

## Therapeutic use of human tissues and organs for transplants: adverse events and biosurveillance actions

*Uso terapêutico de tecidos e órgãos humanos para transplantes: eventos adversos e ações de biovigilância*

*Uso terapéutico de tejidos y órganos humanos para trasplantes: eventos adversos y acciones de biovigilancia*

### ABSTRACT

**Purpose:** To identify evidence in the literature regarding adverse events and biovigilance actions in the process of donation and therapeutic use of human tissues and organs for transplantation. **Method:** An integrative review consulting the following databases: LILACS, MEDLINE, and Embase. Inclusion criteria: Primary studies in English, Spanish and Portuguese, published between 2015 and 2021, about biovigilance in the donation and transplants, risks, and adverse events. **Results:** 10 articles were analyzed, identifying the occurrence of adverse events related to the process of the donation and transplants, biovigilance strategies aiming to reduce risk and increase safety. **Conclusion:** Risks and adverse events can occur in the process of donation and transplantation. Strategies were observed to mitigate the risks and occurrence/recurrence of adverse events, providing assistance with greater quality and patient safety. Nurses have a fundamental role with regard to biosurveillance, as they are present in all stages of the donation and transplants. **Descriptors:** Biosurveillance; Patient Safety; Drug-Related Side Effects and Adverse Reactions; Tissue and Organ Procurement; Transplantation.

### RESUMO

**Objetivo:** Identificar evidências na literatura sobre eventos adversos e ações de biovigilância no processo de doação e uso terapêutico de tecidos e órgãos humanos para transplante. **Método:** Revisão integrativa, utilizando as bases de dados LILACS, MEDLINE e Embase. Critérios de inclusão: estudos primários em inglês, espanhol e português, publicados entre 2015 a 2021, acerca da biovigilância na doação e transplante, riscos e eventos adversos. **Resultados:** Analisados 10 artigos, identificando a ocorrência de eventos adversos referentes ao processo de doação e transplante e estratégias de biovigilância para reduzir riscos e aumentar a segurança. **Conclusão:** Riscos e eventos adversos podem ocorrer no processo de doação e transplante. Observaram-se estratégias, para mitigar os riscos e a ocorrência/recorrência de eventos adversos, propiciando maior qualidade assistencial e segurança ao paciente. O enfermeiro tem papel fundamental no que concerne à biovigilância, estando presente em todas as fases do processo de doação e transplante.

**Descritores:** Biovigilância; Segurança do Paciente; Efeitos Colaterais e Reações Adversas Relacionados a Medicamentos; Obtenção de Tecidos e Órgãos; Transplante.

### RESUMEN


**Objetivo:** Identificar evidencias en la literatura sobre efectos adversos y acciones de biovigilancia en el proceso de donación y uso terapéutico de tejidos y órganos humanos para trasplante. **Método:** Revisión integradora, utilizando las bases de datos LILACS, MEDLINE y Embase. Criterios de inclusión: estudios primarios en inglés, español y portugués, publicados en 2015-2021, sobre biovigilancia en donación y trasplantes, riesgos y eventos adversos. **Resultados:** Se analizaron 10 artículos, se identificó la ocurrencia de efectos adversos referentes al proceso de donación y trasplante, estrategias de biovigilancia para reducir riesgos y aumentar la seguridad. **Conclusión:** Riesgos y efectos adversos pueden ocurrir en el proceso de donación y trasplante. Estrategias para mitigar los riesgos y la ocurrencia/recurrencia de efectos adversos, propician asistencia de mayor calidad y seguridad para el paciente. El enfermero tiene un papel fundamental en la biovigilancia, ya que está presente en todas las etapas del proceso de donación y trasplante.

**Descriptores:** Biovigilancia; Seguridad del Paciente; Efectos Colaterales y Reacciones Adversas Relacionados con Medicamentos; Obtención de Tejidos y Órganos; Trasplante.


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## INTRODUCTION

In the different human health care scenarios, quality and safety have been the focus of attention, study and discussion, and this is no different in the area of organ and tissue donation and transplantation, an area that has been growing in several countries, as well as in Brazil, which has one of the largest public transplant programs. In the last two decades, the World Health Organization (WHO) has worked hard on actions and strategies, in partnership with the member countries, aiming to reduce risks and the occurrence of adverse events and incidents<sup>(1-2)</sup>.

