Outcomes and Predictors of Mortality After Mitral Valve Surgery in High-Risk Elderly Patients: The Heidelberg Experience

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEFG 1 **Sabreen Mkalaluh**
ABCDEFG 1 **Marcin Szczechowicz**
ABCDEFG 1 **Bashar Dib**
ABCDEFG 1 **Gabor Szabo**
ABCDEFG 1 **Matthias Karck**
ABCDEFG 1,2 **Alexander Weymann**

1 Department of Cardiac Surgery, Heart and Marfan Center, University of Heidelberg, Heidelberg, Germany
2 Department of Cardiac Surgery, University Hospital Oldenburg, European Medical School Oldenburg-Groningen, Carl von Ossietzky University Oldenburg, Oldenburg, Germany

Corresponding Author: Alexander Weymann, e-mail: weymann.alexander@googlemail.com
Source of support: Departmental sources

Background: Overall, life expectancy at the age of 80 has significantly increased in the industrialized world and the proportion of this age class undergoing cardiac surgery has also grown. In this context, we have analyzed a contemporary series of octogenarians undergoing mitral valve surgery at our institution.

Material/Methods: We performed a retrospective analysis of 138 consecutive octogenarians receiving mitral valve surgery between January 2006 and April 2017. Preoperative comorbidities, early mortality, postoperative clinical course, and predictors of mortality were examined.

Results: The mean age was 82.4±2.0 years and 50% (n=69) were male. Preoperative comorbidities included history of heart infarction (24.6%, n=34), chronic renal failure (37.7%, n=52), and COPD (27.5%, n=38). A total of 52.9% (n=73) had a history of previous cardiac decompensation, while 20 (14.5%) presented with cardiogenic shock or cardiac arrest. In all, 33 patients (23.9%) underwent emergency surgery. There were only 39 isolated mitral valve procedures, while 99 patients (71.7%) underwent various concomitant procedures. The intensive care unit average length of stay was 5.3±7.5 days. Respiratory complications and sepsis were the most frequent postoperative complications. Emergency surgery and concomitant coronary artery bypass grafting were the most important predictors of early mortality. The overall 30-day mortality was 18.1% (n=25). The mean follow-up time was 1.7±2.3 years.

Conclusions: Octogenarians are increasingly represented in cardiac surgery and combined procedures. Prudent patient selection is necessary for optimizing postoperative outcomes among the elderly. In our seriously ill octogenarian cohort, mitral valve surgery was associated with moderate but acceptable mid-term survival.

MeSH Keywords: Cardiac Surgical Procedures • Mitral Valve Annuloplasty • Mitral Valve Insufficiency

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/906003

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Background

Although age is considered as an independent risk factor for increased mortality and morbidity after cardiac surgery, the proportion of octogenarians admitted to cardiac surgery in Germany has grown from 1% in 1990 to 14.1% in 2015 [1–4]. Especially in the aging population, mitral regurgitation is associated with high morbidity and mortality rates [5]. Furthermore, mitral valve surgery remains controversial in terms of use in octogenarians on grounds of high early mortality and poor long-term survival [6–9]. Various studies at high-volume cardiac centers reported in-hospital and 30-day mortality up to 25% in octogenarians after mitral valve surgery [2,8,10,11]. One- and five-year survival rates after mitral valve replacement were reported as 67–56% and 45–29% versus 71–69% and 59–23% after mitral valve repair [6,8]. Additionally, more and more octogenarians need various combined procedures, which may also be associated with worse survival and higher complications rates [2]. Surgical procedures in this age class present a challenge to surgeons, especially in the era of growing interest in transcatheter mitral valve therapy as a less invasive alternative approach [2,12,13]. The cardiac surgical community should offer effective and safe treatment options for these fragile patients. A number of centers, for example, perform the minimally invasive approach in the mitral valve surgery with acceptable outcome [12,14].

The aim of our study is to investigate the perioperative complications, predictors of mortality, and mid-term survival in patients aged ≥80 undergoing mitral valve surgery in our institution.

