



Original Article

Predictors of major adverse cardiac events following elective stenting of large coronary arteries



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ABSTRACT

Objective: Diameter of the affected coronary artery is an important predictor of restenosis and need for revascularization. In the present study, we investigated the frequency and potential risk factors for major adverse cardiac events following elective percutaneous coronary intervention (PCI) and stenting of large coronary arteries.

Methods: We reviewed the data of elective candidates of PCI on a large coronary artery who presented to our center. Demographic, clinical, angiographic and follow-up data of the eligible patients were retrieved from our databank. The study characteristics were then compared between the patients with and without MACE in order to find out the probable risk factors for MACE in patients with large stent diameter.

Results: Data of 3043 patients who underwent single vessel elective PCI with a stent diameter of ≥ 3.5 mm was reviewed. During a median follow up period of 14 months, 64 (2.1%) patients had MACE. TVR was the most common type of MACE that was observed in 29 patients, while 5 patients had cardiac death. Higher serum levels of creatinine, history of cerebrovascular accident (CVA), and use of a drug eluting stent (DES) were significantly associated with MACE. In the multivariate model, history of CVA (odds ratio = 5.23, $P = 0.030$) and use of DES (odds ratio = 0.048, $P = 0.011$) were the independent predictors of MACE in patients underwent large coronary artery stenting.

Conclusion: This study showed that prior CVA and the use of BMS were the potential risk factors for MACE in patients who were stented on their large coronary arteries.

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1. Introduction

Coronary artery disease (CAD) is a common cause of morbidity and mortality in developed and developing countries.^{1,2} By the advances in the revascularization techniques, particularly percutaneous coronary intervention (PCI), more patients undergo revascularization with single vessel disease.³

Diameter of the affected coronary artery is an important predictive factor for restenosis and need for target vessel revascularization (TVR).⁴ Therefore, the clinical outcome between

small-vessel stenting versus large-vessel stenting can be different as small vessels are more prone to restenosis.^{5,6} On the other hand, type of the stent is another important factor. Drug eluting stents (DES) reduce the risk of restenosis; however, there are some considerations regarding their usage, such as higher price, longer duration of dual antiplatelet therapy that increases the risk of minor and major bleeding, patients' intolerance and some serious complications like late and very late stent thrombosis, especially in the first generation of DES.^{7–10} Thus, it is important to identify the risk factors for MACE in patients who undergo large coronary artery stenting.

In the present study, we investigated the frequency and potential risk factors for MACE following elective PCI and stenting of large coronary arteries in patients who presented to our center.

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2. Methods

In this study, we reviewed the data of elective candidates of PCI on a large coronary artery who presented to our center consecutively from March 2004 to March 2014. Inclusion criteria of this study were: 1) age >18 years; 2) complete clinical profile in the Tehran Heart Center Databank; 3) Being followed-up for at least 9 months, unless developing the study endpoints; 4) Single vessel stenting; 5) stent diameter ≥ 3.5 millimeter. Based on our routine, all patients give an informed consent at the time of admission that their data would be registered in the THC databank and would be used for research purposes anonymously. The protocol of this study was confirmed by the committee of ethics and institutional board of research.

Demographic, clinical, angiographic and follow-up data of the eligible patients were retrieved from the THC databank, which its characteristics has been described elsewhere.^{11,12} Cardiovascular risk factors were also reviewed for each patient, including diabetes mellitus, hypertension, dyslipidemia, smoking, opium abuse, and family history of coronary artery disease as defined institutionally based on the international guidelines.¹³ For blood tests, venous blood samples were obtained before the procedure and routine blood tests, including fasting blood sugar, serum creatinine, and lipid profile was performed for every patient.

All the procedures were performed at the catheterization laboratory of THC using the latest protocols and guidelines as described before.¹⁴ Type of stent was selected to each particular case based on the clinical situation and the interventionist's discretion. All patients received 300–600 mg loading dose of

clopidogrel plus 325 mg aspirin before the intervention and 70–100 IU/kg intravenous unfractionated heparin during the procedure. Clopidogrel (75 mg/d) and aspirin (325 mg/d) were continued for at least 1-month. Then aspirin was tapered to 80 mg for lifelong use while clopidogrel was prescribed for a minimum of 1-month in BMS and 12 months in DES.

Follow-up data were collected prospectively by scheduled inpatient visits or direct telephone interviews. All the events were recorded from the time of intervention. The primary endpoint was the incidence of MACE defined as cardiac death, nonfatal myocardial infarction (MI), target lesion revascularization (TLR) or target vessel revascularization (TVR).

The study characteristics were then compared between the patients with and without MACE in order to find out the probable risk factors for MACE in patients with large stent diameter.

2.1. Statistical analysis

Continuous variables are presented as means \pm standard deviation, or as median and interquartile range boundaries, as appropriate. Categorical variables were expressed as frequency and percentage. Association of the variables with MACE occurrence was assessed using univariate logistic regression model and was reported through odds ratio (OR) with 95% confidence interval (CI). Variables with *p*-values less than 0.1 were entered in a multivariable logistic regression model to find the multiple predictors of MACE. Statistical analyses were conducted applying IBM SPSS Statistics for Windows, version 23.0 (Armonk, NY: IBM Corp.).

