Consensus Conference Report
Maximizing Use of Organs Recovered From the Cadaver Donor: Cardiac Recommendations
March 28–29, 2001, Crystal City, Va

Jonathan G. Zaroff, MD, Conference Co-Chair; Bruce R. Rosengard, MD, Conference Co-Chair; William F. Armstrong, MD; Wayne D. Babcock, BSN; Anthony D’Alessandro, MD; G. William Dec, MD; Niloo M. Edwards, MD; Robert S. Higgins, MD; Valluvan Jeevanandum, MD; Myron Kauffman, MD; James K. Kirklin, MD; Stephen R. Large, MD; Daniel Marelli, MD; Tammie S. Peterson, RN; W. Steves Ring, MD; Robert C. Robbins, MD; Stuart D. Russell, MD; David O. Taylor, MD; Adrian Van Bakel, MD; John Wallwork, MB; James B. Young, MD

Abstract—The shortage of available donor hearts continues to limit cardiac transplantation. For this reason, strict criteria have limited the number of patients placed on the US waiting list to ≈6000 to 8000 per year. Because the number of available donor hearts has not increased beyond ≈2500 per year, the transplant waiting list mortality rate remains substantial. Suboptimal and variable utilization of donor hearts has compounded the problem in the United States. In 1999, the average donor yield from 55 US regions was 39%, ranging from 19% to 62%. This report provides the detailed cardiac recommendations from the conference “Maximizing Use of Organs Recovered From the Cadaver Donor” held March 28 to 29, 2001, in Crystal City, Va. The specific objective of the report is to provide recommendations to improve the evaluation and successful utilization of potential cardiac donors. The report describes the accuracy of current techniques such as echocardiography in the assessment of donor heart function before recovery and the impact of these data on donor yield. The rationale for and specific details of a donor-management pathway that uses pulmonary artery catheterization and hormonal resuscitation are provided. Administrative recommendations such as enhanced communication strategies among transplant centers and organ-procurement organizations, financial incentives for organ recovery, and expansion of donor database fields for research are also described. (Circulation. 2002;106:836-841.)

Key Words: transplantation ■ resuscitation ■ catheterization ■ echocardiography

The shortage of available donor hearts continues to limit cardiac transplantation. For this reason, strict criteria have limited the number of patients placed on the US waiting list to ≈6000 to 8000 per year, although it is estimated that at least 25 000 patients per year would benefit from the procedure. Because the number of available donor hearts has not increased beyond ≈2500 per year, the transplant waiting list mortality rate remains substantial at ≈17% per year overall and 45% for status I patients.

Suboptimal utilization of donor hearts has compounded the problem in the United States. The United Network for Organ Sharing (UNOS) reported a 42% donor yield (2450 heart transplants/5798 potential donors) in 1998. In a 1999 survey from the Association of Organ Procurement Organizations (AOPO), the average donor yield from 55 regions was 39%, ranging from 19% to 62% (unpublished data, 1999 Final Annual Report, Fax Survey Program, AOPO). Regional differences in donor age, cause of death, other donor factors, and the willingness of individual transplant programs to use marginal donors may account for the variability in donor utilization. However, even within the most successful regions, a significant proportion of donor hearts are not transplanted.

This conference was held to assess current evidence regarding the evaluation and management of potential cardiac donors. The committee members were assembled to provide
diverse information and opinions and included thoracic and abdominal transplant surgeons, transplant cardiologists, echocardiographers, organ-procurement agency personnel, clinical researchers in the field of donor management, and representatives from UNOS. The specific objectives of the committee were as follows: (1) to provide recommendations to improve the successful utilization of potential cardiac donors; (2) to determine the accuracy of current methods to assess donor heart function before recovery, the impact of these data on donor utilization, and the potential of aggressive donor management to increase thoracic organ utilization; (3) to examine the wide regional variability in thoracic organ utilization and examine the impact of center size on thoracic organ utilization; and (4) to develop effective and continuing collaboration among the American Society of Transplantation (AST), the American Society of Transplant Surgeons (ASTS), AOPO, the International Society for Heart and Lung Transplantation (ISHLT), UNOS, and the Scientific Registry of Transplant Recipients (SRTR) representatives of the transplant community.

