Should Biatrial Heart Transplantation Still Be Performed? A Meta-analysis

Rafael Fagionato Locali, Priscila Katsumi Matsuoka, Tiago Cherbo, Edmo Atique Gabriel, Enio Buffolo
Universidade Federal de São Paulo, São Paulo, SP - Brazil

Summary

The outcomes of total and bicaval heart transplantation techniques are better than those of the biatrial technique; however, the latter is still considered the gold-standard. The objective of this study was to determine whether the total and bicaval heart transplantation techniques are, in fact, better than the biatrial technique. A systematic review with meta-analysis was carried out. Studies were retrieved from Pubmed™, Lilacs™, Web of Science™, Scirus™, Scopus™, Google Scholar™, and Scielo™ databases, identified by sensitive strategy. Randomized, prospective, and retrospective controlled studies were selected for inclusion. Intra and postoperative parameters were assessed. A total of 11,602 studies were identified and 36 were included in our review. The number of atrial arrhythmias, tricuspid valve regurgitation, deaths, and embolic events, as well as bleeding volume; temporary and permanent pacemaker requirement; and length of stay in the intensive care unit are significantly lower for the total and bicaval techniques than for the biatrial technique. Also, hemodynamic variables such as pulmonary capillary pressure, mean pulmonary artery pressure, and right atrial pressure are lower in total and bicaval transplantation. In prognostic terms, total and bicaval orthotopic heart transplantations are better, than the biatrial transplantation. Therefore, indication of the biatrial technique for transplantation should be the exception, not the rule.

Introduction

Heart transplantation is a widely accepted therapeutic option for the treatment of end-stage heart failure[1,2]. Approximately 3,000 transplantations are performed worldwide every year[3,4].

Although the biatrial transplantation described by Lower and Shumway in 1961[5] is currently considered the gold-standard, two other techniques - the total and bicaval transplantation, were developed with the aim of ensuring better anatomical and physiological graft adaptation and better postoperative outcomes[5-9]. In fact, there are evidences in the literature that better results are obtained with the two techniques described more recently[10-21]. However, these evidences are weak when considered alone, and thus do not ensure an adequate level of evidence, especially because most of them are from retrospective studies with small case series[11,14,22-25].

For this reason, in 2007, Schnoor et al[10] conducted a meta-analysis with the purpose of increasing the statistical power of the evidences that the new techniques are better than the biatrial transplantation[10]. However, these authors excluded retrospective studies from the main assessments; they included the two more recent techniques in a single group and made a limited review of the literature. As such, relevant data may have not been included in the meta-analysis, thus making the evidence incomplete. For this reason, the objective of this study was to determine whether the techniques of total and bicaval heart transplantation are better than the biatrial technique, thus adding to Schnoor et al[10] results.

Key words

Heart transplantation/methods; heart failure; meta-analysis; prospective studies; retrospective studies.

Mailing address: Rafael Fagionato Locali •
Rua 3 de maio, 130, apto 183, Vila Clementino, 04044-020, São Paulo, SP - Brazil
E-mail: rafael.locali@hotmail.com
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Method

Inclusion and exclusion criteria

Study selection

Prospective controlled studies were included, whether randomized or not. Description of the randomization techiques, masking and patient follow-up, as described in the respective methodology of the studies, were not considered as criteria for inclusion. Retrospective studies including control groups were also included.

Studies whose designs did not meet these requirements, like case series and uncontrolled retrospective studies, narrative reviews and systematic reviews of the literature, case reports, letters, brief communications, and experimental animal studies were excluded. Additionally, studies whose results were incomplete, that is, those not reporting information on mean and standard deviation for continuous numeric variables and proportion of events occurred for nominal categorical variables, were also excluded.

Patients

No restrictions were made as to patient gender, age, and ethnicity, or as to the baseline heart diseases that led

to the end-stage heart failure requiring transplantation. Also, no disease or use of medication was considered as an exclusion criterion.

Intervention

Biatrial orthotopic heart transplantation was compared to bicaval transplantation, in which the left atrial anastomosis is performed in a similar fashion to that in Lower and Shumway's technique, however with the anastomosis of both venae cavae made separately, thus preserving the right atrial anatomy[5,8]. Likewise, biatrial transplantation was compared to total transplantation, in which the bicaval technique is used associated with complete removal of the recipient's left atrium, except for the pulmonary vein inlet region, to the right and to the left; in this site the donor's left atrium is anastomosed[9].

Clinical endpoints

Clinical endpoints were distributed into intraoperative and postoperative assessments, and the latter into hemodynamic parameters and morbidities. The intraoperative parameters included extracorporeal circulation time, aortic cross-clamp time, ischemia time, and operative time. The postoperative hemodynamic parameters assessed were mean pulmonary artery pressure, pulmonary capillary pressure, right atrial pressure and cardiac index. In relation to postoperative morbidities, the presence of atrial arrhythmias, mitral and tricuspid valve regurgitation, mortality, number of graft rejections, bleeding volume, embolic events, temporary and permanent pacemaker requirement, mechanical ventilation time, length of hospital stay, and length of stay in intensive care unit were analyzed.

