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Systematic preoperative CT scan is associated with reduced risk of stroke in minimally invasive mitral valve surgery: A meta-analysis☆

Jeremy R. Leonard, Matthew Henry, Mohamed Rahouma, Faiza M. Khan, Matthew Wingo, Irbaz Hameed, Antonino Di Franco, T. Sloane Guy, Leonard N. Girardi, Mario Gaudino *

Department of Cardiothoracic Surgery, Weill Cornell Medicine, New York City, NY, USA

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ABSTRACT

Background: Minimally invasive mitral valve surgery (MIMVS) is performed with increasing frequency. However, patients undergoing MIMVS might be at increased risk of perioperative stroke, mainly due to retrograde aortic embolization during femoral cardio-pulmonary bypass. Pre-operative computed tomography (CT) screening allows visualization of the aorta and femoro-iliac vessels and individualization of the surgical approach. In this meta-analysis, we aim to determine if systematic pre-operative CT screening is associated with decreased incidence of post-operative stroke and other complications following MIMVS.

Methods: A comprehensive review was performed in PubMed (inception-May 2018). Eligible studies included those which reported on MIMVS (mini-thoracotomy, port access or robotic approach) with retrograde arterial perfusion. Studies were separated into two subgroups: systematic pre-operative CT screening (CT-group) and no CT screening (Non-CT). Pooled event rates (PER) for operative mortality, post-operative stroke, perioperative myocardial infarction (MI), and new onset renal failure requiring dialysis were estimated and inter-group comparisons were performed.

Results: Data from 57 studies (13,731 patients) were analyzed (19 CT-group, 38 Non-CT). PER for post-operative stroke was 2.0% with a statistically significant difference between the groups (CT-group: 1.5% versus Non-CT: 2.2%, $P = 0.03$). PER for new dialysis was 1.9%, significantly lower in the CT-group (0.8% versus 2.3% in the Non-CT group, $P = 0.02$). PER for operative mortality was 1.4% with a trend towards better outcomes in the CT-group (0.8% versus 1.6% in the Non-CT group, $P = 0.05$).

Conclusions: Systematic pre-operative CT screening is associated with lower risk of post-operative stroke and need for dialysis and a trend toward lower operative mortality after MIMVS.

1. Introduction

Encouraged by outcomes of laparoscopic procedures in general surgery, cardiac surgeons first began to adopt minimally invasive procedures in the 1990s [1,2]. Among the first to be explored was minimally invasive mitral valve surgery (MIMVS). MIMVS offered the promise of reducing perioperative morbidity and mortality with improved cosmesis. The present day procedure includes several different possible approaches such as right mini-thoracotomy, port-access, and robotic. Typically, the procedure utilizes cardio-pulmonary bypass (CPB) with retrograde perfusion via the femoral vessels. MIMVS is increasingly performed with data from The Society of Thoracic Surgeons Adult Cardiac Surgical Database (STS ACSD) showing an increase from 11.9% to 20.1% of all isolated mitral operations in 2004 and 2008, respectively [3]. One explanation for this rise is an increase in patient satisfaction following MIMVS. In comparison to median sternotomy, the mean incision length is significantly reduced in MIMVS, and significantly fewer patients are dissatisfied with their scar [4]. Additionally, Cohn et al. found that patients report returning to normal activity and "feeling like themselves" four weeks earlier compared to the conventional approach ($P = 0.0002$ and $P = 0.009$, respectively) [2].

Despite its growing popularity among patients, there is concern that MIMVS utilizing retrograde arterial perfusion may be associated with an increased incidence of stroke mainly due to retrograde aortic embolization. Those concerns were mainly generated by a report by Gammie et al. published in 2010. Utilizing the STS ACSD, they reported a post-operative stroke incidence of 1.16% in the conventional median sternotomy cohort and 1.87% in the MIMVS cohort ($P = 0.0001$) [3]. Similarly, in a retrospective cohort of patients undergoing first-time isolated

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

* Corresponding author at: Department of Cardiothoracic Surgery, Weill Cornell Medicine, 525 E 68th St, New York, NY 10065, USA.
E-mail address: mfg9004@med.cornell.edu (M. Gaudino).

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MIMVS via a right mini-thoracotomy, Murzi et al. noted a higher incidence of stroke in patients receiving retrograde compared to antegrade arterial perfusion (3.5% vs 1.1%, $P = 0.005$) [4].

Computed tomography (CT) scans can be employed to evaluate the thoraco-abdominal aorta and femoro-iliac vessels and to individualize the surgical approach to the anatomic and pathologic characteristics of each patient potentially reducing the perioperative risk. For example, Moodley et al. reported that mandatory pre-operative CT scans of the chest, abdomen and pelvis revealed significant subclinical aortoiliac atherosclerosis resulting in a change in surgical approach in 21% of asymptomatic or mildly symptomatic patients scheduled for MIMVS. In the cohort of patients that had their surgical plan altered due to pre-operative CT imaging, there were no documented strokes prior to discharge [5]. However, this study was retrospective and only included robotic MIMVS.

