

Comparison of Zwolle, Cadillac and Syntax-2 risk scores in predicting contrast nephropathy development in patients with ST elevation

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Abstract

Aim: It is known that early prediction of the patients who may develop contrast-induced is nephropathy (CIN) and initiate prophylactic treatment to reduce the risk of morbidity-mortality, hospitalization and prolonged length of stay. In our study, we aimed to compare the Zwolle, Cadillac and Syntax 2 (SS-2) risk scores that are currently used in the management of and predict mortality in patients with ST elevation myocardial infarction (STEMI) in terms of predicting CIN development.

Material and Methods: We enrolled 1622 patients who were diagnosed as STEMI and underwent primary coronary angiography between July 2014 and December 2018. 1381 patients were taken to the final analysis and two groups; CIN - (n=1295) and CIN + (n=86) were formed. Risk scores were compared in terms of CIN prediction.

Results: The mean age of the patients was 62±8 years and 72% of them were males. SS-2, Zwolle and Cadillac scores were significantly higher in CIN+ group (all p values <0.001). A comparative ROC curve analysis was performed for the estimation and clinical use of CIN. In the ROC curve analysis, the cut-off value for SS-2 was 16.7 (AUC:0.82) with a sensitivity of 80.1% and a specificity of 58%. The cut-off value for Cadillac was 1.5 (AUC:0.80), 78% sensitivity and 58% specificity. For Zwolle, the cut-off value was 2.5 (AUC:0.75) and the sensitivity was 73% and the specificity was 69%.

Conclusions: CIN, which develops after coronary angiography in STEMI patients, causes an increase in morbidity and mortality. The risk scores used in STEMI patients, in particular SS-2, may be more useful in predicting the development of CIN than in the Zwolle and Cadillac scores.

Keywords: Zwolle; Cadillac; Syntax 2 score; contrast induced nephropathy.

INTRODUCTION

Various scoring systems have been developed for predicting mortality and morbidity in coronary artery disease. These scoring systems guide both the treatment and follow-up of the patient. Cadillac score predicts short and long-term mortality in patients with ST elevation myocardial infarction (STEMI) by evaluating the patient's basal left ventricular ejection fraction (LV-EF), presence of renal insufficiency, Killip class, the final TIMI flow, the number of diseased vessels, age and anemia. The Zwolle score helps to evaluate the Killip class, TIMI flow, age, number of diseased vessels, presence of anterior infarct, and ischemia duration in STEMI patients in terms of early-safe discharge. Finally, Syntax 2 Score (SS-2) provides idea about long-term mortality with calculating a score based on classical SS -1. Furthermore, in SS-2; age,

creatinine clearance, LV-EF, gender, presence of chronic obstructive lung disease (COPD) and peripheral vascular disease (PVD) are evaluated (1-3).

Contrast-induced nephropathy (CIN) is defined as a sudden deterioration in renal function from 48 hours to 72 hours of contrast medium administration. CIN is the third most common cause of acute nephropathy after dehydration and nephrotoxic drug use (4). It is frequently seen after percutaneous coronary interventional (PCI) procedures. The duration of hospitalization due to CIN that develops after PCI is prolonged and causes an increase in morbidity and mortality. Advanced age, diabetes mellitus (DM), heart failure, presence of chronic renal failure and high levels of contrast agents are important risk factors for CIN development (5-8). Predicting the patients who may develop CIN, and initiating preventive treatments; it is

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extremely important to reduce the morbidity and mortality that may occur and to reduce the risk of hospitalization and prolonged hospitalization.

In this context, in this study, we aimed to compare Zwolle, Cadillac and SS-2 risk scores in terms of predicting CIN development, which are currently used in STEMI patients' treatment management and mortality estimations.

MATERIAL and METHODS

Study population

We enrolled 1622 patients who were diagnosed as STEMI and who underwent primary coronary angiography between July 2014 and December 2018 were included in the study. The study was designed retrospectively. We excluded the patients with systemic inflammatory disease history, autoimmune disease, liver disease, had active infection, severe renal failure (glomerular filtration rate <30 mL/min/1.73m² and dialysis dependent end stage renal disease), had cardiac surgery for emergency coronary revascularization and used contrast media within 10 days. Therefore, 1381 patients were taken to final analysis.

