Advancing Advanced Heart Failure in 2021 Ireland

Written by Dr Emer Joyce, Consultant Cardiologist, Heart Failure / Cardiomyopathies / Mechanical Circulatory Support / Cardiac Transplant - UCD Associate Professor of Medicine

Dr Emer Joyce is a Consultant Cardiologist specializing in Heart Failure, Mechanical Circulatory Support and Cardiac Transplantation at the Mater University Hospital Dublin, having taken up the role in 2018 following 3 years as a Heart Failure and Transplant Cardiologist at the Cleveland Clinic Ohio, USA. Prior to this she completed a 2-year clinical and research fellowship in Advanced Heart Disease at Brigham and Women's Hospital Boston 2013-15 and a 2-year doctoral fellowship in advanced cardiac imaging through Leiden University, Netherlands 2011-13 following which she was awarded a PhD in 2015. She is Chair of the Advanced Heart Failure Subgroup of the National Heart Clinical Program and recent Cardiology Chair of the National Amyloidosis Working Group. She is an Associate Clinical Professor at University College Dublin, an Associate Editor of the Journal of Cardiac Failure and an Editorial Board Member of the European Journal of Heart Failure.

She has published over 60 articles in peer-reviewed medical journals and written several book chapters focused on heart failure, cardiomyopathies, ventricular assist devices and advanced heart disease. She is passionate about educating a new generation of heart failure specialists and driving forward acute, chronic and advanced heart failure care in Ireland, as well as specific cardiomyopathies including amyloidosis and sarcoidosis and HF-intersection subspecialties including cardio-oncology and cardio-obstetrics.

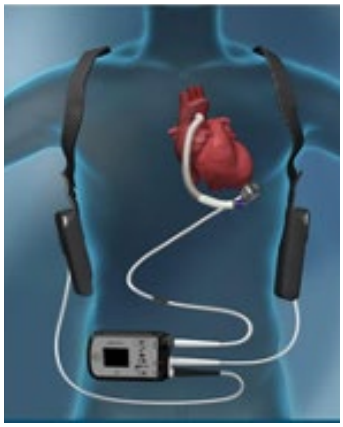
The latter half of the 1960s was a golden period for the development of extraordinary therapies to alter the otherwise terminal course of advanced or end-stage heart failure (HF). The first prototype mechanical heart pump – what we now call "Ventricular Assist device" or VAD - was implanted in a patient with post cardiotomy shock peri-valve surgery by Dr Michael Debakey in 1966. The following year, a temporary form of mechanical circulatory support, the intra-aortic balloon pump (IABP), still in use to this day, was first used successfully. Later that same year, on the 3rd December, 1967, Dr Christiaan Barnard pioneered the first human heart transplant. Though the recipient lived for just 18 days - dying of pneumonia - this was a watershed moment worldwide for the care of these patients. Since then, rapid advancements in anti-rejection therapeutics and evolution of medical and surgical strategies pre, peri and post transplantation have contributed to a median survival of over 12 years and approximately 3,500 heart transplants are now performed each year worldwide.

The Mater University Hospital is the National Cardiac Transplant Center, and since the program kicked off in 1987, has recently reached the milestone number of over 400 heart transplants performed. In the 5-year period leading up to the pandemic, an average of 15-18 heart transplants were carried out each year, with 1-year survival rates of 86%, equivalent to the leading international centers and registries. It remains the gold standard therapy for HF refractory to usual therapies in eligible patients. However, transplantation cannot be relied upon alone as the sole definitive treatment option for end-stage or advanced HF, principally due to a supply-demand mismatch caused by a chronic donor organ shortage. Several coexisting conditions may also render a patient ineligible to derive a reasonable enough benefit from such a major surgery, including mandatory lifelong medications with narrow therapeutic windows and frequently associated adverse effects and complications.

