European Heart Journal (2008) **29**, 1029–1036
doi:10.1093/eurheartj/ehn102



# Prevalence and significance of unrecognized renal insufficiency in patients with heart failure

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*Received 6 August 2007; revised 6 February 2008; accepted 16 February 2008; online publish-ahead-of-print 12 March 2008*

**Aims** Renal insufficiency (RI) is a strong predictor of adverse outcome in patients with heart failure (HF). We aimed to determine the prevalence of RI being unrecognized and its significance in patients hospitalized with HF.

**Methods and results** We analysed data from a prospective survey of 4102 hospitalized patients with HF. RI [defined as estimated glomerular filtration rate (eGFR) $<60$ mL/min/1.73 m$^2$] was present in 2145 (57%) patients but, based on medical records, was unrecognized in 872 [41%, 95% confidence interval (CI) 39–43%] of them. Patients with unrecognized RI were more likely to be women, elderly, and with better functional class, compared with patients with recognized RI. In-hospital and 1 year mortality was significantly higher among patients with recognized and unrecognized RI compared with patients without RI: 6.5 and 7.1 vs. 2.1%, and 38.8 and 30.9 vs. 18.8% ($P < 0.001$), respectively. After adjustment, recognized and unrecognized RI comparably predicted increased in-hospital mortality: odds ratio (OR) and 95% CI of 2.34 (1.43–3.87), $P < 0.001$, and 2.30 (1.45–3.72), $P < 0.001$. After 1 year, recognized RI remained an independent predictor for mortality: OR 1.79 (1.45–2.20), $P < 0.001$, whereas there was a trend for increased mortality predicted by unrecognized RI: OR 1.22 (0.97–1.53), $P = 0.08$.

**Conclusion** A high proportion of RI remains unrecognized among hospitalized patients with HF. As co-morbid RI has important prognostic and therapeutic implications, patients with HF may benefit from routine assessment of GFR.

**Keywords** Glomerular filtration rate • Heart failure • Kidney • Prognosis • Renal insufficiency

Renal insufficiency (RI) is a common co-morbidity among patients with heart failure (HF) and confers excess mortality.[1–6] RI is a major contributor to progressive cardiac damage, whereas HF is often associated with a rapid deterioration of renal function.[7,8] Thus, early diagnosis of chronic RI may promote implementation of treatments that could arrest or reverse the progression of renal damage, enable effective treatment of its complications, and reduce the risk of drug-induced nephrotoxicity.[9,10] It is reasonable that proper manipulation of pharmacological therapy for these high-risk patients could result in better preservation of kidney function.[11]

Recent observations from clinical trials on patients with acute coronary syndrome have suggested that chronic RI is often an unrecognized co-morbidity.[12,13] However, the prevalence and significance of unrecognized RI in patients with HF have not been thoroughly investigated. Thus, we aimed to determine the prevalence of unrecognized RI in an unselected population of patients with HF, using calculated glomerular filtration rate (GFR). In

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addition, we sought to determine the prognostic significance of unrecognized RI, compared with recognized RI and normal renal function.

# Methods

## Patients and data collection

Patient data were extracted from the Heart Failure Survey in Israel 2003 database.[14,15] This survey was conducted in all 25 operating public hospitals in Israel and aimed to record data on all HF patients admitted to the hospital between March and April 2003. The survey included 4102 patients with a diagnosis of either decompensated (acute or acute exacerbation) HF or chronic stable HF (admitted due to other causes). The criteria used for diagnosis of HF were symptoms of HF (at rest or during exertion) and objective evidence of cardiac dysfunction at rest.[16] For each eligible patient admitted with HF, the attending physicians were required to complete a structured form with data regarding patient characteristics, in-hospital course and management, pre-hospital and discharge medications, and admission and discharge diagnoses. We used the Killip classification in all patients regardless of STEMI presence. The first serum creatinine level measured after admission was recorded on the forms. Calculated GFRs are not routinely reported by the participating hospitals' laboratories. The clinicians were asked to indicate the presence of RI (either acute or chronic) among the required pre-specified list of diagnoses. The protocol was approved by the Ethics Committee at each of the participating hospitals.

