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## Elixhauser Comorbidity Score Is the Best Risk Score in Predicting Survival After Mitraclip Implantation

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### ABSTRACT

**Background:** Risk scores to assess life expectancy may be beneficial in clinical decision making in selecting frail patients for MitraClip implantation according to the guidelines. This study was conducted to determine the risk score that performs best in predicting 1-year survival in patients undergoing percutaneous mitral valve repair using the MitraClip.

**Method:** All consecutive patients who underwent a MitraClip implantation between May 2009 and May 2016 were enrolled. The STS-PROM score, EuroSCORE I, EuroSCORE II, ACEF, Charlson comorbidity score, Elixhauser comorbidity score, Guaragna score, OBSERVANT score and Ambler score were calculated. The capacity to discriminate between 1-year survival and 1-year mortality was assessed by the area under the receiver operating characteristic (ROC) curve (c statistic).

**Results:** In the study 152 patients were included, 52% was male and the median age was 78 (interquartile range 69–83). Primary MR was present in 64% of the patients. On average, 1.5 MitraClips were implanted without any procedural mortality. The overall 1-year survival of this cohort was 80%. The Elixhauser comorbidity score showed the largest area under the ROC curve of 0.75 (95% confidence interval: 0.66–0.84). The other tests showed a smaller area under the ROC curve ranging from 0.51 (Guaragna score) to 0.72 (Charlson comorbidity score).

**Conclusion:** The Elixhauser comorbidity score has the best performance in predicting 1-year survival after MitraClip implantation. Therefore, the Elixhauser risk score should be used for making an assessment of 1-year mortality when selecting patients for treatment with the MitraClip.

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**KEYWORDS** Elixhauser comorbidity score; MitraClip; mitral regurgitation; percutaneous mitral valve repair; risk scores

### Introduction

The MitraClip is an alternative treatment option to conventional surgery for high-risk patients with symptomatic moderate-severe to severe mitral regurgitation (MR).<sup>1</sup> The recent updated American Heart Association (AHA)/American College of Cardiology (ACC) guidelines recommend that patient selection for the MitraClip procedure should comprise reasonable life expectancy.<sup>2</sup> Risk scores for predicting procedural mortality may be beneficial and are widely used in cardiac surgery. Risk scores may be beneficial in patient selection in order to meet the guidelines on life expectancy and may prevent overtreatment in this frail population. Nevertheless, as yet no risk score has been developed or validated for predicting survival after MitraClip implantation. Moreover, it is unknown which of the various available risk scores performs best in predicting the 1-year survival. The aim of this study was to determine which risk score performs best in predicting 1-year survival in patients undergoing percutaneous mitral valve repair using the MitraClip.

### Materials and methods

Consecutive patients who underwent MitraClip implantation between May 2009 and May 2016 were included in a prospective cohort. Baseline characteristics were prospectively collected and risk scores were calculated. Baseline medical history and comorbidities were administered using the Tenth Revision of the International Classification of Diseases (ICD-10). Nine commonly used risk scores (see Supplemental materials—online only) were included, consisting of three conventional surgical risk scores (STS-PROM score, EuroSCORE I, and EuroSCORE II), one elective cardiac surgery score (ACEF score), two comorbidity scores (Charlson comorbidity score and Elixhauser comorbidity score), and three valvular heart disease scores (Guaragna score, OBSERVANT score, and Ambler score). The Online STS Adult Cardiac Surgery Risk Calculator was used to prospectively calculate the STS-PROM score. The Elixhauser comorbidity score was calculated according to the point system from Van Walraven and colleagues. (Supplemental Table 1—online only).<sup>3</sup>

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 Supplemental data for this article can be accessed on the [publisher's website](#).

