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CLINICAL RESEARCH
Heart failure and cardiomyopathies

Epidemiology of heart failure in young adults: a French nationwide cohort study

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Abstract

Aims Heart failure (HF) in young adults is uncommon, and changes in its incidence and prognosis in recent years are poorly described.

Methods and results The incidence and prognosis of HF in young adults (18–50 years) were characterized using nationwide medico-administrative data from the French National Hospitalization Database (period 2013–2018). A total of 1,486 877 patients hospitalized for incident HF were identified, including 70 075 (4.7%) patients aged 18–50 years (estimated incidence of 0.44‰ for this age group). During the study period, the overall incidence of HF tended to decrease in the overall population but significantly increased by ∼0.041‰ in young adults ($P < 0.001$). This increase was notably observed among young men (from 0.51‰ to 0.59‰, $P < 0.001$), particularly those aged 36–50 years. In these young men, ischaemic heart disease (IHD) was the most frequently reported cause of HF, whereas non-ischaemic HF was mainly observed in patients ≤ 35 years old. In contrast to non-ischaemic HF, the incidence of IHD increased over the study period, which suggests that IHD-related HF is progressively affecting younger patients. Concordantly, young HF patients presented with high rates of traditional IHD risk factors, including obesity, smoking, hypertension, dyslipidaemia, or diabetes. Lastly, the rates of re-hospitalization (for HF or for any cause) within two years after the first HF event and in-hospital mortality were high in all groups, indicating a poor-prognosis population.

Conclusion Strategies for the prevention of HF risk factors should be strongly considered for patients under 50 years old.

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Structured Graphical Abstract

Key Question

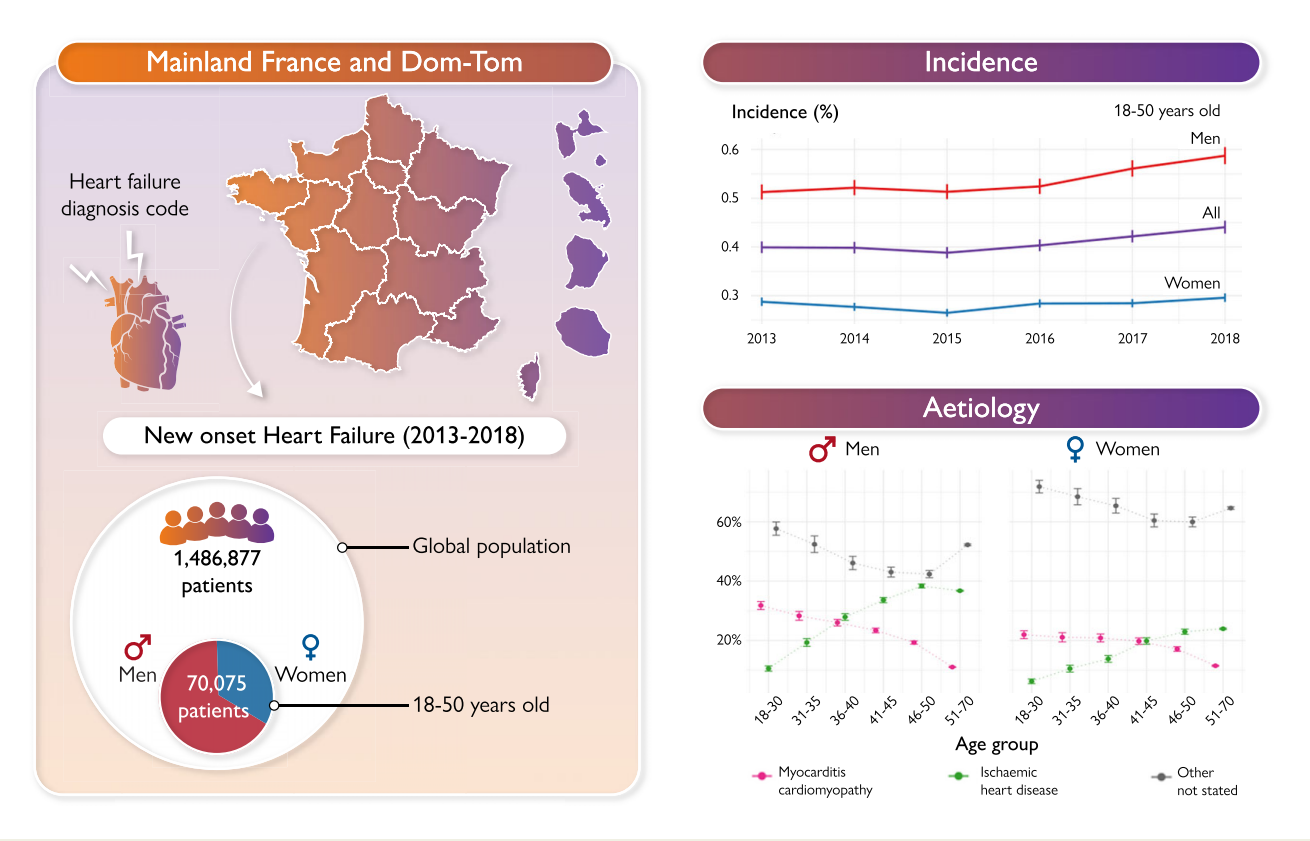
The epidemiology of heart failure (HF) and changes in its incidence and prognosis in patients under 50 years of age are poorly known.

