ABSTRACT

Hypertrophic cardiomyopathy (HCM) is the most common inherited monogenic cardiovascular disease. With extended longevity, the incidence of heart failure (HF) in patients with HCM has been growing exponentially and currently is the predominant mode of demise. The progression to end-stage HF, requiring advanced therapies, is observed in up to 17% of those individuals. Altered ventricular geometry often precludes patients with HCM from even being considered for left ventricular assist device (LVAD) implantation. Therefore, most of those who develop end-stage HF are referred for heart transplantation (HT).

The data on clinical characteristics, their evolution over the years, waitlist outcomes across various heart allocation systems, immediate pre- and postoperative course, and post-HT outcomes in patients with HCM, compared to the most commonly encountered cardiomyopathies, are scarce.

The series of publications opens with a paper titled ***Long-term post-transplantation outcomes in patients with hypertrophic cardiomyopathy: Single-center 35-year experience*.** Its primary objective was to conduct an in-depth analysis of clinical characteristics of patients with hypertrophic cardiomyopathy who underwent heart transplantation, analyze their immediate pre- and post-transplant course along with short- and long-term post-transplantation outcomes. Subsequently, the data and outcomes of patients with hypertrophic cardiomyopathy were contrasted with those of patients with dilated and ischemic cardiomyopathy.

In this single-center study, we retrospectively analyzed and compared data of 319 adult patients who underwent first-time single-organ HT between 1984 and 2019: 24 patients with HCM, 160 with ischemic cardiomyopathy (ICM) and 135 with dilated cardiomyopathy (DCM). At listing, patients with HCM were younger than their ICM and DCM counterparts (41.3±12.9 vs. 56.6±7.9 vs. 48.3±13.3 years, $p<0.01$), less frequently carried a diagnosis of diabetes mellitus (8% vs. 38% vs. 23%, $p<0,01$), peripheral vascular disease (0% vs. 13% vs. 4%, $p=0.01$), essential hypertension (25% vs. 51% vs. 35%, $p=0.03$), hyperlipidemia (30% vs. 94% vs. 39%, $p<0.01$), and at the time of HT were less frequently supported with LVAD (12.5% vs. 26% vs. 26%, $p<0.01$).

Immediately post-HT, recipients with HCM more often than the ICM and DCM groups required prolonged (>7 days) inotropic support (37% vs. 12% vs. 17%, p=0.02), temporary mechanical circulatory support (MCS) (45% vs. 13% vs. 14%, p<0.01), and renal replacement therapy (55% vs. 19% vs. 24%, p<0.01). Post-HT survival among patients with HCM, ICM, and DCM, respectively, was: at 1 year 92% vs. 90% vs. 90%, p=0.97; at 5 years 79% vs. 78% vs. 82%, p=0.59; and at 10 years 67% vs. 62% vs. 69%, p=0.04.

Our study demonstrated that heart transplant recipients with a history of hypertrophic cardiomyopathy were younger and less burdened with comorbidities than their dilated and ischemic cardiomyopathy counterparts. Despite their more challenging immediate postoperative course, recipients with hypertrophic cardiomyopathy showcased comparable with those with dilated and ischemic cardiomyopathy short-term post-transplant survival. While the long-term post-HT survival among recipients with hypertrophic and dilated cardiomyopathy was comparable, recipients with hypertrophic cardiomyopathy had more favorable, than those with ischemic cardiomyopathy, 10-year post-HT survival.

In a paper titled ***Heart Transplantation Outcomes in Patients With Hypertrophic Cardiomyopathy in the Era of Mechanical Circulatory Support***, we assessed at the international level the evolution of clinical profile and outcomes of HT recipients with hypertrophic cardiomyopathy in two eras: before and after the widespread use of mechanical circulatory support (Era 1: 1998-2007 and Era 2: 2008-2017, respectively). Subsequently, the data and outcomes of patients with hypertrophic cardiomyopathy were contrasted with those of patients with ischemic and nonischemic cardiomyopathy.