In this meta-analysis, we aim to determine if systematic pre-operative CT screening is associated with decreased incidence of post-operative stroke and other complications following MIMVS.

2. Methods

This meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [6] and the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) guidelines [7] (Supplementary Table 1).

2.1. Search strategy

PubMed, Ovid MEDLINE and Ovid EMBASE databases were searched to identify studies on MIMVS. Searches were run on May 30, 2018 using the following search terms: 1. "minimally invasive" [Title/Abstract] AND "mitral valve" [Title/Abstract], 2. "robotic" [Title/Abstract] AND "mitral valve" [Title/Abstract].

2.2. Study selection and inclusion criteria

Database searches were conducted, de-duplicated, and screened by two medically qualified preliminary reviewers (JL, MH). A third independent reviewer (MG) confirmed adequacy of studies based on predefined inclusion and exclusion criteria for titles and abstracts. We included only studies reporting the results of isolated MIMVS utilizing retrograde perfusion via femoral artery cannulation in adult patients and reporting stroke among the outcomes. Non-English articles and case series (including sample size of 10 patients or less) were excluded. Full text of initially screened articles was then retrieved for a second round of eligibility screening. Reference lists for articles selected for inclusion were searched and additional studies included (i.e. backward snowballing). The PRISMA flow diagram outlining the study selection process is available in Supplementary Fig. 1. The Newcastle-Ottawa Quality Assessment Scale (NOS) for critical appraisal of eligible studies was used (Supplementary Table 2) [8]. Studies with scores ≥6 were included.

Studies were then divided according to the use of systematic CT screening of the aorta and iliaco-femoral vessels (CT vs. Non-CT group). Studies in which CT screening was adopted in only some patients were excluded from the analysis.

2.3. Outcomes

The primary outcome was postoperative stroke as defined by the authors. Secondary outcomes were operative mortality, perioperative myocardial infarction (MI), new onset renal failure requiring dialysis, and transient ischemic events, all following the authors definition.

2.4. Data extraction and statistical analysis

Extracted variables included the following: study name, publication year, study design, number of patients, age, percentages of female, smoking history, dyslipidemia, coronary artery disease (CAD), hypertension, diabetes mellitus (DM), previous cerebrovascular accident (CVA), peripheral vascular disease (PVD), emergency/urgent surgery, ejection fraction (EF), and previous cardiac surgery, along with numbers of stroke, myocardial infarction, prolonged ventilation/respiratory failure, operative mortality, limb ischemia, new dialysis, wound infection, intensive care unit (ICU)/hospital stay, total procedure time, CPB time, cross-clamp time, follow-up death, and mean follow-up.

Measurement data are reported as mean ± standard deviation. For short term outcomes, pooled event rates (PER) and pooled mean with 95% confidence interval (95%CI) were estimated for the binary and continuous outcomes, respectively. For late outcomes, incidence rates (IRs) were used. Poisson process was used to account for different follow up times of the individual.

Subgroup analyses were used to compare the CT group and Non-CT group. Meta-regression was used to assess the effect of age, gender, smoking history, dyslipidemia, CAD, hypertension, DM, previous CVA, PVD, emergency/urgent surgery and previous cardiac surgery on the primary outcome.

The Cochran Q statistic and the I^2 test were used to assess studies' heterogeneity. If heterogeneity was significant ($I^2 > 75\%$) for the primary outcome, a leave one out sensitivity analysis was performed [9]. Funnel plot and Egger's regression test were used to assess for potential publication bias [10]. A random-effect model (inverse variance method) [10] was used for the whole analysis. Hypothesis testing for equivalence was set at the two-tailed 0.05 level. Analyses were performed using R [11,12] (version 3.3.3 R Project for Statistical Computing) within RStudio (0.99.489, http://www.rstudio.com).

3. Results

3.1. Characteristics of eligible studies and patients included

Among 1203 retrieved searched articles and an additional 9 articles identified by backward snowballing, 57 articles (see references in Appendix) met the inclusion criteria (19 CT group and 38 Non-CT). The mean sample size was 236.6 patients (range 11–2829) and the mean follow up time was 3.00 years (range 0.25–10.40 years).

3.2. Single arm meta-analysis

A total of 13,731 patients were included, baseline characteristics of who are reported in Table 1. Mean age was 59.1 years and ranged from 40.0 to 82.5 years and the percentages of females ranged from 16.0 to 77.8%. DM percent ranged from 0.0 to 32.4%, prior CVA ranged from 0.0 to 17.5%, and PVD ranged from 0.0 to 45.0%.

