Transplant International ISSN 0934-0874

REVIEW

Marginal donor grafts in heart transplantation: lessons learned from 25 years of experience

Thorsten Wittwer and Thorsten Wahlers

Department of Cardiothoracic Surgery, University Hospital of Cologne, Cologne, Germany

Keywords
cardiac allograft acceptance, donor criteria, donor procurement organ utilisation, heart transplantation, marginal donors.

Correspondence
Thorsten Wittwer MD, PhD, MA, Department of Cardiothoracic Surgery, Heart Center, University Hospital of Cologne, Cologne, Germany. Tel.: +49 221 478 32508; fax: +49 221 478 32509; e-mail: Th.Wittwer-Md@t-online.de

Received: 24 August 2007
Revision requested: 14 September 2007
Accepted: 31 October 2007

doi:10.1111/j.1432-2277.2007.00603.x

Summary

Heart transplantation represents an established procedure in end-stage heart failure patients and results in satisfying long-term results. However, this surgical therapy is continuously limited by severe and progredient donor organ shortage in the last years. Therefore, adequate and optimal utilization of all suitable donor organs is mandatory to increase graft availability. Evidence exists that certain 'standard' donor criteria can be significantly liberalized to increase the available donor pool by accepting 'Marginal Donors' who would, under conventional transplant guidelines, be declined as potential organ donors. The aim of this study was to review the available literature with regard to definitions and experiences with 'marginal' donor hearts and to discuss critically the controversies of numerous entities of donor criteria, which might be successfully liberalized. This review is thought to give an up-to-date overview of a modern concept of cardiac allograft acceptance based on a 25-year experience with heart transplantation.

Introduction

Treatment of end-stage heart failure still represents a special challenge as both the patient and the physician must choose between continued medical therapy (5–10% weekly mortality risk), mechanical circulatory support (10–15% operative risk) and a transplant procedure with a significant operative risk [1].

For many years, cardiac transplantation has represented an established procedure in end-stage heart failure patients using the so-called 'Traditional Criteria' for an appropriate heart transplant donor as suggested by Copeland *et al.* [2]. However, over the past two decades, there has been a considerable increase in the numbers of patients annually listed for cardiac transplantation, and strict adherence to those 'standard donor criteria' resulted in a progredient undersupply of available organs [3] with the result of significantly extended waiting times and increased mortality on the waiting list [4].

As a consequence of this severe shortage of donor organs, strict recipient criteria have limited the number of patients placed on the US waiting list to about 8 000 per year [5], although it is estimated that at least 25 000 patients per year would benefit from the procedure [6]. Sub-optimal utilization of donor hearts has compounded the problem worldwide, with the effect that a significant proportion of donor hearts is not transplanted [7], with a maximum 'nonutilization rate' of suitable donors of up to 65% [7–10]. In some countries, approximately 50% of all waiting list patients will never receive a transplant because of extended waiting periods and shortage of organs [11]. Therefore, numerous modified protocols regarding the suitability of potential cardiac donors [12–14] were published over the past 25 years (Fig. 1). Recent evidence confirms that certain donor criteria can be liberalized to increase the available donor pool by accepting 'Marginal Donors' who would, under conventional transplant guidelines, be declined as potential organ donors. [7,15]. Several potential entities are comprised under the terminus 'Marginal Hearts', and each aspect will be illustrated in this review article according to the structure detailed in Table 1. However, special attention has to be drawn to the fact that each assessment, especially of marginal donor grafts, should be made on a

