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

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.

Abstract

Resumo

Methods: Revisão sistemática de estudos observacionais seguindo as recomendações das Diretrizes Metodológicas (REBRATS) e Prefered Reporting Items for Systematic Review and Meta-Analysis (PRISMA). Foram incluídos estudos primários e relatos de caso conduzidos sobre biosurveillance 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

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

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secundarias: 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; falecimento, 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 de ellos para 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 ou perda do enxerto. Destaca-se que os eventos adversos possivelmente ainda são 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. 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. 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).

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) and the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 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. The PECO acronym was used (P - population, E - exposure, C - comparator, O - outcome) 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 to guarantee the blinding of evaluators during peer review and the organization and storage of selected references. Data were collected in March 2021.
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.
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.

<table>
<thead>
<tr>
<th>Author/Year/ Citation</th>
<th>Objective</th>
<th>Design/sample</th>
<th>Interventions</th>
<th>Outcomes</th>
<th>Main results</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>A7 Mareri M, Filippetti M, Ghirardini A, Vespasiano F, Ciaccio P, Costa AP (2011)</td>
<td>To describe the functioning of the EUROCET Portal and the biosurveillance system in Europe.</td>
<td>Case report. Description of the EUROCET Network, Competent Authorities (CA) and Authorized Tissue Establishments (TEs).</td>
<td>Description of the EUROCET Network, Competent Authorities (CA) and Authorized Tissue Establishments (TEs).</td>
<td>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.</td>
<td>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.</td>
<td>Recommendations</td>
</tr>
<tr>
<td>b1 Ali AK (2013)</td>
<td>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.</td>
<td>Cross-sectional observational study. Sample: 12,151 AE reports</td>
<td>Analysis of AE reported to the Adverse Event Reporting System. Adverse events related to drugs used in organ transplant patients were analyzed.</td>
<td>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.</td>
<td>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.</td>
<td>Results</td>
</tr>
<tr>
<td>c3 Stewart DE, et al. (2019)</td>
<td>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.</td>
<td>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.</td>
<td>Analysis of AE reports or near-miss reported in the period from 2012 to 2013, via the online portal or other forms of reporting were analyzed.</td>
<td>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 centers come from just 21 out of 250 institutions. Thirteen (23%) OPOs and 155 (62%) transplant centers reported no events, suggesting substantial underreporting.</td>
<td>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.</td>
<td>Result</td>
</tr>
<tr>
<td>d2 Czerwiński J, Kaliciński P, Danielewicz R (2019)</td>
<td>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.</td>
<td>Prospective, descriptive, cross-sectional observational study. Analysis of 129 reports of AE and AR.</td>
<td>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.</td>
<td>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.</td>
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<th>Recommendations</th>
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</thead>
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<tr>
<td>e6 Eguchi S, et al. (2017)</td>
<td>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.</td>
<td>Observational qualitative study, Case report, Description of three cases.</td>
<td>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.</td>
<td>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.</td>
<td>Recommendations</td>
<td>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.</td>
<td></td>
</tr>
<tr>
<td>T5 Khordad R, Montague E, Nannicelli AP, Woods DM, Ladner DP, Brown A, Holl JL (2018)</td>
<td>To describe an improvement project conducted as part of the United Network for Organ Sharing project.</td>
<td>Case report, Sample: 42 physicians and staff from 10 organ procurement organizations and two transplant centers in the United States participated in the study.</td>
<td>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”.</td>
<td>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, recipient time that was handwritten 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.</td>
<td>Process</td>
<td>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.</td>
<td></td>
</tr>
<tr>
<td>g4 Mathur AK, Stempel-Bartkus C, Enghold K, Thorp A, Dosmann M, Khamash H (2019)</td>
<td>To describe the AE analysis process based on root cause analysis in an organ transplant center and its contributions to process improvement.</td>
<td>Retrospective cross-sectional observational study, Sample: analysis of 1,449 transplant procedures</td>
<td>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 analyses performed as of October 26, 2015 May 14, 2018 - AE by area/organ.</td>
<td>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.</td>
<td>Process</td>
<td>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.</td>
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Continue...
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).

**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.

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

<table>
<thead>
<tr>
<th>Results</th>
<th>Drug reactions(15,20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurotoxicity(15), Long length of hospital stay(15), Surgical reinterventions(15), Falls(16)</td>
<td></td>
</tr>
<tr>
<td>Coma(15), Death(15,17,20), Graft failure or loss(20)</td>
<td></td>
</tr>
</tbody>
</table>

**Processes**

- Underreporting(15,16)
- Communication failures(15,16)
- Failure in information systems and/or documents(14,20)
- Compliance errors(20)
- Errors in decision making(20)
- Errors in the selection and management of the waiting list(20)
- Labeling errors(20)
- Failure to transcribe information and laboratory and immunology results(15)

**Prevention strategies**

- Plan AE prevention and risk mitigation strategies(76)
- Perform risk management(14,15)
- Implement a communication system to support professionals in decision making(16)^6
- Implement a portal to support family members(15)^6
- Create a database of AE situations for analysis and the support of prevention and decision making(15)^6
- Standardize processes(14)^6

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

<table>
<thead>
<tr>
<th>Author/Year/Citation</th>
<th>n Adverse Events</th>
<th>Study follow-up time</th>
<th>MINORS Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ali AK (2019)(16)</td>
<td>12.151</td>
<td>15 years</td>
<td>8</td>
</tr>
<tr>
<td>Steward OE, et al. (2015)(18)</td>
<td>438</td>
<td>1 year</td>
<td>15</td>
</tr>
<tr>
<td>Eguchi S, et al. (2017)(26)</td>
<td>3</td>
<td>Not reported</td>
<td>05</td>
</tr>
<tr>
<td>Khorzad R, et al. (2018)(19)</td>
<td>52</td>
<td>Not reported</td>
<td>11</td>
</tr>
<tr>
<td>Mathur AK, Steinperi-Bartkus C, Engholdt K, Thorp A, Dosmann M, Khamash H (2019)(20)</td>
<td>1.449</td>
<td>2 years and 6 months</td>
<td>11</td>
</tr>
<tr>
<td>Cohen J, Ashkenazi T (2019)(21)</td>
<td>2.826</td>
<td>10 years</td>
<td>10</td>
</tr>
</tbody>
</table>

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**


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


