International Journal of Cardiology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

# SYNTAX score II in patients with coronary artery disease undergoing percutaneous mitral repair with the MitraClip

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ARTICLE INFO

*Article history:*
Received 1 November 2016
Received in revised form 26 January 2017
Accepted 13 February 2017
Available online xxxx

*Keywords:*
Interventional cardiology
Valvular disease
Mitral valve regurgitation
Mitraclip
Syntax score

ABSTRACT

*Background:* Percutaneous mitral valve repair (PMVR) using the MitraClip™ system has become a valuable alternative in patients with severe mitral regurgitation (MR) and high surgical risk. We sought to evaluate the prognostic value of the SYNTAX II score (SSII) in patients with concomitant coronary artery disease (CAD) undergoing a Mitraclip procedure.

*Methods:* In seventy-five consecutive patients who underwent PMVR at the University Heart Center Zürich and the Cardiocentro Ticino, the SSSII was calculated at baseline. Clinical endpoints comprised of all-cause mortality, mitral valve surgery due to failure of PMVR or reoperation, hospitalization for congestive heart failure, heart transplantation and the composite of all four endpoints.

*Results:* Patients were followed for a median of 271 days. And were divided in tertiles of SSII: SSII low ≤46.5 ($n = 25$), SSII mid 46.6–54.4 ($n = 25$) and SSII high ≥54.5 ($n = 25$). Patients in the highest SSII tertile had a lower left ventricular ejection fraction (33% vs. 40% vs. 53%) with a higher log-BNP (3.6 vs. 3.45 vs. 3.16) when compared to SSII mid and SSII low, respectively. However, the anatomical syntax score (SS) did not differ significantly within the tertiles (9.1 ± 6.3 (SSII Low) vs 9.5 ± 7.6 (SSII Mid) vs 10.2 ± 6.7(SSII High), $p = 0.837$). The primary endpoint occurred in 33% of patients ($n = 25$). By multivariate analysis patients in the high SSII tertile (OR = 6.12, 95% confidence interval, [CI] 1.45–25.86, $p = 0.014$) and patients with a history of MI (OR = 3.57, 95% confidence interval, [CI] 1.17–10.88, $p = 0.025$) were at significantly higher risk of experiencing adverse events. Furthermore, in a combined outcome ROC curve analysis, the SSII showed good discrimination with an AUC of 0.73, $p = 0.001$. A cutoff SSII >49 has been identified to have a sensitivity of 83% and specificity of 53% with approximately 45% of the patients experiencing an event during follow-up.

*Conclusion:* Using SSII in CAD patients undergoing PMVR is feasible and of prognostic significance hence widening its clinical utility in valvular heart disease.



## 1. Introduction

The MitraClip™ system is a safe and less invasive, percutaneous alternative to open-heart surgery [14–18,30], which effectively improves functional and clinical outcome in inoperable or high-risk patients [19–21]. While the outcomes of percutaneous mitral valve repair (PMVR) is rather predictable in degenerative mitral regurgitation (MR), patient-related factors have a higher influence on the outcome of PMVR in patients suffering from functional MR (FMR) [1–7]. One frequent and important patient-related factor is the presence of concomitant coronary artery disease (CAD). CAD is a frequent comorbidity in patients with severe mitral regurgitation. In recent registries investigating outcome after MitraCliping prevalence of CAD ranged between 30% and 84.2% and was higher in patients with FMR [21,26–28].

To date, the heart team relies on the Society of Thoracic Surgeons (STS) score or the European system for cardiac operative risk evaluation (EuroSCORE) for objective risk stratifcation of patients with valvular heart disease [8]. The SYNTAX score II (SSII) is a recently developed clinical tool applying a Cox proportional hazards model to the results of the SYNTAX trial [22,23]. For patients with complex coronary artery disease (CAD) SSII has been shown to reliably predict 4-year mortality [22,24,25] and therefore has the potential to assess individual, preprocedural risk.

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http://dx.doi.org/10.1016/j.ijcard.2017.02.049
0167-5273/

In patients with severe MR and CAD the SSII score might be an additional instrument to facilitate multidisciplinary decision-making. Therefore, the purpose of the present study was to evaluate the SSII in patients with CAD undergoing PMVR.

