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Research Article

Long-term Outcomes of Patients with Diabetes Mellitus Undergoing Coronary Revascularization for ST-Segment Elevation Myocardial Infarction: A Single Centre Study

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Abstract

Diabetes mellitus (DM) is a major risk factor for coronary artery disease (CAD) and is associated with a higher incidence of myocardial infarction (MI) and sudden cardiac death (SCD). Patients with DM have higher mortality during the acute period of acute coronary syndrome (ACS), greater morbidity during the postinfarction recovery phase and more frequent re-infarction than patients without DM. Reperfusion therapy with primary percutaneous coronary intervention (PCI) in ST-segment elevation myocardial infarction (STEMI) is associated with higher short-term mortality (30-days) in patients with DM when compared with outcomes in patients without DM. The long-term efficacy of reperfusion therapy with thrombolysis is well established, 8,9 but few data are available on long-term outcomes of PCI for STEMI in patients with DM. We therefore sought to determine long-term outcomes of contemporary PCI in STEMI patients with and without DM.

In a single centre series of 273 patients treated for STEMI in the contemporary era, 17.6% of patients had a diagnosis of DM. Mortality was not different among patients with and without DM at all time points, although the proportion of deaths was numerically greater in DM patients. Management of STEMI in patients with DM was associated with a trend more frequent AKI. Kidney injury is a significant risk factor for long-term mortality, highlighting the importance of mitigating AKI in patients with DM who present with STEMI.

In the present study, mortality at 3 years after STEMI in patients with DM was 18.9%. There was a trend toward adverse outcomes in patients with STEMI and DM compared to patients without DM, although due to the small sample size, none of the comparisons met statistical significance. Additional studies to improve outcomes of patients with DM and STEMI are necessary.

Keywords: *Diabetes Mellitus; Revascularization; AKI*

Background

Diabetes mellitus (DM) is a major risk factor for coronary artery disease (CAD) [1,2] and is associated with a higher incidence of myocardial infarction (MI) and sudden cardiac death (SCD) [3]. Patients with DM have higher mortality during the acute period of acute coro-

nary syndrome (ACS), greater morbidity during the post- infarction recovery phase and more frequent re-infarction than patients without DM [4-7]. Reperfusion therapy with primary percutaneous coronary intervention (PCI) in ST-segment elevation myocardial infarction (STEMI) is associated with higher short-term mortality (30-days) in patients with DM when compared with outcomes in patients without DM [10-14]. The long-term efficacy of reperfusion therapy with thrombolysis is well established [8,9], but few data are available on long-term outcomes of PCI for STEMI in patients with DM [22,23]. We therefore sought to determine long-term outcomes of contemporary PCI in STEMI patients with and without DM.

Methods

Patients

Consecutive patients presenting to the Gold Coast University Hospital (GCUH) in Southport, Australia with STEMI between January 1, 2013 to December 31, 2014 were identified. We collected detailed information including demographics, co-morbidities, medications, prior therapeutic interventions (previous thrombolytic therapy, revascularization procedures), left ventricular ejection fraction (LVEF), coronary anatomy, procedural details of coronary revascularization and outcomes.

Outcome measures

The primary outcomes were short and long-term mortality following PCI for STEMI in patients with and without DM. Survival was determined at 30 days, 1 year and 3 years. The incidence of post-PCI acute kidney injury (AKI), defined as > 25% increase in creatinine at 48 to 72 hours post intervention, and post procedure bleeding complications were also evaluated.

Statistical analysis

Categorical variables were compared using Chi-square tests, continuous variables were compared using nonparametric test. Kaplan Meier plots with log rank tests were generated to determine and compare event rates over time. Multivariable Cox proportional hazards models were then used to determine the impact of diabetes on survival adjusted for clinical covariates. The proportion hazards assumption was tested. All baseline variables recorded were included in risk-adjustment models. Statistical analyses were performed using SPSS. The Gold Coast University Hospital Institutional review board approved this project.