The endpoint of the study was all-cause mortality obtained during follow-up, either from the database itself (in hospital charts) or by matching patient identification numbers with the Israeli National Population Register. Mortality during the first year after index hospitalization was assessed for 99% of patients.

Left ventricular ejection fraction (LVEF) was determined by echocardiography. LVEF data were recorded only if echocardiography was performed within 1 year prior to or during hospitalization. In 70% of 2171 patients with LVEF data, echocardiography was performed during index hospitalization. LVEF classes were classified as follows: normal $\geq$50%, mildly impaired 40–49%, moderately impaired 30–39%, and severely impaired $<$30%.

Efforts to ensure accuracy of data reporting included standardizing the definition of HF and data validation at two time points: (i) during data entry by logical checks incorporated into the data entry interface, which displayed errors and warning signs to alert the data entry operator; (ii) during post-data entry batch checks conducted for missing values, data conflicts, and out of range values. These data conflicts and inconsistencies were resolved and missing data were completed appropriately from the discharge summaries attached to the data forms.

## Definition of recognized and unrecognized renal insufficiency

RI was defined according to the US National Kidney Foundation (NKF) as an eGFR (estimated GFR) of $<$60 mL/min/1.73 m$^2$.[17] We used the modified four-component Modification of Diet in Renal Disease (MDRD) formula to calculate eGFR[18]:

$$\text{eGFR} = 186 \times [\text{serum creatinine level(in mg/dL)}]^{-1.154} \times [\text{age(in years)}]^{-0.203}$$

For women, the product of this equation was multiplied by a factor of 0.742. RI was defined as eGFR $<$60 mL/min/1.73 m$^2$; moderate RI was defined by an eGFR between 30 and 59 mL/min/1.73 m$^2$, and severe RI by an eGFR of $<$30 mL/min/1.73 m$^2$. Unrecognized RI was defined *post hoc* when the diagnosis of RI (eGFR $<$60 mL/min/1.73 m$^2$) was missing from the diagnoses list on the data form. The cohort was stratified into three groups according to RI recognition: (i) patients with recognized RI; (ii) patients with unrecognized RI; and (iii) patients without RI.

## Statistical analysis

Continuous variables were expressed as mean $\pm$ SD or median (interquartile range) when appropriate. Baseline characteristics of the groups were compared by Student's *t*-test for continuous data and by means of $\chi^2$ test for categorical variables and frequencies.

Kaplan–Meier survival curves with the Mantel–Haenszel log-rank test was used to compare crude survival. To adjust for differences in baseline clinical characteristics, co-morbidities, and prescribed medications, multivariable logistic regression analysis was used to examine prognostic factors for in-hospital and 1 year mortality in the whole cohort. Apart from the presence of RI, other pre-specified variables included in the regression models for in-hospital mortality were age, gender, NYHA class $>$1, Killip class $>$1, diabetes, prior myocardial infarction (MI), acute coronary syndrome, haemoglobin, atrial fibrillation, concomitant medications [aspirin, beta-blockers, angiotensin-converting enzyme (ACE)-inhibitors, angiotensin receptor blockers (ARBs), oral anticoagulant], and in-hospital treatment with intravenous diuretics and intravenous inotropes. Variables included in the regression models for 1 year mortality were age, gender, NYHA class $>$1, Killip class $>$1, dyslipidaemia, hypertension, prior MI, prior CABG, prior percutaneous coronary intervention, prior angina, prior stroke, peripheral vascular disease, atrial fibrillation, in-hospital treatment with intravenous diuretics and intravenous inotropes and prescription at discharge for aspirin, oral anticoagulants, beta-blockers, ACE-inhibitors, ARBs, statins, digoxin, spironolactone, vasodilators (calcium channel blockers, nitrates, hydralazine, and alpha blockers), diuretics, and amiodarone. Assumption of linearity for continuous variables was assessed by graphical investigation of logit of crude mortality against categories of these variables and by performing analyses using the continuous variables as quartiles for observing linear trend in the estimated coefficients. We repeated these analyses in a subgroup of patients with LVEF data. To compare the prognostic significance of recognized and unrecognized RI, we performed the same analyses after substituting the status of 'RI recognition' groups as covariates in the model, with patients without RI (eGFR $\geq$60 mL/min/1.73 m$^2$) as a reference group. In a sensitivity analysis, Cox proportional hazards model was performed for the 12 month period of follow-up. Two-sided *P*-values were used accepting $P < 0.05$ to be statistically significant. We did not account for multiple comparisons. All analyses were performed with the SAS software version 8.2.