**Recommendations to Improve the Yield of Donor Evaluation**

Both UNOS\(^1\) and the American College of Cardiology\(^2\) have published guidelines regarding the suitability of potential cardiac donors. Individual centers have published more aggressive guidelines, which have permitted their use of marginal donors, defined as organs that fail to meet 1 or more of the traditional criteria for an optimal cardiac donor. Using organs that otherwise would have been discarded, these centers have provided good recipient outcomes.\(^6\) The available evidence indicates that certain donor criteria can be liberalized. This is particularly true when matching for higher-risk recipients: those with greater short-term mortality while awaiting transplantation or with comorbid factors such as advanced age, prior transplant, or hepatitis C virus (HCV)–positive status. Comments regarding the modifiable criteria follow.

**Extracardiac Factors**

**Age**

Donors >55 years of age may be used selectively in selected higher-risk recipients, although other donor factors such as left ventricular hypertrophy (LVH) and ischemic time may interact synergistically to increase recipient mortality risks.\(^8\)

**Size**

Despite an increased risk associated with small donor size relative to the recipient, a normal-sized (>70 kg) adult male donor is suitable for most recipients.\(^9\) In the case of a small donor, size matching with body mass index or height is more accurate than weight matching.

**HCV-Positive or Hepatitis B Virus–Positive Donors**

HCV-positive or hepatitis B virus (core IgM-negative)–positive donors may be appropriate in selected higher-risk recipients.

**Structural Abnormalities**

**Left Ventricular Hypertrophy**

Mild LVH (wall thickness \(\leqslant 13 \text{ mm by echocardiography}\)) does not preclude transplantation, particularly with shorter ischemic times. Transplantation is inadvisable if both echocardiographic (\(>13 \text{ mm}\)) and ECG criteria for LVH are present. Pseudohypertrophy may be observed by echocardiography in the presence of left ventricular underfilling and should not preclude transplantation.

**Valvular and Congenital Cardiac Abnormalities**

The presence of most valvular and congenital cardiac abnormalities is a contraindication to transplantation. In some cases, however, “bench” repair can be performed on a donor heart with mild or moderate mitral or tricuspid regurgitation or other mild valvular abnormalities, such as a normally functioning bicuspide aortic valve. Repair of a donor heart with a secundum-type atrial septal defect can also be performed.

**Cardiac Catheterization and Coronary Artery Disease**

The conservative recommendations that coronary angiography be performed in male donors >45 years of age and in women donors >50 years of age\(^10\) should be liberalized as follows:

1. Male donor aged 35 to 45 years and female donor aged 35 to 50 years: perform angiography if there is a history of cocaine use or \(\geq 3\) risk factors for coronary artery disease (CAD), such as hypertension, diabetes, smoking history, dyslipidemia, or family history of premature CAD.
2. Male donor aged 46 to 55 years and female donor aged 51 to 55 years: angiography recommended. However, some of these donors should be considered even if angiography cannot be obtained if the heart is being matched with a higher-risk recipient. The presence of donor risk factors for CAD should be factored into this decision.
3. Age >55 years: angiography strongly recommended. An occasional donor can be considered without angiography if being matched with a higher-risk recipient, such as those in urgent need of transplantation because of uncontrollable arrhythmias or hemodynamic deterioration without mechanical support options. The presence of donor risk factors for CAD should be factored into this decision.

