










# The Importance of Reconstituting the Bodies of Organ and Tissue Donors: a Look at Human Dignity

Carlos Alexandre Curylofo Corsi<sup>1\*</sup> , Alan Vinicius Assunção-Luiz<sup>2</sup> , Leonardo Monteiro-Silva<sup>3</sup> , Katia Carmen Gabriel Scarpelini<sup>1</sup> , Rodolfo Leandro Bento<sup>1</sup> , Mayara Segundo Ribeiro<sup>3</sup> , Flávio Luis Garcia<sup>1</sup> ,  
Luís Gustavo Gazoni Martins<sup>1</sup> 

1. Universidade de São Paulo  – Faculdade de Medicina – Hospital das Clínicas – Ribeirão Preto (SP) – Brasil.

2. Comprehensive Health Research Centre – National School of Public Health - Lisboa – Portugal.

3. Centro Universitário Estácio – Ribeirão Preto (SP) – Brasil.

\*Corresponding author: [carlos\\_ccorsi@hotmail.com](mailto:carlos_ccorsi@hotmail.com)

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## ABSTRACT

**Introduction:** Family refusal to authorize the donation of human organs and tissues has remained high over the years. Among the many reasons for not donating, we highlight the lack of information about the process and the family's lack of knowledge about the donor's wishes in life, as well as other issues, such as the appearance of the donor's body after donation. In this sense, it is necessary to bring to light the aspects that permeate the concepts of death, human dignity, and care for the donor's image, especially in the case of tissue donors, where the removal may be more noticeable. **Objectives:** An integrative literature review (ILR) was carried out, seeking to highlight gaps and characterize the process of donating human organs and tissues, with a focus on the reconstruction of the donor's body and human dignity. In addition, the aim was to describe the experience of a professional from a human tissue bank (BTH). **Methods:** Using the PICO strategy, the study's guiding question was drawn up following an IR carried out over the last 10 years, operationalized by controlled descriptors in the SciELO, LILACS, Google Scholar, and PubMed databases. In addition to the search, an experience report was described on the techniques used to reconstruct the donor's body after the tissues used by a BTH located in the interior of the state of São Paulo were harvested. **Results:** Nine specific studies were found on donation and the use of prostheses to reconstruct donated areas. The results show the reasons for family refusal, as well as the care taken by the technical teams in reconstructing donors' bodies. The family's concern about the donor's aesthetic situation influences acceptance for donation, so it is necessary to invest in the safety and quality of the services provided by BTH to reduce family refusal for donation. **Conclusion:** Clear communication and the safety of the processes involved in the procurement of human organs and tissues proved to be the best way to facilitate donation and could thus increase donations.

**Descriptors:** Tissue Donors; Obtaining Tissues and Organs; Collecting Tissues and Organs; Cadavers; Tissue Banks.

## *A Importância da Reconstituição do Corpo de Doadores de Órgãos e Tecidos: um Olhar Sobre a Dignidade Humana*

## RESUMO

**Introdução:** A negativa familiar para autorização da doação de órgãos e tecidos humanos mantém-se elevada ao longo dos anos. Dentre as muitas causas de não efetivação da doação, destacam-se a falta de informação sobre o processo e o desconhecimento da família sobre o desejo do doador em vida, além de outras questões, como a aparência do corpo do doador após a captação. Nesse sentido, torna-se necessário trazer à luz da discussão os aspectos que permeiam os conceitos de morte, dignidade humana e zelo pela imagem do doador, principalmente no caso de doadores de tecidos, nos quais a retirada pode apresentar-se mais perceptível. **Objetivos:** Realizou-se uma revisão integrativa da literatura (RI), buscando evidenciar lacunas e caracterizar o processo da doação de órgãos e tecidos humanos, com foco na reconstrução do corpo do doador e na dignidade humana. Em complemento, também se propôs descrever um relato de experiência de um profissional de um banco de tecidos humanos (BTH). **Métodos:** Por meio da estratégia PICO, elaborou-se a questão norteadora do estudo, após a RI realizada nos últimos 10 anos, operacionalizada por descritores controlados nas bases de dados SciELO, LILACS, Google Acadêmico e PubMed. Adicionado à busca, foi descrito um relato de experiência referente às técnicas de reconstrução do corpo do doador após a captação dos tecidos utilizados por um