# Results

## Patient characteristics

The survey included 4102 consecutive patients hospitalized with a presumptive diagnosis of HF. Of them, 282 patients did not fulfil the inclusion criteria of HF and were excluded from our analysis. GFR could be estimated in 3793 (99%) of the remaining patients.

**Table 1 Baseline clinical characteristics of the cohort, stratified by presence and recognition of renal insufficiency ($n = 3793$)**

| | Estimated glomerular filtration rate | | | *P*-value[a] |
|---|---|---|---|---|
| | ≥60 mL/min/1.73 m$^2$ ($n = 1648$) | <60 mL/min/1.73 m$^2$ | | |
| | | RI unrecognized ($n = 872$) | RI recognized ($n = 1273$) | |
| Age, years | 69 ± 14 | 78 ± 10 | 76 ± 10 | <0.001 |
| Female, *n* (%) | 618 (37) | 546 (63) | 454 (36) | 0.001 |
| Hypertension, *n* (%) | 1159 (70) | 669 (77) | 1024 (81) | 0.009 |
| Diabetes, *n* (%) | 774 (47) | 405 (47) | 747 (59) | <0.001 |
| Dyslipidaemia, *n* (%) | 1004 (61) | 484 (56) | 743 (59) | 0.19 |
| Ischaemic heart disease, *n* (%) | 1306 (79) | 714 (82) | 1094 (86) | 0.01 |
| Previous MI, *n* (%) | 532 (32) | 324 (37) | 593 (47) | <0.001 |
| PVD, *n* (%) | 121 (7) | 64 (7) | 163 (13) | <0.001 |
| COPD, *n* (%) | 309 (19) | 158 (18) | 269 (21) | 0.09 |
| Previous stroke/TIA, *n* (%) | 159 (10) | 122 (14) | 181 (14) | 0.88 |
| Number of hospitalizations during the past year | 1.4 | 1.8 | 2.2 | <0.001 |
| Department of hospitalization, *n* (%) | | | | |
| Internal medicine | 1196 (73) | 713 (82) | 1058 (84) | 0.24 |
| ICCU/Cardiology | 406 (25) | 138 (16) | 169 (13) | |
| LVEF, *n* (%) (*n* = 2171) | | | | |
| ≥50% | 321 (27) | 171 (30) | 223 (25) | 0.017 |
| 40–49% | 308 (25) | 110 (19) | 146 (16) | |
| 30–39% | 302 (25) | 147 (26) | 240 (27) | |
| <30% | 285 (23) | 143 (25) | 282 (32) | |
| Decompensated HF, *n* (%) | 961 (60) | 545 (64) | 792 (64) | 0.91 |
| NYHA class >II, *n* (%) | 517 (32) | 354 (42) | 696 (56) | 0.001 |
| Killip >1, *n* (%) | 998 (60) | 624 (72) | 939 (74) | 0.47 |
| Atrial arrhythmias, *n* (%) | 477 (29) | 348 (40) | 441 (35) | 0.013 |
| Laboratory values | | | | |
| Haemoglobin, gr/dL | 12.8 ± 2.0 | 12.1 ± 1.9 | 11.5 ± 1.9 | <0.001 |
| Urea[b], mg/dL | 34 | 52 | 78 | <0.001 |
| Creatinine[c], mg/dL | 0.9 ± 0.2 | 1.3 ± 0.3 | 2.4 ± 1.3 | <0.001 |
| eGFR, mL/min/1.73 m$^2$ | 84 ± 26 | 48 ± 8 | 32 ± 12 | <0.001 |
| Na, mmol/L | 138 | 139 | 138 | 0.25 |
| K, mmol/L | 4.2 | 4.3 | 4.5 | 0.30 |

Values are counts (%) or means ± standard deviation.
RI, renal insufficiency; MI, myocardial infarction; PVD, peripheral vascular disease; COPD, chronic obstructive pulmonary disease; TIA, transient ischaemic attack; ICCU, intensive cardiac care unit; LVEF, left ventricular ejection fraction; HF, heart failure; NYHA, New York Heart Association; eGFR, estimated glomerular filtration rate.
[a]*P*-value for the comparison between the two groups with RI.
[b]To convert from milligrams per decilitre to millimoles per litre, multiply milligrams per decilitre by 0.357.
[c]To convert from milligrams per decilitre to micromoles per litre, multiply milligrams per decilitre by 88.4.