Key Finding

The incidence of HF significantly increased in young men (18-50 years old) over a 5-year period. This was in line with the presence of increasing rates of traditional cardiovascular risk factors, and the prevalence of ischaemic HF. The prognosis remained poor during the observation period.

Take Home Message

This study highlights the need for active prevention of HF in young people and establishment of specific care pathways for HF patients under 50 years of age.



A French nationwide cohort study of HF in young adults (18–50 years): study design and summary results. Analysis results on 1 486 877 patients (all age groups) hospitalized with incident HF and identified on medico-administrative data from the French National Hospitalization Database (period 2013–18) identified 70 075 patients aged 18–50 years and showed increasing incidence of heart failure and ischaemic heart disease in young men.

Keywords Heart failure • Young people • Ischaemia • Risk factors • Epidemiology

Introduction

Heart failure (HF) is a major clinical and public health challenge that affected ~64.3 million people worldwide in 2017.[1] HF incidence is known to increase with age, and the median age of HF patients in Western countries exceeds 70 years. Therefore, HF is primarily considered to be a disease affecting the elderly, and most HF studies are focused on this group. However, recent studies indicated that the HF burden among the young population (defined as people < 50 years old) is increasing.[2–4] Few specific studies have reported the incidence, aetiologies, and prognostic trends in these younger HF patients.[3,5–7] The rates of HF hospitalizations have remained steady in France, whereas mortality due to HF decreased by ~3% annually during the last decade.[8] The same trends were observed in Sweden, Denmark and Scotland, where mortality due to HF has progressively decreased since the early 1990s.[3,9,10] Whether these favourable trends occur in the general

population of patients with HF independent of age has, to our knowledge, not been examined.

HF is the final stage of a wide range of cardiac impairments, and myocardial ischaemia is the prevailing cause in older patients. However, specific non-ischaemic HF aetiologies (including congenital heart disease, myocarditis, different types of cardiomyopathies, or toxic-related lesions of the myocardium) are more frequently observed among younger patients.[11] Data from the Swedish hospital discharge Registry and from the Framingham Heart Study suggest that the increasing burden of HF earlier in life may be explained by an increase in the prevalence of metabolic (i.e. obesity and diabetes) risk factors for HF combined with a higher attributable weight of these risk factors among younger people.[3,12] These factors are well-known contributors to ischaemic HF that develops in older patients. Whether the incidence of HF cases can be attributed to a change in the incidence of ischaemic or non-ischaemic causes of HF in younger patients has yet to be deciphered.

In this study, we used data from the French National Hospitalization Database (Programme de Médicalisation des Systèmes d'Information, PMSI) to investigate recent trends in HF incidence among patients under 50 years old. We also investigated gender- and age-specific trends in HF incidence and underlying aetiologies in this population.

