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REVIEW ARTICLE

Gastrointestinal Complications after Heart Transplantation: An Integrative Comparative Review between Adult and Pediatric Populations

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ABSTRACT

Objectives: To investigate gastrointestinal complications in the postoperative period of heart transplantation, clinically comparing adult and pediatric populations. **Methods:** An integrative review of observational studies in the PubMed, Embase, and Cochrane Library databases, subjected to screening and methodological quality assessment. **Results:** A clinical age-based dichotomy was identified. The pediatric population presented a higher incidence of complications, characterized by an immunopharmacological profile (pneumatosis intestinalis, drug intolerance) and a benign clinical course. In contrast, adults exhibited a lower incidence but an ischemic-mechanical profile with high lethality in events such as mesenteric ischemia. Additionally, the use of proton pump inhibitors reduced mycophenolate absorption, increasing the risk of acute rejection. **Conclusion:** Complications require stratified management protocols: conservative support and pharmacological adjustment in children and a high index of suspicion for early surgical intervention in adults. Gastric prophylaxis requires rigorous monitoring to avoid interactions that compromise the graft.

Descriptors: Heart Transplantation; Postoperative Complications; Gastrointestinal Diseases; Immunosuppression; Pneumatosis Cystoides Intestinalis.

Complicações Gastrointestinais no Pós-Transplante Cardíaco: Uma Revisão Integrativa Comparativa entre as Populações Adulta e Pediátrica

RESUMO

Objetivos: Investigar as complicações gastrointestinais no pós-operatório de transplante cardíaco, comparando clinicamente as populações adulta e pediátrica. **Métodos:** Revisão integrativa de estudos observacionais nas bases de dados PubMed, Embase e Cochrane Library, submetidos à triagem e avaliação de qualidade metodológica. **Resultados:** Identificou-se uma dicotomia clínica etária. A população pediátrica apresentou maior incidência de complicações, caracterizada por um perfil imunofarmacológico (pneumatose intestinal, intolerância medicamentosa) e curso clínico benigno. Em contraste, os adultos exibiram menor incidência, porém com um perfil isquêmico-mecânico e elevada letalidade em eventos como a isquemia mesentérica. Adicionalmente, evidenciou-se que o uso de inibidores da bomba de prótons reduz a absorção de micofenolato, aumentando o risco de rejeição aguda. **Conclusão:** As complicações exigem protocolos de manejo estratificados: suporte conservador e ajuste farmacológico em crianças e alto índice de suspeição para intervenção cirúrgica precoce em adultos. A profilaxia gástrica requer monitoramento rigoroso para evitar interações que comprometam o enxerto.

Descritores: Transplante de Coração; Complicações Pós-Operatórias; Doenças Gastrointestinais; Imunossupressão; Pneumatose Cistoide Intestinal.

INTRODUCTION

Heart transplantation is the definitive therapy for end-stage heart failure, but non-cardiac complications challenge its long-term success. Among these, gastrointestinal complications (GICs) stand out due to their high morbidity, being responsible for frequent readmissions and, in severe ischemic events, reaching hospital mortality rates of up to 45%. In addition to the direct surgical risk, pharmacological interactions between gastric protectors and immunosuppressants can be silent factors that precipitate graft rejection.

Current literature suggests an important clinical dichotomy: while the adult population predominantly presents with ischemic and degenerative conditions, the pediatric population exhibits a phenotype marked by inflammatory and drug-related disorders, such as pneumatosis intestinalis. Given the fragmentation of this data, the objective of this review was to synthesize evidence from the last 25 years on post-heart transplant GICs, comparing the prevalence, risk factors, and outcomes between adults and children to support more effective management protocols.