Definitions

For the diagnosis of STEMI, we used forth universal definition of myocardial infarction (9). Diabetes mellitus was defined as the use of antidiabetic medication due to elevated blood glucose levels, measurement of a fasting blood glucose level of >126 mg/dL or measurement of a postprandial blood glucose level of >200 mg/dL or a HbA1c level of >6.5. Hypertension (HT) was defined to have a blood pressure value of >140/90 mmHg after two consecutive measurements or previous use of antihypertensive medication. Contrast-induced nephropathy. Increase of creatinine level ≥ 0.5 mg/dl or $\geq 25\%$ above from baseline within 48-72 hours after contrast administration were defined as CIN. Patients with creatinine levels above 1.5mg / dL or in the dialysis program were noted as chronic renal failure. Smoking history was defined as positive for patients who were actively smoking and / or had a smoking history of 1 pack / year until a month ago.

In addition, serum creatinine, blood glucose, lipid levels, basal CK-MB, troponin and hematological indices (hemoglobin, white blood cell, platelet count, and mean platelet volume) were evaluated in all inpatients. Hematological indexes were obtained by using Coulter LH 780 Hematology Analyzer (Beckman Coulter Ireland Inc., Mervue, Galway, Ireland) and biochemical parameters were obtained using Cobas 6000 ce (Roche Diagnostics). Before coronary angiography, all patients underwent echocardiography and LV-EF was measured by Simpson method. SS-2, Cadillac and Zwolle scores were calculated from all patients using an online calculator. The study was approved by the Our Local Ethical Committee.

Statistics

The variables distributed normally were expressed as mean \pm standard deviation and the variables not distributed normally were expressed as median. Categorical variables were expressed as a percentage. While the Mann Whitney U

test or Student T test was used for comparison of numeric variables, the Chi Square test was used for comparison of categorical variables. ROC curve analysis was performed for prediction of CIN development. A p value of <0.05 was considered significant. Data were evaluated by using SPSS Statistics 23 package program (SPSS Inc, Chicago, IL, USA).

RESULTS

The mean age of the patients was 62 \pm 8 years and 72% of them were males. We generated two groups according to CIN. (Group 1, CIN-; n: 1295 and Group 2 CIN+, n: 96). When CIN + and CIN negative groups were compared, no significant difference was found in terms of age, gender, HT, DM, smoking and laboratory values. Sixty-five patients were died during the hospital stay due to the cardiovascular reasons in all study population. Moreover, there was no significant differences in terms of mortality between groups. Eleven patients underwent hemodialysis in CIN + group. The contrast media volume used in CIN + group was mean 240 \pm 45ml and in CIN - group was 210 \pm 25 ml (P=0.06). Baseline demographic and laboratory characteristics of the patients were shown in Table 1.

Table 1. Baseline demographic, laboratory and echocardiographic characteristics of the patients

