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Research paper

Heart failure and chronic kidney disease in a registry of internal medicine wards

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ABSTRACT

Background: The aim of the present study was to evaluate the association between heart failure (HF) and chronic kidney disease (CKD) in tertiary care centers using the clinical records of patients enrolled in internal medicine departments.
Patients and methods: We used the clinical records of 1380 elderly patients to identify patients with a history of HF and CKD using admission ICD codes and glomerular filtration rate (GFR) formulas. Magnitude and strength of such associations were investigated by univariable and multivariable analysis.
Results: Of the 1380 patients enrolled, 27.9% had HF (age 80 ± 7, BMI 27 ± 6 kg/m^2) and 17.4% CKD (age 81 ± 7, BMI 26.8 ± 6 kg/m^2). Both groups were significantly older ($P < 0.0001$) with BMI higher than the patients without those diagnosis ($P < 0.02$). Patients with a history of CKD showed higher non-fasting glycaemia (140 ± 86 vs. 125 ± 63 mg/dL, $P < 0.001$). CKD was significantly associated with HF ($P < 0.0001$). Patients with HF had an estimated GFR lower than patients without HF ($P < 0.0001$). Comorbidity and severity indices were significantly higher in subjects with HF ($P < 0.0001$) and CKD ($P < 0.0001$) than in those without. Multivariable analysis showed a significant association between HF and age (for five years increase OR 1.13, $P < 0.009$), BMI (for each 3 kg/m^2 increase OR 1.15, $P < 0.001$), GFR (for each decrease of 10 mL/min increase OR 0.92, $P < 0.002$) and severity index (IS) (for each 0.25 units increase OR 1.43, $P < 0.001$).
Conclusion: HF on admission is strongly associated with CKD, older age, BMI, and SI. These data focus the value of epidemiological studies such REPOSI in identifying and monitoring multimorbidity in elderly.

1. Introduction

HF is a very common complex syndrome representing the final outcome of the majority of cardiovascular diseases. In developed countries, approximately 1–2% of the adult population is suffering from HF, with an increasing prevalence in elderly [1,2]. Also CKD, due to its large distribution, is now considered one of the most important public health problems, with a prevalence of about 13% in US adult population [3], increased in elderly, and in patients with cardiovascular disease [4]. In Italy, the epidemiology of CKD in the general population was evaluated in studies from small geographical areas, such as GUBBIO study in 1983–1985 (2748 patients aged 25–74 years) and the INCIPE study in 2006 (6200 patients ≥ 40 years old). The Gubbio study showed a prevalence of CKD 3-5 stage of 5.7% in men and 6.2% in women, while in the INCIPE study only gave a total prevalence of CKD of 12.7% (13,2% in men, 12,2% in women) with a prevalence of stage ≥ 3 of 6,7% (6,5% in men, 6,9% in women) [5,6]. Among patients of INCIPE study authors found a greater prevalence of CKD in patients with diabetes, hypertension, and ≥ 80 years old patients [6]. It is likely that the increase in life expectancy will lead to an increased prevalence of both heart and renal failure in a foreseeable future. Several studies showed a close relationship between these two

Abbreviations: CKD, chronic kidney disease; HF, heart failure; GFR, glomerular filtration rate; ICD, International Classification of Diseases; SIMI, Italian Society of Internal Medicine; BMI, Body Mass Index; CIRS, Cumulative Illness Rating Scale; IS, Severity Index; IC, Comorbidity Index; CDK-EPI, Chronic Kidney Disease Epidemiology Collaboration; KDOQI, Kidney Disease Outcomes Quality Initiative; REPOSI, REgistro POliterapie Società Italiana di Medicina Interna.

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syndromes [7,8]. Specifically, in the Second Prospective Randomized Study of Ipobamine on Mortality and Efficacy (PRIME-II study) GFR emerged as the major prognostic factor in patients with HF [7]. The heart and kidney are linked by neuro-hormonal and hemodynamic features, that when unbalanced can determine the "cardio-renal syndrome". This condition has a complex pathophysiologic background yielding several clinical entities, where acute or chronic dysfunction of one organ can induce acute or chronic dysfunction of the other. Data on the cardio-renal syndrome and/or the prevalence and incidence of HF and its relation with chronic renal disease are mainly derived from U.S. studies or from large multinational trials [9].

In our country, such informations in over-60 hospitalized patients are limited and sparse [10,11]. Therefore, the aim of the study was to estimate the prevalence of HF and its association with CKD in consecutive patients admitted to Internal Medicine departments.

2. Patients and methods

One thousand three hundred and eighty patients included in the REgistro POliterapie Società Italiana di Medicina Interna REPOSI) 2010 from 66 Internal Medicine Departments (683 males and 697 females) all of them over sixty-five years old, were enrolled in the study in the period between April 2010 and January 2011. REPOSI is an independent research project born from the collaboration between SIMI and the Mario Negri Institute for Pharmacological Research, performed for the first time in 2008 (REPOSI 2008) and was subsequently repeated in 2010 (REPOSI 2010). The main purpose of this collaborative research project is to create a network/observatory of Internal Medicine departments for the recruitment, monitoring and study of elderly patients, estimating disease prevalence, the predictors of polypathology and polypharmacy and their impact on major clinical outcomes for this class of people. As already described [12–15] patients were recruited in a sequential manner, e.g. all new patients admitted within four different specific weeks (one per season), for a minimum of five patients per week; inclusion criteria in the study were age over 65 years and the acceptance with a signed informed consent. This study was approved by the local Ethics Committee on human research. For each patient the diagnosis formulated at the admission, and corresponding to the medical history, was reported and coded according to the ICD-9-CM (1997 version of the International classification of diseases, 9th revision, and clinical modification) [16].

