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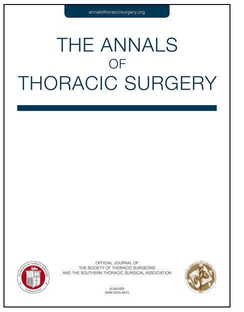

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Running head: Epiaortic ultrasound in CABG

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Abstract

Background: Epiaortic ultrasound (EAU) is a valid imaging method to detect atherosclerotic changes of the ascending aorta and to guide surgical strategies for prevention of cerebral embolism in patients undergoing isolated coronary artery bypass grafting (CABG). However, its use is not widespread.

Methods: The impact of EAU on the outcome after isolated CABG has been investigated in patients from the multicenter E-CABG registry. A systematic review and meta-analysis of the literature was performed to substantiate the findings of this observational study.

Results: Out of 7241 patients from the E-CABG registry, EAU was performed intraoperatively in 673 patients (9.3%). In the overall series, the rates of stroke without and with aortic manipulation were 0.3% and 1.3% (p=0.003). In 660 propensity score matched pairs, EAU was associated with significantly lower risk of stroke (0.6% vs. 2.6%, p=0.007). Literature search yielded five studies fulfilling the inclusion criteria. These studies along with the present one included 11496 patients, of whom 3026 (25.7%) underwent intraoperative EAU and their rate of postoperative stroke was significantly lower than in patients not investigated with EAU (pooled rate, 0.6% vs. 1.9%; RR 0.40, 95%CI 0.24-0.66, I^2 0%). Based on these pooled rates, the number needed to treat to prevent one stroke is 76.9.

Conclusions: Avoiding aortic manipulation is associated with the lowest risk of stroke in patients undergoing CABG. When manipulation of the ascending aorta is planned, EAU is effective in guiding the surgical strategy to reduce the risk for embolic stroke in these patients.

Key words: Stroke; Epiaortic ultrasound; Coronary artery bypass grafting; Cardiac Surgery.

Clinical Trial Registration: Clinicaltrials.gov - NCT02319083

PROSPERO Registration: CRD42019125075

Stroke is an infrequent major complication after coronary artery bypass grafting (CABG) [1], which is associated with significant impairment and increased risk of early death [2]. The pathogenesis of perioperative stroke in patients undergoing cardiac surgery is multifaceted. Manipulation of the ascending aorta is recognized as one the main sources of cerebral embolism [3,4]. Since macroscopical atherosclerotic changes of the ascending aorta can be detected in a significant number of patients, ultrasonographic screening of the ascending aorta is indicated in patients undergoing CABG [5]. Epiaortic ultrasound (EAU) is an accurate imaging method, while aortic palpation and transesophageal ultrasonography have limited sensitivity to detect atherosclerotic changes of the ascending aorta [5]. Once atheromas are identified at EAU, maneuvers to cannulate and clamp the aorta in areas free of atherosclerotic changes or leaving the ascending aorta untouched may prevent dislodgement of aortic atheroma [6-8]. Despite these evidences, the use of EAU in patients undergoing CABG is not widespread and recent guidelines on myocardial revascularization did not mention EAU as a measure to reduce perioperative stroke [9]. The efficacy of EAU to prevent stroke after CABG has been investigated in this multicenter prospective registry. A systematic review of the literature and meta-analysis were performed to substantiate the findings of this observational study.

Patients and Methods

E-CABG registry (Clinical Trials Identifier NCT02319083) is a prospective, multicenter study that enrolled patients undergoing isolated CABG at 16 cardiac surgery centers from Finland, France, Italy, Germany, Sweden and United Kingdom. The study protocol and definition criteria have been previously published [10]. The study was approved by the Institutional Review Board of the participating centers.

For the purpose of this analysis, patients who underwent concomitant carotid revascularization and those who had out-of-hospital cardiac arrest before the index hospitalization were excluded from this analysis. Overall, 7241 patients fulfilled the inclusion criteria and were the subjects of this analysis.