Variables	CIN (-) Group (n=1295)	CIN (+) Group (n=86)	P Value
Age (years)	61.9 \pm 9.26	62.1 \pm 9.57	0.130
Gender (Male %)	72.1	73.5	0.430
DM (%)	37.2	38.1	0.290
HT (%)	43.8	45.2	0.300
Syntax Score II	19.8 (12-26)	27.8 (18-35)	<0.001
Cadillac Score	2 (0-4)	6 (2-9)	<0.001
Zwolle Score	2 (1-3)	4 (2-7)	<0.001
Smoking (%)	37.1	39.1	0.200
CRP(mg/dl)	3.21 (3-6)	3.15 (2.9-5.1)	0.400
Glucose (mg/dl)	114 (97-188.5)	121 (94.5-153.5)	0.830
Creatinine (mg/dl)	1.03 (0.8-1.4)	1.1 (0.8-1.5)	0.500
Na (mg/dl)	137 \pm 2.8	137 \pm 3.1	0.060
K (mg/dl)	4.4 \pm 0.2	4.1 \pm 0.4	0.600
TSH (IU/mL)	1 (0.6-1.5)	0.9 (0.9-1.3)	0.160
T4 (ng/dl)	0.9 \pm 0.2	0.9 (0.3)	0.500
AST (UI/L)	24 (19-34)	25 (20-38)	0.430
ALT (UI/L)	22 (13-32)	23 (18-31)	0.040
Albumin (mg/dl)	4.1 \pm 0.4	4.2 \pm 0.4	0.190
TC (mg/dl)	175 (44.7-186)	190 (152.5-230)	0.570
HDL (mg/dl)	40.2 (13.2-47)	31 (25-43.5)	0.040
LDL (mg/dl)	91 (37.25-87)	136 (98.5-164)	0.029
TG (mg/dl)	122 (104-146)	131 (114.5-201)	0.530
WBC (10 ³ / μ L)	8.1 \pm 2.6	9.5 \pm 2.1	0.150
Hemoglobin(g/dl)	14.8 \pm 1.6	14.1 \pm 1.5	0.780
Platelet (10 ³ / μ L)	246 \pm 65	236 \pm 64	0.160
EF, %	46 \pm 5.4	43 \pm 7.4	0.520
sPAB, mmHg	28 \pm 2.8	30 \pm 3.6	0.780
LA, mm	31 \pm 3.7	33 \pm 4.8	0.660

Abbreviations: DM; diabetes mellitus, HT; hypertension, SS; Syntax score, CRP; C reactive protein, TC; total cholesterol, HDL; high-density lipoprotein, LDL; low-density lipoprotein, TG; triglyceride, WBC; white blood cell, EF; Ejection Fraction, sPAB; systolic pulmonary artery pressure, LA; Left atrium

SS-2, Zwolle and Cadillac scores were significantly higher in CIN+ group (all p values <0.001). A comparative ROC curve analysis was performed for CIN development estimation and clinical use (Table 2). In the ROC curve analysis, the cut-off value for SS-2 was 16.7 (AUC: 0.82) with a sensitivity of 80.1% and a specificity of 58%. The cut-off value for Cadillac was 1.5 (AUC: 0.80), 78% sensitivity and 58% specificity. For Zwolle, the cut-off value was 2.5 (AUC: 0.75) and the sensitivity was 73% and the specificity was 69% (Table 2-3, Figure 1).

Table 2. ROC curve analysis of the risk scores for prediction contrast induced nephropathy

Variables	Cut-off value	AUC	Sensitivity (%)	Specificity (%)
Syntax Score II	16.7	0.82	80.1	58
Zwolle Score	2.5	0.75	73	69
Cadillac Score	1.5	0.80	78	58

Table 3. Comparative ROC curve analysis of the risk scores for prediction contrast induced nephropathy

Variables	P value
Syntax Score II- Zwolle Score	0.030
Syntax Score II- Cadillac Score	0.754
Zwolle Score -Cadillac Score	0.045

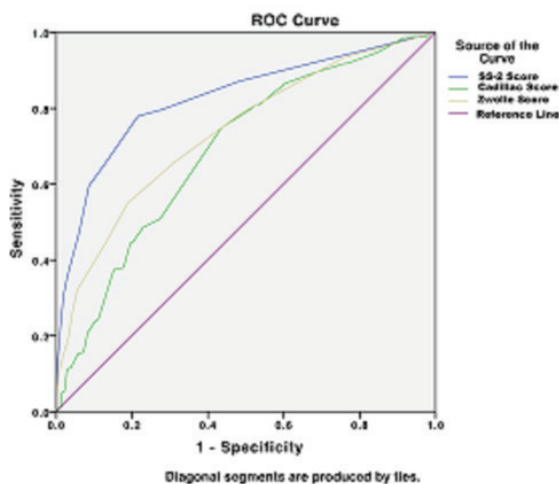


Figure 1. ROC curve analysis of the risk scores for prediction contrast induced nephropathy

DISCUSSION

The development of CIN in STEMI patients is associated with undesirable cardiovascular events and mortality. In our study, we compared the cardiovascular risk scores used in STEMI patients in predicting the development of CIN. As a result, SS-2 had the best estimation value with 0.82 and Zwolle had the lowest predictive value with 0.75.