Using the International Society for Heart and Lung Transplantation Thoracic Organ Transplant Registry, we identified in Era 1: 742 recipients with HCM, 15,964 with nonischemic cardiomyopathy (NICM), and 14,140 with ICM and in Era 2: 1,211 recipients with HCM, 20,394 with NICM, and 12,986 with ICM. Across the two eras, among patients with HCM, the number of HTs increased exponentially (by 63%), as did the rate of recipients with implantable

cardioverter-defibrillator (ICD) in place at the time of HT (67% vs. 89.1%, p<0.01), there was also a trend towards higher rate of patients in the intensive care unit (ICU) at HT (27.1% vs. 32.2%, p=0.07) and statistically significant increase in the rate of patients supported with intra-aortic balloon pump (IABP) (2.4% vs. 6.3%, p<0.01), while the rate of those with good functional status at HT increased (16% vs. 31.1%, p<0.01). Across the two eras, among recipients with HCM there was no difference in 1- and 5-year post-HT survival. In Era 2, at the time when a suitable organ donor was identified recipients with HCM compared to their NICM and ICM counterparts were more frequently in the ICU (32.2% vs. 27.8% vs. 26.4%, p<0.01) and supported with inotropes (44.1% vs. 36.3% vs. 33.8%, p<0.01). In the same era, 1-year and 5-year post-HT survival was more favorable in HCM compared to ICM (85.3% vs. 84.5%, p<0.01; 78.2% vs. 72%, p<0.01, respectively) and comparable to NICM (85.3% vs. 87%, p=0.5; 78.2% vs. 76.1%, p=0.6, respectively).

The current paper is the first one to report the evolution of the clinical profile and post-transplant outcomes in patients with hypertrophic cardiomyopathy at the international level. The higher rate of ICDs in place along with better functional status at the time of HT in the contemporary era suggests significant improvement in the management of these patients. Even though in the contemporary era of widespread mechanical circulatory support use there is a trend among patients with hypertrophic cardiomyopathy awaiting heart transplantation to be more frequently in the intensive care unit and significantly more often supported with intra-aortic balloon pump, their short- and long-term post-transplantation outcomes remain unchanged across eras and favorable compared to those of recipients with ischemic and nonischemic cardiomyopathy.

In a subsequent paper titled ***Impact of the New Heart Allocation System on the Medium-Term Outcomes in Patients With Hypertrophic Cardiomyopathy***, the objective was to investigate whether an introduction of the new heart allocation system in the United States resulted in changes in the waitlist and post-transplant mortality in individuals with hypertrophic cardiomyopathy.

Using the United Network for Organ Sharing Transplant national database we conducted a comparative analysis of the waitlist and post-HT outcomes of the recipients with HCM before and after the US heart allocation system change (Era 1: October 17, 2015, to October 17, 2018 and Era 2: October 18, 2018, to October 18, 2021). In the studied period, we identified 665 patients with HCM who were listed for HT (Era 1: n=304; Era 2: n=361). Under the new heart allocation system, transplant rates were higher (Era 1 and Era 2, at 1 year: 66.8% vs. 72.8%, $p<0.01$; at 3 years: 80.1% vs. 84.7%, $p<0.01$, respectively) while the waitlist mortality remained unchanged. A total of 444 patients with HCM underwent HT (Era 1: n=204; Era 2: n=240). In Era 2, the waitlist time was shorter (151±188 vs. 90±134 days, $p<0.01$) and patients were less frequently supported with inotropes (49.5% vs. 30.8%, $p<0.01$) but more often with an IABP (10.3% vs. 19.6%, $p<0.01$). Across the two analyzed eras (Era 1 and Era 2), post-HT survival was comparable: at 1 year: 92.6% vs. 92.5%, and at 3 years: 89.7% vs. 88.8%, $p=0.6$, respectively.

Our study showed that despite the significant increase in the transplant rate among patients with hypertrophic cardiomyopathy since the new organ allocation system was introduced, both waitlist and post-transplant mortality remained unchanged. Further improvement in the heart allocation system is needed to reduce waitlist mortality in this group.

The series closes with a paper titled ***Hypertrophic Cardiomyopathy: From Medical Treatment to Advanced Heart Failure Therapies***. In this publication, we reviewed the literature on management strategies of patients with HCM at various stages of the disease. For patients with hypertrophic cardiomyopathy who develop advanced heart failure, transplantation remains the gold standard. However, for patients with a left ventricular end-diastolic diameter of 46-70 mm a left ventricular assist device remains a viable option.