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## Statistical analysis

Continuous variables were presented as mean  $\pm$  standard deviation or as median with interquartile range (Q1–Q3). The cumulative survival rates were evaluated with the Kaplan-Meier method. Each individual score was divided into three tertiles, the cutoff values of the tertiles were based on subgroup size and clinical interpretation of the score outcome. The differences between the three tertiles within a risk score were determined based on the log-rank test. The capacity to discriminate between 1-year survival and mortality was assessed by the area under the receiver operating characteristic (ROC) curve (c statistic). The correlation between the 1-year mortality and the risk scores was calculated and resulted in an R-squared value. SPSS software (IBM SPSS Statistics version 23, New York, USA) was used for all statistical analysis. Differences at a  $p$  value  $< 0.05$  were considered statistically significant.

## Results

A total of 152 patients (median age: 78 (interquartile range (IQR) 69–83) years, male: 52%) who underwent MitraClip implantation were included. Baseline characteristics are listed in **Table 1**. Medical history comprised atrial fibrillation in 87 patients (57%), diabetes mellitus in 39 (26%), coronary artery bypass grafting in 32 (21%) and percutaneous coronary intervention in 37 patients

**Table 1.** Baseline characteristics of overall study population.

	Patients undergoing MitraClip (N = 152)	1-year non-survivors (n = 28)
Age at procedure (y)	78 (69–83)	78 (73–82)
Male gender	79 (52%)	20 (71%)
<i>Clinical history</i>		
Atrial fibrillation	87 (57%)	15 (54%)
COPD	36 (24%)	8 (29%)
Coronary artery disease	73 (48%)	15 (54%)
Devices for arrhythmia or conduction disorders	35 (23%)	7 (25%)
Diabetes mellitus	39 (26%)	10 (36%)
Hypertension	93 (61%)	16 (57%)
Previous CABG	32 (21%)	7 (25%)
Previous PCI	37 (24%)	7 (25%)
Previous stroke	17 (11%)	6 (21%)
Previous valve surgery	13 (9%)	7 (25%)
NYHA class $\geq$ III/IV	120 (79%)	26 (93%)
<i>Laboratory findings</i>		
NT-proBNP (ng/L)	2478 (1364–4515)	3874 (1114–6906)
eGFR	55 $\pm$ 24	56 $\pm$ 28
<i>Echocardiographic variables</i>		
MR grade $>3$	111 (73%)	24 (86%)
<i>MR etiology</i>		
Degenerative	47 (31%)	11 (39%)
Functional	98 (65%)	16 (57%)
Mixed	6 (4%)	1 (4%)
LVEF $<30\%$	48 (32%)	8 (29%)

*Note.* CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; NT-proBNP, N-terminal B-type natriuretic peptide; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; TR, tricuspid regurgitation.

(24%). The median N-terminal B-type natriuretic peptide (NT-proBNP) was 1777 ng/L and 48 patients (32%) had a severely impaired left ventricle ejection fraction ( $<30\%$ ).

Global discriminative performance to discriminate between 1-year survival and 1-year mortality of the nine included risk scores are listed in **Table 2**. Of all included scores, the Elixhauser comorbidity score showed the best global discriminative performance (area under the ROC curve: 0.75; 95% confidence interval (CI): 0.66–0.84; log-rank:  $p$  value = 0.001). In patients with degenerative MR, the area under the ROC curve of the Elixhauser comorbidity score was 0.75 (0.60–0.90) and 0.76 (0.64–0.88) in patients with functional MR. In addition, the area under the ROC curve of the Elixhauser comorbidity score was 0.73 (0.62–0.85) in 72% of the patients who underwent a successful procedure (MR grade  $\leq 2$  at discharge) and 0.78 (0.63–0.94) in the other patients. The Kaplan-Meier estimated overall survival rates 30-days, 1-year, and 2-years after MitraClip implantation were respectively  $96.7 \pm 1.5\%$ ,  $79.6 \pm 3.5\%$ , and  $71.0 \pm 4.1\%$ . Kaplan-Meier estimates of overall survival by tertiles of the Elixhauser comorbidity score ( $<11$ ,  $11–15$  and  $>15$ ) are shown in **Figure 1** ( $p$  value = 0.001). The correlation between the 1-year mortality (%) and the Elixhauser comorbidity score is shown in **Figure 2** (R-squared = 0.7134). The other tests had a lower R-squared value ranging from 0.017 (OBSERVANT score) to 0.4627 (Charlson comorbidity score).

