European Journal of Cardio-Thoracic Surgery 2023, 63(6), ezad147
https://doi.org/10.1093/ejcts/ezad147 Advance Access publication 13 April 2023

ORIGINAL ARTICLE

Cite this article as: Doenst T, Berretta P, Bonaros N, Savini C, Pitsis A, Wilbring M *et al.* Aortic cross-clamp time correlates with mortality in the mini-mitral international registry. Eur J Cardiothorac Surg 2023; doi:10.1093/ejcts/ezad147.

Aortic cross-clamp time correlates with mortality in the mini-mitral international registry

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

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

* Corresponding author. Department of Cardiothoracic Surgery, Universitätsklinikum Jena, Am Klinikum 1, 07747 Jena, Germany. Tel: +49-3641-932-2901; fax: +49-3641-932-2902; e-mail: doenst@med.uni-jena.de (T. Doenst).

Received 25 September 2022; received in revised form 20 March 2023; accepted 12 April 2023

Key question

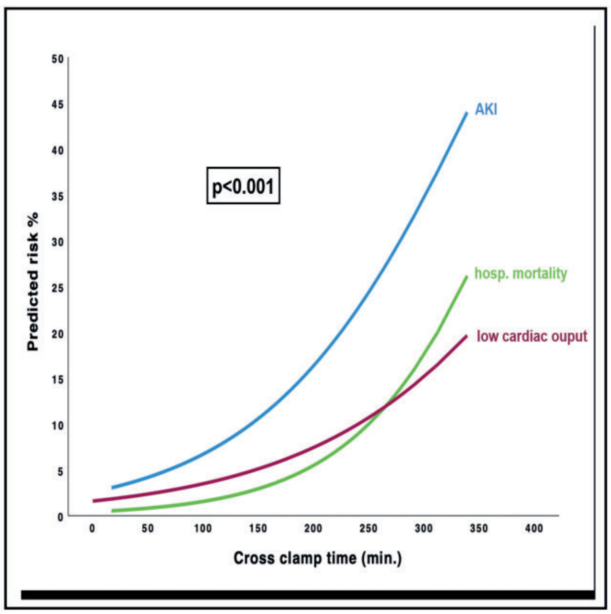
Does aortic cross-clamp times correlate with mortality and clinical outcomes in minimally-invasive mitral valve surgery?

Key finding(s)

Longer aortic cross-clamp times increase mortality, low output and acute kidney injury in min.inv.-mitral valve surgery.

Take-home message

Cross-clamp time is associated with postoperative mortality, heart and kidney failure. Measures to reduce clamp-times may improve outcomes.



Presented at the EACTS Annual Meeting 2022, Milan, Italy, 6 October 2022.

Abstract

OBJECTIVES: Minimally invasive access has become the preferred choice in mitral and/or tricuspid valve surgery. Reported outcomes are at least similar to classic sternotomy although aortic cross-clamp times are usually longer.

METHODS: We analysed the largest registry of mitral and/or tricuspid valve surgery patients (mini-mitral international registry (MMIR)) for the relationship between aortic cross-clamp times, mortality and other outcomes. From 2015 to 2021, 7513 consecutive patients underwent mini-mitral and/or tricuspid valve surgery in 17 international Heart-Valve-Centres. Data were collected according to Mitral Valve Academic Research Consortium (MVARC) definitions and 6878 patients with 1 cross-clamp period were analysed. Uni- and multivariable regression analyses were used to assess outcomes in relation to aortic cross-clamp times.