Patient treatment

Patients were treated according to institutional practice. Aortic anastomosis devices were not used in these patients. EAU was performed to identify any atherosclerotic lesions of the ascending aorta in three institutions. The site and severity of extent of atherosclerosis in the ascending aorta as well as whether the findings at EAU led to changes in the surgical strategy were not recorded. In patients with diseased ascending aorta, the decision of whether to avoid aortic manipulation and modified the site of cannulation and clamping was based on the location and characteristics of the atherosclerotic lesion. Side-bite clamping was believed safe in case of flat atherosclerotic lesions of the posterior wall of the ascending aorta or at the level of the origin of the brachiocephalic trunk, thus far enough from the site of side-bite aortic clamping. Exophytic atherosclerotic lesions were considered an absolute contraindication to aortic manipulation. Aortic manipulation was considered as any maneuver for cannulation and/or clamping of the ascending aorta.For the purpose of this analysis, patient population was stratified according to the policy of epiaortic ultrasound and manipulation of the ascending aorta as follows: EAU+Ao-, epiaortic ultrasound and no aortic manipulation EAU-Ao-, no epiaortic ultrasound and no aortic manipulation; EAU+Ao+, epiaortic ultrasound and aortic manipulation; EAU-Ao+, no epiaortic ultrasound and aortic manipulation.

Outcomes

The main outcome of this study was stroke occurring during the index hospitalization. Secondary outcomes were all-cause hospital and 1-year mortality. Stroke was defined as any focal or global neurological syndrome occurring during the in-hospital stay caused by ischemia and/or hemorrhage not resolving within 24 h. The diagnosis and nature of stroke was made on the basis of findings at computed tomography and/or magnetic resonance imaging of the brain and confirmed by a neurologist. When neurological signs and symptoms disappear before discharge, stroke was defined temporary, otherwise it was defined as permanent. Stroke was defined fatal when was the direct or indirect cause of hospital mortality.

Systematic Review and Meta-analysis

The protocol of this study was registered in the PROSPERO registry (CRD42019125075). Population, intervention, comparator, outcomes, and study design (PICOS) of this analysis are summarized in Supplementary table 1. The population of interest consisted of patients who underwent isolated coronary artery bypass grafting. The intervention of interest was the use of EAU to detected atherosclerosis involving the ascending aorta to guide a strategy for prevention of cerebral embolism from the ascending aorta. Studies comparing the outcomes of patients who underwent EAU and those who were not evaluated with this imaging method were considered for this study. The primary outcome was stroke occurring during the index hospitalization. Stroke was defined according to the definitions used in the included studies. Secondary outcome hospital/30-day mortality after the index cardiac surgery procedure.

Electronic databases of PubMed, Scopus and Google Scholar were searched on February 10, 2019 without date restriction for articles published in English language. Studies including less than 100 patients were excluded from this analysis. Search criteria included different combinations of the following terms: "epiaortic ultrasound", "epiaortic scan", "epiaortic ultrasonography", “aortic ultrasound”, "aortic ultrasonography" AND/OR “coronary” AND/OR “cardiac surgery”. Reference lists of pertinent articles were also reviewed. Reference lists of the retrieved articles were searched for articles of interest as well. Abstracts and full-text articles were independently reviewed, and the data collected by two senior cardiac surgeons (F.B., G.M.). Discrepancies were resolved through consensus. Authors of the retrieved studies were not contacted for missing or additional data. The Quality Assessment Tool for Case Series Studies of the National Heart, Lung and Blood Institute (https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools; access February 10, 2019) was used to assess the methodological quality of the included studies. This meta-analysis complies with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement guidelines [11].