These parameters were not stratified according to the follow-up period of each primary study. In fact, all data relative to each parameter were grouped so as to identify the overall estimate of the intervention, at the expense of the methodological homogeneity of the sample. For studies in which the endpoint was assessed at several timepoints, only data regarding the last timepoint were considered.

Also, no restrictions were made as to the technique used for endpoint assessment in the primary studies. Thus, the results were considered no matter whether obtained by transthoracic or transesophageal echocardiography, or Swan-Ganz catheter, regardless of the specifications of each ultrasound scanner.

Literature review strategy

The PubMed™, Lilacs™, Web of Science™, Scopus™, Scirus™, Google scholar™ and Scielo™ databases were systematically reviewed up to January 2, 2008. For this, the high-sensitivity and low-specificity search strategy was used, based on descriptors, synonyms and acronyms for biatrial, bicaval and total heart transplantation, with no restrictions as to study design, date and language of publication, or country where the study was carried out. This strategy was modified according to the search requirements adopted by each database (Figure 1).

Standardization of the literature review

Study selection

An initial screening of all studies identified by the search strategy in each database was performed using the information contained in their titles and abstracts,[26,27], in order to make an initial selection of the articles that could potencially be included. However, in the studies in which this procedure could not be carried out using the information presented in their title and abstract, the full version was analyzed and the studies were then selected or not[26,27].

All studies selected were reviewed in their full version and after the analysis of the methodology they were included or excluded, according to the inclusion criteria established. Also, the references of all studies selected were analyzed in order to increase the sensitivity of the systematic review. With the same purpose, the articles related to each selected study that were available in each database were also reviewed.

The study screening process was performed by two independent researchers. By the end of this phase, both made comparisons between the studies selected, and the discrepancies found were resolved by consensus.

Assessment of the methodological quality

The quality of the method of every study selected was assessed by two researchers in two different manners. The first consisted of classifying the studies into four categories, from A to D, according to the method used for the randomized distribution[26,27]. The second used the technique developed by Jadad et al[28] in 1996. The assessment of the quality of the method was not used for study inclusion or exclusion, but rather as a predictor of their individual power of evidence.

Data extraction

Data from each study were collected by two researchers. Initially, data collection consisted of the preparation of a standardized form that summarized relevant information for the critical analysis of objectives, methods - internal and external validity, results and conclusions of the primary studies.

Information from the primary studies was systematized in a previously created database for inferential calculations, with the purpose of operationalizing and rationalizing information retrieval.

Statistical analysis

All intraoperative and hemodynamic parameters were considered as quantitative variables of continuous numerical scale. The bleeding volume, mechanical ventilation time, length of stay in the intensive care unit, and length of hospital stay were also included in this category. All other postoperative variables were considered nominal qualitative variables of categorical scale.

Quantitative variables were expressed as the difference of the weighted mean, and qualitative variables as the relative risk, both with 95% confidence interval. The level for rejection of the null hypothesis was set at 5%.

PubMed

(Heart Transplantation OR Transplantation, Heart OR Heart Transplantations OR Transplantations, Heart OR Cardiac Transplantation OR Cardiac Transplantations OR Transplantations, Cardiac OR Transplantation, Cardiac OR Grafting, Heart OR Graftings, Heart OR Heart Grafting OR Heart Graftings OR Heart Lung Transplantation OR Grafting, Heart-Lung OR Grafting, Heart Lung OR Graftings, Heart-Lung OR Heart-Lung Grafting OR Heart-Lung Graftings OR Transplantation, Heart-Lung OR Heart-Lung Transplantations OR Transplantation, Heart Lung OR Transplantations, Heart-Lung OR Heart-Lung Transplantation OR Orthotopic heart transplantation OR (Heart AND (grafting OR grafts OR transplantation [Subheading])) AND (Atria, Heart OR Heart Atrium OR Atrium, Heart OR Left Atrium OR Atrium, Left OR Right Atrium OR Atrium, Right OR Heart Atria OR Atrial anastomoses OR Atrial anastomosis) AND (Vena Cava, Superior OR Cava, Superior Vena OR Cavas, Superior Vena OR Superior Vena Cava OR Superior Vena Cavas OR Vena Cavas, Superior OR Vena Cava, Inferior OR Inferior Vena Cavas OR Vena Cavas, Inferior OR Inferior Vena Cava OR Bicaval anastomosis OR Bicaval anastomoses)

Lilacs

("transplantation, heart" or "heart transplantation" or "transplantation, heart-lung" or "heart-lung transplantation") and ("heart atria" or "heart atrium" or "heart atrium appendage") and ("vena cava, inferior" or "vena cava, superior" or "venae cavae")

