Review Article

Biosurveillance and reporting of adverse events in organ donation and transplantation: a systematic review

Biovigilância e notificação de eventos adversos na doação e transplante de órgãos: revisão sistemática

Biovigilancia y notificación de eventos adversos en la donación y trasplante de órganos: revisión sistemática

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How to cite:
Roza BA, Lazarini LF, Treviso P, Garcia VD, Pierrotti LC, Schirmer J, et al. Biosurveillance and reporting of adverse events in organ donation and transplantation: a systematic review. Acta Paul Enferm. 2023;36:eAPE00101.

DOI
http://dx.doi.org/10.37689/acta-ape/2023AR001011

Keywords
Biosurveillance; Tissue and Organ procurement; Organ transplantation; Medical errors; Near miss

Descritores
Biovigilância; Obtenção de tecidos e órgãos; Transplante de órgãos; Erros médicos; Near miss

Descriptores
Biovigilancia; Obtención de tejidos y órganos; Trasplante de órganos; Errores médicos; Near miss

Submitted
24 January, 2022

Accepted
20 June, 2022

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Abstract

Objective: To synthesize and critically evaluate the scientific evidence from observational studies on biosurveillance systems and adverse event reporting in organ donation and transplantation.

Methods: Systematic review of observational studies following the recommendations of the Methodological Guidelines (REBRATS) and Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA). Primary studies and case reports on biosurveillance and/or adverse events in organ donation and/or transplantation, without restriction of publication date or language were included. Six electronic databases were used in the scientific literature search: Medical Literature Analysis and Retrieval System Online (MEDLINE) (via PubMed), Excerpta Medica Database (Embase), Web of Science, LILACS, Scopus and the electronic library Scielo. A data search was also performed in the following secondary databases: Notify - World Health Organization (WHO), Pan American Health Organization (PAHO) and Google Scholar. The MINORS tool was used to assess the quality of studies.

Results: 551 studies were identified, and after the evaluation steps, eight of them were included in the systematic review. These were divided into results, processes and strategies for preventing adverse events. Regarding the classification of the quality of studies, two obtained a good classification.

Conclusion: The results indicate the occurrence of adverse events at some stage of the organ and tissue donation and transplantation process, such as: adverse drug-related reactions; neurotoxicity; longer length of hospital stay; surgical reinterventions; falls; coma; death; graft failure or loss. The fact that adverse events are possibly still underreported is noteworthy.

Resumo

Objetivo: Sintetizar e avaliar criticamente as evidências científicas oriundas de estudos observacionais sobre sistemas de biovigilância e notificação de eventos adversos na doação e transplante de órgãos.

Métodos: Revisão sistemática de estudos observacionais seguindo as recomendações das Diretrizes Metodológicas (REBRATS) e *Preferred Reporting Items for Systematic Review and Meta-Analysis* (PRISMA). Foram incluídos estudos primários e relatos de caso conduzidos sobre biovigilância e/ou eventos adversos na doação e/ou transplante de órgãos, sem restrição de data de publicação ou idioma. Foram utilizadas seis bases de dados eletrônicas para a realização das buscas na literatura científica: - *Medical Literature Analysis and Retrieval System Online* (MEDLINE) (via PubMed), *Excerpta Medica Database* (Embase), *Web of Science*, LILACS, Scopus e a biblioteca eletrônica Scielo. Realizou-se também busca de dados nas seguintes bases

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Conflicts of interest: Although Roza BA and Schirmer J are respectively Associate Editor and Chief Editor, both did not participate in the peer review process.

secundárias: *Notify - World Health Organization* (WHO), Organização Pan-Americana de Saúde (OPAS) e *Google Scholar.* Para a avaliação da qualidade dos estudos foi utilizada a ferramenta MINORS.

Resultados: Foram identificados 551 estudos, após as etapas de avaliação, foram incluídos oito deles para a revisão sistemática. Estes foram divididos entre resultados, processos e estratégias de prevenção de eventos adversos. Quanto a classificação da qualidade dos estudos, dois obtiveram classificação boa.

Conclusão: Os resultados apontam a ocorrência de eventos adversos ocorridos em alguma etapa do processo de doação e transplante de órgãos e tecidos, como: reações adversas relacionadas a medicamentos; neurotoxicidade; aumento do tempo de hospitalização; reintervenções cirúrgicas; queda; coma; óbito; falha ou perda do enxerto. Destaca-se que os eventos adversos possivelmente ainda são subnotificados.

Resumen

Objetivo: Sintetizar y evaluar críticamente las evidencias científicas provenientes de estudios observacionales sobre sistemas de biovigilancia y notificación de eventos adversos en la donación y trasplante de órganos.

Métodos: Revisión sistemática de estudios observacionales guiada por las recomendaciones de las Directrices Metodológicas (REBRATS) y *Preferred Reporting Items for Systematic Review and Meta-Analysis* (PRISMA). Se incluyeron estudios primarios y relatos de caso realizados sobre biovigilancia o eventos adversos en la donación o trasplante de órganos, sin restricción de fecha de publicación o idioma. Se utilizaron seis bases de datos electrónicas para realizar las búsquedas en la literatura científica: *Medical Literature Analysis and Retrieval System Online* (MEDLINE) (via PubMed), *Excerpta Medica Database* (Embase), *Web of Science*, LILACS, Scopus y la biblioteca electrónica Scielo. También se realizó la búsqueda de datos en las siguientes bases secundarias: *Notify - World Health Organization* (WHO), Organización Panamericana de la Salud (OPS) y *Google Scholar.* Para evaluar la calidad de los estudios se utilizó la herramienta MINORS.

