

PREDICTIVE VALUE OF THE CHA2DS2-VASC SCORE IN DETECTING IN-STENT RESTENOSIS AMONG PATIENTS WHO UNDERWENT PROXIMAL LEFT ANTERIOR DESCENDING ARTERY REVASCULARIZATION WITH DRUG ELUTING STENTS

By

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ABSTRACT

Background: Introduction of coronary stents in the field of interventional cardiology has significantly improved short- and long-term results of the percutaneous coronary interventions but in the same time they became responsible for development of a new entity called neo-intimal hyperplasia (NIH). If overexpressed, NIH can lead to so-called in-stent restenosis (ISR). The CHA2DS2-VASc score has recently been used to predict not only thromboembolic risk in atrial fibrillation (AF) but also adverse events in various cardiovascular diseases.

Objective: Assessment of the predictive value of the CHA2DS2-VASc Score in detecting in-stent restenosis among patients who underwent previous revascularization in proximal left anterior descending (LAD) Artery using drug eluting stents (DES) due to stable angina and acute coronary syndrome.

Patients and Methods: This study was a retrospective observational study conducted over 113 patients with previous history of percutaneous intervention (PCI) to Proximal LAD by DES who presented at our cardiology department catheterization laboratory for coronary angiography due to stable angina or acute coronary syndrome. Angiographic ISR was defined as narrowing $\geq 50\%$ in the stented coronary artery segment.

Results: From total of 113 patients, 38 patients (33.6%) had ISR with CHA2DS2-VASc score equal to or more than 3, (p value =0.033) in ISR group. Also there was a significant relationship between times since PCI of more than 3 years, stent length more than 32 mm and ISR (p value 0.028).

Conclusion: CHA2DS2-VASc score can be used as a simple and effective tool to predict ISR in patients underwent DES implantation in proximal LAD.

Keywords: CHA2DS2-VASc Score, Stent Restenosis, Stable Angina, Acute Coronary Syndromes.

INTRODUCTION

Coronary artery disease has been increasingly treated by coronary stent placement, which has greatly reduced restenosis after

balloon angioplasty (*Alfonso et al., 2014*).

In spite of new medications and development of revascularization techniques, in-stent restenosis

(ISR) after successful percutaneous coronary intervention (PCI) remains one of the most challenging problems in interventional cardiology and limits the efficacy of the procedure (*Ogita et al., 2011*).

The CHA2DS2-VASc score; congestive heart failure (CHF); hypertension; age 75 years (doubled); type 2 diabetes; previous stroke or transient ischemic attack (doubled); vascular disease; age 65-74 years; and sex (female) category has been initially recommended for the assessment of thromboembolic risk in patients with atrial fibrillation (AF) (*Camm et al., 2012*).

Several studies have demonstrated an association of the CHA2DS2-VASc score with cardiovascular prognosis and adverse outcomes in different patient populations, including heart failure, stable coronary artery disease (CAD), and ACS beyond the original AF field (*Orvin et al., 2016, Unal et al., 2016 and Yoshihisa et al., 2016*).

The predictive value of CHA2DS2-VASc score on ISR still remains unclear, although all of the components of the CHA2DS2VASc score are important risk factors for ISR.

AIM OF THE WORK

To assess the predictive value of the CHA2DS2-VASc Score in detecting in-stent restenosis among

patients who underwent previous revascularization in proximal left anterior descending (LAD) Artery using drug eluting stents (DES) due to stable angina and acute coronary syndrome

Study population:

This study included 113 patients with previous history of PCI to proximal LAD by DES who presented at our cardiology department catheterization laboratory for coronary angiography due to stable coronary artery disease or acute coronary syndrome, patients with renal impairments, bleeding tendency, and hemodynamic instability were excluded

Ethics approval and informed consent:

The study protocol was approved by Ain Shams University Faculty of Medicine scientific and ethical committee. Data confidentiality and privacy was maintained. All patients were informed about the registry and written consent was taken.

Methods:

The study is a retrospective observational study with collection of full data including medical history, CHA2DS2-VASc score calculation, drug history, previous PCI history, data of current coronary angiography with pattern and degree of ISR and its significance (“Angiographic”

restenosis means recurrent diameter stenosis (late lumen loss – LLL) >50% within the stent segment or its edges (5 mm segments adjacent to the stent) in follow-up. Clinical restenosis means symptoms or ischemia recurrence with >50% diameter stenosis or >70% diameter stenosis without symptoms).

Statistical analysis:

Using computer software statistical package for the social sciences (SPSS, version 20, SPSS Inc., Chicago, Illinois, USA)

Description of quantitative (numerical) variables was performed in the form of mean ± SD. Description of qualitative (categorical) data was performed in the form of number of cases and percent. Appropriate test of associations was performed using Chi-square test, Independent t-test, Mann Whitney test, repeated measure ANOVA test and Friedman test the significance level was set at p-value of less than 0.05.

