



Mémoire de Maîtrise en médecine No 775

Prediction of myocardial infarction size using the SYNTAX score in patients treated with primary percutaneous coronary intervention for acute STsegment elevation myocardial infarction

Etudiant Jérôme Daellenbach

Tuteur Prof. Eric Eeckhout Service de cardiologie, CHUV

Expert

Prof. Lucas Liaudet Service de médecine intensive adulte, CHUV

Lausanne, décembre 2012

Prediction of myocardial infarction size using the SYNTAX score in patients treated with primary percutaneous coronary intervention for acute ST-segment elevation myocardial infarction

Jérôme Dällenbach¹, Olivier Muller¹, Stéphane Fournier¹, Catalina Trana¹, Nathalie Lauriers¹, Eric Eeckhout¹

¹ Cardiology, University Hospital Center (CHUV), Lausanne, Switzerland

Word count: 2'813

Keywords: SYNTAX score, ST-segment elevation myocardial infraction, primary percutaneous coronary intervention, risk stratification, infarction size

Brief Title:

Prediction of myocardial infarction size using the SYNTAX score in patients treated with PPCI for acute STEMI

Address for correspondence:

Prof Eric Eeckhout Service de cardiologie, CHUV Rue du Bugnon 21 1011 Lausanne Switzerland Fax : +41 21 314 00 13 E-mail : eric.eeckhout@chuv.ch

Objectives

The relevance of the SYNTAX score for the particular case of patients with acute STsegment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PPCI) has previously only been studied in the setting of post hoc analysis of large prospective randomized clinical trials. A "real-life" population approach has never been explored before.

The aim of this study was to evaluate the impact of the SYNTAX score for the prediction of the myocardial infarction size, estimated by the creatin-kinase (CK) peak value, using the SYNTAX score in patients treated with primary coronary intervention for acute ST-segment elevation myocardial infarction.

Methods

The primary endpoint of the study was myocardial infarction size as measured by the CK peak value. The SYNTAX score was calculated retrospectively in 253 consecutive patients with acute ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PPCI) in a large tertiary referral center in Switzerland, between January 2009 and June 2010. Linear regression analysis was performed to compare myocardial infarction size with the SYNTAX score. This same endpoint was then stratified according to SYNTAX score tertiles: low <22 (n=178), intermediate [22-32] (n=60), and high >=33 (n=15).

Results

There were no significant differences in terms of clinical characteristics between the three groups. When stratified according to the SYNTAX score tertiles, average CK peak values of 1985 (low<22), 3336 (intermediate [22-32]) and 3684 (high>=33) were obtained with a p-value <0.0001. Bartlett's test for equal variances between the three groups was 9.999 (p-value <0.0067). A moderate Pearson product-moment correlation coefficient (r=0.4074) with a high statistical significance level (p-value <0.0001) was found. The coefficient of determination (R^2=0.1660) showed that approximately 17% of the variation of CK peak value (myocardial infarction size) could be explained by the SYNTAX score, i.e. by the coronary disease complexity.

Conclusion

In an all-comers population, the SYNTAX score is an additional tool in predicting myocardial infarction size in patients treated with primary percutaneous coronary intervention (PPCI). The stratification of patients in different risk groups according to SYNTAX enables to identify a high-risk population that may warrant particular patient care.

Introduction

Optimal revascularization strategy in patients with coronary disease remains a disputed subject. Several risk scores have been designed and validated for patients presenting with ST-segment elevation myocardial infractions (STEMI) [1-5]. They are mainly patient-based, therefore do not take into account the lesion characteristics and their individual prediction ability is variable [6]. Though the SYNTAX score has primarily been developed to assess the risks of coronary revascularization (either percutaneous or surgical) by integrating the functional impact of coronary disease complexity using anatomic characteristics such as bifurcations, type of occlusions, thrombus, calcifications, tortuosities, bridgings, etc., visualized during coronary angiography [7,8]. This score has largely been validated [9-15] but was almost only limited to elective patients and tough its utility of risk stratifying patients with STEMI is not very well unknown [16].