Material and Methods

Study population

We analyzed a total of 138 consecutive octogenarian patients undergoing elective or emergency mitral valve surgery, with or without concomitant procedures, between January 2006 and April 2017 in our clinic. Most patients suffered from mitral regurgitation due to structural pathology or annular dilation. We included patients with endocarditis, patients who underwent redo surgery, and patients with failed interventional procedures. We stratified our cohort into two groups: isolated mitral valve surgery (repair or replacement) and concomitant procedures (aortic/tricuspid valve procedures or coronary artery bypass grafting).

Surgical procedures

Mitral valve surgery was performed through the conventional median sternotomy as well as right lateral mini-thoracotomy.

Cardiopulmonary bypass was used in all procedures. Arterial cannulation in the ascending aorta or right femoral artery and venous cannulation in venae cavae or femoral vein were performed. Intraoperative transesophageal echocardiography was performed in all cases. Various mitral valve repair techniques were performed. We used, for example, annuloplasty with Edwards ring or Carpentier ring, quadrangular and triangular resection, or chordae tendineae replacement. For the mitral valve replacement, we used the biological prosthesis Hancock II in most cases; two patients received biological Perimount Magna prostheses.

Definitions

Postoperative respiratory insufficiency was defined as re-intubation, tracheotomy, and total intubation >72 hours; postoperative renal failure was defined as necessary for new dialysis or elevation of creatinine level >1 mg/dL as preoperatively level. Postoperative stroke was defined as new permanent or temporary neurological deficit. Emergency surgery was defined as surgery in patients with cardiogenic shock, cardiac arrest, and septic endocarditis. Early mortality was defined as any death occurring within 30 days after surgery.

Statistical analysis

The statistical analysis was performed using SPSS for Mac, version 24 (IBM Corp.). Continuous variables are described as mean ± standard deviation. Categorical variables are presented by absolute numbers and percentages. The Pearson chi-square test was used to investigate the dependence between categorical variables. We used the univariate logistic regression to investigate the influence of relevant variables on 30-day mortality. For assessing the risk factors of short-term mortality, the univariate Cox proportional hazard regression analysis was performed. The results were considered significant at a level of $p<0.05$. The cumulative survival was estimated using the Kaplan-Meier method.

Results

Preoperative data

The mean age was 82.4±2.0 years at the time of surgery, and half of the patients were male (n=69, 50%). The mean body mass index (BMI) was 25.3±3.9 kg/m^2. Preoperatively, 49.3% of the patients (n=68) had a preserved left ventricular systolic function, and 7.2% (n=10) had undergone previous cardiac surgery. A total of 73 patients (52.9%) had a history of previous cardiac decompensation. Severe pulmonary hypertension and relevant tricuspid insufficiency were diagnosed in 64.5% and 32.6% of patients, respectively. In 33 cases (23.9%), emergency surgery was performed; among them, 20 patients (14.5%)

presented cardiogenic shock or cardiac arrest, and 34 patients (24.6%) had experienced myocardial infarctions in their medical history. In all, 112 patients (81.2%) presented with New York Heart Association (NYHA) classification classes III and IV. Three patients already had intra-aortic balloon pump preoperatively. Five patients underwent surgical revision after failed MitraClip procedures. One patient, who had two previous cardiac operations (CABG 10 years and MV replacement five years before), died after failed transcatheter valve-in-valve implantation by cardiologists and following emergency surgical mitral valve replacement. Another patient, after failed transcatheter aortic valve implantation, underwent combined surgical valve procedure.

We observed various etiologies of the mitral valve regurgitation (n=121): structural pathologies (n=107, 77.5%), ischemic cardiomyopathy or post-infarctional (n=11; 8.0%), rheumatic disease (n=1, 0.7%), paravalvular leakage after previous mitral valve replacement (n=1, 0.7%), and degeneration of valve prosthesis (n=1, 0.7%). Endocarditis was to be found in 10 patients (7.2%), while two patients (1.4%) had mitral valve stenosis and another five (3.6%) had combined mitral defect. In Tables 1 and 2, patient demographics and co-morbidities are outlined in detail.