## Discussion

We analyzed the global discriminative performance of nine risk scores on survival among 152 patients who underwent MitraClip implantation. Our study included several surgical, valve-specific and comorbidity scores in order to identify the most suitable risk score.<sup>4–15</sup> To the best of our knowledge, this is the most comprehensive list of risk scores available for patients undergoing percutaneous valvular interventions. The Elixhauser comorbidity score was the best risk score to predict 1-year survival after MitraClip implantation, however it still showed only a fair discrimination (area under the ROC curve: 0.75).

The Elixhauser comorbidity score had the largest area under the ROC curve, although the difference is not significant from the Charlson comorbidity score ( $p = 0.91$  using the DeLong's method). The Elixhauser comorbidity score was the best risk score, but if one has already experience with the Charlson comorbidity score it is acceptable to continue using this risk score.

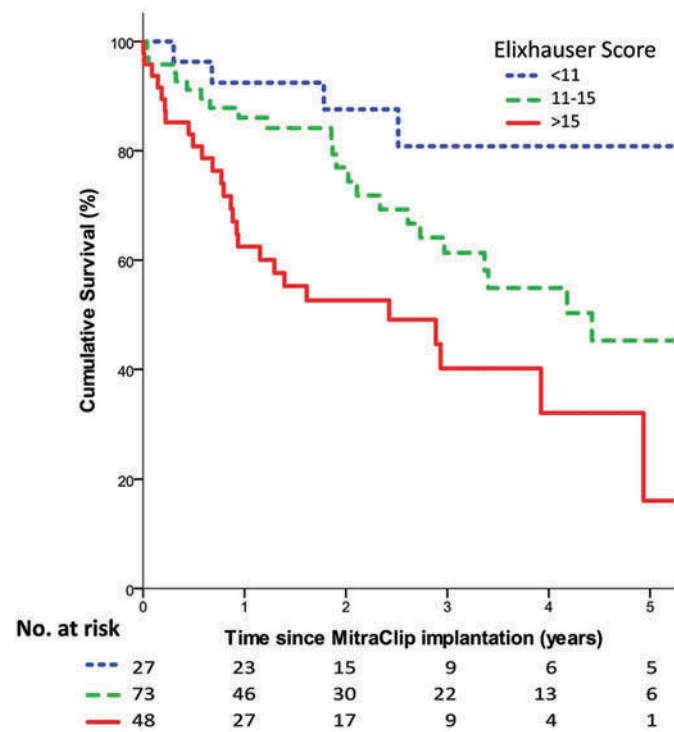
An Elixhauser comorbidity score of  $>15$  can be used as a cut-off value with a 1-year mortality of 38%. This cut-off value is based on the ROC curve and the clinical interpretation of a reasonable life expectancy. The score of  $>15$  is visualized in **Figure 1** as the highest tertile. **Figure 2** provides insight in the chosen cut-off value. The high-risk patients with a score  $>15$  should be considered carefully in the heart team, also with regards to other valve lesions and the clippability of the anatomy of the mitral valve. The prognosis should also be discussed with the patient in order to achieve shared decision-making.