BTH localizado no interior do estado de São Paulo. **Resultados:** Foram encontrados nove estudos específicos sobre doação e utilização de próteses para reconstrução de áreas doadas. Os resultados demonstram os motivos que envolvem a recusa familiar, assim como o cuidado que as equipes técnicas têm na reconstituição do corpo dos doadores. A preocupação da família em relação à situação estética do doador influencia a aceitação para doação, portanto, torna-se necessário investir na segurança e na qualidade dos serviços prestados pelos BTH, a fim de diminuir a recusa familiar para doação. **Conclusão:** A comunicação clara e a segurança dos processos que envolvem a captação de órgãos e tecidos humanos mostraram-se o melhor caminho para facilitar a doação, podendo, assim, aumentar as doações.

**Descritores:** Doadores de Tecidos; Obtenção de Tecidos e Órgãos; Coleta de Tecidos e Órgãos; Cadáver; Banco de Tecidos.

## INTRODUCTION

The donation of human organs and tissues is a surgical procedure that involves the removal, allocation and processing of viable and harmless organs and tissues after family consent in the case of donors with brain death and/or cardiorespiratory arrest<sup>1</sup>. In this way, a single deceased individual can help or save countless lives, reaching more than 20 people, mainly through tissue donation<sup>1-3</sup>.

Organ and tissue donations constitute a safe and effective therapeutic alternative to treat various diseases and clinical conditions, providing a better quality and perspective of life for recipients<sup>2</sup>. In specific cases of tissue use, these present a higher rate of effectiveness and success in transplants, as they do not require donor-recipient histocompatibility, thus presenting lower rejection rates<sup>1,3</sup>. As with organs, the demands for tissue transplants also arise from the consequences of acute and chronic problems caused by various situations, being an increasingly common practice in surgical centers<sup>4,5</sup>.

In recent years, even though it is still insufficient to cover the entire waiting list, there has been an increase in the number of human tissue donors across the country<sup>4</sup>. According to the Brazilian Association of Organ Transplants (*Associação Brasileira de Transplantes de Órgãos-ABTO*), The primary human tissues used in transplantation are corneas, skin, amniotic membrane, valves, bones (femur, tibia, fibula, radius, humerus, ulna, among others), tendons, ligaments, menisci, fascia, cartilage, etc<sup>4,6</sup>.

In the legal sphere, human tissue banks (HTB) are understood as services that have physical facilities and adequate material and human resources, which are responsible for identifying potential donors, also carrying out family interviews, collection, reconstruction of the donor's body, donor, processing, storage and distribution of tissues of human origin, for therapeutic and/or scientific purposes<sup>5-8</sup>. In Brazil, only five accredited HTBs are responsible for harvesting musculoskeletal tissues, located in large centers in the states of São Paulo, Rio de Janeiro, Santa Catarina, and Paraná<sup>6,7</sup>.

HTBs are most requested by orthopedics and dentistry centers, mainly due to the bone tissue (musculoskeletal) available, which can be used in grafting techniques<sup>8</sup>. However, researchers have already shown that more than just implementing the tissue bank and its regulation is needed to meet society's demands, as the entire process depends mainly on the existence of suitable donors and acceptance by their families<sup>7-9</sup>.

It is known that many families fail to accept the donation due to the belief about the image of the cadaver donor after collection, with the image of amputation and/or disfigurement of their body<sup>2</sup>. Therefore, it is up to the professionals responsible for the collection procedure to provide a quality service ethically and coherently, thus preserving the dignity of the donor and family members emotionally involved in their loved one<sup>10</sup>. It is also noteworthy that humanized care ranges from approaching family members regarding donation to collecting and delivering the body<sup>10-12</sup>.

O processo de reconstituição do corpo do doador ainda é pouco conhecido pela população em geral, e até mesmo se configura como tabu, tratando-se de temática pouco explorada nos veículos de informação, o que leva à desinformação e, conseqüentemente, à recusa familiar<sup>2,11,12</sup>.

Given the above, the present work aims to carry out an integrative literature review (IR) to highlight gaps and characterize the process of donating human organs and tissues, focusing on reconstructing the donor's body and human dignity. In addition, it also proposed to describe an experience report from an HTB professional who works in the process of harvesting human organs and tissues.

