European Journal of Cardio-Thoracic Surgery 2023, 63(6), ezad090
https://doi.org/10.1093/ejcts/ezad090 Advance Access publication 9 March 2023

ORIGINAL ARTICLE

Cite this article as: 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. Eur J Cardiothorac Surg 2023; doi:10.1093/ejcts/ezad090.

Risk-related clinical outcomes after minimally invasive mitral valve surgery: insights from the Mini-Mitral International Registry

Paolo Berretta [a,*], Jorg Kempfert[b], Frank Van Praet[c], Loris Salvador[d], Joseph Lamelas[e], Tom C. Nguyen[f], Manuel Wilbring [g], Marc Gerdisch[h], Mauro Rinaldi[i], Nikolaos Bonaros [j], Thierry Folliguet[k], Torsten Doenst [l], Dinh Hoang Nguyen[m], Pierluigi Stefano[n], Tristan Yan [o], Carlo Savini[p], Antonios Pitsis [q], and Marco Di Eusanio[a]

[a] Cardiac Surgery Unit, Lancisi Cardiovascular Center, Polytechnic University of Marche, Ancona, Italy
[b] Department of Cardiothoracic and Vascular Surgery, German Heart Center Berlin, Berlin, Germany
[c] Cardiac Surgery Department, Hartcentrum OLV Aalst, Aalst, Belgium
[d] Division of Cardiac Surgery, S. Bortolo Hospital, Vicenza, Italy
[e] Division of Cardiothoracic Surgery, University of Miami, Miami, FL, USA
[f] Department of Cardiothoracic and Vascular Surgery, University of Texas Health Science Center Houston, McGovern Medical School, Houston, TX, USA
[g] Center for Minimally Invasive Cardiac Surgery, University Heart Center Dresden, Dresden, Germany
[h] Franciscan Health Indianapolis, Indianapolis, IN, USA
[i] Cardiac Surgery Unit, University of Turin, Turin, Italy
[j] Department of Cardiac Surgery, Medical University of Innsbruck, Innsbruck, Austria
[k] Henri Mondor Hospital, University of Paris, Paris, France
[l] Department of Cardiothoracic Surgery, Jena University Hospital, Jena, Germany
[m] University of Medicine and Pharmacy, Ho Chi Minh City, Viet Nam
[n] Cardiac Surgery Unit, Careggi University Hospital, Firenze, Italy
[o] Department of Cardiothoracic Surgery, The Royal Prince Alfred Hospital, Sydney, Australia
[p] Cardiac Surgery Department, Sant'Orsola Malpighi Hospital, University of Bologna, Bologna, Italy
[q] Cardiac Surgery Department, European Interbalkan Medical Center, Thessaloniki, Greece

* Corresponding author. Cardiac Surgery Unit, Lancisi Cardiovascular Center, Polytechnic University of Marche, Via Conca 71, 60126 Ancona, Italy. Tel: +39-0715965353; e-mail: p.berretta@icloud.com (P. Berretta).

Received 15 October 2022; received in revised form 13 February 2023; accepted 8 March 2023

Key question

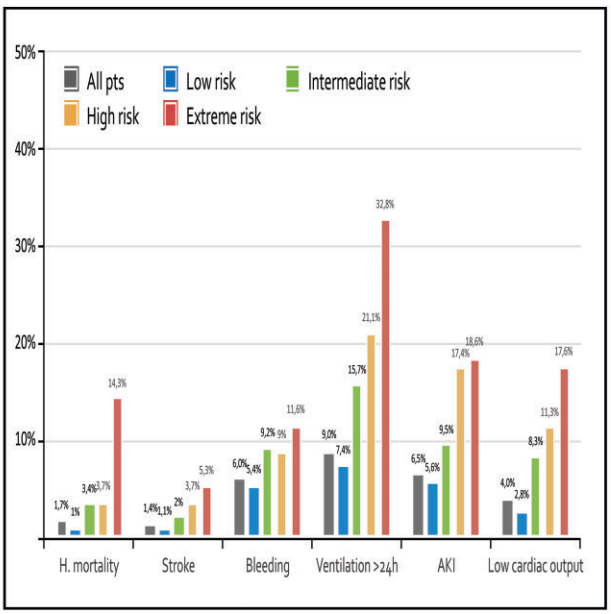
What are the operative results of contemporary mini-mitral surgery according to patient risk profile?

Key finding(s)

Operative results were excellent in low-, intermediate- and high risk patients, but were less satisfacotry in extreme risk.

Take-home message

Our findings may serve as a benchmark for patients whose conditions are being evaluated for any form of mitral valve therapy.



Presented at the 36th Annual Meeting of the European Association for Cardio-Thoracic Surgery, Milan, Italy, 5–8 October 2022.

© The Author(s) 2023. Published by Oxford University Press on behalf of the European Association for Cardio-Thoracic Surgery. All rights reserved.

Downloaded from https://academic.oup.com/ejcts/article/63/6/ezad090/7074178 by Biblioteca di Scienze, Università degli studi di Firenze user on 07 January 2025

Abstract

OBJECTIVES: With the popularization of catheter-based mitral valve procedures, evaluating risk-specific differentiated clinical outcomes after contemporary mitral valve surgery is crucial. In this study, we assessed the operative results of minimally invasive mitral valve operations across different patient risk profiles and evaluated the value of EuroSCORE (ES) II predicted risk of mortality model for risk prediction, in the large cohort of Mini-Mitral International Registry (MMIR).

METHODS: The MMIR database was used to analyse mini-mitral operations between 2015 and 2021. Patients were categorized as low (<4%), intermediate (4% to <8%), high (8% to <12%) and extreme risk (≥12%) according to ES II. The observed-to-expected mortality ratio was calculated for each risk group.

RESULTS: A total of 6541 patients were included in the analysis. Of those, 5546 (84.8%) were classified as low risk, 615 (9.4%) as intermediate risk, 191 (2.9%) as high risk and 189 (2.9%) as extreme risk. Overall operative mortality and stroke rates were 1.7% and 1.4%, respectively, and were significantly associated with patient's risk. The observed mortality was significantly lower than expected—according to the ES II—in all risk categories (observed-to-expected ratio < 1).