Methods

Study design and data source

We performed a retrospective cohort study using data from patients with HF extracted from the Programme de Médicalisation des Systèmes d'Information (PMSI) French national database. The PMSI medical and administrative database contains standardized discharge reports for all patients discharged from all public or private hospitals in France, and it covers a population of ~67 million French people. Each discharge report provides administrative and demographic data, discharge diagnoses, procedures, and comorbidities. Diagnoses are encoded as primary or secondary using the French version of the International Classification of Diseases, 10th revision (ICD-10). Discharge reports are mandatory and serve as the basis for hospital funding. The PMSI database includes a unique anonymous identifier for each patient; this enables all stays by the same patient to be linked, even if the stays were in different establishments.[13]

Patient selection

Patients included in this study were incident cases of HF who were admitted to hospital between 2013 and 2018 in France. These patients were identified in the PMSI database by at least one stay coded with an I50 (ICD-10) diagnosis corresponding to *Heart Failure* and no stay coded with this code in 2011 and 2012. This timeframe was selected as optimal to identify incident HF as we found that a second HF stay occurred in the first 2 years after the first HF events for the very large majority (~85%) of patients (data not shown). We subsequently grouped the patients aged 18–50 years according to gender and age group (18–30, 31–35, 36–40, 41–45, and 46–50 years old) for further analysis. This study complied with rules of the French Data Protection Committee (Commission Nationale Informatique et Liberté, CNIL, MR-005, registration number: F20220208162131).

Extracted variables

We extracted age and gender data at the time of the first hospitalization stay for HF and all hospitalization stay's dates and diagnoses and their outcome (death) from 2011 until 2020, as nationwide hospitalization data were available only after this period (see Supplementary material online, *Tables S1* and *S2*).

Statistical methods

To calculate incidences of HF for each year from 2013 to 2018, the number of new cases of HF was divided by the French population estimate of the corresponding age group. The French population of 2013 was selected as the reference. Annual incidences by age were calculated as the averages over the study period of incidences per age. *P*-values were obtained from χ^2 test statistics for binary variables. Cochran–Armitage trend test was used to assess for changes in incidence over time. The binomial law was used to estimate confidence intervals when possible. Additional statistical methods are reported in Supplementary material online.

For each age group and gender, we then calculated the incidence of patients presenting with the main aetiologies. Patients were classified into one of three aetiological subgroups: ischaemic heart disease (IHD), myocarditis–cardiomyopathy, and other causes (other-not stated) according to ICD-10 codes (see Supplementary material online, *Table S1*). All patients with an ICD-10 code between I20 and I25 within the 2 years prior to or at the time of hospitalization for the first HF event were placed in the IHD group. For patients without an ICD-10 code between I20 and I25, a patient was placed in the myocarditis–cardiomyopathy group if he/she had an ICD-10 code between I40 and I43 within the 2 years prior to or at the time of hospitalization for the first HF event. Finally, remaining patients without these ICD-10 codes were classified in the other group. Incidences of each subgroup were calculated for each age group and gender along with their 95% confidence interval assuming a binomial distribution. A survival analysis with reversed time was performed to explore time to first prior hospitalization using Kaplan–Meier estimates according to aetiology, age group and gender subgroups.

Finally, to investigate the prognosis of patients with HF, we calculated the observed proportion of re-hospitalization for HF for any cause within the 2 years after the first HF event and of hospital death within 2 years or at the time of first HF event by age group, gender, and aetiological subgroup.

Results

General trends

Between 2013 and 2018, we identified 1 486 877 patients hospitalized for incident HF among the 67 million French inhabitants covered in the PMSI database. Among these patients with incident HF, 467 031 (31.4%) were patients aged 18–70 years and 70 075 (4.7%) were patients aged 18–50 years (*Table 1*). About one-third of HF patients aged 18–70 years were women.

