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# Neurological outcomes in minimally invasive mitral valve surgery: risk factors analysis from the Mini-Mitral International Registry

Giovanni Domenico Cresce <sup>a,\*</sup>, Paolo Berretta<sup>b</sup>, Antonio Fiore<sup>c</sup>, Manuel Wilbring <sup>d</sup>, Marc Gerdisch<sup>e</sup>, Antonios Pitsis <sup>f</sup>, Mauro Rinaldi<sup>g</sup>, Nikolaos Bonaros <sup>h</sup>, Jorg Kempfert<sup>i</sup>, Tristan Yan <sup>j</sup>, Frank Van Praet<sup>k</sup>, Hoang Dinh Nguyen<sup>l</sup>, Carlo Savini<sup>m</sup>, Joseph Lamelas<sup>n</sup>, Tom C. Nguyen<sup>o</sup>, Pierluigi Stefano<sup>p</sup>, Gloria Färber<sup>q</sup>, Loris Salvador<sup>a</sup> and Marco Di Eusanio <sup>b</sup>

<sup>a</sup> Division of Cardiac Surgery, San Bortolo Hospital, Vicenza, Italy

<sup>b</sup> Cardiac Surgery Unit, Lancisi Cardiovascular Center, Polytechnic University of Marche, Ancona, Italy

<sup>c</sup> Department of Cardiac Surgery, Hôpitaux Universitaires Henri Mondor, Assistance Publique-Hôpitaux de Paris, Creteil, France

<sup>d</sup> Center for Minimally Invasive Cardiac Surgery, University Heart Center Dresden, Dresden, Germany

<sup>e</sup> Franciscan Health Indianapolis, Indianapolis, IN, USA

<sup>f</sup> Cardiac Surgery Department, European Interbalkan Medical Center, Thessaloniki, Greece

<sup>g</sup> Cardiac Surgery Unit, University of Turin, Turin, Italy

<sup>h</sup> Department of Cardiac Surgery, Medical University of Innsbruck, Innsbruck, Austria

<sup>i</sup> Department of Cardiothoracic and Vascular Surgery, German Heart Center Berlin, Germany

<sup>j</sup> Department of Cardiothoracic Surgery, The Royal Prince Alfred Hospital, Sydney, Australia

<sup>k</sup> Cardiac Surgery Department, Hartcentrum OLV Aalst, Aalst, Belgium

<sup>l</sup> University of Medicine and Pharmacy, Ho Chi Minh City, Vietnam

<sup>m</sup> Cardiac Surgery Department, Sant'Orsola Malpighi Hospital, University of Bologna, Bologna, Italy

<sup>n</sup> Division of Cardiothoracic Surgery, University of Miami, Miami, FL, USA

<sup>o</sup> Department of Cardiothoracic and Vascular Surgery, University of Texas Health Science Center Houston, McGovern Medical School, Houston, TX, USA

<sup>p</sup> Cardiac Surgery Unit, Careggi University Hospital, Firenze, Firenze, Italy

<sup>q</sup> Department of Cardiothoracic Surgery, Jena University Hospital, Jena, Germany

\* Corresponding author. Division of Cardiac Surgery, San Bortolo Hospital, Viale Rodolfi 37, 36100 Vicenza, Italy. Tel: +39-3476473521; fax: +39-0444752768; e-mail: [gd.cresce@yahoo.it](mailto:gd.cresce@yahoo.it) (G.D. Cresce).

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## Neurological outcomes in minimally invasive mitral valve surgery: risk factors analysis from the Mini Mitral International Registry (Mini-Mitral-IR)

### Summary

A total of 7343 patients undergoing minimally invasive mitral valve surgery from 17 Heart Valve Centers were enrolled. Stroke rate was 1.3%. Age, urgent/emergent status and mitral valve replacement emerged as independent predictors of stroke. Preoperative CT-scan affected surgical cannulation strategy and did not lead to improved neurological outcomes.

Multicentric international registry

7343 Mini-MVS

Stroke rate 1.3%

Predictors of stroke: Age, Urgent/emergent status, mitral valve replacement

Legend: Mini-MVS = minimally invasive mitral valve surgery

## Abstract

**OBJECTIVES:** The aim of this study was to examine the incidence and predictors of stroke after minimally invasive mitral valve surgery (mini-MVS) and to assess the role of preoperative CT scan on surgical management and neurological outcomes in the large cohort of Mini-Mitral International Registry.

**METHODS:** Clinical, operative and in-hospital outcomes in patients undergoing mini-MVS between 2015 and 2021 were collected. Univariable and multivariable analyses were used to identify predictors of stroke. Finally, the impact of preoperative CT scan on surgical management and neurological outcomes was assessed.

**RESULTS:** Data from 7343 patients were collected. The incidence of stroke was 1.3% ( $n = 95/7343$ ). Stroke was associated with higher in-hospital mortality (11.6% vs 1.5%,  $P < 0.001$ ) and longer intubation time, ICU and hospital stay (median 26 vs 7 h, 120 vs 24 h and 14 vs 8 days, respectively). On multivariable analysis, age (odds ratio 1.039, 95% confidence interval 1.019–1.060,  $P < 0.001$ ) and mitral valve replacement (odds ratio 2.167, 95% confidence interval 1.401–3.354,  $P < 0.001$ ) emerged as independent predictors of stroke. Preoperative CT scan was made in 31.1% of cases. These patients had a higher risk profile and EuroSCORE II (median 1.58 vs 1.1,  $P < 0.001$ ). CT scan influenced the choice of cannulation site, being ascending aorta (18.5% vs 0.5%,  $P < 0.001$ ) more frequent in the CT group and femoral artery more frequent in the no CT group (97.8% vs 79.7%,  $P < 0.001$ ). No difference was found in the incidence of postoperative stroke (CT group 1.5, no CT group 1.4%,  $P = 0.7$ ).

