Predictors of the Development of Major Adverse Cardiac Events following Percutaneous Coronary Intervention

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Keywords
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Abstract
Background: Coronary artery disease remains the greatest cause of morbidity and mortality worldwide despite the growing access to percutaneous coronary intervention (PCI). Data regarding the factors predicting the development of major adverse cardiac events (MACE) in patients undergoing PCI are, however, lacking in the gulf region. In this study, we analyze demographics and risk profile of all patients undergoing PCI in a tertiary cardiovascular center located in Dubai – UAE. In our study, we aimed to analyze the risk profile of all patients undergoing PCI and determine the independent predictors of MACE.

Methods: Data were collected prospectively on all patients who underwent PCI in our hospital between September 2017 and September 2018. Patients aged 18 years and above were included in the study and there were no exclusion criteria. The definition of MACE was a composite of death, in-hospital recurrent myocardial infarction (MI), in-hospital target vessel revascularization (TVR), and stroke. The patients’ characteristics, risk factor, and demographics were analyzed to identify the predictors of MACE using logistic regression model which is presented in odds ratio. Results: Data were available for 789 patients. Of these, 741 (94%) were male. The mean age was 52 ± 11 years. Twenty-two (3%) patients died, 7 (1%) had an in-hospital recurrent MI, 6 (1%) had in-hospital TVR, and 1 (0.1%) had a stroke. Of the patients who died, 16 (73%) patients presented with cardiogenic shock. Major adverse cardiovascular events occurred in 29 (3.7%) patients. In the multivariable regression model, only cardiogenic shock (odds ratio [OR] = 32.43) and the presence of diabetes mellitus (OR = 3.36) were predictors of MACE. Conclusion: Our study showed that cardiogenic shock and diabetes mellitus are the independent predictors of MACE in patients undergoing PCI.

Introduction

Coronary artery disease (CAD) continues to be one of the major causes of morbidity and mortality worldwide. CAD accounts for about one-third or more of all deaths in individuals over the age of 35 years [1–3]. The World Health Organization reports that CAD is the primary cause of death globally, with estimated death of 17.9 million persons per year (31% of all deaths worldwide); of
these deaths, 85% are due to heart attack and stroke [4]. It is believed that the annual incidence of CAD mortality will increase from 17.9 million to 22.2 million by the year of 2030 if no active interventions are taken [3].

In the UAE, CAD remains a great concern and a leading cause of death in the population, as reported by the Ministry of Health and Prevention. Of all CAD deaths, 22% are due to acute myocardial infarction (MI) [5] despite the growing access to PCI facilities. PCI or PCI with stenting were associated with improved overall outcome and long term safety profile [6, 7]. However, poor prognosis post revascularization was attributed to the development of the major adverse cardiac events (MACE) following PCI [8]. Hence, it is of great importance to study the potential predictors and risk factors for the development of MACE following PCI.

In our study, we aimed to analyze the risk profile of our patients including demographics, the presence of medical comorbidities such as diabetes mellitus, hypertension, and cerebrovascular disease. In addition, the use of thrombolytic therapy and chronic total occlusion PCIs were analyzed. We assessed whether these variables were independent predictors of the development of MACE in patients undergoing PCI.

Materials and Methods

In this study, data were collected prospectively from September 2017 to September 2018. We studied 789 patients who were admitted and underwent PCI in a tertiary cardiovascular center located in Rashid Hospital – Dubai, UAE. We collected data using the Rashid Hospital Percutaneous Coronary Intervention Registry (RHPICIR). The RHPCIR collects a standardized twelve-page case report form for all PCI procedures performed at Rashid Hospital as part of the electronic medical record.

The RHPCIR collects data including demographics and risk factors including age, gender, cardiovascular risk factors, and left ventricular ejection fraction as assessed by transthoracic echocardiogram. Procedural characteristics data including route of arterial access for PCI, the number, type and size of stents per PCI, the door to device time for primary PCI patients, the rate of angiographic success, and adherence to guideline based medical therapy. All patients aged 18 years and above were included in the study including patients with renal impairment, heart failure, history of stroke, and transient ischemic attacks and there were no exclusion criteria. MACE was defined as a composite of death, nonfatal MI, in-hospital target vessel revascularization, and stroke.

In this study, we examined the risk profile of all patients in relation to the development of MACE. The patients’ characteristics were then compared between the population with and without MACE to determine the likely predictors of MACE following PCI.

We hypothesized that the presence of diabetes mellitus, hypertension, dyslipidemia, male gender, current smoking, thrombolytic therapy, chronic total occlusion PCIs, left main coronary artery PCI, previous history of ischemic heart disease, cardiogenic shock on presentation, and out-of-hospital cardiac arrest (OHCA) were independent predictors of MACE. These predictors were compared between patients with and without MACE in order to confirm our assumption.

