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Temporal trends in management and outcomes of patients with acute coronary syndrome according to renal function

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ABSTRACT

Introduction: Recent new therapeutic options have improved outcomes of acute coronary syndrome (ACS) patients. However, data regarding the incremental effect of the improved treatment on patients with renal dysfunction are limited. We sought to evaluate temporal trends in management and outcome of ACS patients according to renal function.

Methods: The study population consisted of all ACS patients enrolled in the Acute Coronary Syndromes Israeli Survey (ACSIS) during 2002–2013. Patients were categorized as normal renal function, mild to moderate and severe renal insufficiency. Patient's characteristics, clinical data and outcomes were compared in each group between 2 time frames - early (2002–2006) vs. late (2008–2013).

Results: The study population included 11,234 patients. Regardless of renal function, patients enrolled in the recent surveys were more frequently selected for an invasive approach and were more commonly treated with guideline-based therapy. Among patients with normal renal function or mild to moderate renal dysfunction the improvement in treatment was associated with a significant reduction in 5-year mortality (10.1% vs. 12.6%, $p = 0.004$, and 36% vs. 41.9%, $p = 0.01$, respectively). On the other hand, outcomes of patients with severe renal insufficiency were unchanged. Multivariate analysis showed that reperfusion was associated with 41% mortality reduction in patients with mild to moderate renal insufficiency (HR = 0.59 CI 95 0.48–0.72, $p < 0.01$%).

Conclusions: Treatment of ACS patients has improved over the past decade. Treatment improvement was associated with a significant mortality reduction in patients with normal renal function and mild to moderate renal dysfunction but not in patients with severe renal dysfunction.

1. Introduction

Chronic renal dysfunction is a frequent comorbidity among patients with acute coronary syndrome (ACS) [1–5]. It has been well demonstrated that even mild renal disease is an independent risk factor for cardiovascular complications and death after acute myocardial infarction [1,2]. Each reduction of the estimated glomerular filtration rate (eGFR) by 10 units was associated with a 10% increase in the risk for death and non-fatal cardiovascular outcomes [1].

The association between renal insufficiency and adverse clinical outcomes is multifactorial and may be partially explained by differences in treatment. Several studies have demonstrated that ACS patients with renal dysfunction were more commonly selected for a conservative rather than an invasive strategy approach with an early coronary angiogram and subsequent angioplasty, compared to patients with normal renal function [1,3,4]. It has also been demonstrated that guideline-based medications such as β-blockers, ACE-inhibitors, statins and anti-platelets were underutilized in ACS patients with renal dysfunction [1,3,4].

Over the last 2 decades the treatment of ACS patients has improved dramatically with the introduction of new technologies in coronary revascularization and more potent medical therapy. These changes have significantly reduced mortality and morbidity of patients with ACS [6]. However, data regarding the incremental effect of these new therapeutic options on patients with renal dysfunction are still limited. A single study has demonstrated a significant reduction in 1-year mortality in patients with acute myocardial infarction and concomitant

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Table 1
Baseline characteristics by kidney function in early versus late survey periods.

	Severe renal insufficiency eGFR < 30 N = 648			Mild to moderate renal insufficiency 30 < eGFR < 60 N = 2598			Normal renal function eGFR > 60 N = 7988		
	Early N = 329	Late N = 319	p	Early N = 1468	Late N = 1130	p	Early N = 4286	Late N = 3702	p
Male gender	192 (58.4)	200 (62.7)	0.294	922 (62.8)	764 (67.6)	0.012	3499 (81.6)	3073 (83.0)	0.116
Age (mean ± SD)	74.17 (11.42)	73.25 (11.67)	0.313	72.45 (10.90)	72.13 (10.91)	0.466	60.22 (12.11)	60.15 (11.98)	0.794
Prior MI	151 (45.9)	143 (45.1)	0.903	567 (38.6)	459 (40.6)	0.322	1006 (23.5)	1011 (27.4)	<0.001
Prior CABG	56 (17.0)	61 (19.1)	0.553	239 (16.3)	191 (16.9)	0.712	361 (8.4)	245 (6.6)	0.003
Prior PCI	43 (13.0)	62 (19.5)	0.011	220 (15.0)	250 (22.1)	<0.001	904 (21.0)	1149 (31.0)	<0.001
COPD	24 (7.3)	23 (7.2)	0.905	83 (5.6)	63 (5.6)	0.766	136 (3.1)	152 (4.1)	0.053
PVD	80 (24.4)	65 (20.4)	0.268	204 (13.9)	152 (13.5)	0.782	263 (6.1)	189 (5.1)	0.053
Prior stroke	69 (21.1)	56 (17.6)	0.298	207 (14.1)	125 (11.1)	0.025	242 (5.7)	220 (5.9)	0.604
Hypertension	254 (77.2)	275 (86.2)	0.004	1079 (73.6)	911 (80.8)	<0.001	2056 (48.0)	2093 (56.6)	<0.001
Diabetes Mellitus	159 (48.3)	202 (63.5)	<0.001	597 (40.7)	534 (47.3)	0.001	1226 (28.6)	1226 (33.1)	<0.001

Abbreviations: eGFR = estimated glomerular filtration rate (ml/min/1.73 m²), MI = myocardial infarction, CABG = coronary artery bypass graft, PCI = percutaneous coronary intervention, COPD = chronic obstructive pulmonary disease, PVD = peripheral vascular disease.

renal dysfunction over the last decade [7]. Nevertheless, it is not clear whether these temporal trends continue over the entire range of renal insufficiency. The current study was aimed to evaluate temporal trends in management and outcome of ACS patients according to their renal function.

