End-Stage Heart Failure - Surgical Therapeutic Options

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Summary

Although medical treatment is the most predominant therapeutic option in end-stage cardiac failure for most patients, it remains palliative, and the prognosis of the disease is considered poor, with its prevalence rising in the last decades. With the introduction of clinical heart transplantation, cardiovascular surgery started to offer a new option implicating significant prognostic improvement to selected population of end-stage heart failure patients. But as transplantation is restricted by the shortage of donor organs, alternative ways of surgical treatment are being investigated. The article focuses on standard treatment with ventricular assist devices and implantable defibrillators, surgical procedures under clinical investigation such as transmyocardial laser revascularization, dynamic cardiomyoplasty, partial left ventriculectomy, permanent mechanical support, and xenotransplantation as possible future options.

Key Words

chronic heart failure, CHF, heart transplantation, ICD, VAD, cardiomyoplasty, TMLR, left ventriculectomy

Introduction

End-stage heart failure will get more and more impact on cardio-vascular medicine in the future decades. With increasing age, this final pathway of almost all cardiac diseases (cardiomyopathy, coronary artery disease, valvular heart disease, complex congenital malformations) will require long term surveillance and treatment of chronic heart failure of increasing parts of the population. The incidence can be estimated as high as 1 to 5 cases per 1,000 population per annum; i. e. 400,000 new cases of heart failure in the United States per year, or 80,000 to 100,000 in Germany [1,2]. The prognosis of chronic heart failure (CHF) remains poor and compares with that of the malignant forms of cancer. The annual mortality from onset of symptoms of moderate and severe chronic heart failure exceeds 20 to 30 % and 30 to 80 %, respectively.

Pathophysiology

The pathophysiological mechanisms resulting in CHF are complex and in part due to the underlying disease. At least the renin-angiotensine-aldosterone system, the arginin-vasopressin system as well as the adrenergic signal transduction pathway are involved; recent findings reveal that alterations in gene expression, most probably leading to the phenomenon of apoptosis as well as both mechanisms together inducing ventricular remodeling are involved in the impairment of left as well as right ventricular function. Nevertheless, the adrenergic system remains the main target of research as well as therapy for CHF. The neurohumoral activation characterized by increased humoral activity, presynaptic facilitation of norepinephrine release and decreased functional activity of the uptake 1 mechanism leads to a down-regulation of the ß-adrenoceptor and this altered ß-adrenoceptor signal transduction results in adverse biological effects on cardiac myocytes [3]. Secondary to these (effects or coincidentally) altered gene expression results in apoptosis and/or remodeling.

Treatment options

Figure 1 outlines medical decision making in CHF and eCAD. Management of chronic heart failure includes general measures, general advice as well as chronic pharmacological therapy and follows distinct guidelines [4] although newer drugs are under continuous investigation. Even acute drug treatment in case of deterioration of CHF using the combination of PDE-III-inhibitors and catecholamines are generally accepted [5,6]. Nevertheless, if this treatment fails, steps

such as the use of a transplant or mechanical support

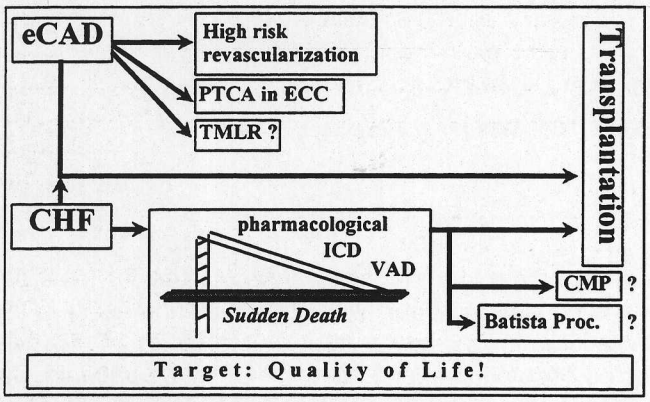

Figure 1. *Therapeutic decision making in end-stage heart failure refractory to conventional chronic medical treatment or coronary artery disease not suitable for revascularization.*

device should be discussed (see Figure 2).