RESULTS

The number of samples that fulfilled the inclusion and exclusion criteria in this study were 113 patients, of them 38 (33.6%) had significant ISR, while 75 (66.4%) had no ISR. The analysis of demographic and clinical data effect on ISR was shown in **table (1)** which showed significant effect of age (p=0.02), diabetes mellitus (p=0.02), CHA2DS2V-VASc SCORE (P=0.03) on ISR.

Table (1): Demographic data and ISR

Parameters	ISR	ISR ≥ 50%	ISR < 50%	p-value
Count (%)		38 (33.6%)	75 (66.4%)	
Age (years)				
Mean ± SD		61.21 ± 7.75	57.53 ± 8.08	0.022
Median (Range)		60.5 (48 – 76)	58 (34 – 80)	
Gender				
Male		32 (84.2%)	60 (80%)	0.587
Female		6 (15.8%)	15 (20%)	
CHF		22 (57.9%)	33 (44%)	0.163
HTN		28 (73.7%)	50 (66.7%)	0.446
DM		25 (65.8%)	33 (44%)	0.029
Vascular disease		1 (2.6%)	4 (5.3%)	0.662
CHA2DS2-VASc score				
Mean ± SD		2.55 ± 1.31	2.08 ± 1.01	0.033
Median (Range)		3 (0 – 5)	2 (0 – 5)	

The ROC curve analysis showed 3 as a cut-off value of CHA2DS2-VASc score as predictor of ISR with sensitivity 55.2%, specificity 66.6% and 75% negative predictive value (Table 2).

Table (2): Conclusion based on ROC curve analysis

Cut-off values	SN % (95% CI)	SP % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	Accuracy	AUROC (95% CI)
CHA2DS2VASc score ≥ 3	55.26% (38.3- 71.4)	66.67% (54.8- 77.1)	45.7% (30.9- 61.0)	74.6% (62.5- 84.5)	62.83%	0.619 (0.523-0.709)

Z = 2.055, p-value = 0.0398.

There was a Significant effect of the time since last PCI (P=0.001), while significant effect of stent length and ISR (Table 3).

Table (3): Relation between last PCI data and ISR

Last PCI data	ISR	ISR $\geq 50\%$	ISR $< 50\%$	p-value
Count (%)		38 (33.6%)	75 (66.4%)	
Time since last PCI (years)				
Mean \pm SD		4.66 \pm 2.65	2.93 \pm 1.67	0.001
Median (Range)		4.5 (1 – 10)	3 (1 – 9)	
Stent diameter (mm)				
Mean \pm SD		3.15 \pm 0.29	3.19 \pm 0.35	0.615
Median (Range)		3 (2.75 – 4)	3 (2.5 – 4)	
Stent length (mm)				
Mean \pm SD		31.21 \pm 10.77	35.68 \pm 10.41	0.028
Median (Range)		28 (18 – 48)	38 (18 – 48)	

DISCUSSION

Several studies have demonstrated an association of CHA2DS2-VASc score with cardiovascular prognosis and adverse outcomes in different pattern population including heart failure, SCAD and ACS beyond the original AF field. The predictive value of the CHA2DS2-VASc score on ISR still remains unclear although all of the components of the CHA2DS2-VASc score are important risk factors for ISR (Farooq *et al.*, 2011). For this reason, the present study was designed to evaluate the predictive value of CHA2DS2-VASc score on the

development of ISR in patients who underwent revascularization by DES.

This study showed a significant relationship between ISR and each of CHA2DS2-VASc score, Age, DM, time since the PCI was done, stent length used. However, non-significant relationship could be concluded between ISR and each of gender, CHF, HTN, vascular diseases, CAD type (stable angina or ACS), DBP, creatinine clearance, the duration of DAPT use, type of P2Y12 inhibitor used (clopidogrel or ticagrelol), use of statins, beta-blockers or nitrates and stent diameter used.

The current study were concordant with *Tocii et al., (2015)* regarding significant relationship with SBP and non-significant relationship between patient gender, CHF, creatinine clearance and use of statins. However, it was discordant with current study showing a significant relationship with use of DAPT and a non-significant relationship with both age and DM.

The study of *Watanabe et al., (2017)* showed concordant results with current study regarding a significant relationship with stent length. However, it showed discordant relationship with current study as it showed a significant relation with both stent diameter and ejection fraction. Difference between the 2 studies may be attributed to the difference in target vessel for each study.