For the purpose of this study, we identified patients with ICD codes at the entrance for congestive HF (428.x, 402.x, 416.x, 425.4, 425.5, and 425.9) and CKD (585.x, 586.x, 403.x, 404.x). For all patients renal function at entry was estimated from serum creatinine using the CKD-EPI formulas [17].

Other admission diagnoses were acquired through a list of 14 different items (one for each system: cardiovascular disease, hypertension, vascular disease, respiratory disease, ear nose and throat diseases, gastrointestinal disease, kidney and genito-urinary disease, metabolic disorders, musculoskeletal disorders, nervous disease) and a score from 1 to 5 was applied depending on the severity of the pathology (1 = absent: no impairment of organ/system; 5 = very severe impairment of organ/treatment is urgent/the prognosis is severe). Through these scores we calculated the CIRS-IS resulting from the first 13 categories scores arithmetic means (excluding the category of psychiatric/behavioral disease) and the "co morbidity index" (CIRS-CI), consisting in the number of categories in which we found a score higher than or equal to 3 (excluding the category of psychiatric/behavioral disease).

2.1. Statistical analysis

We used the Student's *t*-test to compare means and the Chi^2 test to compare proportions. Unadjusted prevalence estimates were obtained form tabular data. Multivariable logistic regression analysis was performed to evaluate the strength of the association between history of HF upon admission and renal disease with adjustment for a pre-defined set of predictors including age, sex, BMI, CIRS-IS, co-morbidity CIRS-CI.

To account for the multi-center nature of the REPOSI data, robust variance estimation was used in all regression models using the Huber-White sandwich estimator, which considers observations as independent across groups (the REPOSI centers in this case).

Analyses were performed using SAS 9.3 (SAS Institute, Cary, NC, USA) and STATA 12.1 (Statacorp, College Station, Tx, US). Statistical significance was set at $P < 0.05$ two-tailed.

3. Results

Table 1 shows the general features of REPOSI populations and the characteristics of patients with and without HF. Over 1380 patients enrolled in this study 633 of them were males (49.6%), 747 females (50.5%); mean age was 79 ± 7.3 years.

Table 1
Demographic and clinical characteristics of the REPOSI population: all patients, patients with and without heart failure (HF).

	All patients $n = 1380$	Patients with HF $n = 383$	Patients without HF $n = 991$	*P*-value*
Age (years)	79.0 (7.3)	80.3 (7.3)	78.5 (7.32)	<0.0001
Female sex (%)	49.6	47.8	50.2	0.4116
Weight (kg)	70.24 (15.2)	72.15 (16.4)	69.5 (14.7)	0.0049
Height (cm)	164.07 (8.8)	163.4 (9.5)	164.3 (8.5)	0.0856
BMI (kg/m^2)	26.04 (5.2)	26.9 (5.9)	25.6 (4.9)	<0.0001
Waist (cm)	93.7 (15.3)	94.53 (16.4)	93.4 (14.8)	0.2715
Systolic BP (mmHg)	133.79 (22.1)	133.3 (23.9)	134.1 (21.7)	0.5416
Diastolic BP min (mmHg)	75.45 (12.1)	75.1 (12.8)	75.6 (11.7)	0.5116
Heart rate (bpm)	80.73 (16.2)	81.9 (16.9)	80.3 (15.8)	0.1052
Blood glucose (mg/dL)	127.68 (67.7)	135.1 (77.6)	124.9 (63.3)	0.0123
Total cholesterol (mg/dL)	163.07 (45.9)	163.9 (44.2)	162.5 (46.5)	0.6349
Serum creatinine (mg/dL)	1.24 (0.9)	1.4 (1.0)	1.2 (0.9)	0.0002
eGFR (mL/min/1.73 m^2)	60.32 (24.2)	53.9 (23.8)	62.7 (23.)	<0.0001
Hemoglobin (g/dL)	11.96 (2.3)	12.1 (2.2)	11.9(2.3)	0.3547
CKD by admission ICD-9-CM (%)	17.4	25.9	14.1	<0.0001
Anemia by admission ICD-9-CM (%)	4.0	4.4	3.8	0.6088
CIRS Severity Index	1.6 (0.3)	1.8 (0.3)	1.6 (0.3)	<0.0001
CIRS Co-morbidity Index	2.9 (1.74)	3.5 (1.71)	2.7 (1.7)	<0.0001

*P-values for the comparison of patients with HF vs. those without HF; BMI: body mass index; BP: blood pressure; eGFR: estimated glomerular filtration rate (4 variable CKD-EPI Equation); CKD: chronic kidney disease; ICD-9-CM: International Classification of Diseases Clinical Modification; CIRS: Cumulative Illness Rating Scale.