Long-term Follow-up of Patients Eligible, Deferred, or Ineligible for Heart Transplantation

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Background: When a patient is referred to a heart transplantation center, the patient and the physician should know the predicted long-term survival according to the first transplant committee decision. The aim of the study was to describe the follow-up of patients with heart failure referred to a heart transplantation center according to the initial decision to include (eligible), exclude (ineligible), or postpone (deferred) cardiac transplantation.

Methods: The study cohort consisted of 852 consecutive patients. Univariate and trend analyses were performed by classification of data into tertiles according to the date of the first visit. The Kaplan-Meier method was used to assess overall survival and probability of receiving a transplant. The Cox hazard model was used to identify predictors of survival.

Results: Transplantation incidence in the 3 groups (eligible, deferred, and ineligible) was 60%, 19%, and 5%, respectively. The 1-, 3-, 5-, and 10-year survival rates were 74%, 58%, 49%, and 37% among eligible patients; 87%, 72%, 62%, and 45% among deferred; and 69%, 50%, 39%, and 19% among ineligible patients ($p < 0.001$). The 10-year survival was 65% for eligible patients who received the transplant and 8.8% for eligible patients who did not receive the transplant. Transplantation was the most powerful predictor of survival.

Conclusion: The initial decision identified 3 groups of patients with different survival rates. Heart transplantation increases the survival of eligible patients at a rate similar to that of less sick subjects for whom heart transplantation can be deferred. J Heart Lung Transplant 2008;27:380–6. Copyright © 2008 by the International Society for Heart and Lung Transplantation.

The periodic reports of the Registry of the International Society for Heart and Lung Transplantation (ISHLT) provide a description of the survival of patients undergoing heart transplantation (HT). According to the last report,[1] the graft half-life is 10 years.

In most analyses of survival after HT, patients are included in the study at the moment of HT. Thus, patients who die during the workup period or while on the waiting list (patients who have the worst life expectancy), or patients who are temporarily removed from the transplant list for clinical improvement (for whom a better outcome is expected)[2–4] are excluded from these evaluations. The waiting list death rate can be established between 10%[5] and 22%.[6] Few attempts have been made to describe a complete survival picture after listing,[7] and to our knowledge, no data are available for patients evaluated for HT. Therefore, our aim was to describe a follow-up study of patients affected by congestive heart failure (CHF) referred to a HT center, according to the initial decision of the transplant committee to add the patient to the waiting list, to exclude the HT, or to delay inclusion in the waiting list.

METHODS

Study Design and Patient Population

This is a cohort study on data collected retrospectively from patients' charts. All CHF patients referred to a HT center for evaluation of HT eligibility between January 1990 and June 1998 were included. The HT center, located in Turin, Italy, is the only one responsible for HT in a region of approximately 4.5 million inhabitants.

The same cardiologist collected data on patients' history, functional status, and the clinical data of previous instrumental tests. When necessary, further tests to collect information needed for transplant eligibility were performed. Then the transplant committee, composed of the cardiologist chief of the HT program, a heart failure cardiologist, a heart surgeon, and a psychologist, decided to classify the patients into 3 groups:

1. "eligible"—advanced CHF patients with clinical indication to HT, and without contraindications;

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2. "deferred"—CHF patients, still without clinical indication for HT, periodically reexamined to determine the best listing time (patients with relative contraindications were also classified in this group); and,
3. "ineligible"—CHF patients with absolute contraindications.

Patients were periodically reevaluated by the transplant committee to determine group classification.

Unfortunately the database regarding the volume of oxygen consumption and the hemodynamic indicators is not available for the whole population. We have those data for all the eligible patients and for most of the deferred, but very few for the ineligible patients, because we did not think it was ethical to refer for hemodynamic evaluation a patient excluded for noncardiac reasons. All patients signed the informed consent for collection of personal and medical data and to use their stored data for research reasons.

Definition of Eligibility

We analyzed the database according to the intention-to-treat method, classifying patients on the basis of the first sub-division into 3 groups (eligible, deferred, or ineligible), whether or not they were subsequently shifted to one of the other groups.

The initial classification as eligible was intended for patients listed within 1 month from their first visit. A complete reevaluation of the indication to HT was performed for all the patients on the waiting list but who did not undergo transplantation within 6 months. Thus, the patients were reclassified eligible, deferred, or ineligible.

The deferred patients could be relisted in the case of a worsening in their clinical status. They were usually followed up by their personal physician and periodically evaluated by the transplant committee (once a year), which could decide to list the patient because of a clinical or functional deterioration or to exclude the patient definitively.

The ineligible patients were referred to their own physician and updated information was collected annually.

Data Acquisition

We evaluated the cohort of patients referred from 1990 to 1998, reviewing all charts, matching patients' names with the HT database, contacting personal physicians to obtain updated information, and querying the official registry for the vital status and the date of death for patients lost to follow-up. Observation began on the day of the initial decision of the transplant committee, or at least within 1 month from the referral. Every change in the status of the patient was recorded; thus, the personal history of each patient was reconstructed.

Statistical Analysis

Univariate analyses were performed to assess associations between patient characteristics and the 3 groups. Trend analysis was performed dividing the patient population in tertiles according to the data of the first visit to the HT center. The first tertile was between January 1990 and March 1993, 26 months; second tertile was between April 1993 and August 1995, 28 months; and the third tertile between September 1995 and June 1998, 22 months. The Kaplan-Meier method was used to assess the overall survival and the probability of transplantation. Differences in survival were compared by the log-rank test. We evaluated the survival probability according to the decision made by the transplant committee using the Cox proportional hazard model, considering eligible patients as a time-dependent covariate. To avoid a selection bias, only variables available for the 3 sub-groups of patients were included into the multivariate statistical analysis. All statistical analyses were performed using SAS software (SAS Institute Inc, Cary, NC).

RESULTS

Study Population

From 1990 to 1998, 880 patients affected by CHF were referred to the HT center to be evaluated for HT eligibility. The 28 patients lost to follow-up were excluded from the analysis. The study population thus consisted of 852 patients (96.8%) classified by the

Table 1. Baseline Patient Characteristics

Characteristic	Eligible	Deferred	Ineligible	*p*-value
Number (%)	227 (26.7)	524 (61.5)	101 (11.8)	
Age Mean ± SD years	52.1 ± 9.9	53.2 ± 8.6	57.9 ± 7.7	<0.001
Males, No. (%)	204 (90)	450 (86)	81 (80)	=0.06
NYHA III-IV, No. (%)	179 (79)	209 (40)	52 (52)	<0.001
Ischemic etiology, No. (%)	102 (44)	142 (27)	31 (30)	<0.001
Tertiles, No. (%)				
1/1990–3/1993	102 (37)	129 (46)	48 (17)	
4/1993–8/1995	54 (19)	200 (71)	29 (10)	<0.001
9/1995–6/1998	71 (25)	195 (67)	24 (8)	

NYHA, New York Heart Association functional class; SD, standard deviation.