The MitraClip procedure is generally performed in elderly patients with many comorbidities who are denied conventional open-heart surgery.<sup>2,16</sup> The conventional surgical risk scores (STS-PROM score, EuroSCORE I, and EuroSCORE II) are used to deny patients conventional open-heart surgery. The scores predict the risk of operative mortality after cardiac surgery and

**Table 2.** Global discriminative performance of the nine included risk scores.

	All patients (N = 152)	1-year survival (n = 124)	1-year mortality (n = 28)	AUC (95% CI)
<i>Conventional surgical risk</i>				
STS-PROM score (%)	3.4 (1.9–5.4)	3.1 (1.8–5.1)	4.8 (2.9–6.6)	0.63 (0.52–0.75)
EuroSCORE I (%)	14.4 (9.4–22)	13.9 (9.0–22)	20.1 (12–35)	0.62 (0.50–0.74)
EuroSCORE II (%)	4.5 (3.1–8.2)	4.3 (3.1–7.3)	7.0 (3.1–11.5)	0.61 (0.48–0.73)
<i>Elective cardiac surgery</i>				
ACEF score (%)	2.1 (1.6–2.8)	2.0 (1.6–2.7)	2.1 (1.5–3.5)	0.53 (0.40–0.68)
<i>Comorbidity</i>				
Charlson score	3 (2–5)	3 (2–4)	4 (4–6)	0.72 (0.62–0.82)
Elixhauser score	14 (11–17)	13 (11–16)	16 (15–20)	0.75 (0.66–0.84)
<i>Valvular heart disease</i>				
Guaragna score	9 (7–11)	9 (7–11)	9 (7–11)	0.51 (0.36–0.65)
OBSERVANT score	6 (3–9)	6 (3–9)	9 (0–11)	0.57 (0.42–0.72)
Ambler score	9 (8–12)	9 (8–11)	11 (8–13)	0.62 (0.49–0.75)

Note. Score values are reported as median (interquartile range). ACEF, value of age, creatinine, and ejection fraction; AUC, area under the curve; CI, confidence interval; EuroSCORE, European System for Cardiac Operative Risk Evaluation; OBSERVANT, Observational Study of Appropriateness, Efficacy and Effectiveness of AVR-TAVR Procedures for the Treatment of Severe Symptomatic Aortic Stenosis; STS-PROM, Society of Thoracic Surgeons – Predicted Risk of Mortality.



**Figure 1.** Kaplan-Meier estimates of overall survival by tertiles of the Elixhauser comorbidity score;  $p$ -value = 0.001.

were not designed to predict the mortality after MitraClip implantation. The valvular heart disease scores (Guaragna score, OBSERVANT score, and Ambler score) could have matched to our population since they were developed for patients undergoing a transcatheter aortic valve replacement. Nevertheless, the valvular scores did not appear to be suitable for the MitraClip population, which is indeed a very specific population. Furthermore, the appropriateness of comorbidity scores (Elixhauser comorbidity score and Charlson comorbidity score) for predicting survival after MitraClip treatment was expected because the MitraClip procedure is generally performed on elderly patients with many comorbidities.<sup>4-6</sup>

Previous studies on risk scores in patients undergoing MitraClip treatment compared only three conventional surgical risk scores (STS-PROM score, EuroSCORE I, and EuroSCORE II) and suggested that these scores all clearly overestimate 30-day or in-hospital mortality in patients undergoing MitraClip implantation.<sup>7,8</sup> The overestimation of the mortality based on the surgical risk scores can also be explained by the fact the MitraClip procedure is a low-risk procedure compared to open-heart surgery.

The two comorbidity scores, Elixhauser comorbidity score and Charlson comorbidity score, were previously compared in predicting mortality in acute myocardial patients and in predicting inpatient death after orthopedic surgery. These studies showed that the Elixhauser comorbidity score was superior to the Charlson comorbidity score.<sup>4-6</sup> These studies, like the current study, used the modified Elixhauser comorbidity score comprising a point system according to Van Walraven and colleagues.<sup>3</sup> The Van Walraven modification simplifies the Elixhauser comorbidity score calculation by eliminating some variables, e.g. hypertension and diabetes. Although calculating a risk score is often complex and time-consuming, simple risk scores like the ACEF score including only age, creatinine, and ejection fraction resulted in our population appearing in a small area under the ROC curve of 0.53 (0.40–0.68).