Statistical Analysis

The analyzed continuous variables were represented as mean ± standard deviation while the analyzed categorical variables were expressed as frequency (n) and a percentage. The variables were analyzed in relation to the occurrence of MACE using the univariate and multivariate logistic regression model. Statistically significance was assumed with a p value of <0.05.

Results

In our study, data were available for 789 patients. Table 1 lists patients’ demographics. The mean age of our patients was relatively young and the vast majority of our patients were male (94%) with a mean age of 52 ± 11 years.

The frequency of MACE between September 2017 and September 2018 was 3.7%. Twenty-two (3%) patients
died, 7 (1%) had an in-hospital recurrent MI, 6 (1%) had in-hospital target vessel revascularization, and 1 (0.1%) had an ischemic stroke as listed in Table 2.

The univariate analysis using logistic regression model showed that the presence of diabetes mellitus (No MACE group \( n = 350 \) [45.9%], MACE group \( n = 21 \) [77.8%] with \( p \) value of 0.005), dyslipidemia (No MACE group \( n = 351 \) [46.1%], MACE group \( n = 7 \) [25.9%] with \( p \) value of 0.019), current smoking (No MACE group \( n = 289 \) [37.9%], MACE group \( n = 5 \) [18.5%] with \( p \) value of 0.023), OHCA (No MACE group \( n = 20 \) [2.6%], MACE group \( n = 6 \) [7.4%] with \( p \) value <0.001), and cardiogenic shock on presentation (No MACE group \( n = 26 \) [3.4%], MACE group \( n = 17 \) [62.9%] with \( p \) value <0.001) were statistically significant factors as shown in Table 3. Further analysis of the statistically significant factors using the multivariate logistic regression model confirmed that the presence of diabetes and cardiogenic shock on presentation were true independent predictors of MACE. Of the patients who died, 17 (70%) patients presented with cardiogenic shock (odds ratio = 32.43, 95% CI: 12.4–84.5). Diabetic patients on the other hand were found to have almost triple the risk of MACE (odds ratio = 3.36, 95% CI: 1.31–8.59) post PCI as shown in Table 4.

### Discussion

We aimed in our study to identify the independent predictors of the development of MACE in our population. To the best of our knowledge, this is the first observational study to analyze the independent predictors of MACE post PCI in our region. We found that patients who present with cardiogenic shock have thirty-two times higher risk of developing MACE following PCI and diabetic patients have triple the risk of developing MACE post PCI. The strong association between cardiogenic shock and MACE was demonstrated in multiple previous studies. In one such example, it was noted that patients with preprocedural cardiogenic shock have a mortality incidence rate of 17.1% and a MACE incidence rate of 28.6% after PCI [9]. In another study by the American College of Cardiology-National Cardiovascular Data Registry, data from 483 patients who underwent emergency PCI for cardiogenic shock were analyzed [10]. Cardiogenic shock was noted to be associated with a high mortality rate reaching up to 60% post PCI [10]. The association between cardiogenic shock and poor overall outcome is likely attributed to the decrease in the cardiac output, resulting in hypotension and reduced coronary and systemic perfusion. This in turn triggers a vasoconstriction reflex as well as systemic inflammation, causing more severe myocardial dysfunction, mortality, and MACE [11].

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### Table 3. Predictors of MACE

| Risk factors                        | No MACE (\( n = 762 \)) | MACE (\( n = 27 \)) | \( p \) value |
|-------------------------------------|--------------------------|---------------------|---------------|
| Male gender, \( n \) (%)            | 715 (93.8)               | 26 (96.3)           | 0.328         |
| Diabetes mellitus, \( n \) (%)      | 350 (45.9)               | 21 (77.8)           | 0.005         |
| Hypertension, \( n \) (%)           | 385 (50.5)               | 13 (48.1)           | 0.538         |
| Previous PCI, \( n \) (%)           | 146 (19.2)               | 4 (14.8)            | 0.466         |
| Current smoking, \( n \) (%)        | 289 (37.9)               | 5 (18.5)            | 0.023         |
| Dyslipidemia, \( n \) (%)           | 351 (46.1)               | 7 (25.9)            | 0.019         |
| CTO PCI, \( n \) (%)                | 16 (2.1)                 | 2 (7.4)             | 0.081         |
| Cardiogenic shock, \( n \) (%)      | 26 (3.4)                 | 17 (62.9)           | 0.000         |
| OHCA, \( n \) (%)                   | 20 (2.6)                 | 6 (7.4)             | 0.000         |
| LMCA PCI, \( n \) (%)               | 23 (3.0)                 | 2 (7.4)             | 0.988         |
| Thrombolytic therapy, \( n \) (%)   | 525 (68.9)               | 21 (77.8)           | 0.874         |

MACE, major adverse cardiac events; PCI, percutaneous coronary intervention; CTO, chronic total occlusion.