Web of Science

((Heart Transplantation OR Transplantation, Heart OR Heart Transplantations OR Transplantations, Heart OR Cardiac Transplantation OR Cardiac Transplantations OR Transplantations, Cardiac OR Transplantation, Cardiac OR Grafting, Heart OR Graftings, Heart OR Heart Grafting OR Heart Graftings OR Heart Lung Transplantation OR Grafting, Heart-Lung OR Grafting, Heart Lung OR Graftings, Heart-Lung OR Heart-Lung Grafting OR Heart-Lung Graftings OR Transplantation, Heart-Lung OR Heart-Lung Transplantations OR Transplantation, Heart Lung OR Transplantations, Heart-Lung OR Heart-Lung Transplantation OR Orthotopic heart transplantation OR (Heart AND (grafting OR grafts OR transplantation))) AND (Atria, Heart OR Heart Atrium OR Atrium, Heart OR Left Atrium OR Atrium, Left OR Right Atrium OR Atrium, Right OR Heart Atria OR Atrial anastomoses OR Atrial anastomosis) AND (Vena Cava, Superior OR Cava, Superior Vena OR Cavas, Superior Vena OR Superior Vena Cava OR Superior Vena Cavas OR Vena Cavas, Superior OR Vena Cava, Inferior OR Inferior Vena Cavas OR Vena Cavas, Inferior OR Inferior Vena Cava OR Bicaval anastomosis OR Bicaval anastomoses))

Scopus

(heart* transplantation* OR cardiac* transplantation* OR heart grafting* OR heart lung transplantation* OR heart-lung grafting* OR heart-lung transplantation* OR orthotopic heart transplantation OR heart graft*) AND (heart atrium* OR left atrium OR right atrium OR heart atria* OR atrial anastomos?s*) AND (superior ven?* cava* OR inferior ven?* cava* OR bicaval anastomos?s*)

Scirus

(heart transplantation OR cardiac transplantation OR heart grafting OR heart lung transplantation OR heart-lung grafting OR heart-lung transplantation OR orthotopic heart transplantation OR heart graft) AND (heart atrium OR left atrium OR right atrium OR heart atria OR atrial anastomoses OR atrial anastomosis) AND (superior vena cava OR inferior vena cava OR bicaval anastomoses OR bicaval anastomosis)

Google Acadêmico

(heart transplantation OR cardiac transplantation OR heart grafting OR orthotopic heart transplantation OR heart graft) AND (heart atrium OR left atrium OR right atrium OR heart atria OR atrial anastomoses) AND (superior vena cava OR inferior vena cava OR bicaval anastomoses)

Scielo

(heart transplantation) AND (heart atria OR heart atrium) AND (vena cava)

Figure 1 - Search strategies used for the identification of the studies.

Results

A total of 11,602 studies were identified, including the articles from all databases, related articles and references of the studies selected. Of these, 89 studies were selected for full text review, of which only 36 were included in this meta-analysis. Twenty two of these studies compared bicaval with biatrial transplantation and 14 compared total with biatrial transplantation. Data from the studies included are summarized in Tables 1 and 2.

Comparison of intraoperative variables in relation to the biatrial and bicaval transplantation shows that the extracorporeal circulation time, aortic cross-clamp time, and operative time are significantly longer in the bicaval transplantation. However, this did not occur with the

Table 1 - Studies included which compared the bicaval and biatrial techniques

Bicaval *versus* biatrial technique									
Nº	Author	Year	Study design	Category	Jadad scale	Operative technique	Nº cases	Age	Gender (M) %
1	Kendall et al[29]	1993	RCT	A	3	Biatrial	30	48 (21-61)	96.0
						Bicaval	30	47 (25-61)	90.0
2	Sarsam et al[30]	1993	RCT	B	1	Biatrial	20	NI	NI
						Bicaval	20	NI	NI
3	Sievers et al[16]	1994	RCT	B	1	Biatrial	10	49.7 ± 13.1	70.0
						Bicaval	8	56.3 ± 9.3	75.0
4	Deleuze et al[31]	1995	RCT	B	1	Biatrial	40	49.8 ± 8	80.0
						Bicaval	41	45.6 ±11	82.9
5	El Gamel et al[18]	1995	RCT	B	1	Biatrial	35	50 ± NI	80.0
						Bicaval	40	53 ± NI	77.5
6	Grant et al[32]	1995	RS	D	0	Biatrial	33	49.2 (45.1-53.4)	88.5
						Bicaval	42	44.1 (39.3-49)	80.6
7	Laske et al[25]	1995	RS	D	0	Biatrial	20	45 ± 10	90.0
						Bicaval	20	48 ± 10	80.0
8	Leyh et al[20]	1995	RS	D	0	Biatrial	12	50.3 ± 10.4	83.3
						Bicaval	15	52.2 ± 10.3	93.3
9	El Gamel et al[33]	1996	RCT	B	1	Biatrial	13	52 ± 8.5	76.9
						Bicaval	24	49 ± 9	70.8
10	Brandt et al[34]	1997	RS	D	0	Biatrial	30	51.6 ± 10.3	86.6
						Bicaval	30	52.8 ± 10.9	90.0
11	El Gamel et al[35]	1997	NRCT	D	1	Biatrial	20	52 ± 4.2	65.0
						Bicaval	20	49 ± 6.1	75.0
12	Traversi et al[19]	1998	NRCT	D	1	Biatrial	22	45 ± 10	93.1
						Bicaval	27	50 ± 12	73.9
13	Aziz et al[21]	1999	NRCT	D	1	Biatrial	105	49 ± 9.9	83.8
						Bicaval	96	47 ± 11.2	87.5
14	Aziz et al[36]	1999	NRCT	D	1	Biatrial	161	NI	NI
						Bicaval	88	NI	NI
15	Grande et al[37]	2000	NRCT	D	1	Biatrial	71	50.4 ± 13.4	78.8
						Bicaval	46	50.9 ± 10.8	80.4
16	Milano et al[22]	2000	RS	D	0	Biatrial	68	50 ± 9	76.0
						Bicaval	75	50 ± 11	76.0
19	Pahl et al[39]	2000	NRCT	D	1	Biatrial	14	14.8 ± 3.4	NI
						Bicaval	5	17.7 ± 3.2	NI
17	Wang et al[38]	2000	RCT	B	0	Biatrial	39	49 ± 12	71.7
						Bicaval	20	46 ± 14	75.0
18	Riberi et al[24]	2001	RS	D	0	Biatrial	72	44 ± NI	81.0
						Bicaval	106	48 ± NI	100
20	Solomon et al[14]	2004	RS	D	0	Biatrial	38	44 ± 13	76.0
						Bicaval	37	45 ± 14	81.0
21	Meyer et al[23]	2005	RS	D	0	Biatrial	48	55.2 ± 12	85.4
						Bicaval	57	55.9 ± 10.4	77.2
22	Park et al[40]	2005	RS	D	0	Biatrial	13	33.1 ± 11.8	76.9
						Bicaval	25	43.6 ± 11	68.0