By the end of the study period, the incidence of HF was estimated to be 3.65‰ in the whole French population and 0.44‰ in the young (18–50 years old) French population. In the whole French population, the overall incidence of HF decreased over the 2013–18 period from 3.99‰ to 3.65‰ ($P < 0.001$, *Figure 1A*), whereas we observed a significant increase of ~0.041‰ in the incidence of HF in the 18–50-year-old group ($P < 0.001$) (*Figure 1B*). This evolution was explained by a significant increase in the incidence of HF among young men (from 0.51‰ to 0.59‰, $P < 0.001$), whereas the incidence of HF among young women remained stable over the study period (~0.28‰). The incidence exponentially increased by age, from ~0.07‰ at 18 years old to 1.31‰ at 50 years old (*Figure 1C*). *Figure 1D* shows that the evolution of incidence of HF according to age was similar for men and women but remained higher in the young male population compared to the young female population at every investigated age. At 50 years old, the incidence of HF was more than two times higher for men than for women (1.84‰ vs. 0.80‰ respectively, $P < 0.001$).

We further described the evolution of HF incidence in men and women aged 18–50 years (*Figure 1E*). We observed a positive change in HF incidence over the study period after 30 years old for men and women, with a maximal change reached in the 36–40 year old age group (+22% for men and +17% for women). In age groups 41–45 and 46–50 years,

Table 1 Patients hospitalized for HF in France between 2013 and 2018

	All (*n*)	Men (%)	Women (%)
Number of patients hospitalized for HF	1 486 877		
18–70 years	467 031	67.94 (67.81; 68.08)	32.06 (31.92; 32.19)
18–50 years	70 075	65.59 (65.23; 65.94)	34.41 (34.06; 34.77)
18–30 years	8260	55.87 (54.79; 56.95)	44.13 (43.05; 45.21)
31–35 years	6210	57.23 (55.99; 58.46)	42.77 (41.54; 44.01)
36–40 years	9699	63.06 (62.09; 64.02)	36.94 (35.98; 37.91)
41–45 years	16 431	68 (67.28; 68.71)	32 (31.29; 32.72)
46–50 years	29 475	69.55 (69.02; 70.08)	30.45 (29.92; 30.98)
51–70 years	396 956	68.36 (68.21; 68.5)	31.64 (31.5; 31.79)

HF, heart failure.

