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Incidence and risk factors for severe renal impairment after first diagnosis of heart failure: A cohort and nested case–control study in UK general practice☆

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ABSTRACT

Objective: We aimed to evaluate the incidence, time-course and risk factors for severe renal impairment (SRI) among incident heart failure (HF) patients.
Methods and results: Patients aged 1–89 years from 2000 to 2005 with incident HF and without SRI or cancer (N = 18,049) were identified from The Health Improvement Network (a primary care database representative of the UK population). Patients with a first ever record of SRI during follow-up were identified and eligible non-cases used as controls (N = 5377; mean age 74 years). Cohort and nested case–control analyses were conducted to identify risk factors for SRI. 2818 patients (15.6%, mean age 75 years) in the HF cohort developed SRI over a mean of 2.84 years with incidence highest in the first year following HF diagnosis. Hazard ratios (HRs) with 95% confidence intervals (CIs) were as follows: diabetes (1.96, 1.80–2.14), hypertension (1.23, 1.14–1.33), peripheral artery disease (1.29, 1.15–1.45), ischemic cerebrovascular disease (1.14, 1.03–1.26), and anemia (1.19, 1.06–1.34). Several cardiovascular medications were associated with SRI in the case–control analysis, odds ratios (95% CIs): 5.07 (3.87–6.64) for all diuretics, 3.22 (2.83–3.66) for potassium-sparing diuretics, 2.40 (1.96–2.93) for thiazide and related diuretics and 3.27 (2.67–4.01) for loop-diuretics.
Conclusion: SRI is a frequent complication in patients with newly diagnosed HF. Comorbidities may contribute to its development and should be adequately treated. Robust clinical trial data on beneficial or possibly deleterious effects of diuretics, especially loop-diuretics and potassium-sparing diuretics, on SRI development in HF patients are warranted.

1. Background

Chronic heart failure (HF) is a clinical syndrome characterized by the involvement of multiple organ systems. In recent years the interaction between heart and kidney disorders has received increasing recognition. Worsening renal function has been recognized as an important and independent predictor for increased mortality and hospitalization rates in patients with HF [1,2]. Furthermore, HF is a risk factor for developing chronic kidney disease (CKD) and vice versa — they are common, often coexist and interact with each other [3,4]. Owing to an aging population, the prevalence of both conditions is increasing, and thus represents major public health problems. The close interaction between the kidney and the heart has been called 'cardiorenal syndrome' or 'renocardiac syndrome' depending on which organ is affected first, and has been classified into five subtypes by Ronco et al. [5].

Risk factors and the time course for declining renal function in patients with HF have not been fully established. Data from clinical trials may not be fully representative of the HF population due to exclusion of certain risk groups, and population-based data on this topic are sparse. Moreover, most of the data on worsening renal function are

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[3] Ana Ruigómez contributed to the study design, the acquisition of data, the analysis and interpretation of the data, writing and reviewing the manuscript, and the decision to submit the manuscript for publication.
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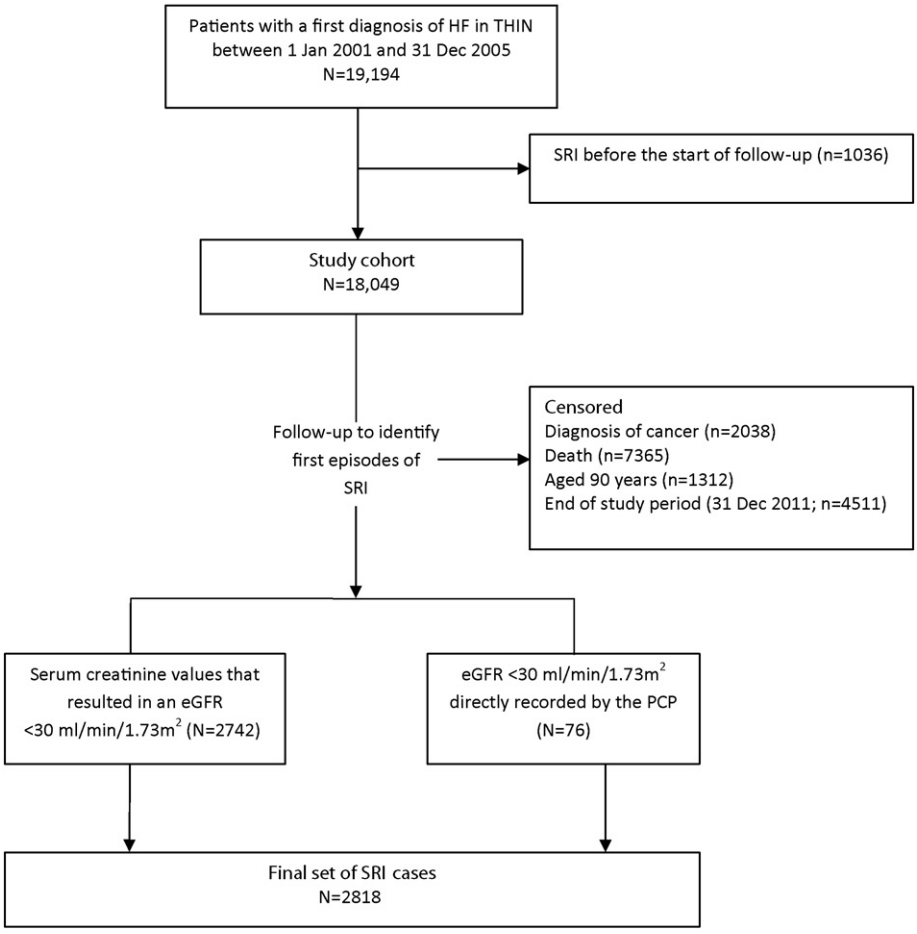