The concept of incidents is described in the literature as events or circumstances that resulted or could have resulted in unnecessary harm to the patient, while risk is defined as the probability of the incident occurring<sup>(1)</sup>. An incident can even be defined as a near miss, adverse event or sentinel event. A near miss is an incident that did not reach the patient but came close to occurring; an adverse event is an incident that resulted in harm to the patient; while a sentinel event is a situation where the harm caused irreversible sequelae or even the death of the patient<sup>(1)</sup>.

In relation to the process of organ and tissue donation and transplantation, the Brazilian National Health Surveillance Agency (*Agência Nacional de Vigilância Sanitária*, ANVISA) defines adverse event and incident as follows<sup>(3)</sup>:

Adverse Event: Any unfavorable occurrence related to the donation, harvesting/collection, evaluation, processing, storage, distribution, and procedure of therapeutic use of cells, tissues, and organs, in a living recipient or donor, which may or may not lead to the transmission of a disease, death, risk to life, disability or incapacity, hospitalization, or even prolongation of diseases or hospitalizations. Incident: Occurrence of a deviation from the operating procedures or from the patient safety policies in the health institution related to the donation, collection/harvesting, evaluation, processing, storage, and distribution of cells, tissues and organs detected during or after the donation or transplantation/infusion/graft/implantation, which may or may not lead to the transmission of a disease, death, risk to life, disability or incapacity, hospitalization, or even prolongation of diseases or hospitalizations, either in a living recipient or donor<sup>(3)</sup>.

In all phases of the donation and therapeutic use of organs and tissues process, risk

is present in *inter vivos* donation as well as in post-mortem donation, and may involve both the donor and the recipient<sup>(3)</sup>. Although transplantation can contribute benefits to the recipients, risk must always be considered, since the process can involve the transmission of diseases, infections, neoplasms, or even lead to other complications<sup>(3-4)</sup>.

Therefore, safety is related to all the stages of the donation and therapeutic use of organs and tissues process, which must be conducted and documented according to what is regulated in the legislation. Safety is considered as one of the dimensions of quality, and systematically analyzing the risks and the occurrence of adverse events makes it possible to identify, prevent and mitigate harm, as well as to improve processes<sup>(5-7)</sup>. The use of indicators can also assist in the monitoring and control of the transplant process, being the tool that makes it possible to assess the processes<sup>(8)</sup>. In this context, it is emphasized that organ donation also depends on trust in the system and on the safety of the process, and that failures can result in problems for the patient and in harmful repercussions for society and health care teams<sup>(9)</sup>.

Developing procedures with quality and safety is a challenge for surveillance systems, institutions, and health professionals. In the context of donation and transplantation, it is necessary to perform risk management, by means of biosurveillance, implementing and developing actions that make it possible to monitor the entire macroprocess<sup>(3)</sup>. In this sense, biosurveillance is defined as a set of monitoring and control actions that covers the cycle of therapeutic use of human cells, tissues and organs, from donation to the clinical evolution of the recipient, aiming to obtain diverse information about risks and adverse events, preventing their occurrence or recurrence<sup>(3)</sup>.

The process of donation and therapeutic use of human tissues and organs for transplantation has significant social relevance because of the benefits of this therapy. However, this is a complex process that involves many professionals from different areas, from donation to the monitoring of the recipient after transplantation, and is also permeated by risks. In view of this scenario, the conduction of this study is justified.

The objective of this study is to identify evidence in the literature on adverse events and

biosurveillance actions in the process of donation and therapeutic use of human tissues and organs for transplantation.

## METHOD

The research is of the integrative review type, a method that aims at gathering and synthesizing the results of research studies on a given topic in a systematic and orderly manner, being an instrument for deepening knowledge on the investigated topic, allowing for the synthesis of published studies and general conclusions of a particular study area<sup>(10)</sup>. Following the theoretical framework by Mendes, Silveira and Galvão<sup>(10)</sup>, the integrative review comprises six stages, namely: identification of the topic and selection of the research question, establishment of the criteria for sample selection, definition of the information to be extracted from the selected articles, analysis of the results, presentation and knowledge synthesis<sup>(10)</sup>.

The research question was elaborated according to the PICO strategy, acronym for Patient or Problem, Intervention, Comparison and Outcomes. Consequently, the following question was elaborated: What is the evidence in the literature on adverse events and biosurveillance actions in the process of donation and therapeutic use of human tissues and organs for transplantation? Therefore: (P) refers to the process of donation and therapeutic use of human tissues and organs; (I) to the biosurveillance actions; and (O) to the adverse events. In this case, (C) for comparison was not used.

