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Original Article

Impaired renal function is associated with adverse outcomes in patients with chest pain discharged from internal medicine wards

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ABSTRACT

Background: Assessment of chest pain is one of the most common reasons for hospital admissions in internal medicine wards. However, little is known regarding predictors for poor prognosis in patients discharged from internal medicine wards after acute coronary syndrome (ACS) rule-out.

Objective: To assess the association of kidney function with mortality and hospital admissions due to ACS in patients with chest pain who were discharged from internal medicine wards following ACS rule-out.

Methods: Included were patients admitted to an internal medicine ward who were subsequently discharged following an ACSrule-out during 2010–2016. The primary endpoint was the composite of all-cause mortality and hospital admission due to ACS at 30-days following hospital discharge.

Results: Included in the study were12,337 patients who were divided into 3 groups according to renal function. Considering patients with an eGFR ≥ 60 ml/min/1.73m^2 as the reference group yielded adjusted hazard ratios for the composite of 30-day all-cause mortality and hospital admission for ACS that increased with reduced eGFR (HR = 2, 95%CI = 1.3–3.3, HR = 4.8, 95%CI = 3–7.6, for patients with eGFR of 45 to 59.9 or < 45 ml/min/1.73m^2, respectively, $p < 0.001$). Similarly, reduced renal function was associated with increased 1-year all-cause mortality (HR = 1.6, 95%CI = 1.2–2.2, HR = 4.5, 95%CI = 3.4–5.9, for patients with eGFR of 45–59.9 or < 45 ml/min/1.73m^2, respectively, $p < 0.001$).

Conclusion: We found an independent graded association between lower eGFR and the risk of death and ACS among patients with chest pain who were discharged from internal medicine wards following an ACS rule-out. The eGFR may be combined in the risk stratification of patients with chest pain.

1. Background

Assessment of chest pain is one of the most common reasons for emergency department visits and hospital admissions in developed countries [1]. While most high risk patients with chest pain are usually admitted to coronary care units or a cardiology ward, the majority of low risk patients are still being admitted to internal medicine wards. Prior studies on risk stratification of patients admitted with chest pain have focused primarily on high risk patients with acute coronary syndrome (ACS) [2]. Although patients with chest pain deemed safe enough for discharge from an internal medicine ward may still be at risk for adverse outcomes, relatively little is known regarding predictors for poor prognosis in this relatively low risk population.

Chronic kidney disease has been associated with both short and long-term adverse outcomes in patients with various cardiovascular conditions including acute coronary syndrome [3,4], congestive heart failure [5] and stroke [6]. A large study covering a community based population of > 1.1 million ambulatory patients demonstrated an independent graded association between reduced estimated glomerular filtration rate (eGFR) and the risk of death, cardiovascular events and hospitalizations [7]. Several studies have investigated the association between renal function and the outcome of patients presenting to the hospital with chest pain. Most of these studies focused on high risk patients who were admitted with an established diagnosis of ACS [8,9]. The few small studies that have evaluated the significance of renal function in risk stratification of low-risk patients with chest pain

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demonstrated contradictory findings [10–12]. The current study was aimed to examine the association between reduced renal function and the risk for future adverse clinical outcomes in low risk patients with chest pain discharged from internal medicine wards following ACS rule-out.

2. Methods

2.1. Patients and design

The Meir Medical Center is a 760-bed academic hospital located in the Sharon district in central Israel. It is the largest hospital in this district, which comprises a mostly urban population of Jews and Arabs. The current study was based on the Meir Medical Center computerized database. All medical information obtained at both the emergency room and internal medicine wards is recorded in the database and can be accessed at the level of the individual patient. The database included a list of all diagnoses, demographic data, laboratory values and medical procedures.

Included in our study were men and women 18 years of age or above who were admitted with a diagnosis of chest pain to an internal medicine ward at the Meir Medical Centre, and were discharged after an ACS rule-out between January 1st, 2010 and June 30, 2016. Since during the study period stress echocardiography and nuclear imaging were not routinely available, ACS rule-out was based mainly on repeated clinical assessment, ECG and highly sensitive troponin-I measurements during hospitalization. ECG assessment of patients was performed repeatedly for each case by both emergency department physicians and by at least one specialist in internal medicine. Patients were considered at low risk and safe enough for discharge from the internal medicine ward if they did not show evidence of ischemia on repeated electrocardiogram, unstable vital signs, abnormal cardiac markers (in at least 2 separate blood samples), serious arrhythmias, or uncontrollable chest pain.

Excluded were patients with an established diagnosis of ACS at the emergency department (the majority was admitted to the cardiology department) or during admission, patients with abnormal cardiac biomarkers regardless of the etiology, and patients at very low risk who were discharged directly from the emergency department. Patients receiving renal replacement therapy were excluded as well.

