

The 500th Heart Transplant - The Steps That Made Ceará a Reference in Heart Transplants in Brazil

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On February 21, 2023, the heart failure (HF) and transplant program at Hospital de Messejana Dr. Carlos Alberto Studart Gomes (HM) set a landmark with its 500th heart transplant completion. In Brazil, this performance is bested only by the Heart Institute (InCor) at the University of São Paulo (USP), consolidating HM as the second-largest transplant center in the country.

Founded in 1933, HM is a tertiary center specialized in the diagnosis and treatment of heart and lung diseases, with an operational capacity of 463 inpatient beds, 70 of which are in the Intensive Care Unit; the HM integrates the healthcare network of the Secretariat of Health of Ceará (SESA), receiving patients from all 184 cities in Ceará and also from other regions of Brazil, both in the Emergency Department and in the 25 outpatient clinics of the Ambulatory Care Center. (Figure 1)

When South African surgeon Christiaan Barnard performed the world's first human heart transplant on December 3, 1967, in South Africa, the procedure was largely considered experimental, and no effective immunosuppressive therapies were available. Just six months later, on May 26, 1968, Dr. Euryclides Zerbini performed the first heart transplant in Latin America at the USP Medical School. However, it was only in the 1980s, with the introduction of cyclosporine, that the field of transplantation gained new momentum and worldwide interest. In Brazil, the inaugural transplant of this so-called “cyclosporine era” was performed in 1984 by Dr. Ivo Nesralla at the Institute of Cardiology of Rio Grande do Sul (ICFUC/RS).

The Beginning of Heart Transplantation in Ceará

The first heart transplant in Ceará occurred in the “cyclosporine era” at Hospital Antônio Prudente on



Figure 1 – Hospital de Messejana Dr. Carlos Alberto Studart Gomes.

February 20, 1993. The team consisted of surgeons José Glauco Lobo Filho (Figure 2A), João Martins de Souza Torres, Francisco Martins de Oliveira, José Maria Furtado Memória Junior, and Haroldo Brasil Barroso, in addition to Dr. Ricardo Lagreca (Natal/RN) as part of the Northeast Program for Heart Transplantation (NE-Tx). João David de Souza (Figure 2B) Neto was the clinical cardiologist, and Fátima Sales and Miguel Arraes were the anesthesiologists. At that time, the NE-Tx provided support by sending collaborators with previous experience in the area, hence the valuable contribution of Dr. Lagreca from Natal.¹ The NE-Tx assisted services from Sergipe, Alagoas, Pernambuco, Bahia, Rio Grande do Norte, and Ceará were discontinued after a few years.

In 1997, still at Hospital Antônio Prudente, a team composed of surgeons Juan Alberto Cosquillo Mejia, Valdeste Cavalcante Pinto Júnior, Waldemiro Carvalho Júnior, Fernando Antônio de Mesquita and Haroldo Brasil Barroso, and anesthesiologist Rogean Nunes, in addition to cardiologists João David de Souza Neto and Patrícia Lopes de Sousa continued the heart transplant program in Ceará. On April 8, 1998, the same group and the pediatric cardiologists Klébica Castelo Branco and Ricardo Sardenberg were responsible for launching pediatric and neonatal transplantation in the North/Northeast regions.

Keywords

Heart Failure; Heart Transplant; Article Historic

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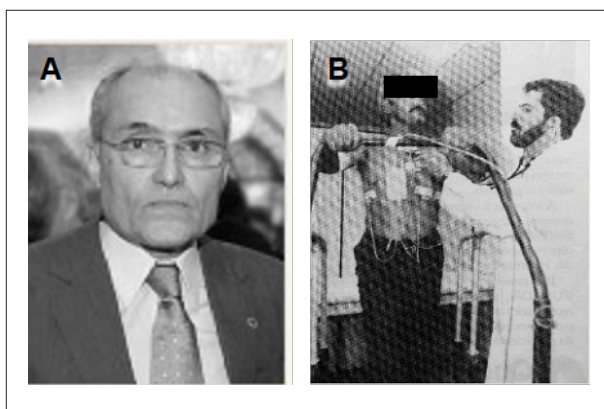


Figure 2 – A) Dr. José Glauco Lôbo Filho; B) Dr. João David de Souza Neto with the second transplanted patient in Ceará (1994).