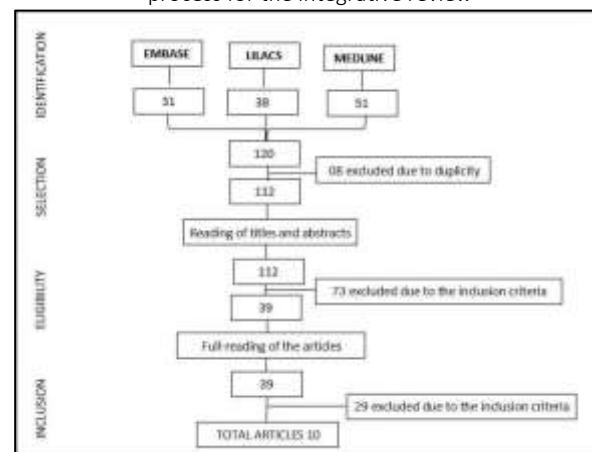
The inclusion criteria were as follows: primary studies published in English, Spanish and Portuguese, published from 2015 to 2021 (the period longer than five years was due to the scarcity of publications on the theme), available in full, and articles with information on biosurveillance in the process of donation and therapeutic use of human tissues and organs for transplantation, their risks, and adverse events.

The articles were identified by means of a search in the literature, conducted in February 2021 in the following databases: Medical Literature Analysis and Retrieval System Online (MEDLINE), consulted via PubMed; *Literatura Latino-americana e do Caribe em Ciências da Saúde* (LILACS), consulted via *Biblioteca Virtual em Saúde* (BVS); and Embase. The search strategies were conducted based on

the following Descriptors in Health Sciences (DeCS): “Biosurveillance”; “Patient Safety”; “Side Effects and Drug-Related Adverse Reactions”; “Tissue and Organ Procurement”; and “Transplant”.

Subsequently, duplicates across the different databases were excluded. Immediately after that, the titles and abstracts were read, excluding the studies that did not meet the inclusion criteria or the theme proposed. A total of 39 articles were selected for the next phase, that is, full reading, which was in charge of two independent evaluators (with experience in the theme under study), aiming to favor validation of the articles selected for the analysis. For this analysis, the evaluators considered the inclusion and exclusion criteria and the research question, resulting in 10 articles, which comprised the final sample of this review (Figure 1).

**Figure 1** - Flowchart corresponding to the study selection process for the integrative review



Source: Study data.

The publications selected for the final sample were analyzed, interpreted in an organized manner and synthesized by preparing a synoptic chart. The quality of the studies was assessed, based on the classification of the levels of evidence, according to the Oxford Centre for Evidence-Based Medicine<sup>(11)</sup>, which classifies studies into five levels: I – systematic review or randomized trials; II – randomized research; III – non-randomized cohort/monitoring studies; IV – case or case-control studies; V – experts opinion or based on regulations and laws.

The data were analyzed according to thematic analysis, with three categories being listed: “Process of organ donation and transplantation”, “Patient safety: multidisciplinary

team, care processes and transition” and “Biosurveillance”.

The presentation of the results and the discussion of the data obtained were descriptive, enabling the reader to know the data related to the adverse events and biosurveillance in the process of donation and therapeutic use of human tissues and organs for transplantation evidenced in the literature.

## RESULTS AND DISCUSSION

A total of 10 articles that met the inclusion criteria were selected to attain the objective

proposed. The largest number of publications was found in the LILACS database (50%), with predominance of the English language (90%) and publication dates between 2015 and 2018, the majority (40%) being from 2016; however, articles published in 2019, 2020 and 2021 were not included, since they did not meet the criteria delimited by the study. In the sample selected there was predominance of studies conducted in Brazil (50%), as well as of papers with level of evidence IV (50%). Chart 1 presents the synthesis of the articles included in this study.

