survival. Patients with hematologic malignancies presented significantly longer survival compared to all other patients with malignant diseases. Since the number of patients of our study is small, we think that more extensive studies are required to confirm these findings.

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