RESULTS: Median age was 65 years (57% male). Median EuroSCORE II was 1.3% (Inpatient Quality Reporting (IQR): 0.80–2.63). Minimally invasive access was either by direct vision (28%), video-assisted (41%) or totally endoscopic/robotic (31%). Femoral cannulation was used in 93%. Three quarters were repairs with 17% additional tricuspid valve surgery and 19% Atrial Fibrillation (AF)-ablation. Cardiopulmonary bypass and cross-clamp times were 135 min (IQR: 107–173) and 85 min (IQR: 64–111), respectively. Postoperative events were death (1.6%), stroke (1.2%), bleeding requiring revision (6%), low cardiac output syndrome (3.5%) and acute kidney injury (6.2%, mainly stage I). Statistical analyses identified significant associations between cross-clamp time and mortality, low cardiac output syndrome and acute kidney injury (all $P < 0.001$). Age, low ejection fraction and emergent surgery were risk factors, but variables of 'increased complexity' (redo, endocarditis, concomitant procedures) were not.

CONCLUSIONS: Aortic cross-clamp time is associated with mortality as well as postoperatively impaired cardiac and renal function. Thus, implementing measures to reduce cross-clamp time may improve outcomes.

Keywords: Minimally invasive valve surgery • Mini-thoracotomy • Myocardial protection • Myocardial ischemia

ABBREVIATION	
MICS	Minimally invasive cardiac surgery

INTRODUCTION

Minimally invasive access has become the preferred choice for surgical treatment of mitral and/or tricuspid valve disease in many centres. In Germany, for instance, the fraction of mitral procedures performed through a mini-right thoracotomy has already surpassed that for sternotomy (56 vs 44%, [1]). In the beginning of minimally invasive cardiac surgery (MICS) hope for superior outcomes [2] met concerns of higher rates of complications [3, 4]. Recent reports [5, 6] and meta-analyses [7] suggest that the results are at least similar to classic sternotomy approaches and safety concerns are not justified.

However, all reports comparing minimally invasive and sternotomy access to the mitral valve share the common finding that aortic cross-clamp times are longer in the minimally invasive groups [4]. Since cross-clamp time in classic sternotomy surgery has been associated with increased mortality [8], the question arises, whether this relationship also exists in minimally invasive cases.

We therefore analysed the largest currently available international registry of minimally invasive mitral and/or tricuspid valve patients (mini-mitral international registry (MMIR)) for the relationship between aortic cross-clamp times and mortality as well as other outcomes.

METHODS

Ethics 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.

International registry and patient data

The MMIR is an independent registry involving 17 international Heart Valve Centres. The centres combined all patients who received mini-mitral operations with or without associated procedures between 2015 and 2021. Perioperative characteristics and in-hospital outcomes of 7513 consecutive patients were collected according to Mitral Valve Academic Research Consortium (MVARC) definitions [9]. Definitions of end-points were as follows: low cardiac output: inotropic support>24 h or the use of temporary mechanical circulatory support.

Acute kidney injury: 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.

Stroke: 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.

Residual MR: Residual Mitral Regurgitation (MR) includes mild, moderate or severe MR (postoperative echo).

Patients who required a second episode of aortic cross-clamping as well as patients who received ventricular fibrillation or beating heart surgery and patients with missing cross-clamp time data were excluded ($n = 635$). The internal review boards (Ethics Committees) of all centres approved participation in the registry and this analysis. There was no requirement for individual informed consent. Outcomes of valvular surgery were recorded based on information from discharge echocardiography.

Statistical analysis

Categorical data are expressed as frequencies and percentages; continuous data are presented as mean ± Standard Deviation (SD) or median with 1st and 3rd quartiles (Q1–Q3) as appropriate. Missing data were not defaulted to zero, and denominators reflect only actual reported data. The cross-clamp time was tested preliminary for any association with the outcome variables by uni-variable regression analysis. If found to be significantly ($P < 0.05$) associated with 1 or more outcome variable, cross-clamp time was tested as independent risk factor within multi-variable models (backward stepwise logistic regression) where the other factors significantly associated with outcome variables were entered as covariates. The variance inflation factor was calculated to assess multicollinearity in the models. Statistical analysis was performed using Statistical Package for Social Sciences version 27.0 (IBM SPSS Inc., Chicago, IL).