CONCLUSIONS: The present study provides an international contemporary benchmark for operative outcomes after minimally invasive mitral surgery. Operative results were excellent in low-, intermediate- and high-risk patients, but were less satisfactory in extreme risk. The ES II model overestimated the in-hospital mortality. We believe that findings from the MMIR may assist surgeons and cardiologists in clinical decision-making and treatment allocation for patients with mitral valve disease.

Keywords: Minimally invasive mitral surgery • Mini-Mitral International Registry • Minimally invasive cardiac surgery

ABBREVIATIONS

CIs	Confidence intervals
ES	EuroSCORE
MMIR	Mini-Mitral International Registry
O:E	Observed-to-expected
OR	Odds ratio
sCr	Serum creatinine

INTRODUCTION

In an era where catheter-based techniques are being proposed as potential alternatives to surgical approaches, more robust evidence to evaluate risk-specific differentiated clinical outcomes after contemporary mitral valve operations is needed. Over the last decade minimally invasive mitral valve surgery has evolved considerably and has become the first choice approach to treat patients with mitral valve disease in many specialized heart valve centres [1–3]. Available data suggest that mini-mitral surgery is associated with improved patient outcomes and faster recovery when compared with the conventional sternotomy approach [4, 5]. However, current evidence is limited to single centres series or national database not specifically focused on mini-mitral operations. The Mini-Mitral International Registry (MMIR), a large multicentric registry specifically focused on mini-mitral surgery, represents a unique opportunity to study a large group of patients who underwent mini-mitral operations. The aims of this study were to assess the operative results of minimally invasive mitral valve operations across different patient risk profiles in the large cohort of MMIR.

PATIENTS AND METHODS

Ethical statement

The study protocol was approved by the local institutional review board of all centres based on the approval of the coordinating centre (n. 2020189, 30 July 2020) and consent of patients was waived.

Study end points

The primary end points included all cause operative mortality, postoperative stroke, low cardiac output, acute kidney injury, respiratory failure, bleeding and repair rate. In addition, lengths of stay and the observed-to-expected (O:E) mortality ratios were assessed. Operative mortality was defined [according to the EuroSCORE (ES) II] as death in the same hospital as the operation took place, before discharge from hospital. Stroke included duration of a focal or global neurological deficit ≥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. Low cardiac output included inotropic support >24 h or the use of temporary mechanical circulatory support. Acute kidney injury involved the maximal change in serum creatinine (sCr) from baseline to 7 days post-procedure as follows: (i) stage 1, increase in sCr to 150–199%, increase of ≥0.3 mg/dl (≥26.4 mmol/l) within 48 h, or urine output <0.5 ml/kg/h for ≥6 h but <12 h, (ii) stage 2, increase in sCr to 200–299% or urine output <0.5 ml/kg/h for ≥12 h but <24 h and (iii) stage 3, increase in sCr to ≥300%, sCr of ≥4.0 mg/dl (≥354 mmol/l) with an acute increase of ≥0.5 mg/dl (44 mmol/l), urine output <0.3 ml/kg/h for >24 h, or anuria for ≥12 h or patients receiving renal replacement therapy. Respiratory failure involved prolonged mechanical ventilation (>24 h), reintubation and tracheostomy. Bleeding included patients who required surgical re-exploration.

Data source and definition

The MMIR was established in 2020 by a consortium of research centres to evaluate the current management and outcomes of minimally invasive mitral valve surgery. The Polytechnic University of Marche, Lancisi Cardiovascular Center (Ancona, Italy) is the Coordinating Center and is responsible for the concept and design, establishing and maintaining the clinical

Downloaded from https://academic.oup.com/ejcts/article/63/6/ezad090/7074178 by Biblioteca di Scienze, Università degli studi di Firenze user on 07 January 2025

database, performing statistical analyses and coordinating and organizing the research projects. Currently, 17 large referral heart valve centres in Europe, America, Oceania and Asia have been included in the registry. Centers were initially invited based on the literature search of international minimally invasive cardiac surgery and mitral surgery expertise hubs with consistent and ongoing academic publication output. Following expert advice was sought from the Research Steering Committee regarding recruitment of other centres. The study population was defined as patients undergoing minimally invasive mitral valve operations with all possible indications, using all available approaches (direct vision, video assisted, fully endoscopic, robotic) and materials except for NeoChord (NeoChord, Inc., St. Louis Park, USA). All consecutive patients were included. The MMIR database was designed specifically to assess patients with mitral valve disease and patients undergoing mini-mitral valve surgery. It includes over 380 variables on clinical data, risk assessment variables, surgery related data, perioperative outcomes, echocardiographic data and long-term outcomes. All centres provided data by using the same definitions and assessment measures according to the current European Society of Cardiology or ACC/AHA/HRS Guidelines, ES II model and Mitral Valve Academy Research Consortium end-point definitions [6–8]. The retrospectively completed data forms were forwarded by the participating MMIR sites to the coordinating centre and reviewed for face validity and completeness. The protocol of the registry is provided in the Supplementary Material.

Population

At the time of writing, 7513 patients were enrolled in the registry (Supplementary Material, Fig. S1). Patients who did not receive minithoracotomy access or underwent concomitant aortic valve replacement and root/ascending aorta repair as well as patients with missing data for calculation of ES II were excluded from the analysis (Fig. 1). Patients were classified as low (ES II <4%), intermediate (ES II 4% to <8%), high (ES II 8% to <12%) and extreme risk (ES II ≥12%). Preoperative, intraoperative and postoperative outcome variables were compared among the 4 groups.