**CONCLUSIONS:** Mini-MVS is associated with a low incidence of stroke, but when it occurs it has an ominous impact on mortality. Preoperative CT scan affected surgical cannulation strategy but did not led to improved neurological outcomes.

**Keywords:** Minimally invasive cardiac surgery • Heart valve surgery • Mitral valve surgery

### ABBREVIATIONS

|          |                                         |
|----------|-----------------------------------------|
| CI       | Confidence interval                     |
| IQR      | Interquartile range                     |
| mini-MVS | Minimally invasive mitral valve surgery |
| MMIR     | Mini-Mitral International Registry      |
| MVS      | Mitral valve surgery                    |
| OR       | Odds ratio                              |

## INTRODUCTION

Neurological injury is a devastating complication after cardiovascular surgery. The incidence of stroke following a cardiac operation ranges from 1.6% to 6% [1–4], and when it occurs it has serious consequences, influencing postoperative mortality rate and patients' quality of life [5]. In the past, an increasing risk of stroke following minimally invasive mitral valve surgery (mini-MVS) compared with standard sternotomy has been reported [6]. However, despite initial concerns about aortic injuries and particularly stroke, recent data from single-centre retrospective studies showed a stroke rate of 0.8–2% [7–9]. Furthermore, a recent meta-analysis showed that, despite longer operative times, mini-MVS, in comparison with sternotomy approach, reduces ICU and hospital stay and does not increase the risk of stroke [10].

In the present study, we aimed to examine the incidence and predictors of stroke in patients undergoing mini-MVS in the largest cohort of patients whose data were collected in the Mini-Mitral International Registry (MMIR) and to assess the role of preoperative CT scan on surgical management and neurological outcomes.

## PATIENTS AND METHODS

### Ethical statement

The study protocol was approved by the local institutional review board (no. 2020189, 30 July 2020). Consent of patients was

waived for the retrospective phase, whereas was obtained for the patients enrolled prospectively.

### Mini-Mitral International Registry and study population

The MMIR is an independent registry involving 17 international heart valve centres. Details of the registry have been published previously [11]. The Centres combined all consecutive patients who received minimally invasive mitral valve operations with or without associated procedures between 2015 and 2021. Perioperative characteristics and in-hospital outcomes of patients were collected according to the current European Society of Cardiology or ACC/AHA/HRS Guidelines [12], EuroSCORE II model [13] and Mitral Valve Academy Research Consortium end point definitions [14].

### Study end points and outcome definitions

The primary end point was to evaluate the incidence and predictors of stroke in patients undergoing mini-MVS. Stroke was defined, according to the Mitral Valve Academy Research Consortium definition, as duration of a focal or global neurological deficit  $\geq 24$  or  $< 24$  h if available neuroimaging documents a new intracranial or subarachnoid haemorrhage or central nervous system infarction or the neurological deficit results in death.

The secondary end point was to assess the role of preoperative CT scan on surgical management and neurological outcomes.

Bleeding was defined as any postoperative haemorrhage requiring surgical revision.

### Statistical analysis

Continuous variables were expressed as mean (standard deviation) and categorical variables as percentages. Where continuous variables did not follow a normal distribution, the median and interquartile range (IQR) were reported. In all cases, missing

data were not defaulted to negative, and denominators reflect only cases reported. The association between covariates and stroke was tested using univariable and multivariable binary logistic regressions. The multivariable model included 18 pre- and intraoperative clinically relevant covariates: sex, age, diabetes, atrial fibrillation, endocarditis, peripheral arteriopathy, previous neurological injury, cerebrovascular arteriopathy, dialysis, previous cardiac surgery, reduced LVEF, urgent/emergent status, arterial cannulation site, myocardial protection, type of mitral valve surgery (MVS), type of valve prosthesis, concomitant tricuspid and atrial fibrillation surgery. The backward stepwise method was used to build the final model (adjusted  $R^2$ : 0.22).

Propensity score matching was used for subgroup analysis (CT scan versus no CT scan). The matched groups were compared using standard univariate statistical tests of association. Details on PS-matching and comparisons were reported in the [Supplementary Material](#). The level of significance,  $\alpha$ , was set at 5%. Statistical analysis was performed using Statistical Package for Social Sciences version 28.0 (IBM SPSS Inc., Chicago, IL, USA).

## RESULTS

### Demographic and baseline data

Perioperative characteristics and in-hospital outcomes of 7513 patients were collected. Patients with missing data on the key study variable—stroke ( $n = 28$ )—and those who received concomitant aortic valve or root/ascending aorta replacement ( $n = 142$ ) were excluded. Subgroup analysis on preoperative CT scan included only patients with available CT scan data.

The analysis then included a total of 7343 patients. Baseline and preoperative characteristics of the populations are shown in Table 1. The median age was 65 years (55–73) with male predominance ( $n = 4239$ , 57.8%) and a median EuroSCORE II of 1.31 (0.81–2.73). A history of neurologic injury was present in 535 patients (7.4%) and an active endocarditis in 272 cases (3.7%), while 560 patients (7.7%) had prior cardiac surgery.

### Perioperative data

Intraoperative variables are resumed in Table 2. The surgical approaches included: direct vision (28.5%), video-assisted (41%), fully endoscopic (27.4%) and robotic (0.7%). Conversion to full sternotomy occurred in 135 cases (1.9%). Femoral artery was the most used cannulation site for cardiopulmonary bypass (CPB) inflow ( $n = 6645$ , 92.8%). The main surgical procedure involved mitral valve repair in 5502 patients (74.9%) and mitral valve replacement in 1840 (25.1%). In 1240 cases (16.9%), a concomitant tricuspid valve surgery was needed. The median CPB and cross-clamp time were 135 (107–172) and 84 min (64–109), respectively. Repeated cross-clamping was observed in 164 patients (2.3%).