Resultados: Se identificaron 551 estudios y, luego de las etapas de evaluación, se incluyeron ocho en la revisión sistemática, que fueron divididos entre resultados, procesos y estrategias de prevención de eventos adversos. Respecto a la clasificación de la calidad de los estudios, dos obtuvieron una clasificación buena.

Conclusión: Los resultados indican casos de eventos adversos ocurridos en alguna etapa del proceso de donación y trasplante de órganos y tejidos, como: reacciones adversas relacionadas con medicamentos, neurotoxicidad, aumento del tiempo de hospitalización, reintervenciones quirúrgicas, caída, coma, fallecimiento, falla o pérdida del injerto. Se destaca que los eventos adversos probablemente aún son subnotificados.

Introduction

The concern with patient safety and the quality of processes involved in health care has mobilized teams and institutions for greater vigilance in the processes. In the area of donation and transplantation, this movement is called biosurveillance and aims at greater safety in procedures involving the therapeutic use of human cells, tissues and organs for transplantation, from donation to the clinical evolution of the recipient and the living donor.[1] In order to contribute to prevent risks and adverse events (AE), the objective of biosurveillance is to obtain information on risks and AE and make it available, and implement measures to monitor and control the processes.[2]

Biosurveillance has been a priority in the world, given its relevance and contribution to the safety of patients and health professionals, in addition to the reduction of costs resulting from AE. An example is the implementation of the biosurveillance process in several countries, such as Canada, United States, United Kingdom, Portugal, Spain, Italy and Australia, which have stood out in the world scenario because of actions implemented, such as the notification of occurrences or even risk situations, the implementation of security measures and the sharing of information and data, contributing to the learning and prevention of new occurrences.[1]

In Brazil, the health surveillance policy was created based on Ordinance GM/MS number 1.660/2009, determining actions under coordination of the National Health Surveillance Agency (Anvisa), for the monitoring, analysis and investigation of AE and technical complaints related to services and products in the post-use/post-marketing phase in the Health Surveillance Notification and Investigation System - VIGIPOS, which includes the use of human cells, tissues and organs with the objective of promoting the population's safe access to these products and in compliance with bioethical and legal principles.[3]

In line with the National Patient Safety Program, Ordinance GM/MS Number 529/2013,[4] on February 20, 2020, RDC Number 339 was approved by the Collegiate Board of Anvisa, which provides for the establishment of the National Biosurveillance System. This is the first regulatory framework related to the topic in Brazil.[2] The project aimed at implementing the National Biosurveillance System takes place through an agreement involving the School of Nursing of the

Universidade Federal de São Paulo (UNIFESP), the United Nations Development Program (UNDP) and the Anvisa.

The first Brazilian biosurveillance report was published in 2020 with the aim to provide the community with information on AE resulting from organ and tissue transplants notified to Anvisa between 2015 and 2018. This established a benchmark for the implementation of monitoring actions in health institutions and the strengthening of surveillance activities, ensuring patient safety and quality processes and services.[5] The publication of this report strengthens activities in the area of biosurveillance.

In the period evaluated, 331 adverse reactions (AR) were reported through the biosurveillance adverse reactions FormSus form; 22 notifications in 2015, 57 in 2016, 128 in 2017 and 124 in 2018, showing an increasing number of notifications between 2015 and 2017 and a slight decrease in 2018. Infections represent most reported AR (34.74%), followed by perioperative complications with 13.6%, and neoplasms with 2.11%. The notifications were made by 56 health institutions, of which 28 services belong to the Sentinela Network.[5] Note that in the period referred to in the report, 91,266 transplants (cells, tissues and organs) were performed in Brazil, possibly indicating underreporting of AE.

This report also aims to promote an increase in notifications, and the notification of occurrences of an AE is a determination of RDC/Anvisa resolution number 55, of December 11, 2015 (which provides for the Good Practices in Human Tissues) and RDC/Anvisa number 214, published on February 7, 2018 (which provides for Good Practices in Human Cells for Therapeutic Use and clinical research).[6,7]

Thus, considering the relevance of the donation and transplant process, its complexity and risks, and biosurveillance initiatives implemented worldwide, including Brazil, we felt the need to perform a systematic review with the aim to synthesize and critically evaluate the scientific evidence from observational studies on biosurveillance systems and AE reporting in organ donation and transplantation.

Methods

This is a systematic review of observational studies in which recommendations of the Methodological Guidelines for the preparation of a systematic review of observational studies (Brazilian Health Technology Assessment Network – REBRATS)[8] and the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA)[9] were adopted as guidance. Primary studies (cross-sectional, cohort and case-control studies) and case reports on biosurveillance and/or adverse events in organ donation and/or transplantation were included, without restriction of publication date or language.

The search strategy was performed according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement.[9] The PECO acronym was used (P - population, E - exposure, C - comparator, O - outcome)[8,10] to elaborate the following guiding question for the review: what is the scientific evidence on biosurveillance systems and AE reporting in organ donation and transplantation?

Five electronic databases were used in the scientific literature search: Medical Literature Analysis and Retrieval System Online (MEDLINE - via PubMed), Excerpta Medica Database (Embase), Web of Science, LILACS, Scopus and the Scielo journal directory. A data search was also performed in the following secondary databases: Notify - World Health Organization (WHO), Pan American Health Organization (PAHO) and Google Scholar.

Controlled descriptors (MeSH, Entree and Health Science Descriptors - DeCS) were used to search for studies; terms were combined using the Boolean operators AND and OR, and the search strategy was guided by MEDLINE (Chart 1) and adapted to the other databases.