Results

The Gold Coast University Hospital (GCUH) is a major tertiary level care facility, which provides revascularization services in Gold Coast and primary PCI is the preferred treatment strategy for STEMI. From January 1, 2013 to December 31, 2014, a total of 273 patients had percutaneous coronary intervention (PCI) for STEMI. All 273 cases had ST-elevation myocardial infarction (STEMI) of which 48 (18%) had a diagnosis of DM. Overall 19 (7%) presented after out-of-hospital cardiac arrest, all of whom were within the non-diabetic group and 6 (2.2%) patients received intravenous thrombolysis prior to transfer for rescue PCI (5 vs 1 in the non- diabetic and diabetic group respectively, $p = 0.95$). The means age was 60.8 ± 12.2 years of age, 83.2% were men. Baseline demographics and clinical characteristics of the study cohort are shown in table 1. There was no difference in age (62.0 vs. 60.5, $p = 0.44$) or female sex (22.9% vs. 15.6%, $p = 0.22$) between patients with and without diabetes mellitus. The presence of co-morbidities including hyperlipidemia and hypertension were significantly higher in the diabetes group, as was weight. At the time of presentation, cardiac troponin was higher and estimated GFR was lower in patients with DM versus those without DM (53.37 vs 35.87, $p < 0.05$ and 76.62 vs 79.63, $p = 0.25$, respectively). Age at presentation and left ventricular function were similar in both cohorts.

	ALL (N = 273)	Non-Diabetic (n = 225)	Diabetic (N = 48)	P-value
Patient Data				
Age	60.77 (12.2)	60.5 (12.01)	62 (12.94)	0.44
Male	227 (83.2%)	190 (84.4%)	37 (77.1%)	0.22
Weight	87.07 (40.31)	83.7 (14.09)	102.5 (90.32)	0.03
Past Medical History				
Hyperlipidemia	113 (41.4%)	83 (36.9%)	30 (62.5%)	0.001
Hypertension	130 (47.8%)	98 (43.8%)	32 (66.7%)	0.004
Smoker	116 (42.5%)	101 (44.9%)	15 (31.3%)	0.04
Ex-Smoker	58 (21.2%)	43 (19.1%)	15 (31.3%)	0.06
Creatinine (umol/L)	93.33 (47.54)	93.17 (49.85)	94.1 (35.2)	0.9
eGFR (mL/min)	79.08 (16.78)	79.63 (16.16)	76.62 (19.26)	0.25
Presenting Features				
Troponin Elevation	38.98 (51.63)	35.87 (46.43)	53.37 (69.75)	0.03
HB	144.12 (17.13)	144 (16.55)	144.71 (19.77)	0.79
Left Ventricular Function (252, 205 and 47)	52.01 (10.25)	52.5 (9.97)	49.7 (11.31)	0.09
Thrombolysis (Referring Hospital)	6 (2.2%)	5 (2.2%)	1 (2.1%)	0.95
Out of Hospital Cardiac Arrest	19 (7%)	19 (8.4%	0	0.04
Values are mean ± SD and n (%)				

Table 1: *Patient baseline characteristics (n = 272).*

Table 2 describes the procedural details of PCI. All patients were referred to the cardiac catheterization laboratory for emergent PCI. Transfemoral arterial access was used in a majority (62%) of patients undergoing PCI. Among patients who underwent PCI, 65% of patients with DM received a Drug Eluting Stent (DES) compared to 54% of patients without DM. Patients undergoing coronary artery bypass grafting were more commonly diabetic. Table 3 describes the stent diameters used in patients with DM. Within the cohort with DM, only 3 patients received a DES < 2.5 mm in diameter.

	ALL (N = 273)	Non-Diabetic (n = 225)	Diabetic (N = 48)	P-value
Primary Coronary Intervention (PCI)	243 (89%)	199 (88.4%)	44 (91.7%)	0.47
PCI Approach				
Radial	106 (38.8%)	89 (39.6%)	17 (35.4%)	0.6
Femoral	170 (62.3%)	138 (61.3%)	32 (66.7%)	0.49
Both	5 (1.8%)	4 (1.8%)	1 (2.1%)	0.89
Coronary Artery Disease				
Left Main and Triple Vessel Disease	5 (1.8%)	5 (2.2%)	0 (0%)	0.3
Left Main and Double Vessel Disease	2 (0.7%)	1 (0.4%)	1 (2.1%)	0.23
Left Main and Single Vessel Disease	2 (0.7%)	0 (0%)	2 (4.2%)	0.002
Triple Vessel Disease	40 (14.7%)	36 (16%)	4 (8.3%)	0.17
Double Vessel Disease	66 (24.2%)	53(23.6%)	13 (27.1%)	0.61
Single Vessel Disease	167 (61.2%)	136 (60.4%)	31 (64.6%)	0.6