### In-hospital outcomes

In-hospital results are shown in Table 3. The overall mortality was 1.7%. The main postoperative complications included stroke (1.3%), bleeding (6%), low cardiac output (3.8%) and dialysis (1.8%). Median ventilation, ICU times and hospital stay were 8 h (IQR 5–13), 24 h (IQR 20–48) and 8 days (IQR 6–11), respectively.

**Table 1:** Patients' characteristics ( $n = 7343$ )

|                                                       | N    | %                |
|-------------------------------------------------------|------|------------------|
| Male                                                  | 4239 | 57.8             |
| Age, <b>median (IQR)</b>                              |      | 65 (55–73)       |
| NYHA class III–IV                                     | 3337 | 47.7             |
| Hypertension                                          | 3896 | 58.1             |
| Diabetes                                              | 653  | 8.9              |
| Smoking                                               | 883  | 13.2             |
| Obesity                                               | 1023 | 14.4             |
| AF                                                    | 2520 | 37.2             |
| PM                                                    | 234  | 3.2              |
| Mitral valve regurgitation ( <b>moderate–severe</b> ) | 6836 | 93.1             |
| Mitral valve stenosis ( <b>moderate–severe</b> )      | 511  | 7.6              |
| Active endocarditis                                   | 272  | 3.7              |
| Cerebrovascular arteriopathy                          | 134  | 1.9              |
| Peripheral arteriopathy                               | 198  | 2.7              |
| History of neurological injury                        | 535  | 7.4              |
| Pulmonary hypertension                                | 2804 | 40               |
| Dialysis                                              | 83   | 1.1              |
| CAD                                                   | 1001 | 14               |
| Chronic lung disease                                  | 662  | 9                |
| Previous cardiac surgery                              | 560  | 7.7              |
| Mitral valve surgery                                  | 322  | 4.4              |
| Aortic valve surgery                                  | 164  | 2.2              |
| CABG                                                  | 149  | 2.1              |
| Root/ascending aorta surgery                          | 51   | 0.7              |
| Other surgery                                         | 89   | 1.2              |
| Reduced LVEF (<50%)                                   | 1305 | 18               |
| Preoperative CT scan                                  | 1750 | 31.1             |
| Critical preoperative state                           | 190  | 2.7              |
| Urgent/emergent status                                | 481  | 6.5              |
| EuroSCORE II, median (IQR)                            |      | 1.31 (0.81–2.73) |

CABG: Coronary Artery Bypass Grafting; IQR: interquartile range; NYHA: New York Heart Association; AF: Atrial Fibrillation; PM: Pace Maker; CAD: coronary artery disease.

### Neurological outcomes

The overall incidence of perioperative stroke was 1.3% ( $n = 95$ ). In-hospital mortality in patients who had stroke was 11.6% ( $n = 11$ ). On multivariable analysis age [odds ratio (OR) 1.039, 95% confidence interval (CI) 1.019–1.060,  $P < 0.001$ ], urgent/emergent status (OR 2.095, 95% CI 1.137–3.857,  $P = 0.02$ ) and mitral valve replacement (OR 2.167, 95% CI 1.401–3.354,  $P < 0.001$ ) emerged as independent predictors of stroke (Table 4).

### CT scan analysis

Patients with available CT scan data were 5626 (76.6%). A preoperative CT scan was made in the 31.1% of patients. These patients had a higher risk profile [median EuroSCORE II 1.58 (IQR 0.9–3.1) vs 1.1 (0.73–2.01),  $P < 0.001$ ] compared with those who did not undergo CT scan (Table 5). When a preoperative CT scan was made, it influenced the choice of arterial cannulation site, being ascending aorta (18% vs 0.4%,  $P < 0.001$ ) more frequent in the CT group and femoral artery more frequent in the no CT group (97.9% vs 80.2%,  $P < 0.001$ ) (Table 6). The incidence of mortality (1.7% and 1.4%,  $P = \text{NS}$ ) and stroke (1.5 vs 1.4%,  $P = \text{NS}$ ) was not different between the CT and no CT groups (Table 7). Even after the propensity score analysis, no differences were found between the CT and no CT groups in terms of in-hospital mortality (1.3 vs 1.5%,  $P = \text{NS}$ ) and stroke (1.2 vs 0.7%,  $P = \text{NS}$ ).

**Table 2:** Operative data

|                                | N    | %             |
|--------------------------------|------|---------------|
| Surgical approach              |      |               |
| Direct vision                  | 2089 | 28.5          |
| Video assisted                 | 3010 | 41            |
| Totally endoscopic             | 2184 | 27.4          |
| Robotic                        | 54   | 0.7           |
| Surgical access                |      |               |
| Anterolateral                  | 5429 | 74            |
| Transaxillary                  | 918  | 12.5          |
| Periareolar                    | 695  | 9.5           |
| Ministernotomy                 | 298  | 4.1           |
| Conversion to full sternotomy  | 135  | 1.9           |
| Arterial cannulation site      |      |               |
| Femoral artery                 | 6645 | 92.8          |
| Axillary artery                | 137  | 1.9           |
| Ascending aorta                | 328  | 4.6           |
| Other                          | 49   | 0.7           |
| Myocardial protection          |      |               |
| Cardioplegia                   | 7123 | 97.6          |
| Ventricular fibrillation       | 149  | 2             |
| Beating heart                  | 26   | 0.4           |
| Aortic cross-clamping type     |      |               |
| External clamp                 | 6040 | 84.3          |
| Endoclamp                      | 1122 | 15.7          |
| Type of surgery                |      |               |
| Mitral valve repair            | 5502 | 74.9          |
| Mitral valve replacement       | 1840 | 25.1          |
| Type of valve prosthesis       |      |               |
| Biological                     | 1341 | 18.4          |
| Mechanical                     | 460  | 6.3           |
| Concomitant tricuspid surgery  | 1240 | 16.9          |
| Concomitant AF surgery         | 1301 | 17.7          |
| LAAA closure                   | 994  | 14.1          |
| Repeated cross-clamping        | 164  | 2.3           |
| CPB time, median (IQR)         |      | 135 (107–172) |
| Cross-clamp time, median (IQR) |      | 84 (64–109)   |

AF: atrial fibrillation; CPB: cardiopulmonary bypass; IQR: interquartile range; LAA: left atrial appendage.