RESULTS

Table 1 shows the demographic data of 6878 consecutive patients. They had a median age of 65 years, and 57% were male. Almost half of all patients were in New York Heart Association (NYHA)-class III–IV. One-third had preoperative atrial fibrillation, 15% had an estimated Glomerular Filtration Rate (eGFR) below 50 ml/min and over 80% had Ejection Fraction (EF) > 50%. Median EuroSCORE II was 1.3% (Inpatient Quality Reporting (IQR): 0.80–2.63). About two-thirds had degenerative MR, 14.3% had functional MR followed by rheumatic, endocarditis or other reasons. The small fraction of patients with moderate MR were all highly symptomatic and indications for surgery came primarily from severe tricuspid regurgitation, tumour or endocarditis.

Table 2 shows the intraoperative characteristics. Minimally invasive access was achieved through the right chest either by direct vision (28%), video-assisted (41%) or totally endoscopic/robotic (31%). The vast majority (93%) was performed with femoral cannulation. In 84% of cases, a transthoracic clamp was used for cross-clamping. Myocardial protection was performed at the discretion of the operating surgeon. Single-shot crystalloid cardioplegia was used in most cases (58%) followed by blood cardioplegia (42%). Mitral valve repair was performed in three quarters and replacement in one-quarter of patients. The majority of replacements were for stenosis and/or rheumatic reasons, followed by endocarditis, redo and replacements for functional MR. Concomitant procedures were performed in one-third of patients (tricuspid surgery 17%, Atrial Fibrillation (AF)-ablation 19%). Median cardiopulmonary bypass time (IQR) was 135 min (107–173) and cross-clamp time was 85 min (64–111). Cross-clamp times were shortest with direct vision (median 72 min, IQR: 55–96) and longest with robotic assistance (median: 129 min, IQR: 99–147 min).

Table 3 shows the postoperative outcomes. In-hospital mortality was 1.6%. Stroke occurred in 1.2%, bleeding requiring revision in 6%, low cardiac output syndrome in 3.5% and acute kidney injury in 6.1% (mainly stage I). Average stay was 1 day in the Intensive Care Unit (ICU) and 8 days in the hospital.

Table 4 shows the results of the uni-variable and Table 5 of the multi-variable statistical analyses. There were significant associations between cross-clamp times and in-hospital mortality, low cardiac output syndrome and acute kidney injury (all $P < 0.001$). There was no relationship to stroke or residual MR. Figure 1 illustrates the increasing risk for in-hospital mortality, low cardiac output syndrome and acute kidney injury with increasing clamp times.

Additional, stepwise analyses for clamp time (Table 6) revealed elevated odds ratios for mortality in the groups with longer clamp times, which was not significant if patients above and below 60 min were compared (Odds Ratio (OR): 1.48; 95% Confidence Interval (CI): 0.87–2.53, $P = 0.2$). Raising the dividing threshold to 90 min (OR: 1.87; 95% CI: 1.28–2.78, $P = 0.002$) or

Table 1: Patients' characteristics ($n = 6878$)

	Frequency	%
Male	3928	57.2
Age, median (IQR)	65 (55–73)	
NYHA class III–IV	3109	47.6
Hypertension	3618	57.7
Diabetes	612	8.9
On insulin	373	5.4
Oral therapy	239	3.5
Dyslipidaemia	1985	31.9
Smoking	810	12.9
Obesity	960	14.3
AF	2366	37.4
Paroxysmal	762	32.2
Persistent	479	20.2
Long-standing persistent	231	9.8
Permanent	620	26.2
Undefined	274	11.6
PM	194	2.8
Renal impairment (eGFR < 85 mm)	3914	58.6
Moderate (eGFR <85 and >50)	2901	43.5
Severe (eGFR < 50)	1013	15.2
Dialysis	73	1.1
CAD	876	13.1
Poor mobility	129	2
Chronic lung disease	620	9
Active endocarditis	254	3.7
Cerebrovascular arteriopathy	116	1.8
Peripheral arteriopathy	170	2.5
Pulmonary hypertension	2620	39.8
Previous cardiac surgery	369	5.4
Mitral valve regurgitation		
Mild	277	4
Moderate	1084	15.8
Severe	5315	77.3
MV disease aetiology		
Degenerative	4362	68.5
Functional	910	14.3
Rheumatic	527	8.3
Endocarditis	290	4.6
Failure of previous MV surgery	172	2.7
Tumour	6	0.1
Mitral valve stenosis		
Mild	168	2.7
Moderate	167	2.7
Severe	314	5
LV function		
Good (LVEF > 50%)	5584	82.3
Moderate (LVEF 31–50%)	1068	15.7
Poor (LVEF 21–30%)	117	1.7
Very poor (≤20%)	13	0.2
Urgent/emergent status	408	5.9
EuroSCORE II, median (IQR)	1.30 (0.80–2.63)	