Over the past 20 years, phenomenal technological advances alongside improved patient selection and post-device management have led to an emergence of VAD therapy as a viable alternative "heart replacement therapy" for patients with advanced HF. The newest generation durable left ventricular assist device (LVAD) is associated with 1-year and 2-year survival rates of >80% and 70% respectively, comparing quite favorably to transplantation, particularly when you consider that LVAD therapy can be applied in a scheduled and timely manner and in patients who may be otherwise ineligible for transplant, for example due to pulmonary hypertension, renal dysfunction or high degree of antibody sensitization. They can be implanted in conjunction with ("bridge to transplant"), or independent of ("destination therapy"), a transplant strategy. Though their incremental survival and quality of life benefits over continued medical therapy for appropriate advanced HF patients are proven, there remain certain challenges in applying this therapeutic strategy more widely, particularly due to infrequent but serious complications such as stroke and right ventricular (RV) failure. Regarding the latter, my former Cleveland Clinic colleagues and I recently published a report on over 300 patients undergoing LVAD implantation where we found that targeted pre-operative hemodynamic optimization can provide useful discrimination of risk regarding likelihood of RV failure. The Mater has been implanting VADs since 2005 to support its transplant program, but recently given significant device improvements and related outcomes, in addition to targeted VAD team development and hiring, the program is beginning to expand.

I took up the first full-time post in advanced HF and cardiac transplantation, a subspeciality of cardiovascular medicine, in the Mater University Hospital in 2018. One of the initial projects I wanted to prioritize was the collection of accurate prevalence data for the syndrome of advanced HF in Ireland, which is a distinct stage of HF with unique resource and therapeutic needs as outlined above. Advanced HF is a clinical syndrome common to multiple forms of cardiovascular diseases, including ischemic heart disease, dilated, hypertrophic and restrictive cardiomyopathies, as well as genetic, valvular and adult congenital heart diseases. Identifying patients who have progressed into this final phase of HF and thus eligible to be evaluated for advanced therapies if appropriate is made more complex by the fact that there is no one clinical course or biomarker or other test that can reliably define exactly when a patient has reached it. Consequently, both lack of contemporaneous epidemiological data and innate difficulties to clinical recognition have imposed barriers to awareness of the condition not just in Ireland but internationally. This has consequences for timing of patient referrals for advanced therapies, meaning referrals may occur when patients are too sick to be considered eligible candidates for either LVAD or transplant, or if still eligible, are at a higher risk of adverse outcomes due to profound degree of debility or end-organ dysfunction.

In 2019 working in tandem with the HF Clinical Program I oversaw the National Advanced HF Prevalence Survey (designed as a simple one-page questionnaire) which was carried out across 21 of Irelands network of nurse-led specialized HF clinics. We found that approximately 5% of an all-comer outpatient HF clinic population, and strikingly two-thirds of a pre-selected HF with reduced ejection fraction aged <65 years cohort, had at least one clinical or biochemical marker potentially suggestive of advanced or impending advanced HF. The clinical indicators most frequently cited were ≥1 HF hospitalization in the prior 12 months and intolerance to renin-angiotensin-aldosterone inhibitors due to hypotension or



Newest Generation LVAD

renal dysfunction. Based on a now likely highly conservative estimate of 90,000 patients living with HF in Ireland (via the 2012 National HF Report), this would equate to a minimum current prevalence of 4,500 patients living with advanced HF in Ireland. The survey results were presented at both the European Society of Heart Failure and Irish Cardiac Society Annual Meetings in 2020. It is my hope that in providing a numerical and demographic insight into the population of patients potentially eligible for referral to an advanced HF center like the Mater, this novel data will aid resource and service planning for the care of these patients.

Providing optimal care for advanced HF patients is not just about one team or center. European best practice models highlight the spoke-and-hub model for optimal HF service delivery, where the secondary or local hospital and GP services providing community-based guideline-directed HF treatment and education are reinforced by more specialist cardiac services in tertiary units, who may then liaise with the advanced HF center hub as required, such as provided by the Mater. Ideally, this model would include a bi- or tri-directional pathway for suitable patients where non-Mater centers and units continue to be involved in the care of patients referred early enough to have time for specific conditions, outstanding medical or psychosocial issues and/or education gaps to be addressed. As Chair of the newly formed Advanced HF Subgroup of the National Heart Program, developing and ultimately resourcing these multi-directional clinical pathways is a key goal. In parallel, my second clinical research priority has been to set up a registry of patients referred to and attending our advanced HF clinic, in order to better understand clinical and non-clinical drivers of referral, patient profiles and disease sub-stages at time of referral, and associated outcomes.