3.3. Short-term outcomes

Overall, 221/13,731 patients experienced a postoperative stroke (PER 2.0%, 95%CI: 1.6–2.4). There was a statistically significant difference between the CT and Non-CT groups (CT group: 1.5%, 95%CI: 1.1–2.0 versus Non-CT 2.2%, 95%CI: 1.7–2.8, P for interaction = 0.03) (Fig. 1 and Table 2). Additional subgroup analysis on PER of stroke based on the underlying disease (degenerative vs others), type of operation (repair vs replacement), use of the endoclamp, and use of a CO_2 line are reported in the Appendix (Supplementary Figs. 2–5). Significantly lower PER for stroke were found in patients with degenerative disease vs other etiologies ($P = 0.02$); no statistically significant differences were found for all other comparisons.

The pooled operative mortality was 1.4% (95%CI: 1.0–1.8) with a trend towards better outcomes in the CT group 0.8% (95%CI: 0.4–1.5) versus 1.6% (95%CI: 1.2–2.2) in the Non-CT group (P for interaction = 0.05). The PER for new dialysis was 1.9% (95%CI: 1.4–2.6), significantly lower in the CT group: 0.8% (95%CI: 0.4–1.9) versus 2.3% (95%CI: 1.7–3.2) in the Non-CT group (p for interaction = 0.02) (Fig. 2A, B and Table 2).

The PER for perioperative MI was 0.8% (95%CI: 0.6–1.0) with no differences between groups (Fig. 2C and Table 2).

Total procedure length was 238.9 min (95%CI: 222.3–255.6 min) with no differences between groups. The pooled mean CPB time and cross-clamp time were 141.4 min (95%CI: 131.7–151.0) and 94.2 min (95%CI: 86.8–101.7), respectively. The pooled rate of prolonged ventilation/respiratory failure, wound infection, and limb ischemia were 5.2% (95%CI: 3.7–7.2), 0.9% (95%CI: 0.6–1.5), and 0.6% (95%CI: 0.3–1.3), respectively, with no intergroup differences (Fig. 2D, Supplementary Fig. 6 and Table 2). The pooled mean ICU stay was 1.84 days (95%CI 1.61–2.07): 1.67 days (95%CI: 0.96–2.37) in the CT group versus 1.66 days (95%CI: 1.48–1.83) in the Non-CT group (P for interaction = 0.98). The pooled mean hospital stay was 7.92 days (95%CI: 6.98–8.85): 8.08 days (95%CI: 5.35–10.82) in the CT group vs 7.66 days (7.03–8.30) in the Non-CT group (P for interaction = 0.77) (Table 2).

No statistically significant difference in terms of transient ischemic events between the 2 groups was found ($P = 0.35$) (Supplementary Fig. 7).

Table 1
Demographics of the included studies in minimally invasive mitral valve surgery (references provided in Appendix).