## METHODS

The present work was carried out in two different stages: the first involved developing the IR of the literature, followed by an experience report from a professional working in human tissue donation and transplants.

### Integrative literature review (IR)

IR is a method that synthesizes knowledge and incorporates the applicability of significant study results into practice<sup>2</sup>. Among the review methods, IR is the broadest, with the advantage of simultaneously including experimental and quasi-experimental research,

which provides a more complete understanding of the topic of interest. It also allows the combination of data from theoretical and empirical literature. Thus, the reviewer can prepare an IR for different purposes, including defining concepts, reviewing theories, or methodological analysis of studies covering a particular topic<sup>13</sup>.

To refine the methodological rigor of an IR, it is strongly recommended to follow the six steps for its preparation: 1) Formulation of the guiding question; 2) Sampling or searching for studies in the literature; 3) Extraction of results; 4) Critical analysis; 5) Analysis and synthesis of review results; and 6) Presentation of the IR<sup>2,13,14</sup>. These steps were performed and described in this study.

Aiming to cover the central databases for the medical and health areas, we carried out a comprehensive search, with different combinations of controlled and uncontrolled descriptors, on the following platforms: SciELO, LILACS, Google Scholar, and PubMed. The article screening period was from August to October 2023.

As a guiding question for this process, following the Joanna Briggs Institute reviewers' manual (JBI)<sup>14</sup>, the following guiding question was proposed: "Is there evidence in the literature about the procedures and protocols regarding the harvesting of musculoskeletal tissues and the process of reconstituting the body of organ and tissue donors?"

The search strategies for each database were developed according to the PICO strategy, in which P = Population of interest, I = Phenomenon of interest, and Co = Expected/found results<sup>14</sup>, as represented in Table 1.

**Table 1.** Controlled descriptors used as a search strategy in the investigated databases.

Controlled descriptors		
	Portuguese	English
P	"Doadores de tecidos"	"Tissue Donors",
I	"Obtenção de órgãos e tecidos"	"Tissue and Organ Procurement"
Co	"Reconstituição de Cadáver", "Cadáver", "Extração de tecidos humanos", "Próteses ósseas", "Dignidade humana"	"Corpse Reconstitution", "Corpse", "Body Reconstruction", "Human tissue extraction", "Bone prostheses", "Human dignity"

Source: Elaborated by the authors.

The descriptors were chosen through searches on the portal Descritores em Ciências da Saúde (DeCS), database tests, and identification of the most used terms in scientific articles in the investigated area. Keywords and accessible terms were included in each search throughout the research.

As this topic is particular, we searched for works published globally in the last 10 years. We included original articles and gray literature in Portuguese and English, such as theses, dissertations, or course completion works.

For inclusion in the work, studies should address and describe materials and techniques for reconstituting cadavers used by HTB and harvesting organs and tissues. Works that only addressed reconstitution techniques for organ donation, secondary articles, protocols, and editorial letters were excluded.

All publications identified in the first screening (initial search in databases) were organized and loaded into Rayyan<sup>13</sup>, data management software for review work that assists in selecting scientific articles. This software allows the removal of duplicates and provides reviewers with convenience in selecting works of interest.

Thus, two independent researchers examined the titles and abstracts of each article selected in the first screening in a double-blind manner. After the screening, the findings were discussed, and conflicts were resolved when the inclusion/exclusion of an article differed between the reviewers. The full texts of the articles selected in this first screening were analyzed again in blind mode according to the inclusion and exclusion criteria. The final sample was reached after consensus, and the data were presented according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) model<sup>15</sup>.