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 were reported. In all cases, missing data were not defaulted to negative, and denominators reflect only cases reported. Comparisons of subgroups were performed using unpaired *t*-test or Mann–Whitney *U*-test (continuous variables) and chi-squared test (categorical variables). Observed in-hospital mortality was divided by mean expected mortality based on the ES II to obtain the O:E mortality ratios. The ratio of O:E mortality was calculated with 95% confidence intervals (CIs) based on the binomial distribution. Multivariable logistic and linear regression models (using backward stepwise algorithm) were estimated to evaluate the effect of patients' risk profile on outcomes. The model was adjusted for residual risk factors for adverse outcomes over and above those included in the ES II (centre volume, preoperative AF, type of mitral valve disease, surgical approach, type of surgery, arterial cannulation site, technique of myocardial protection, type of cardioplegia, cross-clamp time). The variables that achieved $P < 0.25$ in the univariable analysis were included in the multivariable model. The level of significance, α, was set at 5%. Statistical analysis was performed using IBM SPSS Statistics for Macintosh Version 28.0 (IBM Corp. Released 2021. Armonk, NY: IBM Corp).

RESULTS

Patients' characteristics and operative data

This study included 6541 consecutive patients who underwent a mini-mitral operation at MMIR centres from 2015 and 2021. Of those, 84.8% (5546) were classified as low risk, 9.4% (615)

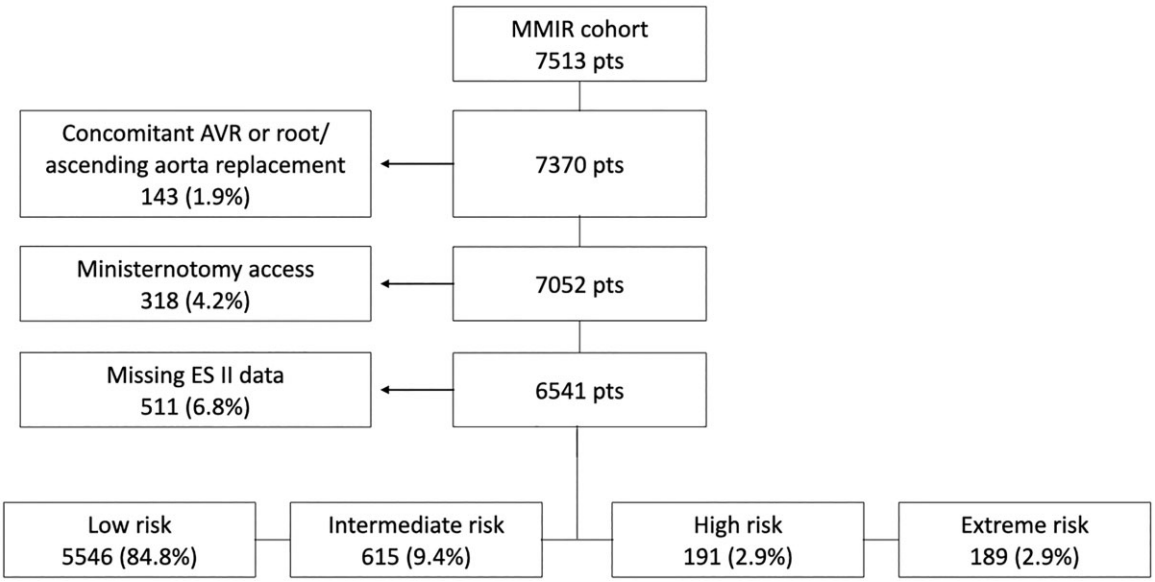


Figure 1: Consolidated Standards of Reporting Trials diagram.

Downloaded from https://academic.oup.com/ejcts/article/63/6/ezad090/7074178 by Biblioteca di Scienze, Università degli studi di Firenze user on 07 January 2025

intermediate risk, 2.9% (191) high risk and 2.9% (189) extreme risk, according to the ES II. The patients' characteristics are reported in Table 1. As expected, higher-risk patients were older and more frequently suffered from serious comorbidities. The probability of valve repair in patients presenting with degenerative mitral valve regurgitation was 92.5% and significantly correlated with patients' risk (low risk 93.3%, intermediate risk 84.4%, high risk 77.5% and extreme risk 65.5%, $p < 0.001$). Higher-risk patients underwent more frequently combined tricuspid and atrial fibrillation surgery with longer CPB and cross-clamp times. The overall MVARC technical success rate was 97.2% with no difference between groups (Table 2).

In-hospital outcomes

In-hospital results are given in Table 3. The overall in-hospital mortality was 1.7%, being 1%, 3.4%, 3.7% and 14.3% in the low-, intermediate-, high- and extreme-risk groups, respectively ($P < 0.001$). The O:E ratios for all risk groups were considerably <1 (low risk, 0.71 [95% CI, 0.63–0.82]; moderate risk, 0.61 [95% CI 0.55–0.79]; high risk, 0.38 [95% CI, 0.21–0.62]; and extreme risk, 0.64 [95% CI, 0.52–0.79]) (Table 4). The rates of main postoperative complications were all in favour for patients in the low-risk category. Higher-risk patients were more likely to have mild postoperative mitral regurgitation, whereas the incidence of