Group	Author year	n	Age mean ± SD	Females (%)	HTN (%)	DM (%)	Prior CVD/CVA (%)	PVD (%)	EF mean ± SD (%)
CT scan	Ad 2015	76	63.00 ± 9.00	35.5	54.0	6.6	4.0	1.3	59.00 ± 8.00
CT scan	Bedeir 2015	57	51.00 (45.00–55.00)*	35.1	50.9	12.3	1.8	5.3	60.00 (57.00–65.00)*
CT scan	Breves 2016	196	62.89 ± 12.34	57.1	NR	NR	NR	NR	NR
CT scan	Gillinov 2018	1000	56.00 ± 10.00	23.0	44.1	1.8	2.2	1.2	60.00 ± 5.10
CT scan	Heuts 2016	11	62.00 ± 10.50	36.4	100.0	NR	9.1	0.0	CAT
CT scan	Ito 2017	250	62.40 ± 14.30	51.2	40.0	7.2	1.6	NR	70.50 ± 8.60
CT scan	Kesavuori 2018	142	59.00 ± 10.80	19.0	33.8	4.2	0.7	NR	CAT
CT scan	Kim 2017	310	48.40 ± 13.70	35.2	31.6	7.4	3.2	NR	63.70 ± 6.70
CT scan	Kiziltan 2015	20	62.00 ± 12.00	45.0	NR	NR	NR	5.0	50.00 ± 11.00
CT scan	Kuo 2018	52	55.10 ± 13.80	65.4	30.8	7.7	11.5	NR	65.50 ± 10.80
CT scan	Lewis 2014	50	73.40 ± 9.30	44.0	82.0	26.0	NR	NR	45.70 ± 14.10
CT scan	Loforte 2010a	45	58.10 ± 11.40	77.8	42.2	11.1	NR	NR	58.00 ± 8.60
CT scan	Murphy 2018	50	62.40 ± 15.00	54.0	42.0	10.0	10.0	NR	55.00 (50.00–60.00)*
CT scan	Navarra 2017	134	57.50 ± 12.00	19.4	26.9	2.2	1.5	2.2	62.70 ± 6.50
CT scan	Rosu 2015	73	59.10 ± 11.10	30.1	NR	NR	NR	NR	NR
CT scan	Sakaguchi 2018	387	56.00 ± 13.00	34.9	37.2	5.7	2.8	0.3	67.50 ± 8.60
CT scan	Suri 2015	487	55.60 ± 11.00	26.1	37.4	2.3	1.4	0.0	64.80 ± 6.30
CT scan	Tarui 2018	162	55.00 ± 11.00	37.7	47.5	12.4	1.2	0.0	66.20 ± 7.00
CT scan	Ward 2014	108	59.00 ± 16.25	38.0	NR	NR	NR	NR	NR
No CT scan	Akowuah 2015	190	61.00 ± 11.00	32.0	34.7	2.6	7.4	NR	CAT
No CT scan	Aybek 2006	241	56.30 ± 14.20	49.8	NR	NR	NR	NR	62.00 ± 12.00
No CT scan	Chen 2013	186	57.00 ± 12.00	40.9	57.0	5.4	1.6	0.0	56.38 ± 9.00
No CT scan	Coyan 2018	91	62.00 ± 16.25	42.9	62.6	11.0	7.7	11.0	60.00 ± 17.50
No CT scan	D'Alfonso 2012	179	40.20 ± 10.10	48.0	NR	NR	NR	NR	62.00 ± 6.00
No CT scan	Davierwala 2013	2829	60.30 ± 13.00	38.8	NR	NR	3.2	NR	56.80 ± 18.90
No CT scan	De Bonis 2017	104	40.00 ± 10.00	52.0	NR	NR	NR	0.0	63.00 ± 5.00
No CT scan	Dogan 2005	20	60.10 ± 12.30	55.0	45.0	NR	NR	0.0	63.40 ± 10.60
No CT scan	Downs 2016	355	59.00 ± 11.60	38.0	55.2	7.3	NR	3.9	57.70 ± 9.10
No CT scan	Efird 2015	641	CAT	39.6	46.8	5.9	2.7	1.7	CAT
No CT scan	Folliguet 2006	25	59.40 ± 11.20	36.0	NR	NR	NR	NR	57.00
No CT scan	Galloway 2009	1071	60.40 ± 14.00	38.3	NR	NR	NR	NR	NR
No CT scan	Gao 2012	22	44.70 ± 9.80	59.1	NR	NR	NR	NR	50.20 ± 13.80
No CT scan	Gersak 2005	105	60.30 ± 12.40	56.2	NR	NR	NR	NR	NR
No CT scan	Goldstone 2013	201	57.10 ± 12.40	33.8	41.8	NR	7.0	2.5	57.00 ± 9.50
No CT scan	Jones 2005	32	67.60 ± 9.75	62.5	46.9	31.3	NR	NR	All above 30.00%
No CT scan	Kitamura 2010	60	61.00 ± 15.00	45.0	73.3	NR	NR	NR	CAT
No CT scan	Lange 2017	97	63.00 ± 12.00	41.2	NR	NR	NR	NR	63.00 ± 11.00
No CT scan	Loforte 2010b	93	58.80 ± 7.80	73.1	45.2	10.8	NR	NR	60.00 ± 9.50
No CT scan	Losenno 2016	40	68.00 ± 14.00	30.0	NR	27.5	17.5	45.0	CAT
No CT scan	Mazine 2013	243	58.16 ± 7.30	39.5	37.9	4.9	6.2	NR	61.05 ± 8.10
No CT scan	Minol 2016	34	82.50 ± 2.00	70.6	94.1	17.7	2.9	NR	59.70 ± 6.90
No CT scan	Minol 2018	146	66.21 ± 4.16	30.8	74.7	5.5	7.5	NR	59.59 ± 2.99
No CT scan	Mishra 2005	430	42.20 ± 8.40	67.4	NR	27.4	9.8	NR	42.00 ± 7.00
No CT scan	Mohr 1999	51	68.10 ± 10.70	66.7	39.2	25.5	NR	NR	57.00 ± 13.00
No CT scan	Muneretto 2015	50	53.00 ± 11.00	38.0	48.0	NR	2.0	8.0	62.00 ± 7.00
No CT scan	Murphy 2006	127	54.00 ± 13.00	42.0	48.8	NR	NR	NR	57.90 ± 9.20
No CT scan	Murzi 2009	25	71.80 ± 12.7	16.0	68.0	24.0	NR	NR	45.00 ± 9.00
No CT scan	Paparella 2017	20	57.00 (44.00–62.00)*	35.0	40.0	0.0	0.0	0.0	56.00 (50.00–58.00)*
No CT scan	Perier 2013	842	56.15 ± 11.62	24.5	52.5	2.4	1.5	NR	64.80 ± 5.20
No CT scan	Petracek 2011	504	65.00 ± 18.00	49.4	59.9	20.0	10.3	NR	55.00 ± 18.75
No CT scan	Qiu 2018	165	51.50 ± 6.80	35.2	21.2	18.8	6.1	NR	59.50 ± 4.00
No CT scan	Reichenspurner 2005	120	62.10 ± 10.50	70.8	NR	NR	NR	0.0	55.80 ± 15.70
No CT scan	Reser 2014	312	61.00 ± 13.10	35.3	55.1	6.1	2.9	4.5	NR
No CT scan	Ryan 2010	220	56.35 ± 12.94	46.4	40.5	7.7	2.7	NR	55.33 ± 10.25
No CT scan	Salman 2018	33	60.00 ± 16.00	48.5	87.9	27.3	NR	39.4	51.79 ± 11.56
No CT scan	Santana 2013	71	67.00 ± 10.00	38.0	94.4	32.4	8.5	NR	27.00 ± 6.00
No CT scan	Vanermen 2000	121	60.00 ± 13.00	44.6	NR	NR	NR	NR	CAT
No CT scan	Woo 2006	25	60.00 ± 3.00	32.0	NR	4.0	16.0	12.0	NR