No matter how well refined outpatient referral tools can be, advanced HF patients still frequently present acutely, often in a cardiogenic shock state, defined by reduced cardiac output, systemic hypotension, tissue hypoperfusion and increased systemic or pulmonary congestion. In parallel with its transplant and durable LVAD programs, our team at the Mater provides a highly specialized menu of temporary mechanical circulatory support devices, which aim to both support the circulation and ideally offload the compromised left and/or right ventricle until either recovery of native function, progression as appropriate to a durable LVAD or cardiac transplant, or transition to palliative-focused care. The HF cardiologist is at the epicenter of what is typically complex, multi-dimensional decision-making. This clinical arena is one in which contemporary randomized controlled trials are severely lacking; consequently it is my goal that the Mater and associated academic facilities forge strong research links with European institutions to both participate in and ultimately develop multi-center randomized clinical trials to drive forward best practice care for this group of patients.

Finally, when we are considering therapeutic options in advanced HF, it is important to remember that outcomes most important to a particular patient may vary. Survival may be less important to many patients than quality of life, less time in the hospital or not being a perceived burden on their caregivers. While many individual hospitals and regions have options for either in-hospital consultation and/or community-based services, a National palliative care strategy tailored to the specific needs of HF patients remains aspirational currently but hopefully achievable in the near future as a relevant and worthy component of our HF spoke-and-hub model.

At the heart of guideline-directed and patient-centered care for advanced HF patients (whether that route takes them to transplant, temporary and/or durable VADs, continued medical care or a combination) lies the multi-disciplinary team: a melting pot of cardiologists of various specialties, cardio-thoracic surgeons, intensive care, perfusion and anesthesia specialists, immunology, microbiology and pathology specialists, nursing specialists across the various domains of care, health and social care professionals, cardiac physiologists and administration staff. Trainees across all the disciplines also contribute very significantly to the success of the program across the triad of clinical, academic and research domains. In particular, an advanced HF fellowship set up since 2018 has become a lynchpin of the service and drives forward increasing awareness of, and exposure to, all aspects of acute, advanced, chronic and subspecialized intersection-based HF care amongst our Cardiology trainees.

In summary, it has been an incredible few decades of growth for advanced HF care in Ireland, and the future looks even brighter, with several key advances poised to come onstream, including safer patient-device profiles in those undergoing LVAD, alternative donation mode / acceptance criteria protocols to increase the donor pool, and a move toward more individualized post-transplant rejection surveillance and immunosuppression strategies. There is no doubt that the COVID-19 pandemic has brought significant and reverberating challenges across multiple domains of the subspeciality. Despite this, it remains an incredibly exciting time to be part of such a dynamic, expert and multi-disciplinary team able to anticipate and respond to these challenges head on. The final word to Dr Christian Baarnard: “Suffering isn’t ennobling, recovery is.”

CARDIO NEWS

New Research on Heart Muscle Damage

Researchers at CÚRAM, the SFI Research Centre for Medical Devices based at NUI Galway, and BIOFORGE Lab, at the University of Valladolid in Spain, have developed an injectable hydrogel that could help repair and prevent further damage to the heart muscle after a heart attack. The results of their research have just been published in the prestigious journal Science Translational Medicine.

Myocardial infarction or heart disease is a leading cause of death due to the irreversible damage caused to the heart muscle (cardiac tissue) during a heart attack. The regeneration of cardiac tissue is minimal so that the damage caused cannot be repaired by itself. Current treatments lack an effective method to prevent death and subsequent cardiac tissue repair following a heart attack.

"This project involved the development and testing of an elastin-based hydrogel derived from a naturally occurring biomaterial in the human body", explains Professor Abhay Pandit, Scientific Director of CÚRAM at NUI Galway and project lead. The hydrogel is based on a family of unique biomaterials, called elastin-like recombinamers, that BIOFORGE-UVa had developed in the search for advanced hydrogels for regenerative medicine. "The hydrogel was developed to mimic the environment around the heart following an infarction and then customised to have the ability to protect and promote regeneration of the cardiac tissue", says Professor Pandit.

The therapeutic effect of multiple injections of this hydrogel into the cardiac tissue was assessed during the first-ever preclinical study of its kind, demonstrating its efficacy for cardiac tissue remodelling following a heart attack.