Heart transplantation in India—are we there yet?

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“To improve is to change; to be perfect is to change often.”

Winston Churchill

The field of heart transplantation in India has had a chequered history. P.K. Sen and colleagues performed India's first, and the world's fourth, heart transplant way back in 1968 [1]. Astonishingly, this was accomplished on the back of a 100 canine heart transplant experiments, a feat which is unthinkable today [2]. It was, however, only in the year 1994 that the first successful heart transplant from a brain dead donor was done in India at the All India Institute of Medical sciences by Professor Venugopal [3]. This was followed soon after by Dr. K.M. Cherian at the Madras Medical Mission hospital in Chennai. However, till the year 2012, the progress in the field was very slow and only a total of about 30 transplants had been done across the country. The state of Tamil Nadu was the first to streamline the process of organ donation and distribution in a very systematic manner [4], with significant contributions from non-governmental agencies [5]. As a consequence, there was a steady increase in the number of donors and hearts transplanted in the state (Fig. 1). Over the next few years, with increasing awareness, organ donation activities spread across the country (Fig. 2). Annually close to 750 organ donations happen in India, with over 200 heart transplants (Fig. 3). It is certainly a matter of great joy for us that the specialty has matured to a stage where a special issue of the

journal is being brought out with contributions from several eminent specialists in the field.

The challenges faced by the heart transplant community in India are very many. The majority of patients referred for transplant are very sick, with over 75% in Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) category 3 or less in our series (Fig. 4). Waiting-list mortality is high, in the absence of affordable implantable left ventricular assist devices. The only realistic bridging strategies available are veno-arterial extracorporeal membrane oxygenation and short-term assist devices like CentriMag™ (Abbott, Chicago, IL). Paediatric donations are uncommon with no organ donation initiatives in paediatric public hospitals. Organ transport is a very big challenge, both within the city and within the country. There is no funding available for airlifting organs. Ours is the only country in the world, where a donor heart is ferried across a vast geographic area on commercial flights [6]. Several of the cities, where organ donations happen, like Erode and Salem in Tamil Nadu or Nellore in Andhra Pradesh and Nanded in Maharashtra, do not have airports which are functional and the driving time to the nearest big city, where transplant is possible, is often more than 5 h. Helicopters are not only expensive but are mostly unavailable and are not allowed to fly between sunset and sunrise, the time when majority of organ retrievals happen! So what happens to those organs? They are wasted, of course. Transporting very sick patients across the country is an even bigger challenge. Air ambulances are expensive and not well equipped. These planes often have very narrow doors and do not have enough electric outlets for infusion pumps and monitors. Immunological monitoring of transplanted patients is also a very big challenge. Protocol endomyocardial biopsies, as advocated by the International Society of Heart and Lung Transplant, are practically not feasible. Modern blood-based immune monitoring tests like AlloGene mapping, IMMUKNOW

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Fig. 1 Trends, over time, of organ donations and heart transplants in Tamil Nadu

(Cylex Inc., Columbia, MD, USA), and cell-free deoxyribonucleic acid (DNA) are not available. The only reliable tests available are echocardiogram and blood tacrolimus levels. Despite these drawbacks, good outcomes are possible. The Kaplan-Meier survival curve of the first 168 patients done in our unit over a 6-year

period, from October 2012 to January 2018, with a follow-up of up to 7 years is shown in Fig. 5. Out of the 31 patients operated before March 2015, 21 are alive. The 5-year survival was 68% in this particular cohort. INTERMACS status of the patient has a great bearing on the outcomes (Fig. 6). In a Cox proportional

Fig. 2 Map of India showing states with organ donation programmes

STATES WITH ORGAN DONATION PROGRAMMES

Fig. 3 Annual heart transplant numbers in the country

hazard survival estimate, the relative hazard of INTERMACS I and II categories are clearly evident (Fig. 7). The ischemic times have progressively increased over the years, reflecting a practice of procuring hearts from more distant locations (Fig. 8), but this does not seem to impact survival (Fig. 9). A detailed outcome analysis of our adult and paediatric transplants is being published elsewhere.