Mean age was 73 years and 43% were female. Acute decompensated HF was encountered in 64% of the patients, NYHA functional class III or IV in 42%, ischaemic heart disease in 82%, and preserved systolic function (ejection fraction ≥50%) in 27% (*Table 1*).

Employing the US NKF criteria,[17] which define RI as eGFR <60 mL/min/1.73 m$^2$, it was found more than half of the patients ($n = 2145$; 57%) had RI: 540 (14%) patients had severe RI and 1605 (42%) had moderate RI. Median (interquartile range) serum creatinine in patients with RI was 1.8 (1.5–2.3) mg/dL [159 (133–203) μmol/L] in men and 1.4 (1.1–1.8) mg/dL [124 (97–159) μmol/L] in women.

## Renal insufficiency is a frequent unrecognized co-morbidity in patients with heart failure

RI was unrecognized by hospital physicians in 872 of 2145 (41%, 95% confidence interval 39–43%) patients with eGFR <60 mL/min/1.73 m$^2$. Specifically, diagnosis of RI was absent in

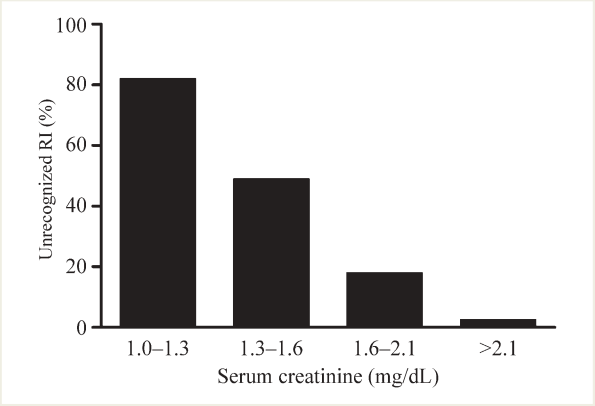


**Figure 1** Per cent of unrecognized renal insufficiency, stratified by quartiles of serum creatinine in patients with renal insufficiency.

53% of patients with moderate RI and in 5% of patients with severe RI.

The prevalence of unrecognized RI was related to levels of serum creatinine, being highest (82%) in the lowest quartile compared with only 2.6% in the highest quartile ($P < 0.001$, *Figure 1*). Likewise, serum creatinine was significantly lower in patients with unrecognized RI, compared with recognized RI: median (interquartile range) 1.3 (1.1–1.5) [115 (97–133) μmol/L] vs. 1.9 (1.6–2.5) [168 (141–221) μmol/L], $P = 0.001$. False-positive diagnosis of RI was made in 2.6% of patients with eGFR >90 mL/min/1.73 $m^2$.

Compared with recognized RI, patients with unrecognized RI were more likely to be women and elderly (*Table 1*). Patients with unrecognized RI had higher LVEF and better functional status before admission, but similar severity of HF on admission (*Table 1*), with similar rates of decompensated HF. They were less likely to have anaemia, diabetes mellitus, ischaemic aetiology for HF, and peripheral vascular disease (*Table 1*), and were less likely to be treated with intravenous inotropes and blood transfusions (*Table 2*), but length of hospital stay was similar (6 days). Prior to admission, the use of ACE-inhibitors in patients with unrecognized and recognized RI was similar and the use of spironolactone was lower in the first group (*Table 2*). At discharge, patients with unrecognized RI were more likely to receive ACE-inhibitors, spironolactone, and digoxin, but less likely to receive statins (*Table 2*).

## Recognized and unrecognized renal insufficiency confers poor prognosis

During the index hospitalization, 181 (4.8%) patients died, whereas 1072 (28.3%) patients died during the first year after admission. Patients with recognized and unrecognized RI had significantly higher in-hospital mortality rates compared with patients without RI: 6.5 and 7.1 vs. 2.1% ($P < 0.05$). This association persisted after 1 year with 38.8 and 30.9% mortality in patients with recognized and unrecognized RI, respectively, vs. 18.8% in patients without RI (log-rank = 110.1, $P < 0.001$, *Figure 2*). The absolute survival difference between the unrecognized RI group and the group without RI increased steadily throughout 1 year (*Figure 2*).