To reduce the risk of nephrotoxicity, contrast left ventriculography can be avoided in donors with technically adequate echocardiograms. Donors with mild CAD should be considered for selected higher-risk recipients. A small series of donor hearts treated with “bench” coronary artery bypass grafting for obstructive coronary lesions resulted in long-term survival for 8 of 10 recipients, with a 65% graft patency at \(\approx 2\) years of follow-up.\(^11\)

**Cardiac Enzymes**

Although cardiac-specific enzymes such as creatine kinase-MB and troponins are routinely obtained by some organ-procurement organizations (OPOs), their role in donor evaluation remains unclear. There is some evidence that
elevated cardiac enzymes are associated with higher recipient inotropic requirements after transplantation and higher rejection rates. There is limited evidence of a relationship between elevated troponin levels and early graft failure. Normal levels of cardiac enzymes are reassuring in cases of donor ventricular dysfunction, because they provide evidence against recent myocardial damage. However, many cardiac donors have elevated cardiac enzymes without evidence of ventricular dysfunction by imaging or hemodynamic criteria. For this reason, elevated cardiac enzymes, viewed in isolation from other donor factors, do not justify nonuse of a donor heart.

Role of Echocardiography

The assessment and management of donor left ventricular dysfunction offers the greatest potential to increase heart donor utilization. According to the 1995 UNOS database, 918 (42%) of 2199 unused donor hearts in the United States were declined because of poor ventricular function. Strong evidence indicates, however, that younger hearts with left ventricular dysfunction can recover normal function over time in the donor and after transplantation into a recipient.

Although echocardiography is effective in screening for anatomic abnormalities of the heart, the use of a single echocardiogram to determine the physiological suitability of a donor is not supported by evidence. In addition, the accuracy of echocardiographic interpretation at donor hospitals may be suboptimal. The Papworth Hospital transplant program in Great Britain increased its donor yield substantially by using a pulmonary artery catheter to guide the physiological assessment and management of ventricular dysfunction. This approach has led to favorable recipient outcomes without the use of echocardiography.

Recommendations for Improving Donor Management

Given that a single echocardiographic assessment may be inaccurate or may fail to predict long-term ventricular contractile function, failure to use a donor heart because of the initial ejection fraction alone is not justified. Hemodynamic and metabolic management should be performed before the organ is declined when donor left ventricular dysfunction is present.

The goals of hemodynamic management are to achieve euvolemia, to adjust vasoconstrictors and vasodilators to maintain a normal afterload, and to optimize cardiac output without relying on high doses of β-agonists or other inotropes, which increase myocardial oxygen demand and deplete the myocardium of high-energy phosphates. Metabolic management includes maintenance of acid-base balance and correction of the hormonal perturbations that occur after brain death and that impair circulatory function. There is evidence that treatment with insulin, corticosteroids, triiodothyronine, and arginine vasopressin improves ventricular performance, raises systolic blood pressure, or reduces inotropic requirements.

Using a combined approach of hemodynamic and metabolic management, the Papworth program in Great Britain has shown that 92% of organs that fail to meet transplantation criteria on initial evaluation can be functionally resuscitated. This has resulted in a 30% expansion of the Papworth donor pool. For this reason, the Papworth approach has been incorporated into the management algorithm described below.

OPOs should use a standard protocol for donor management that includes increased application of pulmonary arterial catheterization. The protocol should be accepted in advance by the regional organ-specific recovery teams and implemented independently by the nurses and/or physicians on the OPO staff. The UNOS critical pathway algorithm has been updated to include the recommendations described below and will be available on the UNOS World Wide Web site in the near future.

It is highly desirable for physicians such as cardiologists, pulmonologists, intensive care specialists, and surgeons to be actively involved in the management of brain-dead donors. A pilot effort in Chicago, Ill, is currently exploring this approach.