RCT - randomized clinical trial; NRCT - non-randomized clinical trial; RS - retrospective study; M - male; NI - not informed.

Table 2 - Studies included which compared the total and biatrial techniques

Total *versus* biatrial technique									
Nº	Author	Year	Study design	Category	Jadad Scale	Operatory technique	Nº cases	Age	Gender (M) %
1	Czer e cols.[41]	1993	NRCT	D	1	Biatrial	26	55 ± 10	NI
						Total	24	56 ± 8	NI
2	Blanche e cols.[42]	1994	RS	D	0	Biatrial	64	53.1 ± 11.5	82.8
						Total	40	58.8 ± 9.7	92.5
3	Bizouarn e cols.[43]	1994	RCT	B	1	Biatrial	11	55 ± 9	90.9
						Total	9	55 ± 6	100
4	Derumeaux e cols.[44]	1995	NRCT	D	1	Biatrial	75	51 ± 12	NI
						Total	20	47 ± 12	NI
5	Freimark e cols.[45]	1995	RS	D	0	Biatrial	8	54.5 ± 10.2	87.5
						Total	8	54.6 ± 11.6	87.5
6	Aleksic e cols.[46]	1996	RS	D	0	Biatrial	60	53.1 ± 11.7	82.0
						Total	66	56.1 ± 10.1	92.0
7	Peteiro e cols.[17]	1996	NRCT	D	1	Biatrial	26	55 ± 9	NI
						Total	11	49 ± 10	NI
8	Rothman e cols.[47]	1996	NRCT	D	1	Biatrial	33	56 ± 8	73.0
						Total	37	49 ± 13	76.0
9	Aleksic e cols.[48]	1997	RS	D	0	Biatrial	15	54 ± 10	73.3
						Total	18	57 ± 10	88.8
10	Beniaminovitz e cols.[49]	1997	NRCT	D	1	Biatrial	10	NI	NI
						Total	10	NI	NI
11	Blanche e cols.[50]	1997	RS	D	0	Biatrial	64	53.1 ± 11.5	83.0
						Total	117	57.2 ± 11	92.0
12	Bouchart e cols.[51]	1997	NRCT	D	1	Biatrial	65	50 ± 11	NI
						Total	30	47 ± 10	NI
13	Bainbridge e cols.[52]	1999	RCT	B	1	Biatrial	29	NI	NI
						Total	29	NI	NI
14	Koch e cols.[11]	2005	RS	D	0	Biatrial	94	50.7 ± 10.7	77.0
						Total	72	49 ± 14	100

RCT - randomized clinical trial; NRCT - non-randomized clinical trial; RS - retrospective study; M - male; NI - not informed.

ischemia time, for which no differences were observed between the two interventions (Table 3). On the other hand, the comparison between the biatrial and total transplantation shows that only the ischemia time is shorter in the biatrial transplantation, with no differences between the groups regarding aortic cross-clamp time and extracorporeal circulation time (Table 3).

However, a smaller number of atrial arrhytmias, deaths and tricuspid valve regurgitation was observed in the postoperative period of the group undergoing the bicaval technique in comparison to the biatrial technique (Figure 2). On the other hand, these data are not valid for the total transplantation, for which only lower incidences of tricuspid valve regurgitation and embolic events were found (Figure 3).