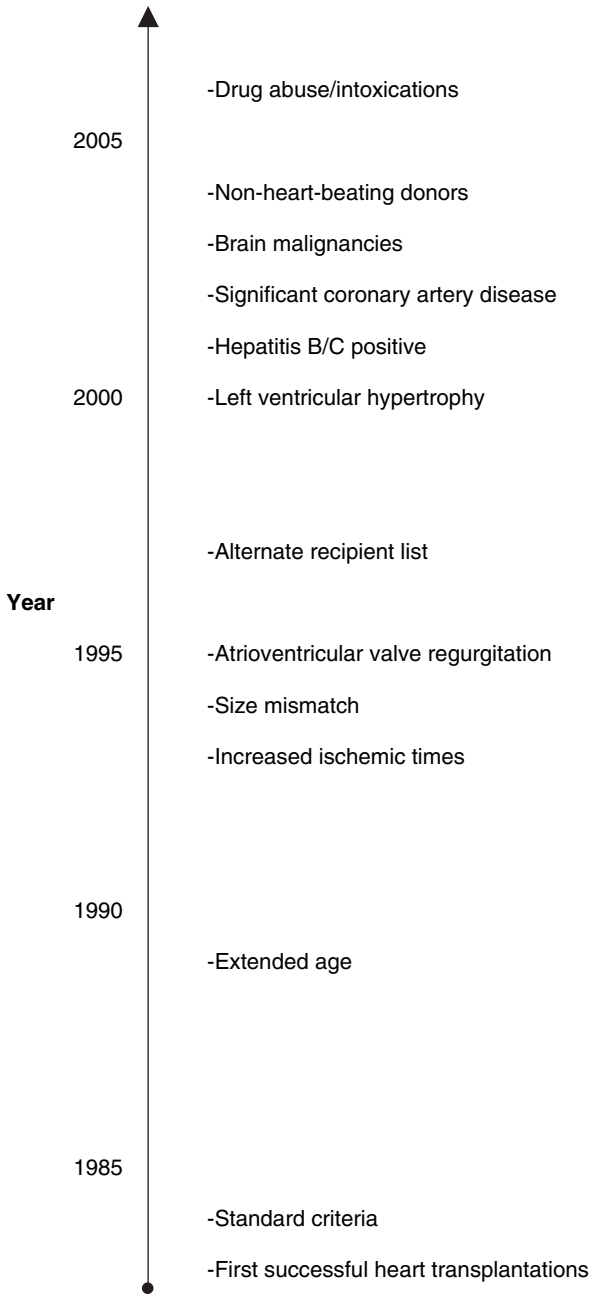

Figure 1 Significant modifications of 'Standard criteria' toward more marginal donors.

recipient-orientated individualized basis rather than using only a theoretical catalogue of specific 'acceptable' values, parameters or conditions.

Extracardiac factors

Age

Expansion of traditional donor criteria in terms of donor age became a standard very early in numerous centers (Fig. 1). In early practice, most institutions excluded donors >40 years of age with extended comorbidities [16,17]. Younger age was thought to protect graft function from the ravage of the catecholamine flood that accompanies brain death [18]. Over time, organ shortage led to increasing acceptance of more marginal, especially older aged donors. Profound evidence exists that the results obtained with donors older than 40 years are not significantly different from those with younger donors below 40 years [19–23]. Latest evidence indicates that even hearts of donors older than 50 years of age result in equivalent survival [24–27], although some authors report increased early mortality and decreased recipient survival with older donor hearts [28–31]. Therefore, in each instance, the risk of accepting an older donor heart must be weighed against the risk of remaining on the waiting list [32]. Bennett *et al.* [33] have clearly shown that increased mortality from an older cardiac donor more than offset the risk of remaining on the waiting list, and Zaroff *et al.* [7] outline that 'donors more than 55 years may be used in selected high-risk recipients'. Generally, older organs should continue to be a viable option for treating heart failure patients [34–36], although the risk for development of cardiac allograft vasculopathy is more pronounced [37,38]. This, in fact, may be a reflection of age-related endothelial dysfunction; therefore, some authors restrict use of older donor hearts to critically ill patients but not to stable transplant candidates [39].

Table 1 Factors and entities of impact on the definition and usability of 'marginal cardiac donors'.