The aim of our study was to evaluate the impact of the SYNTAX score for the prediction of the myocardial infarction size, estimated by the creatin-kinase (CK) peak value, using the SYNTAX score in patients treated with primary coronary intervention for acute ST-segment elevation myocardial infarction, in a well defined region of the French part of Switzerland and based on a real-life registry.

Methods

Patient population

Between January 1st 2009 and June 30th 2010, 402 consecutive patients underwent PPCI for STEMI in a large tertiary referral center in Switzerland. This institution is the

only site performing primary percutaneous coronary intervention (PPCI) in the region (approximately 700'000 inhabitants). Patients with "symptom-to-first-medical-contact" time longer than 12 hours, patients with a previous treatment by fibrinolysis or already hospitalized during their STEMI, patient with previous CABG or directly referred for CABG were excluded. We excluded as well those patients who died during the coronarography but before angioplasty. 345 patients were finally included (**Figure 1**). Coronary angiographies, laboratory values, clinical and demographic data were collected from hospital and catheter laboratory databases. All coronary lesions with a diameter stenosis >=50% in vessels >=1.5 mm were scored using the SYNTAX score algorithm. The online calculator version 2.11 (www.syntaxscore. com) was used.

Study endpoint

The endpoint of the study was myocardial infarction size by using the CK peak value, which is validated as a good quantitative assessment of the extent of myocardial infarction [17,18].

Definition of STEMI

STEMI was defined according to the universal definition of myocardial infarction of the Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction [19].

Statistical Analysis

GraphPad Prism software 5.0d was used to perform statistical analysis. Linear regression analysis was performed to compare myocardial infarction size with the SYNTAX score. The Pearson product-moment, with 95% confidence interval, two-

tailed p-value and the coefficient of determination have been calculated. This same endpoint was then stratified according to SYNTAX score tertiles: low <22 (n=178), intermediate [22-32] (n=60), and high >=33 (n=15). Bartlett's test for equal variances was subsequently calculated between the three groups.

Ethical issues

Our study complies with the Declaration of Helsinki regarding investigations in humans. It had been approved by the Institutional Ethics Committee.

Results

Baseline demographics and clinical outcome

Characteristics of the patients enrolled in this study are summarized in **Table 1**. Median age was 62,0 years. 72,2% of patients was male. There was no significant differences in terms of clinical characteristics between the three groups. Mean peak CK value was 2406 U/L and left ventricular ejection fraction (LVEF) assessed by echocardiography at discharge was 47%. Myocardial infarction localization is summarized in **Table 2**. At 1-year follow-up, all cause mortality rate was 5.80%.

Infarction size prediction with the SYNTAX score

When stratified according to the SYNTAX score tertiles (**Figure 2**), average CK peak values of 1985 U/L (low<22), 3336 U/L (intermediate [22-32]) and 3684 U/L (high>=33) were obtained with a p-value <0.0001. Bartlett's test for equal variances between the three groups was 9.999 (p-value <0.0067). A moderate Pearson

product-moment correlation coefficient (r=0.4074) with a high statistical significance level (p-value <0.0001) was found (**Figure 3**). The coefficient of determination ($R^2=0.1660$) shows that 16.6% of the variation of CK peak value (myocardial infarction size) can be explained by the SYNTAX score, i.e. by the coronary disease complexity.

Discussion

The present study showed that a global risk assessment for patients with STEMI undergoing PPCI has to integrate the anatomical and functional dimension of coronary disease, by means of the SYNTAX score, and not only the patient-based characteristics, even though these are necessary and important variables.