After the searches, the reference list of included studies was manually analyzed in order to find other relevant studies to this review. The search and pre-analysis of selected articles were performed by two independent evaluators using the Rayyan tool[11] to guarantee the blinding of evaluators during peer review and the organization and storage of selected references. Data were collected in March 2021.

Chart 1. Strategy for searching the databases

Database	Search strategy
MEDLINE/PubMed	(("safety management"[MeSH Terms] OR "Safety Culture"[All Fields] OR ("safety"[All Fields] AND "management"[All Fields]) OR ("culture"[All Fields] AND "safety"[All Fields])) AND "management"[All Fields]) OR "safety management"[All Fields] OR ("cultures"[All Fields] AND "safety"[All Fields])) OR "Safety Cultures"[All Fields] OR "Hazard Management"[All Fields] AND "hazard"[All Fields])) OR "Hazard Control"[All Fields] OR ("safety management"[MeSH Terms] OR "Hazard Surveillance Program"[All Fields] AND ("transplants"[MeSH Terms] OR "Transplant"[All Fields] OR "Grafts"[All Fields] OR "Tissue Transplants"[All Fields] OR "tissue"[All Fields])) OR "Organ Transplants"[All Fields] AND ("tissue and organ procurement"[MeSH Terms] OR "Tissue Procurement"[All Fields] OR "Tissue Procurements"[All Fields] OR ("tissue and organ procurement"[MeSH Terms] OR ("tissue"[All Fields] AND "requests"[All Fields])) OR "Organ Donation"[All Fields] OR "tissue and organ procurement"[All Fields] OR ("card"[All Fields] AND "donor"[All Fields])) OR ("tissue and organ procurement"[MeSH Terms] OR ("tissue"[All Fields] AND "organ"[All Fields] AND "procurement"[All Fields]) OR "tissue and organ procurement"[All Fields] OR ("cards"[All Fields] AND "donor"[All Fields])) OR "Donor Card"[All Fields])

After the searches, duplicate articles were excluded. The studies were manually analyzed by two independent reviewers, starting the analysis of articles by title and abstract, based on inclusion/exclusion criteria. Articles that did not meet the inclusion criteria were also excluded. All included articles underwent full-text peer review in order to select eligible articles. The primary outcome analyzed in this review was the notification of AE related to organ and tissue donation and/or transplantation, as well as biosurveillance systems. A third reviewer analyzed studies in which there was no consensus between the first two evaluators.[12]

A data extraction worksheet was used. Studies were identified according to method and outcome for the easier classification and evaluation of each study by two independent reviewers. In case of doubt or disagreement, a third reviewer was called for evaluation.

Study quality and risk of bias were independently assessed by two reviewers using the MINORS tool,[13] which has eight analysis items for studies without a comparative group: 1- Clearly stated aim; 2- Inclusion of consecutive patients; 3- Prospective data collection; 4- Endpoints appropriate to study aim; 5- Unbiased assessment of study endpoint; 6- Follow-up period appropriate to study aim; 7- <5% lost to follow-up; and 8 - Prospective calculation of study size. Each piece of information is classified from zero to two with the following parameters: zero (0) for not reported information; one (1) for reported information, but inadequate; and two (2) for reported and adequate information. The MINORS tool was chosen for assessment of the quality of studies because of the observational design of studies found.

As the outcomes of studies were very different, a meta-analysis or any statistical analysis could not be performed in this review.

To ensure data reliability, this systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO/NHS) under registry number CRD42021225545.

Results

Searches in the six electronic databases resulted in 551 studies; 29 were duplicates and excluded using the Rayyan tool, resulting in 522 studies that went through the selection process by title and abstract, and 499 studies were excluded because they did not meet the pre-established inclusion criteria. Exclusion by title and abstract resulted in the selection of 23 studies that were read in full. After the stage of exhaustive reading of studies in full, another 15 studies were excluded because they did not meet the study objectives. Eight articles remained and were included for qualitative synthesis and analysis. The process of selection of studies is shown in figure 1.

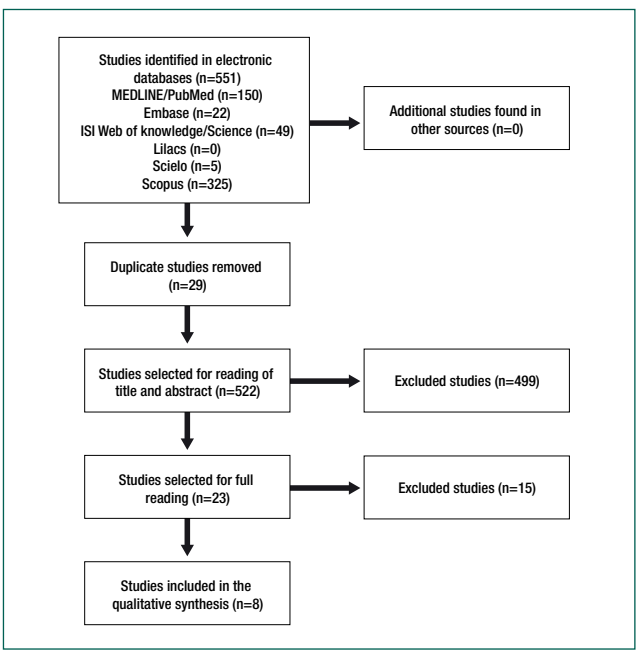

Figure 1. PRISMA flowchart for selection of studies

As for the characteristics of studies, the publication date ranged between 2013-2019, in English and Spanish, studies were conducted in several countries, and the cross-sectional study design predominated. The main characteristics of studies included in the synthesis of this systematic review are displayed in chart 2.