The bicaval and total transplantation are not superior in relation to the biatrial technique as regards the incidence of mitral valve regurgitation and rejection episodes (Figures 2 and 3). Also, mortality for total transplantation was not lower than for biatrial transplantation (Figure 3).

No difference was found for cardiac index between the bicaval and total transplantation groups in comparison to the biatrial transplantation. However, pulmonary capillary pressure, mean pulmonary artery pressure and right atrial pressure were significantly lower with the bicaval technique. On the other hand, only the right atrial pressure was lower in the total transplantation group (Table 4).

Temporary or permanent pacemaker requirement was significantly less frequent in patients treated with the bicaval

Table 3 - Intraoperative parameters

Intervention	WMD (95% CI)	Study references
Bicaval *versus* biatrial transplantation		
Ischemia time	10.13 (-2.43; 22.69)	20-24, 29, 34, 35, 37, 38, 40
ECC time	14.55 (7.79; 21.31)*	14, 24, 25, 29, 31, 34, 35, 37, 38
Aortic cross-clamp time	10.34 (2.00; 18.67)*	14, 23,25
Operative time	17.37 (2.04; 32.09)*	25, 34, 38
Total *versus* biatrial transplantation		
Ischemia time	18.91 (10.70; 27.12)*	11, 17, 42, 43, 45, 47, 48, 51
ECC time	11.97 (-1.67; 25.61)	11, 47, 48, 51
Aortic cross-clamp time	7.67 (0.97; 14.38)	11, 47

*WMD - weighted mean difference; ECC - extracorporeal circulation; * (p < 0.05, in favor of biatrial transplantation).*

transplantation. This was also true for permanent pacemaker implantation in patients undergoing total transplantation.

Also, the postoperative bleeding volume and the length of stay in intensive care unit were lower for the bicaval in comparison to the biatrial technique. However, no differences were found for mechanical ventilation time and length of hospital stay. Likewise, the length of hospital stay for total transplantation was not different from that for biatrial transplantation. The bleeding volume was not different either (Table 5).

Discussion

Despite the remarkable progress of drug treatment for end-stage heart failure, heart transplantation is still the intervention of choice for this syndrome[1,2,11]. However, uncertainty still exists in the literature as to the best technique for this operation.

Both the bicaval and the total orthotopic heart transplantation were introduced as an alternative to the biatrial transplantation technique. They are different from the latter in that they ensure that the anatomical heart geometry is preserved. Thus, there would be theoretically a functional advantage in relation to the orthotopic biatrial transplantation. However, the inconsistent data from the literature are not enough to shake the surgeons' confidence on biatrial transplantation.

A meta-analysis published by Schnoor et al[10] in 2007 showed evidences of possible methodological biases in the systematic review of the literature, and this aroused interest in a new research. Also, given that the bicaval and total techniques are different interventions, it would be interesting to evaluate the advantages and disadvantages of each one separately, since the advantages of one could mask the disadvantages of the other. This is why the present study was conducted.

The criteria for inclusion of studies in this research followed Cochrane's recommendations[53]. However, considering that randomized trials with heart transplantation are difficult to conduct, and this is reflected in the small number of this type of study in the literature, we also included retrospective controlled trials. Uncontrolled trials were excluded for not allowing a meta-analysis[26] to be carried out, differently from what was done in Schnoor et al's study[10].

Furthermore, Schnoor et al[10] did not make strict restrictions as to the study design or the patients' demographic characteristics for inclusion. These authors considered only studies published in English or German, and reviewed only Pubmed™, Cochrane™, and the German Institute of Medical Documentation and Information (which includes EMBASE™ and Medline™) databases. Four journals were handsearched for data collection and experts were consulted[10]. In fact, the review carried out by these authors was not extensive enough to be considered systematic. This fact is evidenced by the considerable difference, in numbers, of data retrieved - 11,602 articles in this study *versus* 109 in theirs.

In this study, the ischemia time was not different between the bicaval and biatrial transplantation; however, it was significantly longer for total transplantation. This finding is similar to that of Schoor et al's[10]. However, these authors do not mention the other intraoperative parameters.

Ischemia time, even when longer as found in some studies, is compensated by a better cardiac performance with the new techniques, since adequate ventricular filling is dependent on a satisfactory atrial function[22,48]. Actually, this benefit is surpassed by possible complications resulting from longer extracorporeal circulation, aortic cross-clamp, and operative times.

The incidence of atrial arrhythmias was lower in the group undergoing bicaval transplantation, like in Schnoor et al's study[10]. This can be explained by the preservation of the sinus node integrity when the more recent techniques are used. Also, modifications in the atrial geometry predispose to atrial arrhythmias, as well as to increased internal pressure, since these events prolong the electric conduction time[34,54,55]. An additional risk for arrhytmias are the acute graft rejection episodes[34,56]. The severity of arrhythmia is known to be proportional to the severity of rejection[34,56].

However, our results showed no differences between the transplantation techniques regarding rejection episodes. Thus, we can presume that the episodes of atrial arrhythmia result mainly from greater deformity and atrial pressure.