After adjustment for other risk factors, patients with both recognized and unrecognized RI were at higher risk for death (*Figure 3*). Compared with patients without RI, unrecognized RI was associated with increased in-hospital mortality risk to the same degree as recognized RI (*Figure 3*). After 1 year, unrecognized RI was still associated with increased mortality, although it did not reach statistical significance (*Figure 3*). Other predictors associated with outcome are presented in *Table 3*. Prescription of ACE-inhibitors, ARBs, oral anticoagulants, beta-blockers, vasodilators, and statins were associated with reduced 1 year mortality (*Table 3*). The Cox proportional hazard analysis (adjusting for the same variables) confirmed the findings from the logistic regression analysis (data not shown).

The strong association between RI and mortality was maintained in a subgroup of 2171 patients with LVEF data. After adjustment for LVEF class, RI was associated with higher risk for in-hospital death [OR = 2.69 (1.46–5.24), $P = 0.002$] and 1 year mortality [OR = 1.50 (1.16–1.94), $P = 0.002$]. Again, unrecognized RI was associated with the same worse prognosis: OR = 2.60 (1.26–5.51) vs. OR = 2.75 (1.42–5.56) for in-hospital mortality, and a trend for higher 1 year mortality OR = 1.25 (0.91–1.72) vs. OR = 1.70 (1.27–2.27).

# Discussion

The main new finding of the present study suggests that RI is a commonly unrecognized co-morbidity among HF patients and confers excess mortality. Physicians providing care for hospitalized patients with HF do not report the presence of RI in almost half of their patients who present with moderate or severe RI. Underdiagnosis is more likely to occur in women, elderly, non-diabetics, and patients with less advanced HF. Early recognition of RI among patients with HF is important, as patients with unrecognized RI have increased mortality risk similar to those patients with recognized RI. Thus, renal function assessment by calculating eGFR should be considered routine test in the evaluation and risk stratification of all patients with HF.

## Unrecognized renal insufficiency and outcome

Renal dysfunction is a powerful predictor of adverse outcomes in HF patients.[9] In a risk stratification analysis of the large Acute Decompensated Heart Failure National Registry[19] comprising 65 275 patient records, serum creatinine ≥2.75 mg/dL (243 μmol/L) was among the three best predictors of long-term mortality.[19] According to a recent report from the same registry, although 63.6% of patients had at least moderate renal dysfunction, as determined by the MDRD equation, only 33.4% of men and 27.3% of women were diagnosed with RI.[6] GFR is the best measure of overall kidney function in health and disease.[20] However, serum creatinine is a weak indicator of renal dysfunction especially in the elderly,[21,22] and in women,[23] mainly due to the relatively low muscle mass in these populations. In our cohort, half of the patients with moderate RI had serum creatinine levels