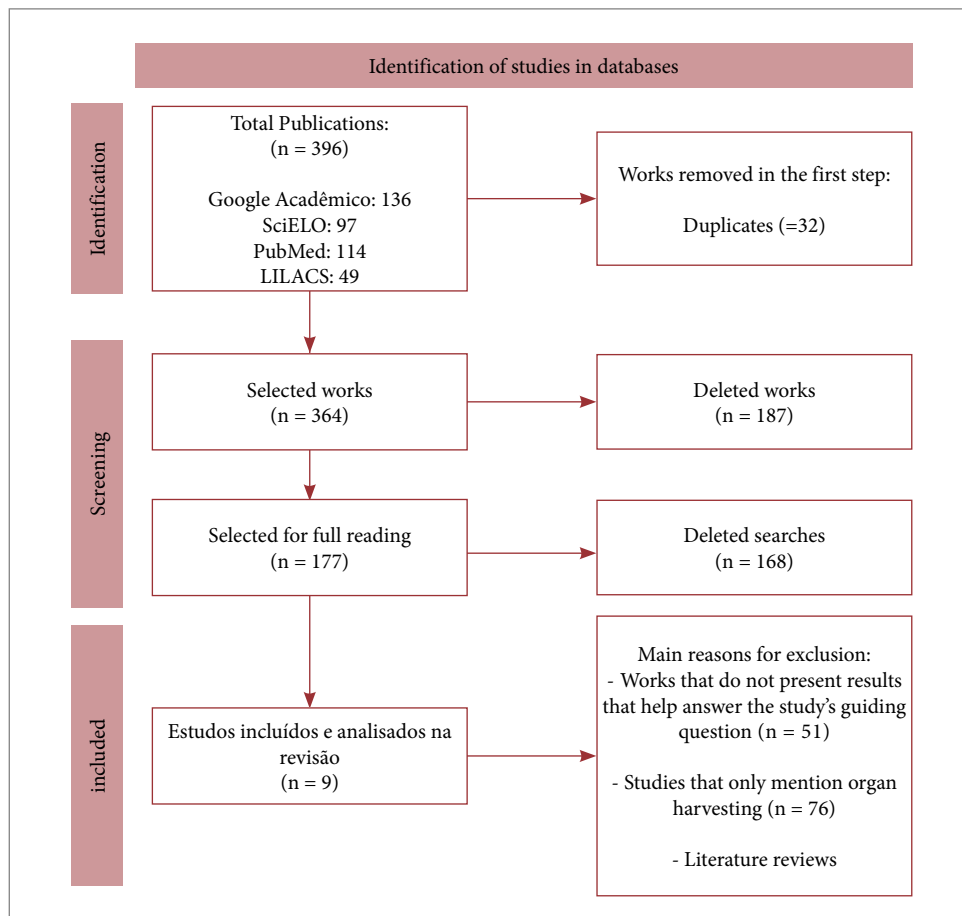
## Experience report

In the second phase of the research, an experience report was described, with a critical-reflective approach, from one of the researchers of the present study who is part of the team at an HTB, a reference in the country, located in a city in the interior of the state of São Paulo. The report described the main techniques for reconstructing a cadaver after human tissue donation and aspects relating to the posture and professionalism of those involved in this process, highlighting the importance of donating musculoskeletal tissues.

## RESULTS

### Integrative literature review (IR)

In the last 10 years, 337 scientific works have been found on the topic under study. After screening, double-blind evaluation, and analyses, nine publications were considered adequate to answer the study's guiding question and included in the final sample. According to the PRISMA model<sup>15</sup>, Figure 1 represents more information about the selection process of works in the databases.



Source: Elaborated by the authors, adapted from PRISMA<sup>15</sup>.

Figure 1. Flowchart with the IR screening and selection steps.

More than half (5/9) of the countries where work on the subject was developed are Brazilian, demonstrating the growth of research in the area of human organ and tissue transplants in the last 10 years in the country. Table 2 represents the most essential characteristics of the works included in the final sample.

Table 2. Main characteristics of the works included in the study.

Author/country	Title	Objective	Comments
Vialle et al. <sup>16</sup> /Brasil	A technique for the reconstruction of the limbs of osteomuscular tissue donors	Demonstrate the technique used to reconstruct limbs from musculoskeletal tissue donors.	The method of reconstructing donor limbs from musculoskeletal tissue developed by the Bone Bank of Paraná is a versatile, low-cost transplant option with good aesthetic results.
Pompeu et al. <sup>17</sup> /Brasil	<i>Aspectos intervenientes na efetivação da doação do tecido ósseo durante o acolhimento e a entrevista familiar para doação de órgãos e tecidos</i>	Understand the aspects involved in the completion of bone tissue donation during reception and the family interview carried out by professionals from the Organ Procurement Organization ( <i>Organização de Procura de Órgãos</i> ) from the perspective of the professional and the potential donor's family member.	The need for educational actions by government bodies was highlighted to raise awareness among the population so that all information is understood in future donation campaigns and possible taboos concerning tissue capture processes and reconstruction of the donor body are avoided.
Pompeu et al. <sup>18</sup> /Brasil	<i>Fatores envolvidos na negativa da doação de tecido ósseo em doadores de órgãos nos hospitais públicos e privados de Ribeirão Preto e região</i>	Determine the prevalence of bone tissue donors and the main variables involved in denying this tissue in organ donors.	Some critical factors that influenced family members' refusal of bone tissue donation were identified: a lack of knowledge about which bones could be removed, how these structures would be reconstituted, and how the donor's body would appear after harvesting.