Figure 3 – Drs. Juan Mejía and João David receiving tribute at the Legislative Assembly.

Accreditation of the Heart Failure and Transplantation Unit of Hospital de Messejana

The establishment of the CNCDO-CE (Central for the Notification, Procurement, and Distribution of Organs and Tissues of Ceará) on June 9, 1998 (SESA Ordinance 797/98) was an important milestone for organ and tissue transplants in Ceará. Nephrologist Eliana Régia Barbosa coordinates the CNCDO-CE and has more than 60 notification centers registered in the National Transplant System. Faced with the success at the Hospital Antônio Prudente, the transplant team organized itself to accredit HM as a transplant center, meeting the CNCDO-CE requirements.

In October 1998, the Heart Failure and Transplantation Unit (UTIC) of the HM was created, with a comprehensive multidisciplinary team that includes nurses, a social worker, a psychologist, a nutritionist, and a secretary, in addition to the complementary services of the HM in anesthesia, dentistry, infectology, pathology, echocardiography, hemodynamics, hematology, pharmacy, physiotherapy and rehabilitation. Currently, the UTIC has a 28-bed medical ward (unit I), a meeting room, 5 outpatient rooms, and its own service desk. Since the program's accreditation, Drs. João David de Souza Neto and Juan Alberto Cosquillo Mejía have been in charge, actively participating in the Technical Chambers of the Ministry of Health and elaborating guidelines, including Brazilian guidelines for HF, heart transplantation, and circulatory assistance mechanics.²⁻¹¹ (Figure 3)

On January 4, 1999, a 39-year-old carpenter named Antônio Pereira de Moura became the first patient to have his heart transplanted at HM, marking the dawn of a new era in cardiology in Ceará. (Figure 4A) A 36-year-old woman donated the organ after a diagnosis of brain death in HM's respiratory ICU; with both recipient and donor placed side by side, the procedure was carried out with a successful ischemia time of less than 90 minutes. Curiously, Moura also debuted the list of HM retransplants after presenting late ventricular failure due to cardiac allograft vasculopathy in 2005. (Figure 4B) The first pediatric heart transplant at HM took place on January 18, 2002; currently, the hospital is recognized for having the second busiest heart transplant program for children in the country.

In July 2001, the 'Prof. Dr. Antônio Lacerda Machado' Research and Experimental Surgery Center (CENPEX) was inaugurated, coordinated by Dr. José Maria Furtado Memória Júnior. CENPEX was responsible for enhancing learning in surgery, especially in transplants, through courses on animal models for heart transplantation. Also during this period, training workshops on heart transplantation were held, supervised by the multidisciplinary team of the Dante Pazzanese Institute of Cardiology under the leadership of Drs. Ricardo Manrique, Jarbas Dikuynsen, and Marco Aurélio Dias da Silva. Fourteen years later, in December 2015, HM itself engaged in actions aimed at disseminating knowledge through the Brazilian Ministry of Health platform for training programs in mechanical circulatory support and cardiac transplantation. The mentoring program was proposed and coordinated by Dr. Juan Mejía with the collaboration of the physiotherapist Maria do Socorro Quintino Farias; it lasted 2 years and consisted of a group of 60 students composed of clinicians, surgeons, nurses and social workers from 5 centers: Hospital Universitário de São Luis (MA), Hospital Ana Nery de Salvador (BA), Hospital Meridional de Vitória (ES), Hospital dos Servidores do Estado (RJ) and Hospital do Coração de Natal (RN).

Routines of the Heart Transplant Program at Hospital de Messejana

Although HM follows most of the routines proposed by the International Society for Heart and Lung Transplantation (ISHLT) guidelines, some particularities are specific to the context in which it operates. The three main indications for heart transplantation are dilated (32%), ischemic (25%), and chagasic (17%) cardiomyopathy.¹² Except for the first 5 cases, all transplants were performed using the bicaval technique; in addition, all patients received a standard 3-drug immunosuppressive regimen with tacrolimus, mycophenolate (mofetil or sodium), and corticosteroids. Azathioprine was never used in the program, and tacrolimus is only converted to cyclosporine or a proliferation signal inhibitor, such as everolimus or sirolimus, in cases of refractory hyperglycemia, renal dysfunction, or persistent rejection.



