Failure Patients [CHAMPION] trial). Once heart failure becomes advanced, regularly scheduled review of the disease course and options with the patient and family is recommended including discussions surrounding end-of-life preferences when patients are comfortable in an outpatient setting. As the disease state advances further, integrating care with social workers, pharmacists, and community-based nursing may be critical in improving patient satisfaction with the therapy, enhancing quality of life, and avoiding heart failure hospitalizations. Equally important is attention to seasonal influenza vaccinations and periodic pneumococcal vaccines that may obviate non–heart failure hospitalizations in these ill patients. When nearing end of life, facilitating a shift in priorities to outpatient and hospice palliation is key, as are discussions around advanced therapeutics and continued use of ICD prophylaxis, which may worsen quality of life and prolong death.



## GLOBAL CONSIDERATIONS

Substantial differences exist in the practice of heart failure therapeutics and outcomes by geographic location. International guidelines produced by the American College of Cardiology/American Heart Association, European Society of Cardiology, and National Institute for Health and Clinical Excellence (United Kingdom) differ in their approach to evaluation of evidence and prioritization of therapy. The penetrance of CRT and ICD is higher in the United States than in Europe. Conversely, therapy unavailable in the United States, such as ivabradine and levosimendan, is designated as useful in Europe. Although ACEIs appear to be similarly effective across populations, variation in the benefits of beta blockers based on world region remains an area of controversy. In oral pharmacologic therapy trials of HFrEF, patients from southwest Europe have a lower incidence of ischemic cardiomyopathy and those in North America tend to have more diabetes and prior coronary revascularization. There is also regional variation in medication use even after accounting for indication. In trials of ADHF, patients in Eastern Europe tend to be younger, with higher ejection fractions and lower natriuretic peptide levels. Patients from South America tend to have the lowest rates of comorbidities, revascularization, and device use. In contrast, patients from North America have the highest comorbidity burden with high revascularization and device use rates. Given geographic differences in baseline characteristics and clinical outcomes, the generalizability of therapeutic outcomes in patients in the United States and Western Europe may require verification.

# 281 Cardiac Transplantation and Prolonged Assisted Circulation

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Advanced or end-stage heart failure is an increasingly frequent sequela of many types of heart disease, as progressively more effective palliation for the earlier stages of heart disease and prevention of sudden death associated with heart disease become more widely recognized and employed (Chap. 279). When patients with end-stage or refractory heart failure are identified, the physician is faced with the decision of advising compassionate end-of-life care or choosing to recommend extraordinary life-extending measures. For the occasional patient who is relatively young and without serious comorbidities, the latter may represent a reasonable option. Current therapeutic options are limited to cardiac transplantation (with the option of mechanical cardiac assistance as a "bridge" to transplantation) or permanent mechanical assistance of the circulation. In the future, it is possible that genetic modulation of ventricular function or cell-based cardiac repair will be options for such patients. Currently, both of the latter approaches are considered to be experimental.

## CARDIAC TRANSPLANTATION

Surgical techniques for orthotopic transplantation of the heart were devised in the 1960s and taken into the clinical arena in 1967. The procedures did not gain widespread clinical acceptance until the introduction of "modern" and more effective immunosuppression in the early 1980s. By the 1990s, the demand for transplantable hearts met, and then exceeded, the available donor supply and leveled off at about 4000 heart transplantations annually worldwide, according to data from the Registry of the International Society for Heart and Lung Transplantation (ISHLT). Subsequently, heart transplantation activity in the United States has remained stable at ~2200 per year, but worldwide activity reported to this registry has decreased somewhat. This apparent decline in numbers may be a result of the fact that reporting is legally mandated in the United States but not elsewhere, and several countries have started their own databases.

### SURGICAL TECHNIQUE

Donor and recipient hearts are excised in virtually identical operations with incisions made across the atria and atrial septum at the mid-atrial level (with the posterior walls of the atria left in place) and across the great vessels just above the semilunar valves. The donor heart is generally "harvested" by a separate surgical team, transported from the donor hospital in a bag of iced saline solution, and reanastomosed into the waiting recipient in the orthotopic or normal anatomic position. The only change in surgical technique since this method was first described has been a movement in recent years to move the right atrial anastomosis back to the level of the superior and inferior venae cavae to better preserve right atrial geometry and prevent atrial arrhythmias. Both methods of implantation leave the recipient with a surgically denervated heart that does not respond to any direct sympathetic or parasympathetic stimuli but does respond to circulating catecholamines. The physiologic responses of the denervated heart to the demands of exercise are atypical but quite adequate for continuation of normal physical activity.

### DONOR ALLOCATION SYSTEM

In the United States, the allocation of donor organs is accomplished under the supervision of the United Network for Organ Sharing, a private organization under contract to the federal government. The United States is divided geographically into eleven regions for donor heart allocation. Allocation of donor hearts within a region is decided according to a system of priority that takes into account (1) the severity of illness, (2) the geographic distance from the donor, and (3) the patient's time on the waiting list. A physiologic limit of ~3 h of "ischemic" (out-of-body) time for hearts precludes a national sharing of hearts. This allocation system design is reissued annually and is responsive to input from a variety of constituencies, including both donor families and transplantation professionals.

At the current time, the highest priority according to severity of illness is assigned to patients requiring hospitalization at the transplantation center for IV inotropic support, with a pulmonary artery catheter in place for hemodynamic monitoring, or to patients requiring mechanical circulatory support—i.e., use of an intra-aortic balloon pump or a right or left ventricular assist device (RVAD, LVAD), extracorporeal membrane oxygenation, or mechanical ventilation. The second highest priority is given to patients requiring ongoing inotropic support, but without a pulmonary artery catheter in place. All other patients are assigned a priority according to time accrued on the waiting list, and matching generally is based only on compatibility in terms of ABO blood group and gross body size.

While HLA matching of donor and recipient would be ideal, the relatively small numbers of patients as well as the time constraints involved make such matching impractical. However, some patients who are "presensitized" and have preexisting antibodies to human leukocyte antigens (HLAs) undergo prospective cross-matching with the