Statistical Analysis

Statistical analyses were performed using SPSS statistical software v. 24.0 (IBM Corporation, New York, USA), Stata v. 14.2 (SAS Institute Inc., Cary, NC, USA), Open Meta-analyst software [12] and Review

Manager software v. 5.3.3 (RevMan, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). Covariates and outcomes were reported as counts and percentages, and as mean ± standard deviation. Mann-Whitney, Chi-square and Fisher exact tests were used to compare baseline and operative covariates. The risk-adjusted rate of stroke was calculated by dividing, for each study subgroups, the observed number of strokes by the expected number of strokes, and by multiplying this ratio by the average event rate of the entire series. The expected numbers of events were estimated using logistic regression including the following baseline and operative covariates: age, gender, anemia, platelets count, estimated glomerular filtration rate, dialysis, use of potent antiplatelet drugs until surgery, prior transient ischemic attack or stroke, extracardiac arteriopathy, diabetes, pulmonary disease, atrial fibrillation, left ventricular ejection fraction ≤50%, recent myocardial infarction, critical preoperative state, prior percutaneous coronary intervention, prior cardiac surgery and emergency procedure, preoperative insertion of intra-aortic balloon pump and amount of red blood transfusion during and after surgery. A one-to-one propensity score matching was performed to adjust the study cohorts for baseline and operative covariates using the nearest neighbour method and a caliper of 0.2 of the standard deviation of the logit of the propensity score (logit=0.81, caliper=0.16). After matching, we used the t-test for paired samples to evaluate the balance between the matched cohorts for continuous variables, the McNemar test for dichotomous variables, and the analysis of the standardized difference. A standardized difference ≤0.10 was considered as an acceptable balance between the study cohorts. The McNemar test were employed to evaluate any difference in the early outcomes of propensity score matched pairs. Survival was estimated by the Kaplan-Meier method and study cohorts were compared with the log-rank test. The outcomes of studies evaluating patients who were evaluated with EAU and those who were not, were pooled with the random-effects method leading to computations of risk ratios (RR) with 95% confidence intervals (CI). The outcomes of retrieved studies are reported as pooled proportions with 95%CI. I^2 statistic was used to estimate the heterogeneity of the studies, with I^2 > 40% as a threshold for significant heterogeneity. Publication bias was assessed by inspecting funnel plot asymmetry. Leave-one-out analysis was performed to estimate the consistency of the findings through the included studies. The number needed to treat to prevent one stroke was estimated based on the crude rates of this observational study and on the pooled rates. A p<0.05 was set for statistical significance.

Results

Overall series

This study included 7241 patients from the E-CABG registry. EAU was employed to detected atherosclerosis of the ascending aorta in 673 patients (9.3%) operated at three out of sixteen centers (99.8%, 64.4% and 0.6% of patients, respectively). Atherosclerosis of any degree involving the ascending aorta was detected in 9.7% of EAU patients (65 out of 673 patients) (Table 1). Advanced age (p<0.0001), diabetes (p=0.021), atrial fibrillation (p=0.001), recent myocardial infarction (p=0.049) and prior transient ischemic attack and/or stroke (p=0.008) (Suppl. Table 1) were independent predictors of diseased ascending aorta at EAU. Among patients who underwent EAU, 14 (2.1%) underwent surgery avoiding manipulation of the aorta and 12 of them had diseased ascending aorta.

The proportion of patients who underwent surgery using different strategies of EAU and aortic manipulation were as follows: EAU+Ao-, 14 patients (0.2%); EAU+Ao+, 659 patients (9.1%); EAU-Ao-, 1090 patients (15.0%); EAU-Ao+, 5478 patients (75.6%). The crude rates of stroke in these groups were as follows: EAU+Ao-, 0% (adjusted rate, 0%); EAU+Ao+, 0.6% (adjusted rate, 0.6%); EAU-Ao-, 0.3% (adjusted rate, 0.3%); EAU-Ao+, 1.4% (adjusted rate 1.4%) (p=0.009, Fig. 1). The crude rates of hospital mortality in these groups were as follows: EAU+Ao-, 0% (adjusted rate, 0%); EAU+Ao+, 1.2% (adjusted rate, 1.3%); EAU-Ao-, 1.4% (adjusted rate, 1.5%); EAU-Ao+, 1.8% (adjusted rate 1.8%) (p=0.498, Fig. 1).

The crude rates of stroke in the no EAU group and in the EAU group were 1.2% and 0.6% (p=0.247), hospital mortality 1.8% and 1.2% (p=0.282), and 1-year mortality 3.5% and 2.9% (p=0.233), respectively (Table 2).