**Chart 1** – Synthesis of the articles included in the study

Reference	Year Country	Design Sample	Interventions	Outcomes	Level of evidence
Pontes <i>et al.</i> (2018) <sup>(12)</sup>	2018 Brazil	Descriptive, retrospective and qualitative study. n=1,090	Analysis of the notifications of incidents.	All the incidents generated harm to the patients, to a greater or lesser degree, in the dimensions of physical harm and subjective harm.	IV
Grossi <i>et al.</i> (2018) <sup>(13)</sup>	2018 Italy	Retrospective cohort study. n=260	Analysis of donors at risk for HCV, HBV and HIV infection and monitoring of the recipients.	There is risk of HCV and HIV transmissibility in organ donation and transplantation. There is the risk of the transmission window period. HBV and HCV transmission affected 12.6% of the patients monitored in this study. There were no cases of HIV transmission.	III
Rosa <i>et al.</i> (2017) <sup>(14)</sup>	2017 Brazil	Quantitative and cross-sectional study. n=60	Application of a questionnaire about safety in the cornea donation process.	Most of the participants feel safe about the donation safety process.	IV
Cristelli <i>et al.</i> (2016) <sup>(15)</sup>	2016 Brazil	Clinical and prospective study. n=39	Analysis of drug treatment in post renal transplant patients.	Treatment-related adverse events: mouth ulcers, dyslipidemia, peripheral edema.	I
Lima <i>et al.</i> (2016) <sup>(16)</sup>	2016 Brazil	Quantitative and cross-sectional. n=74	Analysis of weaknesses related to the drug treatment at hospital discharge of transplanted patients.	Most of the weaknesses were related to the non-prescription of the required medication.	IV
Meng, Yang and Yan (2016) <sup>(17)</sup>	2016 China	Quantitative and retrospective study. n=356	Analysis of postoperative complications in living liver donors.	Most of the complications are related to biliary complications. Minimum severity.	IV
Ribeiro <i>et al.</i> (2016) <sup>(18)</sup>	2016 Brazil	Cohort and retrospective study. n=446	Control group and test group to assess the outcomes of deceased-donor kidney transplantation in sensitized recipients without prior identification of the presence of donor-specific anti-HLA antibodies.	Sensitized individuals presented a higher incidence of infection. There was no difference in graft and patient survival.	III
Czerwiński, Kaliciński and Danielewicz (2015) <sup>(19)</sup>	2015 Poland	Quantitative and retrospective study. n=3,223	Implementation of an online tool to record notifications. Analysis of adverse event notifications.	Most common notifications: early recipient death, early graft loss, transmission of infection. Under-reporting of notifications.	IV

(Continues)

**Chart 1** – Synthesis of the articles included in the study

Reference	Year Country	Design Sample	Interventions	Outcomes	Level of evidence
Stewart <i>et al.</i> (2015) <sup>(20)</sup>	2015 USA	Cohort study. n=438	Notification trend analysis.	Most common notifications: communication failure, failure in donor and/or organ records, conditioning and transport, etc.	III
Weir <i>et al.</i> (2015) <sup>(21)</sup>	2015 USA	Cohort study. n=4,110	Analysis of the incidence of adverse events in kidney transplant recipients.	One third of the transplanted patients suffered adverse events while hospitalized.	III

Source: Study data.

Regarding the adverse events, the publications analyzed list situations such as: surgical complications, drug-related events, readmissions or increased hospitalization time, infections, malignancy, graft loss, patient fall, and death. Failures in processes, implying risk of adverse events, were also described, such as: failures in communication or in health professionals' records; failures in health devices and equipment; failures related to the processes involving medications, such as preparation, administration and prescription; failures in the donation and transplantation process, such as in organ allocation, donor identification, and in the process of conditioning and transporting the donated organ or tissue; lack of knowledge or failure to follow pre-established routines and protocols; and failures in care transition, as described in Chart 2.

Several biosurveillance actions and strategies to mitigate risks and adverse events are proposed in the literature analyzed, such as: importance of interdisciplinary patient care; continuous training of the professionals; adequate staffing of the health care team; implementation and/or review of protocols; mitigation of adverse events; implementation or monitoring of a biosurveillance system with data notification, analysis and dissemination, aiming at promoting safety, as can be seen in Chart 2.

**Chart 2** - Adverse events, failures in processes and biosurveillance strategies

<p><b>Adverse events</b></p> <p>Surgical complications<sup>(15,17)</sup></p> <p>Vascular complications<sup>(17)</sup></p> <p>Adverse effect of drug administration<sup>(15-16,21)</sup></p> <p>Hospitalizations<sup>(12,17-18,21)</sup></p> <p>Infections<sup>(14,17-18,21)</sup></p> <p>Death<sup>(18,21)</sup></p> <p>Graft loss<sup>(15,18)</sup></p>
<p><b>Failures in processes</b></p> <p>Communication and records<sup>(14,20)</sup></p> <p>Failure in health devices and equipment<sup>(20)</sup></p> <p>Failure referring to medications (preparation, administration, prescription)<sup>(20)</sup></p>

Failures in the donation and transplantation process (organ allocation, donor identification, conditioning and/or transport)<sup>(20)</sup>

Lack of knowledge or failure to follow pre-established routines and protocols<sup>(20)</sup>

Care transition<sup>(20)</sup>

**Biosurveillance strategies**

Interdisciplinary assistance/work<sup>(20)</sup>

Training of the team<sup>(13)</sup>

Adequate staffing<sup>(21)</sup>

Protocol implementation or review<sup>(12,21)</sup>

Prophylaxis or preemptive treatment<sup>(18)</sup>

Biosurveillance system with data notification, analysis and dissemination<sup>(19-21)</sup>

Source: Study data.

