International Journal of Cardiology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Time trends in first hospitalization for heart failure in a community-based population

Giulia Lorenzoni [a], Danila Azzolina [a], Corrado Lanera [a], Giorgio Brianti [b], Dario Gregori [a], Diego Vanuzzo [c,d], Ileana Baldi [a,*]

[a] Unit of Biostatistics, Epidemiology and Public Health, Department of Cardiac, Thoracic and Vascular Sciences, University of Padova, Padova, Italy
[b] Department of Prevention, ASS 4 'Medio Friuli', Udine, Italy
[c] National Association of Hospital Cardiologists, ANMCO (Associazione Nazionale Medici Cardiologi Ospedalieri) and Heart Care Foundation (Fondazione per il Tuo Cuore) Onlus, Firenze, Italy
[d] Center for Cardiovascular Prevention, ASS 4 'Medio Friuli', Udine, Italy

ARTICLE INFO

Article history:
Received 29 October 2017
Received in revised form 22 May 2018
Accepted 31 May 2018
Available online xxxx

Keywords:
Heart failure
Incidence
APC analysis

ABSTRACT

Background: This study aims to assess time trends in first hospitalization for heart failure (HF) in a community-based population over the period from 1977 to 2014.
Methods: Population-based cohort study using resources from the "Martignacco project" started in 1977 and promoted by the WHO. Three thousand and sixty-six subjects were involved in the project with follow-up through December 2014. Estimates were made for age-specific incidence rates for the first hospitalization for HF by birth cohort, calendar period, and gender. To disentangle the effects of age, calendar period, and birth cohort on the overall temporal trend in HF, we performed an age-period-cohort (APC) analysis.
Results: An incident hospitalization for HF was reported for 427 subjects. In the APC model, a cohort effect with a turning point in 1930 was observed. After 1930, a sharp decrease in the rate ratios (RRs) occurred in among both genders. The estimated RR in the 1940 birth cohort decreased to 0.43, (95% CI 0.19–0.92), in men and to 0.45, (95% CI 0.16–1.26), in women. A residual effect of calendar period on RR was observed with a plateau in 1995 for women and in 2000 for men, followed by a decline.
Conclusions: The current findings showed that HF hospitalization incidence has declined over the period considered in subjects over 65 years living in a geographically defined community in Northeast Italy. Moreover, the age of birth, calendar period of diagnosis, and birth cohort play an important role in the incidence of the first hospitalization for HF.

1. Introduction

Heart Failure (HF) is a severe and potentially life-threatening condition frequently encountered in everyday clinical practice. Despite recent advances in HF management [1], it continues to represent a large public health burden [2]; it has been estimated to affect approximately 26 million people worldwide [3], and from an economic standpoint, it is associated with high healthcare expenditures [4–7].

Analysing HF epidemiology is crucial to characterize the disease better. In fact, HF represents a complex chronic condition with an onset that is influenced by heterogeneous factors. Understanding HF predictors might help in the development of ad hoc prevention strategies, resulting in a reduction in the burden of such disease. Considering this framework, analysing time trends of HF incidence is crucial, since the analysis of changes in HF incidence over time may assist in better understanding HF contributors. However, epidemiological data on HF incidence trends are sparse and controversial, given the lack of community-based studies on secular trends in HF incidence. The analysis of data from the Framingham study (which enrolled people aged 28–62 years in Framingham, Massachusetts, in 1948) [8] has shown that HF incidence has stabilized among men over the period considered, while it has decreased among women. Survival was found to be improved in both genders. Similarly, a study of HF trends among the population of Olmsted County, Minnesota [9] has shown that HF incidence remained stable over two decades (1979–2000) in both genders, while the 5-year survival rate improved (exception made for the elderly). Conversely, Jhund et al. [10] analysed HF incidence between 1986 and 2003 in Scotland and found that rates of the first hospitalization for HF had increased until 1994 and declined thereafter.