In this context, the rejection episodes can also be related to the degree of tricuspid valve regurgitation[21,57]. In 2002, Aziz et al[57] showed that individuals with moderate or severe tricuspid regurgitation have a higher number and intensity of rejection episodes[57]. On the other hand, the progression of cardiac cellular rejection may be acompanied by edema and papillary muscle dysfunction, or trigger asymmetrical right ventricular contractility and thus lead to tricuspid valve regurgitation[21].

Additionally, the high hydrophillic property of the glucosaminoglycans present in the valve leaflet leads to increased oncotic pressure in the extracellular matrix during cellular rejection, thus causing edema and precluding adequate function[21]. However, in 2003, Aleksic et al[58] showed that patients undergoing total heart transplantation who develop rejection have less hemodynamic consequences than those undergoing biatrial transplantation[58].

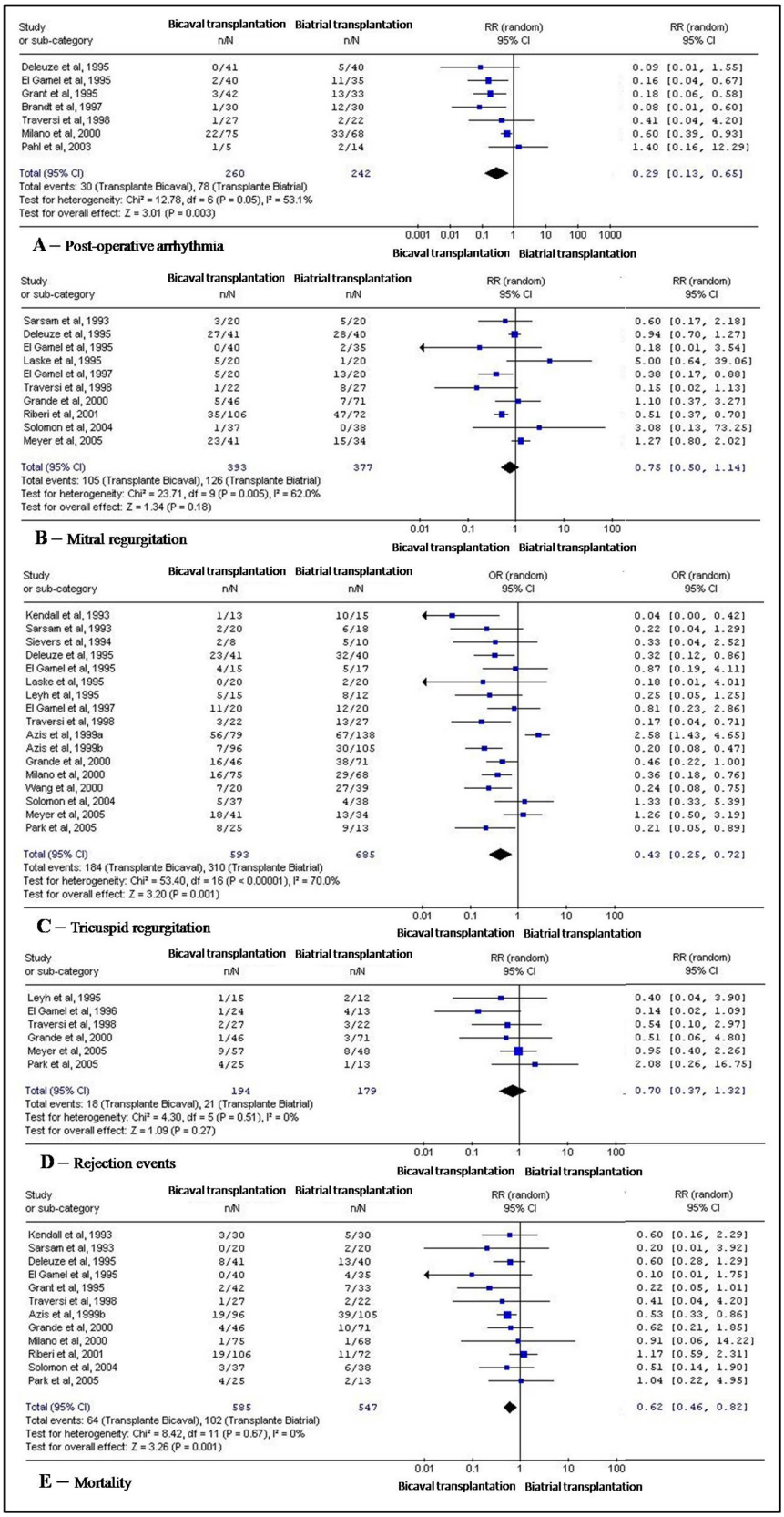

Figure 2 - Bicaval versus biatrial heart transplantation in relation to postoperative parameters.

