

Systematic Review

Cardiac surgery outcomes in patients with antecedent kidney, liver, and pancreas transplantation: a meta-analysis

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Cardiovascular events are among the most common causes of late death in the transplant recipient (Tx) population. Moreover, major cardiac surgical procedures are more challenging and risky due to immunosuppression and the potential impact on the transplanted organ's functional capacity. We aimed to assess open cardiac surgery safety in abdominal solid organ transplant recipients, comparing the postoperative outcomes with those of nontransplant (N-Tx) patients. Electronic databases of PubMed, EMBASE, and SCOPUS were searched. The endpoints were: overall rate of infectious complications (wound infection, septicemia, pneumonia), cardiovascular and renal events (stroke, cardiac tamponade, acute kidney failure), 30-days, 5-years, and 10-years mortality post-cardiac surgery interventions in patients with and without prior solid organ transplantation. This meta-analysis included five studies. Higher rates of wound infection (Tx vs. N-Tx: OR: 2.03, 95% CI: 1.54 to 2.67, $I^2 = 0\%$), septicemia (OR: 3.91, 95% CI: 1.40 to 10.92, $I^2 = 0\%$), cardiac tamponade (OR: 1.83, 95% CI: 1.28 to 2.62, $I^2 = 0\%$) and kidney failure (OR: 1.70, 95% CI: 1.44 to 2.02, $I^2 = 89\%$) in transplant recipients were reported. No significant differences in pneumonia occurrence (OR: 0.95, 95% CI: 0.71 to 1.27, $I^2 = 0\%$) stroke (OR: 0.89, 95% CI: 0.54 to 1.48, $I^2 = 78\%$) and 30-day mortality (OR: 1.92, 95% CI: 0.97 to 3.80, $I^2 = 0\%$) were observed. Surprisingly, 5-years (OR: 3.74, 95% CI: 2.54 to 5.49, $I^2 = 0\%$) and 10-years mortality rates were significantly lower in the N-Tx group (OR: 3.32, 95% CI: 2.35 to 4.69, $I^2 = 0\%$). Our study reveals that open cardiac surgery in transplant recipients is associated with worse postoperative outcomes and higher long-term mortality rates.

Keywords

Cardiac surgery; heart surgery; solid organ transplantation; liver transplantation; kidney transplantation; pancreas transplantation

1. Introduction

According to the latest global report published by the Global Observatory on Donation and Transplantation in 2017, 139,024 transplantation procedures were performed worldwide, of which 90,306 were kidney-, 32,348 liver- and 2243 pancreas transplants (Carmona, 2017). End-stage organ failure is responsible for an increased mortality rate in the general population. The replacement of dysfunctional organs with healthy equivalents through transplantation represents the gold standard treatment. Each year, the number of patients on the waiting list continues to be much larger than both the number of donors and transplants (U.S. Government Information on Organ Donation and Transplantation, 2020).

Nevertheless, most of the patients undergoing abdominal organ transplantation have a higher prevalence of cardiovascular risk factors. Coronary artery disease, stroke, hypertension, dyslipidemia, and diabetes mellitus are among the most common causes of late death in the transplant recipient population (de Mattos et al., 2006; Johnston et al., 2002; Watt et al., 2010). There seems to be an underestimation of the incidence of cardiovascular events, suggesting that other transplant-specific factors may contribute to cardiovascular risk either independently or by interacting with "traditional" risk factors like immunosuppressive drugs (Kasiske et al., 2000; Miller, 2002).

Cardiac surgery after organ transplantation is not uncommon, yet it proved to be more challenging and posed increased risks compared to the general population (Mitruka et al., 1997; Yamamura et al., 2014). Improvements in surgical techniques, immunosuppressive regimens, and perioperative care have resulted in better early and late outcomes after nontransplant-related surgical procedures in transplant recipients.

However, few studies reported that the incidence in postoperative events and mortality among renal and liver transplant patients undergoing heart major surgery is substantially higher than among patients with normal organ function (Alfaro Sanchez et al., 2016; Giakoustidis et al., 2011; Mitruka et al., 1997; Yamamura et al., 2014). There are currently no clear guidelines or solutions for car-