Prior studies evaluating the relevance of the SYNTAX score for the particular case of patients with acute STEMI undergoing primary percutaneous coronary intervention (PPCI) [15-16,20] are substudies based on large prospective randomized trials like STRATEGY (Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent Versus Abciximab and Bare-Metal Stent in Acute Myocardial Infarction) [21], MULTISTRATEGY (Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction Study) [22], SIRTAX (Sirolimus-eluting and paclitaxel-eluting stents for coronary revascularization) [23] and RESOLUTE (A Randomized Comparison of a Zotarolimus-Eluting Stent With an Everolimus-Eluting Stent for Percutaneous Coronary Intervention) [24]. The largest study pools seven coronary stent trials, including those already cited, and "confirms the consistent ability of the SYNTAX score to identify patients who are at highest risk of adverse events" [25].

Except for two studies based on the same population [26,27], a "real-life" population approach has never been explored before. There are limited to highly selected randomized controlled trials patients.

Our results are concordant with the previous studies [14-16,20,25,26]. The SYNTAX score may allow prospective risk stratification of patients undergoing PPCI [14,26] and is able to stratify risk amongst an all-comers population [20].

We established the ability of the SYNTAX score in stratifying infarction size, as in the current study in an all-comers population presenting with STEMI and subsequently treated with PPCI. However, and as already mentioned in prior studies [16,20], improvements can be made with the inclusion of clinical variables. Farooq et al. [28-30] highlighted that "while prognostically useful in risk-stratifying patients [...], in itself appears to carry important information on clinical comorbidity and outcomes for the individual patient. However, [...] the incremental value of adding clinical variables to the SYNTAX score [...] will ultimately prove to be more clinically useful compared with the SYNTAX score alone" [28]. They also noticed how "novel concepts such as the Functional Syntax score, especially if this can be performed noninvasively, and the patient empowered risk-benefit trade-off are all further areas in current development in which additional clinically relevant information may become available" [29]. We share this point of view.

The present study has several limitations. This is a retrospective observation in a limited number of patients. However it has the advantage of being consecutive, homogeneous, including all patients with STEMI undergoing PPCI in a defined period of time and in well-defined region. Furthermore the hospital where this study was

performed is the only center for PPCI of STEMI in this region of the French part of Switzerland.

Conclusion

In conclusion, the syntax score emerges as a useful tool in predicting infarct size during PPCI for STEMI. Further research should probably focus on developing even more accurate risks scores taking also into account clinical scores.

Contribution

All authors contributed equally the study.

Funding

University Hospital Center (Lausanne, Switzerland), Cardiology's research funds.

Conflicts of interest

The authors have no conflict of interest to declare.

References

- 1. Addala S, Grines CL, Dixon SR, et al. Predicting mortality in patients with STelevation myocardial infarction treated with primary percutaneous coronary intervention (PAMI risk score). Am J Cardiol 2004;93:629–32.
- 2. Halkin A, Singh M, Nikolsky E, et al. Prediction of mortality after primary percutaneous coronary intervention for acute myocardial in- farction: the CADILLAC risk score. J Am Coll Cardiol 2005;45:1397–405.
- 3. Morrow DA, Antman EM, Charlesworth A, et al. TIMI risk score for STelevation myocardial infarction: a convenient, bedside, clinical score for risk assessment at presentation: an intravenous nPA for treatment of infarcting myocardium early II trial substudy. Circulation 2000;102:2031–7.
- 4. Eagle KA, Lim MJ, Dabbous OH, et al., for the GRACE Investigators. A validated prediction model for all forms of acute coronary syndrome: estimating the risk of 6-month postdischarge death in an international registry. JAMA 2004;291:2727–33.
- 5. De Luca G, Suryapranata H, van't Hof AW, et al. Prognostic assessment of patients with acute myocardial infarction treated with primary angioplasty: implications for early discharge. Circulation 2004;109:2737–43.
- 6. Lev EI, Kornowski R, Vaknin-Assa H, et al. Comparison of the predictive value of four different risk scores for outcomes of patients with ST-elevation acute myocardial infarction undergoing primary percutaneous coronary intervention. Am J Cardiol 2008;102:6–11.
- 7. Sianos G, Morel MA, Kappetein AP, et al. The SYNTAX score: an angiographic tool grading the complexity of coronary artery disease. EuroIntervention 2005;1:219–27.
- 8. Serruys PW, Onuma Y, Garg S, et al. Assessment of the SYNTAX score in the SYNTAX study. EuroIntervention 2009;5:50–6.
- Serruys PW, Onuma Y, Garg S, et al. 5-year clinical outcomes of the ARTS II (Arterial Revascularization Therapies Study II) of the sirolimus-eluting stent in the treatment of patients with multivessel de novo coronary artery lesions. J Am Coll Cardiol 2010;55:1093–101.
- 10. Valgimigli M, Serruys PW, Tsuchida K, et al. Cyphering the complexity of coronary artery disease using the syntax score to predict clinical outcome in patients with three-vessel lumen obstruction undergoing percutaneous coronary intervention. Am J Cardiol 2007;99:1072–81.
- 11.Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary- artery bypass grafting for severe coronary artery disease. N Engl J Med 2009;360:961–72.
- 12.Capodanno D, Capranzano P, Di Salvo ME, et al. Usefulness of SYNTAX score to select patients with left main coronary artery disease to be treated with coronary artery bypass graft. J Am Coll Cardiol Intv 2009;2:731–8.

