ORIGINAL ARTICLE

THORACIC SURGERY – NOTES FOR ITS HISTORY IN BRAZIL (PART II): LUNG TRANSPLANTATION

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INTRODUCTION

"What magic exists in this activity that keeps these strange types awake, operating all night long, and when day breaks they seem intoxicated by the adrenaline that still insists on circulating?"

José Camargo, thoracic surgeon

Lung transplantation is indicated to improve the quality of life of selected patients who suffer from advanced chronic respiratory insufficiency without responding to other medical interventions. Lung transplantation is well established from the standpoint of operative technique and continues at full pace in Brazil, with new programs being created.

An example comes from the recent pandemic, when lung transplantation was offered as therapy for some patients with COVID-19 who presented persistent respiratory insufficiency, despite several weeks or months of support in the intensive care unit[1-3].

Pulmonary transplantation arrived in Brazil after being well grounded in operative technique, in the use of anti-rejection drugs, as well as advances in pulmonary preservation, allowing longer ischemia time with less reperfusion injury[4]. Consistent with this fact, there was advancement in understanding the mechanism of rejection and infection.

The first Brazilian pulmonary transplant occurred in Porto Alegre, in May 1989. It was also the first in Latin America. The author was José de Jesus Peixoto Camargo, surgeon at the Pereira Filho Pavilion of the Santa Casa of Porto Alegre. It was a 27-year-old man, suffering from bronchiolitis obliterans, who received a left lung transplant and survived more than nine years, dying from infectious complications resulting from bronchiolitis and bronchiectasis, associated with pulmonary tuberculosis that he developed eight years after the transplant.

From then on, more Brazilian centers created transplant programs. The implementation of each service incorporated infrastructure that guaranteed multidisciplinary care. The emphasis of these programs was due to: care for the donor, selection of recipients, adequate rehabilitation of candidates during the waiting time, anesthetic and surgical training in the management of pertinent technical peculiarities, highly qualified intensive care, and follow-up of a regulated, inflexible, and permanent postoperative protocol. Thus, one understands how we arrived at the current moment to be reported in the form of history.

The historiographic material (method) collected by the authors was based on reading scientific texts, informative materials, and oral reports. It follows the methodological line of the previous article[5](Part I) whose events served to build the history of the specialty in Brazil, under the pioneering work of José de Jesus Peixoto Camargo.

We will divide the history of transplantation in Brazil into acts, just as in Part I, taking as reference relevant points of scientific evolution, up to the present day.

ACT 1: HISTORY OF LUNG TRANSPLANTATION IN BRAZIL

"Regardless of what stimulus may have moved them, they are all irreversibly contaminated by the unquenchable need to expand their own limits, convinced that the energy that springs from this obstinacy will justify their lives."

José Camargo, thoracic surgeon

The history of lung transplantation in Brazil begins with experimental work in the early 1970s. Noteworthy is the thesis by Eimar Delly de Araújo entitled "Lung Transplantation: technical problems and evaluation of immediate results," defended at the Federal University of Rio de Janeiro, with the objective of evaluating the feasibility of the operative technique. Araújo was the leading thoracic surgeon at the Marcílio Dias Hospital[6].

If the experimental works were the first steps

toward the sedimentation of lung transplantation, what really motivated them was the success of cases in Canada, starting in 1983. It wasn't long before the first pulmonary transplant in Brazil occurred in 1989, in Porto Alegre.

With the arrival of cyclosporine, Brazilians became enthusiastic about the idea of performing transplants in various areas. Encouraged by the Canadian results, José Camargo decided to seek details of the pulmonary technique, as well as the clinical elements to support the idea to implement it in Brazil, even knowing that the lung was the worst organ to be transplanted, due to complications evidently more frequent than with other transplants. Therefore, he knew there was a long way to go until its definitive incorporation into the modern therapy of advanced pulmonary diseases.

The pulmonary transplant program remains active at the Pereira Filho Pavilion of the Santa Casa de Misericórdia of Porto Alegre, and José Camargo continues as coordinator. José Camargo, in addition to being a thoracic surgeon at the Santa Casa de Misericórdia Hospital of Porto Alegre, became, in 2012, a professor-doctor at the Federal University of Rio Grande do Sul (UFRS) with the thesis "Bronchial complications in lung transplantation: predictive factors and therapeutic alternatives."