Figure 4 – A) Antonio Pereira de Moura, the first heart transplant recipient at Hospital de Messejana; B) Antonio Pereira de Moura completing 20 years of transplantation on 04/01/2019.

After 6 months, prednisone is weaned when possible, and while immunosuppression with mycophenolate has been associated with a higher rate of *Trypanosoma cruzi* reactivation,¹³ the HM protocol does not require mycophenolate dose adjustment or mandatory switch to azathioprine in chagasic patients. Search for acute rejection and suspected cases of Chagas disease reactivation are monitored employing routine surveillance endomyocardial biopsies (EMB) according to established international standards. However, despite the ISHLT guidelines recommending approximately 14 EMB per patient in the first post-transplant year,¹⁴ the frequency of EMB at HM in the first year after heart transplantation has been considerably lower, roughly 3 to 5; this is due in part to financial restrictions but mainly to the risk of severe complications associated with EMB, including ventricular perforation and EMB-related tricuspid valve damage.¹⁵ Even so, Chagas disease rejection or reactivation rates are not higher than those reported in surveys by other services.¹²

The median survival of HM transplanted patients is 9.5 (95%CI, 8.5 – 10.5) years, with overall survival rates at 1, 5, and 10 years of 73%, 60%, and 46%, respectively.¹² The main cause of post-transplant death in HM is infection (36%), followed by rejection (27%) and graft vascular disease (20%).

Artificial Heart in the Northeast

With the official launch of the Artificial Heart Program by the Government of the State of Ceara in March 2008, HM was a pioneer in the field of mechanical circulatory support (MCS) devices in Northeast Brazil, with the implantation of an AB5000 as a bridge to transplantation (BTT). (Figure 5) Between 2008 and 2019, 19 adult patients underwent implantation of an MCS as a BTT, of which 8 CentriMag (Thoratec Corp, Pleasanton, CA), 6 AB5000 (ABIOMED Inc, Danvers, MA), and 5 venoarterial extracorporeal membrane oxygenation (VA-ECMO, Maquet Getinge Group, Rastatt, Germany), with median support of 18 days (ranging from 0 to 176 days).^{12,16}

In 2012 and 2015, a partnership between surgeons Juan Mejía and Cristiano Caldeira (from Tampa General Hospital) resulted in the Pan American Workshop for



Figure 5 – First patient to receive an MCS (AB5000) as a bridge to transplant. After a successful heart transplant, he currently leads a normal life in the countryside.

Mechanical Circulatory Support & Heart Transplant at the Center for Advance Medical Learning e Simulation (CAMLS) in Tampa (Florida/USA). Around 200 professionals from all over Brazil (18 from Ceará) and Latin America were present at the first symposium.

The Messejana Hospital and the UTIC during the COVID-19 pandemic

Even during the COVID-19 pandemic, the CNCDO-CE and the UTIC program remained active, following the Brazilian Association of Organ Transplants (ABTO) protocols. (Figure 6) Due to the reallocation of beds and human resources, the UTIC assumed preferentially remote assistance between March and July 2020, supporting 504 patients at distance: 361 with HF and 143 with transplants. This number represents an approximate reduction of 48% of the 972 patients seen in the same period of the previous year. During remote follow-up, the hospitalization rate of patients with HF declined from 24% to 12%, while that of transplant recipients increased from 10% to 20%. This finding can be explained by the large number of procedures that transplant recipients have to undergo in the first months and years after transplantation, including EMB and rescue immunosuppressive therapies, which in general require hospitalization.¹⁷

Although there was no difference in reported deaths between 2019 and 2020, there was a relative increase of 5 times more deaths in HF patients hospitalized during the pandemic. This may be due to greater prioritization for hospitalized individuals with more severe disease and a worse prognosis.