- Capodanno D, Di Salvo ME, Cincotta G, et al. Usefulness of the SYNTAX score for predicting clinical outcome after percutaneous coronary intervention of unprotected left main coronary artery disease. Circ Cardiovasc Interv 2009;2:302–8.
- 14.Wykrzykowska J, Garg S, Girasis C, et al. Value of the SYNTAX score (SX) for risk assessment in the "all-comers" population of the randomized multicenter LEADERS Trial. J Am Coll Cardiol 2010;56:272–7.
- 15.Girasis C, Garg S, Raber L, et al. Prediction of 5-year clinical outcomes using the SYNTAX score in patients undergoing PCI from the sirolimus eluting stent compared with paclitaxel eluting stent for coronary revascularisation (SIRTAX) trial. Abstract presented at: American College of Cardiology meeting; March 14–16, 2010; Atlanta, GA.
- 16.Garg S, Sarno G, Serruys PW, et al. Prediction of 1-year clinical outcomes using the SYNTAX score in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention: a substudy of the STRATEGY (Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent Versus Abciximab and Bare-Metal Stent in Acute Myocardial Infarction) and MULTISTRATEGY (Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction Study) trials. JACC Cardiovasc Interv. 2011 Jan;4(1):66-75.
- 17.Shell WE, Kjekshus JK, Sobel BE. Quantitative assessment of the extent of myocardial infarction in the conscious dog by means of analysis of serial creatine phosphokinase activity. J Clin Invest. 1971 Dec;50(12):2614-25.
- 18. Roberts R, Henry PD, Sobel BE. An improved basis for enzymatic estimation of infarct size. Circulation. 1975 Nov;52(5):743-54.
- 19. Wijns W, Kolh P, Danchin N, et al. Guidelines on myocardial revascularization. Eur. Heart J. 2010 oct;31(20):2501–55.
- 20.Garg S, Serruys PW, Silber S, et al. The prognostic utility of the SYNTAX score on 1-year outcomes after revascularization with zotarolimus- and everolimus-eluting stents: a substudy of the RESOLUTE All Comers Trial. JACC Cardiovasc Interv. 2011 Apr;4(4):432-41.
- 21.Valgimigli M, Percoco G, Malagutti P, et al. Tirofiban and sirolimus-eluting stent vs abciximab and bare-metal stent for acute myocardial infarction: a randomized trial. JAMA 2005;293:2109–17.
- 22.Valgimigli M, Campo G, Percoco G, et al. Comparison of angioplasty with infusion of tirofiban or abciximab and with implantation of sirolimus-eluting or uncoated stents for acute myocardial infarction: the MULTISTRATEGY Randomized Trial. JAMA 2008;299:1788–99.
- 23. Windecker S, Remondino A, Eberli FR, et al. Sirolimus-eluting and paclitaxeleluting stents for coronary revascularization. N Engl J Med 2005;353:653-662.