Renal function, weight loss, and solid tumor without metastasis were the major factors influencing mortality from the variables in the Elixhauser comorbidity score. The factors renal function and previous malignancy are known predictors of mortality after MitraClip implantation.<sup>17-19</sup> Weight loss has not yet been thoroughly investigated for its risk for mortality, but could reflect a patient's nutritional status and impaired prognosis. Limiting the analysis to predict mortality only to the clinical variables renal function, weight loss, and solid tumor without metastasis was inferior to the modified Elixhauser comorbidity score.

The extent to which the outcomes can be generalized is limited due to a limited number of patients. In the future, our findings require validation in other patient populations undergoing a MitraClip treatment to enhance external validity.

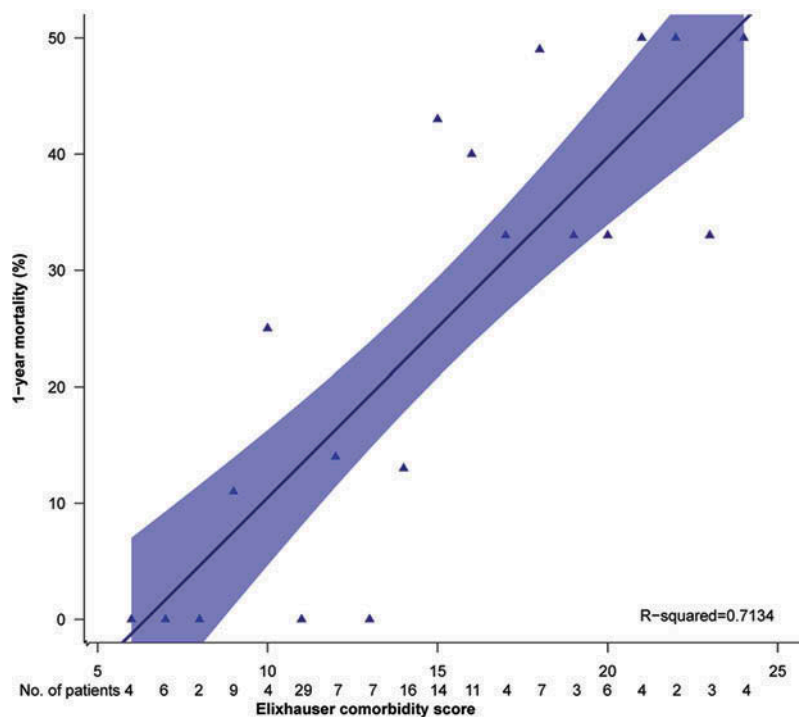


Figure 2. Correlation between the 1-year mortality (%) and the Elixhauser comorbidity score; R-squared = 0.7134.

## Conclusion

Risk scores may be used in selecting patients for percutaneous mitral valve repair using the MitraClip to meet the guidelines obligations to assess life expectancy. The Elixhauser comorbidity score had the best performance in predicting 1-year survival after MitraClip implantation. Therefore, the Elixhauser risk score should be used in clinical decision making, when a 1-year mortality assessment is required when selecting patients for treatment with the MitraClip.

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## Disclosure statements

Juliëtte F. Velu has no conflict of interest; Stijn D. Haas has no conflict of interest; Martijn S. Van Mourik has no conflict of interest; Karel T. Koch has no conflict of interest; M. Marije Vis has no conflict of interest; José P. Henriques has no conflict of interest; Renée B. Van Den Brink has no conflict of interest; S. Matthijs Boekholdt has no conflict of interest; Jan J. Piek has no conflict of interest; Berto J. Bouma has no conflict of interest; Jan Baan, Jr. is proctor for Abbott Vascular MitraClip and receives an unrestricted research grant from Abbott Vascular.

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