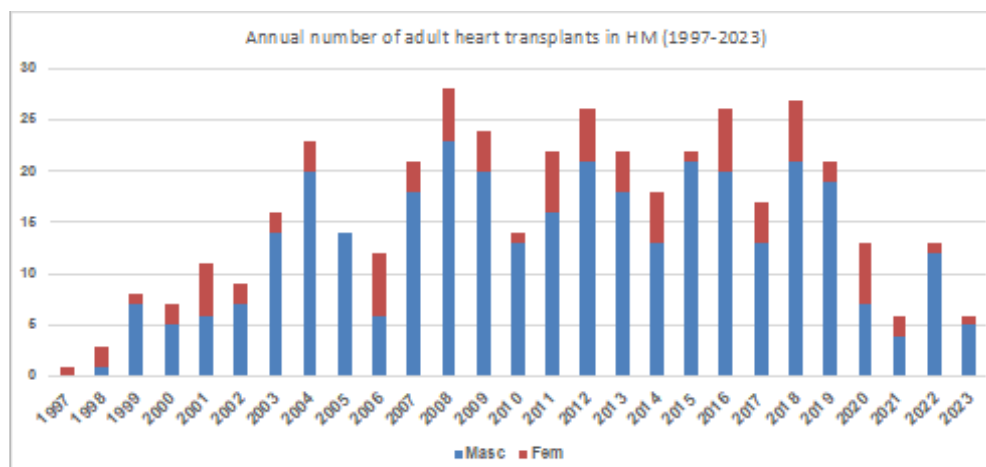


Figure 6 – Annual number of adult heart transplants in HM (1997-2023) according to gender, with a significant reduction during the COVID-19 pandemic.

Conclusion

Brazil has the world's largest public organ transplant system in the world. The history of HF and heart transplantation in Brazil is intertwined with the history of cardiology in Ceará and HM. Over 25 years, HM has added procedures and services incorporated after the transplant program, including 24-hour availability of echocardiography and interventional cardiology services and its own pathology laboratory.

The UTIC grew, becoming a reference for patients who did not have a specialized outpatient clinic in Brazil and receiving recurring recognition by the Best Practice in Cardiology (BPC) program, the result of a tripartite collaboration of the American Heart Association, the *Sociedade Brasileira de Cardiologia* and the Brazilian Ministry of Health.¹⁸

For this to happen, we owe gratitude to the entire clinical and multidisciplinary team and complementary sectors, directors, health secretaries, and governors. A special acknowledgment and gratitude to the family members and, above all, to the donor, who is essential for the success of the organ transplant (Figure 7).

Author Contributions

Conception and design of the research: Vieira JL, Sobral MGV, Alves VM, Almeida GPL, Fernandes JR, Sugette JFV, Ximenes ALP, Mejia JAC, Souza Neto JD; Acquisition of data: Vieira JL, Sobral MGV, Alves VM, Almeida GPL, Fernandes JR, Marinho LLE, Vasconcelos GG, Trompieri DFM, Santos GS, Diniz RMV; Analysis and interpretation of the data: Vieira JL, Mejia JAC, Souza Neto JD; Writing of the manuscript: Vieira JL, Santos GS, Diniz RMV, Sugette JFV, Ximenes ALP, Mejia JAC, Souza Neto JD; Critical revision of the manuscript for important intellectual content: Vieira JL, Mejia JAC, Souza Neto JD.

Potential conflict of interest

No potential conflict of interest relevant to this article was reported.

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Study association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

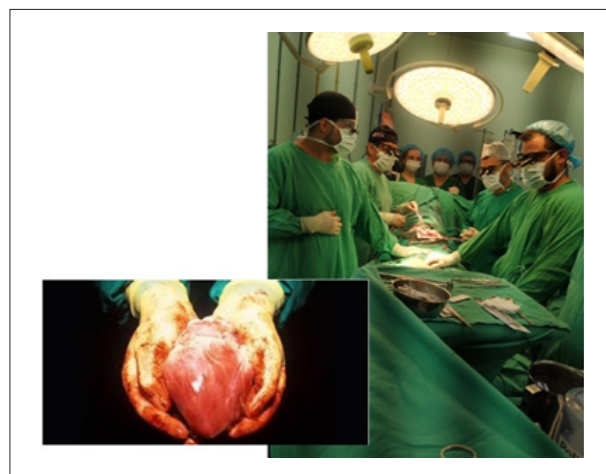


Figure 7 – The 500th heart transplant.

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