- 24.P.W. Serruys, S. Silber, S. Garg et al. Comparison of zotarolimus-eluting and everolimus-eluting coronary stents. N Engl J Med 2010;363(2):136-46.
- 25.Garg S, Sarno G, Girasis C, et al. A patient-level pooled analysis assessing the impact of the SYNTAX (synergy between percutaneous coronary intervention with taxus and cardiac surgery) score on 1-year clinical outcomes in 6,508 patients enrolled in contemporary coronary stent trials. JACC Cardiovasc Interv. 2011 Jun;4(6):645-53.
- 26.Magro M, Nauta S, Simsek C, et al. Value of the SYNTAX score in patients treated by primary percutaneous coronary intervention for acute ST-elevation myocardial infarction: The MI SYNTAXscore study. Am Heart J. 2011 Apr;161(4):771-81.
- 27.Magro M, Nauta ST, Simsek C, et al. Usefulness of the SYNTAX score to predict "no reflow" in patients treated with primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. Am J Cardiol. 2012 Mar 1;109(5):601-6.
- 28. Farooq V, Brugaletta S, Serruys PW. Contemporary and evolving risk scoring algorithms for percutaneous coronary intervention. Heart. 2011 Dec;97(23):1902-13.
- 29. Farooq V, Brugaletta S, Serruys PW. The SYNTAX score and SYNTAX-based clinical risk scores. Semin Thorac Cardiovasc Surg. 2011 Summer;23(2):99-105.
- 30.Farooq V, Brugaletta S, Serruys PW. Utilizing risk scores in determining the optimal revascularization strategy for complex coronary artery disease. Curr Cardiol Rep. 2011 Oct;13(5):415-23.

Table 1

Table 1. Baseline demographics & outcome		SYNTAX tertiles		
Gender and age		Low (%)	Intermediate (%)	High (%)
Male gender (n, %)	249 (72.2)	73.0	70.0	46.7
Age (mean ± SD)	61.96 ± 12.8	63.3	63.9	67.5
Cardiovascular Risk Factors (%)				
Dyslipidemia	52.0	52.8	62.7	50.0
Diabetes	24.0	21.3	28.8	35.7
Hypertension	48.8	41.1	44.1	71.4
Family history	13.2	12.4	13.6	14.3
Obesity	25.4	23.0	23.7	42.9
Smoking	53.5	55.6	55.9	28.6
Previous cardiovascular history (%)				
Prior PCI or MI	11.9	10.1	15.0	6.7
Outcome		Low	Intermediate	High
Peak CK (mean ± SD)	2406 ± 1905	1985	3336	3684
LVEF (mean % ± SD)	47.19 ± 11.85	50.0	44.4	41.4

Table 2

Table 2. Myocardial infarction localization

Inferior (%)	32.2
Anterior (%)	46.1
Posterior (%)	1.7
Infero-posterior (%)	9.6
Lateral (%)	2.6
Antero-latero-posterior (%)	0.6
Infero-lateral (%)	4.6
Postero-lateral (%)	0.3
Undefined (%)	2.3



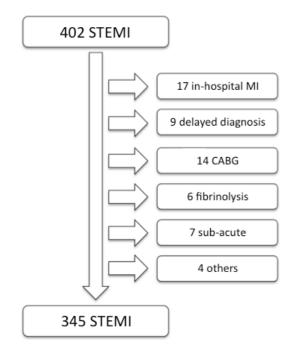


Figure 2

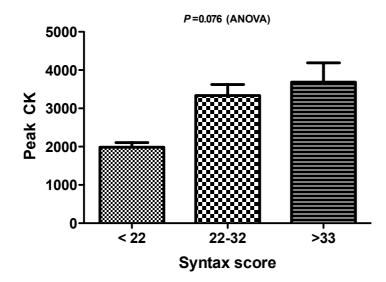


Figure 3

P < 0.0001 (Pearson)