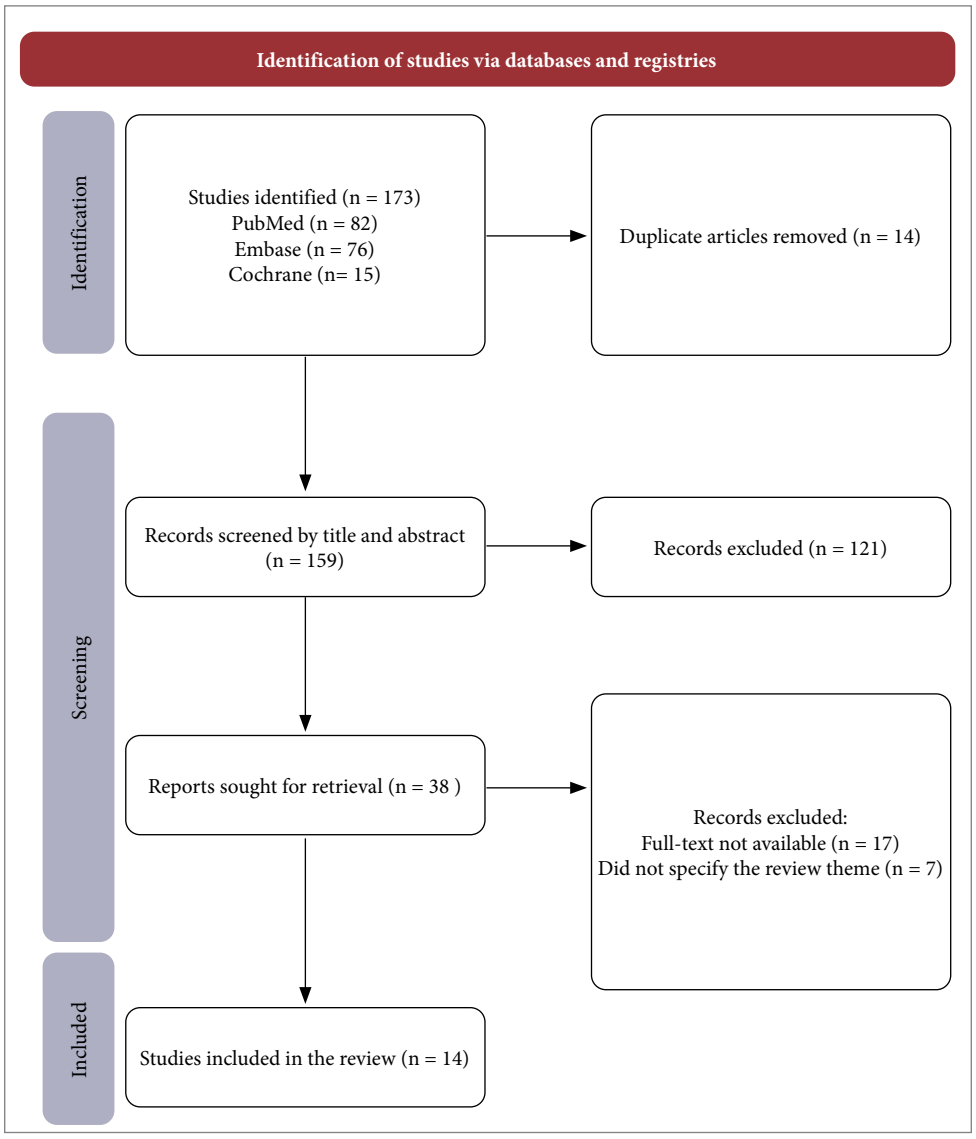
METHODS

The following research question guided this integrative review: What are the predominant GICs, their respective risk factors, and the clinical outcomes observed in heart transplant recipients, based on the literature of the last 25 years? Regarding the sample composition, rigorous eligibility criteria were defined, prioritizing the inclusion of primary observational studies of a quantitative nature, specifically prospective, retrospective cohorts and cross-sectional designs. The population of interest included heart transplant recipients across pediatric and adult age groups. The literature search covered the period from January 1998, a milestone selected to represent the consolidation of contemporary immunosuppression regimens and surgical techniques, to October 2025, without geographical or linguistic limitations. Conversely, the following were excluded: secondary publications (such as systematic, narrative, or other integrative reviews), editorials, letters to the editor, preclinical or animal experimental models, and manuscripts for which full-text access was not feasible.