**Table 3:** In-hospital outcomes

|                                     | N    | %          |
|-------------------------------------|------|------------|
| In-hospital mortality               | 122  | 1.7        |
| Delirium                            | 402  | 6.2        |
| Intubation time (h), median (IQR)   |      | 8 (5–13)   |
| Bleeding requiring revision         | 420  | 6          |
| New-onset AF                        | 1063 | 15.8       |
| Definitive PM implantation          | 453  | 6.2        |
| Myocardial infarction               | 59   | 0.8        |
| Low cardiac output syndrome         | 273  | 3.8        |
| Dialysis                            | 115  | 1.8        |
| Vascular complications              |      |            |
| Major vasc. complications           | 86   | 1.3        |
| Minor vasc. complications           | 42   | 0.6        |
| Thoracic wound complications        | 104  | 1.4        |
| Redo for early valve repair failure | 59   | 0.9        |
| ICU stay (h), median (IQR)          |      | 24 (20–48) |
| Hospital stay (days), median (IQR)  |      | 8 (6–11)   |

AF: atrial fibrillation; IQR: interquartile range; PM: Pace Maker.

**Table 4:** Multivariable analysis for stroke

| Variable                 | P-value | OR/HR | 95% CI      |
|--------------------------|---------|-------|-------------|
| Age                      | <0.001  | 1.039 | 1.019–1.060 |
| Urgent/emergent status   | 0.02    | 2.095 | 1.137–3.857 |
| Reduced LVEF             | –       | –     | –           |
| Mitral valve replacement | <0.001  | 2.167 | 1.401–3.354 |

CI: confidence interval; OR: odds ratio.

## DISCUSSION

In the present study, we evaluated the neurological outcomes and predictors of stroke after mini-MVS using data from the largest worldwide registry for mini-MVS. Moreover, we assessed the role of preoperative CT scan on surgical management and neurological outcomes.

The main results are as follows: (i) while the incidence of stroke in mini-MVS was very low, when it occurs had an ominous impact on mortality, (ii) advanced age, coronary artery disease, urgent emergent status and mitral valve replacement were significant predictors for stroke and (iii) preoperative CT scan performed in selected higher-risk patients affected surgical strategy and likely led to improved neurological outcomes.

Mini-MVS has been adopted for >30 years, since Carpentier reported the first successful case [15]. During these years, the minimally invasive techniques have greatly evolved and nowadays have become the routine approach in many specialized high-volume centres. However, there is still doubt about associated risk and detractors of the minimally invasive cardiac surgery claim that patients are exposed to a greater neurological risk. In 2010, a consensus statement of the International Society of Minimally Invasive Coronary Surgery stated that in patients with mitral disease, minimally invasive surgery could be an alternative to conventional surgery, but with an increasing risk of stroke [16]. Potential reasons for the increased risk of stroke included: incomplete or ineffective de-airing, retrograde aortic flow during CPB, use of CO<sub>2</sub> insufflation, air embolism, prolonged cross-clamp and CPB time and the use of endoaortic balloon. Recently, data from 2 large meta-analyses disproved this assumption showing comparable results between mini-MVS and full sternotomy MVS [17, 18]. Our study confirmed that mini-MVS is associated with a very low incidence of neurologic injury. In MMIR, the overall incidence of stroke was 1.3% being only 1.1% in the isolated MVS. These results compare favourably with those reported by other international registries on conventional MVS [19]. These improvements may be explained by the evolution in terms of technology and surgeons' experience, which allowed to overcome some technical challenges like worse exposure and de-airing.

Although the incidence was very low, the occurrence of stroke remains a devastating complication after cardiac surgery. In MMIR, the mortality rate was 7 times higher in patients with postoperative stroke (11.6% vs 1.5%). On multivariable logistic regression, we have identified 3 preoperative and 1 intraoperative risk factors independently associated with the development of postoperative stroke: advanced age, urgent/emergent status and