Surgical data

Surgical data are illustrated in detail in Table 3. Overall, mean duration of the surgery was 271±84 minutes, with mean cardiopulmonary bypass (CPB) time of 164±58 minutes and a mean cross clamp time of 98±35 minutes. Isolated mitral valve surgery was performed in 39 cases (28.3%). Overall, 34.1% patients (n=47) received MV repair and 66% (n=91) had MV replacement. A total of 99 patients (71.7%) underwent various concomitant procedures: 31 (22.5%) had aortic valve replacement, 52 (37.7%) had coronary artery bypass grafting (CABG), and 44 (31.9%) had tricuspid valve repair. One patient had aortic root replacement due to an intraoperative injury.

Early outcome

In-hospital outcomes and early mortality in relating to surgical procedures are summarized in Tables 4 and 5. The overall 30-day mortality was 18.1% (n=25), while combined procedures were not associated with significantly higher rate than isolated mitral valve procedures (p=0.2). Redo surgery had no influence on early mortality (p=0.8). Octogenarians showed high incidence of major postoperative complications. The incidence of cerebrovascular events was 7.2% (n=10) and postoperative hemorrhage requiring exploration was 2.9% (n=4). In all, 14 patients (10.1%) received inferior pericardiotomy due to pericardial tamponade. One patient suffered postoperative myocardial infarction (0.7%). The mean mechanical ventilation time was

Table 1. Patients' preoperative characteristics.

Characteristics	Value
Number of patients	138
Age [years]	82.4±2.0
Female	69 (50%)
Body mass index [kg/m²]	25.3±3.9
Emergency surgical indication	**33 (23.9%)**
Including cardiogenic shock	20 (14.5%)
Preoperative intubation	2 (1.4%)
Preoperative intraaortic balloon pump	3 (2.2%)
Preserved left ventricular systolic function	**68 (49.3%)**
New York Heart Association functional class	
I	8 (5.8%)
II	18 (13%)
III	79 (57.2%)
IV and shock	33 (23.9%)
Disease of the mitral valve	
Infective endocarditis	10 (7.2%)
Mitral valve regurgitation	121 (87.7%)
Mitral valve stenosis	2 (1.4%)
Combined mitral defect	5 (3.6%)
Relevant disease of other valves	
Aortic stenosis	20 (14.5%)
Aortic regurgitation	47 (34%)
Tricuspid regurgitation	45 (32.6%)
Previous cardiac valvular interventions	
Failed Mitra Clip	5 (3.6%)
Failed transcatheter aortic valve implantation	1 (0.7%)
Failed transcatheter mitral valve-in-valve implantation	1 (0.7%)

63±114 hours. A total of 10 patients (7.2%) had to be re-intubated and 17 (12.3%) received tracheotomy. In 19.6% (n=27) of the cases, severe acute renal failure occurred and temporary dialysis was necessary. Due to postoperative bradycardia, in 10 patients (7.2%), pacemaker implantation was carried out. We observed relatively high incidence of sepsis (n=14, 10.1%) and pneumonia (n=18, 13%). Sternal wound infection occurred

Table 2. Patients' medical history.

Characteristics	Value
Comorbidities	
Arterial hypertension	120 (86.9%)
Coronary artery disease	109 (79%)
Previous percutaneous coronary angioplasty	21 (15.2%)
Previous myocardial infarction	34 (24.6%)
Smoking	27 (19.6%)
Hyperlipidaemia	71 (51.4%)
Peripheral vascular disease	21 (15.2%)
Chronic obstructive pulmonary disease (COPD)	38 (27.5%)
Diabetes mellitus	39 (28.3%)
Stroke	14 (10.1%)
Transient ischemic attack	4 (2.9%)
Previous cardiac surgery	10 (7.2%)
Atrial fibrillation (chronic or paroxysmal)	84 (69.9%)
Preoperative sinus rhythm	101 (73.2%)
Non-terminal chronic kidney disease	52 (37.7%)
Dialysis	2 (1.4%)
Pneumonia or sepsis	17 (12.4%)
Previous cardiac decompensation	73 (52.9%)
Pulmonary hypertension	89 (64.5%)
Previous cardiac surgery	
Coronary artery bypass grafting	3 (2.2%)
Aortic valve replacement	5 (3.6%)
Mitral valve replacement	4 (2.9%)
Tricuspid valve repair	1 (0.7%)
Number of previous cardiac operations	
1	8 (6%)
2	2 (1.4%)

Table 3. Surgical data.