The data collection phase was based on a systematic review of the electronic databases MEDLINE (via PubMed), Embase, and the Cochrane Library. For the formulation of the search strategy, the controlled vocabulary Medical Subject Headings (MeSH 2024) was used, defining two central thematic areas: heart transplantation and gastrointestinal disorders. The final syntax was constructed by combining descriptors and free terms with the Boolean operators AND and OR, resulting in the following combination: ("Heart Transplantation" [MeSH] OR "Cardiac Transplantation" OR "Heart Transplant" OR "Cardiac Transplant*") AND ("Gastrointestinal Diseases" [MeSH] OR "Digestive System Diseases" [MeSH] OR gastrointestinal OR digestive OR "GI" OR "gastrointestinal complication*" OR "digestive complication*" OR "GI complication*"). It should be noted that the strategy was properly adapted for the Embase database, respecting the indexing specifics of the Emtree thesaurus.

The selection of studies was carried out independently by two researchers using the Rayyan platform for reference management. The screening process consisted of two phases: first, a critical review of titles and abstracts was conducted to exclude articles; then, the preselected articles were submitted for full-text review to confirm eligibility. Discrepancies that arose during the evaluation were resolved through consensus among the reviewers. To ensure methodological transparency, the entire flow of identification, screening, eligibility, and final inclusion (accounting for exclusions and their reasons) was systematized in a flowchart (Fig. 1), in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines[1]. It should be clarified that, although the present study is conceptually classified as an integrative review, as it allows for the inclusion of diverse methodological designs to promote a broad and comparative understanding of the phenomenon, it was decided to incorporate guidelines and tools characteristic of systematic reviews. This rigorous methodological approach was adopted to maximize transparency and reproducibility and minimize bias during the search and selection process.

Data extraction was performed independently by the reviewers using a standardized spreadsheet form (Microsoft Excel®) to compile the information. The extraction protocol included the following variables: bibliographic identification (authorship, year, and country of origin), methodological design, sample size, demographic profile of the population (pediatric versus adult), typology of GICs, correlated risk factors, and clinical outcomes, including mortality rates and impact on graft function. Subsequently, the findings were descriptively synthesized and categorized to enable comparative analysis across age groups. Finally, the assessment of methodological quality and risk of bias was conducted by the same pair of researchers, applying specific instruments for each design: the Newcastle-Ottawa Scale (NOS) for cohort and case-control studies, and the Joanna Briggs Institute (JBI) checklist for case series and other descriptive studies. The prospective application of these quality assessment scales ensured that the integrative synthesis was based solely on methodologically valid and reliable evidence.



Source: Elaborated by the authors.

Figure 1. Flowchart for identifying, selecting, and including studies in the integrative review.

RESULTS

The systematic search yielded 14 studies that met the eligibility criteria (Table 1). The analyzed sample comprised predominantly retrospective cohorts and observational studies, totaling more than 1,400 transplant patients directly evaluated in the subgroups of interest. The methodological quality assessment, conducted mainly using the NOS scale, revealed that most studies presented moderate to high quality (≥ 6 stars). The overall incidence of GICs varied substantially among the cohorts. In adult populations, the incidence of serious complications requiring emergency intervention or consultation ranged from 7.5% to 8.8%.[2,3] In contrast, series focused on pediatric patients reported higher rates, reaching 34.5% in an institutional cohort, driven mainly by infections and mycophenolate mofetil (MMF)[4] intolerance.

Inflammatory and infectious disorders accounted for a significant portion of morbidity. *Clostridium difficile*-associated diarrhea had a cumulative incidence of 14.9% in adults, with severe hypogammaglobulinemia (IgG < 400 mg/dL) identified as the only independent risk factor [risk ratio (RR) [5,8]] for its development[9]. Similarly, cytomegalovirus (CMV) gastrointestinal disease manifested as the predominant form of late tissue-invasive disease, affecting 29% of high-risk patients (D+/R- serology) after the end of prophylaxis, with a negative impact on long-term graft vasculopathy-free survival[10,11].

