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Review article

The promising future of ventricular restraint therapy for the management of end-stage heart failure

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ABSTRACT

Complicated pathophysiological syndrome associated with irregular functioning of the heart leading to insufficient blood supply to the organs is linked to congestive heart failure (CHF) which is the leading cause of death in developed countries. Numerous factors can add to heart failure (HF) pathogenesis, including myocardial infarction (MI), genetic factors, coronary artery disease (CAD), ischemia or hypertension. Presently, most of the therapies against CHF cause modest symptom relief but incapable of giving significant recovery for long-term survival outcomes. Unfortunately, there is no effective treatment of HF except cardiac transplantation but genetic variations, tissue mismatch, differences in certain immune response and socioeconomic crisis are some major concern with cardiac transplantation, suggested an alternate bridge to transplant (BTT) or destination therapies (DT). Ventricular restraint therapy (VRT) is a promising, non-transplant surgical treatment wherein the overall goal is to wrap the dilated heart with prosthetic material to mechanically restrain the heart at end-diastole, stop extra remodeling, and thereby ultimately improve patient symptoms, ventricular function and survival. Ventricular restraint devices (VRDs) are developed to treat end-stage HF and BTT, including the CorCap cardiac support device (CSD) (CSD; Acorn Cardiovascular Inc, St Paul, Minn), Paracor HeartNet (Paracor Medical, Sunnyvale, Calif), QVR (Polyzen Inc, Apex, NC) and ASD (ASD, X. Zhou). An overview of 4 restraint devices, with their precise advantages and disadvantages, will be presented. The accessible peer-reviewed literature summarized with an important considerations on the mechanism of restraint therapy and how this acquaintance can be accustomed to optimize and improve its effectiveness.

1. Introduction

HF is a complicated pathophysiological syndrome where an irregular functioning of the heart leads to insufficient blood supply to the body organs. Numerous factors can add to HF pathogenesis, including myocardial infarction (MI), coronary artery disease (CAD), genetic factors, ischemia or hypertension etc. 2/3 of the HF cases occur in patients who have MI [1]. After MI, diverse physiological and molecular changes modulate cardiomyocytes composition, changes in protein, gene expression and a series of multifaceted remodeling responses [2]. MI induced left ventricular (LV) remodeling is now liable for approximately 70% of the 4.9 million cases of HF in the US [3]. After ventricular dilatation it's hard to reverse and showed long lasting results [4]. Although it is appealing to mark the association between MI and HF simply to a reduction in the amount of healthy myocardium contributing to ejection, the majorities of patients who suffer an MI are initially well-compensated hemodynamically and only expand symptomatic HF over time as the LV remodels in reaction to the MI. In addition to a loss of contractile myocardium, the degree of LV remodeling and systolic mutilation is related to the compliance, size, and geometry of the infarct region [5–7]. According to New York Heart Association (NYHA) II–III classification, the patient suffering from mild to moderate

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HF, lifestyle modifications and use of conventional HF medications are frequently unbeaten in improving symptoms and survival rate [8]. In addition, the implantation of an implantable cardioverter-defibrillator (ICD) with or without cardiac resynchronization therapy (CRT) stand for typical therapies for patients with low left ventricular ejection fractions (LVEF). However, ischemic heart disease (IHD)-associated HF patients should be evaluated for possible catheter-based interventions or surgical procedure. Advance HF patients NYHA IV classifications have constant symptoms regardless of the implantation of ICDs, CRT and best medical treatment having regular hospitalization and deprived quality of life (QOL) [8] with 1-year mortality rate up to 50%. Chronic heart failure (CHF) generally occurs due to continuous LV remodeling and the progressive loss of heart functions, leading to abnormalities in systolic or diastolic function [9]. The heart transplantation is a gold standard for advanced HF but is scarce by the donor pool limitation and socioeconomic crisis creating a need for alternate efficient BTT or DTs. [10]. Ventricular restraint therapy (VRT) is a non-transplant surgical option for HF during which the whole ventricular surface is wrapped with a prosthetic material [11,12]. The fundamental hypothesis to deliver restrain by decreasing transmural myocardial pressure (P_{tm}) and mixed venous oxygen saturation (mVO_2) and thus improve mechanical efficacy of ventricles [13]. So provide diastolic support and to prevent adverse ventricular remodeling. Current restraint devices have led to improvements in left ventricle (LV) volume, ejection fraction (EF), and sphericity index, correlating with reverse remodeling as shown in Fig. 1. Cautions to adverse LV remodeling and decrease LV wall stress in CHF have been persuaded via pharmacological or biological agent, cardiac intervention or surgery. Left ventricular passive support devices (LVSD) are surgically implanted to bound progressive dilatation through restraint, reducing wall stress and thus restoring standard LV sphericity [14]. Left ventricle assist device (LVAD) like VRDs used as a targeted therapy for advanced stage HF management and as a BTT [15]. Here we will focus on VRDs in relation to the heart and will discuss the reported therapeutic approaches for the management of HF. VRT is a promising, non-transplant surgical therapy in which the overall goal is to wrap the dilated failing heart with prosthetic material. VRD is different from direct cardiac compression device (DCC) in terms of the designed, just to treat advanced-stage HF due to dilated ventricles and it can prevent and adverse ventricle remodeling [16]. Furthermore, it consists of a flexible biocompatible material wrap around the heart without any driveline, pressure sensing and ECG system. Cardiomyoplasty is a surgical technique wherein the sub-totally mobilized latissimusdorsi muscle is wrapped around the heart and inspired to contract in synchrony with cardiac systole [17]. Clinical active cardiomyoplasty was initially reported in 1930 and it has a long history of more than 80 years of scientific research [18]. In 1985 Carpentier performed 1st successful clinical cases in Paris, a subset of patients showed significant improvement in LVEF and NYHA functional class, but no significant change in cardiac substantial pressure was observed [19]. Cardiomyoplasty provides a basic foundation to VRT, and later on series of devices were developed and their effects were monitored in animal models to investigate ventricular dilatation [20]. VRT can recover the adverse remodeling of the myocardium as shown in studies [21,22]. Basic VTDs including CorCap CSD (Acorn Cardiovascular Inc, St Paul, Minn), Paracor HeartNet (Paracor Medical, Inc, Sunnyvale, Calif), QVR (Polyzen Inc, Apex NC) [23,24] and ASD (ASD, X. Zhou) [25] are developed for the management of end-stage HF. However, CSD and HeartNet take effect by inertly physical shaping and thus have great compliance in application [26]. Although QVR device was developed to adjust and measure the ventricular restraint level (AMVR) [27] while, ASD is a combination of all operational VRDs by delivering pharmacological [28] and biological (stem cells) agents, and can determined the AMVR of the heart.