2.2. Renal function assessment

Serum creatinine levels were recorded at hospital admission. The estimated glomerular filtration rate (eGFR) was calculated using the simplified Modification of Diet in Renal Disease (MDRD) formula]:

eGFR = 186 × [serum creatinine (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.

Patients were stratified into 3 groups according to the National Kidney Foundation chronic kidney disease (CKD) staging: An eGFR ≥ 60 ml/min/1.73 m^2 (CKD stages 1–2), an eGFR of 45–59.9 ml/min/1.73 m^2 (CKD stages 3a) and an eGFR of < 45 ml/min/1.73 m^2 (CKD stages 3b–5).

2.3. Study endpoints

The primary endpoint was the composite of all-cause mortality and hospital admission due to ACS at 30-days following hospital discharge. The secondary endpoints were 1-year all-cause mortality and 1-year hospital admission for ACS. Mortality data were collected from the National Social Security records. Information regarding the specific causes of death was not available to us. Hospital admissions for ACS only included those patients who were admitted to the same hospital. Considered were only discharge diagnosis of ACS.

2.4. Ethical considerations

The study was approved by the local institutional ethics committee in keeping with the principles of the Declaration of Helsinki. In accordance with Ministry of Health regulations, the institutional ethics committee did not require written informed consent since data were collected anonymously from the computerized medical files, with no active participation of patients.

2.5. Statistical analysis

Data are presented as numbers and percentages for nominal parameters and as means and standard deviations for continuous parameters. Differences between the eGFR groups were analyzed with chi-square or Fisher's exact test, as appropriate. Continuous variables were examined for normality (Shapiro-Wilk test) and data were analyzed accordingly. The *t*-test was used for normally distributed variables and the Mann-Whitney for non-parametric variables. A logistic regression model was applied to estimate odds ratios for 1-year ACS. A multivariate logistic regression model was performed to adjust for all clinically relevant baseline parameters with statistical significance in univariate analyses. It included the following variables: age, gender, hypertension, current smoking, dyslipidemia, diabetes mellitus, heart failure, prior coronary disease, atrial fibrillation and chronic obstructive pulmonary disease. A Cox proportional hazard model was applied to estimate hazard ratios for the primary and secondary endpoints. $P < 0.05$ was considered statistically significant. Data were analyzed with SPSS Version 21 (IBM Corporation, Armonk, NY, USA).

3. Results

The 12,337 patients included in the study had a mean age of 58.2 ± 13 years and their mean eGFR was 71 ± 20 ml/min/1.73 m^2. Of the study population, 9374 (76%) patients had an eGFR ≥ 60, 2031 (16%) had an eGFR of 45–59.9 ml/min/1.73m^2 and 932 (8%) patients had an eGFR < 45 ml/min/1.73m^2. Patients with reduced renal function were older and more frequently females. The prevalence of most coexisting conditions at baseline including hypertension, diabetes mellitus and prior cardiovascular disease increased with decreasing eGFR (Table 1).

The composite endpoint of 30-day all-cause mortality and hospital admission for ACS occurred more frequently among patients with reduced renal function (Fig. 1). Unadjusted 30-day all-cause mortality and ACS admissions rates were 0.6% among patients with eGFR ≥ 60 ml/min/1.73 m^2, 1.7% among those with eGFR of 45–59.9 ml/min/1.73 m^2 and 4.6% among patients with eGFR < 45 ml/min/1.73 m^2 ($p < 0.001$). Differences in the 30-day composite endpoint remained significant even following a multi-variate adjustment for all relevant baseline characteristics (Table 2). Considering the patients with an eGFR ≥ 60 ml/min/1.73 m^2 as the reference group yielded adjusted hazard ratios for all-cause death and hospital admission for ACS that increased in an independent graded association with reduced eGFR (HR = 2, 95%CI = 1.3–3.3, HR = 4.8, 95%CI = 3–7.6, for patients with eGFR of 45 to 59.9 or < 45 ml/min/1.73 m^2, respectively, $p < 0.001$).

We further compared the diagnostic performance of renal function and other clinically important baseline characteristics in predicting the composite of 30-day all-cause mortality and hospital admission for ACS using a receiver operating characteristic (ROC) curve. The highest AUC was demonstrated for eGFR (0.68, 95%CI = 0.62–0.74) followed by age (0.64, 95% CI = 0.60–0.67). Other baseline characteristics including diabetes mellitus (0.58, 95%CI = 0.52–0.63), history of heart failure (0.56, 95%CI = 0.51–0.61), history of ACS (0.51, 95%CI = 0.45–0.56) and male gender (0.53, 95%CI = 0.48–0.58) demonstrated significantly lower AUC suggesting their lower accuracy in predicting 30-day adverse outcomes.

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