2. Methods

2.1. Study population

The Acute Coronary Syndromes Israeli Survey (ACSIS) is a biennial, 2-month survey carried out in all intensive coronary care units and cardiology departments in Israel. The study population consisted of patients with ACS (ST-elevation and non ST-elevation myocardial infarction and unstable angina pectoris) and renal dysfunction included in the ACSIS surveys during 2002–2013. Study physicians recorded all clinical and demographic data on pre-specified forms for consecutive participants. The diagnosis of ACS was based on clinical, electrocardiographic and enzymatic criteria and patients were managed at the discretion of each center. Informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

2.2. Renal function assessment

Serum creatinine levels were recorded at presentation to the hospital. The eGFR was calculated using the simplified Modification of Diet in Renal Disease (MDRM) formula: eGFR = 186 × [sCr (in mg/dl)] − 1.154 × [age(in years)] − 0.203. For women the product of this equation was multiplied by a factor of 0.742.

Renal failure was defined as eGFR below 60 ml/min/1.73 m^2 and patients were divided into 3 groups: **normal renal function** (eGFR ≥ 60 ml/min/1.73 m^2), **mild to moderate renal insufficiency** (eGFR below 60 but above 30 ml/min/1.73 m^2) and **severe renal insufficiency** (eGFR below 30 ml/min/1.73 m^2). Patient's characteristics, clinical data and outcomes were compared in each group between 2 time frames - Early (2002–2006) vs. late (2008–2013).

2.3. Outcomes

The primary outcome of the study was all-cause mortality at 1 and 5 years. Mortality rates were determined for all participants from hospital charts and by matching the identification numbers of the patients with the Israeli National Population Registry. The secondary outcome was all-cause mortality at one month.

2.4. Statistical analysis

Categorical variables were expressed as percentage of available data and continuous variables were expressed as mean ± SD. The study cohort was stratified into three groups according to the renal function and each group data were compared between early and late surveys. Characteristics of study participants were compared using chi-square test for categorical variables and Student's *t*-test or Wilcoxon rank tests, as appropriate for continuous variables. Kaplan-Meier survival curves with the log-rank test were used to compare all-cause mortality during 1-year and 5 years. Cox proportional hazard model was used to evaluate the effects of patients' characteristics on 1 year all-cause mortality by renal insufficiency groups (severe, mild-moderate). Results are presented as Hazard Ratio (HR) and 95% confidence interval (95% CI). A p-value of <0.05 was considered significant. Statistical analyses were carried out using R version 3.2.5 (2016-04-14).

3. Results

A total of 11,234 ACS patients were enrolled in the ACSIS between 2002 and 2013. Of them, 7988 had normal kidney function and 3246 had renal insufficiency. Among patients with renal dysfunction, 2598 (80%) presented with mild to moderate renal insufficiency and 648 (20%) had severe renal insufficiency. The latter was more common in patients enrolled in the late compared to the early surveys (22% and 18%, respectively).

3.1. Baseline and admission characteristics of early versus late surveys

Baseline characteristics according to renal function are shown in Table 1. Mean age of patients with normal renal function, mild to moderate, and severe renal insufficiency was 60, 72 and 74 years respectively. Regardless to renal function, the prevalence of most baseline characteristics did not differ significantly between patients included in early and recent surveys. However, patients enrolled in the

Table 2
Trends in clinical presentation, and treatment modalities by kidney function in early versus late survey.

	Severe Renal Insufficiency eGFR < 30 N = 648			Mild to Moderate Renal Insufficiency 30 < eGFR < 60 N = 2598			Normal Renal Function eGFR > 60 N = 7988		
	Early	Late	p	Early	Late	p	Early	Late	p
Non ST elevation MI	168 (51.4)	176 (55.2)	0.604	634 (43.2)	580 (51.3)	<0.001	1340 (31.3)	1406 (38.0)	<0.001
ST-elevation MI	127 (38.8)	116 (36.4)	0.570	580 (39.5)	403 (35.7)	0.050	2195 (51.2)	1700 (45.9)	<0.001
Unstable Angina	32 (9.8)	27 (8.5)	0.655	254 (17.3)	147 (13.0)	0.003	748 (17.5)	596 (16.1)	<0.001
Coronary angiography	97 (29.8)	126 (40.1)	0.008	735 (50.3)	680 (60.6)	<0.001	2601 (61.0)	2352 (64.4)	0.002
PCI	58 (8.9)	85 (26.6)	0.008	448 (30.5)	456 (40.4)	<0.001	1799 (42.0)	1677 (45.3)	0.003
Aspirin	238 (75.6)	249 (83.3)	0.024	1265 (88.0)	1027 (92.4)	<0.001	4074 (95.6)	3578 (97.0)	0.001
Antiplatelets	115 (36.5)	207 (69.2)	<0.001	765 (53.4)	852 (76.6)	<0.001	2923 (68.6)	3170 (86.1)	<0.001
ACE-I/ARB	146 (46.3)	128 (40.1)	0.133	1066 (74.2)	859 (76.0)	0.322	3087 (72.5)	2916 (78.8)	<0.001
Statins	175 (55.6)	233 (78.2)	<0.001	1047 (72.8)	1011 (90.8)	<0.001	3559 (83.4)	3504 (95.0)	<0.001

Abbreviations: eGFR = estimated glomerular filtration rate (ml/min/1.73 m²), MI = myocardial infarction, PCI = percutaneous coronary intervention, ACE-I = angiotensin converting enzyme inhibitor, ARB = angiotensin II receptor blocker.

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