Table 1: Demographics

	Total ($n = 6541$), n (%)	ES II <4% ($n = 5546$), n (%)	ES II 4–8% ($n = 615$), n (%)	ES II 8–12% ($n = 191$), n (%)	ES II ≥12% ($n = 189$), n (%)	P-Value
Male	3819 (58.4)	3371 (60.8)	272 (44.2)	79 (41.4)	97 (51.3)	<0.001
Age. median (IQR)	65 (55–73)	63 (53–72)	73 (66–78)	76 (69–79)	75 (67–78)	<0.001
NYHA class III–IV	3050 (47.2)	2261 (41.3)	453 (74.4)	159 (83.7)	177 (94.1)	<0.001
Hypertension	3395 (57.4)	2798 (54.6)	363 (72.3)	125 (86.2)	109 (76.8)	<0.001
Diabetes	544 (8.3)	350 (6.3)	110 (17.9)	39 (20.5)	45 (23.8)	<0.001
Dyslipidemia	1800 (30.5)	1453 (28.4)	217 (43.3)	68 (46.9)	62 (43.7)	<0.001
Smoking	672 (11.4)	595 (11.6)	54 (10.8)	12 (8.3)	11 (7.7)	0.4
Obesity (BMI > 30)	910 (14.2)	741 (13.7)	111 (18.7)	25 (13.3)	33 (17.6)	0.005
Atrial fibrillation	2226 (37.2)	1765 (34)	287 (56.9)	86 (58.9)	88 (62.4)	<0.001
Pacemaker	213 (3.3)	103 (1.9)	56 (9.3)	30 (15.9)	24 (12.7)	<0.001
Renal impairment (eGFR < 85)	3691 (57.8)	2860 (52.9)	496 (83.5)	170 (90.4)	165 (87.8)	<0.001
Dialysis	67 (1)	30 (0.5)	14 (2.3)	11 (5.8)	12 (6.3)	<0.001
CAD	887 (13.8)	586 (10.8)	146 (24)	75 (39.7)	80 (42.6)	<0.001
Poor mobility	131 (2)	78 (1.4)	27 (4.5)	12 (6.3)	14 (7.4)	<0.001
Chronic lung disease	523 (8)	354 (6.4)	82 (13.3)	36 (18.9)	51 (27)	<0.001
Active endocarditis	233 (3.6)	162 (2.9)	32 (5.3)	14 (7.4)	25 (13.2)	<0.001
Cerebrovascular arteriopathy	119 (1.8)	61 (1.1)	26 (4.2)	13 (6.8)	19 (10.1)	<0.001
Peripheral arteriopathy	188 (2.9)	83 (1.5)	34 (5.5)	28 (14.7)	43 (22.8)	<0.001
Pulmonary hypertension	2604 (41.5)	1954 (36.6)	379 (64.5)	128 (70.7)	143 (81.3)	<0.001
Previous cardiac surgery	491 (7.5)	159 (2.9)	137 (22.3)	78 (40.8)	117 (61.9)	<0.001
Mitral valve surgery	275 (4.2)	102 (1.8)	78 (13)	33 (17.5)	62 (32.8)	<0.001
Aortic valve surgery	149 (2.3)	40 (0.7)	38 (6.3)	27 (14.3)	44 (23.3)	<0.001
CABG	130 (2)	19 (0.4)	35 (5.9)	28 (14.9)	48 (25.5)	<0.001
Thoracic aorta surgery	51 (0.8)	15 (0.3)	19 (3.2)	8 (4.2)	9 (4.8)	<0.001
Critical preoperative state	188 (2.9)	76 (1.4)	41 (6.8)	20 (10.6)	51 (27)	<0.001
Preoperative CT angiography	1450 (27.9)	1208 (26.2)	159 (40.2)	47 (46.5)	36 (39.6)	<0.001
Mitral valve disease etiology						<0.001
Degenerative	4424 (69.9)	4058 (75.1)	253 (44.5)	61 (34.2)	52 (29.1)	
Functional	942 (14.9)	696 (12.9)	145 (25.5)	54 (30.3)	47 (26.3)	
Rheumatic	479 (7.6)	377 (7)	74 (13)	16 (9)	12 (6.7)	
Other	484 (7.6)	272 (5)	97 (17)	47 (26.4)	68 (38)	
Mitral valve regurgitation						<0.001
Mild	266 (4.1)	179 (3.2)	49 (8)	12 (6.3)	26 (13.8)	
Moderate	1091 (16.7)	862 (15.6)	133 (21.6)	47 (24.6)	49 (25.9)	
Severe	4983 (76.3)	4341 (78.4)	412 (70)	126 (65.9)	104 (55)	
Mitral valve stenosis						<0.001
Mild	135 (2.2)	88 (1.7)	24 (4.7)	10 (6.8)	13 (9.1)	
Moderate	178 (3)	118 (2.3)	30 (5.9)	13 (8.9)	17 (11.9)	
Severe	310 (5.2)	248 (4.8)	45 (8.8)	11 (7.5)	6 (4.2)	
LV function						<0.001
LVEF > 50%	5288 (81.9)	4685 (85.7)	405 (66.7)	102 (54)	96 (51.1)	
LVEF 31–50%	1031 (16)	724 (13.2)	167 (27.5)	72 (38.1)	68 (36.2)	
LVEF 21–30%	120 (1.9)	54 (1)	31 (5.1)	12 (6.3)	23 (12.2)	
LVEF ≤20%	14 (0.2)	6 (0.1)	4 (0.7)	3 (1.6)	1 (0.5)	
Urgent/emergent status	437 (6.7)	225 (4.1)	93 (15.4)	45 (23.8)	74 (39.2)	<0.001

BMI: body mass index; CAD: coronary artery disease; ES: EuroSCORE; IQR: interquartile range; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association.

Downloaded from https://academic.oup.com/ejcts/article/63/6/ezad090/7074178 by Biblioteca di Scienze, Università degli studi di Firenze user on 07 January 2025