**Table 5:** Patients' characteristics (N = 5626)

| Characteristics                                       | Overall cohort                   |                                     |                                    | Propensity-matched cohort        |                                     |                                    |
|-------------------------------------------------------|----------------------------------|-------------------------------------|------------------------------------|----------------------------------|-------------------------------------|------------------------------------|
|                                                       | CT group<br>(n = 1750),<br>N (%) | No CT group<br>(n = 3876),<br>N (%) | Standardized<br>mean<br>difference | CT group<br>(n = 1185),<br>N (%) | No CT group<br>(n = 1185),<br>N (%) | Standardized<br>mean<br>difference |
| Male                                                  | 977 (55.9)                       | 2328 (60.2)                         | -15.6                              | 504 (42.5)                       | 479 (40.4)                          | 6.4                                |
| Age, <b>median (IQR)</b>                              | 65 (54–73)                       | 64 (55–72)                          | 8.4                                | 64 (53–73)                       | 64 (52–72)                          | 3.6                                |
| NYHA class III–IV                                     | 820 (47.3)                       | 1618 (42.5)                         | 13.1                               | 523 (44.1)                       | 473 (39.9)                          | 8.8                                |
| Hypertension                                          | 965 (58.5)                       | 2243 (57.9)                         | 2.2                                | 687 (58)                         | 667 (56.3)                          | 5.3                                |
| Diabetes                                              | 201 (11.5)                       | 265 (6.8)                           | 14.3                               | 92 (7.8)                         | 100 (8.4)                           | -4.2                               |
| Smoking                                               | 252 (15.4)                       | 422 (10.9)                          | 16.8                               | 143 (12.1)                       | 169 (14.3)                          | -8.1                               |
| Obesity                                               | 217 (13.2)                       | 570 (15)                            | -8.9                               | 154 (13)                         | 136 (11.5)                          | 4.7                                |
| AF                                                    | 707 (40.4)                       | 1420 (36.7)                         | 14.7                               | 441 (37.2)                       | 402 (33.9)                          | 9.7                                |
| PM                                                    | 81 (4.6)                         | 80 (2.1)                            | 11.8                               | 33 (2.8)                         | 28 (2.4)                            | 3.1                                |
| Mitral valve regurgitation ( <b>moderate-severe</b> ) | 1597 (91.3)                      | 3631 (93.8)                         | -9.8                               | 1118 (94.3)                      | 1101 (92.9)                         | 5.1                                |
| Mitral valve stenosis ( <b>moderate-severe</b> )      | 216 (12.3)                       | 195 (5)                             | 23.6                               | 86 (7.3)                         | 72 (6.1)                            | 3.6                                |
| Active endocarditis                                   | 79 (4.5)                         | 124 (3.2)                           | 7.8                                | 51 (4.3)                         | 45 (3.8)                            | 2.5                                |
| Cerebrovascular disease                               | 50 (2.9)                         | 61 (1.6)                            | 6.4                                | 22 (1.9)                         | 17 (1.4)                            | 2.6                                |
| Peripheral arteriopathy                               | 38 (2.2)                         | 49 (1.3)                            | 7.7                                | 21 (1.8)                         | 13 (1.1)                            | 1.8                                |
| History of neurological injury                        | 193 (11.8)                       | 218 (5.6)                           | 18.4                               | 84 (7.1)                         | 95 (8)                              | -2.4                               |
| Pulmonary hypertension                                | 564 (32.3)                       | 1490 (38.7)                         | -14.2                              | 406 (34.3)                       | 417 (35.2)                          | -2.6                               |
| Dialysis                                              | 27 (1.5)                         | 32 (0.8)                            | 9.8                                | 14 (1.2)                         | 11 (0.9)                            | 2.1                                |
| CAD                                                   | 237 (14.4)                       | 485 (12.5)                          | 7.7                                | 141 (11.9)                       | 114 (9.6)                           | 5.3                                |
| Chronic lung disease                                  | 199 (11.4)                       | 287 (7.4)                           | 13.1                               | 94 (7.9)                         | 90 (7.6)                            | 0.9                                |
| Previous cardiac surgery                              | 106 (6.1)                        | 158 (4.1)                           | 7.8                                | 58 (4.9)                         | 44 (3.7)                            | 3.6                                |
| Mitral valve surgery                                  | 42 (2.4)                         | 90 (2.3)                            | 2.3                                | 23 (1.9)                         | 24 (2)                              | -0.3                               |
| Aortic valve surgery                                  | 42 (2.4)                         | 38 (1)                              | 4.7                                | 18 (1.5)                         | 9 (0.8)                             | 1.1                                |
| CABG                                                  | 32 (2)                           | 44 (1.1)                            | 3.3                                | 19 (1.6)                         | 10 (0.8)                            | 2.8                                |
| Root/ascending aorta surgery                          | 18 (1)                           | 15 (0.4)                            | 2.4                                | 10 (0.8)                         | 3 (0.3)                             | 1.2                                |
| Other surgery                                         | 22 (1.3)                         | 32 (0.8)                            | 2.1                                | 15 (1.3)                         | 13 (1.1)                            | 0.9                                |
| Reduced LVEF (<50%)                                   | 345 (20)                         | 649 (17)                            | 11.3                               | 208 (17.6)                       | 174 (14.7)                          | 6.3                                |
| Critical preoperative state                           | 54 (3.1)                         | 94 (2.4)                            | 6.5                                | 30 (2.5)                         | 30 (2.5)                            | -                                  |
| Urgent/emergent status                                | 124 (7.1)                        | 234 (6)                             | 5.2                                | 75 (6.3)                         | 75 (6.3)                            | -                                  |
| EuroSCORE II, median (IQR)                            | 1.58 (0.9–3.1)                   | 1.1 (0.73–2.01)                     | 14.9                               | 1.41 (0.83–2.94)                 | 1.29 (0.91–2.13)                    | 9.4                                |

AF: atrial fibrillation; CABG: coronary artery bypass grafting; IQR: interquartile range; NYHA: New York Heart Association.