In case of medical treatment failure or technical impossibility of revascularisation heart transplantation is the accepted therapeutic tool for the treatment of end-stage heart failure. The shortage of donor organs necessitates to bridge the lacking time to the point of getting a donor organ by mechanical devices. Reducing the risk of sudden cardiac death due to ventricular fibrillation during waiting time "electrical bridging" by use of an implantable cardioverter-defibrillator becomes more and more common. In addition, if heart transplantation is contraindicated ICD implantation offers an independent therapeutic option in heart failure patients. Only in case of contraindication new procedures currently undergoing clinical evaluation like

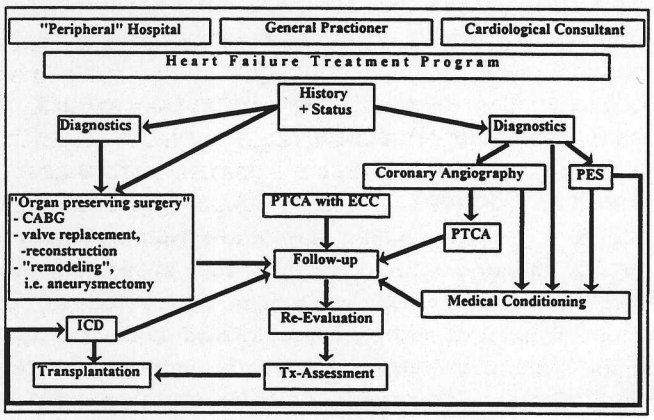

Figure 2. *Heart Failure Treatment Program*

cardiomyoplasty, partial left ventriculectomy or transmyocardial laser revascularisation may be used [9].

Heart transplantation

Heart transplantation represents the mode of treatment of choice for end-stage heart failure. The selection and treatment of candidates considered for heart transplantation has been standardized during the last five years [7,8]. Indications as well as contraindications are well defined [9] even if borderline conditions like severely elevated pulmonary vascular resistance, history of malignancy, pediatric transplantation as well as patients on mechanical assist devices are under clinical evaluation and remain on discussion.

Transplantation significantly improves survival, exercise capacity as well as quality of life compared to the pretransplant physical and mental condition. Recent results in patients on triple immunosuppressive regimen have shown a five year survival of 70 % [10]; avoidance of chronic corticosteroid administration seems to be closely correlated to lower incidence of graft atherosclerosis.

The longterm outcome after heart transplantation depends on the surveillance program and the skills and experience of the team involved in the clinical follow-up. Main problems are represented by accelerated graft atherosclerosis, post transplant lymphoproliferative disorders as well as the acquisition of opportunistic infections; the later became less important in the recent years.

Bridge to transplant

The severe shortage of donor organs (especially in times of fundamental legal discussions) has focused research and clinical efforts on mechanical assist devices. All devices (left as well as biventricular ones) in clinical use are able to support patients circulation at least for months until a donor organ is available. Proper selection of candidates for mechanical bridging as well as the timing of the operation result in an acceptable outcome: 60 % of the patients are transplanted [11]. The results of heart transplantation after multiorgan recovery during mechanical assist do not differ from those after elective transplantation [12]. Long term assist (as first step to permanent replacement) is limited by the imminent risk of thromboembolic events and device infection. Even if the problem of permanent energy provision could be solved the problem of biocompatibility remains the most important topic for technical development; genetic engineering of inner surfaces like endothelialisation should become one of the options of the year 2000 and beyond.