AF: Atrial Fibrillation; CAD: Coronary Artery Disease; eGFR: estimated Glomerular Filtration Rate; IQR: Inpatient Quality Reporting; LV: Left Ventricular; LVEF: Left Ventricular Ejection Fraction; MV: Mitral Valve; NYHA: New York Heart Association; PM: Pacemaker.

Table 2: Operative data

	Frequency	%
Surgical approach		
Direct vision	1919	27.9
Video-assisted	2831	41.2
Totally endoscopic	2072	30.1
Robotic	51	0.7
Surgical access		
Anterolateral	5134	74.7
Transaxillary	797	11.6
Periareolar	637	9.3
Ministernotomy	307	4.5
Conversion to full sternotomy	128	1.9
Arterial cannulation site		
Femoral artery	6278	93.1
Axillary artery	104	1.5
Ascending aorta	333	4.9
Other	30	0.4
Aortic cross-clamping type		
External clamp	5779	84.1
Endoclamp	1095	15.9
Cardioplegia		
Crystalloid	3973	58.1
Blood	2859	41.8
Type of surgery		
Mitral valve repair	5224	76
Mitral valve replacement	1653	24
Associated procedures	2186	31.8
Tricuspid surgery	1140	16.6
AF surgery	1272	18.5
Aortic valve replacement	128	1.9
Root/ascending aorta surgery	10	0.1
LAAA closure	964	14.7
CPB time (min), median (IQR)	135 (107–173)	
Cross-clamp time (min), median (IQR)	85 (64–111)	

AF: Atrial Fibrillation; IQR: Inpatient Quality Reporting; LAAA: Left Atrial Appendage Aneurysm.

120 min (OR: 3.02; 95% CI: 2.01–4.54, $P < 0.001$) revealed significantly increased odds ratios, illustrating the increasing mortality risk with increasing clamp times (Fig. 2). Other independent risk factors for mortality were age, reduced ejection fraction and emergent or urgent surgery (all $P < 0.001$). However, variables of 'increased complexity' such as redo, endocarditis, associated procedures or the type of cardioplegia were included in the multivariable analysis and did not emerge as risk factors.

DISCUSSION

We demonstrate in this large multicentre registry analysis, that aortic cross-clamp time is associated with mortality as well as postoperatively impaired cardiac and renal function. Thus, implementing measures to reduce cross-clamp time may improve outcomes.

The observed relationship may have been expected and are corroborative as other analyses found similar relationships before, although primarily in sternotomy cases [8]. Yet, it is exactly that observation that sparked this analysis because the repeatedly documented similarity in outcome [7] (or even superiority with minimally invasive access [5]) questions this relationship in MICS. We here demonstrate that simply operating without opening the sternum does not offset the relationship between cardioplegic ischaemia time and mortality. The literature provides reports of mitral valve repair in large series where clamp times differed between 5 and 22 min between sternotomy and MICS cases (mean difference 14 min) [6]. Translating these differences to our results, the additional clamp time would also translate into an increase in mortality risk due to minimally invasive access. Thus, if there is indeed no difference between MICS and sternotomy, MICS must confer a protective effect somehow that outweighs any additional detrimental effect of the longer clamp times in MICS. Our analysis does not contain a sternotomy cohort, which may serve as comparator. Thus, it is difficult to relate the results to outcomes from such cases. However, if one would extrapolate the odds ratio results from the multivariable analysis, 20 min of extra