### Process of organ donation and transplantation

The process of organ and tissue donation and transplantation is complex, involving several stages, from the identification of the potential donor to the monitoring after the transplant and throughout the transplanted person's life. It is also a process that involves professionals from different areas and academic backgrounds, as well as different health care sectors and institutions. The complexity of this entire macroprocess, the long treatment and the vulnerability of the immunosuppressed patient, among others, are factors that can interfere with patient safety<sup>(21)</sup>.

In this scenario, the transplanted patient is vulnerable to the occurrence of incidents and/or adverse events, such as infections (bacterial, fungal or viral)<sup>(12,14,18-19,21)</sup>, adverse reactions related to drug administration<sup>(15-16,21)</sup>, infusion reactions<sup>(21)</sup>, surgical complications<sup>(15,17)</sup>, organ rejection<sup>(15,18)</sup> and death<sup>(18,21)</sup>. There is risk of disease transmission through the transplanted organ and/or tissue, and the complications can impact on the function of the grafted organ, on quality of life, and on survival of the transplanted individual<sup>(22)</sup>. It is worth mentioning that immunosuppression is also a factor that contributes to the advent of infections and that it is not always related to adverse events, but as a result of the immunosuppression situation<sup>(23)</sup>.



In a scenario where there is shortage of donors<sup>(17)</sup> and an increasing number of patients entering the transplant waiting list, thinking about the safety of both the donor and the recipient is imperative and, therefore, defining and following safety criteria is of great relevance. The careful evaluation of the donors and of the organs and tissues, such as viability, size and possible injuries, among others, is fundamental for patient safety<sup>(17)</sup>. It is noteworthy that, in *intervivos* donation, safety is of even greater relevance, since the donor is a healthy individual who by no means should suffer any harm related to the donation<sup>(17)</sup>.

There are situations evidencing that the evolution of scientific knowledge and the insertion of new technologies provide changes in health care through quality, agility and precision. However, the complexity of the procedures and treatments can imply the occurrence of assistance-related harm, requiring technical and scientific knowledge from the care team to provide quality and safe care<sup>(12-13)</sup>. The events that affect or have the potential to affect patient safety can be due to the following: human error, process failures and communication failures, among others<sup>(20-21)</sup>.

### **Patient safety: multidisciplinary team, care processes and transition**

Multidisciplinary work, the dynamics and the interaction between the professionals and the different teams are extremely relevant for care continuity to the patient, as well as for the safety of the care to be provided<sup>(16)</sup>. Remembering that everyone is at the service of the patient, care quality and safety should be everyone's goal. Professionals with non-aggregating behavior can negatively interfere with team interaction and communication, compromising patient safety. The performance of the multidisciplinary team engaged in safe care is a crucial factor for patient safety<sup>(16)</sup>.

In this context, the nurse acts throughout the organ and tissue donation and transplantation process, performing care and managerial activities. The magnitude and complexity of the care provided by nurses, in the different phases of the process, require qualified education, training, and constant surveillance, aiming at the safety of the patient and of the professionals involved.

A number of studies point out that failures in the processes or in communication between

professionals and different teams are intrinsically involved in avoidable adverse events<sup>(14,20)</sup>, implying delayed laboratory test results and errors in conditioning, transport and labeling of the organ/tissue, which can result in disposal of the donated organ or in complications to the transplanted patient<sup>(20)</sup>. The following are also highlighted as causes of adverse events: lack of knowledge or failure to follow pre-established routines and protocols<sup>(14,20)</sup>, lack of equipment or materials needed for assistance, whether clinical, surgical, inpatient or outpatient, and delay of essential information for the donation and transplantation process, such as laboratory test results, among others<sup>(14,20)</sup>.

Another key factor in care quality and safety is knowledge and mastery of the scientific evidence, protocols and institutional routines<sup>(14)</sup>. However, a number of studies indicate that there are still gaps in the training of health professionals and that lack of training and knowledge can jeopardize both donation and use of the donated organs and tissues<sup>(14)</sup>. These situations can be considered as avoidable adverse events or even as near misses<sup>(20)</sup>.

