Should we Try to Determine the Specific Cause of Cardiac Tamponade?

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Introduction. The causes of cardiac tamponade vary and it has been suggested that underlying causes should be sought in all cases. The purpose of this study was to determine the causes of cardiac tamponade in our environment, distinguishing between specific and idiopathic causes, and analyzing the proportion and causes in the subgroup of patients with relapsing tamponade.

Patients and method. We retrospectively studied all patients who underwent therapeutic pericardiocentesis between 1985 and 2001. The clinical and radiographic features and macroscopic characteristics of the pericardial fluid were analyzed. The final diagnosis in each patient was based on the clinical history, follow-up, pericardial fluid cytology, and pericardial biopsy, if available.

Results. Ninety-six patients were included (52 men/44 women), mean age 56.1 ± 16.1 years. The cause of pericardial effusion was neoplasm in 50 patients (52.1%), 14 idiopathic pericarditis (14.6%), 12 renal failure (12.5%), 7 iatrogenic cases (7.3%), 4 mechanical tamponades (4.2%), 2 tuberculosis (2.1%), and 7 other causes (7.3%). Thirty-five patients had relapsing tamponade; only 2 of them had idiopathic pericarditis (5.7%). We found no significant differences in age, development time, extracted volume or fluid features between tamponade of specific or idiopathic origin.

Conclusions. Most of the cardiac tamponades in our series had a specific cause. This made it necessary to identify a specific underlying cause in each case, especially in relapsing effusions. However, we did not find any variable suggestive of the cause of the disease.

Key words: Cardiac tamponade. Pericardial effusion. Pericardium.

¿Debemos pensar en una etiología específica en pacientes con taponamiento cardíaco?

Introducción. La etiología del taponamiento cardíaco es muy diversa, por lo que se ha planteado la necesidad de realizar un cribado de la posible causa subyacente en todos los casos. Nuestro objetivo fue determinar las causas del taponamiento en nuestro medio, distinguiendo entre específicas e idiopáticas, así como analizar la proporción y la etiología del subgrupo de taponamientos recidivantes.

Pacientes y método. Se realizó un estudio retrospectivo de los pacientes tratados con pericardiocentesis terapéutica entre 1985 y 2001. Se recogieron las características clínicas, radiológicas y macroscópicas del líquido extraído en cada caso. El diagnóstico etiológico se basó en datos de la historia clínica, evolución, citología del líquido pericárdico y biopsia, si se disponía de ésta.

Resultados. Se incluyeron a 96 pacientes (52 varones y 44 mujeres; edad media 56,1 ± 16,1 años). La etiología fue en 50 pacientes neoplásica (52,1%); en 14, idiopática (14,6%); en 12, urémica (12,5%); en 7, iatrogénica (7,3%); en 4, mecánica (4,2%); en 2, tuberculosa (2,1%); y en 7 (7,3%) otras causas. En 35 pacientes el taponamiento recidió; de ellos, sólo dos presentaban una pericarditis idiopática (5,7%). No encontramos diferencias significativas en cuanto a la edad del paciente, el tiempo de evolución, el volumen extraído o las características del líquido, entre los taponamientos debidos a una pericarditis idiopática o a etiologías específicas.

Conclusiones. La mayoría de los taponamientos cardíacos de nuestra serie presentan una etiología específica. Esto obliga a descartar una causa subyacente en todo taponamiento, especialmente en los casos de recidiva. Sin embargo, no encontramos ninguna variable que nos oriente hacia la etiología del cuadro.

Palabras clave: Taponamiento cardíaco. Derrame pericárdico. Pericardio.
pericardial effusion. Its diagnosis is based on demonstrating hemodynamic impairment in the presence of moderate or severe pericardial effusion. It can develop as a complication of pericardial effusion of any cause.\(^1\) Its treatment is pericardiocentesis, which also has a relatively high diagnostic performance (around 30%).\(^2\) Nevertheless, diagnostic pericardiocentesis has a low performance (5%), which is why it is reserved for cases of suspicion of purulent pericarditis or long-standing pericardial effusion without a clear diagnosis.