Extracardiac factors	Age
	Ischemic time
	Size
	Virology status
Heart-related variables	Left ventricular hypertrophy
	Valvular/congenital abnormalities
	Coronary artery disease
Brain death-related factors	Intracranial hemorrhage
	Penetrating head injury
	Brain malignancies
	Drug/substance intoxications
	Various
Impact of optimal donor management	Metabolic/endocrine management
	Hemodynamic assessment
	Coronary evaluation
	Echocardiographic evaluation
Nonheart-beating donation	

Ischemic time

Prior to acceptance of especially older allograft, other accompanying factors have to be examined carefully; In

several studies, the authors [29,40] revealed that aside from donor age and donor ischemic times, both significant independent predictors of negative outcome, recipients did worse when they had received an older heart with a longer ischemic time. Ischemic times exceeding 3–4 h were found to be predictive of early mortality [29,30,41,42] because of an association with significantly reduced postoperative biventricular function and increased inotropic requirements [43,44]. Furthermore, prolonged graft ischemia has also been associated with a trend toward increased intensive care unit and hospital stay [43,44]; therefore, subtile handling of controllable factors such as graft ischemic time can help increase the probability of survival.

Alternate recipient list, 'old-for-old-program'

In the context of advanced age, the 'alternate recipient list' proposed by Laks *et al*. [45,46] has served as a useful method of transplanting high-risk recipients who fail to meet standard criteria [47]. These patients are offered 'high-risk' hearts, i.e. with extensive coronary artery disease (CAD), etc., only if these grafts are not able to be placed into any patient on the regular waiting list and therefore would otherwise have been discarded. On follow-up, recipient survival was shown to be equivalent to standard list patients [48,49]. However, some authors describe a significant mortality in the alternate list group [47,50]. The most common donor risks for alternate recipients were high inotropic requirements, left ventricular hypertrophy (LVH), or hepatitis C seropositivity. However, given the lack of other treatment options for these patients, this risk is considered justifiable [46]. The alternate list brings forth the question of age cutoffs, and generally it is considered appropriate to allocate older donors only to older recipients in accordance with current UNOS policy that all donors younger than 18 years be offered to recipients younger than age of 18 [51]. In this way, the alternate heart transplantation waiting list resembles the so-called 'Old-for-Old' allocation program in renal transplantation, which allows successful expansion of the donor and recipient pool without affecting patient and graft survival [5,52,53].

According to recent evidence [49], the second most common reason for alternate listing is amyloidosis. As the treatment of choice in AL amyloidosis is the concept of heart transplantation followed by stem cell transplantation [54], use of extended donor criteria might be successfully applied to patients with cardiac amyloidosis. This concept does not show any significantly inferior outcome to standard donor criteria in standard recipients but represents a significant survival advantage in a very specific cohort of terminally ill patients [55].

Since the inception of the alternate list, the reported acceptable outcome has subsequently led to many of these 'marginal' donors being used for patients on the regular list. This appears to be a natural evolution, as over time, improved preservation techniques [56] together with optimized donor management and recipient care lead to good outcome even with a marginal donor organ. In the future, an alternate list may not even exist anymore, because donors will either be acceptable or unacceptable for all recipients [47].

Size

Despite an increased risk associated with small donor size relative to the recipient, a normal-sized adult male of about 75 kg is considered to be suitable for most recipients [30]. In the specific case of a small donor, size matching with body mass index or height is more accurate than weight matching [7], but generally undersized hearts have been used successfully with excellent long-term outcomes [57]. Although recipient obesity is known to have an adverse effect on survival [58], extended donor weight above 90 kg represents also an independent risk factor for recipient late death [16]. Hearts from obese donors may have very early atherosclerotic changes that escape detection during donor evaluation and may predispose to graft vasculopathy. Endothelial dysfunction is an early marker of vascular damage caused by atherosclerotic disease and occurs especially in obese subjects [59]. Aside from these facts, in assessing the suitability of a certain organ offer one has to assess specifically the match between the characteristics of this donor heart and the specific risk-profile of the recipient in terms of potentially critical factors like a significant and fixed pulmonary hypertension, which would require maximized attention with regard to donor/recipient size and weight ranges. However, this again illustrates the general necessity for a recipient-oriented and much individualized assessment process when accepting organ offers, especially from marginal donors.