Highly trained health care teams are the key to successful donation and transplantation<sup>(14)</sup>. In a study carried out with medical professionals, concerning safety in the corneal donation process, 68% reported feeling safe in the process, while 31% revealed not feeling safe for this condition, justifying the situation by the scarce information in that respect, limited contact with potential donors, and disinterest in the subject matter. The authors point out that the stabilization trend or even the reduction in the number of donations can be a reflection of the unpreparedness of professionals in identifying potential donors and in approaching the potential donor's family<sup>(14)</sup>.

In general, both the potential donor and the recently transplanted person are critical patients who demand multiple care, and assistance safety and quality must be guaranteed, such as, among many other care measures, in the manipulation of catheters, in the administration of medications, and in the careful evaluation of the patient, mitigating the risks of incidents<sup>(12)</sup>.

In this context, various types of care require interaction and interdisciplinary work, such as care related to drug treatment, to changes in the patients' lifestyle and their adherence to the guidelines regarding self-care, and to preparation for hospital discharge. In this care, the

interdisciplinary approach can infer greater patient safety, involving not only the medical professional and the nurse, but also the pharmacist, nutritionist, psychologist, social worker and physical therapist<sup>(16)</sup>. It is worth pointing out that each profession has its own specific knowledge, and all are important and complementary in the provision of care. Thinking about educational actions, involving interprofessional performance and articulation, can contribute more effective results in patient care.

Faulty processes are also computed as a cause of adverse events<sup>(20)</sup>, as well as weaknesses in the structure of the institutions, which can exert a negative impact and affect patient care. In a study that analyzed 438 adverse events related to the donation and transplantation process, the results indicate that 44% of the situations that involved failures in patient safety were related to failures in the institutional processes, or to communication failures and, in some situations, these failures resulted in loss/disposal of viable organs for transplantation<sup>(20)</sup>. Examples include: switching laterality; mislabeling the recipient containing the organ; increasing the cold ischemia time beyond the maximum limit; sterility violation; freezing the organ; damage in the vessels or in the organ structure during the harvesting procedure; or preparing the organ for grafting<sup>(20)</sup>.

Other aspects can also affect the safety of the assistance processes, such as: insufficient materials and equipment needed for assistance; failure to perform exams and procedures; failure in the conditioning and/or transport of organs and tissues; insufficient surgical instruments or in poor conditions; inadequate control of surgical instruments, with risk of intracavitary object retention; shortage of intensive care and inpatient unit beds; and failure in shift change or patient transfer (care transition)<sup>(16,20)</sup>.

The issue of patient safety takes on special importance in situations of care transition, such as when the patient is transferred to other units or institutions and even at hospital discharge<sup>(16)</sup>. Communication in this process is a critical factor for safety<sup>(16,20)</sup>. In order to transfer a patient from one unit to another, clear communication and information exchange between the health professionals are mandatory. The person who transfers the patient must inform the professionals at the receiving unit about the

patient's status – clinical conditions, risks, complications and care provided, among others – thus enabling safe care continuity. Care transition is a process that stands out in the Nursing team work by the dynamics inherent to this profession, present 24 hours a day in direct and continuous patient care.

One issue that stands out in the processes of care transition or even hospital discharge is pharmacotherapy, taking into account that the use of medications by these patients is complex, increasing the risk of errors in the administration of drugs, due to misunderstanding of guidelines by the patient and/or family, or even to the incorrect or incomplete transfer of information between professionals or from them to the patient, in addition to involving multiple actions, such as multi-professional and inter-institutional actions<sup>(16)</sup>. A strategy to facilitate the patient's understanding regarding the drug treatment is, in addition to verbal and written guidance, making use of instruments that enable direct contact with the patient and facilitate their understanding, such as the use of symbols, colors and/or figures that can illustrate what is described in the medical prescription<sup>(16)</sup>.

The adverse events resulting from drug treatment can be related to several factors, such as not prescribing the required medication to the patient, underdosing or overdosing, unavailability of the medication in the access network, prescriptions written incorrectly or illegibly, inadequate selection of the medication, non-compliance with the schedule/interval for drug administration and non-adherence, among others<sup>(16)</sup>.