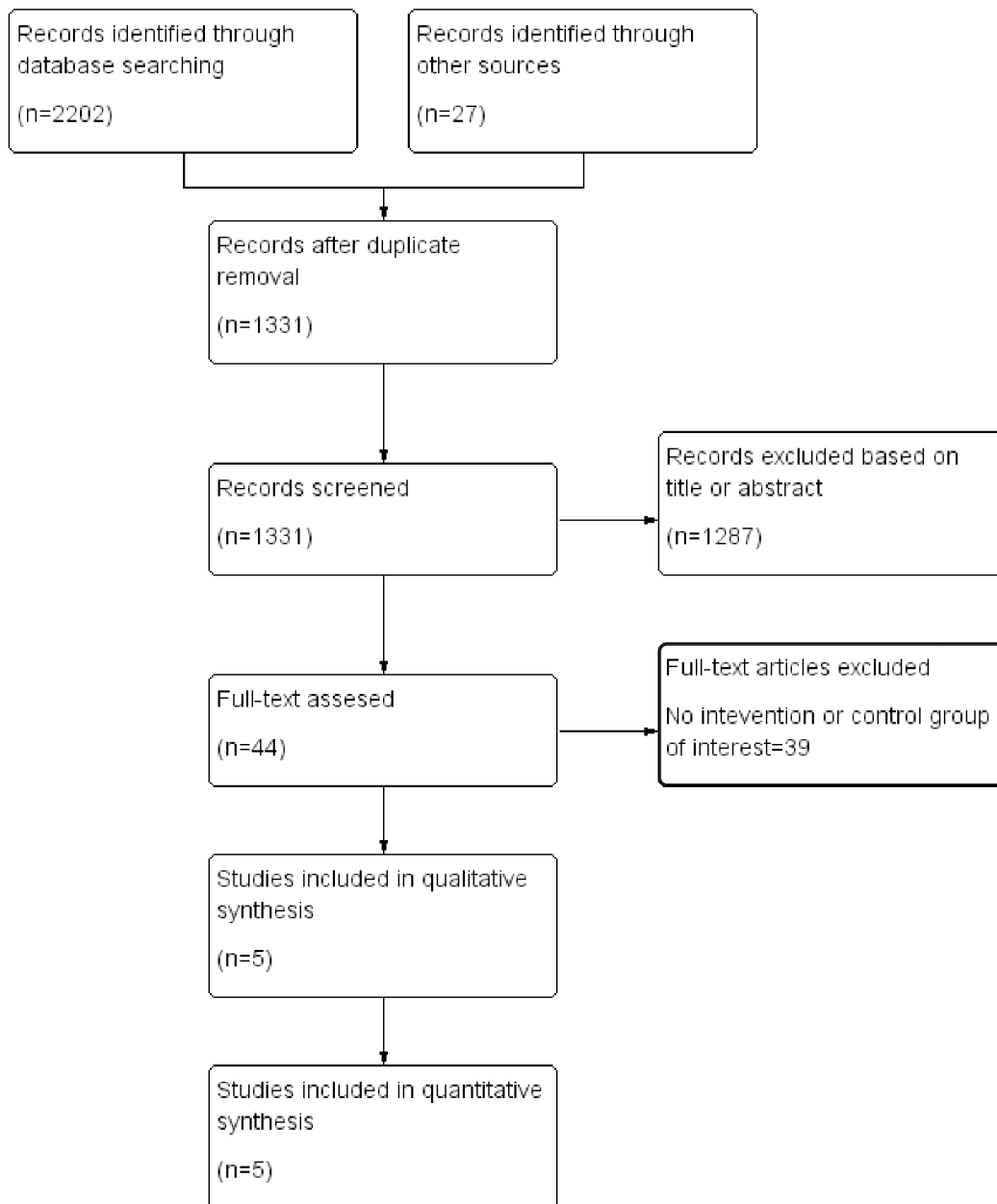


Fig. 1. PRISMA flow diagram of the selection process. PRISMA flow diagram representing the selection process of papers used for meta-analysis, study of the cardiac surgery outcomes and individual cases pooled analysis in patients with solid abdominal transplantation.

diac surgery's risk-benefit ratio in abdominal transplant patients.

The purpose of this meta-analysis is to assess cardiac surgery safety in abdominal solid organ transplant recipients by comparing the postoperative outcomes (in terms of major adverse cardiovascular and cerebrovascular events, short- and long-term mortality) in adult patients that had previously undergone either a kidney, liver, pancreas and pancreas-kidney transplant surgery compared with nontransplant patients.

2. Materials and methods

2.1 Search

We interrogated three electronic databases: PubMed, EMBASE, and SCOPUS from the inception of these databases to September 1st, 2020. We used the following query terms: "car-

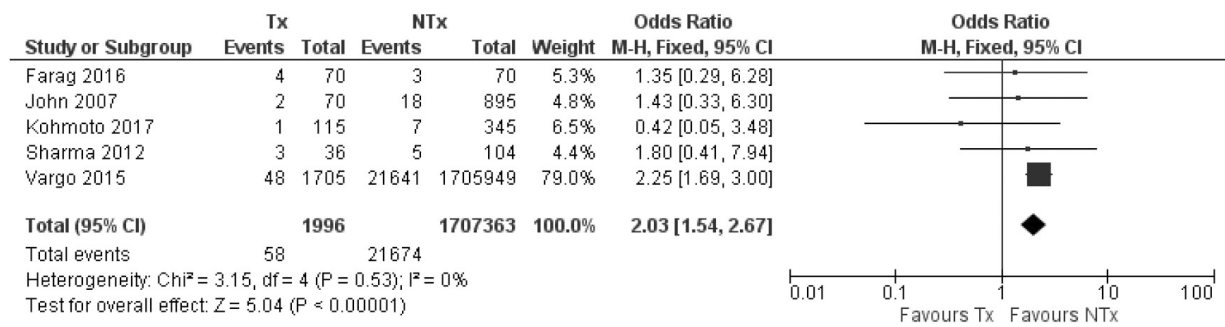
diac surgery", "heart surgery", "solid organ transplantation", "liver transplantation", "kidney transplantation", "pancreas transplantation". Two authors (A.E.B. and M.E.) independently scanned titles and abstracts and performed an additional check of references in relevant articles. When there was a lack of consensus, we asked the opinion of the third senior reviewer (G.T.).

The literature's systematic search was performed following PRISMA (the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement). The PRISMA Flowchart is available in Fig. 1.