Until a clinical trial can be performed to measure the independent effects of hemodynamic management and hormonal resuscitation, the current shortfall of donor hearts mandates aggressive donor management. Given the currently available evidence, the following approach is recommended (and summarized in the Figure):

1. Conventional management, before the initial echocardiogram
   a. Adjust volume status (target central venous pressure 6 to 10 mm Hg)
   b. Correct metabolic perturbations, including:
      ● Acidosis (target pH 7.40 to 7.45)
      ● Hypoxemia (target PO2 > 80 mm Hg, O2 saturation >95%)
      ● Hypercarbia (target PCO2 30 to 35 mm Hg)
   c. Correct anemia (target hematocrit ≥30%, hemoglobin ≥10 g/dL)
   d. Adjust inotropes to maintain mean arterial pressure ≥60 mm Hg. Norepinephrine and epinephrine should be tapered off rapidly in favor of dopamine or dobutamine.
   e. Target=doxamine <10 μg · kg⁻¹ · min⁻¹ or dobutamine <10 μg · kg⁻¹ · min⁻¹

2. Obtain an initial echocardiogram
   a. Rule out structural abnormalities (substantial LVH, valvular dysfunction, congenital lesions)
   b. If left ventricular ejection fraction is ≥45%, proceed with recovery (consider aggressive management as shown below to optimize cardiac function before recovery) with final evaluation in the operating room.
   c. If left ventricular ejection fraction is <45%, aggressive management with placement of a pulmonary arterial catheter and hormonal resuscitation is strongly recommended.

3. Hormonal resuscitation
   a. Triiodothyronine (T3): 4-μg bolus, then continuous infusion at 3 μg/h
   b. Arginine vasopressin: 1-U bolus, then continuous infusion at 0.5 to 4 U/h, titrated to a systemic vascular resistance of 800 to 1200 dyne · s⁻¹ · cm⁻⁵
   c. Methylprednisolone: 15-mg/kg bolus

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d. Insulin: 1 U/h minimum. Titrate to maintain blood sugar 120 to 180 mg/dL

4. Aggressive hemodynamic management
   a. Initiated simultaneously with hormonal resuscitation
   b. Placement of pulmonary artery catheter
   c. Duration of therapy ≥ 2 hours
   d. Adjustment of fluids, inotropes, and pressors every 15 minutes based on serial hemodynamic measurements to minimize use of α-agonists and meet the following target (Papworth) criteria:
      - Mean arterial pressure > 60 mm Hg
      - Central venous pressure 4 to 12 mm Hg
      - Pulmonary capillary wedge pressure 8 to 12 mm Hg
      - Systemic vascular resistance 800 to 1200 dyne·s·cm⁻⁵
      - Cardiac index > 2.4 L·min⁻¹·m⁻²
      - Dopamine < 10 µg·kg⁻¹·min⁻¹ or dobutamine < 10 µg·kg⁻¹·min⁻¹

   If these hemodynamic criteria are achieved, it is appropriate to proceed to recovery. Repeat echocardiography may be useful in cases of borderline donor suitability, although outcomes data are currently limited on this issue.

   **Recommendations to Improve Organ Recovery**

   Ideally, a set of established criteria for heart suitability would allow for regional evaluation and recovery, which would increase the efficiency of the process. However, changing the current system of recovery will require time and patience given the inherent conservatism related to the mortality of early allograft dysfunction. For this reason, a logical first step would be to attempt regional donor evaluation and management before widespread regional recovery is attempted. However, pilot efforts at regional recovery should be encouraged.

   With regard to the recovery procedure itself, there is no clear superiority of any of the currently approved preservative solutions. In multorgan recovery procedures, many centers recommend that the inferior vena cava be vented in the abdomen by cannulation of the abdominal inferior vena cava with an efficient venous cannula, which will facilitate uniform cooling of the
organ utilization.

Administrative Recommendations

Alternate Recipient List

The purpose of an alternate recipient list is to match certain recipients, who might be excluded from a standard list because of advanced age or other characteristics, with marginal donor hearts that would otherwise go unused. From 1992 to 2000, the University of California at Los Angeles transplanted 260 donor hearts that were classified as marginal because of abnormalities that included age over 55 years, ejection fraction <50% with inotropes, high-dose inotropes, CAD, mild LVH by echocardiography, hepatitis B and C, and recent cardiac arrest (Daniel Marelli, MD, unpublished data, 2001).