Intervention				
Single PCI	196 (72.2%)	162 (72%)	35 (72.9%)	0.7
Multi PCI	45 (16.5%)	37 (16.4%)	8 (16.7%)	0.68
Plain Old Balloon Angioplasty	11 (4%)	9 (4%)	2 (4.2%)	0.96
Emergency Coronary Artery Bypass Graft (CABG)	21 (7.7%)	16* (7.1%)	5 (10.4%)	0.44
CABG and PCI	6 (2.2%)	3** (1.3%)	3*** (6.3%)	0.04
Failed PCI	12 (4.4%)	11 (4.9%)	1 (2.1%)	0.39
Stent				
Drug Eluting Stent	152 (55.7%)	121 (53.8%)	31 (64.6%)	0.32
Bare Metal Stent	94 (34.4%)	80 (35.6%)	14 (29.2%)	0.98
Both	5 (1.8%)	4 (1.8%)	1 (2.1%)	0.89
Failed	12 (4.4%)	11 (4.9%)	1 (2.1%)	0.39
Not attempted	18 (6.6%)	15 (6.7%)	3 (6.3%)	0.92
Values are mean ± SD and n (%)				

Table 2: *Procedural details.*

**4 failed and went for CABG.*

*** 2 went for CABG after a single and multi-vessel stent.*

***3 CABG performed after single PCI with BMS.

	Diabetic (N = 50)
Stent	
Drug Eluting Stent - Single Stent	26 (52%)
2.25 mm	1(2%)
2.5 mm	4 (8%)
2.75 mm	5 (10%)
3.0 mm	13 (26%)
3.5 mm	3 (6%)
Drug Eluting Stent - Multiple Stents	6 (12%)
2.0 mm and 3.5 mm	1 (2%)
2.25 mm and 3.0 mm	1 (2%)
2.5 mm and 3.0 mm	1 (2%)
2 * 2.5 mm and 3.5 mm	1 (2%)
2 * 3.0 mm	1 (2%)
3.0 mm and 4.0 mm	1 (2%)
Bare Metal Stent - Single Stent	14 (28%)
2.5 mm	3 (6%)
3.0 mm	5* (10%)
3.5 mm	4** (8%)
4.0 mm	1 (4%)
Bare Metal Stent - Multiple Stent	1 (2%)
3 * 2.75 mm	1 (2%)
CABG	3(6%)
Values are mean ± SD and n (%)	

Table 3: *Diabetic Cohort who received PCI.*

**: Two patients went onto surgery.*

***: One patient went on to CABG.*

Table 4 describes the medications at the time of hospital discharge. The majority of patients with STEMI were discharged on aspirin (99%) and a P2Y12 receptor antagonist (94%). Patients who were not discharged on a P2Y12 inhibitor were generally patients without DM who underwent CABG. Statins, angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) and beta-blockers were prescribed to 97%, 89% and 83% of patients, respectively. There was no observed statistically significant difference between the medications on discharge between the 2 groups.

	ALL (N = 261)	Non-Diabetic (N = 214)	Diabetic (N = 47)	P-value
Medication on Discharge				
P2Y12 Receptor Antagonist	254 (94.4%)	209 (94.6%)	45 (93.8%)	0.82
Ticagrelor	179 (66.3%)	146 (65.8%)	33 (68.8%)	0.69
Clopidogrel	76 (28%)	64 (28.7%)	12 (25%)	0.61
None	15* (5.6%)	12* (5.4%)	3 (16.7%)	0.82
Aspirin	267 (98.5%)	220 (98.7%)	47 (97.9%)	0.7
Beta Blocker	226 (83.4%)	185 (83%)	41 (85.4%)	0.68
ACE I or ARB	241 (88.9%)	195 (87.4%)	46 (95.8%)	0.9
Statin	263 (97%)	217 (97.3%)	46 (95.8%)	0.59
Values are mean ± SD and n (%)				

Table 4: *Post procedural care.*

**All went to CABG and did not receive a stent.*

Outcomes are shown in table 5. A similar proportion of patients died at 30 days, including 6% of patients with DM and 4% of those without DM. TIMI major bleeding was similar in both cohorts. Patients with DM had a higher proportion of patients with AKI than those without DM (22% vs 8%, $p < 0.05$).