CAT, categorical; CT, computed tomography; CVD/CVA, cerebrovascular disease/accident; DM, diabetes mellitus; EF, ejection fraction; HTN, hypertension; NR, not reported; PVD, peripheral vascular disease.
* Median (IQR).

3.4. Long-term outcomes

IR for late mortality was 1.3% (95%CI 0.9–1.8), and it was significantly lower in the CT group versus the non-CT group (0.7%, 95%CI 0.4–1.2 versus 1.7%, 95%CI 1.1–2.4) (p for interaction = 0.009) (Table 2).

Funnel plot of observed and imputed studies (Trim and fill method) and leave one out analysis for the primary outcome revealed robustness of the results (Egger's intercept = 0.44, $P = 0.12$) (Supplementary Fig. 8). The cumulative analysis for the primary outcome is shown in Supplementary Fig. 9. The number of studies used for each outcome analysis is reported in Table 2.

3.5. Meta-regression

Age (Beta = 0.07, $P < 0.0001$), female gender (Beta = 0.02, $P = 0.005$), CAD (Beta = 0.03, $P < 0.0001$), hypertension (Beta = 0.01, $P = 0.014$), DM (Beta = 0.05, $P < 0.0001$), previous stroke (Beta = 0.10, $P < 0.0001$), PVD (Beta = 0.05, $P < 0.0001$), emergency/urgent surgery (Beta = 0.06, $P < 0.0001$), previous cardiac surgery (Beta =