Table 1. Characteristics of the studies included in the integrative review on digestive complications in heart transplant recipients.

Title/Quality	Periodical/ year	Author/ location	Type of study	Sample/ profile	Risk factors	Complications	Outcome
Serious gastrointestinal complications after cardiac surgery and associated mortality[2] – High quality: seven/nine stars (NOS)	Ann Thorac Surg 2021	Elgharably et al./USA	Retrospective cohort study	Adults (n = 329 transplant recipients)	The transplant procedure itself was an independent risk factor ($p < 0.001$); advanced age; reoperation.	Incidence of 8.8% (n = 29); includes: mesenteric ischemia, GI bleeding, and perforation.	Hospital mortality increased from 1.6% (without complications) to 14% in the presence of GIC.
Changing trends in abdominal surgical complications following cardiac surgery in an era of advanced procedures. A retrospective cohort study[3] – Moderate quality: six/nine stars (NOS)	Int J Surg 2015	Ashfaq et al./ USA	Retrospective cohort study	Adults (n = 56 transplant recipients; 133 advanced heart failure)	Complexity of the surgical procedure (advanced heart failure).	Emergency GI consultations: 7.5% (n = 10); abdominal surgeries: n = 3; obstruction and cholecystitis predominated.	No mortality (0%) directly related to abdominal causes in the advanced heart failure group.
Early mortality after cardiac transplantation: should we do better?[5] – High quality: seven/nine stars (NOS)	J Heart Lung Transplant 2005	Luckraz et al./United Kingdom	Retrospective cohort (autopsy-based)	Adults (n = 75 deaths analyzed)	Previous ischemic heart disease; use of dopamine (associated, but without evident severe shock).	Fatal GIC (n = 7, 9.3% of deaths); severe pancreatitis (n = 5); intestinal ischemia (n = 1); mixed (n = 1).	Gastrointestinal complications were the fourth leading cause of death in the first 30 days.
Pneumatosis intestinalis after pediatric thoracic organ transplantation[6] – Moderate quality: six/nine stars (NOS)	Pediatrics 2002	Fleenor et al./USA	Case-control study	Pediatric (n = 116; cases n = 8)	Age < 5 years; black race; prednisone dose > 0.5 mg/kg/day; tacrolimus > 11 ng/mL.	Pneumatosis intestinalis: 7% (n = 8); symptoms: bloody diarrhea (n = 6), abdominal pain.	Benign evolution in all cases with conservative treatment; no deaths or intestinal resection required.
Predictors of re-hospitalization time during the first year after heart transplant[7] – High quality: eight/nine stars (NOS)	Heart Lung 2008	Jalowiec et al./USA	Prospective cohort study	Adults (n = 269)	High doses of prednisone; use of MMF; cyclosporine.	Overall prevalence of 27%; ulcers/ gastritis (9%); gallstones/ pancreatitis (7%).	GI complications were significant independent predictors ($p<0.001$) for increased rehospitalization time during the first year.
Fontan-associated protein-losing enteropathy and post-heart transplant outcomes: A multicenter study[8] – High quality: seven/nine stars (NOS)	J Heart Lung Transplant 2019	Schumacher et al./USA	Multicenter cohort study	Mixed/pediatric (n = 52)	Immunosuppressive regimens without MMF were associated with higher mortality.	Recurrence of PLE: n = 4 (8%).	Complete resolution of enteropathy in 98% of survivors; relapses resolved without sequelae.
Complications after pediatric heart transplantation - 9 years single centre experience[4] – Low/moderate quality: three/nine stars (NOS-Abstract)	Cardiol Young 2016	Kis et al./ Hungary	Retrospective cohort study	Pediatric (n = 29)	Use of MMF (causes 60% of GIC); *C. difficile* infection.	High incidence (34.5%, n=10); MMF intolerance (n=6); infectious enteritis (n=4); *de novo* IBD (n=1).	Symptoms resolved after conversion from MMF to everolimus; no direct deaths from GI.
Clostridium difficile-associated diarrhea in heart transplant recipients: is hypogammaglobulinemia the answer?[9] – High quality: eight/nine stars (NOS)	J Heart Lung Transplant 2007	Muñoz et al./Spain	Retrospective cohort study	Adults (n = 235)	Severe hypogammaglobulinemia (IgG < 400 mg/dL) was the only independent risk factor (RR [5,8]).	Diarrhea due to *C. difficile*: 14.9% (n = 35); included one case of toxic megacolon.	High recurrence rate (28.6%); incidence was significantly reduced with IVIG replacement.
Clinical features and outcomes of delayed-onset primary cytomegalovirus disease in cardiac transplant recipients[10] – Moderate/ high quality: seven/nine stars (NOS)	J Heart Lung Transplant 2007	Kijpittayarit-Arthurs et al./USA	Retrospective cohort study	Adults (n = 31)	Acute rejection grade ≥ 2 (trend, hazard ratio 2.46); diabetes was a protective factor.	Invasive CMV GI disease: n=6 (66% of CMV cases); predominated over pneumonitis.	High clinical recurrence rate (33%); no association with cardiac allograft vasculopathy (CAV) in this cohort.

