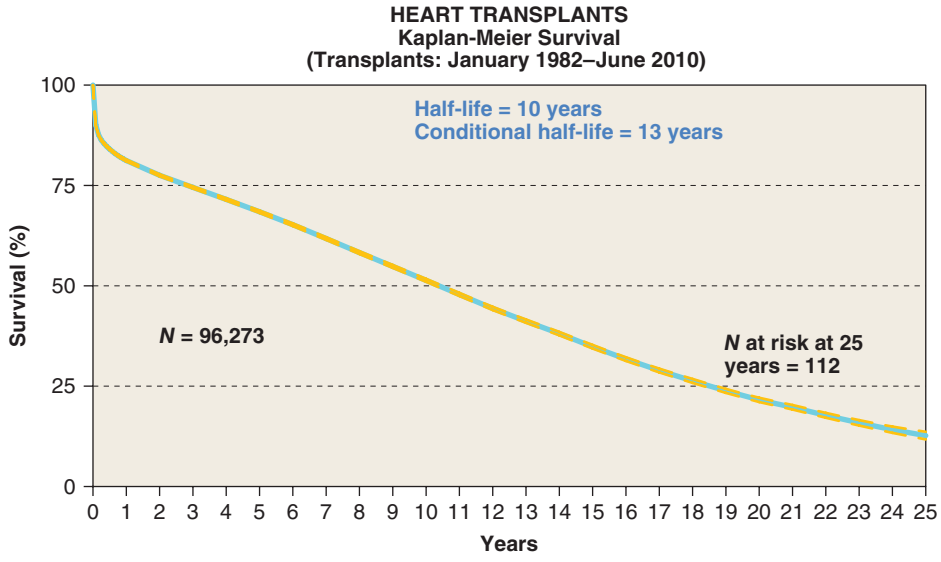

FIGURE 281-1 Global survival rates after heart transplantation since 1982. Rates were calculated by the Kaplan-Meier method, which incorporates information from all transplant recipients for whom any follow-up has been provided. Because many patients are still alive and some patients have been lost to follow-up, the survival rates are estimates rather than exact figures because the time of death is not known for all patients. Therefore, 95% confidence limits are provided. *(From J Stehlik et al: J Heart Lung Transplant 31:1052, 2012.)*

donor; these patients are commonly multiparous women or patients who have received multiple transfusions.

INDICATIONS/CONTRAINDICATIONS

Heart failure is an increasingly common cause of death, particularly in the elderly. Most patients who reach what has recently been categorized as stage D, or refractory end-stage heart failure, are appropriately treated with compassionate end-of-life care. A subset of such patients who are younger and without significant comorbidities can be considered as candidates for heart transplantation. Exact criteria vary in different centers but generally take into consideration the patient's physiologic age and the existence of comorbidities such as peripheral or cerebrovascular disease, obesity, diabetes, cancer, or chronic infection.

RESULTS

A registry organized by the ISHLT has tracked worldwide and U.S. survival rates after heart transplantation since 1982. The most recent update reveals survival rates of 83% and 76% 1 and 3 years after transplantation, respectively, or a posttransplantation "half-life" of 10.00 years (Fig. 281-1). The quality of life of survivors is generally excellent, with well over 90% of patients in the registry returning to normal and unrestricted function after transplantation.

IMMUNOSUPPRESSION

Medical regimens employed to suppress the normal immune response to a solid organ allograft vary from center to center and are in a constant state of evolution, as more effective agents with improved side-effect profiles and less toxicity are introduced. All currently used regimens are nonspecific, providing general hyporeactivity to foreign antigens rather than donor-specific hyporeactivity and also causing the attendant, and unwanted, susceptibility to infections and malignancy. Most cardiac transplantation programs currently use a three-drug regimen that includes a calcineurin inhibitor (cyclosporine or tacrolimus), an inhibitor of T cell proliferation or differentiation (azathioprine, mycophenolate mofetil, or sirolimus), and at least a short initial course of glucocorticoids. Many programs also include an initial "induction" course of polyclonal or monoclonal antibodies to T cells in the perioperative period to decrease the frequency or severity of early posttransplantation rejection. Most recently introduced have been monoclonal antibodies (daclizumab and basiliximab) that block the interleukin 2 receptor and may prevent allograft rejection without additional global immunosuppression.

Cardiac allograft rejection is usually diagnosed by endomyocardial biopsy conducted either on a surveillance basis or in response to clinical deterioration. Biopsy surveillance is performed on a regular basis in most programs for the first year postoperatively (or the first 5 years in many programs). Therapy consists of augmentation of immunosuppression, the intensity and duration of which are dictated by the severity of rejection.

LATE POSTTRANSPLANTATION MANAGEMENT ISSUES

Increasing numbers of heart transplant recipients are surviving for years following transplantation and constitute a population of patients with a number of long-term management issues.

Allograft Coronary Artery Disease Despite usually having young donor hearts, cardiac allograft recipients are prone to develop coronary artery disease (CAD). This CAD is generally a diffuse, concentric, and longitudinal process that is quite different from "ordinary" atherosclerotic CAD, which is more focal and often eccentric. The underlying etiology most likely is primarily immunologic injury of the vascular endothelium, but a variety of risk factors influence the existence and progression of CAD, including nonimmunologic factors such as dyslipidemia, diabetes mellitus, and cytomegalovirus (CMV) infection. It is hoped that newer and improved immunosuppressive modalities will reduce the incidence and impact of these devastating complications, which currently account for the majority of late posttransplantation deaths. Thus far, the immunosuppressive agents mycophenolate mofetil and the mammalian target of the rapamycin (mTOR) inhibitors sirolimus and everolimus have been shown to be associated with short-term lower incidence and extent of coronary intimal thickening; in anecdotal reports, institution of sirolimus was associated with some reversal of CAD. The use of statins also is associated with a reduced incidence of this vasculopathy, and these drugs are now used almost universally in transplant recipients unless contraindicated. Palliation of CAD with percutaneous interventions is probably safe and effective in the short term, although the disease often advances relentlessly. Because of the denervated status of the organ, patients rarely experience angina pectoris, even in advanced stages of disease.

Retransplantation is the only definitive form of therapy for advanced allograft CAD. However, the scarcity of donor hearts makes the