HCV-positive or HBV-positive donors

As nearly all recipients of kidney transplants from HCV-positive donors became infected with the virus [60], many thoracic transplant centers do not accept HCV-positive donors [17] as seroconversion also occurs following heart transplantation of infected organs [61]. Transplantation of HCV-positive grafts to HCV-positive recipients is undesirable for two specific reasons: firstly, there is more than one strain of hepatitis C virus, and, secondly, the prevalence of antiviral antibody does not guarantee immediate immunity [62]. Although in a recent Consensus Conference Report [7], both hepatitis B-posi-

tive and/or hepatitis C positive donors are considered to be appropriate 'in selected higher-risk recipients', hepatitis seropositivity is known to be associated with cardiac allograft vasculopathy and therefore predicts outcome following heart transplantation [63,64].

Heart-related variables

Left ventricular hypertrophy

Especially with short ischemic times, mild LVH is considered not to preclude cardiac transplantation but becomes inadvisable because of significantly increased peri-operative risk if both echocardiographic evaluation with a wall thickness >13 mm and standard electrocardiogram (ECG) criteria are present [7,65].

Valvular and congenital cardiac abnormalities

While the presence of most valvular and congenital cardiac abnormalities in the donor graft is a contraindication to heart transplantation, there are very few instances of mild-to-moderate mitral or tricuspid insufficiency or secundum-type atrial septal defects in which 'bench' repair or repair at later time points post-transplant can be performed with good results [7,66,67].

Coronary artery disease

Post-transplant CAD has been identified as one of the causes of worse long-term outcome in recipients of organs from older donors, as these organs may carry with them pre-existing CAD [24,68–70]. Costanzo *et al.* [69] found that at the end of 5 years, 42% of patients had developed CAD, 7% of those with a severe extent. Death or retransplantation occurred in two-thirds of patients with severe CAD; therefore, more aggressive screening for existing CAD both pre- and post-transplant is important in identifying organs at risk for disease. Recently, Grauhan *et al.* [71] described an overall prevalence of donor-transmitted coronary atherosclerosis of 7.0%, and he stated that donor screening without coronary angiogram overlooks a significant proportion of coronary lesions. In that study, the prevalence of donor transmitted CAD in recipients who underwent coronary angiography within 6 months post-tranplantation was 5.2%, whereas it was 15.1% on autopsy in those recipients who died within 6 months without coronary angiogram. Among all patients with early graft failure, prevalence was as high as 22.8% indicating that donor CAD represents a significant risk factor for early graft failure [72]. Furthermore, some authors stated that transmitted CAD increases the risk of accelerated allograft vasculopathy [73,74], while additionally there are reports that native CAD shown by angiography in heart transplant recipients predicts a 3–5 times greater relative risk for cardiac events like myocardial infarction, heart failure and sudden death [75,76]. However, more recent studies indicate that deleterious transplant vasculopathy (TVP) as a result of chronic rejection is multifactorial and that atherosclerotic plaque in the donor heart may not necessarily progress to TVP [77–80]. Instead, using serial Intravascular Ultrasound (IVUS) measurements, Li *et al.* [81] demonstrated that pre-existing donor atherosclerotic lesions do not accelerate the development of TVP either at the site of pre-existing donor atherosclerosis or elsewhere within the same artery. Although coronary arterial revascularization procedures can be performed in the recipient subsequently [82], little has been reported so far on systematic use of donor hearts with significant CAD. In a recent study, Marelli *et al.* [83] reported their experiences with the use of donor hearts with mild-to-moderate CAD in recipients who were either urgent candidates or would otherwise not have been transplanted for various reasons (alternate group). In 59% of those recipients, simultaneous bypass grafting of donor vessels was performed backtable at the time of heart transplantation using recipient conduits, mostly saphenous vein, but rarely the left anterior descending artery. Besides the reported favourable intermediate-term results with regard to survival, overall graft patency at 2 years was 82%.