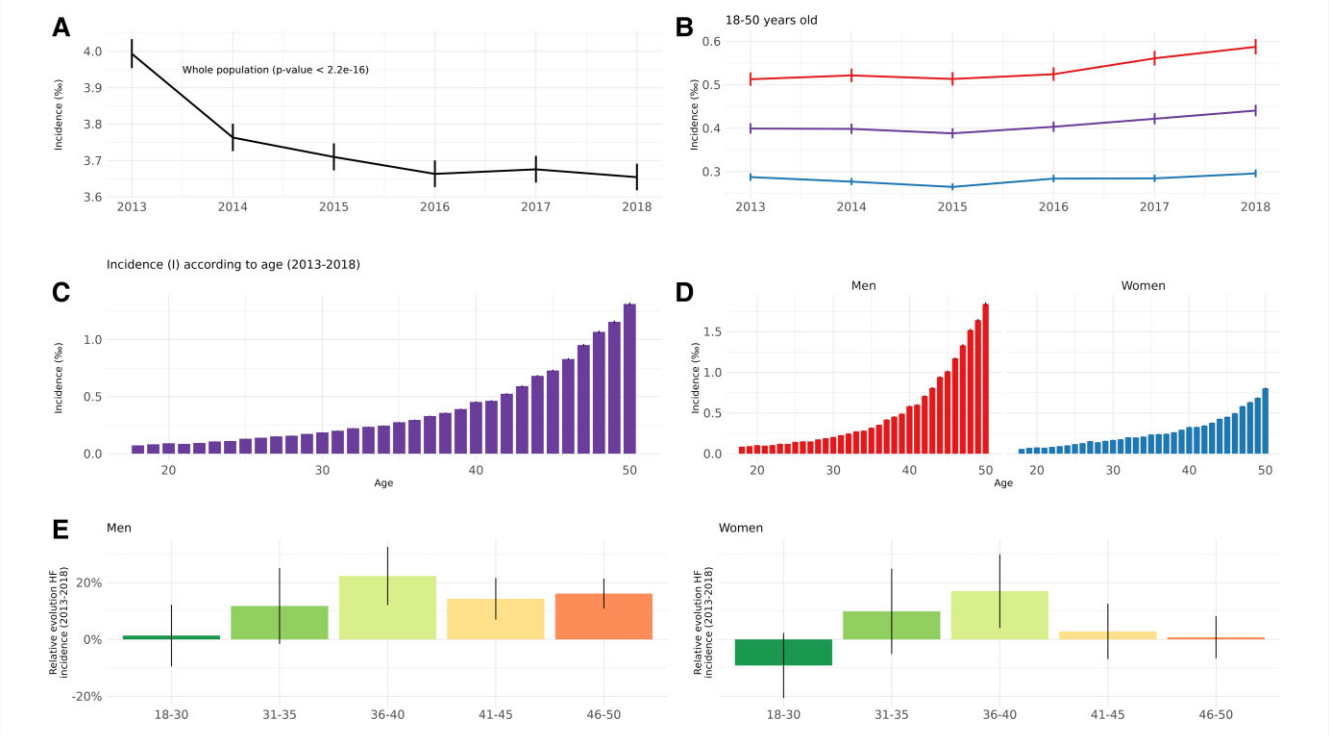


Figure 1 (*A*) Incidence of heart failure in the French population (all age groups) from 2013 to 2018. (*B*) Standardized incidence of heart failure in the 18–50-year-old French population. (*C*) Incidence of heart failure according to age from 2013 to 2018 in the young French population (18–50 years) assessed in this study. (*D*) Incidence of heart failure according to age from 2013 to 2018 in men and women. (*E*) Relative evolution of incidence of heart failure between 2013 and 2018 in the young population according to age group and gender.

changes observed in men were much higher (+16% and +14%, respectively) than those in women (+3% and +1%, respectively) (*Figure 1E*).

Underlinying heart failure causes and trends in prevalence over the study period

Figure 2A shows the incidence of HF hospitalizations with a concomitant diagnosis or a diagnosis within the prior 2 years of either myocarditis–cardiomyopathy, IHD, or other causes according to gender and age group. Myocarditis–cardiomyopathy and IHD diagnoses were found in 23% and 20%, respectively, of patients aged 18–50 years, whereas these incidences were 11% and 30% for patients aged 51–70 years. We also found that the incidence of IHD-related HF was positively associated with age, whereas the incidence of patients with a myocarditis–cardiomyopathy diagnosis significantly decreased with age in both genders. Myocarditis–cardiomyopathy diagnostic codes were more frequently found in the youngest HF patients and decreased across all age

