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Original Article

Temporal trends in the outcomes of patients with acute myocardial infarction associated with renal dysfunction over the past decade

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ABSTRACT

Background: Patients with renal dysfunction (RD) who present with acute myocardial infarction (AMI) are at a high risk for subsequent cardiovascular morbidity and mortality. We sought to evaluate changes in the short and long term mortality of AMI patients with RD compared to patients with normal renal function over the last decade.

Methods: This study based on 4 bi-annually surveys was performed from 2002 to 2010 and included 9468 AMI patients, that were followed for 1 year, of whom 2770 (29%) had reduced estimated GFR ([eGFR] < 60 ml/min/m^2). Among patients with reduced eGFR: 1251 patients (45%) were included in the 2002–2005 surveys (early period) and 1519 (55%) in the 2006–2010 surveys (late period).

Results: Patients with RD were more likely to have advanced cardiovascular disease, multiple comorbidities and higher in-hospital, 30-day, and 1-year mortality rates (8.1%,12.3% and 23% vs. 0.7%, 1.7% and 4%, respectively; all $p < 0.001$). Patients with RD enrolled during the late survey periods were more likely to undergo primary PCI and be discharged with current evidence based medical treatment. 1-year mortality rates were significantly lower among patients with RD who were enrolled during the late vs. early survey periods: 22% vs. 25% respectively; (Log-rank P-value <0.001). Consistently, multivariate analysis showed that patients with RD who were enrolled during the late survey periods displayed a lower adjusted risk for 1-year mortality (HR 0.83; CI[0.70–0.94] P = 0.01).

Conclusions: Prognosis of patients with RD admitted with AMI has significantly improved over the last decade, possibly due to an improvement of pharmacological and non-pharmacological management.

1. Introduction

The association between renal dysfunction and acute coronary syndrome (ACS) is increasingly recognized; moreover renal dysfunction is associated with a higher frequency of hypertension, diabetes, previous myocardial infarcts (MI), as well as older age. Furthermore, the prevalence of cardiovascular diseases rises with the decline in renal function, as patients with impaired renal function have more severe coronary artery disease [1–5].

Many patients with decreased renal function are treated less aggressively with therapeutic interventions and risk factor modification [6,7]. It is well established that progressive renal deterioration is associated with poor outcome [8–10]. Impaired renal function is an independent predictor of death in patients with ST elevation myocardial infarction (STEMI) [11].

Over the years new medical technologies and therapeutic agents have been introduced for the management of acute MI (AMI) patients that have significantly improved morbidity and mortality in this population [12]. However, data regarding the incremental benefits of these newer management strategies in AMI patients with impaired renal function are limited.

The aim of the present study was to evaluate temporal trends in the outcomes associated with renal dysfunction in AMI patients who were enrolled in the biannual Acute Coronary Syndrome Israeli Surveys (ACSIS) from 2002 through 2010.

2. Methods

2.1. Study population

The ACSIS (Acute Coronary Syndrome Israeli Survey) registry is a biannual prospective observational national survey of all patients with

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definite diagnosis of AMI hospitalized in all of the 25 coronary care units in Israel, during a 2-month period (June and July).

During each survey, patient data are collected by means of the comprehensive pre-specified case report forms. Details of the ACSIS registry have been previously reported [13].

The present study data were derived from ACSIS surveys conducted in the years: 2002, 2004, 2006, 2008 and 2010. From 2002 to 2010, 11,536 patients, during a two-month period bi-annually, were enrolled into the ACSIS surveys, of whom 9468 (82%) had available data regarding baseline serum creatinine and were included in the present study. Serum creatinine result was obtained during the first day of the index hospitalization.

2.2. Follow-up

Patient management was at the discretion of the attending physicians. Admission and discharge diagnoses were recorded as determined by the attending physicians, based on clinical, electrocardiographic, and biochemical (elevated troponin and/or creatine kinase (CK)-MB levels) criteria. Data were collected by dedicated study physicians and checked for consistency and completeness. Available data included demographic information, historical and clinical data, including in-hospital medical management and performed procedures. In-hospital complications were recorded on pre-specified forms by dedicated medical personal. In-hospital, 30-day post discharge and 1-year outcome were ascertained by hospital chart review, telephone contact and use of the Israeli National Population Registry. Study protocol was approved by the participating institute review boards and corresponds to the Helsinki declaration.

2.3. Definition and endpoints

Renal dysfunction: based on the serum creatinine level measured on admission, the estimated glomerular filtration rate (eGFR) was assessed using the Modification of Diet in Renal Disease formula (MDRD) [14]: eGFR (ml/min/1.73 m^2) = 186.3 × serum creatinine (mg/dl) − 1.154 × age − 0.203 × 1.212 (if patient is black) × 0.742 (if female). Patients were categorised based on eGFR to patients without significant renal disease (eGFR ≥60 ml/min/1.73 m^2) and those with renal disease (eGFR <60 ml/min/1.73 m^2), as defined by the National Kidney Foundation [15].

The ACSIS survey periods over the past decade were categorized as early (years: 2002–2005) and late period (years: 2006–2010).

Diagnosis of diabetes and hypertension were based on medical history.

The primary study end point was all-cause mortality at 1-year. Secondary endpoint included in-hospital death and 30-day mortality.