Chart 2. Synthesis of articles included in the study

	Author/Year/ Citation	Objective	Design/sample	Interventions	Outcomes	Main results	Category
A7	Mareri M, Filippetti M, Ghirardini A, Vespasiano F, Ciaccio P, Costa AP (2011)[14]	To describe the functioning of the EUROCET Portal and the biosurveillance system in Europe.	Case report. Description of the EUROCET Network, Competent Authorities (CA) and Authorized Tissue Establishments (TEs).	Description of the EUROCET Network, Competent Authorities (CA) and Authorized Tissue Establishments (TEs).	There are 33 countries linked to EUROCET and 57 CAs, 3,974 TEs are registered: 1,108 for tissues, 1,480 for hematopoietic progenitor cells and 1,386 for assisted reproduction.	Based on cooperation with the CAs, EUROCET represents them in the European Network. The Portal contributes to the biosurveillance system in Europe. State members of the EU rely on the web portal and database, which contributes to decision-making based on facts and guidelines.	Recommendations
b1	Ali AK (2013)[15]	To identify and characterize risks and serious AE associated with exposure to BRM (Biologic Response Modifiers) in organ transplant patients in a real-world environment.	Cross-sectional observational study. Sample: 12,151 AE reports	Analysis of AE reported to the Adverse Event Reporting System. Adverse events related to drugs used in organ transplant patients were analyzed.	A total of 12,151 notifications classified as serious events were analyzed. Of these, 6,749 (55%) related to sirolimus; 2,317 (19%) to mycophenolate; 1,067 (9%) to cyclosporine; 841 (7%) to tacrolimus; 725 (6%) related to antithymocyte immunoglobulin and 452 (4%) to others. Types of AE reported: neurotoxicity; hospitalization or longer length of hospital stay; reinterventions; coma; death.	The use of Biologic Response Modifiers for prophylaxis against transplant rejection is associated with serious AE that can be fatal. Transplant specialists must be cautious when prescribing these drugs to transplant patients and monitor patients' progress in terms of safety, tolerability, and transplant outcomes during the exposure period.	Results
c3	Stewart DE, et al. (2015)[16]	To describe an AE review process based on root cause analysis in an organ transplant center and its contributions to the improvement of the process.	Retrospective cross-sectional observational study. Notifications of safety situations in the period from 2012 to 2013, via the online portal or other means of generating reports.	Transplant-related AE or near miss reported in the period from 2012 to 2013, via the online portal or other forms of reporting were analyzed.	Between 2012 and 2013, 438 adverse event reports were received through the online portal or other forms of reporting, and about half were self-reports. Communication failure (22.8%) was the most common type of event. Events considered as avoidable errors led to the disposal of organs and near misses. Among events reported by the Organ Procurement Organization (OPOs), half came from just 10 out of 58 institutions, while half of the events reported by *centros* came from just 21 out of 250 institutions. Thirteen (23%) OPOs and 155 (62%) transplant centers reported no events, suggesting substantial underreporting	In one year, 438 AE were reported, and 50% of these were self-reports. The most common event was related to communication failure. The study evidences the underreporting of AE.	Result
d2	Czerwiński J, Kaliciński P, Danielewicz R (2015)[17]	To provide an introduction to everyday organ transplant practices from national and European legislative initiatives to monitor and manage SAREs (Serious Adverse Reactions and Events) in order to ensure the quality of organ donation from both deceased and living donors and the safety of donors and recipients in living transplants.	Prospective, descriptive, cross-sectional observational study. Analysis of 129 reports of AE and AR.	Analysis of 129 reports of AE and AR from the period between 2012 and 2013, referring to living donors and recipients, from the total of 3,223 transplanted organs.	In the analyzed period, 3,223 transplants were performed, with 17 serious AE and 112 AR documented (events in 0.5% and reactions in 3.4% of cases).	The purpose of the SARE registry is to collect and manage occurrences related to living donors and recipients, due to the quality of the donor, the organ and the process of collection and management of the organ until implantation. The SARE monitoring system aims at self-assessment, development and dissemination of information about the potential dangers of organ transplantation. Considering the small number of SARE referred to Poltransplant in 2012 (n = 64) and 2013 (n = 65), during which the monitoring system was fully implemented, the authors indicate there was underreporting. According to the authors, underreporting results from the fear of transplant centers to reveal possible failures.	Results

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Continuation.