Characteristics	Value
Emergency surgery	33 (23.9%)
Intraoperative data	
Median sternotomy as a primary approach	125 (90.6%)
Lateral thoracotomy as a primary approach	15 (10.9%)
Bicaval cannulation	122 (88.4%)
Femoral vessels cannulation	16 (11.6%)
Operation time [min]	271±84
Cardiopulmonary bypass (CPB) time [min]	164±58
Cross-clamp time [min]	98±35
Lowest intraoperative body temperature [°C]	33.0±1.9
Type of mitral valve surgery	
Median sternotomy – mitral valve replacement	87 (63.1%)
Median sternotomy – mitral valve reconstruction	38 (27.5%)
Lateral thoracotomy – mitral valve replacement	4 (2.9%)
Lateral thoracotomy – mitral valve reconstruction	9 (6.5%)
Concomitant procedures – also, performed in various combinations	
Coronary artery bypass grafting (CABG)	52 (37.7%)
Tricuspid valve reconstruction (TVr)	44 (31.9%)
Aortic valve replacement (AVR)	31 (22.5%)
Isolated mitral valve surgery	**39 (28.3%)**
Number of concomitant procedures	
1	76 (55.1%)
2	21 (15.2%)
3	3 (2.2%)
Intraoperative transfusions	
Packed red cells [ml]	1350±1800
Platelets [ml]	323±700
Fresh frozen plasma [ml]	719±1379

in one patient (0.7%). The octogenarians required on average a prolonged intensive care unit stay (5.3±7.5 days), as well as hospital length of stay. They were discharged from the hospital after an average of 19.0±13.4 days. Furthermore, the need for blood products in this patient group was relatively high: 1,350±1,800 mL of red blood cells, 323±700 mL of platelets, and 719±1379 mL of fresh frozen plasma.

Predictors of mortality

Detailed data are given in Table 6. Emergency surgery, NYHA class IV, postoperative necessity of dialysis, intubation ≥72

Table 4. Adverse events and outcomes.

Characteristics	Value
Postoperative outcomes	
ICU length of stay, LOS [days]	5.3±7.5
Total hospital LOS [days]	19±13.4
Intubation time [hours]	63±114
Overall 30-days mortality	25 (18.1%)
Mid-term mortality	47 (34%)
Follow up time [years]	1.75±2.3
Postoperative adverse events	
Extracorporeal membrane oxygenation (ECMO)	1 (0.7%)
Intraaortic balloon pump (IABP)	8 (5.8%)
Revision due to bleeding	4 (2.9%)
Revision due to wound infection	1 (0.7%)
Revision due to pericardial tamponade	14 (10.1%)
New-onset kidney failure requiring dialysis	27 (19.6%)
Cerebrovascular events	10 (7.2%)
Pacemaker implantation	10 (7.2%)
Symptomatic transitory psychotic syndrome	27 (19.6%)
Pneumonia	18 (13%)
Sepsis	14 (10.1%)
Mediastinitis	0
Acute myocardial infarction	1 (0.7%)
Cardiopulmonary resuscitation	8 (5.8%)
Re-intubation	10 (7.2%)
Tracheotomy	17 (12.3%)
Intubation ≥72 hours	26 (18.9%)

Table 5. Early mortality rate related to the surgical procedures.

Characteristics	30-day mortality
Total	25 (18.1%)
Isolated mitral valve surgery (n=39)	4 (10.3%)
Repair	0
Replacement	4 (10.3%)
Combined mitral valve surgery	
With CABG (n=52)	14 (26.9%)
With tricuspid repair (n=44)	7 (15.9%)
With aortic replacement (n=31)	7 (22.6%)
One concomitant procedure (n=75)	15 (20%)
More than one concomitant procedure (n=24)	6 (25%)
Emergency surgery (n=33)	12 (36.4%)

did not influence 30-day mortality. Blood transfusion was a surrogate parameter.

Survival

The mean follow-up was 1.7±2.3 years and the one-year survival rate was 73% (Figure 1).

The significantly best survival rates were observed in patients who had electively undergone isolated MV repair. Among the concomitant procedures, only CABG was associated with a significant reduction of 30-day survival (p=0.04). There was no valve-related re-operation or intervention in the short follow-up time.