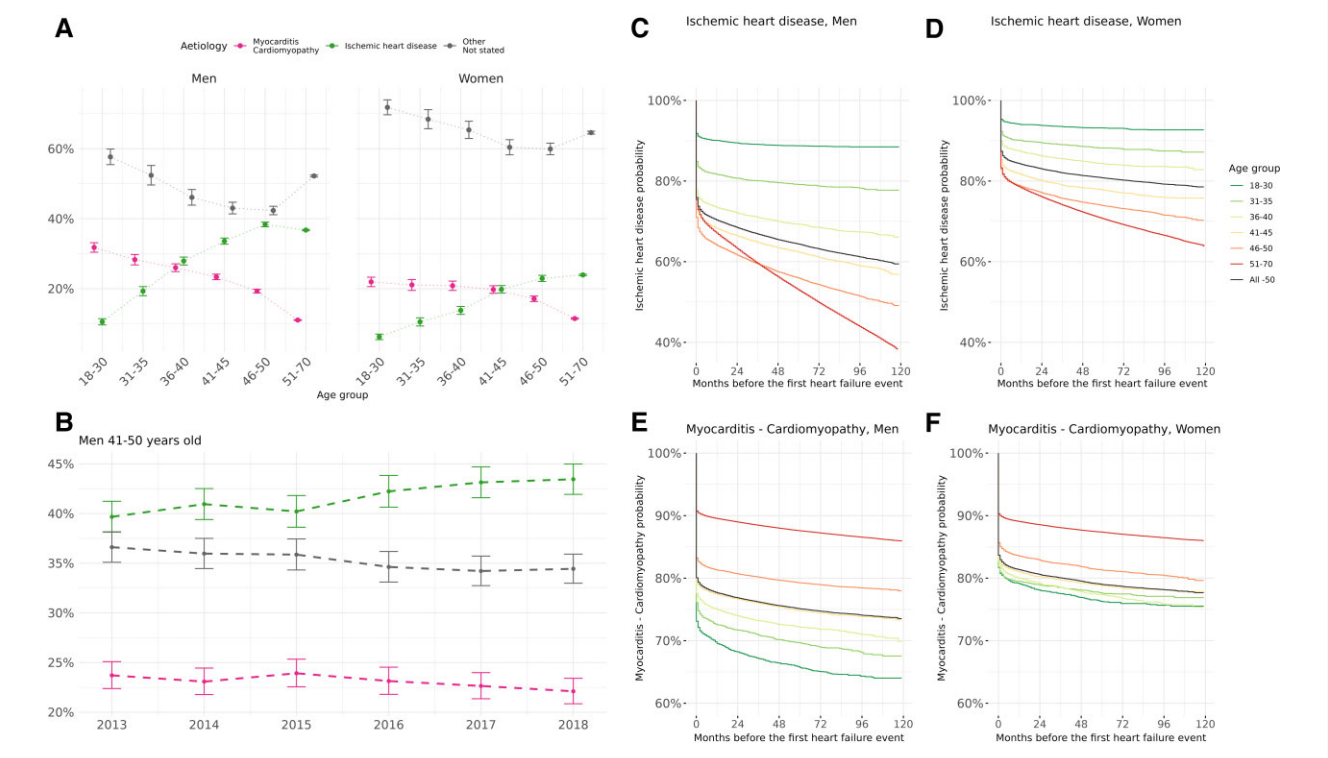


Figure 2 (*A*) Concomitant diagnosis [myocarditis–cardiomyopathy (red), ischaemic heart disease (green), or other-not stated (grey)] either within the 2 years prior to or at the time of hospitalization for heart failure for men and women according to age group. (*B*) Relative evolution of incidence of myocarditis–cardiomyopathy (red), IHD (green), or other-not stated (grey) over the 2013–18 study period in the young male population aged 41–50 years. (*C*/*D*) Kaplan–Meier estimations of having a prior ischaemic heart disease preceding the first heart failure hospitalization according to age group in men (*C*) and women (*D*). (*E*/*F*) Kaplan–Meier estimations of having a prior myocarditis/cardiomyopathy preceding the first heart failure hospitalization according to age group in men (*E*) and women (*F*). $P < 0.001$ for all comparisons.

groups from 32% to 11% in men and from 22% to 11% in women. Reciprocally, the incidence of IHD-related HF patients was minimal for the youngest HF patients (10% and 6% in men and women, respectively) but was more likely than myocarditis–cardiomyopathy at a younger age for men than for women (36–40 years old for men vs. 41–45 years old for women). The incidences of patients diagnosed with IHD-related HF in the 46–50-year-old age group (38% and 23% in men and women, respectively) were similar to those observed in the 51–70-year-old age group (37% and 24% in men and women, respectively), suggesting that a plateau was reached by age 46 for both genders. The large and heterogeneous group of patients in the other group (i.e. patients without a concomitant diagnosis of either myocarditis–cardiomyopathy of IHD within the prior 2 years or at the time of hospitalization) showed no qualitative differences between age groups, but a difference between genders was detected, with rates higher in women than in men ($P < 0.001$). Corresponding data to *Figure 2A* are provided in Supplementary material online, *Table S3*.

We identified a significant increase in HF incidence in young men aged 41–50 years over the 2013–18 study period (*Figure 1E*). A significant increase in the incidence of IHD-related HF (from 40% to 43%, $P < 0.001$, *Figure 2B*) occurred, whereas incidences of a concomitant diagnosis of myocarditis–cardiomyopathy or other-not stated diagnoses decreased or were stable over the study period (*Figure 2B*; Supplementary material online, *Table S4*).