Table 2: Operative data

	Total (*n* = 6541), *n* (%)	ES II <4% (*n* = 5546), *n* (%)	ES II 4–8% (*n* = 615), *n* (%)	ES II 8–12% (*n* = 191), *n* (%)	ES II ≥12% (*n* = 189), *n* (%)	*P*-Value
Surgical approach						<0.001
Direct vision	1480 (22.6)	1202 (21.7)	177 (28.8)	59 (30.9)	42 (22.3)	
Video assisted	2816 (43.1)	2500 (45.1)	198 (32.2)	56 (29.3)	62 (33)	
Totally endoscopic	2184 (33.4)	1787 (32.3)	237 (38.5)	76 (39.8)	84 (44.7)	
Robotic	55 (0.8)	52 (0.9)	3 (0.5)	–	–	
Surgical access						<0.001
Anterolateral	4927 (75.3)	4121 (74.3)	490 (79.7)	156 (81.7)	160 (84.7)	
Transaxillary	917 (14)	821 (14.8)	74 (12)	18 (9.4)	4 (2.1)	
Periareolar	697 (10.7)	604 (10.9)	51 (8.3)	17 (8.9)	25 (13.2)	
Conversion to full sternotomy	113 (1.7)	84 (1.5)	16 (2.7)	4 (2.1)	9 (4.8)	<0.001
Arterial cannulation site						<0.001
Femoral artery	6206 (97)	5314 (97.9)	554 (93.3)	172 (91.5)	166 (88.3)	
Axillary artery	115 (1.8)	69 (1.3)	31 (5.2)	7 (3.7)	8 (4.3)	
Ascending aorta	27 (0.4)	16 (0.3)	4 (0.7)	2 (1.1)	5 (2.7)	
Other	49 (0.8)	28 (0.5)	5 (0.8)	7 (3.7)	9 (4.8)	
Myocardial protection						<0.001
Cardioplegia	6362 (97.8)	5486 (99.3)	555 (92.2)	170 (89.9)	151 (79.9)	
Ventricular fibrillation	116 (1.8)	33 (0.6)	39 (6.5)	15 (7.9)	29 (15.3)	
Beating heart	26 (0.4)	5 (0.1)	8 (1.3)	4 (2.1)	9 (4.8)	
Cardioplegia type						<0.001
Blood	2352 (36.2)	2220 (40.2)	97 (16.1)	17 (9)	18 (9.5)	
Crystalloid	4016 (61.8)	3264 (59.1)	460 (76.5)	153 (81)	139 73.5	
Type of surgery						<0.001
Mitral valve repair	4981 (76.2)	4486 (80.9)	345 (56.1)	88 (46.1)	62 (32.8)	
Mitral valve replacement	1478 (22.6)	990 (17.9)	263 (42.8)	101 (52.9)	124 (65.6)	
Replacement due to unsuccessful repair	81 (1.2)	69 (1.2)	7 (1.1)	2 (1)	3 (1.6)	
Mitral valve repair technique						
Annuloplasty ring	4923 (98.5)	4443 (98.7)	338 (98)	86 (98.7)	56 (90.3)	<0.001
Artificial chords	3073 (62.6)	2879 (65.1)	143 (43.1)	28 (32.2)	23 (37.1)	<0.001
Resection	778 (16)	571 (16.6)	32 (9.8)	10 (11.6)	5 (8.1)	0.04
Sliding	122 (2.5)	115 (2.6)	5 (1.5)	–	2 (3.2)	0.6
Edge to edge	111 (2.3)	96 (2.2)	10 (2.9)	3 (3.5)	2 (3.2)	0.7
Associated procedures	1968 (30.1)	1473 (26.6)	306 (49.8)	91 (47.6)	98 (51.9)	<0.001
Tricuspid surgery	1084 (16.6)	732 (13.2)	209 (34)	69 (36.5)	74 (39.1)	
Atrial fibrillation surgery	1197 (18.3)	969 (17.5)	147 (23.9)	42 (22.1)	39 (20.6)	
LAA closure	938 (14.6)	741 (13.4)	137 (22.3)	33 (17.3)	27 (14.3)	<0.001
Repeated X-clamping	155 (2.4)	146 (2.6)	6 (1)	3 (1.6)	–	0.008
CPB time (min), median (IQR)	136 (108–174)	134 (106–170)	149 (120–184)	146 (120–182)	154 (122–195)	<0.001
Clamp time (min), median (IQR)	84 (63–110)	84 (63–108)	88 (64–115)	85 (66–112)	92 (61–125)	0.04
Technical success	6217 (97.2)	5268 (97.1)	590 (98.2)	183 (97.9)	176 (95.1)	0.1

CABG: coronary artery bypass grafting; CPB: cardiopulmonary bypass; CT: Computed tomography; eGFR: Estimated Glomerular Filtration Rate; ES: EuroSCORE; IQR: interquartile range; LAA: left atrial appendix.

moderate to severe mitral regurgitation was similar between groups (Fig. 2). The association between patient's risk profile and risk for adverse outcomes are displayed in Table 5. After adjusting for the other measured covariates, an increase in ES II was related to an increase in risk of all adverse outcome measures. On multivariable analysis, ES II [odds ratio (OR) 1.081, 95% CI 1.046–1.117], mitral valve replacement (OR 1.813, 95% CI 1.047–3.139) and cross-clamp time (OR 1.015, 95% CI 1.009–1.022) emerged as independent predictors of in-hospital mortality (Table 6).

DISCUSSION

With the popularization of catheter-based mitral valve procedures, an evaluation of surgical results after contemporary mitral valve operations has become crucial. The use of MMIR allowed us to provide a real world picture of demographics as well as differentiated, risk-specific clinical outcomes of patients undergoing mini-mitral operations. The main findings can be summarized as follows: (i) the vast majority of patients who received mini-mitral surgery were at low surgical risk, (ii) in MMIR less-invasive mitral operations were performed with very low rates of mortality and morbidity, (iii) the rate of mitral valve repair was excellent and significantly correlated with patients' risk and (iv) the ES II consistently overestimated mortality in all risk categories.

Contemporary risk profiles of patients undergoing mini-mitral valve surgery skew towards low operative risk: 84.8% of patients had a low mortality risk (ES II <4%) and only 5.8% had a high or extreme risk (ES II ≥8%). Similar distributions of patient by risk have been previously reported in conventional mitral valve surgery [9], indicating that low-risk patients continue to constitute the majority of patients referred to surgical treatment. Indeed, nearly half of patients who meet indications for mitral valve surgery are not offered this therapy due to the perception of elevated surgical risk or the advanced age [10]. Our results showed that a minimally invasive approach to mitral valve surgery can be accomplished with very low operative mortality and morbidity rates. In MMIR cohort, the overall mortality was 1.7% and the

Downloaded from https://academic.oup.com/ejcts/article/63/6/ezad090/7074178 by Biblioteca di Scienze, Università degli studi di Firenze user on 07 January 2025