### Table 4. Multivariate analysis of the predictors of MACE

| Multivariate analysis                   | Odds ratio | \( p \) value | 95% CI        |
|----------------------------------------|------------|---------------|---------------|
| Diabetes mellitus, \( n \) (%)        | 3.360      | 0.029         | 1.313–8.596   |
| Current smoking, \( n \) (%)          | 0.493      | 0.128         | 0.166–1.464   |
| Dyslipidemia, \( n \) (%)             | 0.577      | 0.506         | 0.215–1.490   |
| OHCA, \( n \) (%)                     | 1.447      | 0.826         | 0.376–5.572   |
| Cardiogenic shock, \( n \) (%)        | 32.435     | 0.000         | 12.438–84.586 |

CI, confidence interval; CTO, chronic total occlusion; PCI, percutaneous coronary intervention.
Similar to our findings, patients with diabetes mellitus were found to have less favorable angiographic outcomes following coronary stent placement and higher incidence of MACE compared to the nondiabetic patients as investigated in multiple previous studies [12–14]. Diabetes was associated with higher incidence of death, MI, reinterventions, and increased risk of restenosis [12]. Importantly, diabetic patients with good risk factor control and managed on diet or oral hypoglycemic medications had similar outcomes to the nondiabetic population post PCI [14]. Several causative factors were suggested to explain the impact of diabetes mellitus on the adverse outcome post PCI. One such example is the decreased resistance of the myocardium to the ischemic insult due to the poor collateral flow [15]. The PROSPECT study showed that type 2 diabetic patients tend to have coronary atherosclerotic lesions characterized by a large necrotic core, thin-cap fibroatheroma, and high calcium content [16]. These characteristic lesions favor plaque instability and degradation, and predict future MACE independent of myocardial ischemia [16].

In the univariate analysis, we found MACE to be associated with OHCA. This association is likely attributed to delays in the prehospital “chain of survival.” Up to 80% of patients with OHCA present in coma despite the successful resuscitation and the return of the spontaneous circulation [17], which indicates post-resuscitation brain injury, the severity of which may vary from no or mild disability to permanent vegetative state or brain death [17]. Death from neurologic injury was reported more than 3 times as frequently as death from a cardiac cause in post cardiac arrest patients [18]. Several factors leading to the poor overall outcome including unwitnessed cardiac arrest, late arrival of a prehospital team without basic life support (>10 min), presence of an initial non-shockable rhythm, and more than 20 min of advanced life support without return of the spontaneous circulation indicating a remote likelihood for neurological recovery [17]. The majority of MACE were driven by in-hospital mortality [19].

Thrombolytic therapy of left main coronary artery stenting and previous history of PCI were not associated with higher incidence of MACE, unlike the hypothesis formulated at the commencement of this study. In the univariate analysis, MACE was found to be associated with current smoking, dyslipidemia, and OHCA, but this significance did not hold with the multivariate analysis.

Study Limitations

There were several limitations to this study. First, this is an observational study from only one center in our region. Further studies are needed to investigate the clinical outcome following PCI. Second, we did not analyze several complications following PCI such as contrast-induced nephropathy, vascular access injuries, and bleeding. Third, there is no long-term follow-up to the enrolled patients of this study. Fourth, the relatively low incidence of MACE in our patients limited the power of this study.

Conclusion

In conclusion, cardiogenic shock and the presence of diabetes were found to be independent predictors of MACE. The incidence of MACE in patients undergoing PCI in our center is relatively low (3.7%).

Statement of Ethics

This study is done and complies with the guidelines of human subjects of Helsinki Declaration. It was approved by the Dubai Scientific Research Ethics Committee (DSREC) with the following ethics approval reference number: DSREC-01/2019/_03 dated 31 January 2019, for Dubai Health Authority Hospitals. Patients signed in the medical record system and the general information consent to use their de-identified data for the purpose of education and research.

Conflict of Interest Statement

The authors report no relationships that could be construed as a conflict of interest.

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Author Contributions

All authors contributed in the work and consent for publication. N.A.: writing the research manuscript, data collection, and data analysis. N.S.: conceiving the research idea, data collection, data analysis, proposal writing. F.O.B.: idea conception. A.A., M.A., J.A., M.G., and G.A.: idea conception and data collection.

Data Availability Statement

The data that support the findings of this study are not publicly available due to security reasons. However, the data are available upon reasonable request from the corresponding author N.A.
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