The crude rates of stroke in patients who underwent CABG without and with manipulation of the ascending aorta were 0.3% and 1.3% (p=0.003), hospital mortality 1.4% and 1.8% (p=0.342), and 1-year mortality 3.2% and 3.5% (p=0.364), respectively.

Propensity score matching analysis

Propensity score matching results in 660 pairs of patients with balanced covariates as confirmed by the post-matching standardized differences (Table 1). Among these matched pairs, the rates of stroke in the no EAU group and in the EAU group were 2.6% and 0.6% (p=0.0.007), hospital mortality 3.5% and 1.1% (p=0.006), and 1-year mortality 5.4% and 2.8% (p=0.008), respectively (Table 2). One-year mortality was significantly higher in patients who suffered stroke postoperatively (38.5% vs. 3.5%, Log-rank test, p<0.0001). Based on the adjusted rates of stroke, the number needed to treat to prevent one stroke was 53.0.

Systematic Review and Meta-analysis

Two-hundred and twenty-six records were identified (Suppl. table 3). Five studies fulfilled the inclusion criteria [13-17] and, including the present one, form the basis of this meta-analysis (Suppl. Fig. 1). The main characteristics of the included studies are summarized in Table 3 and Supplementary table 4. None of these studies reported on risk estimates adjusted for baseline and/or operative covariates. The study by Nakamura et al. [16] included in the EAU group seven patients who underwent cerebrovascular revascularization before CABG. In the study by Joo et al. [17] included control patients in whom the status of the ascending aorta was estimated using transesophageal ultrasound.

Overall, these studies included 11496 patients, of whom 3026 (25.7%) underwent intraoperative EAU and their rate of postoperative stroke was significantly lower than in patients who were not investigated with EAU (pooled rate, 0.6% vs. 1.9%; RR 0.40, 95%CI 0.24-0.66, I^2 0%, no significant publication bias, Suppl. fig. 2). Leave-one-out analysis confirmed the consistency of these findings through the studies (Suppl. fig. 3).

After excluding the studies by Nakamura et al. [16] and Joo et al. [17], EAU was still associated with significantly lower risk of stroke (RR 0.37, 95%CI 0.18-0.77, I^2 15%). Four studies evaluated the impact of EAU on hospital mortality, which was similar to that of patients not investigated with EAU (1.6% vs. 1.8%, RR 0.80, 95%CI 0.53-1.21, I^2 0%, no significant publication bias) (Suppl. figs. 4-5).

Based on these pooled rates, the number of patients needed to treat to prevent one stroke was 77.

Comment

The main findings of the present study can be summarized as follows: 1) avoidance of aortic manipulation is associated with the lowest risk of stroke in patients undergoing CABG; 2) EAU was not performed in most of European centres participating to this prospective registry; 3) EAU-guided surgical strategy may reduce the risk of stroke in patients undergoing CABG.

This study confirmed that leaving the ascending aorta untouched is the treatment of choice to reduce the risk of stroke after CABG as recently shown by a large network meta-analysis [7]. These findings prove that the ascending aorta is the main source of debris embolism secondary to aortic cannulation, clamping and suture of proximal anastomoses. Based on these evidences, myocardial revascularization using the internal mammary grafts without aortic manipulation seems to be a straightforward policy for stroke prevention, but this technique has been adopted in only 16% of our patients not evaluated by EAU. This surgical strategy implies the adoption of off-pump surgery with intrathoracic artery-based revascularization in all patients, though not all surgeons are familiar with this technique. Here lies the importance of ultrasound screening of the ascending aorta, which may effectively guide the surgeon to modify the surgical plan only in presence of atherosclerosis changes [7]. Rosenberg et al. [18] reported on changes in the surgical strategy after EAU in 4.6%. These changes consisted in circulatory arrest, no aortic cross clamp, ventricular fibrillatory arrest and off -pump surgery. EAU screening has been shown to effectively guide surgical strategy also in patients undergoing other major cardiac surgery procedures as reported by Rosenberg et al. [18]. Hangler et al. [19] reported changes of the surgical strategy in 26% of patients undergoing CABG (alternate cannulation and/or clamping site, single clamping, beating heart surgery and extra-anatomic bypass grafting). Shimokawa et al. [20] modified the surgical strategy in 36% of patients with favourable results. In particular, EAU led to recognize the importance of off-pump surgery in patients with atherosclerotic ascending aorta [21,22] and, more recently, the benefit of avoiding aortic clamping in these patients [23]. However, most of studies reporting on the potential benefits of using EAU failed to compare the results of EAU-driven surgical strategy with a control, non-EAU screened population. This systematic review showed that only a few comparative studies exist on this topic and these were not adjusted for baseline differences. Furthermore, the importance of off-pump surgery without aortic manipulation in patients with severe atheroma of the ascending aorta has been only more recently recognized, whilst this technique was not adopted in early studies.