Adverse events may not only occur during the patient's hospitalization, but also after discharge<sup>(16)</sup>. Strategies such as teaching the patient and family member/caregiver about signs and symptoms of changes or complications can be useful in preventing harms<sup>(16)</sup>. The complications resulting from the adverse events also imply additional costs to the health institutions<sup>(12)</sup>, as a result of the need for longer hospitalizations or readmissions<sup>(12,18)</sup> and of the performance of procedures (invasive or not) that would not be necessary if the adverse event had not occurred – such as laboratory or imaging tests – or even mitigation of harms<sup>(12)</sup>.

The damage that failures in processes and structures cause to care, quality, safety and outcomes becomes evident. According to the

literature, incidents and adverse events related to care in organ and tissue donation and transplantation are not uncommon<sup>(12)</sup>. It is necessary to invest in training, as well as in risk management and constant surveillance, in order to increase patient care safety in the process of organ and tissue donation and transplantation<sup>(19)</sup>.

### **Biosurveillance and improvement strategies for patient safety**

Biosurveillance concerns the surveillance aspects in the area of organ, tissue and cell donation and transplantation, involving monitoring actions from donor selection, extraction, preparation, conditioning and distribution, until the graft is performed in the recipient. This is a process aimed at obtaining information about adverse events and at preventing their occurrence<sup>(24-25)</sup>. With the support of the World Health Organization (WHO), several countries have implemented biosurveillance systems, such as Italy, Spain, France, Portugal, United States and Australia, among others<sup>(24)</sup>. In Brazil, the implementation of the National Biosurveillance System took place through Collegiate Board Resolution (*Resolução de Diretoria Colegiada, RDC*) No. 339 on February 20<sup>th</sup>, 2020<sup>(25)</sup>, being a milestone for patient safety.

After being reported, the adverse events are analyzed and transformed into information that can be used as data to update and guide the health professionals, aiming to mitigate risks, prevent the occurrence of new adverse events, improve the quality of the processes, and increase patient safety.

Biosurveillance plays an important role in the process of evidencing information about adverse events<sup>(12,19)</sup>. For several reasons, many institutions and professionals still resist reporting incidents and adverse events, and there is even scarcity of publications evidencing their occurrence. A number of authors describe that, even in the context of prospective cohort studies, there is difficulty in identifying incidents in the area of transplants, a population considered to be at risk for potential adverse events<sup>(12)</sup>.

In a study conducted with 4,110 kidney transplant recipients, where the authors sought to verify the risk of adverse events related to the use of medications, the results only touch on the surface of potential adverse events in the transplanted population<sup>(12)</sup>. However, they point

out that the data found, such as septic shock, diabetic coma, hypoglycemia and drug interactions, among others, are sufficient to increase the health professionals' concern with their practice, in addition to generating subsidies that provide increased patient safety<sup>(12)</sup>.

The actual number of incidents and adverse events related to donation, transplantation, and care of transplanted patients is unknown<sup>(19-20)</sup>. Markedly uneven reports of incident and adverse event occurrence across the transplant institutions suggest that safety situations are still underreported<sup>(19-20)</sup>; there are institutions where notification is null, suggesting substantial under-reporting of incidents and adverse events.

In a study that analyzed 438 adverse events notified to the Organ Procurement and Transplantation Network (OPTN), over a one-year period, the data indicated that 50% of the events notified came from one-third of the registered institutions, that is, most of the transplant institutions or centers did not report any adverse event during a year, clearly evidencing under-reporting<sup>(20)</sup>. Such situation can be related to the fact that notifications are still voluntary<sup>(20)</sup>. Mandatory notification of any adverse event could evidence a greater number of situations that involve care safety and, thus, it would be possible to propose strategies to contain such events.

Notification allows for the dissemination of lessons learned, enabling prevention of recurrence<sup>(20)</sup>. Notifying involves detailing what happened and verifying risk and safety situations, preparing analysis reports after the events (debriefing) and reinforcing that patient safety is improved, when patient care provision systems and processes are improved and investments are made in people training, rather than blaming individuals. The analysis and dissemination of safety data are essential to understand the main risk factors and situations, in order to promote the safety culture<sup>(20)</sup>.

In this context, taxonomy is also important both regarding safety in communication and processes and for the analysis of safety situations and the prevention of adverse events<sup>(15,20)</sup>. The WHO proposes a patient safety taxonomy, which has been widely used and followed by several countries, expanding the dissemination of knowledge on the theme<sup>(25)</sup>. In addition to that, relevant institutions have significantly contributed to biosurveillance, including the WHO, the United



Network for Organ Sharing (UNOS), Notify Library and ANVISA, among others.