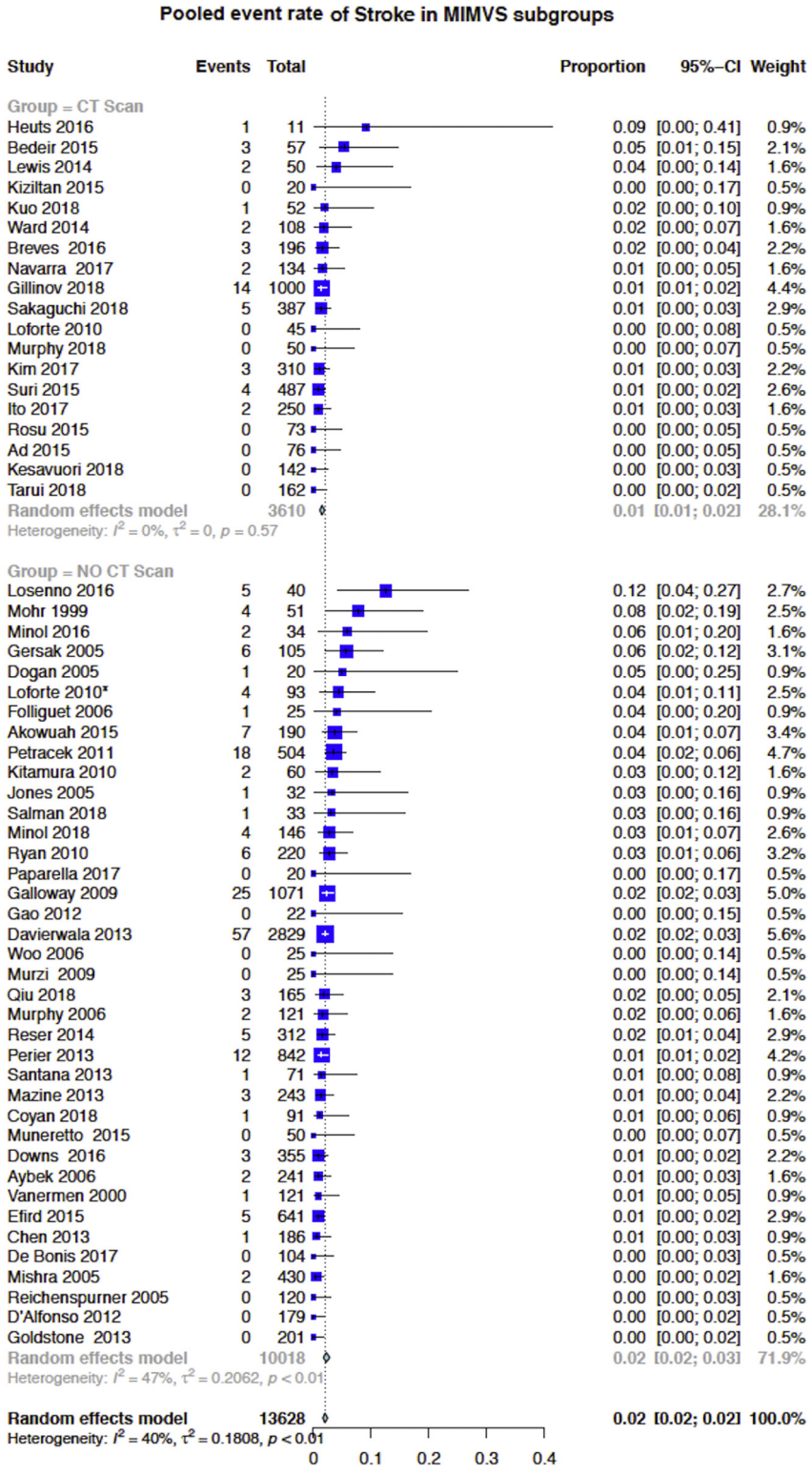

Fig. 1. Pooled event rate of stroke in MIMVS subgroups. 95% CI, 95% confidence interval, MIMVS, minimally invasive mitral valve surgery.

0.02, $P < 0.0001$), and no CT screening (versus CT screening) (Beta = 0.45, $P = 0.007$) were associated with post-operative stroke (Supplementary Table 3).

4. Discussion

Since the publication by Gammie et al. in 2010, there has been a growing concern that MIMVS may be associated with an increased risk of post-operative stroke. This is particularly relevant given the rising trend in less invasive approaches with approximately one-quarter of all procedures for mitral regurgitation being performed this way in 2008 according to the STS ACSD [3].

The reported increase in post-operative stroke associated with MIMVS has been postulated to be secondary to peripheral (femoral) cardiopulmonary bypass resulting in potential retrograde embolization from the distal aorta to the cerebral circulation [5]. For this reason, some

Table 2
Outcomes summary for single arm meta-analysis among minimally invasive mitral valve surgery (MIMVS) cohort.

	Studies	Proportion (95%CI)	Heterogeneity (I^2, *P*-value)	tau^2
Stroke in MIMVS (All)	57	0.0198 [0.0162; 0.0243]	40.2%, $P = 0.0012$	0.1808
Stroke in MIMVS (CT screened)	19	0.0146 [0.0109; 0.0195]	0.0%, SGD-P = 0.0338	0
Stroke in MIMVS (no CT screen)	38	0.0221 [0.0172; 0.0282]	47.2%, SGD-P = 0.0338	0.2062
Operative mortality in MIMVS (all)	57	0.0136 [0.0103; 0.0181]	47.8%, $P < 0.0001$	0.4191
Operative mortality in MIMVS (CT screened)	18	0.0080 [0.0043; 0.0149]	34.7%, SGD-P = 0.0516	0.5756
Operative mortality in MIMVS (no CT screen)	39	0.0160 [0.0116; 0.0219]	51.7%, SGD-P = 0.0516	0.3934
MI in MIMVS (all)	20	0.0078 [0.0059; 0.0104]	0.0%,$P = 0.6838$	0
MI in MIMVS (CT screened)	6	0.0077 [0.0032; 0.0184]	0.0%, SGD-P = 0.9659	0
MI in MIMVS (no CT screen)	14	0.0079 [0.0058; 0.0108]	2.9%, SGD-P = 0.9659	0.0122
Renal failure/dialysis in MIMVS (All)	36	0.0187 [0.0136; 0.0256]	61.9%, $P < 0.0001$	0.4138
Renal failure/dialysis in MIMVS (CT screened)	11	0.0083 [0.0036; 0.0190]	50.2%, SGD-P = 0.0225	0.9198
Renal failure/dialysis in MIMVS (no CT screen)	25	0.0233 [0.0168; 0.0323	60.4%, SGD-P = 0.0225	0.3015
Prolonged ventilation/respiratory failure in MIMVS (all)	25	0.0519 [0.0372; 0.0719]	80.53%, $P < 0.0001$	0.5356
Prolonged ventilation/respiratory failure in MIMVS (CT screened)	8	0.0478 [0.0285; 0.0791]	79.6%, SGD-P = 0.7303	0.4407
Prolonged ventilation/respiratory failure in MIMVS (no CT screen)	17	0.0537 [0.0350; 0.0815]	79.6%, SGD-P = 0.7303	0.5797
Wound infection in MIMVS (all)	39	0.0089 [0.0055; 0.0145]	63.4%, $P < 0.0001$	1.1880
Wound infection in MIMVS (CT screened)	13	0.0096 [0.0048; 0.0195]	36.3%, SGD-P-0.8262	0.5556
Wound infection in MIMVS (no CT screen)	26	0.0087 [0.0046; 0.0163]	69.4%, SGD-P = 0.8262	1.4423
Limb ischemia in MIMVS (all)	12	0.0063 [0.0030; 0.0131]	0.0%, $P = 0.9537$	0
Limb ischemia in MIMVS (CT screened)	6	0.0048 [0.0017; 0.0135]	0.0%, SGD-P = 0.4606	0
Limb ischemia in MIMVS (no CT screen)	6	0.0083 [0.0029; 0.0235]	0.0%, SGD-P = 0.4606	0
Late mortality (all)	32	IR = 0.0125 [0.0087; 0.0180]	87.2%, $P < 0.0001$	0.6414
Late mortality (CT screened)	9	IR = 0.0071 [0.0043; 0.0116]	41.5%, SGD-P = 0.0090	0.2217
Late mortality (no CT screen)	22	IR = 0.0165 [0.0111; 0.0244]	86.8%, SGD-P = 0.0090	0.5062
CPB time-in minutes (all)	53	Mean = 141.3631 [131.7079; 151.0183]	99.6%, $P = 0$	1260.4527
Cross-clamp time-in minutes (all)	49	Mean = 94.2181 [86.7500; 101.6862]	99.6%, $P = 0$	699.8058
ICU stay- in days (all)	37	Mean = 1.8384 [1.6098; 2.0669]	99.5%, $P = 0$	0.4077
Hospital stay- in days (all)	44	Mean = 7.9151 [6.9763; 8.8539]	99.7%, $P = 0$	9.6798
Total procedure length- in minutes (all)	22	Mean = 238.9358 [222.2738; 255.5978]	99.0%, $P = 0$	1517.1067