The routine use of EAU is a potential strategy which might reduce the incident of post-operative strokes if surgeons focused on stroke prevention using different techniques to avoid aortic manipulation when indicated.

This study does not address the value of clamp-less proximal anastomosis devices in preventing stroke. However, the present results suggest that an EAU-guided strategy may achieve excellent results without incremental costs related with the use of such devices. In a very large study from the Japan Adult Cardiovascular Surgery Database, Saito et al. [24] reported a similar stroke rate of 1.4% after off-pump surgery both with an anastomosis device and side-bite clamping. A stroke rate of 1.2% was reported in large series using the Heartstring device in patients screened with EAU [25]. Concerns exist regarding the increased number of embolic debris with the use clamp-less anastomosis devices compared with side-bite clamping in patients undergoing off-pump surgery [26]. In patients without or low-grade atherosclerosis of the ascending aorta, Halkos et al. [26] observed that the number of high-intensity transient signals in the middle cerebral arteries was significantly larger with the use of clamp-less anastomosis devices than with site-bite clamping. The effect of using clamp-less anastomosis devices on cerebral embolic events was directly related to the number of devices used [26].

The present study is not exempted from several limitations, although is the largest study evaluating the impact of EAU in patients undergoing CABG. First, data on the severity and sites of atherosclerosis in the ascending aorta were not recorded in this registry and cannot be retrieved retrospectively. Second, we do not have specific data on the modification of surgical strategy in patients with diseased ascending aorta. Third, EAU were used mainly in two centers by surgeons with experience in off-pump surgery. This may be a source of bias, but these results should be view in the context of a rather low rate of stroke among patients who underwent CABG with aortic manipulation. Fourth, aortic anastomosis devices were not used in these patients and this prevents the analysis of the potential impact of these devices in patients screened by EAU for atherosclerosis of the ascending aorta. Fifth, in this multicenter study, only two Institutions widely adopted an EAU-based surgical strategy and this may introduce a further bias in to this analysis. We were aware of this possible bias which cannot be overcome with mixed-effect analysis. This is the reason why we performed a concomitant meta-analysis, which confirmed that an EAU-based surgical strategy had a preventative effect on postoperative stroke which was of the same magnitude of that demonstrated in previous comparative studies. Finally, despite EAU-based surgical strategy was adopted only in less than 10% of cases, post-hoc sample size estimation based on matched-control study design showed that the sample size of propensity score matched pairs was enough large as we would have needed 172 cases per study group in order to verify the significance of stroke rate difference herein observed (2.6% vs. 0.6%, power 0.800, alpha 0.050).

In conclusion, these results suggest that avoiding aortic manipulation is associated with the lowest risk of stroke in patients undergoing CABG. When manipulation of the ascending aorta is planned, EAU is effective in guiding the surgical strategy to reduce the risk for embolic stroke in these patients.

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Table 1. Baseline characteristics and operative data of patients undergoing coronary surgery in the participating centers.