	Author/Year/ Citation	Objective	Design/sample	Interventions	Outcomes	Main results	Category
e6	Eguchi S, et al. (2017)[18]	To describe the donor advocacy program established by Nagasaki University Hospital and launched for living donors of liver, bone marrow, kidney, lung, and other organs.	Observational qualitative study. Case report. Description of three cases.	The study describes how the University of Nagasaki Hospital established and implemented a Donor Advocacy Team (DAT): a risk management program for initiation in the event of severe, persistent, or fatal impairment of an organ, tissue, or cell transplant from a living donor.	The Nagasaki University Hospital has established a risk management system called the DAT and a system of communication and response to local government, mass media, academic transplant societies and the Japan Organ Transplant Network. DAT functions: to provide assistance to donors, their family and the medical staff involved and communicate accurate information to the public without delay; risk management team, composed of physicians and professionals from different areas, such as risk manager, counselor, spokesperson, responsible for legal matters, bioethicist and social worker.	The study describes the risk management process called DAT and establishes quick and effective communication strategies for professionals and institutions involved in the donation and transplant process and the population.	Recommendations
f5	Khorzad R, Montague E, Nannicelli AP, Woods DM, Ladner DP, Brown A, Holl JL (2018) [19]	To describe an improvement project conducted as part of the United Network for Organ Sharing project.	Case report. Sample: 42 physicians and staff from 10 organ procurement organizations and two transplant centers in the United States participated in the study.	An interdisciplinary team conducted a Process Failure Modes and Effects Analysis, laboratory simulations of organ labeling during purchase, and a heuristic evaluation of a labeling software application to inform the design of TransNet, a system that uses barcode on the organ retrieval point. A total of 42 physicians and staff from 10 organ procurement organizations and two transplant centers across the United States participated. Processes covered: key features of the redesigned labeling system include independent, dual input of label information into the software application, a barcode machine on each organ label, and a portable printer for printing labels at the "point of use"	The new labeling, TransNet, became mandatory since June 2017. The survey conducted with early adopters after one year of use, indicates the process is safer and more efficient. Implications for practice: results of this study suggest that the application of quality planning methods, common in other sectors, when redesigning a health care process, are valuable and revealing, and should be adopted more widely. Future evaluation of the effectiveness of TransNet in reducing security incidents is critical. Process Failure Modes and Effects Analysis revealed 146 potential failures, of which 34 (23%) were associated with a verification step in organ labeling and 56 (38%) had the potential to harm a patient or result in organ loss. The greatest potential for damage failures was underlying low frequency causes (1 in 10,000 or less in 37 failures, 1 in 5000 for 14 failures, and 1 in 2000 for 2 failures). Three failures had causes with a moderate frequency of 1 in 1000. Two were related to the omission of critical information (eg, hepatitis B status, *piçamento* time that was handwritten and to the outer packaging labels, and one was related to a data entry/ transcription error that can occur when entering immunology laboratory results into the donor management software, DonorNet.	The risks and incidents found refer to sample labeling errors due to unreliable source information and data entry errors during the registration of donors in the electronic OPO system. Study resulted in comprehensive identification of organ labeling risks. The findings indicate that the design of TransNet, a system implemented in OPOs in the United States in 2014, has now become mandatory.	Process
g4	Mathur AK, Stemper-Bartkus C, Engholdt K, Thorp A, Dosmann M, Khamash H (2019)[20]	To describe the AE analysis process based on root cause analysis in an organ transplant center and its contributions to process improvement.	Retrospective cross-sectional observational study. Sample: analysis of 1,449 transplant procedures	Analysis of quality improvement domains identified in departmental case reviews at a high-volume transplant center. Specific areas of process improvement vary by stage of treatment: transplant center / pre-transplant / donation: Operative and perioperative care / Post-transplant / donation care. Descriptive statistics from departmental case analyzes performed as of October 26, 2015 May 14, 2018 - AE by area/by organ.	In 30 months, 1,449 transplant and living donor procedures were analyzed, with a total of 45 deaths and 31 graft losses; 91 notifications: 43 related to kidney transplant; 24 to liver; 10 to pancreas; 6 to heart; 3 to lung; 5 related to the living donor. Seventy-nine action plan items were identified in the improvement domains, including errors in clinical decision making, communication, compliance, documentation, selection, waiting list management, and administrative processes. The average time to review was 83 days and six days to complete the action plan. Clinical decision-making in the pre-transplant phase was identified as an opportunity for improvement in all programs.	The analysis of reported cases provides a robust approach to the review of transplant AE. The AE review process begins with the occurrence and reporting of an AE, including patient deaths, graft losses, and other patient safety events. This process includes thorough review of the narrative timeline, multidisciplinary discussion, and creation of action plan items aimed at improving processes using quality improvement methods.	Process

Continue...

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	Author/Year/ Citation	Objective	Design/sample	Interventions	Outcomes	Main results	Category
h8	Cohen J, Ashkenazi T (2019)[21]	To describe the implementation and use of a centralized medical advisory service (MAS), based on a telephone service (aimed at mapping the safety, quality and standardization of the donation process).	Prospective, observational, quanti-qualitative study.	Analysis of a centralized MAS created in 2007 to answer questions from healthcare professionals about organ safety, determination of brain death and donor management. Data collected from 2007 to 2017 included the number and context of consultations and the average number of organs transplanted.	Sample: 2,826 consultations to the centralized MAS from 2007 to 2017. The context of consultations shows the formulation of protocols related to donor infections and malignancy and difficulties identified regarding the determination of brain death and subsequent implementation of solutions.	Study describes the implementation and use of a centralized MAS, based on a telephone service. Authors suggest that this model can provide a valuable resource to improve the safety, quality and standardization of the donation process.	Recommendations

After the analysis of studies, AR and AE related to results and processes could be identified, as well as strategies and recommendations for better safety in the transplant process (Chart 3).

Items of the MINORS scale are rated as 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). The maximum score is 16 for non-comparative studies and 24 for comparative studies. Such analysis showed that the study by Mareri[14] obtained lower scores (chart 4).