	ALL (N = 273)	Non-Diabetic (N = 225)	Diabetic (N = 48)	P-value
30 Day Outcomes				
30 day mortality	11 (4%)	8 (3.6%)	3 (6.3%)	0.39
30 day TIMI Major Bleeding	13 (4.8%)	11 (5%)	2* (4.3%)	0.84
Creatinine ≥ 25 at 48 - 72 hours post intervention	27 (10.3%)	17 (7.8%)	10 (21.7%)	0.005
	ALL (N = 226)	**Non-Diabetic (N = 182)**	**Diabetic (N = 44)**	
1 Year Mortality	20 (8.8%)	14 (7.7%)	6 (13.6%)	0.3
	ALL (N = 185)	**Non-Diabetic (N = 148)**	**Diabetic (N = 37)**	
3 Year Mortality	26 (14.1%)	19 (12.8%)	7 (18.9%)	0.84
Values are mean ± SD and n (%)				

Table 5: *30 Day, 1 year and 3 year outcomes.*

**One patient had Major bleed and died in cardiogenic shock.*

Table 5 describes the 30-day, 1 year and 3-year outcomes. Patients were followed for a median of 296 days (IQR 4 - 1489). Mortality at 30 days was 6% among patients with diabetes and 4% in those without non-diabetic group. At 1 year, mortality was 14% among patents with DM and 8% in the group without DM. Loss of follow up at 1 year was 18% and 12% in the non-diabetic and diabetic groups respectively. At 3 years, 19% of patients with DM died versus 13% of patients without diabetes. There were no differences in mortality among patients with and without diabetes (12.5% vs. 12.0%, p = 0.99; aHR 1.03, 95% 0.42-2.53, adjusted for age/sex). There was no difference in the incidence of stent thrombosis (p = 0.89) or major bleeding (p = 0.84) between the groups with and without diabetes. There was a trend towards more AKI in the cohort with DM.

Discussion

In a single centre series of 273 patients treated for STEMI in the contemporary era, 17.6% of patients had a diagnosis of DM. Mortality was not different among patients with and without DM at all time points, although the proportion of deaths was numerically greater in DM patients. Management of STEMI in patients with DM was associated with a trend more frequent AKI.

Acute kidney injury following PCI for STEMI may be due hemodynamic instability and the adverse renal effects of iodinated contrast media. Radiocontrast-induced nephropathy (RCIN) is a potentially preventable complication in patients with pre-existent renal disease and/or conditions, which could lead to renal disease in the long-term. It is defined as an increase in serum creatinine by 0.5 mg/dL or 25% above baseline 48 hours after exposure to radiocontrast [17,18]. It is the third leading cause of hospital-acquired acute renal failure [17,19,20] and is a widely debated and discussed topic in modern cardiovascular medicine. Although there is risk stratification schemes available [16], these may not always be feasible to use prior to emergency revascularization for STEMI. Strategies and protocols for post procedure renal protection are important and may help reduce the incidence of AKI. Several pharmacological agents have been evaluated as prophylactic agents to prevent AKI. However, through various large studies, none of them have been proven to be effective and simple measures like pre-hydration, cessation of nephrotoxic drugs and limiting the amount of contrast use are the mainstay of therapy for prophylaxis [17,18]. Kidney injury is a significant risk factor for long-term mortality, highlighting the importance of mitigating AKI in patients with DM who present with STEMI [21].

Limitations of the Study

There are a number of important limitations. First, this was a single centre retrospective audit of electronic medical records of consecutive STEMIs presenting to a large regional PCI centre. Laboratory data were not available in all cases. Loss to follow up occurred in 68 cases. Experienced operators at this high-volume academic centre performed all PCI procedures. Outcome's reported here may not be applicable to other centres. Due to the relatively small sample, the study is under-powered for meaningful comparisons of the group with and without diabetes.

Conclusion

In the present study, mortality at 3 years after STEMI in patients with DM was 18.9%. There was a trend toward adverse outcomes in patients with STEMI and DM compared to patients without DM, although due to the small sample size, none of the comparisons met statistical significance. Additional studies to improve outcomes of patients with DM and STEMI are necessary.

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