	Overall series			*Propensity score matched pairs*		
Covariates	*No EAU no. 6568*	*EAU no. 673*	*Standardized difference*	*No EAU no. 660*	*EAU no. 660*	*Standardized difference*
Baseline risk factors						
Age (years)	67.1±9.2	68.2±9.2	0.116	68.3±9.4	68.2±9.2	0.017
Female	893 (16.2)	108 (16.4)	0.004	101 (15.3)	109 (16.5)	0.033
Body mass index (kg/m^2)	27.6±4.2	27.6±4.2	0.021	27.2±4.2	27.6±4.1	0.093
eGFR (mL/min/1.73 m^2)	82±25	83±26	0.051	83±27	83±26	0.024
Hemoglobin (g/L)	137±16	133±18	0.244	133±18	133±18	0.015
Dialysis	57 (1.0)	7 (1.1)	0.003	10 (1.5)	6 (0.9)	0.055
Diabetes	1788 (32.5)	144 (21.9)	0.242	119 (18.0)	146 (22.1)	0.102
Recent myocardial infarction	1783 (32.4)	229 (34.7)	0.049	226 (34.2)	227 (34.4)	0.003
Prior stroke/transient ischemic attack	300 (5.5)	30 (4.6)	0.041	32 (4.8)	31 (4.7)	0.007
Atrial fibrillation	427 (7.8)	54 (8.2)	0.016	52 (7.9)	54 (8.2)	0.011
Pulmonary disease	564 (10.3)	62 (9.4)	0.028	66 (10.0)	63 (9.5)	0.015
Extracardiac arteriopathy	1232 (22.4)	108 (16.4)	0.152	101 (15.3)	108 (16.4)	0.029
Left ventricular ejection fraction ≤50%	1584 (28.8)	142 (21.6)	0.166	156 (23.6)	141 (21.4)	0.054
Prior PCI	1124 (20.4)	91 (13.8)	0.176	101 (15.3)	93 (14.1)	0.035
Prior cardiac surgery	246 (4.5)	23 (3.5)	0.050	6 (0.9)	4 (0.6)	0.035
Critical preoperative state	281 (5.1)	98 (14.9)	0.330	85 (12.9)	92 (13.9)	0.003
Preop. IABP	188 (3.4)	54 (8.2)	0.205	43 (6.5)	53 (8.0)	0.058
Emergency procedure	246 (4.5)	23 (3.5)	0.050	22 (3.3)	23 (3.5)	0.008
Diseased ascending aorta	206 (3.1)	65 (9.7)	0.269	21 (3.2)	59 (8.9)	0.243
EuroSCORE II (%)	2.6±3.8	3.6±4.9	0.124	3.6±6.7	3.5±4.4	0.017
Operative data						
Off-pump surgery	214 (3.9)	179 (27.2)	0.678	30 (4.5)	184 (27.9)	0.667
Ascending aorta left untouched	1090 (16.6)	14 (2.1)	0.515	14 (2.1)	8 (1.2)	0.071
No. of distal anastomoses	2.7±0.8	3.6±0.9	1.000	2.7±0.8	3.6±0.9	1.000
BIMA grafting	1868 (34.0)	275 (41.7)	0.161	213 (32.3)	274 (41.5)	0.192
RBC units transfused	1.2±2.4	1.5±2.0	0.124	1.6±3.0	1.4±1.8	0.052

Continuous variables are reported as mean and standard deviation. Categorical variables are reported as counts and percentages (in parentheses). EAU, epiaortic ultrasound; eGFR: estimated glomerular filtration rate according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation; PCI: percutaneous coronary intervention; IABP, intra-aortic balloon pump; BIMA: bilateral internal mammary artery, RBC, red blood cell.

Table 2. Outcomes in the overall series and in propensity score matched pairs.

	Overall series			*Propensity score matched pairs*		
Outcomes	*No EAU no. 6568*	*EAU no. 673*	*p-value*	*No EAU no. 660*	*EAU no. 660*	*p-value*
Stroke	78 (1.2)	4 (0.6)	0.247	17 (2.6)	4 (0.6)	0.007
Permanent stroke	55 (0.8)	3 (0.4)	0.366	13 (2.0)	3 (0.5)	0.021
Fatal stroke	12 (0.2)	1 (0.1)	1.000	5 (0.8)	1 (0.2)	0.219
Hospital mortality	115 (1.8)	8 (1.2)	0.282	23 (3.5)	7 (1.1)	0.006
1-year mortality	3.5%	2.9%	0.233	5.4%	2.8%	0.008

Binary outcomes are reported as counts and percentages (in parentheses) and survival as percentages. EAU, epiaortic ultrasound.