**Table 6:** Operative data (N = 5626)

| Characteristics               | Overall cohort                |                                  |         | Propensity-matched cohort     |                                  |         |
|-------------------------------|-------------------------------|----------------------------------|---------|-------------------------------|----------------------------------|---------|
|                               | CT group<br>(n = 1750), N (%) | No CT group<br>(n = 3876), N (%) | P-value | CT group<br>(n = 1185), N (%) | No CT group<br>(n = 1185), N (%) | P-value |
| Surgical approach             |                               |                                  | <0.001  |                               |                                  | <0.001  |
| Direct vision                 | 795 (45.5)                    | 989 (2.5)                        |         | 467 (39.4)                    | 342 (28.9)                       |         |
| Video assisted                | 507 (29)                      | 1697 (43.8)                      |         | 347 (29.3)                    | 433 (36.5)                       |         |
| Totally endoscopic            | 401 (22.9)                    | 1177 (30.4)                      |         | 332 (28)                      | 410 (34.6)                       |         |
| Robotic                       | 46 (2.6)                      | 8 (0.2)                          |         | 38 (3.2)                      | 1 (0.1)                          |         |
| Surgical access               |                               |                                  | <0.001  |                               |                                  | <0.001  |
| Antrolateral                  | 806 (46.1)                    | 2939 (75.8)                      |         | 615 (51.9)                    | 788 (66.5)                       |         |
| Transaxillary                 | 570 (32.6)                    | 348 (9)                          |         | 298 (25.2)                    | 152 (12.8)                       |         |
| Periareolar                   | 80 (4.6)                      | 583 (15)                         |         | 62 (5.2)                      | 244 (20.6)                       |         |
| Ministernotomy                | 293 (16.8)                    | 5 (0.1)                          |         | 210 (17.7)                    | 1 (0.1)                          |         |
| Conversion to full sternotomy | 39 (2.2)                      | 56 (1.4)                         | 0.04    | 31 (2.6)                      | 19 (1.6)                         | 0.1     |
| Arterial cannulation site     |                               |                                  | <0.001  |                               |                                  | <0.001  |
| Femoral artery                | 1317 (80.2)                   | 3791 (97.9)                      |         | 955 (80.6)                    | 1169 (98.6)                      |         |
| Axillary artery               | 15 (0.9)                      | 39 (1)                           |         | 11 (0.9)                      | 10 (0.8)                         |         |
| Ascending aorta               | 296 (18)                      | 17 (0.4)                         |         | 212 (17.9)                    | 4 (0.3)                          |         |
| Other                         | 14 (0.9)                      | 27 (0.7)                         |         | 7 (0.6)                       | 2 (0.2)                          |         |
| Myocardial protection         |                               |                                  | <0.001  |                               |                                  | <0.001  |
| Cardioplegia                  | 1719 (98.2)                   | 3798 (98)                        |         | 1170 (98.7)                   | 1158 (97.7)                      |         |
| Ventricular fibrillation      | 13 (0.7)                      | 69 (1.8)                         |         | 5 (0.4)                       | 25 (2.1)                         |         |
| Beating heart                 | 18 (1)                        | 7 (0.2)                          |         | 10 (0.8)                      | 2 (0.2)                          |         |
| Aortic cross-clamping type    |                               |                                  | <0.001  |                               |                                  | 0.006   |
| External clamp                | 1658 (96.2)                   | 3524 (92)                        |         | 1121 (95.6)                   | 1086 (93)                        |         |
| Endoclamp                     | 65 (3.8)                      | 306 (8)                          |         | 51 (4.4)                      | 82 (7)                           |         |

Continued



**Table 6:** Continued

| Characteristics                | Overall cohort                |                                  |         | Propensity-matched cohort     |                                  |         |
|--------------------------------|-------------------------------|----------------------------------|---------|-------------------------------|----------------------------------|---------|
|                                | CT group<br>(n = 1750), N (%) | No CT group<br>(n = 3876), N (%) | P-value | CT group<br>(n = 1185), N (%) | No CT group<br>(n = 1185), N (%) | P-value |
| Type of surgery                |                               |                                  | <0.001  |                               |                                  | <0.001  |
| Mitral valve repair            | 1202 (68.7)                   | 3213 (82.9)                      |         | 893 (75.4)                    | 976 (82.4)                       |         |
| Mitral valve replacement       | 548 (31.3)                    | 662 (17.1)                       |         | 292 (24.6)                    | 209 (17.6)                       |         |
| Concomitant tricuspid surgery  | 361 (20.6)                    | 654 (16.9)                       | <0.001  | 230 (19.4)                    | 186 (15.7)                       | 0.02    |
| Concomitant AF surgery         | 250 (14.3)                    | 757 (19.5)                       | <0.001  | 184 (15.5)                    | 159 (13.4)                       | 0.2     |
| LAA closure                    | 270 (15.4)                    | 592 (15.3)                       | 0.8     | 191 (16.1)                    | 157 (13.2)                       | 0.03    |
| Repeated cross-clamping        | 40 (2.3)                      | 104 (2.7)                        | 0.4     | 25 (2.1)                      | 32 (2.7)                         | 0.4     |
| CPB time, median (IQR)         | 140 (114–176)                 | 134 (103–178)                    | <0.001  | 142 (113–176)                 | 133 (106–176)                    | <0.001  |
| Cross-clamp time, median (IQR) | 83 (64–109)                   | 80 (59–107)                      | 0.004   | 85 (65–111)                   | 82 (61–106)                      | 0.005   |

AF: atrial fibrillation; CPB: cardiopulmonary bypass; IQR: interquartile range; LAA: left atrial appendage.