From that first case, some centers followed with implementation in Brazil and lung transplantation gained greater dimension, giving greater diversity to thoracic surgery and pneumology. For most thoracic surgeons in Brazil, that end of the decade would give to the following one, the radiance of one of the most brilliant pages of Brazilian medicine.

As early as 1990, isolated cases were observed at the Escola Paulista de Medicina (Vicente Forte and José Ernesto Succi) and in Belo Horizonte (Fernando Eloi de Almeida); however, these experiences did not gain continuity, nor did similar isolated efforts by surgeons elsewhere in the country.

When analyzing this thread of history, the idea becomes clear that transplant centers tend to be long-lived and obtain better results when there is multidisciplinarity. The following are fundamental: pulmonologists, infectious disease specialists, nurses, physiotherapists, nutritionists, social workers, and psychologists for patients on the waiting list and in the postoperative period. Thus highlighted Adib Jatene, cardiovascular transplant surgeon and professor at the University of São Paulo (USP): "I don't believe in people who save, but in structures that work."

In 1990, one of the structures that became established was the Hospital de Clínicas of USP, which performed nine unilateral transplants. They had a five-year pause and, in 2000, moved to INCOR-USP, today led by Paulo Pego-Fernandes, to resume the program and consolidate it as one of the most important transplant centers in Brazil and the world. In 2003 they performed the first double lung transplant, and since then they have continued innovating without stopping8. In March 2012, the group achieved a notable feat: the first transplant in Brazil and Latin America using a lung reconditioned by ex vivo pulmonary perfusion (EVPP). The method restores lungs from donors, initially rejected, and they become feasible to be implanted in the recipient, increasing the organ utilization rate.

In Rio de Janeiro, in November 1999, Carlos Henrique Boasquevisque, after long and fruitful training in Toronto, returned to Hospital do Fundão of the Federal University of Rio de Janeiro and formed a group in partnership with the Pulmonology departement. They performed 29 transplants with good results until the end of the program in 2007. After a pause of almost 14 years, Rio de Janeiro resumed lung transplantation in the private network.

Next, the Hospital de Clínicas of the Federal University of Minas Gerais, starting in 2003, performed a series of 22 cases, led by Silvio Paulo, Nilson Amaral, and Guilherme Ribeiro. One of the mentors of the program was the pioneer José Camargo. Then the trio traveled to Toronto for improvement. The program as since been deactivated, however it is already being reconditioned for a second phase, and José Camargo returns to be the mentor of this new era.

In 2009, the Hospital de Clínicas of Porto Alegre, which has an academic link with the Federal University of Rio Grande do Sul, hosted the first lung transplant, done by Amarilio Macedo. Cristiano Feijó, current coordinator, was part of the initial team, whose academic training in transplantation occurred at the Santa Casa de Misericórdia of Porto Alegre itself, under the auspices of José Camargo. Today, in addition to pulmonologists and intensive care physicians, there is a solid multidisciplinary team with a nutritionist, psychologist, nurse, social worker, and physiotherapist maintaining the program breathing without difficulties.

Outside the south-southeast axis, Fortaleza, led by Antero Gomes Neto, created a transplant center at Hospital de Messejana in 2011, giving the north-northeast region the opportunity to be part of this important chapter of Brazilian surgery9. The program was also inspired by Porto Alegre, given that Gomes Neto was an intern at the Pereira Filho Pavilion and an eyewitness to the first Brazilian case. The first case in the state of Ceará was of a 46 year old patient, suffering from pulmonary emphysema. The Service remains structured and is now led by Israel Medeiros, trained by the INCOR-USP group (São Paulo).

In the COVID-19 pandemic, in November 2020, Marcos Samano and the transplant group at Hospital Albert Einstein performed the first lung transplant in a patient who had been on mechanical ventilation for three months and another three months on ECMO. It was not the only case. Samano himself and more institutions and services continued performing transplants because of COVID-19.

ACT II: THE PIONEER'S VIEW

"To compensate for all the effort expended there is the most genuine of gratitudes, that of one who is grateful for life.