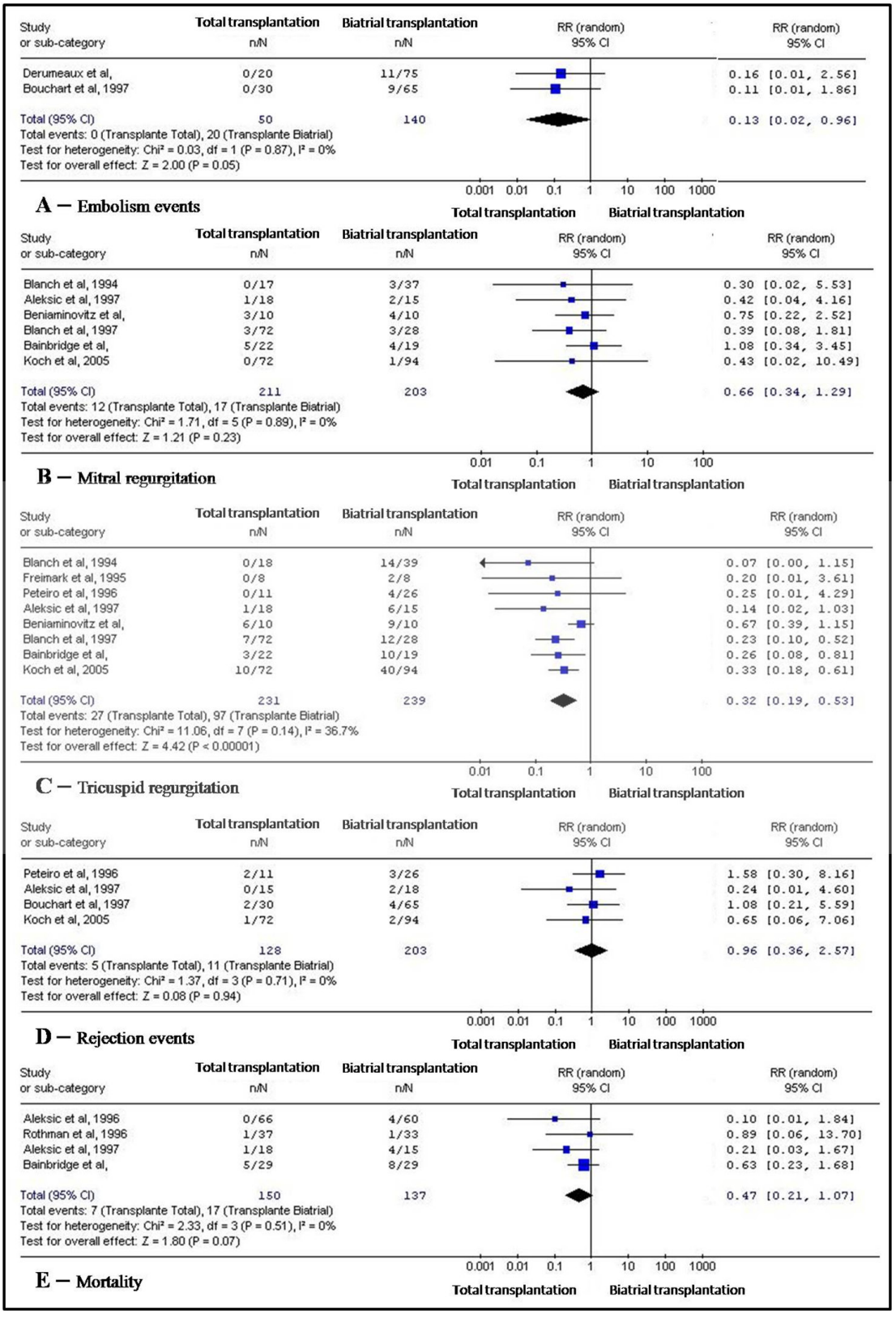

Figure 3 - Total versus *biatrial transplantation in relation to postoperative parameters.*

Table 4 - Hemodynamic parameters in the postoperative period

Intervention	WMD (95% CI)	Study references
Bicaval *versus* biatrial transplantation		
Cardiac index	0.36 (-0.09; 0.81)	18-20, 22, 31, 37, 39
Pulmonary capillary pressure	-1.06 (-1.96; -0.16)*	18-20, 31, 38
Mean pulmonary artery pressure	-3.07 (-4.95; -1.19)*	18, 20, 21, 31, 38
Right atrial pressure	-3.16 (-4.96; -1.36)*	18, 19, 21, 31, 30, 34, 38
Total *versus* biatrial transplantion		
Cardiac index	0.13 (-0.03; 0.30)	43, 46, 45, 48, 49, 51
Pulmonary capillary pressure	-0.59 (-2.87; 1.70)	43, 45, 46, 48, 49, 51
Mean pulmonary artery pressure	-1.28 (-5.34; 2.78)	43, 45, 46, 48
Right atrial pressure	-1.67 (-2.64; -0.69)*	43, 46, 48, 49

*WMD - weighted mean difference; * (p < 0.005, in favor of the bicaval or total transplantation).*