Continue...

Table 1. Continuation.

Title/Quality	Periodical/ year	Author/ location	Type of study	Sample/ profile	Risk factors	Complications	Outcome
Cytomegalovirus infection and disease reduce 10-year cardiac allograft vasculopathy-free survival in heart transplant recipients[11] – Moderate/high quality: seven/nine stars (NOS)	BMC Infect Dis	Johansson et al./Sweden	Retrospective cohort study	Adults (n = 226)	Serological mismatch (donor+/recipient-)	Invasive CMV GI disease: n=8 (3.5% of the total cohort; 30% of invasive CMV cases).	Patients with GI/ CMV disease showed lower graft vasculopathy-free survival and lower 10-year overall survival.
Hypogammaglobulinemia after heart transplantation: use of intravenous immunoglobulin replacement therapy in relapsing CMV disease[12] – Low quality: Case series (JBI)	Int Immunopharmacol 2005	Sarmiento et al./Spain	Interventional case series	Adults (n = 5)	Hypogammaglobulinemia secondary to rejection therapy (thymoglobulin/ pulses).	GI disease due to CMV (n = 4); gastric perforation (n = 1); hepatitis (n = 1).	Complete resolution of symptoms and viral clearance after adding IVIG to ganciclovir.
Biliary surgery after heart transplantation[13] – Low quality: Case series (JBI)	Am J Surg 1998	Menegaux et al./France	Case series	Adults (n = 18 operated patients)	Cyclosporine-induced lithogenesis (hemolysis and biliary alterations)	Symptomatic cholelithiasis (n = 13); acute cholecystitis (n = 3).	Mortality and rejection rate: 0%; laparoscopic cholecystectomy proved to be safe and definitive.
Proton pump inhibitor co-medication reduces mycophenolate acid drug exposure in heart transplant recipients[14] – Moderate quality: five/ nine stars (NOS)	J Heart Lung Transplant 2009	Kofler et al./ Germany	Pharmacokinetic cohort study	Adults (n = 33)	Pantoprazole use drastically reduced mycophenolic acid absorption.	Acute rejection: 33.3% (n = 7) in the pantoprazole group vs. 8.3% in the control group (due to interaction).	Significant reduction in exposure to the immunosuppressant, leading to a higher risk of rejection and vasculopathy.
Comparison of survival and readmission rates in patients 65 and older undergoing heart transplantation or LVAD implantation[15] – Low quality: three/nine stars (NOS)	J Heart Lung Transplant 2018	Imamura et al./USA	Comparative cohort study	Elderly (n = 20)	Advanced age (65-72 years).	Infection was the primary complication (36%); GI bleeding was rare following transplantation (vs. 20% in patients with left ventricular assist devices).	One-year survival rate of 95%, superior to left ventricular assist device therapy.

