

Diagnostic Accuracy of Mortality on a Population of Heart Transplant Patients

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ABSTRACT

Background

Although morbidity and mortality rates in heart transplant have been extensively analyzed, most mortality studies and mortality registries in heart transplant patients are based on clinical data. Isolated communications of necropsies performed in heart transplant patients have been reported.

Objective

To determine the importance of pathological studies for the diagnosis of the causes of death in a heart transplant program.

Material and Methods

Between January 1990 and January 2005 all dead transplant patients were included. The final diagnosis of the cause of death was confirmed with necropsy or biopsy of a solid organ. The causes of death assessed were early graft failure, cellular rejection, graft vascular disease, neoplasms and others.

Results

Seventy three patients underwent heart transplantation during the study period. Thirty one patients died. The cause of death was certified in 61% of cases by 12 necropsies and 7 solid organ biopsies. Cellular rejection greater than grade III was the most frequent cause of death. Histopathology studies differed from the clinically suspected cause of death in 12.9% of cases.

Conclusion

Clinical and pathological information derived from post mortem studies is an indicator of the reality of our practice and constitutes an underlying mainstay for understanding transplant patients and for their further management; in this sense, performing necropsies is of vital importance for these patients.

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Key words > Heart Transplant - Necropsy - Diagnosis

BACKGROUND

Heart failure is one of the most important issues in Public Health, with an increasing prevalence due to improved survival in the population and a better management of coronary artery disease. (1, 2) There are several strategies of treatment depending on the patient's clinical stage; orthotopic heart transplant is, so far, the most effective treatment for end-stage heart failure.

One-year survival has increased up to almost 86% as a consequence of better surgical techniques and

immunosuppressive therapies. In addition, mortality related to infections and acute rejection has decreased; however, graft vascular disease has emerged as the main cause of long-term morbidity and mortality. (3, 4)

Although morbidity and mortality in heart transplant have been extensively analyzed, most studies and registries of mortality in transplant patients are based on clinical data, (3) which are sometimes controversial due to the type of patients assessed: patients with few symptoms, with atypical presentations or with low-prevalent diseases. Isolated communica-

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tions of autopsies performed in heart transplant patients have been reported. (5)

Our hospital's Heart Transplant Program has a permanent staff of pathologists on duty that has enabled us to perform a great number of autopsies. The aim of this study was to determine the importance of pathological studies for the diagnosis of the causes of death in a heart transplant program.

MATERIAL AND METHODS

We conducted a descriptive and retrospective study. Between January 1990 and January 2005 all dead transplant patients were analyzed. The final diagnosis of the cause of death was classified as *definite* in all deaths confirmed with autopsy or biopsy of a solid organ, *probable* in dead patients with clinical suspicion and laboratory data or image scans available, and *unknown* in those with no record of clinical data. The reason for hospitalization was considered the cause of death in cases of multiple pathological findings. In addition, the causes of death assessed were early graft failure, cellular rejection graded as International Society of Heart and Lung Transplantation (ISHLT), 1990, greater than grade III, (6) infection, graft vascular disease, neoplasms and other causes. Early graft failure was identified as primary and unspecific graft failure. Variables are expressed as percentages.

RESULTS

Between January 1990 and January 2005, 73 patients underwent heart transplantation. Survival rate at 1, 5 and 10 years was 80%, 65% and 50%, respectively. Thirty one patients died; 27 deaths occurred at hospital and 4 outside (the final diagnosis of death was unknown in 2 patients and probable in the remaining 2 patients). Global survival was 221.9 (0-93.1) months. Fifty eight percent of deaths occurred during the first year (Figure 1).

A definite diagnosis of death was made in 61% of cases (19/31) (12 autopsies and 7 biopsies). Cellular rejection greater than grade III was the most frequent cause of death (Figure 2). The cause of death was confirmed by autopsy in 12.9% of the cases. The causes of death are listed in Table 1.

DISCUSSION

Early graft failure was the main cause of perioperative death, while cellular rejection and infections were most frequent 30 days after the transplant. These findings are consistent with the data reported by the registry ISHLT (4) and the Spanish Heart Transplantation Registry (7).

Autopsy has been historically considered the gold standard for the diagnosis of the cause of death. This kind of practice has evolved since the 17th century and is useful to show the incidence of organic diseases or to discover the medical causes of death. (8) For several reasons, this practice is no longer habitual in our environment, especially in transplant patients. Nevertheless, several published papers have encouraged

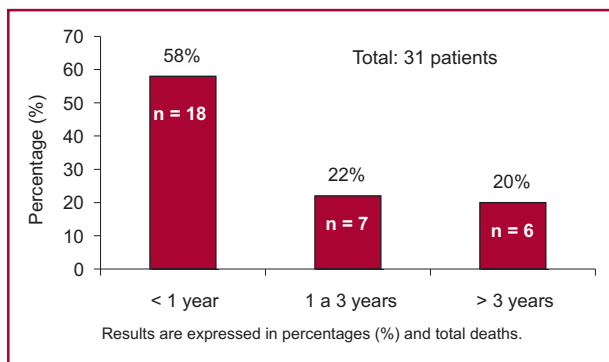


Fig. 1. Mortality in transplant patients in our center during different periods of time.