Table 3. Characteristics of studies included in the meta-analysis.

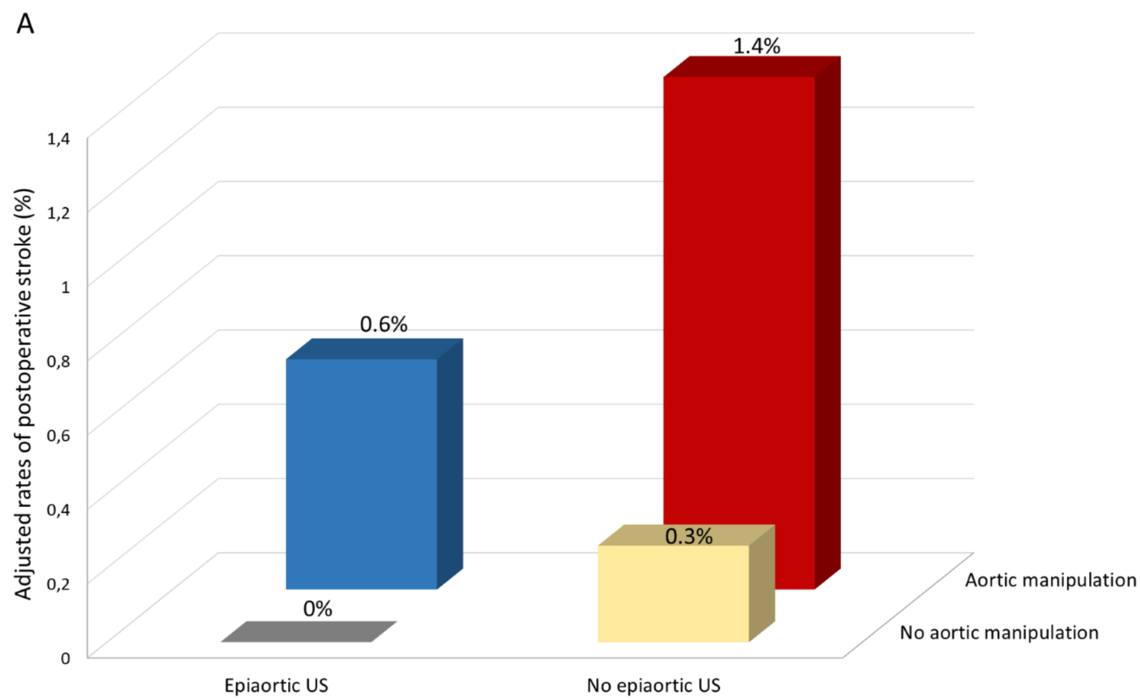
Author	Year	Country	Design	Multicenter study	EAU No. of patients	EAU Stroke (%)	No EAU No. of patients	No EAU Stroke (%)
Duda	1995	USA	R	No	195	0.0	164	3.1
Zingone	2006	Italy	R	No	419	1.7	268	3.4
Biancari	2007	Finland	R	No	228	0.4	204	3.9
Nakamura[a]	2008	Japan	RCT	No	238	0.4	247	2.8
Joo[b]	2013	Korea	R	No	1 273	0.6	1 019	1.3
Present study	2019	International	P	Yes	673	0.6	6 568	1.2