Source: Elaborated by the authors.

In the spectrum of surgical and ischemic complications, high mortality was observed. Mesenteric ischemia, although present in a smaller fraction of cases, was associated with a devastating hospital mortality rate of 45%[2]. Biliary disease was also prevalent, with symptomatic cholelithiasis and acute cholecystitis representing the main surgical indications; in these cases, laparoscopic cholecystectomy proved to be safe, with 0% mortality and no episodes of procedure-induced rejection[13].

Analysis of risk factors revealed distinct patterns among age groups. In children, prednisone doses greater than 0.5 mg/kg/day and serum tacrolimus levels above 11 ng/mL increased the risk of pneumatosis intestinalis sevenfold and sixfold, respectively6. In adults, the complexity of the surgical procedure, advanced age, and the need for reoperation were consistent predictors of complications[2,3]. Additionally, concomitant use of proton pump inhibitors (pantoprazole) reduced the absorption of mycophenolic acid, and was associated with a higher rate of acute rejection (33.3% vs. 8.3%) in the treated group[14].

Regarding clinical outcomes, GICs significantly impacted prognosis. They were identified as the fourth leading cause of death in the first 30 days post-transplant, accounting for 9.3% of early deaths in a series of autopsies[5]. In addition to mortality, GICs were independent predictors ($p < 0.001$) for increased length of hospital stay in the first year[7]. However, specific conditions such as protein-losing enteropathy (PLE) have shown an excellent prognosis after transplantation, with complete resolution of symptoms in 98% of survivors[8].

DISCUSSION

This integrative review synthesized evidence from 14 studies spanning more than two decades, confirming that GICs remain a significant cause of morbidity and mortality after heart transplantation. In an innovative approach, stratified data analysis

identified two distinct clinical phenotypes of complications, determined by the recipient's age group: an immunopharmacological profile in the pediatric population and an ischemic-mechanical profile in the adult population (Table 2). This dichotomy challenges the uniform screening approach and suggests the need for age-specific protocols stratified by major complications, their incidence, and prognosis (Table 3).

Table 2. Comparative table between the two phenotypes analyzed.

Category of analysis	Pediatric population	Adult population
Reported incidence	Elevated; reported in up to 34.5% of cohorts, frequently associated with drug intolerance and infections[4].	Moderate to low for severe events; ranging from 7.5% to 8.8% for complications requiring emergency surgical intervention or specialized consultation[2,3].
Main etiology	Immunological and pharmacological; strongly linked to elevated serum levels of immunosuppressants such as tacrolimus, high doses of corticosteroids[6] and physiology of previous congenital heart disease[8].	Ischemic and degenerative; associated with surgical complexity, reoperation, prolonged aortic clamping time[2] and pre-existing comorbidities such as atherosclerosis[5].
Typical complications	Pneumatosis intestinalis: gas in the intestinal wall in 7% of cases6; PLE: recurrence of a pre-existing condition[8]; mycophenolate intolerance: cause of 60% of GI complaints[4].	Mesenteric ischemia: a rare but devastating event[2]; severe pancreatitis: responsible for premature deaths[5]; biliary disease: frequent cholelithiasis and acute cholecystitis[13]; infections: *C. difficile* 9 and CMV GI disease[10].
Specific risk factors	Age < 5 years and black race: main predictors for pneumatosis[6]; prednisone dose: > 0.5 mg/kg/day increases the risk 7 times[6]; tacrolimus level: > 1 ng/mL at presentation[6].	Hypogammaglobulinemia: IgG < 400 mg/dL increases the risk of *C. difficile* by 5.8-fold[9]; use of proton pump inhibitors: reduces mycophenolate absorption and increases rejection[14]; CMV D+/R- serostatus: high risk for late invasive disease[11].
Mortality and prognosis	Generally benign; pneumatosis: 0% mortality with conservative management[6]; PLE: complete resolution in 98% of survivors[8]; intolerance: resolution after switching to everolimus[4].	High lethality in ischemic events; mesenteric ischemia: hospital mortality of 45%[2]; overall impact: GIs were the fourth leading cause of early death (9.3% of deaths)[5]; safety: laparoscopic cholecystectomy had 0% mortality[13].