Findings from these studies suggest that the incidence of HF over the last 30 years may have stabilized. These observed trends might be the joint result of several factors affecting the onset of HF over time, such as the progressive demographic shift (age effect), the improvement of clinical management of HF (period effect), and the improvement in population well-being (cohort of birth effect). However, the common

* Corresponding author at: Unit of Biostatistics, Epidemiology and Public Health, Department of Cardiac, Thoracic and Vascular Sciences, University of Padova, Via Loredan, 18, 35131 Padova, Italy.
E-mail address: ileana.baldi@unipd.it (I. Baldi).

https://doi.org/10.1016/j.ijcard.2018.05.132
0167-5273/© 2017 Published by Elsevier B.V.

approach to the study of age, period of diagnosis, and birth cohort effects on HF incidence has not fully explored the separate roles of these time dimensions. Few studies have reported on the use of combined analyses to disentangle the age-period-cohort (APC) effects. The age effect in HF incidence has been well described, showing that the risk of HF increases exponentially in the elderly [11]. However, period and cohort effects are more difficult to understand separately. Improvements in healthcare over time, particularly the introduction of angiotensin-converting enzyme (ACE) inhibitors, spironolactone, and β-blockers, may be period effects, which can modify the time trends in incidence rates. Cohort effects can result from changes in well-being between generations.

To obtain a reliable explanation for the time trends in first hospitalization for HF, the APC dimensions are addressed using a unique analysis that can provide a separation of the individual effects. Using a combined approach of estimating APC effects, the aim of this study is to unravel the separate effects of age, period and cohort on first hospitalization for HF within a geographically defined community in Northeast of Italy that was enrolled in the "Martignacco project" [12] in 1977 and followed up for 37 years.

2. Methods

2.1. Study population

The "Martignacco project", promoted by the World Health Organization (WHO), was started in 1977 with the aim of evaluating the impact of health promotion interventions on cardiovascular health in middle-aged (40–59 years) subjects. Two comparable communities in the Friuli Region of Northeastern Italy were selected: Martignacco was chosen as the intervention area, and San Giorgio di Nogaro was designated the control area. The intervention consisted of both the development of initiatives aimed at promoting healthy lifestyles among the community (e.g., cooking classes, smoking cessation support programs) and the regular follow-up of subjects with increased cardiovascular risk at the time of enrolment. The project is ongoing, and details are available elsewhere [12, 13].

The cohort data for the present analysis refers to the 3066 subjects (1324 and 1742 drawn from the geographical area of Martignacco and San Giorgio di Nogaro, respectively) enrolled in 1977 and followed up through December 31, 2014, by means of a computerized record linkage system with administrative sources on healthcare use.

2.2. The Italian National Health Service

The principle of universal provision of services, regardless of ability to pay, was introduced in 1978 by the first health care reform, which established the Italian National Health Service (NHS). In Italy, the NHS provides health services free of charge (in-patient care and general practitioner consultations) or at a minimal charge (outpatient care and prescription drugs). Some particular circumstances such as disability, chronic diseases, the status of inability, low income (based on the previous year's gross income) or >65 years of age entitle patients to co-payment fee exemption. It is worthwhile to note that the exemption is not a deterministic function of age, since from one hand individuals can be exempted before age 65 in case of chronic health problems or unemployment status and, on the other hand, are not entitled to the exemption after 65 if their family income is above the threshold level.

Since the Italian NHS provides universal coverage with standard care to all Italian citizens, the inequality in health care access is not a matter of insurance status. However, the universal coverage does not necessarily imply an equitable health care access. In fact, in Italy, it has been observed that the health care access could be affected by the socioeconomic status [14–16].

All exemptions from co-payment were retrieved for the study participants. Since exemptions may have a different period of validity (lifetime or periodically renewed), those referring to the same subject and condition were considered as a single one with an overall duration given by sum of the single pieces. Conversion of former or regional coding to the current nomenclature (http://www.salute.gov.it/BancheDati/anagrafi/MCR) was performed.

2.3. Heart failure identification

A HF event is defined as the first occurrence in the study period of a hospitalization with a primary diagnosis of HF (428) or hypertensive HF (402.01, 402.11, and 402.91), according to the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM). As reported in a literature review [17], this choice ensures a high positive predictive value (97%) in identifying incident HF.