## 2. Methods

### 2.1. Patient selection

We included 75 consecutive patients who underwent PMVR using the MitraClip™ System at the University Heart Center Zurich (57 patients) and the Cardiocentro Ticino (18 patients) between February 2009 and July 2015. All patients had a history of coronary artery disease and suffered from symptomatic moderate-to-severe (3+) or severe (4+) MR. Patients with previous bypass-surgery were excluded from the analysis. Patients were assessed by an interdisciplinary Heart Team and assigned to MitraClip according to local institutional practice in accordance with the European Society of Cardiology European Association for Cardio-Thoracic Surgery guidelines on the management of valvular heart disease [8]. Complete anatomical SYNTAX score (SS) and SSII were calculated for every patient using the online scoring system (http://www.syntaxscore.com), with adoption of the PCI score value where syntax score II was concerned. Patients were stratified according to tertiles of SSII: low tertile ≤46.5 ($n = 25$), mid tertile 46.6–54.4 ($n = 25$); and high tertile ≥54.5 ($n = 25$).

All Patients gave written informed consent for the procedure and data collection. Patients were followed within the nationwide MitraSwiss registry, which was approved by the local ethics committee.

### 2.2. SYNTAX score II

The SSII score was designed for risk assessment of patients with complex coronary artery disease in purpose of choosing the optimal revascularization method, be it surgical or percutaneous [22]. It combines extension and complexity of native coronary artery disease (anatomical SS,LM disease) with 6 clinical variables (gender, age, left ventricular ejection fraction, peripheral vascular disease, creatinine clearance and chronic obstructive pulmonary disease) and was found to be a predictor of 4-year mortality [22].

### 2.3. MitraClip procedure

Percutaneous MitraClip implantation was performed in a hybrid operating room under general anesthesia with transesophageal and fluoroscopic guidance, as previously described [30]. After access of the left atrium by trans-septal puncture, the MitraClip (a polyester-covered cobalt-chronium clip) was advanced through a 24-French catheter-based delivery system. One or more clips were deployed aiming to reduce MR without creating a relevant trans-valvular gradient. Acute procedural success (APS) was defined as successful implantation of one or more clips with reduction of the MR to <2+.

**Table 1**
Baseline characteristics.

| | Overall population $n = 75$ (%) |
|---|---|
| Age (y) | 78 ± 8 |
| Gender (male) | 46 (61) |
| BMI | 25 ± 5 |
| Hypertension | 61 (81) |
| Dyslipidemia | 36 (48) |
| Diabetes mellitus | 15 (20) |
| Previous MI | 22 (29) |
| Previous PCI | 43 (57) |
| Previous valve surgery | 6 (8) |
| Previous vascular surgery or of the thoracic aorta | 7 (9) |
| History of congestive heart failure | 21 (28) |
| Atrial fibrillation | 32 (43) |
| Previous ischemic stroke | 5 (7) |
| COPD | 11 (15) |
| Renal failure | 22 (29) |
| NYHA functional Class | |
| I/II | 14 (19) |
| III | 43 (57) |
| IV | 18 (24) |
| Baseline LVEF | 43 ± 17 |
| Mitral regurgitation | |
| Moderate to severe | 12 (16) |
| Severe | 63 (84) |
| MR aetiology | |
| Functional MR | 39 (52) |
| Degenerative MR | 30 (40) |
| Mixed MR | 6 (8) |
| Anatomical SYNTAX score | 9.6 ± 6.8 |
| SYNTAX score II | 50.8 ± 10.1 |

Values are mean ± SD or n (%). BMI = Body mass index; COPD = Chronic obstructive pulmonary disease; MI = Myocardial infarction; MR = Mitral regurgitation; NYHA = New York Heart Association; PCI = Percutaneous coronary intervention.