Table 3: In-hospital outcomes

	Total (*n* = 6541), *n* (%)	ES II <4% (*n* = 5546), *n* (%)	ES II 4–8% (*n* = 615), *n* (%)	ES II 8–12% (*n* = 191), *n* (%)	ES II ≥12% (*n* = 189), *n* (%)	*P*-Value
In-hospital mortality	112 (1.7)	57 (1)	21 (3.4)	7 (3.7)	27 (14.3)	<0.001
Stroke	90 (1.4)	61 (1.1)	12 (2)	7 (3.7)	10 (5.3)	<0.001
Delirium	391 (6.6)	305 (5.9)	53 (10.7)	14 (9.7)	19 (13.5)	<0.001
Intubation time (h), median (IQR)	8 (5–13)	7.8 (5–12)	10 (6–19)	13 (7.4–23.3)	15 (10–60)	<0.001
Respiratory insufficiency	533 (9)	380 (7.4)	78 (15.7)	30 (21.1)	45 (32.8)	<0.001
Bleeding	393 (6)	297 (5.4)	57 (9.2)	17 (9)	22 (11.6)	<0.001
Transfusions (U), median (IQR)	0 (0–1)	0 (0–1)	0 (0–2)	1 (0–3)	2 (0–5)	<0.001
New onset atrial fibrillation	887 (14.9)	792 (15.3)	63 (12.8)	18 (12.5)	14 (9.9)	0.1
Definitive pacemaker	167 (2.6)	110 (2)	29 (4.8)	14 (7.4)	14 (7.4)	<0.001
Myocardial infarction	58 (0.9)	50 (0.9)	5 (0.8)	2 (1.1)	1 (0.5)	0.9
Periprocedural (≤48 h)	51 (0.8)	43 (0.8)	5 (0.8)	2 (1.1)	1 (0.5)	
Spontaneous (>48 h)	7 (0.1)	7 (0.1)	–	–	–	
Low cardiac output	257 (4)	154 (2.8)	49 (8.3)	21 (11.3)	33 (17.6)	<0.001
Acute kidney injury						<0.001
Stage 1	231 (3.9)	180 (3.5)	25 (5)	13 (9)	10 (7.1)	
Stage 2	54 (0.9)	34 (0.7)	8 (1.6)	6 (4.2)	1 (0.7)	
Stage 3	102 (1.7)	74 (1.4)	15 (3)	6 (4.2)	15 (10.7)	
Postoperative dialysis	74 (1.2)	40 (0.8)	15 (3)	4 (2.8)	15 (10.7)	<0.001
Vascular complications						0.007
Major	85 (1.4)	69 (1.3)	10 (1.8)	1 (0.6)	5 (2.9)	
Minor	40 (0.6)	31 (0.6)	4 (0.7)	3 (1.8)	2 (1.2)	
Thoracic wound complications	101 (1.6)	86 (1.6)	8 (1.3)	4 (2.1)	3 (1.6)	0.9
Residual MR (after valve repair)						<0.001
Mild	837 (18.4)	717 (17.4)	75 (24.8)	24 (32)	21 (42)	
Moderate	77 (1.7)	69 (1.7)	7 (2.3)	1 (1.3)	–	
Severe	9 (0.2)	5 (0.1)	1 (0.3)	3 (4)	–	
ICU stay (h), median (IQR)	24 (20–48)	23.5 (20–48)	24 (20–96)	40 (20–120)	72 (22–216)	<0.001
Hospital stay (days), median (IQR)	8 (6–12)	8 (6–11)	10 (7–15)	11 (8–17)	12 (8–23)	<0.001

ES: EuroSCORE; ICU: intensive care unit; IQR: interquartile range; MR: mitral regurgitation.

incidence of stroke was 1.4%. As expected, whereas low-risk patients showed low rates of adverse events, patients at increased risk suffered from worse outcomes. Operative mortality remained good in intermediate (3.4%) and high risk groups (3.7%) but was less satisfactory in extreme risk (14.3%). Nevertheless, all these results compare favourably with those reported by other international registries on conventional mitral valve surgery [9, 11]. Multiple factors may explain this observation. First, the proven clinical benefits of minimally invasive mitral valve techniques. In this regard, multiple studies demonstrated that mini-mitral operations are associated with reduced short-term morbidity and faster recovery, when compared with conventional mitral surgery [4, 5]. Second, the high level of volume and experience with mitral valve operations and minimally invasive cardiac surgery techniques by the MMIR participating centres. It is well-recognized that good outcomes are strictly associated with relatively high individual and centre volumes [5, 12, 13]. In our study, the observed mortality was significantly lower than expected in all risk groups. This may suggest that, in experienced centres, less-invasive techniques can be extended to patient who have less optimal surgical risk with satisfactory results. As previously reported for conventional valve surgery [14], the ES II consistently overestimated risk for mini-mitral operations, regardless of the patient's risk. It has to be noted, however, that an increase in ES II remains related to an increase in risk of all adverse outcomes (Table 5). Our findings suggest that achieving an O:E ratio ≤0.7 may be a realistic goal for all mini-mitral programs in heart valve referral centres.

In MMIR, the entire strategic approach to the procedure seems not influenced by the use of less-invasive accesses. The minimally invasive techniques allowed for the full spectrum of mitral repair and replacement techniques to be performed, including concomitant procedures. In particular, tricuspid valve repair was performed in 17% of cases and AF ablation in 42% of patients presenting with preoperative AF, which are consistent with data observed in patients receiving full sternotomy mitral valve operations [11]. Mitral valve repair is the recommended treatment for severe mitral regurgitation and is performed in nearly 60% of patients undergoing mitral valve surgery according to national databases [5, 15, 16]. It has been suggested that less-invasive approaches may lead to surgical compromise, with the surgeon adjusting their repair techniques and resulting in reduced quality repair and lower repair rate [17]. As less-invasive techniques are increasingly used, and mitral valve surgery has recently extended to asymptomatic patients, it is crucial that the surgical access not compromise the valve repair outcome. Our results argue against this assumption. In the MMIR cohort the overall repair rate was 76.2%, with 98.1% of cases showing no or mild residual mitral valve regurgitation postoperatively (Fig. 2). These values included a large number of patients with dysfunctional mitral valve due to ischaemic mitral regurgitation with severe restriction of leaflets, rheumatic valve disease and infective endocarditis, which were not amenable for repair. When considering only patients presenting with degenerative mitral valve regurgitation, the rate of valve repair increases to 92.5%. This observed high adoption rate of valve repair techniques was 25% higher than that observed in

Downloaded from https://academic.oup.com/ejcts/article/63/6/ezad090/7074178 by Biblioteca di Scienze, Università degli studi di Firenze user on 07 January 2025

Table 4: Observed and expected mortality by predicted risk of mortality group

Variable	Observed mortality%	Expected mortality %	O:E ratio	95% CI
EuroSCORE II <4	1	1.4	0.71	0.627–0.816
EuroSCORE II 4–8	3.4	5.6	0.61	0.550–0.789
EuroSCORE II 8–12	3.7	9.8	0.38	0.211–0.616
EuroSCORE II >12	14.3	22.3	0.64	0.522–0.791

CI: confidence interval; O:E: observed to expected.