2.4. Statistical analysis

The number of first hospitalizations for HF and the incidence rate (per 1000 person years), along with 95% confidence intervals (95% CI), were calculated both overall and stratified by gender, age, period, and geographic area. Denominators for these rates were measured in years of observation time for each cohort member, beginning in June 1977 until the occurrence of an HF event or the end of follow-up. Subjects who died before experiencing an HF event were censored at that time.

Age-specific incidence rates of first hospitalization for HF by birth cohort and gender were estimated. For this purpose, age at hospitalization was split into six 10-year increment age groups, from 45 to 95+ years, and birth cohort was split into five 5-year increment age groups, from 1915 to 1940.

To try to disentangle the effect of age, calendar period, and birth cohort on the overall temporal trend for HF during the period from 1977 to 2014, we fitted an APC model [18] to the data.

To overcome the identifiability problem of APC analysis, we set the cohort function at zero at 1930 (median of birth date) and constrained the period effects to be zero, on average, with zero slope. Different parameterizations can be chosen; however, they do not affect the effect curve. With the chosen parameterization, age effects can be interpreted as incidence rates for the first hospitalization for HF in the reference cohort of 1930, cohort effects as the rate ratios (RRs) relative to the reference cohort and period effects as the residual rate ratios relative to the age-cohort estimation. This approach assesses whether period has the same effect on all age groups and/or whether all birth cohorts have similar patterns (decreasing, increasing or stable incidence rates).

Computations were implemented with R software [19] (version 3.4.0) using the "rms", "EPI", and "PopEpi" packages.

3. Results

The study cohort included 3066 subjects. Two thousand seven hundred and fifty-two subjects were entitled to a co-payment exemption during the follow-up. Of these, 422, 615 and 958 were exempted for diabetes, neoplasms, and hypertension, respectively. In addition to that, such analysis showed a high proportion of low-income exemptions (Table S1 Supplementary material).

3.1. HF incidence

A total of 427 individual patients in the study cohort ($n = 3066$) were discharged from the hospital for the first time with HF over the 37-year time span. One thousand six-hundred and thirty-four subjects (52%) died during the follow-up period. Of these, 123 also had a hospitalization for HF.

Table 1 shows that the incidence of first hospitalization for HF increases with age and is higher for males. For the calendar period component, a crude increase in HF incidence from 2000 onwards was evident

Table 1
Number of first hospitalizations for heart failure (HF), person-years (P-years), incidence rates (IR) (×1000), and 95% confidence intervals (95% CI) according to age at first hospitalization, gender, period of first hospitalization and geographic area.

	HF	P-years	IR (×1000)	95% CI
Age at first hospitalization for HF (years)				
45–55	1	5299	0.2	0–1.3
55–65	26	20,323	1.3	0.9–1.9
65–75	116	26,285	4.4	3.7–5.3
75–85	208	16,240	12.8	11.2–14.7
85–95	75	3509	21.4	17.0–26.8
95+	1	23	43.8	6.2–311.0
Gender				
Female	212	38,630	5.5	4.8–6.3
Male	215	33,049	6.5	5.7–7.4
Period				
1985–1990	9	15,302	0.3	0.3–1.1
1990–1995	37	14,573	2.5	1.8–3.5
1995–2000	69	13,205	5.2	4.1–6.6
2000–2005	117	11,500	10.2	8.5–12.2
2005–2010	93	9646	9.6	7.9–11.8
2010–2014	102	7453	13.7	11.3–16.6
Geographical area				
Martignacco	182	31,087	5.9	5.1–6.8
San Giorgio Di Nogaro	245	40,592	6.0	5.3–6.8
Overall	427	71,679	6.0	5.4–6.5

Please cite this article as: G. Lorenzoni, et al., Time trends in first hospitalization for heart failure in a community-based population, Int J Cardiol (2017), https://doi.org/10.1016/j.ijcard.2018.05.132