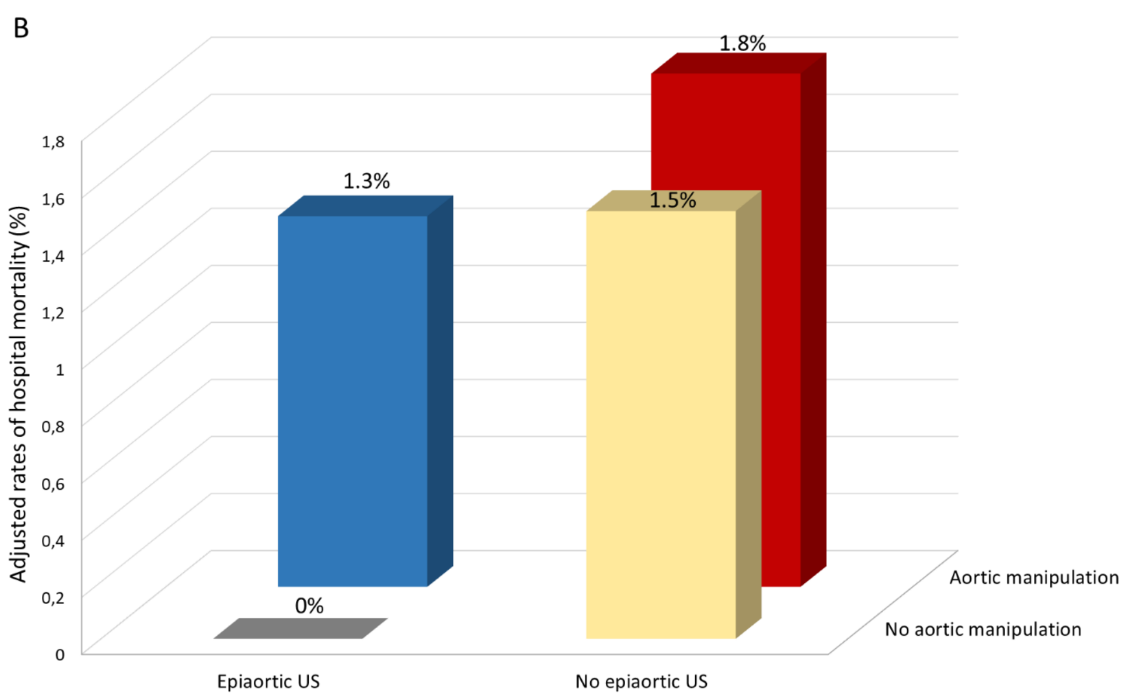
EAU, epiaortic ultrasound; R, retrospective; P, prospective; RCT, randomized controlled trial.
a, Intervention group: 7 patients of the intervention group underwent concomitant cerebrovascular revascularization;
b, Control group underwent transesophageal ultrasound for evaluation of the ascending aorta.

Figure legends

Figure 1. Adjusted rates of stroke (A) and hospital mortality (B) according to the use of epiaortic ultrasound and aortic manipulation in patients undergoing isolated coronary artery bypass grafting.

Figure 2. Forest plot of the risk of stroke in patients who underwent isolated coronary artery bypass grafting with and without intraoperative epiaortic ultrasound (EAU).


A
Adjusted rates of postoperative stroke (%)
1,4
1,2
1
0,8
0,6
0,4
0,2
0
1.4%
0.6%
0.3%
0%
Aortic manipulation
No aortic manipulation
Epiaortic US
No epiaortic US


B
Adjusted rates of hospital mortality (%)
1,8
1,6
1,4
1,2
1
0,8
0,6
0,4
0,2
0
1.8%
1.3%
1.5%
0%
Aortic manipulation
No aortic manipulation
Epiaortic US
No epiaortic US

	EAU		No EAU			Risk Ratio	
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**Year**
Duda 1995	0	195	6	164	3.1%	0.06 [0.00, 1.14]	1995
Zingone 2006	7	419	9	268	26.7%	0.50 [0.19, 1.32]	2006
Biancari 2007	1	228	8	204	5.9%	0.11 [0.01, 0.89]	2007
Nakamura 2008	1	238	7	247	5.8%	0.15 [0.02, 1.20]	2008
Joo 2013	8	1273	13	1019	33.1%	0.49 [0.20, 1.18]	2013
Present study 2019	4	673	78	6568	25.3%	0.50 [0.18, 1.36]	2019
Total (95% CI)		**3026**		**8470**	**100.0%**	**0.40 [0.24, 0.66]**	
Total events	21		121				

Heterogeneity: Tau² = 0.00; Chi² = 4.65, df = 5 (P = 0.46); I² = 0%
Test for overall effect: Z = 3.58 (P = 0.0003)

Risk Ratio
M-H, Random, 95% CI