**Table 2 Treatment of patients with recognized and unrecognized renal insufficiency**

| | Estimated glomerular filtration rate | | | *P*-value[a] |
|---|---|---|---|---|
| | ≥60 mL/min/1.73 m$^2$ (*n* = 1648) | <60 mL/min/1.73 m$^2$ | | |
| | | RI unrecognized (*n* = 872) | RI recognized (*n* = 1273) | |
| Medications on admission, *n* (%) | | | | |
| Aspirin | 961 (58) | 502 (58) | 786 (62) | 0.05 |
| Oral anticoagulants | 255 (16) | 184 (21) | 247 (19) | 0.34 |
| ACE-inhibitors | 885 (54) | 457 (52) | 623 (49) | 0.11 |
| ARBs | 100 (6) | 74 (9) | 132 (10) | 0.15 |
| Beta-blockers | 763 (46) | 424 (49) | 685 (54) | 0.018 |
| Loop diuretics | 783 (48) | 586 (68) | 993 (78) | 0.001 |
| Spironolactone | 207 (13) | 135 (16) | 255 (20) | 0.007 |
| Digoxin | 216 (13) | 153 (18) | 167 (13) | 0.005 |
| Amiodarone | 85 (5) | 90 (10) | 180 (14) | 0.009 |
| Statins | 545 (33) | 280 (32) | 492 (39) | 0.002 |
| NSAIDs | 26 (2) | 9 (1) | 16 (1) | 0.64 |
| In-hospital treatment, *n* (%) | | | | |
| IV inotropes | 88 (5) | 56 (6) | 127 (10) | 0.004 |
| IV vasodilators | 195 (12) | 90 (10) | 137 (11) | 0.74 |
| IV diuretics | 931 (57) | 602 (69) | 888 (70) | 0.72 |
| Blood transfusion | 71 (4) | 62 (7) | 137 (11) | 0.004 |
| Thoracocentesis | 33 (2) | 17 (2) | 48 (4) | 0.016 |
| Swan–Ganz catheter | 3 (0.2) | 3 (0.3) | 5 (0.4) | 0.86 |
| Medications on discharge, *n* (%) | | | | |
| Aspirin | 1138 (71) | 516 (64) | 782 (66) | 0.19 |
| Oral anticoagulants | 290 (18) | 181 (22) | 225 (19) | 0.08 |
| ACE-inhibitors | 1098 (68) | 495 (61) | 542 (46) | <0.001 |
| ARBs | 116 (7) | 84 (10) | 128 (11) | 0.71 |
| Beta-blockers | 964 (60) | 458 (56) | 683 (58) | 0.48 |
| Loop diuretics | 1042 (65) | 665 (82) | 967 (82) | 0.91 |
| Spironolactone | 329 (20) | 193 (24) | 233 (20) | 0.03 |
| Digoxin | 236 (15) | 143 (18) | 153 (13) | 0.004 |
| Amiodarone | 124 (8) | 89 (11) | 155 (13) | 0.14 |
| Statins | 668 (42) | 281 (35) | 482 (41) | 0.004 |

RI, renal insufficiency; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blockers; NSAID, non-steroidal anti-inflammatory drugs; IV, intravenous.
[a]*P*-value for the comparison between the two groups with RI.

≤1.4 mg/dL (124 μmol/L). Values in this range are considered 'normal' or near-normal by many physicians and may explain our finding that RI was unrecognized in more than half of the patients with moderate RI. Poor recognition of RI in patients with cardiac disease is also in accordance with findings from studies in primary care settings.[23,24] In one such study, RI was recognized in only 22.4% of patients, which increased to 85.1% after eGFR was automatically reported by the local laboratory coupled with an educational programme.[23]

Perhaps the most intriguing result of our study was the similar excess risk for in-hospital mortality among the recognized and unrecognized RI groups, despite the fact that patients in the former group had more severe RI. This may be related to the fact that even subtle elevations (as low as ≥0.3 mg/dL) of serum creatinine after admission have been associated with markedly increased in-hospital mortality, irrespective of baseline serum creatinine.[25] As only admission serum creatinine was recorded, we were unable to determine whether more patients in the unrecognized RI group had worsening renal function rather than unchanged RI. At 1 year, patients with unrecognized RI who survived the index hospitalization still had a higher risk for mortality compared with patients with normal renal function. One might have expected to find a worse long-term outcome in the unrecognized RI group compared with the recognized RI group due to consequences of non-recognition. However, after 1 year, we found higher mortality in the recognized RI group, probably due to the established linear association between the severity of RI and long-term outcome.[3,4]