José Camargo, thoracic surgeon

It was during an American congress in 1986, when the Toronto group presented the first results of lung transplantation, that José Camargo decided he would do the same at Santa Casa of Porto Alegre, contaminated as he was with the embryonic idea from the 70s, when he did

experimental work in the laboratory of the Cardiology Institute of Porto Alegre. For three consecutive years he participated in all the seminars organized by the Toronto group, and in parallel began the preparation of the Pereira Filho Pavilion, of the Santa Casa de Misericórdia, to receive the challenge. The starting point was the creation of an Intensive Care Unit with regular shifts with trained intensive care specialists.

Even before they were ready, they already had a listed patient. In November 1988, a 27-year-old young man, from Vargeão do Oeste, in Santa Catarina, was admitted to the hospital, from which he would never leave again, unless his destroyed lungs could be replaced. The suffering but hopeful presence of that young man represented an important increase in responsibility and anguish for the group, which began to live with a patient whose life depended on how bold and competent they could be. Waiting list meant the expectation for a donor, a figure, at that time, as eagerly awaited as feared.

On May 15, 1989, José Camargo was informed of the existence of a patient from Novo Hamburgo, close to Porto Alegre, with head trauma, transferred from the Emergency Room to Hospital São Francisco, at Santa Casa, with the confirmed diagnosis of brain death. The blood type, chest size, and pulmonary function were adequate for the transplant. There were hours of great expectation while the final immunological compatibility tests were being performed.

At 10 p.m. they were informed of the compatibility. The young patient from Vargeão alternated between laughter and tears when he was prepared for surgery. Shortly after midnight, they went to the surgical center of Hospital São Francisco, where the abdominal transplant teams (Santo Vitola, Guido Cantisani and Maria Lucia) received them with a kindness capable of easing the fear of a beginner. Camargo reported: "I suspect they have no idea how grateful I am for that reception."

After the left lung was removed - soon placed in a basin, immersed in chilled saline and protected by sterile drapes - the journey back to the Pereira Filho Pavilion began, embracing the precious cargo. At that time the current walkways did not exist, so that, without direct access, along with Dagoberto Godoy, one of the clinicians involved in the program, they traveled the long route inside the Santa Casa, to the central courtyard; then through the external corridor to the Pereira Filho Pavilion. It was a cold autumn dawn, but probably the trembling had nothing to do with the temperature. He reported in one of his writings: "on this long journey, being as we were, two fraternal and supportive partners, we had not exchanged a single word. Today the explanation is obvious: we were in panic." And certainly only the overflowing adrenaline was capable of antagonizing the fear that, otherwise, would paralyze them.

From the moment of arrival in the operating room, a series of valuable realizations emerged: the indispensability of competent and trustworthy partners, the importance of the team's extensive experience in highly complex procedures, and, above all, the recognition that the most critical moments of a surgeon's life are inevitably experienced in profound solitude.

The complete silence of the team during the procedure, punctuated only by anticipation of the next announced step, confirmed that the greatest solitude belonged to the one who made the decisions.

When, after the implant was completed, the lung expanded, oxygenation normalized, and everything else seemed wonderful, the transformation emerged: everyone, excited, started talking at the same time, because from that point on, everyone knew what to do. The generalized exultation after completing the procedure, the embraces of solidarity, the uncontained emotion of José Felicetti (surgeon), the euphoria of Artur Burlamaqui (anesthesiologist), the joy of Leduína, responsible for cleaning the surgical block at dawn. Everything was archived with the care that definitive experiences deserve, which certainly placed May 16, 1989 as a milestone in Brazil's achievements and a dividing line in their lives as doctors.

José Camargo wrote: "Six hours after the transplant was finished, it would already justify our decision to run all the risks, even knowing that, whatever happened, we would never be the same again. But one cannot forget the emotional density of having been, for hours, divided between the fragile courage to do it and the terrifying fear of not succeeding."

Regarding that donor cadaver, José Camargo recently wrote: "This is the feeling that manages, in the consecration of kindness, to occupy the shattered heart of one who, at the limit of atrocious suffering, sublimates their pain to spare unknown families. Enchanted by what generosity can do, I continue looking for a gesture of love greater than this. In vain, until now."

ACT III: LIVING DONOR TRANSPLANTATION

"There will never be a stronger doctor-patient relationship, nor a more definitive partnership than this one that was born from the certainty of timed death, and raced against time and materialized in the reconquest of life with dignity."