Table 3: In-hospital outcomes

	Frequency	%
In-hospital mortality	107	1.6
Stroke	79	1.2
Delirium	372	6.2
Intubation time (h), median (IQR)	8 (5–13)	
Re-intubation/tracheostomy	225	3.3
Bleeding requiring revision	380	5.8
New onset AF	1005	15.9
Definitive PM implantation	454	6.6
Myocardial infarction	54	0.8
Periprocedural (≤48 h)	47	0.7
Spontaneous (>48 h)	7	0.1
Low cardiac output syndrome	234	3.5
Acute kidney injury	366	6.1
Stage 1	215	3.6
Stage 2	49	0.8
Stage 3	102	1.7
Dialysis	103	1.7
Vascular complications	120	1.9
Major vascular complications	*82*	*1.3*
Minor vascular complications	*38*	*0.6*
Thoracic wound complications	97	1.4
MV insufficiency (after MV repair)		
Mild	810	17.7
Moderate	64	1.4
Severe	8	0.2
Redo for early-valve repair-failure	49	0.8
ICU stay (h), median (IQR)	24 (20–48)	
Hospital stay (days), median (IQR)	8 (6–11)	

AF: Atrial Fibrillation; IQR: Inpatient Quality Reporting; MV: Mitral Valve; PM: Pacemaker.

Table 4: Univariate association between cross-clamp time and postoperative outcomes

Variable	*P*-Value	OR/β	95% CI
In-hospital mortality	<0.001	1.014	1.009 to 1.019
Stroke	0.7	1.002	0.995 to 1.008
Low cardiac output	<0.001	1.009	1.005 to 1.012
AKI	<0.001	1.010	1.007 to 1.013
Residual MR (mod–sev)	0.2	1.004	0.998 to 1.011
Death/low output/AKI	0.9	1.000	0.998 to 1.002
ICU stay	<0.001	−0.176	−0.244 to −0.109
In-hospital stay	0.4	−0.004	−0.12 to 0.004

AKI: Acute Kidney Injury; CI: Confidence Interval; OR: Odds Ratio.

Table 5: Multivariable analysis (backward stepwise logistic regression)

Variable	*P*-Value	OR/HR	95% CI
For in-hospital mortality			
Age (per year)	<0.001	1.060	1.037–1.084
Chronic lung disease	0.02	1.873	1.103–3.179
Peripheral arteriopathy	0.03	2.269	1.077–4.779
Dialysis	<0.001	5.128	1.939–13.562
Reduced LVEF (<50%)	<0.001	2.608	1.671–4.070
Previous cardiac surgery	0.01	2.201	1.185–4.091
Urgent/emergent status	<0.001	4.147	2.460–6.992
Cross-clamp time (per min)	<0.001	1.018	1.012–1.023
For low cardiac output			
Hypertension	0.03	1.410	1.039–1.913
Reduced LVEF (<50%)	<0.001	2.139	1.571–2.912
Pulmonary hypertension	0.02	1.423	1.064–1.903
Urgent/emergent status	<0.001	2.652	1.761–3.996
Cross-clamp time (per min)	<0.001	1.009	1.005–1.012
Mitral valve replacement	<0.001	2.459	1.838–3.288
For acute kidney injury (AKI)			
Age (per year)	–	–	–
eGFR	<0.001	0.99	0.986–0.995
Obesity	0.013	1.477	1.087–2.007
Diabetes	0.04	1.425	1.018–1.994
Reduced LVEF (<50%)	<0.001	1.549	1.198–2.003
Urgent/emergent status	<0.001	2.010	1.394–2.897
Cross-clamp time (per min)	<0.001	1.012	1.009–1.015
Associated procedures	–	–	–

AKI: Acute Kidney Injury; CI: Confidence Interval; eGFR: estimated Glomerular Filtration Rate; HR: Hazard Ratio; OR: Odds Ratio; LVEF: Left Ventricular Ejection Fraction.

cross-clamp time would translate into 36% additional risk (OR for in-hospital mortality per min: 1.018; Table 5). Although risk in the entire cohort was low with <2% total mortality, the relative increase is still not negligible, although it is only 1 aspect in the context of a complex operation.