As the economy of the country improves and more centres embark on this journey, the results can only get better. The quality of life in survivors is excellent. With

increasing transplant activity, there was felt a big need for a dedicated society to address the requirements and aspirations of this speciality. This became a reality with the formation of the Indian Society of Heart and Lung Transplant (INSHLT), with the first conference held in New Delhi, which was very successful with active participation from several members from ISHLT (inshlt.org.in). It is to be hoped that with the establishment of such a society, we will have a national registry of outcome data from several centres, which will help, amongst other things, in having a national database on organ

Fig. 4 Interagency registry for mechanically assisted circulatory support. INTERMACS status of patients referred for transplant

Fig. 5 Kaplan-Meier estimation of medium-term survival of the first 168 heart transplant recipients in our series

utilization. At this time, we have no national data on either the number of transplants performed, number of donations and organs on offer, organs utilised and the reasons for not utilising. The Web sites of the state transplant authorities have some information, but the national figures have to be compiled. The Web site of National Organ and Tissue Transplant Organisation (NOTTO) is spectacularly bereft of any such information. As a consequence, at any meeting, if we provide data that we have collected, we are always

confronted with ... but where are the official figures?? Recently, NOTTO, the central federal agency for overseeing all transplant-related activities in the country (NOTTO director, personal communication), announced the formation of a national-level expert committee to oversee the transplant activity of all the organs including the heart and lungs. This, indeed, is a very welcome step. At the time of writing this article, heart transplants have been done in over a dozen states, a remarkable growth story in just a few years.

Fig. 6 Kaplan-Meier survival curve stratified by INTERMACS category

Fig. 7 Cox regression analysis of effect of INTERMACS category on survival after heart transplant

Cox regression-based test for equality of survival curves

INTERMACS	Events observed	Events expected	Relative hazard
1	7	2.81	3.3314
2	12	5.93	2.7161
3	25	31.86	1.0434
4	6	9.10	0.8703
5	0	0.29	0.0000
Total	50	50.00	1.0000

LR chi2(4) = 12.64

Pr>chi2 = 0.0132

The modern era of mechanical circulatory support started with the first HeartMate II implant in 2012 and a HeartWare HVAD system implant soon after, both in Chennai at the Fortis Malar hospital. Since then, there has been a modest growth in this field, hampered to a very large extent by the fact that there is no public funding or reimbursement possible and the expenses have to be borne by the patient (Fig. 10).

Where do we go from here?

More cardiologists need to get involved in heart failure programmes. Their lack of interest is puzzling. In the

Indian Heart Journal, the foremost journal addressing the needs of the cardiological community in our country, there is not even a subsection on heart failure! Articles on transplantation have to be uploaded in the invasive cardiology section! Liver transplants, which started in India a good decade after heart, are now very commonplace and are being done in several centres across the country in large numbers [7]. They, of course, have the advantage of living donors. Surely, that cannot be the only reason, nor can it be the cost. Liver transplants do not cost any less. Hopefully with time, the interest among the cardiology community will increase leading to earlier referrals of better risk patients.

Fig. 8 The box plot clearly shows the changes in the median ischemic time over two time periods. The whiskers of the plot show the minimum and maximum values and the edges of the box represent the 25th and 75th percentiles. The horizontal line is the median value or the 50th percentile

Fig. 9 Kaplan-Meier survival curve stratified by ischemic time

We need a reference laboratory in every state which can do all the tests that are needed, whether it is a donor-specific antibody or panel reactive antibody tests at a reasonable cost. This has to be a national initiative. We need to engage with the insurance and state funding agencies to cover the cost of heart transplants, so that more patients are able to afford this expensive procedure. State funding for transplants, at this point, is restricted to a few states only. Ideally, every state in the country should have one multi-organ transplant centre

of excellence in a public hospital with state-of-the-art infrastructure.

In this issue, we have excellent contributions from some of the leading authorities in the world. I am certain that you will find them informative, interesting and useful. I sincerely hope that some of the contents of this issue will stimulate young minds in our specialty to perhaps look towards a career in treating patients with advanced heart failure.

Fig. 10 Graph shows the trends in the country in the usage of implantable pumps (CFVAD) and short-term pumps (CENTRIMAG)

Compliance with ethical standards

Conflict of interest The author declares that there are no conflicts of interest.

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