CIN is seen 48-72 hours after contrast enhancement and although various bio mediators, renal vasoconstriction and direct tubular damage have been reported in the pathophysiology, the exact etiology remains unknown.

Current guidelines suggest using hypoosmolar contrast agents, iv hydration and avoid of pre-post procedural nephrotoxic agents to prevent development of CIN. Moreover, in a study; N acetyl cysteine with saline solutions was offered before PCI. However, in spite of the recommended treatments, the development of CIN is not completely prevented (5-8).

The fact that angiography is the first-choice method in the diagnosis of coronary artery disease and contrast agents are still required in angiography, therefore frequency of CIN is increased clinical practice. As a result; CIN causes to prolonged hospitalization time and leading to an increase in costs. In this context, early detection and early intervention of patients who may develop contrast nephropathy is important to reduce complications.

There are various approaches to predicting CIN development. In particular, Mehran scoring (MS) is currently being used in the estimation of patients who may develop CIN after PCI. In the MS, hypotension, intra-aortic balloon use, congestive heart failure, age > 75, presence of anemia, presence of diabetes, basal creatinine clearance and contrast media volume are considered(1,10,11). In SS2, Cadillac and Zwolle comparison, SS2 is the best predictor; similarly to MS, it adds age and creatinine clearance to the calculation. Secondly, the Cadillac of 0,80 is jointly with MS; renal failure, age and anemia are evaluated. Zwolle also has only age in common with the MS. The SS-2 and Cadillac CIN predictions may be high in the evaluation of creatinine clearance and age, similar to MS(1-3, 12-17).

Conventional risk factors for the development of CIN are hypotension, renal insufficiency, cardiac failure, excessive contrast use, DM, use of nephrotoxic agent and advanced age(18). One of these risk factors is heart failure evaluated by measurement of EF. Cadillac and SS-2 score are evaluated directly and Zwolle evaluates heart failure by considering anterior infarction. SS-2 takes into account the patient's coronary artery anatomy and coronary complexity in scoring. Similarly, Zwolle and Cadillac risk scores assess coronary anatomy, but consider patients only with 3-vessel disease. From this point of view, it is observed that SS-2 scoring takes all coronary arteries individually and makes a more comprehensive evaluation. Rencuzogulları et al. showed that SS-2 provides better prediction of CIN and hemodialysis requirement than SS(19). Furthermore, PRECISE-DAPT and TIMI risk index can predict CIN, it has proved in studies performed by Cinar et al(20, 21). In this context, SS-2 may be helpful in predicting the development of CIN in patients with STEMI, as the SS-2 has the most comprehensive assessment and has the highest predictive value from these three-risk scoring.

Although risk scores are widely used to predict cardiovascular events, their association on CIN development are not known. In this context, the risk scores can be calculated before the procedure and early detection of risky patients can be achieved and the risk of

CIN development can be reduced by using methods such as isoosmolar contrast agent or hydration.

Limitations

There were various limitations in our study. First, the study was designed retrospectively. The small number of patients can be considered as a limitation. Finally, the major adverse cardiac events could be stated in patients with CIN.

CONCLUSION

CIN development after PCI causes an increase of morbidity and mortality in patients with STEMI. The risk scores used in patients with STEMI, especially SS-2, may be more useful than the Zwolle and Cadillac scores in order to predict CIN development.

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Ethical approval: This work has been approved by the Institutional Review Board: The study was approved by the Our Local Ethical Committee.