The traditional concept that cardiac tamponade is of idiopathic origin in most cases\(^2-4\) has been questioned in recent years. Consequently, specific, frequently neoplastic, etiologies are gaining in relevance as the underlying cause of tamponade.\(^5-6\) Nevertheless, few series support this hypothesis\(^2,4,7\) although this information is crucial for the management of patients with cardiac tamponade. However, it necessarily requires that an exhaustive investigation be made of potentially treatable underlying processes.

For this reason, we designed a study to determine the causes of cardiac tamponade in our setting and the proportion of specific and idiopathic causes, centering especially on «primary» cardiac tamponade, that is, those without a clear cause \textit{a priori}. In addition, we analyzed the subgroup of cardiac tamponades that tended to recur. Finally, we sought variables that were significantly related with the ultimate cause of cardiac tamponade.

**PATIENTS AND METHOD**

The study was carried out in the Hospital General of Alicante from January 1985 to October 2001. This is a 900-bed tertiary hospital that has cardiology, cardiac surgery, oncology, internal medicine, and nephrology departments, which were the main sources of cardiac tamponades in our series. It is the reference hospital of the province of Alicante for cardiac and hemodynamic surgery. During the period of time analyzed, most of the patients in the province with cardiac tamponade requiring pericardiocentesis or surgical drainage were sent to our hospital, which is why we have a representative distribution of all the possible causes of the condition.

All the samples of pericardial fluid obtained in this period were investigated retrospectively and the medical histories of these patients were collected. Among them, those corresponding to patients who required drainage pericardiocentesis for cardiac tamponade were selected. The patients in which pericardial liquid was obtained for merely diagnostic purposes were excluded (for example, massive chronic effusion, or long-standing, undiagnosed effusion in the course of cardiac surgery or a post mortem study) (n=20). The group of patients whose medical history was not available or who were lost to follow-up after pericardiocentesis was excluded (n=15).

The following variables were obtained from each patient: clinical data (age, sex, main symptoms, duration of the condition, physical examination); radiological characteristics (increased cardiothoracic index and association with pleural effusion), and data corresponding to the pericardial fluid extracted (volume, gross appearance, biochemical values, cytology, and microbiology).

In our center the diagnostic protocol proposed by the Hospital Vall d’Hebron for the study of pericardial disease was followed.\(^2,3\) The final etiological diagnosis of cardiac tamponade was based on data in the medical history and later follow-up, as well as the cytology and pericardial biopsy in cases in which these studies were made. Recurrences of cardiac tamponade were also studied.

The cardiac tamponades were divided into the following categories:

1. Cardiac tamponades of neoplastic origin, including those that appeared in the context of a malignant disease and those that lead to the diagnosis of a neoplasm as a result of the study of pericardial fluid.
2. Iatrogenic tamponades, consisting of the tamponades that were directly related with an invasive surgical or medical procedure.
3. The third group included patients with chronic renal failure who were either predialysis or in hemodialysis and developed cardiac tamponade, in the absence of another cause to explain it.
4. The etiology was considered tuberculous in patients in which Koch bacilli were demonstrated in the pericardial fluid or any other site of the organism.
5. Mechanical causes included cardiac tamponade secondary to dissecting aortic aneurysm, thoracic trauma, or cardiac ruptures after myocardial infarction.
6. The section «other causes» included pericardial effusion secondary to hypothroidism, purulent pericarditis, heart failure, postpericardiotomy syndrome, and other systemic diseases (one case was associated with thrombotic thrombocytopenic purpura).
7. Finally, cardiac tamponade was denominated «idiopathic» when no underlying cause was found (including cardiac tamponade after acute pericarditis.
of supposedly viral origin) at the time the clinical condition appeared or later.

All the samples of pericardial fluid were processed for microbiology, with culture of aerobe and anaerobe organisms, biochemical findings (glucose and proteins), leukocyte count, and cytological examination.

In the statistical analysis, quantitative variables were expressed as mean ± standard deviation, and qualitative variables were expressed as percentages. Statistical analysis was made with the Chi-square test for discrete variables and the Student t test and ANOVA for continuous variables. The level of statistical significance was P<.05.

RESULTS

The study included 103 pericardial fluid samples from 96 patients, 51 men and 44 women, of ages ranging from 18 to 84 years (mean 56.1±16.1).