Sixty-six of the 260 marginal donor hearts were used for alternate-list recipients, and the remainder were used for status I and II patients on the standard list. Although use of marginal donors in alternate recipients was associated with increased early mortality, the intermediate-term results have been favorable.23 On the basis of this evidence, the use of an alternate list has the potential to increase the use of marginal donors when applied in large-volume centers. This approach also limits the redistribution of available organs from younger recipients to older patients. However, alternate recipient lists have not yet been widely implemented by transplant centers, and some aspects of this approach remain controversial.

Communication Strategies

Before declining a donor heart, a transplant center’s surgeons and cardiologists should discuss the limiting characteristic(s) of the donor and consider management options. In addition, each OPO and transplant center should have a feedback mechanism regarding donor utilization and management. This should take the form of a quality-assurance program, which will audit cases of nonutilized donors and provide feedback regarding errors in donor management and utilization.

Because placement of marginal donor hearts often requires discussion between an OPO and a large number of transplant centers, novel communication strategies should be explored. One possible approach would be to post detailed information about a marginal heart on a secure Internet site that is hosted by the OPO and accessed by regional transplant centers. These centers could then simultaneously indicate their interest in accepting the donor. Another strategy would be for regional transplant centers to alert the OPOs of their willingness to accept a marginal donor for a higher-risk recipient, with updates provided on a weekly basis. This would allow OPOs to more efficiently match marginal donors to appropriate recipients.

Expansion of Donor Databases

Although the Cardiac Transplant Research Database, UNOS, AOPO, and ISHLT offer detailed information regarding recipient characteristics and outcome, there are inadequate data describing donor characteristics and utilization outcomes. Specifically, data from serial hemodynamic measurements and a detailed recording of management strategies should be noted. These data should facilitate the development of models that can estimate the mortality risk for a given donor-recipient match. Ultimately, the availability of this information should expedite the use of a greater number of marginal donors.

Financial Issues

Numerous financial disincentives impede the broader use of marginal donor hearts. It is critical to provide incentives that will encourage physicians to participate in the management of brain-dead donors. In many settings, donor management itself is not reimbursed, and prolonged evaluation and management are expensive for OPOs. In addition, prolonged donor management and delayed recovery may be costly and inconvenient for donor hospitals. Importantly, no reimbursement is provided for on-site transplant team evaluations that fail to yield a suitable heart, which is particularly problematic for distant donor evaluations. Finally, Medicare accreditation decisions focus on 1-year recipient mortality and do not consider the waiting-list acuity and mortality at a given center, which also leads to conservative use of marginal donors.

The creation of financial incentives for OPOs, transplant programs, and donor hospitals that encourage aggressive management of marginal donors should increase utilization. Such incentives are essential if regional donor evaluation, management, and recovery are to be developed in the United States.

Logistical Issues

Because cardiothoracic surgeons do not limit their practices solely to transplantation, the efforts of organ recovery and transplantation often interfere with scheduled operations. Donor heart recovery primarily occurs at night, which creates a further disincentive to evaluate a marginal organ. For this reason, optimal organ utilization requires that transplant centers have adequate staffing and established infrastructures that can maximize efficiency. Concentration of expertise in fewer centers with greater volume and resources would likely increase the successful utilization of marginal donors.

Future Research

Despite the fact that the shortage of donors is the primary limiting factor in the clinical application of organ transplantation, insufficient attention has been given to clinical studies involving the evaluation and management of brain-dead donors. Therefore, it is recommended that a coordinated effort to comprehensively analyze donor evaluation and management be undertaken. An initial study, which has preliminary approval of both AST and ASTS, will test the validity of echocardiography to determine the functional suitability of donor hearts compared with physiological measurements obtained via right heart catheterization. In addition, the benefits of aggressive hemodynamic management and hormonal resuscitation will be evaluated. Other studies
will be required to address the issues of infrastructure and logistics. For example, OPOs should examine the effect of having physicians directly involved in donor management, and pilot efforts at regional donor management and organ recovery should be undertaken. A biennial meeting on donor issues sponsored jointly by the AST, ASTS, and ISHLT would also be highly desirable.

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References
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