Another aspect that needs to be considered in the context of myocardial protection and cross-clamp times is the type of cardioplegia. The majority of centres used crystalloid cardioplegia, followed in frequency by blood cardioplegia. While individual surgeon opinions may opt for one in much greater favour than for the other, the literature has repeatedly failed to demonstrate significant differences between different types of cardioplegia [10]. Similarly, in our analyses, the type of cardioplegia did not emerge as risk factor in the multi-variable analysis.

The findings highlight the importance of measures that help keeping cross-clamp times low. Maintaining a certain case load appears important as practice increases operative speed. The association of case load and operative outcome has been documented by several investigators [11, 12], although many other factors are likely to contribute to this association besides cross-clamp time. Patient selection and adopting complexity to one's own level of expertise may be other ways to keep cross-clamp times low, because complex repairs take longer than simple ones and experienced surgeons may perform complex repairs in the same time as inexperienced surgeon need for simpler repairs. This rationale brings us to appropriate surgical training. Our findings here can be interpreted as a strong statement for simulating minimally invasive surgery (i.e. training the handling of instruments, needles and knot tying in

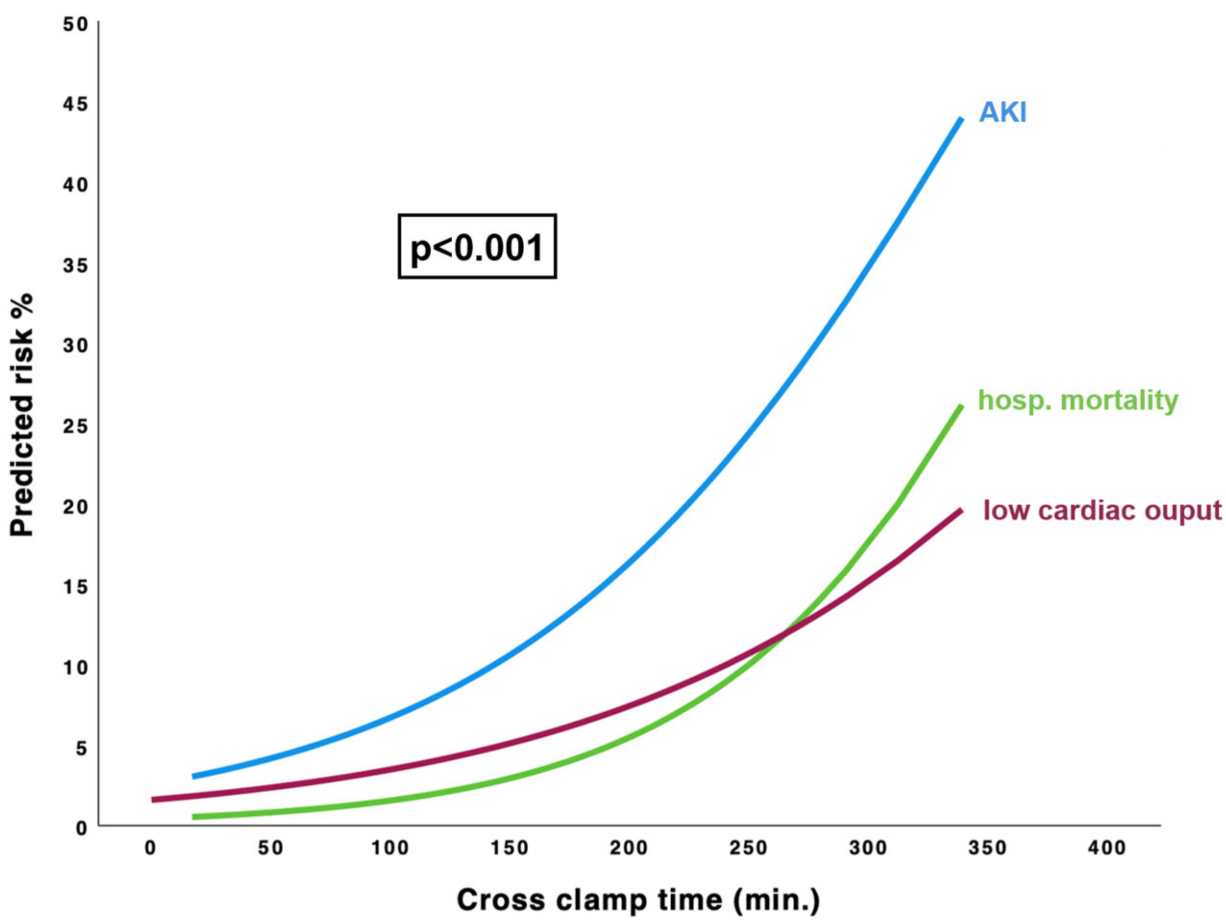