The most frequent main symptom was dyspnea (n=57, 59.4% of the cases), followed by chest pain (n=21, 21.9%) and hemodynamic instability (although hemodynamic instability, by definition, is associated with all cardiac tamponades, it was the main reason for consultation in only 5 patients). Coughing was the symptom that motivated the visit in 2 patients (2.1%), and in another 2 it was a constitutional syndrome with anorexia, asthenia, and weight loss. In 49 patients (51%), pericardial effusion was associated with the presence of pleural effusion.

Of the 103 fluid specimens obtained, the gross appearance was hematic in 40 (38.8%), serohematic in 33 (32.0%), serous in 28 (27.2%), purulent in 1 (1.0%), and chylous in 1 (1.0%).8 Analysis of only the tamponades of neoplastic origin disclosed similar proportions.

The final diagnoses of the 96 patients are shown in Figure 1: neoplasm in 50 patients (52.1%), idiopathic in 14 patients (14.6%), renal insufficiency in 12 (12.5%), iatrogenesis in 7 (7.3%) (4 ventricular perforations during pacemaker implantation and 3 postoperative cardiac tamponades with anticoagulation in excess of therapeutic levels), mechanical causes in 4 patients (4.2%) (including 2 dissecting aneurysms of the aorta, cardiac rupture after acute extensive anterior myocardial infarction, and a case after chest injury), 2 of tuberculous origin (2.1%), and 7 (7.3%) due to other causes (1 hypothyroidism, 2 heart failures, 1 purulent pericarditis due to Streptococcus pyogenes, 2 postpericardiotomy syndromes, and 1 associated with thrombotic thrombocytopenic purpura).

The main cause of cardiac tamponade of malignant origin was pulmonary neoplasm in 22 patients (44%), followed by breast carcinoma in 6 patients (12%), and a neoplasm of unknown origin in spite of exhaustive study in another 6 (12%). Three patients had an ovarian neoplasm and 3 had gastric carcinoma. The remaining patients had one each of lymphoma, chronic myeloid leukemia, carcinoma of the base of the tongue, rectal neoplasm, melanoma, prostate neoplasm, uterine cervix cancer, and sarcoma of the right atrium. In some cases of recurrent neoplastic cardiac tamponade, additional measures were carried out, like opening a pericardial window (n=6) or intrapericardial instillation of mitoxantrone (n=5) or tetracyclines (n=2).

In an analysis of just the cardiac tamponades without an underlying disease, in which no etiological estimate of probability at the time of admission could be identified (the so-called «primary» cardiac tamponades),2,3 there were 31 cases: 13 incipient neoplasms (diagnosed as a result of the episode of cardiac tamponade) (41.9%), 14 idiopathic pericarditis (45.2%), 2 cases of tuberculosis (TB) (6.5%), 1 patient with hypothyroidism (which was found through the study protocol of pericardial effusion) (3.2%), and 1 purulent pericarditis (3.2%) (Figure 2). Of the 13 incipient neoplasms, 5 were pulmonary, 3 of unknown origin, 1 rectal adenocarcinoma, 1 sarcoma of the right atrium, 1 prostate carcinoma, 1 ovarian neoplasm, and 1 cancer of the uterine cervix.

In 84 of the 96 patients we collected data on the long-term follow-up: 10 cases of idiopathic pericarditis and 74 cardiac tamponades of specific origin. In these patients, cardiac tamponade recurred in 35 patients, of which only 2 (5.7%) had an idiopathic etiology. In 26 cases the cause was neoplastic, in 2 a long-term postpericardiotomy complication, in 2 renal insufficiency, 1 iatrogenesis (after cardiac surgery, with excessive anticoagulation), 1 hypothyroidism, and 1 case of TB. There was no recurrence in the patients with purulent pericarditis, heart failure, mechanical causes, or thrombotic
thrombocytopenic purpura.

In Tables 1 and 2, the clinical characteristics and pericardial fluid in each etiological subgroup are described, as well as the $P$ value obtained in the statistical analysis. The ultimate cause of tamponade showed no statistically significant relation with any of the variables analyzed: age, sex, duration of the clinical condition, association with pleural effusion, volume of pericardial fluid extracted, gross appearance or biochemical composition of the fluid (glucose, proteins, and cell count). Therefore, we encountered no clinical findings suggestive of the cause of tamponade. Nevertheless, the appearance of recurrences showed a statistically significant relation with etiology, with a clear tendency toward an association between the evolution to recurrence and the underlying disease, especially neoplasms.

