Heart failure continues to be one of the few problems in cardiovascular medicine that is increasing in frequency. It is a major public health problem in the United States. Approximately five million people in this country have heart failure. There are about a half of a million patients who receive a diagnosis of heart failure for the first time each year. Heart failure is responsible for approximately 12 to 15 million office visits and approximately 6.5 million hospital days each year. Nearly 300,000 patients die of heart failure as a primary or contributory cause each year, and the number of deaths has increased steadily despite advancements in treatment. It is primarily a disease of the elderly. Approximately 5 to 10% of people > 65 years old have heart failure. It is the most common Medicare diagnosis-related group, and more Medicare dollars are spent for the diagnosis and treatment of heart failure than for any other diagnosis. In the United States, approximately five million dollars are spent annually on drugs for the treatment of heart failure.1

As we use new developments and innovations in the treatment of coronary artery disease and valvular heart disease, patients tend to live longer and subsequently develop heart failure. End-stage congestive heart failure is a disease that has a very poor prognosis, with mortality rates > 50% in severe cardiomyopathies. Our understanding of the pathophysiology of heart failure has come quite a long way since the 1960s and 1970s when it was thought that it was primarily a “pump problem.” We now know that heart failure is a neurohormonal syndrome; as research continues, we have come a long way in using medications such as β-blockers and angiotensin-converting enzyme inhibitors in the treatment of this disease. Much controversy has existed in the use of long-term intermittent inotropic infusions in patients with end-stage congestive heart failure. There is some belief that long-term infusions may even shorten the patient’s life span, but many clinicians have seen the beneficial effects of long-term intermittent inotropic infusions. In the past, there was a very small study done whereby patients who were receiving dobutamine experienced sudden death with increased frequency vs the control group. This study, in my opinion, was flawed because of the fact that it was a small study; in addition, the patients who were infused at the time had potassium levels that were low. The concern is that dobutamine and inotropic infusions may increase the incidence of arrhythmogenic death.2 This has been the controversial issue that has separated the different schools of thought of the physicians who treat heart failure. Some advocate the use of inotropic infusions intermittently as a way for symptomatic improvement, as well as for care of the patient and improving their quality of life, while others argue that this method of treatment may shorten the patient’s life span and may not be beneficial.

In this issue of CHEST (see page 1198), Nanas and colleagues present a study of long-term intermittent dobutamine infusion combined with oral amiodarone for end-stage heart failure. This randomized, double-blinded, placebo-control study included 30 patients with congestive heart failure who were refractory to standard therapy. The patients were receiving digoxin, enalapril, spironolactone, and diuretics, and then were subsequently randomized to intermittent dobutamine infusion vs placebo. All patients had a radionuclide left ventricular ejection fraction of < 35%, and all patients received amiodarone therapy orally. Their hypothesis was that dobutamine would improve the hemodynamics of these patients and amiodarone would counteract the possible serious proarrhythmic effect of dobutamine. The patients were subsequently followed up by the same team of physicians in the same ICUs. It was then subsequently noted that the patients who were receiving biweekly dobutamine infusions along with amiodarone had a 57% relative reduction in death rate during the first year of follow-up and a 41% absolute reduction in mortality at 1 year. This was better than the placebo group.

Obviously, this study by no means will settle the controversy of “to infuse or not” in end-stage heart failure. Nonetheless, this is a novel pilot study that is well designed and does show an improved survival benefit with dobutamine infusion. The good news from this study is that it does not show that it decreases the patient’s life span. This study sets the stage for future studies that are desperately needed in this ever-evolving arena of heart failure. New therapeutic measures such as maximizing angiotensin-converting enzyme inhibition and using carvedilol3 need to be included in future studies that are done with patients receiving inotropic outpatient intermittent infusions. The data that we have collected and the lessons that we have learned from implantable cardiac defibrillator trials, as well as biventricular pacing in patients with severe cardiomyopathy and heart failure, have to be included in future trials with or without inotropic infusions in end-stage heart failure. As this disease continues to increase in frequency, especially as the population continues to increase in age, physicians who care for these patients must continue to keep up with this rapidly advancing and changing field of heart failure.

In summary, this study shows that at least we do not decrease the life span of the patient, and this can

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be used as a model for future studies. Obviously, it is advisable that when the physician decides to infuse, the patient should be adequately informed about the possibility that infusion therapy may shorten his/her life span. Nonetheless, it has been shown that patients who have a severe cardiomyopathy with significant heart failure that is refractory and with multiple hospitalizations may benefit symptomatically from inotropic infusions and their quality of life seems to improve. Whether this improvement is solely the result of the inotropic infusions or secondary to the fact that the physician carefully follows up the patient after every infusion and then adjusts the medical therapy, is a question that remains to be answered.

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**The Clinical Practice of Lung Transplantation in North America**

Evidence-based medicine is most effectively applied in clinical scenarios, which are complex, expensive, and high-risk. In lung transplantation, applying evidence-based medicine is problematic because it involves diverse phenotypes (emphysema vs cystic fibrosis) and different surgical options (single vs double lung transplantation). Furthermore, irrespective of the frequency of advanced lung disease, lung transplantation is offered only to a select few. Therefore, to obtain evidence in the field of lung transplantation solely based on randomized controlled studies is pragmatically difficult. Alternative data sets may be equally effective in providing insight into clinical practice.¹

In 1998, selection criteria for lung transplantation were published in an international consensus statement.² This publication included all major international stakeholders and forged a discipline of common practice. Other groups followed this principle, including the Munch-Vienna collaboration and the European Australian investigators group.³ The study by Levine et al in this issue of CHEST (see page 1225), on behalf of the transplant network of the American College of Chest Physicians, is another example of the merits of collaborative data sharing. A Web-based questionnaire that was focused on common clinical problems was applied to transplant programs across North America. Its simplicity is its strength. The results are validated by closely replicating registry data pertaining to questions on the utilization of immunosuppression.

Interesting patterns of practice and uncertainty emerge. In general, prior to transplantation there appears to be a broad consensus. However, the data provided by Levine et al suggest that these criteria are being challenged. Following transplantation, a contrasting divergent approach to problems highlights the absence of published management guidelines.

The selection of patients for lung transplantation is central to the management of advanced lung disease. Age is perhaps the simplest but potentially the most controversial issue with respect to candidate selection. Published international guidelines recommend 60 years of age for single lung transplantation, and 55 years of age for double sequential lung transplantation. In contrast, 20% of programs offer single lung transplantation to patients > 65 years of age, and 25% offer double lung transplantation to patients > 60 years of age. This emerging practice is probably most pertinent to idiopathic pulmonary fibrosis patients, for whom there is no pharmacologic treatment that prevents disease progression and death. However, older recipients may demand tailored immunosuppression in light of immunosenescence and the infectious complications seen in other elderly organ transplant groups.⁴

The selection of patients colonized or infected with antibiotic-resistant organisms is another controversial area. A body of evidence has highlighted the importance of genomovar classification of Burkholderia cepacia, with poor outcome following transplantation being associated with B cenocepacia (genomovar III).⁵ However, a third of programs consider B cepacia globally to be an absolute contraindication.

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