**Table 7:** In-hospital results

| Characteristics                     | Overall cohort                |                                  |         | Propensity-matched cohort     |                                  |         |
|-------------------------------------|-------------------------------|----------------------------------|---------|-------------------------------|----------------------------------|---------|
|                                     | CT group (n = 1750),<br>N (%) | No CT group (n = 3876),<br>N (%) | P-value | CT group (n = 1185),<br>N (%) | No CT group (n = 1185),<br>N (%) | P-value |
| In-hospital mortality               | 29 (1.7)                      | 53 (1.4)                         | 0.4     | 15 (1.3)                      | 18 (1.5)                         | 0.7     |
| Stroke                              | 26 (1.5)                      | 53 (1.4)                         | 0.7     | 14 (1.2)                      | 8 (0.7)                          | 0.2     |
| Delirium                            | 177 (10.1)                    | 218 (5.6)                        | <0.001  | 103 (8.7)                     | 60 (5.1)                         | <0.001  |
| Intubation time (h), median (IQR)   | 8 (5–15)                      | 7 (5–12)                         | <0.001  | 8 (5–14)                      | 7 (5–12)                         | <0.001  |
| Bleeding requiring revision         | 95 (5.5)                      | 260 (6.7)                        | 0.02    | 63 (5.3)                      | 66 (5.6)                         | 0.8     |
| New-onset AF                        | 270 (15.4)                    | 567 (14.6)                       | 0.4     | 191 (16.1)                    | 189 (15.9)                       | 0.9     |
| Definitive PM implantation          | 53 (3)                        | 72 (1.9)                         | 0.008   | 39 (3.3)                      | 24 (2)                           | 0.07    |
| Myocardial infarction               | 12 (0.7)                      | 33 (0.8)                         | 0.5     | 9 (0.8)                       | 12 (1)                           | 0.2     |
| Low cardiac output syndrome         | 126 (7.7)                     | 114 (2.9)                        | <0.001  | 79 (6.7)                      | 41 (3.5)                         | <0.001  |
| Dialysis                            | 35 (1.8)                      | 42 (1.1)                         | 0.03    | 18 (1.5)                      | 13 (1.1)                         | 0.5     |
| Vascular complications              | 29 (1.7)                      | 78 (2)                           | 0.05    | 20 (1.7)                      | 27 (2.3)                         | 0.1     |
| Major vasc. complications           | 15 (0.9)                      | 59 (1.5)                         |         | 9 (0.8)                       | 19 (1.6)                         |         |
| Minor vasc. complications           | 14 (0.8)                      | 19 (0.5)                         |         | 11 (0.9)                      | 8 (0.7)                          |         |
| Thoracic wound complications        | 50 (2.9)                      | 41 (1.1)                         | <0.001  | 7 (0.6)                       | 17 (1.4)                         | 0.06    |
| Redo for early valve repair failure | 12 (0.7)                      | 35 (0.9)                         | 0.6     | 12 (1)                        | 7 (0.6)                          | 0.3     |
| ICU stay (h), median (IQR)          | 23 (18–48)                    | 24 (19–48)                       | <0.001  | 23 (19–48)                    | 24 (19–48)                       | 0.2     |
| Hospital stay (days), median (IQR)  | 9 (8–15)                      | 8 (6–11)                         | <0.001  | 9 (7–14)                      | 7 (6–10)                         | <0.001  |

AF: atrial fibrillation; IQR: interquartile range.

mitral valve replacement. These results are consistent with those reported in most series where age has been identified as a strong predictor of postoperative stroke due to the underlying conditions [20, 21]. Moreover, our findings get stronger what showed in a recent meta-analysis comparing MV repair over replacement, showing postoperative neurological complications in favour of repair over replacement [22]. Although in the past retrograde perfusion was associated with an increased risk of stroke and postoperative delirium [23], in the present study, the site of cannulation did not affect neurological outcomes.

Another topic of discussion is the need of preoperative CT scan screening in minimally invasive surgery. It is well known that it is very useful to assess preoperatively the chest anatomy and to identify the presence of peripheral vascular disease as well as potential contraindications, such as severely calcified aortopathy. Recent data showed that systematic preoperative CT scan screening seems to be associated with lower risk of postoperative stroke and need for dialysis after mini-MVS [24]. In MMIR, a preoperative CT scan was not routinely performed in all cases and was

predominantly made in higher-risk patients. Performing CT scan in such selected patients resulted in similar incidence of mortality (1.7% and 1.4%,  $P = \text{NS}$ ) and stroke (1.5% vs 1.4%,  $P = \text{NS}$ ) between the CT group and the no CT group. However, CT scan influenced the choice of cannulation site, being ascending aorta more frequently cannulated in the CT group and femoral artery more frequently cannulated in the no CT group.

## Limitations

Despite the strength of our multicentre international registry study, it is a retrospective observational analysis, with its intrinsic limitations. Moreover, indication and subsequent type of mini-MVS were assessed independently by each local institution that was responsible for the data collection and transmission. This study provides no information about the prevalence of mitral annulus calcification that it is a major risk factor for complications including stroke. The comparison of mortality in patients with and without stroke is merely descriptive and was not adjusted for confounders.

## CONCLUSIONS

The present study showed that mini-MVS is associated with a low incidence of perioperative stroke, but when it occurs it has an ominous impact on mortality. Age, urgent/emergent status and mitral valve replacement emerged as independent predictors of stroke. In our experience, preoperative CT scan, performed in selected higher-risk patients, affected surgical cannulation strategy and did not led to improved neurological outcomes.

## SUPPLEMENTARY MATERIAL

[Supplementary material](#) is available at *EJCTS* online.

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## DATA AVAILABILITY

All relevant data are available on request to the authors.

## Author contributions

**Giovanni Domenico Cresce:** Investigation; Writing—original draft. **Paolo Berretta:** Data curation; Formal analysis. **Antonio Fiore:** Investigation. **Manuel Wilbring:** Investigation. **Marc Gerdisch:** Investigation. **Antonios Pitsis:** Investigation. **Mauro Rinaldi:** Investigation. **Nikolaos Bonaros:** Investigation. **Jorg Kempfert:** Investigation. **Tristan Yan:** Investigation. **Frank Van Praet:** Investigation. **Hoang Dinh Nguyen:** Investigation. **Carlo Savini:** Investigation. **Joseph Lamelas:** Investigation. **Tom C. Nguyen:** Investigation. **Pierluigi Stefano:** Investigation. **Gloria Färber:** Investigation. **Loris Salvador:** Conceptualization. **Marco Di Eusanio:** Conceptualization; Writing—review & editing.