CPB, cardiopulmonary bypass; CT computed tomography; ICU, intensive care unit; IR, incidence rate; MI, myocardial infarction; MIMVS, minimally invasive mitral valve surgery; SGD-P, *P*-value for subgroup difference; TIA, transient ischemic attack.

centers utilize alternative methods of cannulation including central aortic cannulation and axillary cannulation. Although alternative cannulation sites were not studied in our paper, it would be interesting to look at this subgroup of the MIMVS population in the future. Others advocate the use of carbon dioxide insufflation of the surgical field to help protect the cerebral circulation from another source of emboli [13]. The known increased solubility of CO_2 compared to room air in blood is sought out to prevent air embolus in addition to other de-airing maneuvers. In ours study the use of CO_2 did not affect the PER for stroke, but the sample size for this comparison was limited and a Type 2 error cannot be excluded.

In the paper by Gammie, stroke incidence was 1.16% in the conventional median sternotomy cohort and 1.87% in the MIMVS cohort ($P = 0.0001$) [3]. Of note, this analysis included all centers participating in the STS Database with the average volume of MIMVS per center at three cases per year.

Our study involved 13,731 patients which is slightly less than half the 28,143 patients reported on by Gammie. In our analysis, the PER for post-operative stroke was 2.0%, 2.2 % in the Non-CT group, and 1.5% in the CT group ($P = 0.03$). Our meta-analysis was restricted to papers with a sample size of at least 10 cases and most studies had many more than this, suggesting that our population comprised surgical groups which perform MIMVS more frequently than the STS average.

The significant difference seen between the CT group and the Non-CT group in this meta-analysis is encouraging. While it is difficult to compare the two cohorts, the PER in the CT group for post-operative stroke was 1.5% in comparison to the stroke rate seen in the conventional median sternotomy group of 1.16% reported by Gammie.

Along with the reduction of post-operative stroke obtained by pre-operative imaging of the aorta and its branches, we have also found a decreased risk of new need for hemodialysis post-operatively in the CT group. Since the onset of renal failure in the immediate post-operative period can be related to an embolic event, this finding is supportive that pre-operative CT screening would also reduce post-operative strokes given that they share a similar mechanism.

Finally, the use of pre-operative CT scans led to a trend towards decreased operative mortality. The STS study found no difference in operative mortality between the conventional and less-invasive groups (OR 1.13, CI 0.84–1.51, $P = 0.419$) and an overall operative mortality of 1.75%. However, results from our meta-analysis showed the PER for operative mortality was 1.4% with a trend towards better outcomes in the CT group (0.8% vs. 1.6%, $P = 0.052$).

While these results all support the use of pre-operative CT scanning, it must be acknowledged that this strategy has the potential risks of contrast induced nephropathy, radiation exposure, and is associated with increased cost. Non-contrasted CT scanning can be considered as an alternative option for visualization of atherosclerotic disease in patients with impaired renal function.

Finally, it has to be reminded that a valuable alternative to retrograde perfusion is to cannulate the ascending aorta making a larger incision and using a retractor, which still allows to perform a minimally invasive approach, potentially reducing the risk of stroke.