Figure 1: Relationship of predicted risk and mortality for acute kidney injury (Acute Kidney Injury (AKI), blue line), low output syndrome (red line) and in-hospital mortality (green line).

Table 6: Univariate association between cross-clamp time and postoperative outcomes

Variable	*P*-Value	OR	95% CI
>60 min			
In-hospital mortality	0.2	1.480	0.865–2.532
Stroke	0.5	1.235	0.690–2.210
Low cardiac output	0.2	1.235	0.876–1.741
AKI	0.03	1.359	1.036–1.784
Residual MR (mod–sev)	0.3	1.369	0.765–2.449
Death/low output/AKI	0.8	0.976	0.818–1.164
>90 min			
In-hospital mortality	0.002	1.868	1.257–2.777
Stroke	0.5	0.860	0.543–1.363
Low cardiac output	0.05	1.296	0.995–1.687
AKI	<0.001	1.846	1.492–2.283
Residual MR (mod–sev)	0.3	1.277	0.816–1.998
Death/low output/AKI	0.5	0.946	0.812–1.102
>120 min			
In-hospital mortality	<0.001	3.022	2.012–4.538
Stroke	0.71	1.108	0.618–1.984
Low cardiac output	<0.001	1.824	1.351–2.464
AKI	<0.001	2.167	1.706–2.753
Residual MR (mod–sev)	0.2	1.427	0.839–2.427
Death/low output/AKI	0.1	1.157	0.949–1.410

AKI: Acute Kidney Injury; CI: Confidence Interval; OR: Odds Ratio.

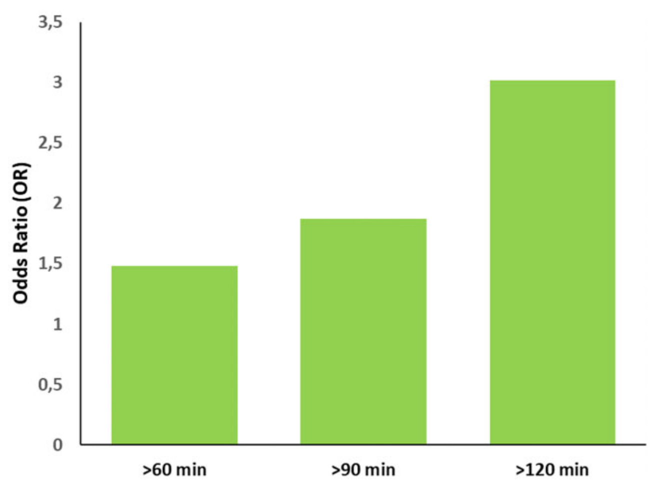


Figure 2: Odds ratios for in-hospital mortality from stepwise multivariable analyses for increasing cut-offs of aortic cross-clamp time. Note that the higher the clamp time cut-off, the greater mortality risk.

mock models) aiming to reduce the required time for the live process. Other technical aspects may be the use of direct vision or applying knot tying devices that may also help to reduce clamp times but did not emerge as specific factors in this analysis.