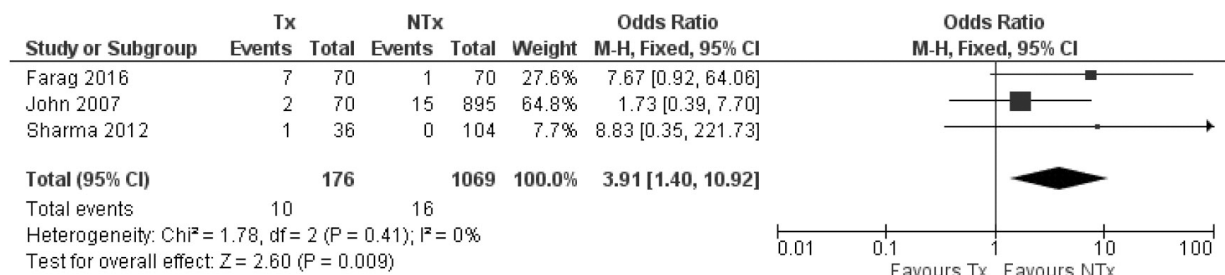
2.2 Eligibility

Relevant articles were assessed to fulfill the inclusion criteria (Table 1) without restrictions for publication language.

A



B



C

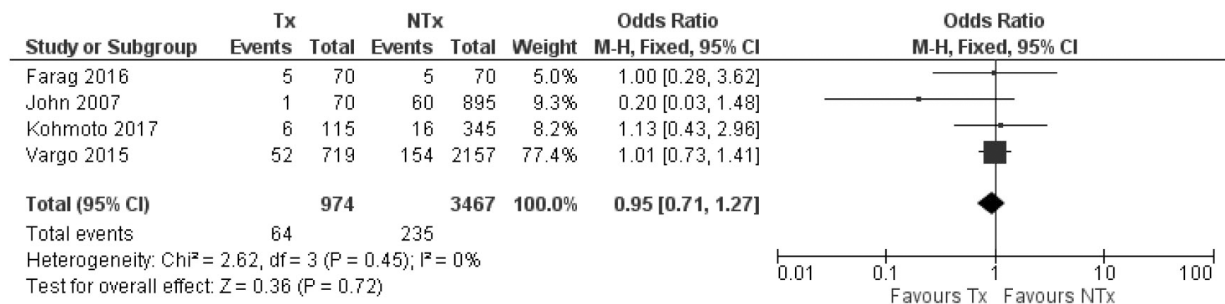


Fig. 2. Postprocedural infectious complications. (a). Wound infection. Forest plot of the meta-analysis depicting the comparison of postoperative wound infection after cardiac surgery in patients with and without previous abdominal solid organ transplantation. (b). Septicemia. Forest plot of the meta-analysis depicting the comparison of postoperative septicemia after cardiac surgery in solid abdominal organ transplant recipients with patients without abdominal transplantation history. (c). Pneumonia. Forest plot of the meta-analysis depicting the comparison of postoperative pneumonia after cardiac surgery in patients with and without previous abdominal solid organ transplantation.

2.3 Outcome parameters

The endpoints were as follows: the overall rate of postprocedural infection, pneumonia, stroke, cardiac tamponade, acute kidney failure, 30-days, 5-years, and 10-years mortality between patients with previous solid abdominal organ transplantation and patients without a history of transplantation, undergoing heart surgery.

2.4 Data collection and extraction

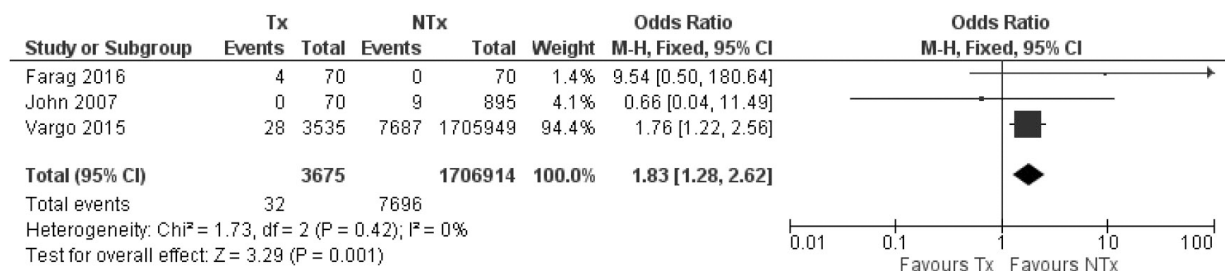
The same reviewers extracted data from retrieved manuscripts and registered in standard tables. When the ratio of events and not raw data were available, we calculated the event number from the described ratio and total cohort. We used the Web plot digitizer to digitalize data from Kaplan-Meier Survival Curves. We calculated crude mortality using the method described by Tierney et al.: Events in current interval = [(Number at risk at start + number

at risk at the end)* (%Event free at the start - %Event free at the end)]/(%Event free at start + %Event free at the end) (Tierney et al., 2007).