Table 1

General characteristics of the study population and univariate analysis of the characteristics related to major adverse cardiac events.

Characteristic	Total (n=3043)	MACE free (n=2979)	MACE (n=64)	Odds ratio	95% confidence interval	P-value
Age, year	57.1 \pm 10.5	57.1 \pm 10.4	56.7 \pm 10.8	0.99	0.97–1.02	0.774
Male gender, n (%)	2367 (77.8)	2317 (77.8)	50 (78.1)	1.02	0.56–1.85	0.947
BMI, kg/m ²	27.9 \pm 4.3	27.9 \pm 4.3	27.6 \pm 4.7	0.98	0.92–1.04	0.592
EF, %	50.0 \pm 10.3	50 \pm 10.2	48.7 \pm 10.7	0.99	0.96–1.01	0.295
Diabetes mellitus, n (%)	688 (22.6)	672 (22.6)	16 (25.0)	1.14	0.64–2.02	0.649
Hypertension, n (%)	1358 (44.6)	1328 (44.7)	30 (46.9)	1.09	0.66–1.79	0.725
Dyslipidemia, n (%)	1931 (63.4)	1892 (64.2)	39 (60.9)	0.87	0.52–1.45	0.591
Smoking, n (%)	902 (29.6)	881 (29.7)	21 (32.8)	1.15	0.68–1.96	0.585
Opium, n (%)	334 (11.0)	330 (11.7)	4 (7.1)	0.59	0.20–1.61	0.296
Family history of CAD, n (%)	575 (18.9)	562 (19.0)	13 (20.3)	1.08	0.58–2.01	0.793
Past medical history						
CVA, n (%)	44 (1.4)	41 (1.4)	3 (4.7)	5.02	1.14–22.0	0.032
Renal failure, n (%)	52 (1.7)	50 (1.7)	2 (3.1)	1.88	0.44–7.93	0.386
CHF, n (%)	10 (0.3)	9 (0.7)	1 (3.1)	4.42	0.54–36.02	0.164
COPD, n (%)	45 (1.5)	44 (3.5)	1 (3.1)	1.13	0.15–8.51	0.901
Total cholesterol, mg/dl	173.6 \pm 46.9	173.6 \pm 47.0	177.9 \pm 44.3	1	0.9–1.01	0.524
Triglyceride, mg/dl	151.0 [110.0, 212.0]	150.0 [110.0, 212]	165.0 [135.0, 227.5]	1	0.99–1.00	0.406
LDL, mg/dl	102.6 \pm 38.0	102.6 \pm 38.0	103.8 \pm 38.4	1	0.99–1.00	0.837
HDL, mg/dl	40.3 \pm 10.4	40.3 \pm 10.4	39.5 \pm 9.1	0.99	0.96–1.02	0.61
Fasting blood sugar, mg/dl	100.0 [89.0, 120.0]	100.0 [89.0, 120.0]	106.0 [90.0, 128.0]	1	0.99–1.01	0.18
Creatinine, mg/dl	1.1 [0.9, 1.2]	1.1 [0.9, 1.2]	1.1 [0.9, 1.3]	1.57	1.07–2.31	0.02
Hb A1c, %	7.9 [6.7, 9.5]	7.9 [6.8, 9.5]	8.2 [6.2, 10.2]	0.97	0.78–1.19	0.775
Hb, mg/dl	14.2 \pm 1.7	14.2 \pm 1.7	14.0 \pm 1.9	0.93	0.71–1.21	0.611
Target vessel, n (%)						
LAD	1602 (52.6)	1575 (52.9)	27 (42.2)	0.65	0.39–1.07	0.093
LCX	355 (11.7)	343 (11.5)	12 (18.8)	1.15	0.69–1.92	0.569
RCA	1086 (35.7)	1061 (35.6)	25 (39.1)	1.77	0.93–3.53	0.078
Stent length >20 mm, n (%)	1678 (55.1)	1646 (55.3)	32 (50.0)	0.81	0.49–1.32	0.404
Type of stent, n (%)						
BMS	1115 (36.8)	1081 (36.4)	34 (53.1)	Reference	–	–
DES	1918 (63.2)	1888 (63.6)	30 (46.9)	0.5	0.30–0.83	0.007

BMI: Body mass index; BMS: Bare metal stent; CAD; Coronary artery disease; CHF: Congestive heart failure; COPD: Chronic obstructive pulmonary disease; CVA: Cerebrovascular accident; DES: Drug eluting stent; EF: Ejection fraction; HB: Hemoglobin; LAD: Left anterior descending artery; LCX: Left circumflex artery; LDL: Low density lipoprotein; MACE: Major adverse cardiac events; RCA: Right coronary artery.

*P-value < 0.05 was considered as statistically significant.