Continue...

**Table 2.** Continuation.

Author/country	Title	Objective	Comments
Vanholder et al. <sup>19</sup> /União Europeia	Organ donation and transplantation: a multi-stakeholder call to action	Review policy and clinical measures that should be considered to increase access to transplantation and improve post-transplant outcomes.	They indicate that one main reason for refusing donations concerns bone harvesting, which can alter the donor's body.
Jawoniyi et al. <sup>10</sup> /Reino Unido	Organ donation and transplantation: awareness and roles of healthcare professionals – A systematic literature review	Investigate the role of health professionals in the organ donation and transplant process.	The health professional must be appropriately specialized to carry out an appropriate and humanized approach to the donors' families, enabling the acceptance of conscious and educated donation.
Santos et al. <sup>9</sup> /Brasil	Trend analysis of organ and tissue donation for transplantation	Identify the trend in tissue and organ donation from brain-dead donors between 2001 and 2016 registered by an organ procurement organization in the city of São Paulo.	It is reported that factors related to donation refusal may be associated with the lack of information to family members about aspects of the surgery, body reassembly and use of such organs and tissues.
Srivastava & Mani <sup>20</sup> /Índia	Deceased organ donation and transplantation in India: promises and challenges	Analyze ongoing efforts being implemented to encourage organ transplantation.	It was identified that there are still challenges, including the interaction of sociocultural factors, beliefs, and superstitions that result from a lack of communication and organizational support. These factors impact negative opinions and refusal to donate. The main factor is the lack of information about using the collected organs and tissues and the deformation of the donor's body.
Schmidt et al. <sup>21</sup> /Alemanha	Fresh osteochondral allografts-procurement and tissue donation in Europe	Highlight Europe's current human organ and tissue donation situation, focusing on bone processing and possible safety and quality concerns.	It was identified that among the main barriers to accepting the donation is the need for knowledge of the situation in which the donor's body will be after the extraction of bone tissue, highlighting the scarcity of work with this approach and objectives.
Hage et al. <sup>22</sup> /Brasil	Bone tissue donation: tendency and hurdles	Identify the percentage of bone tissue donation in situations of brain death and the trend in the donation rate of this tissue in an organ procurement organization in the city of São Paulo from 2001 to 2016	A significant increase in the rate of bone donation has been observed, but more is still insufficient to meet the demand. This rise is attributed to educational and awareness-raising initiatives about the collection process, donor body restructuring, and using collected tissues and organs. The positive impact of this surge in donation rates is not just in the numbers but in the lives being saved and improved, underscoring the urgency of addressing the organ and tissue shortage. This gives us hope for a future where such shortages are a thing of the past.

Source: Elaborated by the authors.

## Experience report

With the technical, practical, and philosophical experience and years of experience in an HTB, it is clear that there is excellent potential in donating human organs and tissues. This potential can save lives that are still waiting (even at this very moment), distressed by years of waiting in transplant queues, uninterrupted consultations, and exhaustingly prolonged treatments, seeing time disappear with the delay, time that doesn't stop. It does not regress and only restlessly increases the reality of non-arrival.

In this sense, a remarkable potential emerges, little explored and/or publicized. It is found in the opportunity in which only a donating family can change the reality placed on them by life, or rather, death.

However, after this endpoint in life, there is an urgent need for the possibility of donating human organs and tissues as a generous act of love and compassion for others, making it a possible mechanism for overcoming, or rather, coping with, a painful phase of life. I struggle so that, finally, acceptance emerges from the ruins and chaos characterized by irreversibly losing someone so loved.