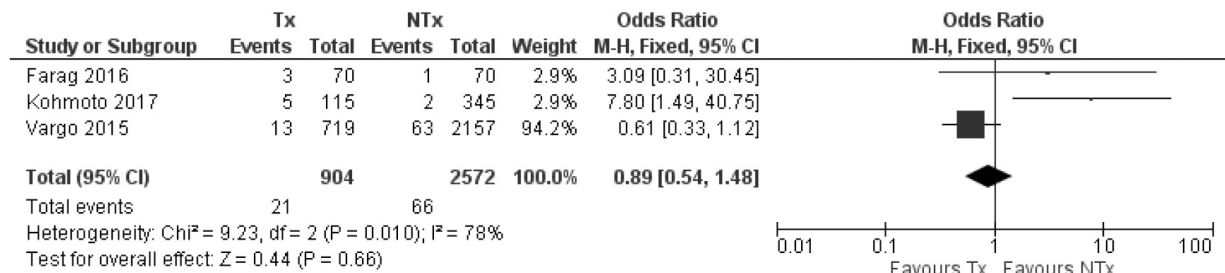
2.5 Data synthesis

Review Manager (RevMan) Version 5.3 (Nordic Cochrane Centre, The Cochrane Collaboration, 2012, Copenhagen, Denmark) software was used to generate the pooled effect size with odds ratio (OR) and 95% confidence intervals (CI) by Mantel-Haenszel method and random effect model for dichotomous data. For continuous data, we used mean difference (MD) and 95% confidence intervals by the Inverse Variance method and random effect model. I² statistics were used to evaluate the heterogeneity of studies. We considered 0% to 25% as low, 26% to 50% as moderate, 51% to 75% as high, and > 75% as very high heterogeneity.

A



B



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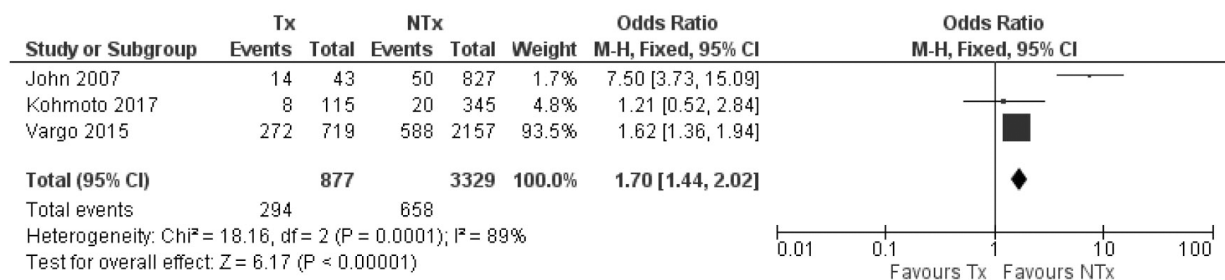


Fig. 3. Postprocedural cardiovascular and renal complications. (a). Tamponade. Forest plot of the meta-analysis depicting the comparison of postoperative tamponade after cardiac surgery in patients with and without previous abdominal solid organ transplantation. (b). Stroke. Forest plot of the meta-analysis depicting the comparison of postoperative stroke after cardiac surgery in solid abdominal organ transplant recipients with patients without abdominal transplantation history. (c). Kidney failure. Forest plot of the meta-analysis depicting the comparison of postoperative kidney failure after cardiac surgery in solid abdominal organ transplant recipients with patients without abdominal transplantation history.

Conversion to mean and standard deviation (SD), when median and IQR was available, was performed following the methods published by Luo et al. (2018) and Wan et al. (2014). The pooled sample mean and pooled standard deviation for selected studies was calculated according to the recommendation of the Cochrane Handbook for Systematic Reviews. Dichotomous data were compared with the Chi-square test, continuous data with the Student *t*-test. A *P*-value lower than 0.05 was considered significant for each test. We used MedCalc Statistical Software version 14.8.1 (2014; <http://www.medcalc.org>); MedCalc Software bvba, Ostend, Belgium) to perform the statistical analysis.

2.6 Risk of bias in included studies

The risk of publication bias was assessed Newcastle-Ottawa Quality Assessment Scale for cohort studies (Table 2).

3. Results

3.1 Literature search and study selection

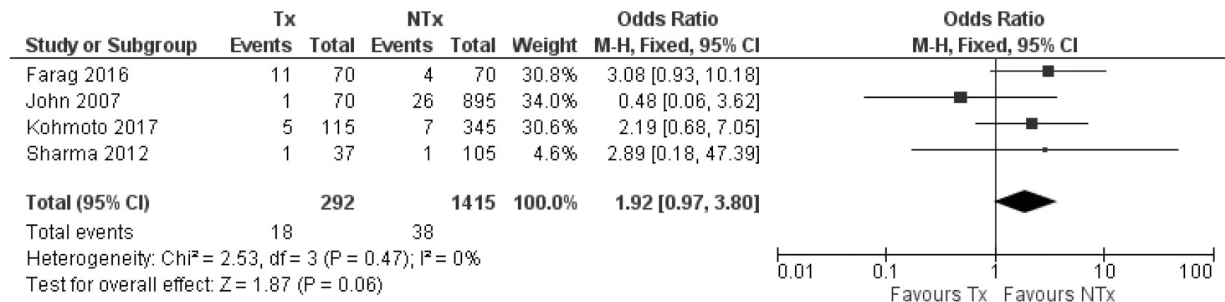
The digital search identified a total of 2202 titles. After duplicates removal, a total of 1253 references were screened by title and abstract. There were 44 articles selected for full-text analysis.