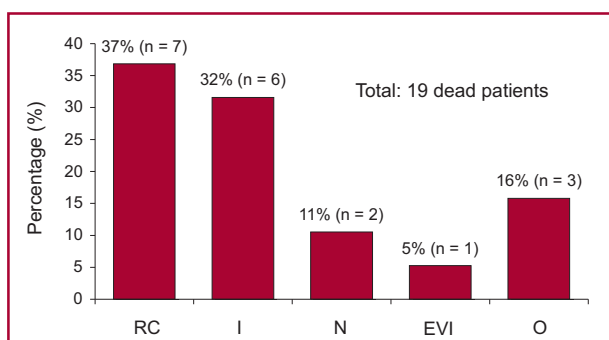


Fig. 2. Causes of death in patients with a definite diagnosis Results are expressed in percentages (%) and total deaths. CR: Cellular rejection I: Infection. N: Neoplasm. GVD: Graft vascular disease O: Other causes.

Table 1. Discrepancies between clinical diagnosis and data from autopsy

	Clinical diagnosis	Autopsy diagnosis
1	Acute pulmonary thromboembolism	Grade IV severe acute rejection
2	Unknown infection	Invasive aspergillosis
3	Unknown infection	Cytomegalovirus encephalitis
4	Severe cellular rejection	Graft vascular disease

the use of this practice as a useful tool for medical education, research and professional development. (9)

Interestingly, in our study the cause of death was diagnosed by autopsy in 12.9% of cases, and differed from the clinically suspected diagnosis. In 1999, Zarbo et al. reported the results of 2479 post-mortem examinations performed in 248 hospitals. In 39.7% of the examinations, the autopsy showed that the cause of death was a major disease that had not been clini-

cally suspected. (10) Rastan et al. demonstrated that the autopsies of a population of patients who died as a consequence of heart surgery revealed clinically relevant information in a significant number of cases and they found discrepancies between clinical and postmortem determinations of cause of death in 23.1% of cases. (11)

Our single-center study included a small number of patients; however, we believe that histopathology plays a fundamental role in a transplant program, not only for patients' follow-up through endomyocardial biopsies but also to contribute to a better understanding and for future management of transplant patients. For this reason, we find it necessary to continue performing autopsies as a source of medical learning and development.

CONCLUSION

Despite the presence of modern screening studies, autopsies keep on revealing premortem clinical diagnostic errors in about 30% of cases. Histopathological diagnosis confirmed the etiology in a high number of patients and rectified the diagnosis in 12.9% of cases; in this sense, we strongly believe that clinical and pathological information derived from post mortem studies is an indicator of the reality of our practice and constitutes an underlying mainstay of the reality of our medical practice. In this way we may advance in the knowledge of diseases, in particular of those with new therapies under research.

RESUMEN

Certeza diagnóstica en la mortalidad de una población de pacientes con trasplante cardíaco

Introducción

A pesar de que la morbimortalidad en el trasplante cardíaco ha sido motivo de extenso análisis, la mayoría de los estudios y registros de mortalidad en pacientes trasplantados se basan sobre datos clínicos. En la bibliografía existen comunicaciones aisladas de autopsias en pacientes con trasplante cardíaco.

Objetivo

Determinar la importancia de la realización de estudios anatomopatológicos para el diagnóstico de causa de muerte en un programa de trasplante cardíaco.

Material y métodos

Se incluyeron todos los pacientes con trasplante cardíaco fallecidos entre enero 1990 y enero 2005. El diagnóstico definitivo de la causa de muerte fue corroborado por autopsia o biopsia de órgano sólido. Las causas de muerte evalua-

das fueron falla precoz del injerto, rechazo celular, infección, enfermedad vascular del injerto, neoplasia y otros.

Resultados

Durante el período en estudio 73 pacientes fueron sometidos a trasplante cardíaco; de ellos, fallecieron 31. Se obtuvieron 12 autopsias y 7 biopsias de órgano sólido que certificaron la causa de muerte (61%). La causa de muerte más frecuente fue el rechazo celular mayor de grado III. En el 12,9%, la anatomía patológica difirió de la sospecha clínica de la causa de muerte.

Conclusión

La información clinicopatológica derivada de estudios *post mortem* es un indicador de nuestra realidad asistencial y se constituye en un pilar fundamental para el conocimiento y el manejo futuro de los pacientes trasplantados, por lo que consideramos que la realización de autopsias en estos pacientes es de vital importancia.

Palabras clave > Trasplante de corazón - Autopsia - Diagnóstico

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