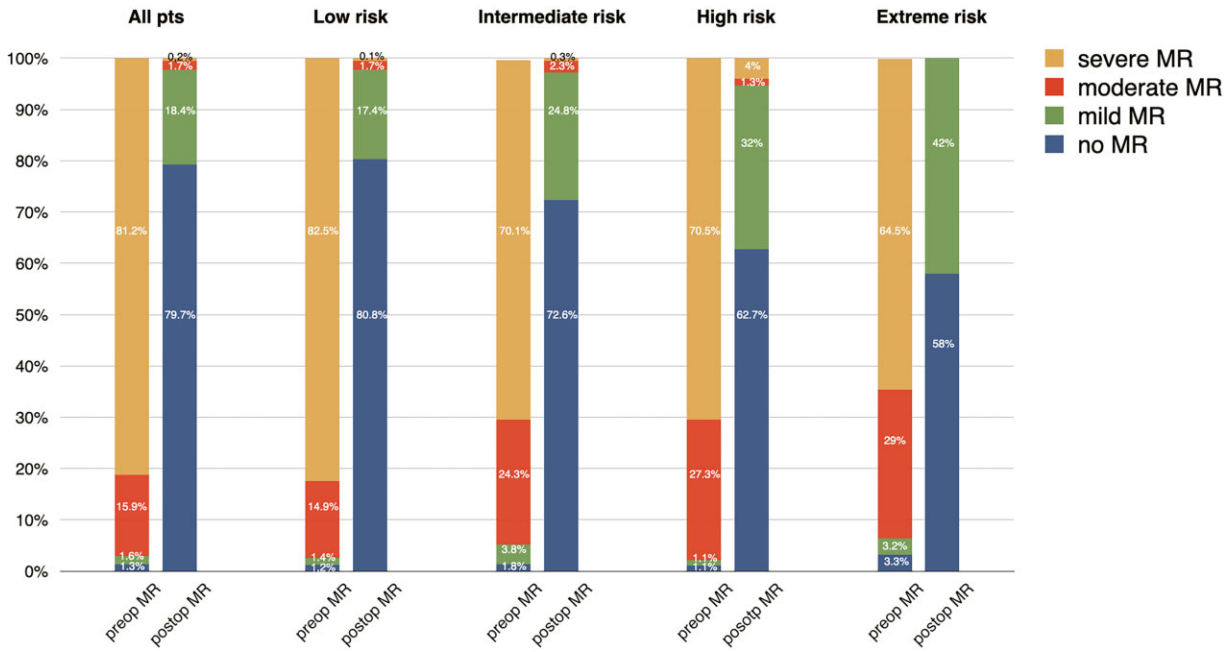


Figure 2: Reduction of mitral valve regurgitation according to patient risk, in patients undergoing valve repair.

Table 5: Impact of patients' risk profile on clinical outcomes

Variable	*P*-Value	Impact of EuroSCORE II (per 1-U increase), adjusted OR/β (95% CI)
In-hospital mortality	<0.001	1.081 (1.046–1.117)
Stroke	0.02	1.052 (1.008–1.097)
Low cardiac output	<0.001	1.099 (1.068–1.132)
Acute kidney injury	<0.001	1.104 (1.075–1.134)
Respiratory failure	<0.001	1.089 (1.066–1.118)
Bleeding	0.005	1.040 (1.012–1.070)
ICU stay (β coefficient)	<0.001	0.215 (0.132–0.240)
In-hospital stay (β coefficient)	<0.001	0.120 (0.092–0.147)

CI: confidence interval; ICU: intensive care unit; OR: odds ratio.

Table 6: Multivariable analysis for in-hospital mortality

Variable	*P*-Value	OR	95% CI
Mitral valve replacement	0.03	1.813	1.047–3.139
Type of cardioplegia	–	–	–
Cross clamp time	<0.001	1.015	1.009–1.022
EuroSCORE II	<0.001	1.081	1.046–1.117
Case volume	–	–	–

CI: confidence interval; OR: odds ratio.

the STS database in patients receiving conventional mitral valve operations [5] and this proportion even increases when considering higher-risk patients [9]. In addition, just 1.2% of patients with an initial attempt at repair ultimately received replacement (Table 2), resulting in a valve repair rate of 98.8% among the valves that were deemed to be highly reparable intraoperatively. We do believe these findings support definitely that less-invasive techniques are not associated with reduced repair rate than those reported with conventional approach, when performed by experienced surgeons.

Downloaded from https://academic.oup.com/ejcts/article/63/6/ezad090/7074178 by Biblioteca di Scienze, Università degli studi di Firenze user on 07 January 2025

Limitations

This study has the limitations of any observational registry involving no adjudication of patient inclusion and data collection. There is no core laboratory to review images, and the investigators are responsible for data reporting from their own institutions. MMIR is built on a voluntary participation; therefore, our data are limited to sites with a mini-mitral program that agree to participate in the registry. The participating centres are tertiary referral centres. As a result, our findings may not reflect management or represent patients treated and followed at non-tertiary centres. Finally, no long-term data are currently available in the MMIR.