Figures 2C–F are Kaplan–Meier estimations of having an IHD or a myocarditis–cardiomyopathy diagnostic code, respectively, before the first HF event for men and women according to age group. Overall, these time-reversed graphs showed that HF cause was reported at the time of HF hospitalization for the majority of patients aged < 50 years, both for IHD and for myocarditis–cardiomyopathy. In contrast, the incidence of patients with a known IHD prior the first HF event was much more important in patients aged 51–70 years (*Figure 2C and D*), but this pattern was not observed for myocarditis–cardiomyopathy (*Figure 2E and F*). Overall, these data show that the ischaemic origin of HF became highly prevalent in men > 40 years old and in women > 45 years old but not in younger patients with very premature HF.

We next looked at the prevalence of diagnostic codes related to cardiovascular risk factors, lifestyle habits, and other cardiac and non-cardiac disorders in these patients. We found that the overall burden of comorbidity in this young HF population was substantial. *Table 2* shows that the population of young HF patients had more major HF risk factors (and often multiple factors) than anticipated in such a young population in France.[14–17] Indeed, the classical atherosclerotic risk factors (i.e. smoking, hypertension, dyslipidaemia, diabetes, or obesity) were substantially high and significantly more frequent in patients with IHD than in patients with myocarditis–cardiomyopathy or others diagnosis. Similarly, unhealthy lifestyles habits (smoking, alcohol or drug use) and cancer were frequently found in this population, regardless of gender. We further looked to temporal trends in HF risk factors (see Supplementary material online, *Figure S1*) and found a significant increase in the rates of smoking habits and obesity over the study period in patients presenting incident HF, whereas the rates of other risk factors were stable or decreasing.