Chart 3. Findings related to results, processes and strategies for preventing adverse events

Results
Adverse drug-related reactions[15]
Neurotoxicity[15]
Longer length of hospital stay[15]
Reinterventions[15]
Coma[15]
Death[15,17,20]
Graft failure or loss[15]
Falls[16]
Processes
Underreporting [16,17]
Communication failures[16,19]
Failure in information systems and/or documents[19,20]
Compliance errors[20]
Errors in decision making[20]
Errors in the selection and management of the waiting list[20]
Labeling errors[19]
Failure to transcribe information and laboratory and immunology results[19]
Prevention strategies
Plan AE prevention and risk mitigation strategies[19]
Perform risk management[18,19]
Implement a communication system to support professionals in decision making[18,21]
Implement a portal to support family members[14]
Create a database of AE situations for analysis and the support of prevention and decision-making [14]
Standardize processes[14]

Chart 4. Classification of study quality and risk of bias according to the MINORS tool

Author/Year/Citation	n Adverse Events	Study follow-up time	MINORS Score
Mareri M, et al.(2011)[14]	3.974	2 years	04
Ali AK (2013)[14]	12.151	15 years	8
Stewart DE, et al. (2015)[16]	438	1 year	15
Czerwiński J, Kaliciński P, Danielewicz R (2015)[17]	14.129	1 year	14
Eguchi S, et al. (2017)[18]	3	Not reported	05
Khorzad R, et al. (2018)[19]	52	Not reported	11
Mathur AK, Stemper-Bartkus C, Engholdt K, Thorp A, Dosmann M, Khamash H (2019)[20]	1.449	2 years and 6 months	11
Cohen J, Ashkenazi T (2019)[21]	2.826	10 years	10

Discussion

The results of the study show scientific evidence of AE occurring at some stage of the organ donation and transplantation process, such as adverse drug reactions,[15] neurotoxicity,[15] longer length of hospital stay,[15] surgical reinterventions,[15] falls,[16] coma,[15] death,[16,17,20] and graft failure or loss.[20] Note that AE reporting data are possibly still underreported.[22,23]

A study conducted by Estrada et al.[24] in a university hospital institution in Bogotá describes the occurrence of AE and related risk factors, and indicates the lack of prevention as one of the main causes for occurrence of AE. It shows that the occurrence of AE led to an increase in the average length of hospital stay of 17.5 days, in addition to serious complications, such as death, and also reports that most of the analyzed AEs were preventable and more than 80% of them were classified as serious.

Risk is present in any care activity and at any stage of donation and transplantation. However, the occurrence of an AE follows a path in which safety

barriers are often overcome. Risks can be managed and mitigated, and in general, AE can be prevented if safety protocols are followed, respecting the safety culture of the institution.[25]

In a study conducted in Colombia and published in 2018,[26] the causes of 164 AE reported in a hospital were analyzed, and the following were described as causes of AE: carelessness of professionals, incorrect identification of patients, and failure to follow institutional routines and protocols. The study also indicated that 58% of the AE analyzed were preventable. In addition to these causes, drug-related AE are also significant in healthcare, accounting for 45% of AE related to drugs or medicinal substances in therapeutic use in the US.[27]

The results show that failure in processes and activities, or failure to follow protocols and recommendations are related to the occurrence of AE.[28] The analyzed studies bring the following as causes of the occurrence of AEs: failures in communication;[16,19] failure in recording information in systems and documents;[19,20] in addition to errors in the transcription of information and laboratory and immunology results;[19] compliance errors, that is, failure to follow routines and protocols;[20] errors in decision making;[20] errors in the management of the waiting list;[20] and errors in the labeling of donated organs or tissues.[19] These situations put the donated organ/tissue and the recipient at risk, and also exert impact on the safety and reliability of the donation and transplant process.

Underreporting endorses the importance of reflecting and discussing safety and failure to follow protocols and prevention measures, and denotes the importance of a safety culture perspective.[29] Analyzing the reasons for non-reporting is also essential to improve records and have more data to support risk mitigation and AE prevention measures. According to Almeida, de Jesus and Morais,[22] the policy of punishment for those who fail is still predominant in several institutions, inhibiting notification by professionals. The authors indicate that in order to establish a safety scenario in institutions, a behavior of continuous learning must be adopted, based on notifications and the analysis of how they happened, seeking strategies to improve care and administrative process.[22]

The studies analyzed in this review address the need to plan and invest in AE prevention strategies and the management and mitigation of risks.[18,19] Some of the strategies aimed at greater safety in decision-making at various stages of the donation and transplant process are the implementation of safe communication tools and a communication system to support professionals on the front line, in direct patient care, or even in the area of donation and transplantation management.[18,21] The family and society should also be included with regard to effective communication in relation to guidelines and self-care, the flow of care, clarification of doubts and also information on how donation and transplants occur.[14]

Standardizing processes was also one of the strategies found in this study.[21] The standardization of processes provides greater alignment of practices, reducing the risk of failure and following what is stipulated in the institution, based on guidelines and scientific evidence. However, each individual must be assisted in their uniqueness.

Each stage of the organ and tissue donation and transplantation process is performed with rigor, ethics and moral, following legal precepts. However, the eventual occurrence of failures, AE, non-conformities or failure to follow predetermined flows and protocols can result in the loss of the potential donor, in the impossibility of donated and viable organs to be transplanted, in harm to the recipient, in addition to other losses.[30]

Organizing a database of AE or near-miss AE situations for further analysis and providing training or continuing education contribute to the safety culture, to risk management, to support prevention and decision-making by professionals directly or indirectly involved in the care and management process of donation and transplantation.[14,31,32]

Implementing the management of biosurveillance systems aimed at mapping risks, analyzing AE and proposing measures for their prevention in the donation and transplant process are actions that have been developed in several countries, such as

Italy, Spain, United States, Australia and in Brazil by means of the Health Surveillance Agency.[2,33]

In this context, data from the present review present scientific evidence on biosurveillance systems and notification of AE in the process of organ and tissue donation and transplantation, highlighting the consequences of the occurrence of AE and related causes, in addition to presenting strategies to mitigate risks, prevent the occurrence of errors and make the team more prepared and qualified to act with greater safety and quality in the process of donation and transplantation of organs and tissues.