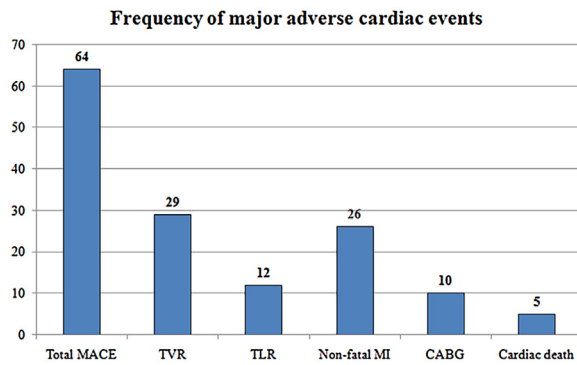


Fig. 1. Frequency of total MACE and its subtypes in the study population. (CABG: Coronary artery bypass graft; MACE: Major adverse cardiac events; MI: Myocardial infarction; TLR: Target lesion revascularization; TVR: target vessel revascularization).

3. Results

For this study, from a total of 29508 procedures, data of 3043 patients who underwent single vessel elective PCI with a stent diameter of ≥ 3.5 mm and met our study criteria were reviewed. The median follow-up period was 14 months. Mean age of the study population was 57.1 ± 10.5 and 77.8% were males. Dyslipidemia (63.4%) was the most common cardiovascular risk factor among them and left anterior descending artery was the most common revascularized artery (52.6%) (Table 1).

Within the follow up period, 64 (2.1%) patients had MACE. TVR was the most common type of MACE that was observed in 29 patients, while 5 patients had cardiac death (Fig. 1).

In the univariable regression analysis, history of cerebrovascular accident (CVA) ($P=0.032$), serum creatinine ($P=0.020$) and type of stent ($P=0.007$) were potential predictors for MACE as shown in Table-1. In the multivariable model, and after the inclusion of potential confounders, history of CVA and type of stent were the major predictors of MACE in our study ($P=0.030$ and $P=0.011$, respectively) (Table 2).

4. Discussion

In this study, we found that prior CVA and the use of BMS were potential risk factors for MACE in a cohort of patients with PCI on large coronary arteries. The incidence of MACE in our study was 2.1% within a median follow-up period of 14 months.

Diameter of the culprit vessel seems to have no effect on the clinical outcome of the PCI and MACE as shown by previous studies.^{6,15} However, several studies have shown that patients who received BMS in large coronary arteries had a worse survival than the drug eluting stent (DES) recipients.^{16,17} On the other hand, patients with BMS tend to be more prone to TVR.¹⁸ Because several type of DES stents were used in our patients, we could not relate this effect to a specific type of stent or its drug, but our finding is in line with all previous studies that showed a better clinical outcome

with DES.^{19,20} It has been shown that DES significantly reduces TVR and thereby total MACE.²¹

Despite the previous evidence that the stent length was a predictor for stent thrombosis,²² the proportion of patients with stent length above 20 mm was not different between the study groups and almost half of the patients within each group had a stent length above 20 mm. Therefore, it seems that the common belief that longer stents are more prone to thrombosis and complications may not come true for high diameter stents.

A more recent study on the use of new generations of DES in the left main artery PCI showed a lower chance of mortality in these patients in comparison with coronary artery bypass graft (CABG).²³ However, we still consider patients with left main coronary artery stenosis for CABG in our center. On the other hand, use of DES was accompanied by better clinical outcomes as compared with BMS use, even in the elderly patients.²⁴ Both studies confirm our findings that the type of stent can influence the outcome of PCI in large coronary arteries.

The second risk factor for MACE in our study was prior CVA. CVA is normally considered as one of the complications following PCI; however, its role as a risk factor for MACE seems to be underestimated to date. It is probable that presence of prior CVA as a comorbidity makes the patients more susceptible to MACE but proving this demands further investigations.

4.1. Study limitation

Although we studied a large number of patients with large vessel stenting, the main limitation of our study is the limited duration of follow-up (median 14 months) and thereby relatively low frequency of MACE that limited the power of our study to find other potential risk factors of MACE in our study. Furthermore, based on practice protocol in our center, patients with significant left main stenosis are normally referred to coronary artery bypass grafting (CABG) surgery. Hence, our result cannot be extended to patients with isolated left main stenting.

5. Conclusion

In conclusion, this study on patients who were stented on their large coronary arteries showed that the rate of MACE was 2.1% and prior CVA and the use of BMS were the potential risk factors for MACE. However, the length of the stent did not influence the frequency of MACE. For detecting the definite predictors for MACE following PCI on large coronary arteries, larger studies with longer follow-up duration are required.

Conflict of interest

None declared.

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Table 2

Adjusted multivariable model for the predictors of major adverse cardiac events following the stenting of large coronary arteries.

Characteristic	Odds ratio	95% confidence interval	P-value
Previous CVA	5.23	1.17–23.14	0.03
Serum Creatinine (each 1 mg/dL increase)	1.46	0.98–2.17	0.058
LAD stenting	0.81	0.44–1.50	0.51
LCX stenting	1.56	0.73–3.26	0.249
Type of stent (DES)	0.48	0.28–0.84	0.011

CVA: Cerebrovascular accident; DES: Drug eluting stent; LAD: Left anterior descending artery; LCX: Left circumflex artery.

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