Limitations

This study is limited by its retrospective nature and the lack of a control group with sternotomy access. However, the knowledge of the existence of the relationship of aortic cross-clamp time and mortality may help to enforce efforts to speed up our minimally invasive game.

CONCLUSION

In minimally invasive mitral valve surgery, aortic cross-clamp time is associated with mortality as well as postoperatively impaired cardiac and renal function. Thus, implementing measures to reduce cross-clamp time may improve outcomes.

Conflict of interest: Nikolaos Bonaros received scientific grants from Edwards Lifesciences and Corcym and speaker's honoraria from Edwards Lifesciences, Medtronic, and Vascular Graft Solutions. Jorg Kempfert received speaker's honoraria from Edwards, Medtronic, Artivion, and Abbott. All other authors have nothing to declare.

DATA AVAILABILITY

The data underlying this article are available in the article.

Author contributions

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

Reviewer information

European Journal of Cardio-Thoracic Surgery thanks Walter Randolph Chitwood Jr, Jules R Olsthoorn and the other, anonymous reviewer(s) for their contribution to the peer review process of this article.

ACKNOWLEDGEMENT

We thank Mr Benjamin May for his editorial assistance.

REFERENCES

[1] Beckmann A, Meyer R, Lewandowski J, Markewitz A, Blaßfeld D, Böning A. German Heart Surgery Report 2021: the Annual Updated Registry of the German Society for Thoracic and Cardiovascular Surgery. Thorac Cardiovasc Surg 2022;70:362–76.

[2] Murzi M, Solinas M, Glauber M. Is a minimally invasive approach for re-operative mitral valve surgery superior to standard resternotomy? Interact CardioVasc Thorac Surg 2009;9:327–32.

[3] 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.

[4] Doenst T, Lamelas J. Do we have enough evidence for minimally-invasive cardiac surgery? A critical review of scientific and non-scientific information. J Cardiovasc Surg (Torino) 2017;58:613–23.

[5] Sá M, Van den Eynde J, Cavalcanti LRP, Kadyraliev B, Enginoev S, Zhigalov K *et al.* Mitral valve repair with minimally invasive approaches

vs sternotomy: a meta-analysis of early and late results in randomized and matched observational studies. J Card Surg 2020;35:2307–23.
[6] Doenst T, Diab M, Sponholz C, Bauer M, Färber G. The opportunities and limitations of minimally invasive cardiac surgery. Dtsch Arztebl Int 2017;114:777–84.
[7] Sündermann SH, Czerny M, Falk V. Open vs. minimally invasive mitral valve surgery: surgical technique, indications and results. Cardiovasc Eng Technol 2015;6:160–6.
[8] Doenst T, Borger MA, Weisel RD, Yau TM, Maganti M, Rao V. Relation between aortic cross-clamp time and mortality–not as straightforward as expected. Eur J Cardiothorac Surg 2008;33:660–5.
[9] 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.
[10] Allen BS. Myocardial protection: a forgotten modality. Eur J Cardiothorac Surg 2020;57:263–70.
[11] Chikwe J, Toyoda N, Anyanwu AC, Itagaki S, Egorova NN, Boateng P *et al.* Relation of mitral valve surgery volume to repair rate, durability, and survival. J Am Coll Cardiol 2017;S0735-1097(17)30677-0. doi: 10.1016/j.jacc.2017.02.026.
[12] Khera R, Pandey A, Koshy T, Ayers C, Nallamothu BK, Das SR *et al.* Role of hospital volumes in identifying low-performing and high-performing aortic and mitral valve surgical centers in the United States. JAMA Cardiol 2017;2:1322–31.