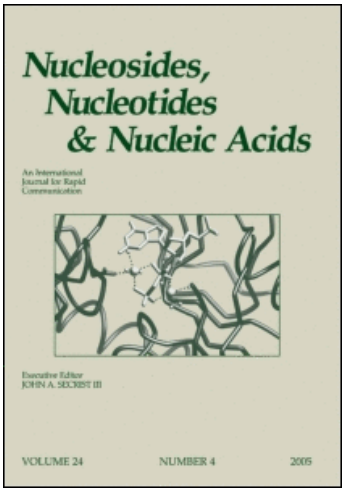

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ASSOCIATION OF IMPROVED CARDIAC FUNCTION IN DONORS WITH C34T MUTATION OF THE AMP DEAMINASE 1 GENE

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▫ *Possession of the C34T mutation in AMP deaminase (AMPD1) gene has been shown to be associated with attenuation of the progression of heart failure and improved survival in ischemic heart disease. In this study, we examined the frequency of the mutation in the heart with good and poor cardiac function and in healthy controls. We found that there was no difference in the frequency of the mutation between the patients with heart failure and healthy controls. However, the frequency of the mutation in the healthy donor hearts was much higher when compared to healthy controls or donors with failing hearts.*

Keywords AMP Deaminase, C34T Mutation, Heart Transplantation, Organ Donors

INTRODUCTION

Shortage of donors is the main factor limiting number of cardiac transplantation.[1] It is estimated that in 20–30% of cases, cardiac function of potential donors is so severely affected that hearts cannot be used. The mechanisms for this remains poorly understood. Possession of the C34T mutation in AMPD1 gene has been shown to be associated with attenuation of the progression of heart failure[2] and improved survival in ischemia heart disease.[3] In this study, we examined whether the C34T mutation of AMPD1 is protective for cardiac function in donors.

MATERIALS AND METHODS

The presence of the C34T mutation was assayed by single-stranded conformational polymorphism (SSCP) and restriction fragment length polymorphism

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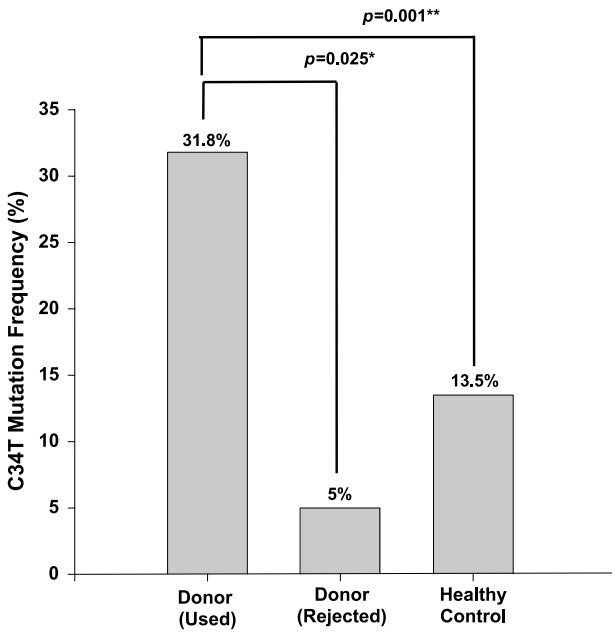

FIGURE 1 The C34T mutation frequency in each group. Statistical significance was calculated using Fisher's exact test (*) or χ^2 test (**).

(RFLP) analysis on heart biopsies. Donors were assessed by tranoesophageal echocardiography at the time of harvesting. Those with an ejection fraction >40% (associated with good hemodynamics) were used for transplantation (n = 22) and a right ventricular biopsy taken at the time of transplantation. Donors with the ejection fraction <40% (associated with poor hemodynamics) were considered unsuitable for transplantation (rejected donors, n = 10). A small piece from the left apex was taken for analysis. Blood samples from 207 healthy volunteers were also genotyped.

RESULTS

The frequency of C34T mutation in each group was calculated according to the number of mutant alleles (Figure 1). The frequency of the C34T mutation in the used donors (31.8%) was significantly higher than in rejected donors (5%, p = 0.025) or in healthy control group (13.5%, p = 0.001). However, there was no difference between heart failure and healthy control group.

DISCUSSION

The high frequency of C34T AMPD1 mutation in heart donors with good ventricular function strongly suggests that this mutation protects cardiac function.

Therefore, we conclude that high incidence of AMPD1 gene mutation in donors with good cardiac function could have clinical implications to donor selection and may help to develop new treatment of heart failure.

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