These very promising results demonstrate proof of the concept of accepting donors with CAD. One may consider brain death as a stress test such that if subsequent ECG or echocardiography is favourable, the chance of an older donor having CAD is probably low. This screening strategy without use of coronary angiography is though to enable efficient selection of older donors for hearts [83,84] with the understanding that additional presence of LVH including ECG changes generally precludes use of such donor hearts [65]. Generally, the additional use of statins and recipient conduits in terms of concurrent or postponed coronary artery bypass grafting (CABG) might account for satisfactory results of some studies with use of CAD donor hearts [67,83, 85–87].

Impact of the mode of brain death

Currently, with regard to cardiac transplantation, most organ donors are brain dead, and in some countries, i.e. Germany, documentation of brain death is mandatory prior to organ harvesting. Generally, 'head trauma' represents the most common cause of death in heart donors worldwide. However, the specific mode of brain death has an important impact on the extent of the accompanying cardiac dysfunction such as elevated cardiac enzymes, arrhythmias and impaired contractility [88].

Cranial causes of brain death

Atraumatic intracranial bleeding

Spontaneous or atraumatic intracranial bleeding (aICB) occurs in 39.3% of brain death donors [89] and experience shows that hearts from donors with aICB are associated with negative outcome following transplantation [65]. Experimental evidence suggests that aICB is associated with a catecholamine surge that can cause cardiac dysfunction [90–92]. Interestingly, both type and extent of myocardial injury are directly related to the type of brain injury, and the frequency of contraction band necrosis or coagulative myocytolysis was found to be significantly higher in patients with spontaneous brain hemorrhage than in those with head trauma [92]. Recently, it was confirmed that donor brain death caused by aICB is a potential risk factor for early post-transplantation mortality [89]. However, that study also suggests that aICB status is one of many risk factors that can be present in a donor, none of which, when present alone, precludes organ donation and successful transplantation.

Penetrating head injury

In experimental animals, acute increase in intracranial pressure as a result of explosive brain injury caused upregulation in pro-inflammatory cascades and an exaggerated catecholamine response [93,94]. Especially, the latter catecholamine surge is considered to be problematic as Wahlers [95] has shown that high-dose catecholamine levels are a significant donor-related risk factor for early post-transplantation mortality. Penetrating cerebral trauma results in neutrophil-mediated endothelial damage, the formation of circulating platelet and protein aggregates and widespread changes in capillary and membrane permeability [96]. The combination of these effects could expose more immonoreactive areas in the donor organs and thereby render the allograft at a higher level of antigenicity. This higher immunological activity might explain that in a recent study, recipients from projectile brain injury (PBI) donors had significantly higher incidences of severe rejection with decreased recipient survival following heart transplantation [97]. Therefore, PBI donors, especially when other risk factors in combination are present, are considered to be 'higher-risk' donors, and cautious use of such cardiac allografts, especially in low-risk recipients, may lead to improved outcome following heart transplantation [97].

Brain malignancies

As a rare cause of brain death, donors with primary brain malignancies carry the theoretical risk of malignancy transmission to the recipient. However, recent evidence exists that tumor transmission seems to be extremely low; therefore, in the context of increased donor organ shortage, acceptance of all otherwise suitable cardiac allografts harvested from donors with primary brain malignancies is recommended, provided that no remote metastases are detectable at the time of procurement screening [98].

Extracranial causes of brain death

Drug abuse

Many transplant centers continue to decline heart donors because of history of drug abuse as some reports suggest that using these donors might have a negative impact on post-transplant outcomes. For instance, chronic use of alcohol has been shown to impact post-heart transplant graft function and survival. Freimark *et al.* [99] reported that heart transplant recipients who received an organ from an alcohol abuser had significantly lower 1- and 2-year survival rates when compared with the nonalcoholic group. The authors postulated that the presence of subclinical cardiomyopathy may be a contributing factor associated with these results. In another study by Houyel *et al.* [100], an increased risk of early graft dysfunction without survival disadvantage compared to a nonalcohol abuser cohort was described. In contrast, other reports show that grafts from alcohol abusers did not show any long-term survival disadvantages with 89.6% survival at 4 years and good functioning grafts at time of discharge [61].