**DISCUSSION**

In the first large series of patients with pericardial disease, acute idiopathic pericarditis was considered the cause of most of cardiac tamponades, although other conditions had a higher rate of evolution to tamponade. This finding was found fundamentally in cases of primary pericardial disease (that is, pericardial disease with no clear etiology $a$ priori), although it held true in series of primary and secondary pericardial effusion and in both young and older patients. According to this premise, it is not imperative to carry out an exhaustive search for the underlying processes in patients with cardiac tamponade, except in cases of a torpid evolution or high suspicion of a specific etiology in light of the basic examinations.

Nevertheless, in the recent years we are seeing a growing relevance of specific etiologies as the basis for cardiac tamponade, mainly neoplasms. We confirmed this tendency in our series, neoplasms being the cause of more than half of the cardiac tamponades investigated. As an explanation of this phenomenon we note an improvement in diagnostic techniques, the prolongation of survival in patients with advanced neoplasms, and improvements in the cytological techniques that, in expert hands, often suggest a neoplastic origin of the condition. In fact, in our series, even in the case of «primary» cardiac tamponades, although the most frequent cause continues to be idiopathic pericarditis (45.2%), most patients had an underlying process, predominantly neoplasms (41.9%).

Among the cardiac tamponades of neoplastic origin, the main cause in this series was lung cancer (44% of the malignant cardiac tamponades), as in previous series in the literature. The high proportion of neoplasms of unknown origin (12%) with a positive

**TABLA 1. Clinical characteristics of the overall group of patients studied and each etiological subgroup**

<table>
<thead>
<tr>
<th>Age</th>
<th>Men (%)</th>
<th>Days of evolution</th>
<th>Recurrences* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>56.5±15.9</td>
<td>52 (54.2)</td>
<td>28.9±53.7</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>54.2±20.4</td>
<td>8 (57.1)</td>
<td>60.6±117.0</td>
</tr>
<tr>
<td>Neoplastic</td>
<td>57.6±12.1</td>
<td>28 (56.0)</td>
<td>26.4±31.5</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>57.0±4.2</td>
<td>2 (100.0)</td>
<td>33.5±37.5</td>
</tr>
<tr>
<td>Uremia</td>
<td>53.1±22.5</td>
<td>6 (50.0)</td>
<td>21.6±36.6</td>
</tr>
<tr>
<td>Mechanical</td>
<td>60.2±22.1</td>
<td>2 (50.0)</td>
<td>12.2±13.7</td>
</tr>
<tr>
<td>Iatrogenic</td>
<td>69.3±7.3</td>
<td>4 (57.1)</td>
<td>8.0±7.4</td>
</tr>
<tr>
<td>Others</td>
<td>44.1±16.2</td>
<td>2 (28.6)</td>
<td>24.3±43.5</td>
</tr>
</tbody>
</table>

$P$ refers to the 84 patients in whom long-term follow-up was carried out.

**TABLA 2. Association with pleural effusion and characteristics of the pericardial fluid extracted in the overall group of patients and in each of the etiological subgroups**

<table>
<thead>
<tr>
<th>Pleural (%)</th>
<th>Fluid Volume</th>
<th>Hematic Fluid* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>51 (53.1)</td>
<td>932±600</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>6 (42.9)</td>
<td>863±742</td>
</tr>
<tr>
<td>Neoplastic</td>
<td>33 (66.0)</td>
<td>1051±563</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>1 (50.0)</td>
<td>710±198</td>
</tr>
<tr>
<td>Uremia</td>
<td>5 (41.7)</td>
<td>557±426</td>
</tr>
<tr>
<td>Mechanical</td>
<td>2 (50.0)</td>
<td>454±406</td>
</tr>
<tr>
<td>Iatrogenic</td>
<td>2 (28.6)</td>
<td>1143±592</td>
</tr>
<tr>
<td>Others</td>
<td>2 (28.6)</td>
<td>989±713</td>
</tr>
</tbody>
</table>

$P$ refers to the 84 patients with hematic or serohematic pericardial fluid versus patients with serous effusion; patients with purulent pericardial fluid were excluded.
cytological study for malignant cells but no identifiable primary neoplasm should be emphasized. The fact that we have few post mortem studies (n=3), together with the rapid and somber evolution of these patients, explains this high percentage.