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## REFERENCES

- [1] Newman MF, Mathew JP, Grocott HP, Mackensen GB, Monk T, Welsh-Bohmer KA *et al.* Central nervous system injury associated with cardiac surgery. *Lancet* 2006;368:694–703.
- [2] Selnes OA, Gottesman RF, Grega MA, Baumgartner WA, Zeger SL, McKhann GM *et al.* Cognitive and neurologic outcomes after coronary-artery bypass surgery. *N Engl J Med* 2012;366:250–7.
- [3] Raffa GM, Agnello F, Occhipinti G, Miraglia R, Lo Re V, Marrone G *et al.* Neurological complications after cardiac surgery: a retrospective case-control study of risk factors and outcome. *J Cardiothorac Surg* 2019;14:23.
- [4] Liu Y, Chen K, Mei W. Neurological complications after cardiac surgery. *Curr Opin Anaesthesiol* 2019;32:563–7.
- [5] Russo A, Grigioni F, Avierinos J-F, Freeman WK, Suri R, Michelena H *et al.* Thromboembolic complications after surgical correction of mitral regurgitation. *J Am Coll Cardiol* 2008;51:1203–11.
- [6] Cheng DC, Martin J, Lal A, Diegeler A, Folliguet TA, Nifong LW *et al.* Minimally invasive versus conventional open mitral valve surgery: a meta-analysis and systematic review. *Innovations (Phila)* 2011;6:84–103.
- [7] Davierwala PM, Seeburger J, Pfannmueller B, Garbade J, Misfeld M, Borger MA *et al.* Minimally invasive mitral valve surgery: “The Leipzig experience”. *Ann Cardiothorac Surg* 2013;2:744–50.
- [8] Grant SW, Hickey GL, Modi P, Hunter S, Akowuah E, Zacharias J. Propensity-matched analysis of minimally invasive approach versus sternotomy for mitral valve surgery. *Heart* 2019;105:783–9.
- [9] Cao C, Gupta S, Chandrakumar D, Nienaber TA, Indraratna P, Ang SC *et al.* A meta-analysis of minimally invasive versus conventional mitral valve repair for patients with degenerative mitral disease. *Ann Cardiothorac Surg* 2013;2:693–703.
- [10] Sá MPBO, Van den Eynde J, Cavalcanti LRP, Kadyraliev B, Enginöev S, Zhigalov K *et al.* Mitral valve repair with minimally invasive approach vs sternotomy: a meta-analysis of early and late results in randomized and matched observational studies. *J Card Surg* 2020;35:2307–23.
- [11] Berretta P, Kempfert J, Van Praet F, Salvador L, Lamelas J, Nguyen TC *et al.* Risk-related clinical outcomes after minimally invasive mitral valve surgery: insights from the mini-mitral international registry (MMIR). *Eur J Cardiothorac Surg* 2023;63:eza090.
- [12] Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J *et al.*; ESC/EACTS Scientific Document Group. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J* 2022;43:561–632.
- [13] Nashef SAM, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR *et al.* EuroSCORE II. *Eur J Cardiothorac Surg* 2012;41:734–45.
- [14] Stone GW, Adams DH, Abraham WT, Kappetein AP, Généreux P, Vranckx P *et al.*; for the Mitral Valve Academic Research Consortium (MVARC). Clinical trial design principles and endpoint definitions for transcatheter mitral valve repair and replacement: part 2: endpoint definitions. *J Am Coll Cardiol* 2015;66:308–21.
- [15] Carpentier A, Loumet D, Carpentier A, Le Bret E, Haugades B, Dassier P *et al.* Chirurgie à coeur ouvert par vidéo-chirurgie et mini-thoracotomie. Premier cas (valvuloplastie mitrale) opéré avec succès [Open heart operation under videosurgery and minithoracotomy. First case (mitral valvuloplasty) operated with success]. *C R Acad Sci III* 1996;319:219–23.
- [16] Falk V, Cheng DC, Martin J, Diegeler A, Folliguet TA, Nifong LW *et al.* Minimally invasive versus open mitral valve surgery: a consensus statement of the international society of minimally invasive coronary surgery (ISMICS) 2010. *Innovations (Phila)* 2011;6:66–76.
- [17] Sündermann SH, Sromicki J, Rodriguez Cetina Bieffer H, Seifert B, Holubec T, Falk V *et al.* Mitral valve surgery: right lateral minithoracotomy or sternotomy? A systematic review and meta-analysis. *J Thorac Cardiovasc Surg* 2014;148:1989–95.e4.
- [18] Al Otaibi A, Gupta S, Belley-Cote EP, Alsagheir A, Spence J, Parry D *et al.* Mini-thoracotomy vs. conventional sternotomy mitral valve surgery: a systematic review and meta-analysis. *J Cardiovasc Surg (Torino)* 2017;58:489–96.
- [19] Udesch R, Natarajan P, Jeevanantham V, Gleason TG, Badhwar V, Thirumala PD. Perioperative strokes following surgical correction of mitral valves: a systematic review and meta-analysis. *Eur Neurol* 2017;78:63–70.
- [20] Sultan I, Bianco V, Kilic A, Jovin T, Jadhav A, Jankowitz B *et al.* Predictors and outcomes of ischemic stroke after cardiac surgery. *Ann Thorac Surg* 2020;110:448–56.
- [21] Whitlock R, Healey JS, Connolly SJ, Wang J, Danter MR, Tu JV *et al.* Predictors of early and late stroke following cardiac surgery. *CMAJ* 2014;186:905–11.
- [22] Di Tommaso E, Rapetto F, Guida GA, Zakkar M, Bruno VD. Benefits of mitral valve repair over replacement in the elderly: a systematic review and meta-analysis. *J Card Surg* 2021;36:2524–30.
- [23] Murzi M, Cerillo AG, Miceli A, Bevilacqua S, Kallushi E, Farneti P *et al.* Antegrade and retrograde arterial perfusion strategy in minimally invasive mitral-valve surgery: a propensity score analysis on 1280 patients. *Eur J Cardiothorac Surg* 2013;43:e167–72–e172. Jun
- [24] Leonard JR, Henry M, Rahoma M, Khan FM, Wingo M, Hameed I *et al.* Systematic preoperative CT scan is associated with reduced risk of stroke in minimally invasive mitral valve surgery: a meta-analysis. *Int J Cardiol* 2019;278:300–6.