Five full-text articles that compared clinical outcomes, early and late mortality after cardiac surgical procedures in solid abdominal organ transplant recipients with patients without transplantation history were retrieved (Farag et al., 2017; John et al., 2007; Kohmoto et al., 2018; Sharma et al., 2013; Vargo et al., 2015).

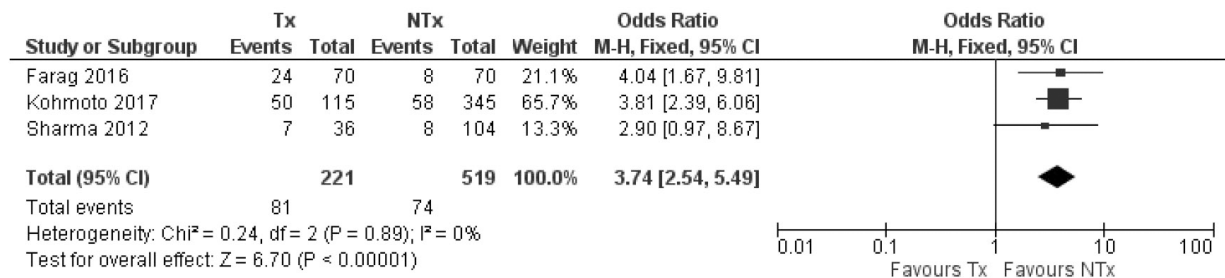
3.2 Study characteristics and risk of bias

The characteristics of the selected studies are presented in Table 3. All studies were appreciated to have a good quality design (Table 3).

A



B



C

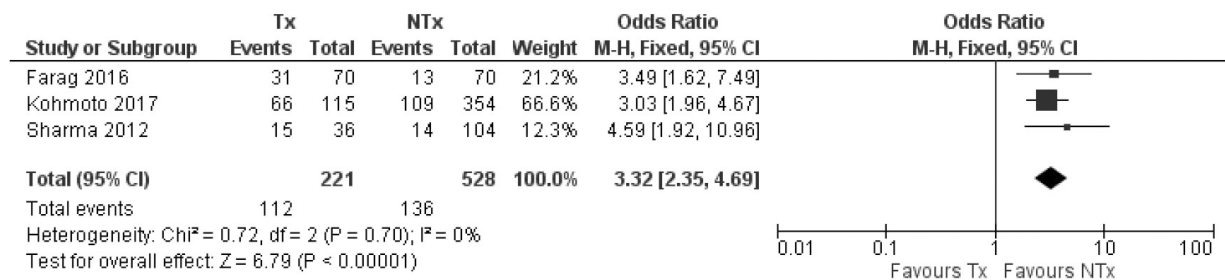


Fig. 4. Survival data. (a). 30-days mortality. Forest plot of the meta-analysis depicting the comparison of 30-days mortality after cardiac surgery in patients with and without previous abdominal solid organ transplantation. (b). 5-years mortality. Forest plot of the meta-analysis depicting the comparison of 5-years mortality after cardiac surgery in patients with and without previous abdominal solid organ transplantation. (c). 10-years mortality. Forest plot of the meta-analysis depicting the comparison of 10-years mortality after cardiac surgery in patients with and without previous abdominal solid organ transplantation.

3.3 Patient and periprocedural characteristics

The final analysis included 1,711,189 patients with 3826 transplant recipients (Tx) and 1,707,363 patients without transplantation history (N-Tx). Only patients with solid abdominal organ transplants (kidney, liver, pancreas, kidney-pancreas) were included in the Tx group. All types of cardiac surgery were taken into account.

Baseline characteristics and periprocedural data distinguishing each group are summarized in Table 4. Patients with a transplant history included in the Tx group were younger (58.06 ± 10.55 vs. 65.50 ± 11.80 , $P < 0.0001$), had higher rates of hypertension (88.31% vs. 74.82%, $P < 0.0001$) and congestive heart failure (28.97% vs. 23.4%, $P < 0.0001$). Meanwhile, N-Tx patients were more commonly male (66.28% vs. 68.36%, $P = 0.006$), had higher rates of previous myocardial infarction (38.33% vs. 31.27%, $P = 0.03$), stroke (7.56% vs. 6.61%, $P = 0.03$), and had higher body

mass index levels (26.41 ± 5.75 vs. 28.5 ± 5.67 , $P < 0.0001$). Additionally, N-Tx patients were more commonly smokers (51.07% vs. 31.5%, $P = 0.0011$) with a higher prevalence of chronic obstructive pulmonary disease (21.22% vs. 10.73%, $P < 0.0001$). The average time interval between transplantation and cardiac surgery was 7.96 ± 7.04 .

We aimed to compare the difference in periprocedural data between the liver and a kidney transplant cohort. Except that renal transplant recipients were younger (62.42 ± 7.15 vs. 57.38 ± 11.12 , $P = 0.04$), no significant differences were reported (Table 5).

3.4 Study endpoints - safety and survival in Tx compared to N-Tx group.

The outcomes for each of the included studies and the main findings of this meta-analysis are summarized in Fig. 2-4.

Table 1. Inclusion criteria for selected studies.

Criteria	
Population	Patients with previous abdominal solid organ transplantation
Intervention	Open-heart surgical procedures
Comparators	Heart surgery in nontransplant recipients
	Survival
Outcomes	At least in-hospital mortality
	Safety
	At least post-procedural infectious and cardiovascular events.
	Randomized Control Trials
Type of study	Observation Studies
	Propensity Score Match studies
Language	No restriction

Table 2. Newcastle-Ottawa quality assessment scale (NOS) for assessing the quality of cohort studies in meta-analyses.

