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Arrhythmogenic mortality in heart-transplant candidates

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Abstract Sudden cardiac death represents a major problem in patients awaiting heart transplantation (HTx). A retrospective analysis of 1019 patients accepted for HTx revealed a high actuarial risk for sudden death accounting to 14 % after 1 year and 20 % after 2 years waiting time. Unterlying disease and hemodynamic characteristics had no predictive value. The use of implantable cardioverter/defibrillator therapy is discussed.

Key words Heart transplantation · Sudden cardiac death · Myocardial death · Implantable cardioverter/defibrillator therapy

Introduction

The therapeutic option of heart transplantation (HTx) is limited by the scarcity of donated organs, leading to increasing waiting times for patients in end-stage heart failure. Advances in the medical treatment of congestive heart failure and the broadening acceptance of mechanical support systems have decreased the risk of myocardial death [1]. The incidence of sudden cardiac death in this patient group is, therefore, focusing interest [2].

Patients and methods

For evaluation of the risk of sudden cardiac death in patients awaiting HTx, a retrospective analysis was performed in 1554 patients who were evaluated for HTx at our institution from 1985 through 1994. Of these, 1019 patients were accepted for HTx and entered the study group, while 535 patients were not considered as transplant candidates for medical reasons. Complete follow-up of the study group was accomplished by serial reevaluation via the referring physician and the transplant center. Patient demographics, hemodynamic profile, and follow-up data were stored in a database and analyzed using SPSS software for statistical and actuarial work-up. Values are given as mean ± standard deviation. P values below 0.05 were considered significant.

Results

The mean age of patients entering the study was 45 ± 12 years and of these 608 patients had a dilated cardiomyopathy (DCM), 313 patients revealed an ischemic cardiomyopathy (ICM) due to end-stage coronary disease, and 98 patients suffered from miscellaneous disorders leading to terminal myocardial failure. Of the 1019 patients in the study group, 485 patients were transplanted after a mean waiting period of 13 ± 11 months, 363 patients remained waiting for a mean follow-up of 13 ± 22 months, and 171 patients died after 8 ± 11 months while awaiting HTx. Of these, 69 patients died in hospital and 102 as outpatients. Causes of in-hospital mortality were documented ventricular tachyarrhythmia in 28 patients (40 %) and refractory myocardial failure in 40 patients (59 %); 1 patient sustained a non-cardiac death. Outpatient deaths were sudden in 55 patients (54 %), myocardial in 28 patients (27 %) and not determinable in 19 patients (19 %). Within the whole group, incidence of sudden and myocardial deaths revealed no significant differences with regard to patient hemodynamics including cardiac index (CI) and radionuclide left ventricular ejection fraction (LVEF), as well as with regard to the underlying disease. Interestingly, the incidence of sudden cardiac death rose with increasing waiting periods, thus occurring significantly later than myocardial failure as the

Table 1 Patients characteristics of the study group (*CI* cardiac index, LVEF left ventricular ejection fraction, *DCM* dilated cardiomyopathy, *ICM* ischemic cardiomyopathy)

	Total group	Sudden death	Myocardial death	
CI	1.4 ± 1.0 l/min per m^2	1.7 ± 1.0 l/min per m^2	1.3 ± 1.0 l/min per m^2	n.s.
LVEF	9.9 ± 12.9 %	16.1 ± 15.7 %	9.1 ± 12.1 %	n.s.
DCM	60 %	68 %	62 %	n.s.
ICM	31 %	32 %	38 %	n.s.
Waiting period	12 ± 21 months	13 ± 15 months	6 ± 9 months	$p < 0.05$

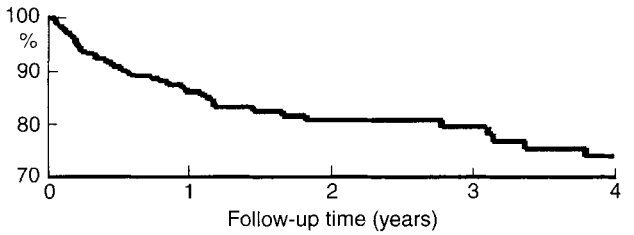

Fig. 1 Actuarial freedom from sudden cardiac death

cause of death in the evaluated population of transplant candidates (Table 1).

Actuarial analysis of survival, according to the Kaplan-Meyer method, was calculated with transplanted patients censored and terminal events grouped as: (1) all deaths, (2) myocardial deaths, and (3) sudden cardiac deaths. This analysis revealed an actuarial survival prior to heart transplantation in the population of accepted candidates of 52.9 ± 2.7 % at 1 year, 47.2 ± 2.9 % at 2 years, and 42.1 ± 3.1 % at 4 years, with 51 of the 1019 patients remaining at risk. Actuarial risk for myocardial death was calculated as 23.4 ± 2.5 % at 1 year, 32.1 ± 3.2 % at 2 years and 39.4 ± 3.9 % at 4 years. Actuarial risk for sudden cardiac death in patients awaiting HTx was predicted as 13.8 ± 2.1 % at 1 year, 19.3 ± 2.8 % at 2 years and 28.1 ± 3.9 % at 4 years (Fig. 1).

Discussion

The results of our retrospective analysis clearly reveal that sudden cardiac death is a major hazard for patients prior to HTx, accounting for 40 % of the overall mortality and representing an actuarial risk of 20 % within 2 years. Risk of sudden cardiac deaths showed no significant differences with regard to the underlying disease and patient hemodynamics. Thus, especially with regard to the limitations of a retrospective study, it was not possible to define a subgroup of patients, within the whole population of transplant candidates, that is especially at risk. The finding that the underlying disease process has no significant influence on the risk of sudden cardiac death is supported by other large evaluations of patients in severe heart failure [3]. Furthermore, there are currently no established risk factors or diagnostic markers for sudden cardiac death in patients with chronic heart failure, and no correlation between the degree of ventricular arrhythmias and sudden cardiac death could be demonstrated [4]. In contrast, prolonged waiting periods for transplant candidates increase the risk of sudden death significantly. This, together with the advances in the medical treatment of severe heart failure [5], emphasize the need for control of arrhythmogenic mortality in patients considered for heart transplantation [6].

Interventional approaches including implantation of an automatic implantable cardioverter/defibrillator (ICD) should be considered, since pharmacological approaches have proven ineffective or even dangerous [7]. ICD therapy has proven to be the sole effective means of prevention of sudden cardiac death due to ventricular tachyarrhythmias in patients with severe impairment of left ventricular function [8]. Furthermore, the non-thoracotomy approach for ICD implantation represents a safe method with virtually no mortality, that implies no additional risk or operative difficulties at the time of cardiac transplant [9]. To assess the feasibility of this cost-intensive therapeutic "bridging approach" towards cardiac transplantation, a prospective and randomized study is needed for the evaluation of the effect of ICD implantation on the overall outcome in this high risk patient population.

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