Cocaine use has been associated with similar findings in the literature. While one report warns about the potential implications on outcomes associated with use of donor hearts from patients with cocaine abuse [101], another large single-center study raises questions about these concerns [102]. As a consequence, there is the latest evidence that a history of substance abuse associated with a potential heart transplant donor does not have a significant impact on overall post-heart transplant survival, graft function or risk of graft vasculopathy [61].

Intoxications

Carbon monoxide poisoning. In a consensus study, most heart transplant surgeons considered allografts of victims of carbonmonoxide-(CO)-poisoning unsuitable for heart transplantation as extended pathologic changes in the myocardium following CO-poising are described [103,104]. In the literature, there is contradictory evidence concerning this topic; while some have some negative experience with CO-poisoned donors [105,106], others report on successful use such victims as a cardiac allograft donor [107–110]. There is, however, a very poor

correlation between blood carboxy-hemoglobin level, tissue carboxy-hemoglobin level, and the degree of organ damage [111]. Thus, the best way to assess the suitability of CO-poisoned donors is not the carboxy-hemoglobin level at admission and thereafter, but the pulmonary gas exchange and hemodynamic stability several hours after the injury. As a conclusion, allografts from CO-poisoned donors seem to be suitable, if there are no signs of severe hemodynamic dysfunction in combination with a normal ECG and physiologic levels of transaminases [109]. Extensive Swan-Ganz catheter (SGC) assessment of the cardiocirculatory function seems to be essential [112].

Antidepressants. Cyclic antidepressant intoxication is a major cause of death from intoxication [113]. Compared with new tetracyclic antidepressants, tricyclic antidepressants have significant effects on the cardiovascular system. Most commonly, such effects include postural hypotension, sinus tachycardia, direct depression of the myocardium, and ventricular arrhythmia [114]. Intoxication mostly appears as cardiac toxicity and neurologic complications. The heart is usually hyperactive, with supraventricular tachycardia and a high cardiac output [115]. Evidence in the literature concerning suitability of donors poisoned with cyclic antidepressants is very poor; however, some authors report satisfying results in very selected cases emphasizing that the serum drug concentration in the donor has to be returned to normal and that the heart has to be without any noteworthy damage in an extensive hemodynamic assessment including serial Swan-Ganz catheter measurements [116].

Another class of antidepressants are serotonin antagonists. Cardiac effects reported in intoxication with those drugs include hypertension, tachycardia, ST depression, junctional rhythm, bigeminy, ventricular tachycardia and QTc prolongation associated with ventricular tachycardia.

Besides, from the even longer plasmatic half life of some serotonin antagonists (e.g. fluoxetine) as compared to tricyclic antidepressants, successful heart transplantation can be performed in very selected cases with high-risk recipients [117].

Others. In other rare cases, successful cardiac transplantation was reported using donors poisoned with methaqualone, benzodiazepine, barbiturates, insulin, cyanide, methanol and acetaminophen [118]. Follow up studies have shown good actuarial survival rates with marginal or compromised organs after 1 year [119], which might support the use of poisoned donors for heart transplantation in selected cases.

Impact of 'optimal donor management'

General implications

Management of 'marginal' hearts should include donor graft 'resuscitation' and re-evaluation [120] thus allowing potential organ rescue and utilization. The main goals of optimal hemodynamic management are to achieve isovolemia, to adjust vasoconstrictors and vasodilators to optimize cardiac output without relying on high doses of ß-agonists or other inotropes, which increase myocardial oxygen demand and deplete the myocardium of high-energy phosphates [121–123]. Metabolic management comprises maintenance of acid–base balance [124] and correction of the hormonal perturbations that occur following brain death and that impair circulatory function. Strong evidence exists that treatment with insulin, corticosteroids [120,125], tri-iodothyronine [126,127] and arginine vasopressin [128,129] improves ventricular performance, raises systolic blood pressure and reduces inotropic requirements.