Study Author, year	Selection				Comparability	Exposure		
	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at the start of the study	Comparability of cohorts based on the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts
(John et al., 2007)	* (b)	*	* (a)	*	-	* (b)	* (a)	* (a)
(Sharma et al., 2013)	* (a)	*	* (a)	*	*	* (b)	* (a)	* (a)
(Vargo et al., 2015)	* (a)	*	* (a)	*	*	* (b)	* (a)	-
(Farag et al., 2017)	* (a)	*	* (a)	*	*	* (b)	* (a)	* (a)
(Kohmoto et al., 2018)	* (a)	*	* (a)	*	*	* (b)	* (a)	* (a)

The guidelines of the Newcastle-Ottawa Scale interpretation. A "good" quality score required 3 or 4 stars in selection, 1 or 2 stars in comparability, and 2 or 3 stars in outcomes. A "fair" quality score required two stars in selection, 1 or 2 stars in comparability, and 2 or 3 stars in outcomes. A "poor" quality score reflected 0 or 1 star(s) in selection, or 0 stars in comparability, or 0 or 1 star(s) in outcomes.

Table 3. Summary of the included studies.

Author	Year	Country	No. of Centres	Type of study	Time period	Type of surgery	Transplanted organ	Patient group	No. of patients per group	Follow-up
(Kohmoto et al., 2018)	2017	USA	1	Retrospective observational- Propensity score-matched 1 : 3	2000-2016	CABG, Valve surgery, CABG + Valve surgery, Other	Kidney Kidney-Pancreas Liver	TX N-TX	115 345	K-Tx 39 months [IQR: 12 to 82] KP-Tx 71months [IQR: 31 to 123] L-Tx 51 months [IQR: 26 to 114]
(Farag et al., 2017)	2016	Germany	1	Prospective observational pair-matched 1:01	2000-2013	CABG, Valve surgery, Ascending Aorta surgery, Other	Kidney Liver	Tx N-Tx	70 70	32 months
(Vargo et al., 2015)	2015	USA	1000 (NIS)	Retrospective observational- Propensity score-matched 1 : 3	2004-2008	CABG, Valve surgery, Thoracic Aorta surgery, Combination	Kidney Pancreas Liver	Tx N-Tx	719 (2322) 2157 (1 705 949)	-
(Sharma et al., 2013)	2012	Australia	1	Prospective Observational, cross-matched	1997-2010	CABG, Valve surgery, CABG + Valve surgery	Kidney Liver	Tx N-Tx	36	Tx- 4.5 ± 3.2 years N-Tx 3.9 ± 3.2 years
(John et al., 2007)	2007	USA	1	Retrospective	1995-2005	CABG, Valve	Kidney	Tx N-Tx	70 104	

CABG - Coronary Artery Bypass Grafting, NIS - Nationwide Inpatient Sample, Tx- Transplanted group, N-Tx - Non-Transplanted Group, K-Tx - Kidney transplantation, KP-Tx - Kidney-Pancreas transplantation, L-Tx - Liver Transplantation .

The meta-analysis revealed that the infectious postoperative complications such as wound infection (Tx vs. N-Tx: OR: 2.03, 95% CI: 1.54 to 2.67, $I^2 = 0\%$) and septicemia (Tx vs. N-Tx: OR: 3.91, 95% CI: 1.40 to 10.92, $I^2 = 0\%$) had significant lower rates in patients without transplantation history. Despite that, there was no difference pneumonia occurrence (OR: 0.95, 95% CI: 0.71 to 1.27, $I^2 = 0\%$).

Cardiac tamponade (Tx vs. N-Tx: OR: 1.83, 95% CI: 1.28 to 2.62, $I^2 = 0\%$) and kidney failure (Tx vs. N-Tx: OR: 1.70, 95% CI: 1.44 to 2.02, $I^2 = 89\%$) had also a higher incidence in transplant recipients, but no significant difference in post-procedural stroke rate (OR: 0.89, 95% CI: 0.54 to 1.48, $I^2 = 78\%$) was noticed.

No significant difference in 30-day mortality was observed (OR: 1.92, 95% CI: 0.97 to 3.80, $I^2 = 0\%$). Meanwhile, 5-years (OR: 3.74, 95% CI: 2.54 to 5.49, $I^2 = 0\%$) and 10-years mortality rates were significantly lower in the N-Tx group (OR: 3.32, 95% CI: 2.35 to 4.69, $I^2 = 0\%$).

4. Discussion

This study is the first meta-analysis to evaluate the short- and long-term consequences of open cardiac surgery in solid abdominal organ transplant patients versus non-transplant patients.

Our meta-analysis reveals that prior solid abdominal organ transplantation is associated with higher long-term mortality after major cardiac surgery. However, in the short term, not mortality but infectious complications are significantly higher in the group of transplanted individuals.

The (abdominal) transplanted population is a susceptible cohort to higher cardiovascular events rates with an estimated rate of 19% (de Mattos et al., 2006). Moreover, renal recipients' annual cardiovascular mortality rate is increased from 0.28% (in the general population) to 0.54%, where it accounts for 55% of the overall mortality. In comparison, up to 10% of the late mortality in the same category of patients has been ascribed to cardiovascular diseases (Rabkin et al., 2002, 2001).