As implications of the findings for the health area, the study highlights the importance of safe care practices, of performing activities inherent to the process of donation and transplantation of organs and tissues with quality and safety for all involved, whether a donor, recipient and professionals. In clinical practice, it is relevant to report risk situations, near miss and AE, and based on these occurrences, perform an analysis of the event in order to contribute to greater safety and process improvement.

For future studies, we recommend the analysis of the safety culture in institutions where donation and transplants are performed.

A limitation of the study was the impossibility of performing statistical analysis and meta-analysis based on its results, and because it is a systematic review of observational studies, the possibility of confounding variables that can generate erroneous measures of association. Another limiting factor is the scarcity of studies related to biosurveillance and studies describing the occurrence of AE in the process of donation and transplantation of organs and tissues, due to the incipient notification of AE by professionals and health institutions. Furthermore, until the moment of the search, no randomized clinical studies were identified.

Conclusion

The implementation of management in the biosurveillance system has been a strategy adopted by several countries, including Brazil, with the aim to promote the notification of AE that occurred during the organ and tissue donation and transplantation process, analyze the reported events and propose preventive and risk reduction measures. The results indicate the occurrence of AE at some stage of the organ and tissue donation and transplantation process, such as: adverse drug-related reactions; neurotoxicity; longer length of hospital stay; surgical reinterventions; falls; coma; death; graft failure or loss. Note that AE are possibly still underreported and their causes are not always clear. The studies analyzed show that failure in processes, in following protocols and guidelines, in communication, in reporting information, and in the transcription of information and exam results, as well as labeling errors of conditioned organs and tissues, among others, contribute to the occurrence of AE. Thus, the fact that biosurveillance systems may contribute to the quality, safety and greater reliability of the organ and tissue transplant and donation process stands out.

References

1. Roza B, Kusahara D, Pessoa J, Treviso P, Oliveira P, Leite R, et al. Modelos e iniciativas de biovigilância e transplante: uma revisão narrativa. Vigil Sanitária Debate. 2019;7(4):10-6.
2. Agência Nacional de Vigilância Sanitária (ANVISA). Resolução de Diretoria Colegiada RDC Nº 339. Dispõe sobre a instituição do Sistema Nacional de Biovigilância. Brasília (DF): ANVISA; 2020 [citado 2020 Maio 25]. Disponível em: http://portal.anvisa.gov.br/documents/10181/3146460/RDC_339_2020_.pdf/b7b60dd9-ba54-4d91-b6db-8d3a2d369afb
3. Brasil. Ministério da Saúde. Portaria Nº 1.660, de 22 de julho de 2009. Institui o sistema de notificação e investigação em vigilância sanitária Vigipos, no âmbito do sistema nacional de vigilância sanitária, como parte integrante do sistema único de saúde SUS. Brasília (DF): Ministério da Saúde; 2009 [citado 2020 Maio 25]. Disponível em: https://bvsms.saude.gov.br/bvs/saudelegis/gm/2009/prt1660_22_07_2009.html
4. Brasil. Ministério da Saúde. Portaria Nº 529. Institui o Programa Nacional de Segurança do Paciente (PNSP). Brasília (DF): Ministério da Saúde; 2013 [citado 2020 Maio 25]. Disponível em: http://bvsms.saude.gov.br/bvs/saudelegis/gm/2013/prt0529_01_04_2013.html
5. Agência Nacional de Vigilância Sanitária (ANVISA). Relatório de dados de eventos adversos 2015 a 2018. Biovigilância no Brasil. Brasília (DF): ANVISA; 2020 [citado 2021 Fev 22]. Disponível em: http://portal.anvisa.gov.br/documents/33868/3055469/1o+Relat%C3%B3rio+de+dados+de+Biovigil%C3%A2ncia/325bb60c-f1cf-46fe-97a4-0e06e27e8a76
6. Agência Nacional de Vigilância Sanitária (ANVISA). Resolução da Diretoria Colegiada-RDC nº 55. Dispõe sobre as Boas Práticas em Tecidos Humanos e Terapêutico. Brasília (DF): ANVISA; 2015 [citado 2020 Maio 25]. Disponível em: http://portal.anvisa.gov.br/documents/10181/2718376/RDC_55_2015_.pdf/57eb6007-b35e-4d15-992d-51118966450c?version=1.0

7. Agência Nacional de Vigilância Sanitária (ANVISA). Resolução da Diretoria Colegiada-RDC nº 214. Dispõe sobre as Boas Práticas em Células Humanas para Uso Terapêutico e pesquisa clínica, e dá outras providências. Brasília (DF): ANVISA; 2018 [citado 2021 Fev 22]. Disponível em: http://portal.anvisa.gov.br/documents/10181/3078078/%281%29RDC_214_2018_.pdf/8acbc5cb-bca6-4725-b9de-da584e3c024a

8. Brasil. Ministério da Saúde. Secretaria de Ciência, Tecnologia e Insumos Estratégicos. Departamento de Ciência e Tecnologia. Diretrizes Metodológicas: elaboração de revisão sistemática e metanálise de estudos observacionais comparativos sobre fatores de risco e prognósticos. Brasília (DF): Ministério da Saúde; 2014 [citado 2021 Fev 22]. Disponível em: https://bvsms.saude.gov.br/bvs/ct/PDF/diretrizes_metodologias_estudos_observacionais.pdf

9. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.