Another point worth mentioning, which is consistent with recent series of pericardial effusion, is the growing importance of iatrogenesis as a cause, due to the increase in the use of invasive techniques in cardiology, such as percutaneous coronary interventions\(^1\) (with an incidence of cardiac tamponades of about 0.2%\(^{14}\)) or cardiac surgery. In certain series the frequency of iatrogenesis reaches 17.6%,\(^4\) a figure that depends on patient selection and the type of hospital in which the cases are recorded.

Tuberculosis, which for years was an important cause of cardiac tamponade, has been decreasing notably in our country,\(^5,6\) with only a few demonstrated cases of tuberculosis in similar series in Spain. However, in other countries (including the U.S.) it continues to be an etiology found mainly in the population of Asian and African origin.\(^5,7\) Nowadays, most cases of tuberculous cardiac tamponade are seen in patients with AIDS.\(^8,9\) In our series only one patient had HIV infection, in this case concomitantly with chronic kidney failure in dialysis, which we interpreted as the underlying cause of cardiac tamponade since all the pericardial fluid cultures were negative. This low proportion of seropositive patients probably conditions the results of our series, since the etiological spectrum is very different in HIV-positive patients. Such patients have a high prevalence of infectious causes (fundamentally tuberculosis) and occasional neoplasms in immunocompetent patients, such as lymphoma or Kaposi’s sarcoma.\(^9,10\)

The early treatment of severe thoracic infections (empyema, mediastinitis, pneumonia) has made it possible to reduce purulent pericarditis to anecdotal figures, as confirmed by our series, in which we found only one case due to \textit{S. pyogenes}.

We did not find any case of cardiac tamponade in patients with connective tissue diseases. Although pericardial effusion is frequent in such cases, the evolution to cardiac tamponade is exceptional.\(^11,12\) For that reason, the need for screening for rheumatological diseases in cases of cardiac tamponade with no other data suggesting their presence could be contemplated.

There is a generalized tendency among clinicians to consider the finding of hematic fluid by pericardiocentesis as a sign of poor prognosis, consistent with etiologies like neoplasm or tuberculosis.\(^13\) This affirmation was not sustained in our series because we found no significant differences in the relation between the appearance of the pericardial fluid and the underlying cause.

No clinical finding was related with either specific causes of cardiac tamponade or idiopathic pericarditis. Likewise, the characteristics of the pericardial fluid (volume, appearance, or laboratory findings) did not allow the cause of effusion to be predicted. Cytological study and biopsy were the only useful diagnostic tools, as has been reported in earlier series of cardiac tamponades.\(^24\)

The rate of recurrences is clearly higher in specific pericardial effusions. In our study, more than half of the neoplastic effusions tended to recur after pericardiocentesis. In contrast, only two of the 14 idiopathic tamponades (14.3%) recurred. This finding obliges us to intensify diagnostic efforts in cardiac tamponades that reappear after correct treatment, in order to find the underlying process that exists in more than 90% of cases, according to our series.

**Limitations of the study**

The population in which the data of the study were obtained consisted of patients hospitalized in a tertiary care center. Consequently, there probably was a certain selection bias that could overvalue some causes, like neoplasms, uremia, or iatrogenic cases, which are found in a larger proportion in reference hospital centers than in the general population. For the same reason, other etiological groups like idiopathic pericarditis, could have been underestimated because patients were studied in other hospitals. This was the case of most of these patients, who were excluded because later follow-up data could not be collected.

The etiological investigation and long-term follow-up of each patient could have been influenced by the clinician who carried out the study. Nonetheless, the fact that we had a pre-established protocol for the study of pericardial disease (the protocol proposed by the Hospital Vall d’Hebron) minimizes this possible bias by unifying the diagnostic and therapeutic attitude in different cases.

**CONCLUSION**

The main cause of cardiac tamponade in our setting was neoplasms, idiopathic cases constituting only 15% of all cardiac tamponades. This finding obliges us to screen for various specific etiologies in the case of cardiac tamponade requiring therapeutic pericardiocentesis.

No clinical variable allows the cause of effusion to be determined. A large proportion of recurrent pericardial effusions after tamponade are associated with a specific etiology, fundamentally neoplasms.
REFERENCES