A particularly unique risk element that appears to multiply the prevalence of cardiovascular risk factors and subsequently the development of cardiovascular disease is represented by the pharmacological immunosuppression in transplanted individuals, among which the use of calcineurin inhibitor was directly linked to severe hypertension and dyslipidemia (Rabkin et al., 2002).

Hypertension is prevalent in > 70% of transplant recipients and is associated with allograft failure, death with a functioning allograft, atherosclerotic cardiovascular diseases, and disorders of cardiac function (Kasiske et al., 2004). Meanwhile, 50% to 60% of kidney transplant recipients have dyslipidemia, strongly associated with atherosclerotic cardiovascular diseases in chronic kidney disease (CKD) and non-CKD populations (Kasiske et al., 2004). Obesity is also a frequent posttransplantation complication, while new-onset diabetes has a cumulative incidence of 5.9% at six months and 29.8% at 15-years posttransplantation (Friedman et al., 2003).

Like dyslipidemia, new-onset diabetes has been associated with allograft loss and death with a functioning allograft (Cosio et al., 2002; Gill, 2008; Kasiske et al., 2003). In our study, there was a significant difference between the two groups regarding the prevalence of hypertension and congestive heart failure, while con-

trary to what was previously reported, obesity and dyslipidemia had a lower prevalence in the transplanted population.

Three out of the five studies have reported data regarding the average interval between transplantation and cardiac surgery. The combined mean and standard deviation was approximately eight years. Musci et al. also reported similar data with an interval of 7.26 years in a renal transplant population (Musci et al., 2007). This variable's impact on short- and long-term outcomes can not be accurately estimated as there is no similar data in the control group. Also, no comparison within the transplanted population was reported based on the average interval between transplantation and cardiac surgery. Further studies that compare the transplanted graft age's influence on postoperative outcomes are necessary as this could be a lead-time bias source.

Our meta-analysis revealed that open cardiac surgery in abdominal transplant recipients might be challenging and hazardous, owing to an increased risk of infection, with higher rates of septicemia and wound infections. In particular, opportunistic infections are considered among the most feared in transplant patients due to immunosuppression therapy (Christiansen et al., 1997). Although the authors of the included studies reported infections of the lower respiratory tract, we found no difference in pneumonia between groups (Basic-Jukic et al., 2015; Bolman et al., 1984). Cardiac tamponade and kidney failure also had a higher incidence in transplant recipients, yet this could also be influenced by the higher prevalence of long chronic kidney dysfunction among renal transplant recipients.

We found no significant difference in 30-days mortality. Some authors even report a 100% survival rate after 30-days in patients with prior transplants who undergo valve replacement surgery (Bozso et al., 2019). This finding led to the conclusion that there would be no justification for the delay that so often accompanies the application of appropriate therapy in patients with prior transplantation, since cardiac therapeutic interventions could be carried out with relative impunity (Bolman et al., 1984).

A significant difference is observed when it comes to long-term mortality, with significantly higher rates after 5- and 10- years follow-up. This might be a strong argument to reconsider the proper approach in the surgical treatment of cardiac pathologies in this population and focus on other less-invasive transcatheter alternatives.

The relevance of accounting for renal transplantation status before choosing between open heart surgery and transcatheter approaches for coronary revascularization has indeed been highlighted by a propensity-matched control study based on six years of registry data. The study aimed to assess the postoperative incidence of renal dysfunction in patients with kidney-transplantation history undergoing coronary revascularization therapy either by percutaneous coronary interventions (PCI) or coronary arteries bypass grafting (CABG) from 2008 to 2014. There was a significantly higher incidence of both acute kidney injury (OR 2.20, 95% CI 1.91 to 2.54, $P = 0.0001$) and acute kidney injury requiring dialysis (OR 2.50, 95% CI 1.49 to 4.19, $P = 0.001$) in patients who underwent CABG compared with patients who underwent PCI. Despite that, no statistically significant difference in the in-hospital mortality between the PCI and CABG cohorts (OR 1.33, 95% CI 0.94 to 1.87, $P = 0.104$) was found (Taduru et al., 2017).

Table 4. Summary of individual pooled data and comparison between groups.

Parameters	No. of studies	No. of Tx patients	No. of N-Tx patients	Tx	N-Tx	P-value
				Mean ± SD or (%)	Mean ± SD or (%)	
Demographics						
Age	5	3826	1.707.363	58.06 ± 10.55	65.50 ± 11.80	< 0.0001
Male	5	3826	1.707.363	66.28%	68.36%	0.006
Congestive Heart Failure	3	3675	1.706.914	28.97%	23.40%	< 0.0001
NYHA –class IV	2	185	2135	16.75%	11.89%	NS
Previous myocardial infarction	4	291	1414	31.27%	38.33%	0.03
Peripheral vascular disease	5	3826	1.707.363	10.29%	9.98%	NS
Prior Stroke	5	3826	1.707.363	6.61%	7.56%	0.03
Diabetes mellitus	5	3825	1.707.363	27.42%	26.53%	NS
Hypertension4	291	1414	88.31%	74.82%	< 0.0001	
Obesity	2	185	415	28.64%	27.95%	NS
BMI	2	185	1240	26.42 ± 5.76	28.51 ± 5.67	
COPD	3	3641	1.706.123	10.73%	21.22%	< 0.0001
Smoking history	3	176	1069	37.50%	51.07%	0.001
Dyslipidaemia	3	176	1069	59.09%	68.38%	0.002
Type of surgery						
CABG only	5	3826	1.707.363	59%	70%	< 0.0001
Valve surgery only	5	3826	1.707.363	25.37%	16%	< 0.0001
CABG and Valve surgery	4	3756	1.707.293	14.80%	13%	0.002
Intraoperative data						
CPB time –minutes	4	291	1414	132.375 ± 65.9417	147.1262 ± 65.3887	0.0005
Aortic cross-clamp time- minutes	4	291	1414	86.1653 ± 45.5276	102.9047 ± 49.2664	< 0.0001