10. Latorraca CO, Rodrigues M, Pacheco RL, Martimbianco AL, Riera R. Busca em bases de dados eletrônicas da área da saúde: por onde começar. Diagn Tratamento. 2019;24(2):59-63.

11. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. 2016;5:210.

12. Lopes-Júnior LC, Lima RA, Olson K, Bomfim E, Neves ET, Silveira DS, et al. Systematic review protocol examining the effectiveness of hospital clowns for symptom cluster management in paediatrics. BMJ Open. 2019;9:e026524.

13. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (minors): development and validation of a new instrument. ANZ J Surg. 2003;73(9):712-6.

14. Ali AK. pharmacovigilance analysis of serious adverse events reported for biologic response modifiers used as prophylaxis against transplant rejection: a real-world postmarketing experience from the US FDA adverse event reporting system (FAERS). Int J Org Transplant Med. 2013;4(2):62-71.

15. Czerwiński J, Kaliciński P, Danielewicz R. Serious adverse events and reactions in organ donation and transplantation: a web-net tool- based nationwide system for reporting and monitoring. Ann Transplant. 2015;20:243-8.

16. Stewart DE, Tlusty SM, Taylor KH, Brown RS, Neil HN, Klassen DK, et al. Trends and patterns in reporting of patient safety situations in transplantation. Am J Transplant. 2015;15:3123-33.

17. Mathur AK, Stemper-Bartkus C, Engholdt K, Thorp A, Dosmann M, Khamash H. Identifying patterns of adverse events of solid organ transplantation through departmental case reviews. Mayo Clin Proc Innov Qual Outcomes. 2019;3(3):335-43.

18. Khorzad R, Montague E, Nannicelli AP, Woods DM, Ladner DP, Brown A, et al. Redesigning transplant organ labeling to prevent patient harm and organ loss. Progress Transplant. 2018;28(3):271-7.

19. Eguchi S, Soyama A, Nagai K, Miyazaki Y, Kurihara S, Hidaka M, et al. The donor advocacy team: a risk management program for living organ, tissue, and cell transplant donors. Surg Today. 2017;47(8):980-5.

20. Mareri M, Filippetti M, Ghirardini A, Vespasiano F, Ciaccio P, Costa AP. The EUROCET Network: Support for Coding, Vigilance and Surveillance. Transfus Med Hemother. 2011;38:352-6.

21. Cohen J, Ashkenazi T. The implementation and utilization of an organ donation dedicated medical advisory service: A descriptive study. Clin Transplant. 2019;33(11):e13711.

22. Almeida HO, De Jesus AM, Morais CR. Eventos adversos relacionados à assistência em serviços de saúde: um desafio para segurança do paciente. Cad Grad Cien Biol Saude. 2020;6(2):11.

23. Maia, CS, Freitas DR, Gallo LG, Araujo WN. Notificações de eventos adversos relacionados com a assistência à saúde que levaram a óbitos no Brasil, 2014-2016. Epid Serv Saúde. 2018;27(2):1-10.

24. Estrada-Orozco K, Gaitán-Duarte H, Moreno S, Moreno-Chaparro J. Eventos hospitalares notificáveis: incidência e fatores contribuintes no serviço de cirurgia de um hospital de alta complexidade em Bogotá, Colômbia, 2017. Colombian J Anestesiology. 2019;47(1):5-13.

25. Hessels A, Paliwal M, Weaver SH, Siddiqui D, Wurmser TA. Impact of patient safety culture on missed nursing care and adverse patient events. J Nurs Care Qual. 2019;34(4):287-94.

26. Gonzalez CE, Restrepo LD. Sucesos adversos relacionados con el acto quirúrgico en una institución de salud de tercer nivel. Rev Cubana Salud Pub. 2018;44(3):1-14.

27. Riaz M, Brown JD. Association of adverse drug events with hospitalization outcomes and costs in older adults in the USA using the Nationwide Readmissions Database. Pharmaceut Med. 2019;33(4):321-9.

28. Xelegati R, Gabriel CS, Dessotte CA, Zen YP, Évora YD. Eventos adversos relacionados ao uso de equipamentos e materiais na assistência de enfermagem a pacientes hospitalizados. Rev Esc Enferm USP 2019;53:e03503.

29. Siman AG, Cunha SG, Brito MJ. The practice of reporting adverse events in a teaching hospital. Rev Esc Enferm USP. 2017;51:e03243.

30. Knihs NS, Cabral AS, Magalhães AL, Barra DC, Lanzoni GM, Silva OM. Avaliação da cultura de segurança no processo de doação de órgãos. Rev Bras Enferm. 2020;73(2):e20180514.

31. Ramírez E, Martín A, Villán Y, Lorente M, Ojeda J, Moro M, et al. Effectiveness and limitations of an incident-reporting system analyzed by local clinical safety leaders in a tertiary hospital: Prospective evaluation through real-time observations of patient safety incidents. Medicine (Baltimore). 2018;97(38):e12509.

32. Maguire EM, Bokhour BG, Wagner TH, Asch SM, Gifford AL, Gallagher TH, et al. Evaluating the implementation of a national disclosure policy for large-scale adverse events in an integrated health care system: identification of gaps and successes. BMC Health Serv Res. 2016;16(1):648.

33. Treviso P, Amorim MH, Schimer J, Roza BA. Biovigilância: qualidade e segurança no processo de doação e transplante de órgãos e tecidos [Editorial]. Rev Sobecc. 2020;25(1):1-2.