José Camargo, thoracic surgeon

José Camargo was also a pioneer in living donor pulmonary transplantation. The first performed outside the USA. Date: September 17, 1999, ten years after that first transplant. This journey began in January 1997, when he participated in a course at the American Congress of the STS (Society of Thoracis Surgeons), in Los Angeles. The enthusiasm of Dr. Vaughn Starnes, an important American transplant surgeon, was contagious. The technique seemed quite simple for someone who already had considerable experience in pulmonary transplantation with cadaveric donors. From then on, in all the many lower lobectomies performed, for the most varied indications, he began to dissect the vessels of the lobe that was going to be removed with the eyes of someone who thinks that one day he might reimplant it in another patient.

Soon after, a patient appeared who showed up with frightening bronchiolitis and dyspnea that only allowed him short phrases and forced him to sleep leaning over pillows.

Figure 1 *José Camargo and Jesse Teixeira with residents (1989), in a meeting in Rio de Janeiro, after second lung transplant case.*

With that shortness of breath he did not even tolerate the supine position, which forced him to be anesthetized on his knees on the operating table, because he could not tolerate the supine position.

It was Bruno Palombini, pulmonologist, who presented the case, with the story that he had already consulted the California group who had considered the indication correct for living donor transplantation. It was the moment, as there were already conditions for such a surgery.

The support of the clinical team was decisive during that entirely unprecedented preoperative period, in which two healthy individuals would be surgically mutilated so that their beloved son might have one final chance of survival.

The clinical team was led by Beatriz Moraes and Marlova Caramori, supportive and friendly to the point that none of them issued any kind of criticism for entering that type of adventure. But, more than generous, they seemed confident that they were doing the right thing, and they were moved by the suffering of that child. They displayed competence in managing a situation that has as a crushing characteristic the total absence of margin for errors. Twelve more transplants occurred with this duo, until the arrival of a new team.

That was something new and exciting to the point of changing the benchmarks of normality. José Camargo confessed in one of his texts that, despite great experience in pediatric surgery, accustomed to exchanging reassuring caresses with distressed parents at the door of the surgical block, he only truly realized the size of the predicament they were in when, for the first time, an entire family entered to be operated on.

It was six hours driven by pure adrenaline, supported by impeccable anesthesia conducted by Artur Burlamarqui and Fabio Amaral, and which counted on the invaluable help of Fernando Lucchese, who brought the best extracorporeal machine they had in the house to actively participate in the operation. Then he continued with Aldemir Nogueira, who from then on took on the task.

José Carlos Felicetti was his surgical partner for about 30 years in which he proved to be the best and most reliable partner anyone could have. Then Spencer Camargo arrived, who was also fascinated by the idea of transplantation, along with some residents in training. Some of these residents followed the long mission of transplanting lungs in other lands.

Twenty-four hours after the first living donor transplant, the patient was extubated and the initial evolution was very smooth, until after an acute rejection, there was information that there was tuberculosis in the right lung removed for transplantation. Tuberculostatic drugs were immediately started, frightened by the idea that he had been using immunosuppressive drugs and with potentially circulating bacilli.

Two weeks after the transplant, on a beautiful sunday morning, the boy woke up screaming in pain and saying he couldn't feel his legs. It was a side effect of cyclosporine, which is neurotoxic in children. When he was discharged from the hospital, they knew they would never be the same again and that new and crushing challenges were on the way. After that there were unforgettable victories and devastating defeats.

FINAL ACT

"Certainly the fascination of an activity in which the line between success and failure is so narrow, contributed to attracting restless spirits and promised to cradle them with emotions that cannot be understood by the complacent and that conflicts with the belief of those who think that peace is synonymous with happiness."

José Camargo, thoracic surgeon

Brazil adopted pulmonary transplant surgery after the arrival of cyclosporine to combat rejection. The pioneering work at Santa Casa of Porto Alegre occurred in May 1989, followed by cutting-edge centers: São Paulo, Rio de Janeiro, Belo Horizonte, Porto Alegre (Hospital de Clínicas) and Fortaleza.

Today Brazil is one of the major lung transplant centers in Latin America and the world, whose results are encouraging and stimulating for a generation of promising surgeons.

It is hoped that the current lineage of fellow thoracic surgeons may find some inspiration in this historiographic testimony and that pulmonary transplants gain more support in health policy, so that it can stimulate and encourage more surgeons to continue advancing. And that all patients with advanced pulmonary diseases who meet the clinical indication criteria can benefit from this therapeutic measure, above all challenging.

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