Tx- Transplantation, N-Tx - No Transplantation, BMI-Body Mass Index, COPD- Chronic obstructive pulmonary disease, CABG- Coronary Artery Bypass Grafting, CPB- Cardiopulmonary Bypass.

Table 5. Comparison between liver transplant and kidney transplant recipients.

	Total Liver Tx Kohmoto-Vargo-Sharma	Total Kidney Tx Kohmoto-Vargo-Sharma	P-value
Risk Factor Demographics			
Number of patients	762	2824	
Age at heart surgery (years)	62.42 ± 7.15	57.3839 ± 11.130	0.0357
Gender (males)	19/24 (79.16%)	84/112 (75%)	0.8657
Cardiac procedure			
CABG	471/762 (61.81%)	1635/2824 (57.89%)	0.0563
CABG and Valve	4/24 (16.66%)	15/112 (13.39%)	0.9244
Valve	183/762 (24.01%)	710/2824 (25.14%)	0.5532
Other	1/24 (4.16%)	11/112 (9.82%)	0.6236
Comorbidities			
Previous MI (%)	8/24 (33.33%)	31/112 (27.67%)	0.7683
PVD (%)	6/24 (25%)	26/112 (23.21%)	0.9382
CVA (%)	1/24 (4.16%)	17/112 (15.17%)	0.2658
Diabetes mellitus (%)	13/24 (54.16%)	51/112 (45.53%)	0.5869
Hypertension (%)	20/24 (83.33%)	101/112 (90.17%)	0.5409

Tx -Transplantation, CABG- Coronary Artery By-pass Grafting, MI- Myocardial Infarction, PVD-Peripheral Vascular Disease, CVA- Cerebrovascular Accidents.

Finally, transcatheter valve implantation procedures also proved to be an effective and safe method to treat kidney transplant recipients with high-grade aortic stenosis, associated with lower morbidity and mortality than conventional open-heart surgery. No severe complications such as acute renal failure (post-intervention creatinine [mg/dl] at 24 h 1.88 ± 0.77; 48 h 1.93 ± 0.84; 72 h 1.81 ± 0.78; discharge 1.87 ± 0.76), nosocomial infection, or in-hospital mortality occurred and a 100% survival was re-

ported after a 1-year follow-up. Meanwhile, the same authors reported a 30-day-mortality of 11.1% and a 1-year-mortality of 16.7% in the group that had undergone surgical aortic valve replacement (SAVR). Additional postoperative complications in the SAVR group were acute renal failure, sepsis, cerebral hemorrhage, re-thoracotomy, and prolonged hospitalization (Fox et al., 2013).

5. Limitations

This meta-analysis has some notable limitations. Firstly, there were two prospective and three retrospective studies. Four of them were pair-matched, among which there were two propensity score-matched studies. Vargo *et al.* (Vargo *et al.*, 2015) reported the outcomes in both ways, before and after 1 : 3 propensity matching. We mainly focused on the outcomes reported after propensity matching, except in those cases where data were unavailable to protect patient confidentiality as specified in the data users agreement. Secondly, in one study, 5- and 10- years mortality was calculated from the Kaplan-Meier survival curve, which can be inaccurate (Kohmoto *et al.*, 2018).

Thirdly, John *et al.* did not include the liver alone and pancreas alone transplant recipients in the analysis due to the small number of cases (John *et al.*, 2007). Fourthly, Kohmoto *et al.* (Kohmoto *et al.*, 2018) and Vargo *et al.* (2015) included the patients who underwent both on- and off-pump procedures, while the other three analyzed only the cases in which the procedure was performed under cardio-pulmonary by-pass. Fifthly, all types of cardiac surgeries were considered irrelevant to their level of risk and prognosis.

6. Conclusions

Given the growing number of abdominal organ transplant procedures and complex cardiovascular diseases that require open-heart surgery even in this particular category of patients, a solid background of evidence and indications/contraindications is needed for proper management of these tricky situations. Our meta-analysis sheds light on the short-term significant infectious risks and increased long-term mortality induced by open heart surgery in transplant patients. We believe that alternatives to classical surgery (such as minimally invasive surgery or transcatheter interventions) must be found, significantly where substantial evidence predicts major and unjustified complications.

Authors' contributions

Concept/design: AEB, AB, GT;
Data collection: AEB, AB;
Data analysis/interpretation: all authors;
Drafting article: all authors;
Critical revision of article: AB, GT;
Approval of article: all authors.

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Conflict of Interest

The authors declare no conflict of interest.

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