Table 5 - Interventions, events and length of hospital stay

Intervention	RR/WMD (95% CI)	Study references
Bicaval *versus* biatrial transplantation		
Temporary pacemaker	RR 0.56 (0.44; 0.70)*	14, 18, 19, 22, 25, 32, 33, 37, 38
Permanent pacemaker	RR 0.25 (0.09; 0.69)*	18, 23, 31, 32, 34, 37
Mechanical ventilation time	RR 0.29 (-12.2; 12.77)	14, 31, 34
Bleeding volume	DMP -141.08 (-245.08; -37.07)*	18, 33, 37
Length of stay in ICU	DMP 0.49 (-0.20; -1.18)*	14, 23, 25, 34
Length of hospital stay	DMP -0.53 (-5.28; 4.22)	14, 22, 23, 34, 37
Total *versus* biatrial transplantion		
Permanent pacemaker	RR 0.08 (0.02; 0.34)*	41, 46, 48, 50, 52
Bleeding volume	DMP 167.32 (-99.22; 433.86)	51, 52
Length of hospital stay	DMP -2.28 (-4.78; 0.23)	45, 48, 51

*ICU - intensive care unit; RR - long-term relative risk; WMD - weighted mean difference. * (p < 0.005, in favor of bicaval or total transplantation).*

In fact, the most recent transplantation techniques, especially the bicaval one, show better postoperative hemodynamic results than biatrial transplantation, that is, lower pulmonary capillary, and pulmonary artery and right atrial pressures. Similar findings were presented by Schnoor et al, who showed lower right atrial and pulmonary artery pressures[10]. However, unlike these authors' results, the cardiac index was not different between the groups in our study.

In 2002, Aziz et al[57] assessed these same parameters and showed that pulmonary artery, right atrial and right ventricular systolic pressures are correlated with a high incidence of tricuspid regurgitation in transplanted patients[57]. This finding is corroborated by that of Rees et al's study[59].

Actually, these authors' findings confirm our own, since a lower incidence of tricuspid regurgitation was identified in patients transplanted using the bicaval or total techniques; these patients also had better hemodynamic outcomes[10]. Furthermore, Schnoor et al[10] showed identical results for tricuspid regurgitation. On the other hand, these authors also found a lower incidence of mitral regurgitation, unlike in our study, in which no significant difference was found regarding this condition[10].

Tricuspid valve regurgitation is a common complication of heart transplantation, and is correlated with the development of right ventricular failure, kidney and liver failure and, consequently, with worse long-term outcomes[13,14,57]. In light of these facts, some authors proposed prophylactic tricuspid anuloplasty at the moment of transplantation, or in a new, further intervention[13]. In 2007, Marelli et al[13] described a new technique for bicaval transplantation with the aim of further reducing the incidence of this complication[13]. The mechanism through which tricuspid regurgitation develops is multifactorial. There is an association of acute graft edema; papillary muscle dysfunction; preoperative annular dilatation; change in the right atrial anatomic geometry with subsequent worsening of the functional integrity of the valvular apparatus; lesion of the subvalvular apparatus during endomyocardial biopsy; cyclic atrial tortion during ventricular systole and diastole; and asynchronous contraction of the donor and recipient atrial compartments[21,57].

Additionally, in 2002, Aziz et al[57] showed that the survival of patients with moderate/severe tricuspid regurgitation is insatisfactory in comparison to that of patients with other degrees of valve regurgitation[57]. In fact, we found lower mortality in patients undergoing the bicaval technique, similar to Schnoor et al's findings[10]. The explanation that Aziz et al[57] give to this finding is a worsened ventricular function associated with renal lesion due to low blood flow and immunosupressor toxicity that would lead to lower survival[57].

Our results also showed that systemic embolism, another complication of biatrial heart transplantation, with an incidence ranging from 2 to 15%, is also significantly decreased with the total transplantation technique[24]. Schnoor et al's findings are similar[10].

In 1997, Bouchart et al[51] analyzed this aspect and demonstrated that the possible formation of left atrial thrombus or embolic events were strongly predictable by the identification of spontaneous echo contrast in transesophageal echocardiography[51]. This finding is defined as the presence of swirling smoke-like echos within the atrial cavity, and was observed in all patients with a history of peripheral embolism or left atrial thrombus[51].

In fact, this atrial thrombogenic tendency results from

the asynchronous contraction of the donor's and recipient's atrial components, as well as from the presence of atrial arrhythmias[24,51]. In this regard, it is worth recalling that lower rates of atrial arrhythmias and subsequent less temporary or permanent pacemaker requirement were found in our study with the bicaval and total transplantation techniques. These findings were similar to those of Schnoor et al's study[10].

Other advantages of the more recent transplantation techniques are lower mortality rates, lower bleeding volume, and shorter length of stay in intensive care unit. The only result not concurrent with that of Schnoor et al's was the length of stay in intensive care unit, which was not significant[10].

In light of these facts, the superiority of the bicaval and total techniques demonstrated both in the present study and in Schnoor et al's is undebatable[10]. For this reason, the biatrial transplantation technique should no longer be considered the gold standard for transplantation, and should only be used in selected cases and special situations. Thus, today there is no more room for questioning whether there are advantages of the bicaval or total techniques over the biatrial technique, but rather for searching for possible advantages of one technique over the other and thus provide patients with the best treatment.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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