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REFERENCES

- Littnerova S, Kala P, Jarkovsky J, et al. GRACE Score among Six Risk Scoring Systems (CADILLAC, PAMI, TIMI, Dynamic TIMI, Zwolle) Demonstrated the Best Predictive Value for Prediction of Long-Term Mortality in Patients with ST-Elevation Myocardial Infarction. *PLoS One* 2015;10:e0123215.
- Liu YH, Liu Y, Tan N, et al. Predictive value of GRACE risk scores for contrast-induced acute kidney injury in patients with ST-segment elevation myocardial infarction before undergoing primary percutaneous coronary intervention. *Int Urol Nephrol* 2014;46:417-26.
- Kul S, Uyarel H, Kucukdagli OT, et al. Zwolle risk score predicts contrast-induced acute kidney injury in STEMI patients undergoing PCI. *Herz* 2015;40:109-15.
- Deek H, Newton P, Sheerin N, et al. Contrast media induced nephropathy: a literature review of the available evidence and recommendations for practice. *Australian critical care: official journal of the Confederation of Australian Critical Care Nurses* 2014;27:166-71.
- Honicker T, Holt K. Contrast-Induced Acute Kidney Injury: Comparison of Preventative Therapies. *Nephrol Nurs J* 2016;43:109-16.
- John M. Contrast-Induced Nephropathy (CIN): current state of the evidence on contrast media and prevention of CIN. *AHRQ Comparative Effectiveness Reviews* 2016;18.
- Ando G, Trio O. Contrast-Induced Nephropathy After Primary Percutaneous Coronary Intervention: The Need for a Unifying Definition. *Am J Cardiol* 2017;119:169.
- McDonald RJ, McDonald JS, Newhouse JH, et al. Controversies in Contrast Material-induced Acute Kidney Injury: Closing in on the Truth? *Radiology* 2015;277:627-32.
- Thygesen K, Alpert JS, Jaffe AS, et al. Fourth Universal Definition of Myocardial Infarction (2018). *J Am Coll Cardiol* 2018;72:2231-64.
- Sato A, Hoshi T, Kakefuda Y, et al. Effect of the Mehran risk score for the prediction of clinical outcomes after percutaneous coronary intervention. *J Cardiol* 2015;66:417-22.
- Abellas-Sequeiros RA, Raposeiras-Roubin S, Abu-Assi E, et al. Mehran contrast nephropathy risk score: Is it still useful 10 years later? *J Cardiol* 2016;67:262-7.
- Serruys PW, Onuma Y, Garg S, et al. Assessment of the SYNTAX score in the Syntax study. *EuroIntervention* 2009;5:50-6.
- Askin L, Akturk E. Association between SYNTAX II score and electrocardiographic evidence of no-reflow in patients with ST-segment elevation myocardial infarction. *Turk Kardiyol Dern Ars* 2018;46:455-63.
- Nerlekar N, Ha FJ, Verma KP, et al. Percutaneous Coronary Intervention Using Drug-Eluting Stents Versus Coronary Artery Bypass Grafting for Unprotected Left Main Coronary Artery Stenosis: A Meta-Analysis of Randomized Trials. *Circ Cardiovasc Interv* 2016;9.
- Cid Alvarez AB, Gomez-Pena F, Redondo-Diequez A, et al. Prognostic impact of SYNTAX II score in patients with ST-elevation myocardial infarction undergoing Primary Percutaneous Coronary Intervention: analysis of a 4-year all-comers registry. *EuroIntervention* 2018;4.
- Palmerini T, Genereux P, Caixeta A, et al. Prognostic value of the SYNTAX score in patients with acute coronary syndromes undergoing percutaneous coronary intervention: analysis from the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial. *J Am Coll Cardiol* 2011;57:2389-97.
- Head SJ, Farooq V, Serruys PW, et al. The SYNTAX score and its clinical implications. *Heart* 2014;100:169-77.
- Mamoulakis C, Tsarouhas K, Fragkiadoulaki I, et al. Contrast-induced nephropathy: Basic concepts, pathophysiological implications and prevention strategies. *Pharmacol Ther* 2017;180:99-112.
- Rencuzogullari I, Cagdas M, Karakoyun S, et al. Association of Syntax Score II with Contrast-induced Nephropathy and Hemodialysis Requirement in Patients with ST Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention. *Korean Circ J* 2018;48:59-70.
- Cinar T, Karabag Y, Ozan Tanik V, et al. The investigation of TIMI risk index for prediction of contrast-induced acute kidney injury in patients with ST elevation myocardial infarction. *Acta Cardiol* 2019;25:1-8.
- Cinar T, Tanik VO, Arugaslan E, et al. The association of PRECISE-DAPT score with development of contrast-induced nephropathy in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Cardiovasc Interv Ther* 2019;34:207-15.