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Editorial

Relative roles of heart transplantation and long-term mechanical circulatory support in contemporary management of advanced heart failure — a critical appraisal 10 years after REMATCH

Keywords: Heart transplantation; Advanced heart failure; Mechanical circulatory support

The number of patients with heart failure (HF) is growing. In the United States and Europe alone, with >700 million inhabitants, there are more than seven million patients with heart failure. In the United States, heart failure is a major public health problem affecting over 5.8 million men and women with over 670,000 newly diagnosed patients each year. HF contributes to over 250,000 deaths a year, results in 2.4—3.5 million hospitalizations a year, 12—15 million outpatient office visits a year and total costs estimated at 39.2 billion dollars a year [1]. The prevalence of advanced heart failure (AdHF), constituting between 1 and 10% of the heart failure population, is estimated to total between 70,000 and 700,000 patients in the US. From a regional heart failure care perspective, for example, in the Greater Los Angeles area with >10,000,000 population, the prevalence of heart failure is estimated at >100,000 people, and those with AdHF >10,000 people. AdHF carries a prognosis similar to cancer. After publication of the REMATCH study [9], while heart transplantation donor organ numbers remain constant worldwide [2], the relative contribution of long-term mechanical circulatory support devices (MCSDs), either as destination or alternative to transplantation MCSD (ATT) or long-term bridge to transplantation (BTT), is increasing. This Editorial addresses the changing relationship between heart transplantation (HTx) and mechanical circulatory support device (MCSD) therapy in the treatment of patients with AdHF, with a special emphasis on the historical perspective of heart transplantation and contemporary challenges in this changing scenario. Heart transplantation evolved through different phases of development. We discuss the role of heart transplantation in relationship to MCSD over three different phases which we have somewhat arbitrarily divided into an (1) early clinical phase (1958—1977), (2) established standard of care phase (1978—2000), and (3) competing standard of care phase (2001—ongoing).

Early clinical phase of HTx (*1958—1977*): The early clinical phase was, after the groundbreaking accomplishment of technique development in the dog model [3], initiated by the spectacular first human transplantations by Christiaan Barnard (Groote Schuur Hospital, Kapstadt, South Africa) and Adrian Kantrowitz (Maimonides Hospital, Brooklyn, USA), in 1967 and Norman Shumway (Stanford University Hospital, Palo Alto, USA) in 1968. A transitional period of struggle for medical and societal acceptance followed. This period also marked the first commitment by the US-NIH to develop MCSD through funding for the development of the Artificial Heart in 1964. The first clinical implantations of artificial hearts were paralleling the first HTx reports. The professional paradigm of this period could be summarized as: 'Both therapies are applicable to humans yet are clinically immature'. After the results at Stanford University [4] showed evidence of a survival benefit from the first 109 Htx recipients over contemporary control patients in a non-randomized analysis, this all-or-none evidence, along with the introduction of cyclosporine, provided the basis for HTx to enter the next phase of development worldwide.

Established standard of care phase of HTx (*1978—2000*): Over the following years more than 200 heart transplantation centers emerged worldwide, prompting the founding of the umbrella of the International Society for Heart and Lung Transplantation (ISHLT). The annual number of HTx worldwide reached a ceiling of 4000. During this phase, the implantation of the Jarvik-7 Total Artificial Heart into Barney Clark in 1982 and the subsequent Jarvik-7 implantations were portrayed as clinically immature 'halfway' technology and ethically questionable. While HTx became the gold standard in the treatment of AdHF, MCSD was undergoing a critical professional and societal evaluation. The professional paradigm could be summarized as: 'While HTx has evolved to a mature lifesaving and quality-of life enhancing therapy for selected AdHF patients, MCSD therapy is still struggling to demonstrate a beneficial role in the care of AdHF patients except for selected BTT patients'. During this time period medical therapy for AdHF had substantially improved. In the year 2000, the collaborative Eurotransplant/German Transplantation Society-sponsored COCPIT (Clinical Profiles and

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Comparative Outcomes in Transplantation) Study called into question the undisputed survival benefit of HTx over alternative organ-repairing therapies [5] and called for a scientific comparison, for example by randomized controlled trial design, comparing HTx to alternative therapies [6,7].

Competing standard of care phase of HTx (2001—ongoing): HTx therapy has shown steady but incremental improvements in outcomes [8] through improved patient selection with extended indications, extended donor acceptance, improved monitoring and immunosuppression. In 2001, the groundbreaking randomized controlled REMATCH trial demonstrated, using the first generation HeartMate I Left Ventricular Assist Device (LVAD), a survival and quality-of-life benefit of MCSD in transplant-ineligible patients [9]. The second generation HeartMate II LVAD improved the survival and quality of life even more [10,11]. Currently, the 1-year survival in HeartMate II LVAD patients is around 85% and therefore reaching similar intermediate-term outcomes as HTx. Although HTx has maintained its highly visible role as established therapy for selected AdHF patients, it remains notably limited by donor organ availability. In contrast, MCSD therapy is achieving similar outcomes as HTx but is available in potentially unlimited numbers. The professional paradigm could be summarized as: 'While HTx is maintaining its mature lifesaving and quality-of life enhancing role for selected AdHF patients, MCSD therapy is rivaling the outcome of HTX, at least over midterm ranges and has the advantage to be available in unlimited numbers. Therefore, direct comparison of both approaches with respect to long-term survival and quality of life are appropriate'.

Perspective: From our responsibility towards an integrated and accountable heart failure care concept, it seems timely to place the changing roles of HTx and MCSD therapies in the context of a broader vision of comprehensive regional AdHF models with the long-term goals to (1) improve the care of the individual AdHF patient, (2) improve the care for the AdHF population in the region, and (3) provide this care in the most cost-effective way. Translating these long-term goals into regional heart failure care models and taking the Greater Los Angeles Area as an example, we have to offer to our patients with AdHF different options including (1) optimal lifestyle changes as well as medical, interventional, and surgical cardiac repair (estimated between 10,000 and 100,000 patients/year), (2) long-term mechanical circulatory support (ATT MCSD) (estimated 100—1000/year), (3) HTx (estimated 100—200/year), and (4) quality-of-life-emphasizing palliative care (estimated 5000—10,000/year).

Upon referral and evaluation, we need to empower our patients with AdHF to make well informed personal choices, connect the chosen evidence-based care plans to primary care practitioners, cardiologists, advanced practices nurses, regional hospitals, and long-term facilities in a care continuum, provide world class heart transplantation medicine, expand state-of-the art lifetime assist heart pump therapy, integrate quality-of-life-emphasizing options during the entire course of illness, and unite all of the region's providers to create integrated, comprehensive, patient-centered, and accountable models of heart failure care.

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