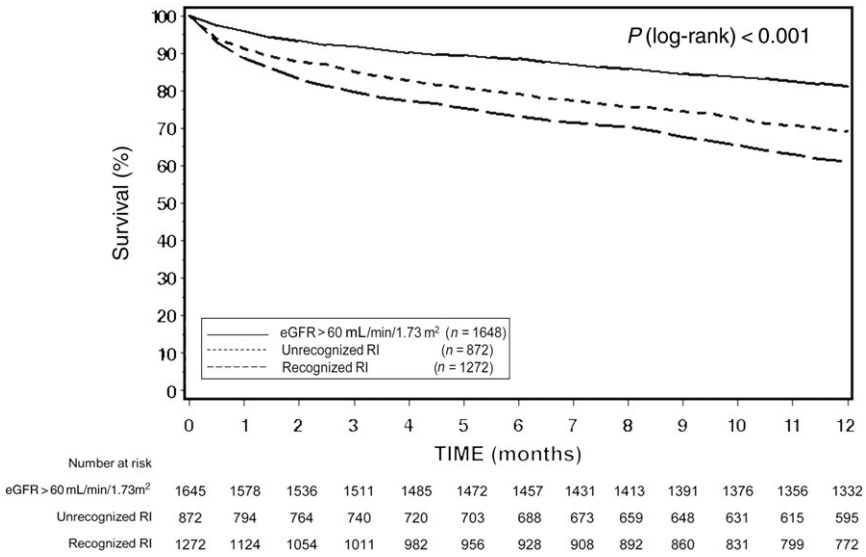


**Figure 2** Kaplan–Meier survival curves of patients with recognized renal insufficiency, unrecognized renal insufficiency, and patients with estimated glomerular filtration rate $\geq$60 mL/min/1.73 $m^2$.

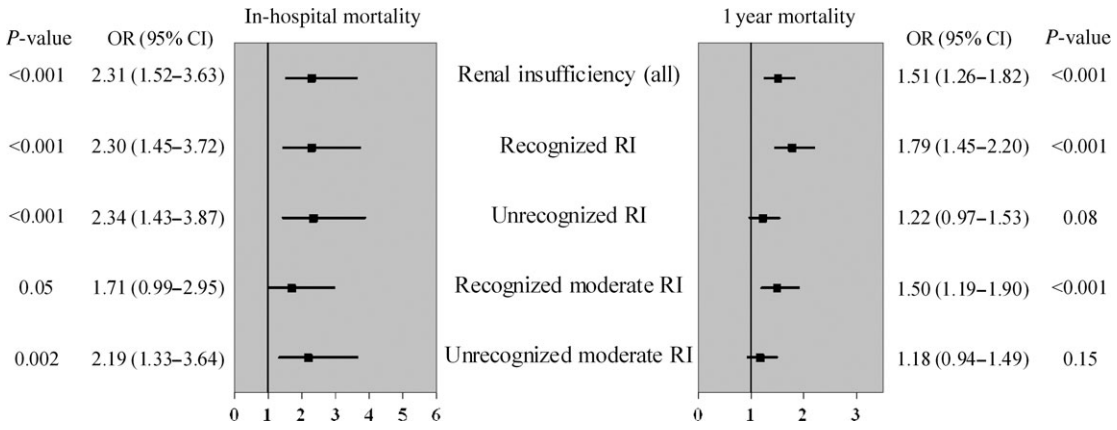


**Figure 3** Prognostic value of unrecognized and recognized renal insufficiency for in-hospital and 1 year mortality.

Corsonello *et al.*[26] showed that hospitalized elderly patients with apparently normal serum creatinine, but impaired renal function according to GFR estimation, were exposed to a higher risk of adverse drug reactions from drugs such as diuretics, ACE-inhibitors, and digoxin, comparable with that observed in patients with overt RI. Specifically, the risk of digoxin cardiac toxicity has been shown to increase even in patients with only mild renal impairment.[26] In our cohort, more patients with unrecognized RI received ACE-inhibitors and spironolactone at discharge, compared with patients with recognized RI. These drugs have been shown to improve survival in patients with HF. However, initiation of these drugs, and especially their combination, in HF patients with RI should be done cautiously with closer monitoring for the appearance of hyperkalaemia and worsening renal function.[27] Notably, in the multivariable analysis, digoxin and spironolactone, two drugs which were more frequently prescribed to patients with unrecognized RI, were associated with increased 1 year mortality. Facing the paucity of evidence from prospective trials in HF patients with significant renal dysfunction, further research is needed to guide appropriate pharmacological treatment in this growing subset of patients.[7]

## Limitations

We are aware of several limitations in our study. First, only initial measurements of serum creatinine were included in the structured data forms. It is possible that renal function deteriorated or improved during hospital course. We attempted to overcome