With such a detailed approach, organs which at first assessed as marginal and/or unacceptable had the potential to improve and thus be utilized, resulting in an increase of utilization rates from only 39–58% [8,125] with excellent results in experienced centers [130].

Metabolic disorders: donor sodium level

Brain death results in an impairment of cerebral regulatory processes leading to central diabetes insipidus and serum sodium levels that range above normal values [131,132]. Donor hyponatremia is generally believed to cause myocardial stunning and an increased incidence of primary graft failure following heart transplantation as intracellular sodium concentrations contribute to reperfusion injury [133]. Therefore, donor sodium levels exceeding 150 mmol/l are commonly recognized as a risk factor that may be associated with adverse outcome following HTx, although few reports in the field of liver transplantation indicate that there might be no correlation between donor hypernatremia and outcome [134]. However, recent evidence exists that also in heart transplantation, there is no impact of donor serum sodium concentration on postoperative outcome [135–137]. Therefore, donor hyponatremia might be considered an epiphenomenon of brain death and it serves as an indicator of sub-optimal donor management with the need for careful donor examination, but it does not contribute to adverse outcome. Thus, refusal of such grafts as proposed by some authors [138] is not justified unless there are additional significantly critical recipient-related conditions, which in combination preclude transplantation of such grafts.

Role of cardiac catheterization

Some reports have recommended to perform coronary angiography in all male donors >45 years of age and in all women >50 years of age [71,139]. However, latest agreement suggests to liberalize these recommendations in younger donors to cases with positive risk factor anamnesis and in older donors to the age group >55 years [7]. Generally, donors with mild CAD should be considered for selected higher-risk patients, although a small series of donor hearts treated with 'bench' coronary artery bypass grafting for obstructive coronary lesions resulted in long-term survival with a 65% graft patency at 2 years of follow-up [140].

Role of echocardiography

The aggressive assessment and optimal management of donor left ventricular dysfunction offer a tremendous potential to increase cardiac donor utilization as a significant proportion of hearts are declined for reasons of 'poor ventricular function' [141]. However, strong evidence indicates that grafts from younger donors with left ventricular dysfunction can completely recover to normal function over time in the donor [142] and following transplantation into a recipient [3,143]. Although echocardiography is very effective in screening for anatomical, especially valvular anomalies of the heart, use of a single echo examination in terms of a 'snapshot assessment' of pump function to determine the physiological suitability of a donor graft is not well supported by evidence [7]. Instead, better physiological assessment and donor management of ventricular dysfunction are achieved by SGC investigations, which have led to favourite long-term outcomes [125,144]. By serial SGC investigations, specific physiologic targets as mean blood pressure >60 mmHg, central venous pressure <12 mmHg, pulmonary capillary wedge pressure <12 mmHg, left ventricular stroke work index >15 g m/m^2 while on only one single inotrope can be achieved resulting in specified hemodynamic categories [144].

Therefore, SGC assessment is considered to be a useful tool that permits initial assessment of donor hemodynamics, followed by appropriate intervention and reassessment of the circulation as often as needed, resulting in a remarkable amount of 'resuscitated' donor hearts. Such protocols confirm earlier findings that expansion of the donor pool based on functional criteria is possible and safe [125].

Nonheart-beating donors (NHBD)