2.4. Statistical methods

Patients with normal eGFR were compared to those with reduced eGFR, by comparing categorical variables using the Chi-square test and continuous data using the unpaired Student's t-test or Mann Whitney test, as appropriate. Similarly, patients in the reduced eGFR group were further compared according to their survey period early (2002–2005) vs. late (2006–2010) using the same statistical methods described. Rates of reduced eGFR prevalence were calculated, and trend analysis was performed using the Mantel–Haenszel method.

Survival curves were constructed using the Kaplan–Meier method, and unadjusted comparisons of survival curves were performed using the Log-rank test.

Multivariate logistic regression analysis was used to evaluate factors associated with in-hospital and 30-day outcomes, whereas multivariate Cox proportional hazards regression modeling was used to evaluate factors associated with 1-year mortality. The following pre-specified covariates were introduced in all above described regression multivariate models in addition to dichotomized eGFR (<60 vs. ≥60 ml/min/1.73 m^2): age, gender, smoking status, hypertension, diabetes, history of CABG, prior PCI, prior MI, admission Killip class, STEMI (vs. non-STEMI), presence of Q-wave on discharge ECG, survey period (categorized as early [years: 2002–2005] vs. late [years: 2006–2010]), and left ventricular ejection fraction (LVEF) determined during hospitalization (dichotomized at LVEF <40%), PCI in STEMI, thrombolysis in STEMI, in-hospital events of heart failure and events of atrial fibrillation or flutter during hospitalization. Additionally, we evaluated mortality risk associated with reduced eGFR in subjects with kidney dysfunction (GFR < 60 ml/min/1.73 m^2) by introducing eGFR as a continuous covariate in addition to the covariates detailed above.

To evaluate whether outcome differences between the two survey periods (late vs. early) differed significantly based on the presence of renal dysfunction, an interaction term for survey period by RD (<60 vs. ≥60 ml/min/m^2) was included in the Cox regression model.

For all analyses, a two-sided $P < 0.05$ was considered statistically significant. Data were analyzed using SPSS software, version 20 (IBM, Chicago, IL).

3. Results

3.1. Characteristics of patients by renal function groups

A total of 9468 patients with AMI and eGFR data have been included in the 5 surveys (Table 1), of whom 6698 (71%) patients had eGFR ≥60 ml/min/m^2, and 2770 had eGFR <60 ml/min/m^2 (29%). As

Table 1
Patient characteristic by renal function group.

	eGFR ≥ 60 (n = 6698)	eGFR < 60 (n = 2770)	P-value
Age (mean ± SD)	60.1 ± 11	72.8 ± 10	<0.001
Female gender	1194 (18%)	1022 (37%)	<0.001
Smoking	1217 (18%)	621 (23%)	<0.001
History of:			
Diabetes mellitus	2017 (30%)	1260 (45%)	<0.001
Hyperlipidemia	4244 (63%)	1787 (64%)	0.91
Hypertension	3416 (51%)	2137 (77%)	<0.001
Prior MI	1684 (25%)	1130 (41%)	<0.001
Prior TIA/CVA	390 (6%)	394 (14%)	<0.001
Index event			
ST elevation MI	3321 (49%)	1060 (38%)	<0.001
Non ST elevation MI	3276 (48%)	1527 (55%)	<0.001
Undetermined ECG[a]	201 (3%)	184 (7%)	0.01
LVEF (mean ± SD) (%)	48.6 ± 11	43.8 ± 12.8	<0.001
GFR (mean ± SD) (ml/min/m^2)	85.7 ± 18	42.3 ± 14	<0.001
Killip class III–IV	237 (4%)	452 (16%)	<0.001
Primary PCI in STEMI	1632 (72%)	479 (76%)	0.054
Thrombolysis in STEMI	590 (18%)	137 (13%)	<0.01
CHF in hospital	411 (6%)	461 (17%)	<0.001
New AF in hospital	139 (4%)	169 (11%)	<0.001
Days in CCU	4.3 ± 3.6	5.3 ± 4.6	<0.01
Days in hospital	5.9 ± 6	7.9 ± 7	<0.001
In hospital mortality	47 (0.7%)	224 (8.1%)	<0.001
30 day mortality	114 (1.7%)	341 (12.3%)	<0.001
1 year mortality	265 (4%)	647 (23%)	<0.001
Discharge medications			
ACE I/ARB	5031 (75%)	1889 (69%)	<0.001
Aspirin	6466 (96%)	2369 (86%)	<0.001
ADP antagonists	5015 (75%)	1581 (58%)	<0.001
β blocker	5505 (82%)	2009 (74%)	<0.001
Statins	5937 (88%)	2087 (77%)	<0.001

Abbreviations: MI = myocardial infarction, TIA = transient ischemic attack, CVA = cerebro vascular accident, LVEF = left ventricular ejection fraction, GFR = glomerular filtration rate, PCI = percutaneous coronary intervention, STEMI = ST elevation MI, AF = atrial fibrillation, CCU = coronary care unit, ACE I = angiotensin converting enzyme inhibitor, angiotensin receptor blocker, ADP = adenosine diphosphate.

[a] Patients with: paced rhythm, left bundle branch block and marked intra-ventricular conduction delay.