**Table 2**
Characteristics of low, mid and high tertiles of SYNTAX score II.

| SSII tertiles | Low (≤46.5) ($n = 25$) | Mid (46.6–54.4) ($n = 25$) | High (≥54.5) ($n = 25$) | *p*-Value |
|---|---|---|---|---|
| Age | 79.6 ± 8.2 | 77 ± 8.8 | 75 ± 6.7 | 0.225 |
| BMI | 24.9 ± 4.6 | 24.5 ± 4.2 | 25 ± 5.3 | 0.89 |
| Diabetes mellitus | 2 (8%) | 5 (20%) | 8 (32%) | 0.12 |
| Dyslipidemia | 11 (44%) | 12 (48%) | 13 (52%) | 0.957 |
| Hypertension | 21 (84%) | 20 (80%) | 20 (80%) | 1 |
| Previous MI | 5 (20%) | 9 (36%) | 8 (32%) | 0.532 |
| Previous PCI | 10 (40%) | 19 (70%) | 14 (56%) | 0.05 |
| Left main disease | 8(32%) | 7 (28%) | 6 (24%) | 0.947 |
| Previous ischemic stroke | 1 (4%) | 3 (12%) | 1 (4%) | 0.609 |
| Renal failure | 3 (12%) | 11 (44%) | 8 (32%) | 0.06 |
| Creatinine | 111 ± 42 | 151 ± 71 | 135 ± 51 | 0.046 |
| GFR | 55.19 ± 17 | 39.16 ± 16 | 41.2 ± 16 | 0.006 |
| PAD | 1 (4%) | 1 (4%) | 5 (20%) | 0.112 |
| COPD | 2 (8%) | 1 (4%) | 8 (32%) | 0.015 |
| Baseline HGB | 123 ± 19.1 | 117 ± 18.3 | 121 ± 19.8 | 0.491 |
| History of CHF | 5 (20%) | 7 (28%) | 9 (36%) | 0.505 |
| Baseline LVEF | 53.5 ± 13 | 40 ± 15 | 33 ± 15.7 | <0.001 |
| Baseline log-BNP | 3.16 ± 0.47 | 3.45 ± 0.36 | 3.6 ± 0.54 | 0.009 |
| Severe MR (4+) | 18 (72%) | 24 (96%) | 21 (84%) | 0.08 |
| Functional MR | 12 (48%) | 12 (48%) | 15 (60%) | 0.736 |
| Implantation of ≥2 clips | 15 (60%) | 15 (60%) | 17 (68%) | 0.87 |
| Anatomical Syntax score(SS) | 9.1 ± 6.3 | 9.5 ± 7.6 | 10.2 ± 6.7 | 0.837 |

Values are mean ± SD or n (%).
CHF = congestive heart failure; COPD = Chronic obstructive pulmonary disease; HGB = Hemoglobin; Log-BNP = Logarithm of brain natriuretic peptide; MI = Myocardial infarction; MR = Mitral regurgitation; PAD = peripheral artery disease; PCI = Percutaneous coronary intervention.

### 2.4. Follow-up and endpoints

Clinical assessment and TTE were performed at baseline, discharge, 1, 3, 6, and 12 months, and yearly thereafter. In case of an event, hospital charts were reviewed, or the cardiologist or primary care physician was contacted.

Clinical endpoints comprised of all-cause mortality, mitral valve surgery due to failure of PMVR or reoperation, hospitalization for congestive heart failure (CHF), heart transplantation and the composite of all four endpoints.

### 2.5. Statistical analysis

Continuous variables are expressed as mean ± SD or median with interquartile ranges (IQR), and were compared using 1-way ANOVA, Student's *t*-test, Kruskal-Wallis or Mann-Whitney as appropriate. Categorical data are presented as frequency (percentages) and were compared using the Fisher exact or the chi-square test. Variables with a significant Odds Ratio ($p < 0.05$) in a univariable analysis model for the prediction of different outcomes were included in an Enter-Method multivariable Logistic regression model to find independent predictors of studied outcome. Calibration was determined by the Hosmer-Lemeshow goodness-of-fit test. For discrimination the C-statistics and ROC curves were constructed to assess the ability of the SSII, to predict combined outcome. All probability values and confidence intervals were 2-sided. A probability value of <0.05 was considered significant, and all tests were 2-tailed. All analyses were performed with SPSS version 21.0 software (SPSS Inc., Chicago, Ill).

## 3. Results

### 3.1. Patient characteristics

The cohort comprised of 75 patients (46 males; mean age 78 ± 8 years). All patients had MR grade 3+ or 4+ with more than two third (81.3%) being classified in New York Heart Association (NYHA) functional class III or IV. Functional MR was present in 52% of the total study population, whereas 40% of patients had degenerative MR, and

Please cite this article as: S. Obeid, et al., SYNTAX score II in patients with coronary artery disease undergoing percutaneous mitral repair with the MitraClip, Int J Cardiol (2017), http://dx.doi.org/10.1016/j.ijcard.2017.02.049