It is in this gap that this transformation mechanism can exist. When we think about donation as a "bridge" between life-death-life, which can provide the bereaved with overcoming, we think about the gift in the "yes" of a donating family.

Inspired by this "yes," we believe it is possible to continue providing dignity to humanity, memory, identity, and, above all, the body of our donor. In a harmonious, truthful, and empathetic way, we create internal protocols for interviews with family

members and prepare scripts and questionnaires to facilitate communication in critical situations. Therefore, an employee trained by our HTB travels with the Organ Procurement Organization (OPO) team will participate in interviews and explain in detail to family members what will be removed, how it will be reconstructed, where it will be located and how to prepare and send the offered fabrics, clearly and objectively.

In the hospital's carpentry service, replacement prostheses are made for the donated areas, mainly those used for donating musculoskeletal tissues, which are biodegradable and articulated, ready to be placed on the donor dignifiedly (Fig. 2a, b). Furthermore, a few months after the donation, HTB sends the donor family a letter of thanks signed by the institution's clinical director (Fig. 2c).

Finally, we believe that these small "interpersonal gestures" bring us closer to family members, thus rescuing the fraternity that moves us, makes us equal, and makes us human.



Source: Elaborated by the authors

**Figure 2.** Representative photographs of some donation processes adopted by an HTB in 2024. a and b use prostheses to reconstruct the donor's body, with the areas where the tissues were removed; c: model letter of thanks to donor families.

Likewise, another important factor is the remarkable dignity of reconstructing the donor's body, especially in visible areas, as in the case of donating corneas for transplants. Among the many existing techniques for collecting corneas, one of the most used by the country's Eye and Tissue Banks is Ocular Enucleation (total surgical removal of the eyeball). Therefore, after its removal, care is taken to fill the cavity with absorbent cotton for tamponade and then use a Specific Orbital Cavity Reconstructor (RECO) (Reco, Ribeirão Preto, São Paulo, Brazil) in order to get as close as possible to the previous appearance of the face. In addition, using a Small Disposable Applicator Brush (Haste Aplik) - adapted from the dental industry - (Angelus Odonto, Londrina, Paraná, Brazil) instant superglue (cyanoacrylate) is applied to the entire waterline of the donor's eye, then the upper and lower mobile eyelids are carefully brought together. In this way, it is possible to protect the donor's image, as well as preserving the family and loved ones from any embarrassment.

Therefore, after years of working in an HTB as professionals who participate in conversations with family members to explain all procedures—removal of human organs and tissues, reconstitution of the donor's body, and the purpose of this donation—we highlight the importance of awareness and clarification so that the long-awaited “yes” occurs. Countless lives can be helped and saved.

## DISCUSSION

The donation and transplantation of human organs and tissues are directly related to the various dilemmas addressed in the themes of death and dying. Therefore, working professionals must base their approaches on proven scientific guidelines and pay attention to the popular and cultural roots of the region where they work<sup>2</sup>.

There are several definitions of death<sup>23</sup>. Although it involves meanings and aspects that transcend human and scientific understanding, the most concrete definition of death, in the physiological sense, is the loss of vital functions, resulting in the definitive cessation of the life of an organism or human being<sup>5-7</sup>.

In this context, Santos et al.<sup>9</sup> states that the family can only donate when it truly understands and accepts the donor's finitude. Furthermore, the dilemma of acceptance (or non-acceptance) arises from the lack of explanation about aspects involving surgery, body reconstruction, use, and destination of donated organs and/or tissues<sup>9</sup>. Many donations are refused due to a lack of understanding of the diagnosis of brain death on the part of family members, as well as a lack of clarity and adequate explanation by the professionals responsible for communicating the diagnosis of a family member's death, despite their physiological functions being evident to the eyes of those who see it<sup>2,17,18,23</sup>.

HTB professionals are responsible for searching for donors, obtaining family consent, collecting tissues and reconstructing the donor's body dignifiedly, avoiding disfigurement, as provided for in Article 26 of Decree No. 9,175, of 2017<sup>5</sup>. Then, the body must be adequately restored to be handed over to family members for burial<sup>16</sup>. It is worth mentioning that, due to this legal protection, organ and tissue donors do not require burial in a sealed coffin.