4.1. Limitations

A limitation which is inherent to this study stems from the use of retrospective cohort studies in our pooled analyses. This comes along with the limitation of reporting bias for each of the studies included. Also, different in expertise between the different studies cannot be accounted for using a meta-analytic approach. Nevertheless, the use of the Newcastle-Ottawa Quality Assessment Scale to guarantee that studies included were of high quality does improve the reliability of these results. The study is also strengthened by strict adherence with PRISMA and MOOSE guidelines. We also acknowledge that patients included in this study were relatively young (mean age: 59.1 years, range: from

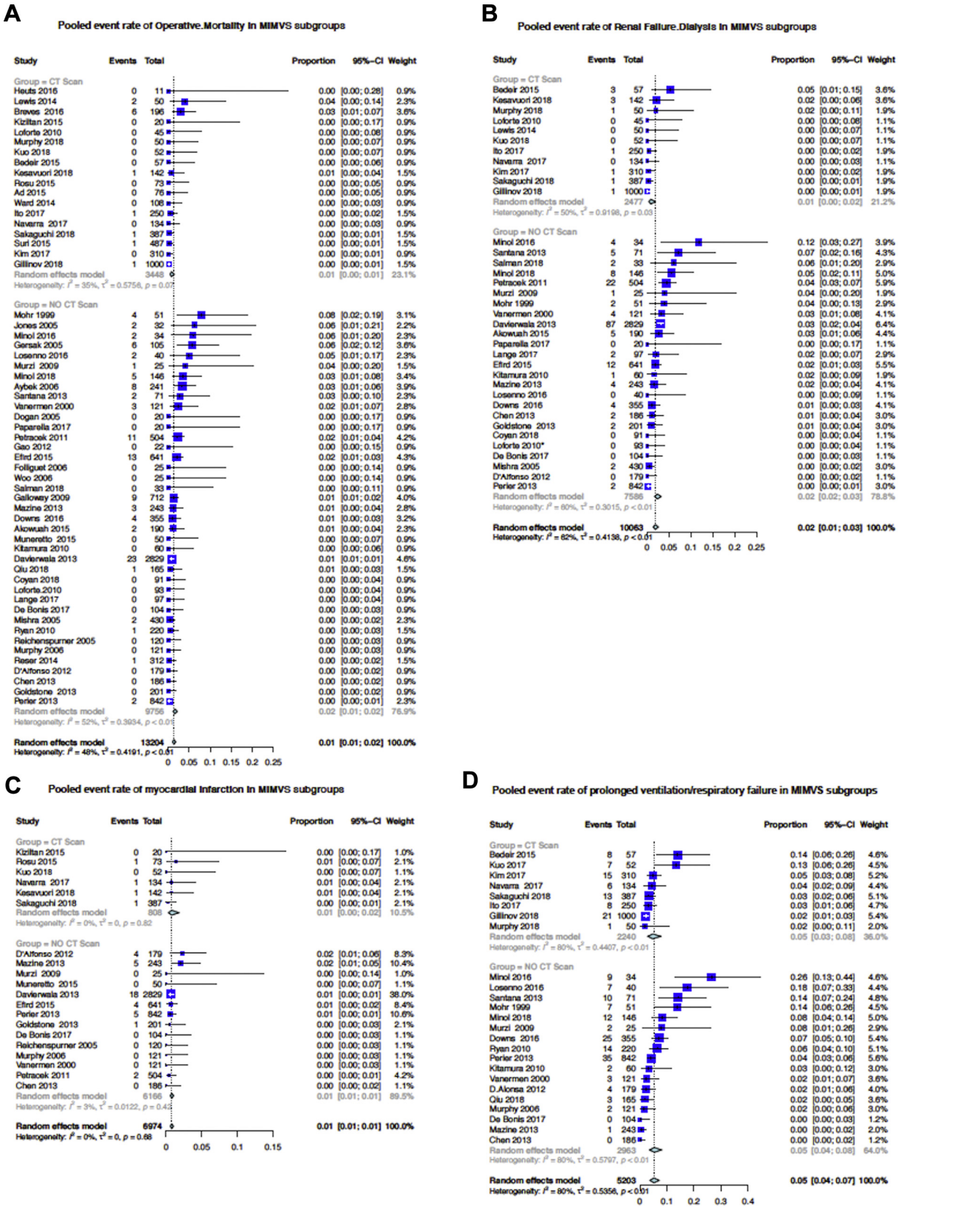

Fig. 2. Pooled event rate of operative mortality (A), renal failure/dialysis (B), myocardial infarction (C), and prolonged ventilation/respiratory failure (D) in MIMVS subgroups. 95% CI, 95% confidence interval, MIMVS, minimally invasive mitral valve surgery.

40.0 to 82.5 years) and with a relatively preserved EF, hence at lower risk for mitral surgery and for stroke; results might therefore not apply to higher-risk cohorts. Also, despite being statistically significant, the absolute difference in terms of postoperative stroke between the CT and Non-CT groups was 0.7%. Nevertheless, this analysis represents the most solid evidence in regards to our study question since there are currently no prospective randomized investigational trials on it in publication.

5. Conclusion

Our results suggest that systematic pre-operative CT screening is associated with significantly reduced risk of post-operative stroke in MIMVS with retrograde arterial cannulation.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2018.12.025.

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