Fig. 1. Identification of SRI cases. eGFR, estimated glomerular filtration rate; PCP, primary care practitioner; HF, heart failure; SRI, severe renal impairment; THIN, The Health Improvement Network.

derived from patients with acute decompensated HF, while there is a paucity of information on worsening renal function in patients with chronic HF [6]. Unfortunately there exists no commonly agreed definition of worsening renal function in HF. Furthermore, in a real-world clinical practice setting there is no standardized monitoring of renal function at defined time-intervals as could be undertaken in a clinical trial. Due to these limitations, we decided that for the present study in a UK general practice setting, we would take the first recorded occurrence of severe renal impairment during follow-up, as defined in the Methods section, as the outcome variable. The aim of this study was to describe the incidence, time course and risk factors for developing severe renal impairment (SRI) in a population-based cohort of patients with newly diagnosed HF, with long-term follow-up. The study protocol was reviewed and approved by an independent scientific review committee (reference number 13-030).

2. Methods

2.1. Study cohort of patients with HF

We carried out a cohort study with nested case–control analyses using data from The Health Improvement Network (THIN), a computerized database containing anonymized patient medical records from general practices in the UK [7,8]. Clinical events including symptoms, medical diagnoses, laboratory tests, referrals to specialists and hospital admissions are entered using Read codes [9]. The database is representative of the UK population with regard to age, sex and geographic distribution, and has been validated for use in pharmacoepidemiological research [7,8]. A previously identified cohort of patients aged 1–89 years between 1 January 2000 and 31 December 2005 with a first ever diagnosis of HF (inception cohort) and no previous diagnosis of cancer comprised our initial study cohort (N = 19,194). Patients with HF were identified by automated computer searches for HF Read codes and semi-automatic review of patient records was undertaken to obtain data on symptoms, signs and diagnostic tests. Patients were excluded from the cohort if the diagnosis was recorded at death or post mortem. At the time of diagnosis, approximately half (54.1%) of the patients were ambulatory and managed by the primary care practitioner (PCP) only, while 27.3% were referred to a consultant and 18.6% had a related hospitalization [10]. Among a random sample of the HF cohort (n = 200), 84% had the diagnosis of incident HF validated by their PCP (*Ruigómez A, unpublished data*). For this current study, we excluded individuals with SRI before the diagnosis of HF, leaving a final study cohort of 18,049 HF patients.

2.2. Severe renal impairment case definition and ascertainment

The identification of SRI cases is depicted in Fig. 1. The study cohort was followed from the day after the HF diagnosis (start date) until the earliest of the following: first recorded

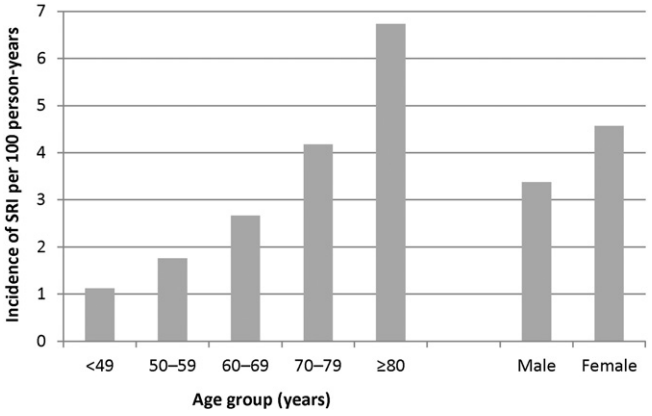

Fig. 2. Incidence of SRI per 100 person-years by age group, and by sex. SRI, severe renal impairment.