Due to the difficulty of acceptance, many HTBs choose to capture only the tissues of the lower limbs, making it possible to collect larger bones with a large amount of material, resulting in a better aesthetic result for the corpse. One of the biggest concerns for families who agree to donate their loved one's organs and tissues is the aesthetic situation in which they will be presented<sup>19,20</sup>. This factor has proven to be important when families make decisions when many choose not to donate due to taboos regarding the tissue extraction process<sup>19-21</sup>.

Therefore, it is crucial to invest in the safety and quality of reconstitution services used by HTB to reduce family refusal to donate<sup>17,18</sup>. The IR carried out in this work, the experience report described here, and some articles included bringing different reconstruction techniques for continuous improvement of the services provided by HTB and, consequently, greater acceptance<sup>16,20-22</sup>.

For example, the Bone Bank of Paraná uses metal rebars, silicone tubes, and nylon clamps to reconstitute musculoskeletal tissues, a technique considered easy to perform and apply, providing satisfactory aesthetic results<sup>16</sup>. This technique differs from the experience report, which uses biodegradable wooden prostheses but follows a similar limb insertion and suturing style.

The decision to donate, which is the family's sole responsibility, often generates conflicts and questions for those involved since not all potential donors verbally expressed their wish in favor of donation during their lifetime<sup>2,9,10</sup>. From an ethical point of view, this decision is personal. It may generate divergence among family members when making the decision, mainly due to a need for knowledge about the possibility of donating different types of organs and tissues and their cultural symbolism, among other factors<sup>9,10</sup>.

Therefore, it is necessary to consider the practices studied on the subject, use the reconstruction techniques described here, and/or improve them to contribute to the donation process. It is possible to carry out these technical activities through a humanitarian scope, based on empathy and care, capable of providing support for overcoming, offering support, care, and sensitivity<sup>23,24</sup>.

Considering these issues, subsidies that acquire concreteness through reception so that the family feels welcomed and safe in the face of bad news are effectively within the health professional's reach. Therefore, it is necessary to exercise an attitude based on ethical principles, understanding that this family will regret how difficult it was to go through this moment of mourning and encouraging them to be happy when remembering the trust and welcome they received<sup>24</sup>.

Notably, more humanized professional training for health professionals can adequately prepare them for these moments of contact with donors' families and, possibly, contribute to greater acceptance of informed donation, breaking taboos related to organ and tissue transplantation.

As relevant and necessary as the issues that permeate this topic are, it is clear that few studies in the current literature address human dignity in the donation of human organs and tissues. Therefore, more robust, replicable, and standardizable studies are required. This study has the limitations of using only some databases available in the literature and taking an exclusively qualitative approach to the topic.

## CONCLUSION

Based on the results of the IR carried out, focused on the critical categories emphasized in the field of donation, harvesting, and reconstruction of the donor's body, significant gaps were identified in the process of donating human organ and tissue transplants in Brazil, especially concerning respect for the restructuring of the donor's body. It was also noticed that many challenges must be overcome to expand the harvesting of organs and tissues on the national scene. Clear and adequately guided communication with family members emerges as the best way to increase the number of donations, considering that one of the main concerns presented lies in the reconstitution of the donor's body.

The experience report presented here demonstrated the restructuring process conducted by professionals from a reference HTB in Brazil, highlighting, once again, the importance of a humanized and empathetic approach toward the donor and his family. Given the above, the present study indicates the need for new research and techniques aimed at reconstituting the donor's body, aiming at its wide dissemination in the community, and awareness actions that can favor breaking taboos, enabling a higher rate of donation acceptance by family members.

## CONFLICT OF INTEREST

The authors declare the absence of conflicts of interest and the non-use of artificial intelligence in this study.

## AUTHOR'S CONTRIBUTION

**Substantive scientific and intellectual contributions to the study:** CACC, AVAL, LMS; **Conception and design:** CACC, AVAL, LMS, KCGS, RLB; **Data analysis and interpretation:** CACC, AVAL, LMS, KCGS, RLB; **Article writing:** CACC, AVAL, LMS, MSR; **Critical revision:** CACC, AVAL, LMS, MSR; **Final approval:** FLG, LGGM.

## DATA AVAILABILITY STATEMENT

All dataset were generated or analyzed in the current study.

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