CONCLUSIONS

The MMIR is currently the largest worldwide registry that provides a contemporary picture of operative outcomes after minimally invasive mitral surgery in referral centres. Operative results were excellent in low-, intermediate- and high-risk patients, with very low mortality and morbidity rates. Conversely, extreme risk patients showed less satisfactory procedural and clinical outcomes. In MMIR, the ES II model overestimated in-hospital mortality. Thus, our findings could serve as a benchmark for patients in all risk categories whose conditions are being evaluated for any form of mitral valve therapy.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

Conflict of interest: Nikolaos Bonaros receives speaker's honoraria from Edwards, Lifesciences and Medtronic; institutional grant from Edwards Lifesciences and Corcym; and travel grants from Abbott, Medtronic and Edwards Lifesciences. Jorg Kempfert receives speaker honoraria from Edwards, Medtronic, Artivion and Abbott. The other authors have nothing to disclose.

DATA AVAILABILITY

The data underlying this article will be shared on reasonable request to the corresponding author.

Author contributions

Paolo Berretta: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Software; Validation; Writing—original draft; Writing—review & editing. **Jorg Kempfert:** Investigation; Methodology; Validation; Visualization. **Frank Van Praet:** Investigation; Validation; Visualization. **Loris Salvador:** Investigation; Validation; Visualization. **Joseph Lamelas:** Investigation; Validation; Visualization. **Tom C. Nguyen:** Investigation; Validation; Visualization. **Manuel Wilbring:** Investigation; Validation; Visualization. **Marc Gerdisch:** Investigation; Supervision; Validation. **Mauro Rinaldi:** Investigation; Supervision; Validation. **Nikolaos Bonaros:** Investigation; Validation; Visualization. **Thierry Folliguet:** Investigation; Supervision; Validation. **Torsten Doenst:** Investigation; Validation; Visualization. **Nguyen Hoang Dinh:** Investigation; Supervision; Validation. **Pierluigi Stefano:** Investigation; Validation; Visualization. **Tristan Yan:** Investigation; Validation; Visualization. **Carlo Savini:** Investigation; Validation; Visualization. **Antonios Pitsis:** Investigation; Validation; Visualization. **Marco Di Eusanio:** Conceptualization; Investigation; Methodology; Project administration; Supervision; Validation; Visualization.

Reviewer information

European Journal of Cardio-Thoracic Surgery thanks Samuel Heuts, Francesco Pollari and the other anonymous reviewer(s) for their contribution to the peer review process of this article.

REFERENCES

[1] McClure RS, Athanasopoulos LV, McGurk S, Davidson MJ, Couper GS, Cohn LH. One thousand minimally invasive mitral valve operations: early outcomes, late outcomes, and echocardiographic follow-up. J Thorac Cardiovasc Surg 2013;145:1199–206.
[2] 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.
[3] Glauber M, Miceli A, Canarutto D, Lio A, Murzi M, Gilmanov D *et al.* Early and long-term outcomes of minimally invasive mitral valve surgery through right minithoracotomy: a 10-year experience in 1604 patients. J Cardiothorac Surg 2015;10:181.
[4] 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.
[5] Nissen AP, Miller CC, Thourani VH, Woo YJ, Gammie JS, Ailawadi G *et al.* Less invasive mitral surgery versus conventional sternotomy stratified by mitral pathology. Ann Thorac Surg 2021;111:819–27.
[6] Stone GW, Adams DH, Abraham WT, Kappetein AP, Généreux P, Vranckx P *et al.*; Mitral Valve Academic Research Consortium MVARC. Clinical trial design principles and endpoint definitions for transcatheter mitral valve repair and replacement: part 2: endpoint definitions: a consensus document from the mitral valve academic research consortium. J Am Coll Cardiol 2015;66:308–21.
[7] Nashef SA, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR *et al.* EuroSCORE II. Eur J Cardiothorac Surg 2012;41:734–45; discussion 744.
[8] Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ *et al.*; ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J 2017;38:2739–91.
[9] Chatterjee S, Rankin JS, Gammie JS, Sheng S, O'Brien SM, Brennan JM *et al.* Isolated mitral valve surgery risk in 77,836 patients from the Society of Thoracic Surgeons database. Ann Thorac Surg 2013;96:1587–95; discussion 1594.
[10] Mirabel M, Iung B, Baron G, Messika-Zeitoun D, Détaint D, Vanoverschelde JL *et al.* What are the characteristics of patients with severe, symptomatic, mitral regurgitation who are denied surgery. Eur Heart J 2007;28:1358–65.
[11] Gammie JS, Chikwe J, Badhwar V, Thibault DP, Vemulapalli S, Thourani VH *et al.* Isolated mitral valve surgery: the society of thoracic surgeons adult cardiac surgery database analysis. Ann Thorac Surg 2018;106:716–27.
[12] Gammie JS, O'Brien SM, Griffith BP, Ferguson TB, Peterson ED. Influence of hospital procedural volume on care process and mortality for patients undergoing elective surgery for mitral regurgitation. Circulation 2007;115:881–7.
[13] Weiner MM, Hofer I, Lin HM, Castillo JG, Adams DH, Fischer GW. Relationship among surgical volume, repair quality, and perioperative outcomes for repair of mitral insufficiency in a mitral valve reference center. J Thorac Cardiovasc Surg 2014;148:2021–6.
[14] Ad N, Holmes SD, Patel J, Pritchard G, Shuman DJ, Halpin L. Comparison of EuroSCORE II, original EuroSCORE, and The Society of Thoracic surgeons risk score in cardiac surgery patients. Ann Thorac Surg 2016;102:573–9.
[15] Messika-Zeitoun D, Candolfi P, Enriquez-Sarano M, Burwash IG, Chan V, Philippon JF *et al.* Presentation and outcomes of mitral valve surgery in France in the recent era: a nationwide perspective. Open Heart 2020;7:e001339.
[16] Beckmann A, Meyer R, Lewandowski J, Markewitz A, Gummert J. German Heart Surgery Report 2020: the annual updated registry of the German Society for Thoracic and Cardiovascular Surgery. Thorac Cardiovasc Surg 2021;69:294–307.
[17] Anyanwu AC, Adams DH. Should complex mitral valve repair be routinely performed using a minimally invasive approach. Curr Opin Cardiol 2012;27:118–24.

Downloaded from https://academic.oup.com/ejcts/article/63/6/ezad090/7074178 by Biblioteca di Scienze, Università degli studi di Firenze user on 07 January 2025