Discussion

Considering the increasing proportion of the elderly worldwide, it is not surprising that octogenarians are more and more commonly being referred to cardiac surgery. In Germany, the proportion of patients ≥80 years who have undergone cardiac surgery has increased from 1.0% in 1990 to 14.1% in 2015 [1]. In various studies, the age ≥80 years was associated with a higher risk of postoperative complications and moderate long-term survival [2,6,11].

In recent literature, 30-day mortality rates vary between 2.7% and 25% for isolated mitral valve surgery and up to 20.4% after combined procedures were usually reported in elective cases [2,6,10,11,15,16]. In our cohort, mitral valve replacement was more common than valve repair. This fact is also described in the

hours, and prolonged inotropic support with adrenalin could be defined as predictors of 30-day and overall mortality in follow-up time. However, concomitant CABG, a predictor of early mortality, was not associated with worse short-term survival. In contrast, tricuspid regurgitation did not influence early mortality, but only late mortality. Mitral valve replacement was identified as a predictor of early mortality. Failed MitraClip intervention in medical history was not a significant predictor of mortality. Surprisingly, diabetes mellitus, concomitant aortic or tricuspid surgery, BMI, COPD, endocarditis, and redo surgery

Table 6. Predictors of mortality (p<0.05 is considered as statistically significant).

Factor	Logistic regression analysis for predictors of 30-day mortality		Cox regression analysis for predictors of mortality in follow-up	
	OR (95% CI)	p Value	OR (95% CI)	p Value
Gender		0.272		0.1
Emergency surgical indication	4 (1.6, 10.1)	0.003	2.1 (1.16, 3.79)	0.014
Diabetes		0.6		0.94
Chronic kidney disease		0.4		0.074
BMI		0.07		0.08
Previous cardiac surgery		0.8		0.97
Tricuspid valve regurgitation		0.56	0.4 (0.2, 0.8)	0.01
Impaired LVF		0.08		0.2
COPD		0.19		0.2
NYHA class	2.2 (1.1, 4.4)	0.034	1.95 (1.2, 3.1)	0.006
Preoperative failed mitral valve interventional therapy		0.336		0.1
Endocarditis		0.32		0.052
Mitral valve replacement	4.9 (1.37, 17.17)	0.014		0.34
Concomitant AKE		0.14		0.27
Concomitant TKR		0.4		0.45
Concomitant CABG	8.8 (1.1, 71.6)	0.04		0.1
Number of concomitant procedures		0.11		0.56
Need for use of adrenalin postoperatively	8.1(2.9, 22.5)	0.000	3.05 (1.53, 6.08)	0.002
Intubated ≥72 h	5.13 (1.97, 13.4)	0.001	4.26 (2.32, 7.84)	0.000
Dialysis postoperatively	6.6 (2.6, 16.9)	0.000	4.3 (2.4, 7.75)	0.000
Transfusions of packed red cells	1 (1, 1)	0.008	1 (1, 1)	0.000
Psychotic syndrome		0.6		0.78

literature [17]. It could be explained by the fact that due to high degeneration of valve structure, valve repair may not be possible. Chikwe et al. determined that concomitant CABG with mitral valve replacement was associated with increased early and mid-term mortality. Moreover, elective MV replacement was associated with the 90-day mortality rate of 31.6% [6].We observed an overall 30-day mortality of about 10.3% in isolated mitral valve surgery (0% in MV repair and 10.3% in MV replacement) versus insignificantly higher rates with 15.2% in combined procedures (*p*=0.2). Furthermore, we could identify CABG as the only concomitant procedure that is a significant predictor of early mortality. About a quarter of our collective underwent emergency surgery. This subgroup demonstrated a large proportion of 30-day mortality. In 105 elective patients, we observed a 12.4% 30-day

mortality rate, compared with 36.4% in the 33 emergency cases. At this point, it should be discussed whether the decision to get surgery was taken too late. Conforming to our findings, emergency surgery was already identified as an independent risk factor for decreased survival [6,11,18,19]. Endocarditis could not be identified as a predictor of mortality, as mentioned by different statements in the recent literature [18,19].