Mortality on the waiting list remains unfortunately 30 %. 40 to 50 % of the patients awaiting heart transplantation as well as those with end-stage heart failure not suitable for this treatment option die from sudden cardiac death. Therefore, the use of implantable cardioverter-defibrillator systems (ICD) are more and more accepted as a bridge to transplant or isolated antiarrhythmic treatment. Improvement of survival of patients with coronary artery disease with high risk for ventricular arrhythmia has been proved [13]. Following recommendations for antiarrhythmic treatment in patients after myocardial infarction [14] as well as patients awaiting transplantation [15] result in significant reduction of mortality in both patient groups. Therefore, ICD-treatment with shock option, antitachycardiac pacing as well as integrated diagnostic options using sophisticated holter systems has established ICD-implantation as an independent therapeutic tool in end-stage heart failure. Reduction of size as well as simplified technical features of ICDs in use for bridging to transplant should result in lower prices and therefore, offer the opportunity of broader (prophylactic?) use in these patients.

Surgical procedures under clinical investigation

Shortage of donor organs is limiting heart transplantation to carefully selected patient groups without contraindications and severe probability for post transplant survival. Patients with general symptomatic atherosclerotic disease, patients of higher ages as well as patients with chronic infections or history of malignancy are usually excluded from organ transplantation. In those cases, surgical procedures without yet proven long-term effect can be considered under clinical study conditions: transmyocardial laser revascularisation (TMLR), cardiomyoplasty as well as partial left ventriculectomy.

Transmyocardial laser revascularisation

In ischemic heart disease with native coronary arteries not feasible for direct revascularisation the creation of laser induced transmyocardial channels should hypothetically either result in ventriculo-coronary collaterals or induce angioneogenesis by molecular mechanisms not yet clearly understood [16,17]. Neither szintigraphic nor PET-perfusion investigations, nor morphological studies have revealed the cause for the subjective improvement [18] of the patients. The mortality rate after two years of 30 to 35 % is in the same range as in patient groups with conservative treatment. In those patients not suitable for heart transplantation for different reasons Carpentier and Chachques recommended the surgical technique of dynamic cardiomyoplasty [19]. Due to its plasticity the normal skeletal muscle can be trained and transformed into a fatigue resistant muscle by chronic electrical stimulation. Wrapping of the cardiomyopathic heart by the latissimus dorsi muscle results in subjective improvement of the patient. This improvement can not be clearly demonstrated by hemodynamic measurements, but long-term outcome compared to patients in historical treatment groups seems to be positively affected [20]. The mechanism of action is still under investigation; factors contributing to the clinical effect may be improved systolic function by squeezing, improved diastolic function by stenting, reducing ventricular wall stress by thickening as well as myocardial revascularisation due to development of collaterals between skeletal and myocardial muscle. Combination of dynamic cardiomyoplasty with ICD implantation may result in an improved outcome in subgroups suffering from severe arrhythmias.

Partial left ventriculectomy

Partial left ventriculectomy [21], known as "Batista procedure", is an attractive idea for surgical reverse remodeling of the dilated left ventricle. Partial resection of the left ventricle restoring normal geometry and "wringing" mechanics during systolic ejection will result in reducing wall stress and improving myocardial performance while normalising its oxygen demand/supply ratio. This attractive therapeutic idea should be further evaluated in randomised clinical studies.

Future developments

Transplantation of thoracic organs will continue to play an important clinical role in the year 2000 and beyond; the shortage of donor organs will remain a depressant factor as well. This will result into the development of alternative options like xenotransplantation [20] or permanent mechanical implants. Even if the development of transgenic animals will not result in the availability of "xenotransplant organs on request", research in this field will contribute to the development of immunosuppressive regimes to induce long-lasting immunetolerance. At the beginning of the next millennium the development of permanent mechanical implants should provide options for permanent heart replacement, at least in chronic heart failure patients of higher ages. Prolonged mechanical unloading of chronic dilated ventricles [23] may become an independent treatment option leading to reverse remodeling or reversal of apoptotic mechanisms [24]. The combination of the principles of dynamic cardiomyoplasty and artificial

heart may result in implantable devices driven by transformed skeletal muscle [25,26].

Besides these future horizons an interdisciplinary approach performed within heart failure treatment programs supported by cardiologists as well as cardiac surgeons offers the opportunity of individualized treatment of heart failure patients reaching from optimised medical treatment up to transplant.

Treatment of chronic end-stage heart failure will remain one of the medical, social and financial challenges of the future.

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