UNOS, a North American network that acts as the Organ Procurement Organization (OPO) and Process Safety Committee, has been seeking integrity of incident, adverse event and near miss notifications, in addition to leveraging this data, in order to identify opportunities for process improvements throughout the donation and transplantation system<sup>(20)</sup>. The objective of using biosurveillance tools is to evidence the occurrence of safety-related incidents and adverse events to raise awareness about the importance of process surveillance, encourage safety self-assessments across the transplant institutions, and improve patient safety<sup>(14,19)</sup>. The Notify Library, linked to the WHO, provides publications regarding safety in the process of organ and tissue donation and transplantation, allowing institutions and professionals broad access to publications and reports on the occurrence of adverse events, potential risks and patient safety.

Being aware of adverse events that can occur and that other teams and institutions are experimenting with certain types of safety precautions can lead to improvements in the system, by promoting self-assessment of the own processes, risk analysis, and susceptibility to errors<sup>(20)</sup>. Sharing information that contributes to improving process safety, and therefore patient safety, is considered as a high priority action<sup>(20)</sup>.

Safety data have also been used to devise new guiding policies and documents<sup>(20)</sup>. For example, the OPTN network has approved a policy that requires checking (checklist) the organ/tissue upon receipt, to verify data such as donor ID (donor identification code), which organ, laterality (if any), and other information the service deems necessary. In addition to that, other improvement projects have been implemented, such as TransNet, which aims at mitigating the failures during organ and tissue transport<sup>(20)</sup>.

The analysis of the adverse events that have occurred shows that a single safety incident is often due to multiple contributing factors. To improve patient safety, obtaining various perspectives increases the likelihood of identifying vulnerabilities in care provision.

Patient safety in health care is the basic principle of care quality<sup>(12,17,20)</sup>. In this context, the literature points out strategies to increase patient safety in the donation and transplantation

process, such as implementing or reviewing protocols<sup>(7,12)</sup>; conducting studies on good practices and evidence in care<sup>(12)</sup>; constant monitoring and analysis of factors indicative of clinical, surgical, and process changes<sup>(17)</sup>; collection, analysis and monitoring of quality indicators<sup>(12)</sup>; analysis and notification of the occurrence of incidents or adverse events<sup>(9,15,20)</sup>; and continuous training of professionals<sup>(12,20)</sup>.

Thus, the disclosure of adverse events and harm mitigation measures in the scientific community aims at promoting broad knowledge of situations that may occur and, thus, create strategies to prevent their occurrence or recurrence<sup>(20)</sup>. The importance of biosurveillance and the continuous search for best practices and greater patient safety is thus ratified<sup>(12,19,20)</sup>.

## CONCLUSION

The adverse events related to the process of donation and therapeutic use of human tissues and organs for transplantation identified in this study encompass surgical and vascular complications, events related to drug administration, readmissions or increased hospitalization times, infections, malignancy, graft loss, falls and death. Likewise, failures in processes involving risk of adverse events were identified, such as: failures in communication or in health professionals' records; failure in health devices and equipment; failure related to the processes involving medications, such as preparation, administration and prescription; failures in the donation and transplantation process, such as failures in organ allocation, donor identification and conditioning and transportation of the donated organ or tissue; lack of knowledge or failure to follow pre-established routines and protocols; and failure in care transition.

The biosurveillance actions and strategies to reduce risks and the occurrence of adverse events in the process of tissue and organ donation and transplantation identified in this study include the following: importance of patient care in an interdisciplinary way; continuous training of the professionals, as well as adequate staffing of the assistance team; implementation or even review of protocols; adverse event prophylaxis; implementation and follow-up of the biosurveillance system with notification, data analysis and dissemination, aiming at promoting safety and at reducing the occurrence or recurrence of adverse events.

As for the contributions to the Nursing area, the results presented allow for greater knowledge about the theme under study, providing subsidies for greater safety in the process of donation and therapeutic use of human tissues and organs for transplantation, a process in which the role of the nurse is emphasized, as a professional who works in the different donation and transplantation stages.

It is important to note that the conclusions presented by this study cannot be generalized, as the articles included in this integrative literature review listed research studies with their level of evidence mostly established at IV. This evidence is considered to be less robust and lacking in methodological strategies that include the synthesis of the best scientific evidence, in other words, from systematic reviews or randomized clinical trials.

New studies are suggested that can identify and analyze risks, adverse events, and especially actions to reduce risks and increase safety and quality in the process of organ and tissue donation and transplantation.

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