Source: Elaborated by the authors.

Table 3. Main GCIs after heart transplantation: incidence and prognosis

Complication (reference)	Prevalent population	Reported incidence	Mortality/prognosis
Pneumatosis intestinalis[6]	Pediatrics	7% of cases.	The course is generally benign; mortality is 0% with conservative management.
Mycophenolate intolerance[4]	Pediatrics	High; accounts for 60% of gastrointestinal complaints in this population.	Benign course; symptoms resolved after switching to everolimus.
PLE[8]	Pediatrics/ mixed	Recurrence occurs in 8% of cases (most often in those with a history of congenital heart disease).	Good long-term prognosis; complete resolution in 98% of survivors.
Mesenteric ischemia[2,5]	Adult	A rare but devastating event (the overall incidence of complications in adults ranges from 7.5% to 8.8%).	High case fatality rate; hospital mortality rate of 45%.
Severe pancreatitis[5]	Adult	Reported as a cause of premature deaths (GICs were the fourth leading cause of death).	High lethality (responsible for four premature deaths).
Biliary disease[13] (cholelithiasis and cholecystitis)	Adult	Frequent [symptomatic cholelithiasis (n = 13); acute cholecystitis (n = 3)]	Excellent surgical prognosis; laparoscopic cholecystectomy with 0% mortality.
Infections (*C. difficile*)[9]	Adult	Frequent, affecting up to 14.9% of adult recipients.	It requires clinical management and is frequently associated with severe hypogammaglobulinemia.
Infections (invasive CMV GI disease)[10,11]	Adult	Frequent, accounting for up to 66% of invasive CMV cases in some cohorts	High risk for late invasive disease in D+/R- serology; reduces long-term vasculopathy-free survival.

Source: Elaborated by the authors.

In the pediatric population, the synthesis reveals a "severity paradox": although the incidence of complications is high, reaching 34.5% in some cohorts4, the clinical course is predominantly benign. Pneumatosis intestinalis emerged as the most prominent complication in this group, strongly associated with the use of high doses of corticosteroids (> 0.5 mg/kg/day) and supratherapeutic levels of tacrolimus[6]. Unlike what is observed in adults or neonates with necrotizing enterocolitis, pneumatosis in pediatric heart transplant recipients, despite presenting with alarming symptoms such as bloody diarrhea, had zero mortality and responded uniformly to conservative management6. Additionally, recurrence of PLE proved to be a transient event, with complete resolution in 98% of survivors, and should not contraindicate transplantation[8].

In stark contrast, the adult profile is characterized by a lower incidence of mild events, but excessive lethality in major complications. Mesenteric ischemia, although less frequent than in other cardiac surgeries, presented a hospital mortality rate of 45%[2]. Autopsy study analysis corroborated these data, positioning severe GICs (including pancreatitis and bowel infarction) as the fourth leading cause of death within the first 30 days post-transplant[5]. Factors such as reoperation due to bleeding, prolonged aortic clamping time, and the use of vasopressors have been identified as crucial triggers for this vascular catastrophe[2]. Therefore, unlike in children, where monitoring focuses on medication adjustment, in adults, any acute abdominal pain should raise suspicion of ischemia requiring immediate surgical intervention.

A finding of particular pharmacological relevance highlighted by this review is the hidden danger in gastric prophylaxis. The study by Kofler et al.[14] demonstrated that concomitant pantoprazole (a proton pump inhibitor), frequently prescribed to mitigate dyspeptic symptoms, drastically reduces MMF absorption, resulting in a significantly higher acute rejection rate (33.3% vs. 8.3%) in the treated group. This data introduces a new safety paradigm: symptomatic GI treatment may inadvertently compromise cardiac graft integrity, necessitating rigorous therapeutic monitoring or a change in gastric protectant class.