We observed prolonged CPB and cross-clamp times due the high proportion of combined procedures (71.7%). The ICU and in-hospital length of stay was also relatively long. Others series showed similar results [2,11,12]. Additionally, Deschka et al. reported a 56.5% in-hospital mortality rate for patients who were ≥80 years of age after cardiac surgery if they stayed longer than
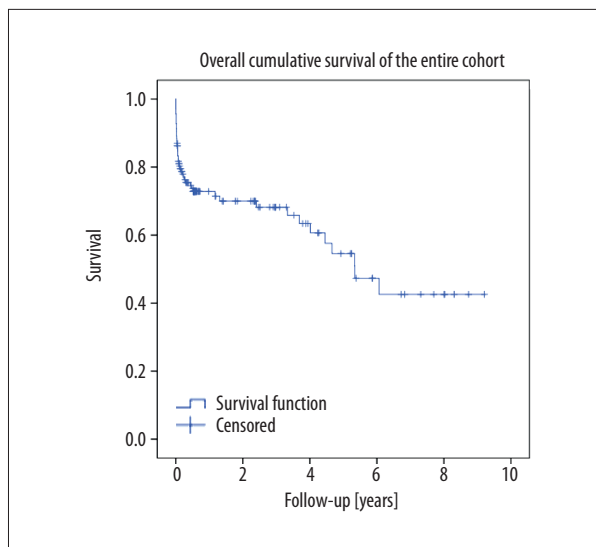
Figure 1. Overall cumulative survival of the entire cohort.

five days in the intensive care unit [20]. This fact underlines the complexity of clinical courses of octogenarians. Octogenarians show a higher risk for major postoperative complications due to preoperative high-risk conditions [12]. We observed acceptable rates of bleeding, strokes, and acute renal failure, which are comparable to the already reported results [2,10].

In Germany, we observed an increasing number of catheter-based mitral valve procedures [21]. Puls et al. presented the largest data for one-year outcome after transcatheter mitral valve interventions (TRAMI) in a total of 828 patients with a median age of 76 years. One-year mortality was 20.3%, with 14.1% of re-hospitalized patients due to cardiac decompensation, and 17.8% due to other cardiovascular reasons [21]. Although the MitraClip implantation as minimally invasive intervention could be more indulgent, the survival is comparable to the complex combined surgical procedures or to emergency valve surgery. Basing on a cohort aged ≥80, Alozie et al. reported better results in terms of postoperative residual mitral regurgitation (MR); MR ≥2 in 0% in surgical group versus 23.8% after MitraClip and a one-year mortality in the MitraClip group of 21.4% versus 9.5% in the surgical group [1]. Additionally, significant number of these patients required MV surgery to treat the residual MR [22]. Seeburger et al. reported promising results with acceptable survival in octogenarians who underwent minimally invasive mitral valve surgery with high repair

rates [23]. Furthermore, Ondrus et al. reported similar 30-day and long-term outcomes, comprising MitraClip with minimally invasive mitral valve repair in a younger patient collective (mean age 75±9 years) [24]. We have a modest experience with minimally invasive mitral valve surgery in octogenarians, however, with good outcome and survival.

In our study group surgical revision was performed in five cases after failed MitraClip with acceptable survival (one death nine days after surgery). Such experiences were reported with comparable results [25,26]. Nevertheless, mitral valve surgery after failed interventional procedures remains complex and presents surgical challenges.

Our study had various limits. First, it was a single-center retrospective study with a small number of octogenarians undergoing mitral valve surgery. Furthermore, we did not have long-term data about survival and quality of life. We did not include echocardiographic follow-up data and could not make comparison with younger patients, patients after MitraClip, or patients undergoing only medical therapy.

Conclusions

Mitral valve surgery beyond the age of 80 years could be a suitable treatment option. Our results should encourage us to differentiate indications for surgical therapy and interventional concepts. Age should not be considered as the only contraindication for surgery. Overall preoperative conditions of patients (e.g., NYHA class or history of cardiac decompensation) should be clearly taken into consideration. Our present study demonstrates that early mortality seems to be dependent on the type of procedures. We believe that the decision for timing of surgery in elderly patients with severe mitral regurgitation remains a challenging clinical problem and should be discussed in a timely manner.

Furthermore, we believe that prudent patient selection can optimize the outcome and survival rates of octogenarians after mitral valve surgery.

Conflict of interest

None.

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