Currently, most of the suitable grafts are retrieved from brain-dead heart-beating donors. However, about 35 000 people in the US are killed from firearms while 47 000 deaths are related to motor vehicle accidents [145]. If just some of these acutely injured people after unsuccessful resuscitation were candidates for nonheart-beating organ donation, this might increase the number of available organs by up to 20–30% [146,147]. In 1995, at the first international workshop on NHBD in Maastricht, consensus was reached about donor management protocols, and four different categories of NHB donors were defined as the so-called 'Maastricht classification' [148]. Ever since, the practice of NHBD has increasingly become a part of transplant programs worldwide; within Eurotransplant, 6% of all kidney donors in the year 2005 were NHBD [149]. Although there are very few reports indicating that NHBD programs might have only little impact on potential thoracic organ recovery [150], even in thoracic organ transplantation, use of NHBD has become an option and is clinically used in pulmonary transplantation with increasing tendency [151,152]. Furthermore, there is growing evidence that even heart transplantation could be performed using NHBD, as isolated instances of clinical transplantations have been reported yet [153]. Experimentally, encouraging results are reported recently with pig heart transplantation from NHBD after 30 min of normothermic ischemia [154–156]. Although this experimentally successful concept might not be transferable to standard clinical practice in the near future, it could be anticipated that at least donor hearts with prolonged ischemia >4 h and/or hearts from donors with a variable amount of cardiac arrest prior to organ harvest could be an additional source of donor grafts. At least, the sophisticated experimental concepts of recovery of donor hearts from NHBD, i.e. mode of controlled reperfusion, etc., can successfully be used in very marginal heart donors whose grafts are currently rejected even by high-volume transplant units with extended 'marginal donor' protocols because of a significantly increased risk of primary graft failure [156].

Conclusion

'Certainly it makes little sense to replace one diseased heart with another' is a well-known quote by DePasquale [157]. Agreement exists that the major aim of transplantation is to avoid using an inferior organ in a critically ill patient awaiting heart transplantation [158]. However, as waiting lists for heart transplantation continue to grow, continuous changes in practice patterns of donor heart usage are the most demanding. The increasing use of older donor hearts will possibly be necessary as the numbers of available grafts continue to decline. It is believed that about 15 000 patients would potentially benefit from a heart transplant, if the acceptance criteria included

Table 2 Acceptance criteria for heart transplantation using marginal donors (according to Massad. *Cardiology* 2004; 101: 79).

Age up to 65 years
Undersizing or oversizing by more than 20% body weight
Prolonged hospitalization
History of chest trauma
Open cardiac massage
Elevation of myocardial enzyme levels
Prolonged cardiopulmonary resuscitation (>5 min)
Transient hypotension (>30 min)
High-dose vasopressor requirement
Wall motion abnormalities by echocardiography
Long-distance procurement (>1000 miles)
Persistent conduction disturbances
Cold ischemia time up to 4–5 h
Bypassable one- or two-vessel disease
Correctable valvular dysfunction by echocardiography

'marginal' donors up to 55 years of age, and about 40 000–70 000 patients would benefit, if the acceptance age was extended to 65 years [159]. However, regardless of the changes made in the acceptance of marginal donors, any such mechanism will not be considered successful unless recipient graft survival rates in center-specific outcome analyses remain acceptable. This implies that the decision making on whether a certain donor heart would be suitable for successful transplantation is based on an individualized and recipient-oriented assessment procedure, which is the responsibility of the transplanting physicians and which has to be based on the specific profile of risk factors and critical conditions of the particular recipient.

As a consequence, because of the potential risk for the recipient in terms of short-term outcome, personal inspection especially of such 'marginal' or 'very marginal' donor organs by the harvesting team of the transplanting hospital is considered helpful by some well known transplant surgeons [158] but interferes somewhat with some national trends to establish 'regional explanting teams', which are not affiliated to the transplanting center of the specific recipient of that particular marginal donor heart.

As a conclusion, there is considerable evidence that use of marginal donors generally results in satisfying results and therefore is justifiable to alleviate the progredient donor organ scarcity. In our own experience, establishment and coherent use of specifically liberalized acceptance criteria for marginal donors (Table 2) have been safe and successful for several years and are generally confirmed by others [158]. The strict use of the so-called 'Papworth protocol' of marginal donor management [125], together with comprehensive monitoring of the donor, has been shown to have the potential to increase substantially the numbers of donor hearts without adverse effects on the recipient [160].

Authorship

T Wittwer contributed by reviewing world literature, acquisition of data, analysis and interpretation of data. In addition he was responsible for drafting the article, revision of the article corresponding to comments by the expert reviewers and final approval of the version to be published. T Wahlers contributed substantially to conception and design, critical revision of the article for important intellectual content, revision of the article corresponding to comments by the expert reviewers and had final approval of the version to be published.

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