Cho (2017) studied risk factors influencing ISR in ACS presentation. This study was able to show results regarding ISR in all CAD types (SCAD and ACS). It showed concordance with current study regarding a non-significant relation with sex, HTN, use of DAPT, Clopidogrel use, statins use and HBA1c. It showed a non-significant relation with age and DM which is discordant with the current study. This study was able to show that age, DM and use of clopidogrel are independent risk factors influencing ISR in ACS presentation.

The significant relationship between DES ISR and CHA2DS2-VASc score is consistent with another study conducted in 700 patients which was able to show significant relationship between BMS ISR and CHA2DS2-VASc score at cut off value of equal to or more than 3 (*Alfonso et al., 2017*).

Significant relationships with age, DM, & stent length were found in another study conducted on 407 patients *Kurtul et al., (2018)*, while CHA2DS2-VASc score at cut off value of equal to or more than 4 showed significant relationship to BMS-ISR, However, it was discordant with current study regarding significant relationship with gender, HTN CHF, creatinine clearance, HbA1c and stent diameter used.

Concordant results regarding insignificant relation with gender, DBP, HTN, HBA1c, CHF, Medical treatment offered and creatinine clearance were found (*Wang et al., 2018*), However it showed discordant results with current study because it denied a significant relationship with Age and SBP. Probable reason for discordance is the difference in sample size.

CONCLUSION

This study was able to show a significant relationship between ISR and each of CHA2DS2-VASc score, Age, DM, time since the PCI was done, stent length used. However, non-significant relationship could be concluded between ISR and each of gender, CHF, HTN, vascular diseases, CAD type (stable angina or ACS), uncontrolled DBP, creatinine clearance, HBA1c, use of DAPT, the duration of DAPT use, type of P2Y12 inhibitor used (clopidogrel or ticagrelol), use of statins, beta-blockers or nitrates and stent diameter used. This means that in the further years after more research in this aspect, the CHA2DS2-VASc score can be used as a prognostic tool in detecting in-stent restenosis among

patients who underwent previous revascularization due to stable angina or acute coronary syndromes.

LIMITATIONS

It is a retrospective study. The sample was not large.

Conflict of interest statement:

The authors have no conflicts of interest to declare.

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القيمة التنبؤية لنتاج شادس2 فاسك (CHADS2VAsc) لتوقع ضيق الدعامات الدوائية التي تم تركيبها للمرضي في الشريان التاجي الأيسر الامامي النازل حسن شحاته، رنا ايمن، ياسر جمعه، إيهاب الفقي

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خلفية البحث: أدي اكتشاف الدعامات إلي تجسن نتائج التدخلات القلبية علي المدى القصير و البعيد و لكنه أدي إلي ظهور ظاهرة جديدة تعرف بتكاثر الخلايا داخل الدعامة مما قد يؤدي إلي ضيقها و يستخدم ناتج شادس2 فاسك (CHAD2VASC) ليس فقط لتحديد خطورة التجلطات في مرضي الذبذبة الأذينية ولكن في العديد من أمراض القلب.

الهدف من البحث: دراسة القيمة التنبؤية لنتاج شادس2 فاسك (CHADS2VAsc) لتوقع ضيق الدعامات الدوائية التي تم تركيبها للمرضي في الشريان التاجي الأيسر الامامي النازل وذلك في حالات الذبذبة الصدرية المستقرة أو متلازمة الشريان التاجي الحادة.

المرضي و طرق البحث: إشتمل البحث علي المرضي الذين سبق لهم تركيب دعامات في الشريان التاجي الأيسر النازل الامامي والذين حضروا لعمل قسطرة علي الشرايين التاجية بمستشفيات جامعة عين شمس نتيجة الذبذبة الصدرية المستقرة او متلازمة الشريان التاجي الحادة و تم تعريف ضيق الدعامة بوجود ضيق أكثر من 50% من قطر الدعامة.

نتائج البحث: التحق بهذه الدراسة مائه و ثلاثه عشر مريضاً، كان منهم ثمانية و ثلاثون مريضاً يعانون من ضيق بالدعامه و ناتج شادس2 فاسك عندهم أكبر من او يساوي 3 وهي علاقة هامة، كما أوضحت الدراسة علاقة هامة بين مدة وضع الدعامه (أكثر من 3 سنوات) و طول الدعامه (أطول من 32 مم) و حدوث الضيق في الدعامه.

الاستنتاج: ناتج شادس 2 فاسك (CHADS2VAsc) هو طريقة بسيطة وفاعلة للتنبؤ بضيق الدعامات التي تم تركيبها في الشريان التاجي الأمامي الأيسر النازل.

الكلمات الدالة: ناتج شادس 2 فاسك (CHADS2VAsc)، حدوث الضيق في الدعامات، حالات الذبحه الصدرية المستقرة، و متلازمة الشريان التاجي الحادة.