2. Ventricular restraint therapy (VRT)

VRT refers to the treatment approach, which is achieved by surrounding the organ with protective and supportive biomaterial without having direct contact with the blood. This concept is old and adopted by more than one century. In cardiomyoplasty, a distinctive pacemaker is implanted to improve the skeletal muscle contraction and improve ventricular function in HF [29]. The implantation procedure of latissimusdorsi muscle is relatively simple and can be easily placed around heart through the thoracotomy [30]. First multicenter FDA approved phase II study showed that cardiomyoplasty improves symptoms and cardiac performance [31]. Non-randomized trial also showed hemodynamic improvement, significant changes in exercise tolerance and survival rate in patients [32]. However, the C-smart trial failed to show statistically significant improvement in survival rate and mVO_2 consumption in 1 year [33]. Unfortunately, the results of different studies showed a deviation of early and late mortality in cardiomyoplasty trials conducted on more than 1000 patients [34] but provide a basic foundation to VRT. Two of these interventional therapies were studied in human clinical trials and others are still in the initial safety study. Here, we will discuss salient features of all VRDs.

2.1. CorCap CSD

The Acorn CorCap (Acorn Cardiovascular, Inc, St Paul, MN) was the first and most extensively studied VRD that has undergone human trials [35] as shown in Fig. 2C. This device is made of a multi filamentous fiber (Fig. 2A & B) and the implantation procedure of Acorn CorCap is relatively simple and can be easily placed around heart through a median sternotomy and secured with 8–10 polypropylene sutures circumferentially around the atrioventricular (AV) groove. The degree of tightness should be adjusted to achieve 5% reduction in heart diameter and should not affect the diastolic function or myocardial mal-perfusion [47]. The major function of the device is to decrease the amount of

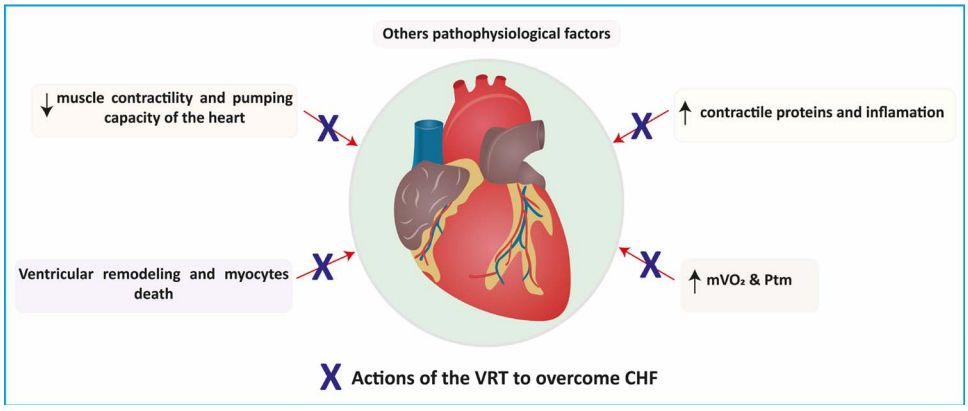

Fig. 1. Actions of the VRT to overcome CHF.