In the context of infectious complications, the review highlights a shift in the clinical spectrum of CMV and *C. difficile*. Late CMV disease (after the end of prophylaxis) manifested predominantly as invasive gastrointestinal disease, and no longer as pneumonitis, negatively impacting long-term graft vasculopathy-free survival[10,11]. Meanwhile, *C. difficile* diarrhea has been established as a marker of humoral immunodeficiency, with severe hypogammaglobulinemia (IgG < 400 mg/dL) being its main independent predictor[9]. Intravenous immunoglobulin (IVIG) replacement has been shown to reduce the incidence of this complication, suggesting that gastrointestinal management should include active immunological monitoring.

Finally, regarding elective surgical interventions, laparoscopic cholecystectomy has proven to be a safe procedure for managing symptomatic biliary disease in transplant recipients, with no mortality or induction of rejection[13]. However, the emergency surgery scenario for patients with advanced heart failure or recent transplant recipients remains challenging, although mortality has proven to be lower than historically reported in previous decades[3].

It is imperative to acknowledge the inherent limitations of this review. The almost exclusive predominance of retrospective, single-center observational studies introduces an inherent information bias, since data collection depended on medical records that often lack standardization in recording gastrointestinal complaints and the exact severity of symptoms over the years. Additionally, there is significant heterogeneity in the methodological designs included in the literature, ranging from small case series to historical cohorts, which, coupled with the lack of consensus among authors on the strict definitions of what constitutes a "gastrointestinal complication," makes a formal quantitative meta-analysis unfeasible and limits the ability to infer causality from the findings.

However, despite these methodological barriers, the consistency of the data regarding age dichotomy and pharmacological risks provides a solid scientific basis for updating clinical practices. The synthesis of these findings points to the need for differentiated protocols: in pediatrics, the priority should be conservative management and careful adjustment of immunosuppressants (such as the use of everolimus instead of mycophenolate in cases of intolerance)[4];n adults, a high index of suspicion and early diagnosis of acute ischemic abdomen is necessary, as well as extreme caution with prescriptions and drug interactions that affect the absorption and effectiveness of immunosuppression.

CONCLUSION

GICs are frequent events that negatively impact morbidity and hospital resources in the postoperative period of heart transplantation. This review highlighted a clear phenotypic distinction: the pediatric population presents an immunopharmacological profile marked by pneumatosis and drug intolerance, with a benign course, while the adult population is susceptible to an ischemic-mechanical profile, characterized by a lower incidence but higher lethality.

Additionally, the identification of hidden risks in routine prophylaxis with proton pump inhibitors highlights that indiscriminate gastric protection can precipitate acute rejection via unfavorable drug interactions. The clinical application of these findings points to the urgent need to abandon uniform approaches in favor of stratified protocols that prioritize fine-tuning immunosuppression and surveillance of opportunistic infections in children, and maintaining a high index of suspicion for early surgical intervention in adults, to optimize long-term graft and patient survival.

CONFLICT OF INTEREST

Nothing to declare.

AUTHOR'S CONTRIBUTION

Substantive scientific and intellectual contributions to the study: Azevedo JLR, Fonseca Neto OCL; **Conception and design:** Azevedo JLR, Fonseca Neto OCL; **Data analysis and interpretation:** Azevedo JLR; **Article writing:** Azevedo JLR; **Critical revision:** Fonseca Neto OCL; **Final approval:** Azevedo JLR, Fonseca Neto OCL.

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Not applicable.

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DECLARATION OF USE OF ARTIFICIAL INTELLIGENCE TOOLS

In strict compliance with transparency and research ethics guidelines, we declare that no artificial intelligence tools or language modeling technologies were used for the design, data collection, analysis, writing, or revision of the content of this manuscript. All work was entirely developed by the authors.

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