**Table 3 Multivariable predictors of 1 year mortality[a] ($n = 3501$)[b]**

| Variables | OR (95% CI) | *P*-value |
|---|---|---|
| Age (per 10 year increase) | 1.28 (1.18–1.39) | <0.001 |
| Recognized RI | 1.79 (1.45–2.20) | <0.001 |
| Unrecognized RI | 1.22 (0.97–1.53) | 0.08 |
| NYHA class >1 | 1.47 (1.12–1.93) | 0.006 |
| Killip >1 | 1.38 (1.12–1.69) | 0.002 |
| LVEF ≤30% vs. LVEF >50% ($n = 2032$)[c] | 1.31 (0.91–1.88) | 0.064 |
| Past MI | 1.38 (1.13–1.68) | 0.001 |
| Past stroke | 1.59 (1.25–2.02) | <0.001 |
| Haemoglobin (per 1 gr/dL decrease) | 1.11 (1.06–1.16) | <0.001 |
| Dyslipidaemia | 0.83 (0.69–0.99) | 0.034 |
| Digoxin[d] | 1.41 (1.11–1.78) | 0.005 |
| Spironolactone | 1.36 (1.11–1.66) | 0.069 |
| Beta-blockers | 0.84 (0.70–1.00) | 0.046 |
| ACE-inhibitors | 0.83 (0.69–0.99) | 0.040 |
| Statins | 0.80 (0.66–0.97) | 0.025 |
| Vasodilators | 0.78 (0.65–0.93) | 0.005 |
| Oral anticoagulants | 0.60 (0.47–0.77) | <0.001 |
| ARBs | 0.57 (0.41–0.80) | 0.001 |

See text for the list of covariates included in analyses. RI, renal insufficiency; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; MI, myocardial infarction; ACE, angiotensin-converting enzyme; ARBs, angiotensin receptor blockers.
[a]Only the covariates with statistically significant (or marginally significant) ORs.
[b]*n* corresponds to the number of patients with no missing values for the response or explanatory variables.
[c]Derived from a separate analysis in the subgroup of patients with LVEF data.
[d]All medications were prescribed at discharge.

this limitation by searching for a diagnosis of RI both in the admission and discharge diagnoses lists which were part of the data collection form. Secondly, the MDRD equation, similar to the Cockroft–Gault equation, was derived from populations with stable chronic kidney disease, which is frequently not the case in patients admitted because of HF. We chose to use the MDRD equation, currently the recommended method for estimating renal function,[10] and which has recently been used in other studies of patients with combined cardiac and renal dysfunction.[3,6,28] A recent small study showed that the MDRD equation adequately predicted GFR in patients with advanced HF, with higher accuracy than the Cockroft–Gault equation.[29] Moreover, body weight, which is frequently higher than the true 'dry' weight in HF patients, is not needed in this equation. Thirdly, it is possible that renal dysfunction was known but simply not recorded on the data form. However, we believe that as long as eGFR is not calculated, RI might be overlooked in a considerable number of patients, especially when serum creatinine levels are only mildly elevated. Finally, for the purpose of this work, we used a dichotomous acceptable definition for RI (<60 mL/min/1.73 $m^2$). It is important to point out that the association of RI with a worse prognosis exists across a wide range of RI severity.

## Summary and implications

Among hospitalized patients with HF, unrecognized RI is a common, independent predictor of increased mortality. However, a high proportion (41%) of RI remains clinically unrecognized. With the expanding population of HF patients, it is important to identify the subset of patients with HF who are at the highest risk for poor outcomes, so that clinicians can treat modifiable risk factors. The ability to identify chronic RI may promote early implementation of treatment that might arrest or delay the progression of renal damage, enable effective treatment of its complications, and reduce the risk of drug-induced nephrotoxicity. Thus, we suggest the routine use of calculated eGFR, preferably routinely reported by the local laboratory along with serum creatinine, to enhance early recognition of RI in HF patients.

## Acknowledgement

We thank all the physicians and nurses at the participating hospitals for their help during the course of the study.

**Conflict of interest:** none declared.

## Funding

The Heart Failure Survey in Israel 2003 was supported by the Israel Center for Disease Control; the Israel Medical Association; and Teva, Pfizer, MSD, Aventis, Medtronic, Dexxon, Levant, Medisson, Neopharm, Novartis, and Schering-Plough. Funding to pay the Open Access publication charges for this article was provided by the Neufeld Cardiac Research Institute, Tel-Aviv University, Tel-Aviv, Israel.

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