Table 2 Distribution of concomitant diagnoses among young people with HF

Diagnostic		Men				Women				All genders $n = 70\,075$	*P*-value IHD in Men vs. Women
		Myo-cardio $n = 11\,349$	IHD $n = 16\,855$	Others $n = 17\,755$	All aetiologies $n = 45\,959$	Myo-Cardio $n = 5038$	IHD $n = 4719$	Others $n = 14\,359$	All aetiologies $n = 24\,116$		
Lifestyle habits	Alcoholism, *n* (%)	2666 [23.5 (22.7; 24.3)]	3060 [18.2 (17.6; 18.8)]	3774 [21.3 (20.7; 21.9)]	9500 [20.7 (20.3, 21)]	342 [6.8 (6.1; 7.5)]	411 [8.7 (7.9; 9.6)]	1233 [8.6 (8.1; 9.1)]	1986 [8.2 (7.9, 8.6)]	11486 [16.4 (16.1; 16.7)]	< 0.001
	Smoking, *n* (%)	3651 [32.2 (31.3; 33.0)]	8908 [52.9 (52.1; 53.6)]	4934 [27.8 (27.1; 28.5)]	17493 [38.1 (37.6, 38.5)]	1026 [20.4 (19.3; 21.5)]	2111 [44.7 (43.3; 46.2)]	2657 [18.5 (17.9; 19.2)]	5794 [24.0 (23.5, 24.6)]	23287 [33.2 (32.9; 33.6)]	< 0.001
	Drug use, *n* (%)	242 [2.1 (1.9; 2.4)]	354 [2.1 (1.9; 2.3)]	671 [3.8 (3.5; 4.1)]	1267 [2.8 (2.6, 2.9)]	49 [1,0 (0.7; 1.3)]	75 [1.6 (1.3; 2.0)]	244 [1.7 (1.5; 1.9)]	368 [1.5 (1.4, 1.7)]	1635 [2.3 (2.2; 2.4)]	0.031
Cardio-vascular risk factors	Arterial hypertension, *n* (%)	3279 [28.9 (28.1; 29.7)]	6407 [38.0 (37.3; 38.8)]	5313 [29.9 (29.3; 30.6)]	14999 [32.6 (32.2, 33.1)]	1533 [30.4 (29.2; 31.7)]	1995 [42.3 (40.9; 43.7)]	4040 [28.1 (27.4; 28.9)]	7568 [31.4 (30.8, 32.0)]	22567 [32.2 (31.9; 32.6)]	< 0.001
	Gestational hypertension, *n* (%)	0.00	0.00	0.00	0.00	362 [7.2 (6.5; 7.9)]	166 [3.5 (3.0; 4.1)]	1072 [7.5 (7.0; 7.9)]	1600 [6.6 (6.3, 7.0)]	-	-
	Obesity, *n* (%)	2560 [22.6 (21.8; 23.3)]	4478 [26.6 (25.9; 27.2)]	3454 [19.5 (18.9; 20.1)]	10492 [22.8 (22.4, 23.2)]	1266 [25.1 (23.9; 26.4)]	1489 [31.6 (30.2; 32.9)]	3602 [25.1 (24.4; 25.8)]	6357 [26.4 (25.8, 26.9)]	16849 [24.0 (23.7; 24.4)]	< 0.001
	Diabetes type 1, *n* (%)	302 [2.7 (2.4; 3.0)]	1111 [6.6 (6.2; 7.0)]	781 [4.4 (4.1; 4.7)]	2194 [4.8 (4.6, 5.0)]	178 [3.5 (3.1; 4.1)]	517 [11.0 (10.1; 11.9)]	789 [5.5 (5.1; 5.9)]	1484 [6.2 (5.9, 6.5)]	3678 [5.2 (5.1; 5.4)]	< 0.001
	Diabetes type 2, *n* (%)	1038 [9.2 (8.6; 9.7)]	3227 [19.2 (18.6; 19.8)]	1841 [10.4 (9.9; 10.8)]	6106 [13.3 (13.0, 13.6)]	495 [9.8 (9.0; 10.7)]	1034 [21.9 (20.7; 23.1)]	1566 [10.9 (10.4; 11.4)]	3095 [12.8 (12.4, 13.3)]	9201 [13.1 (12.9; 13.4)]	< 0.001
	Dyslipidaemia, *n* (%)	1001 [8.8 (8.3; 9.4)]	5289 [31.4 (30.7; 32.1)]	1499 [8.4 (8.0; 8.9)]	7789 [16.9 (16.6, 17.3)]	387 [7.7 (7.0; 8.5)]	1194 [25.3 (24.1; 26.6)]	970 [6.8 (6.4; 7.2)]	2551 [10.6 (10.2, 11.0)]	10340 [14.8 (14.5; 15.0)]	< 0.001
	Chronic renal failure, *n* (%)	913 [8.0 (7.6; 8.6)]	1391 [8.3 (7.8; 8.7)]	2124 [12.0 (11.5; 12.5)]	4428 [9.6 (9.4, 9.9)]	440 [8.7 (8.0; 9.6)]	568 [12.0 (11.1; 13.0)]	1640 [11.4 (10.9; 12.0)]	2648 [11.0 (10.6, 11.4)]	7076 [10.1 (9.9; 10.3)]	< 0.001
	Sleep apnoea, *n* (%)	823 [7.3 (6.8; 7.8)]	1262 [7.5 (7.1; 7.9)]	1375 [7.7 (7.4; 8.2)]	3460 [7.5 (7.3, 7.8)]	197 [3.9 (3.4; 4.5)]	275 [5.8 (5.2; 6.5)]	758 [5.3 (4.9; 5.7)]	1230 [5.1 (4.8, 5.4)]	4690 [6.7 (6.5; 6.9)]	< 0.001
Other cardiac diagnosis	Arrhythmia, *n* (%)	4241 [37.4 (36.5; 38.3)]	4995 [29.6 (29.0; 30.3)]	4940 [27.8 (27.2; 28.5)]	14176 [30.8 (30.4, 31.3)]	1400 [27.8 (26.6; 29.1)]	1209 [25.6 (24.4; 26.9)]	2853 [19.9 (19.2; 20.5)]	5462 [22.6 (22.1, 23.2)]	19638 [28.0 (27.7; 28.4)]	< 0.001
	Pulmonary embolism, *n* (%)	388 [3.4 (3.1; 3.8)]	373 [2.2 (2.0; 2.5)]	987 [5.6 (5.2; 5.9)]	1748 (3.8 (3.6, 4.0)]	196 [3.9 (3.4; 4.5)]	161 [3.4 (2.9; 4.0)]	992 [6.9 (6.5; 7.3)]	1349 [5.6 (5.3, 5.9)]	3097 [4.4 (4.3; 4.6)]	< 0.001
	Primary pulmonary hypertension, *n* (%)	370 [3.3 (2.9; 3.6)]	311 [1.9 (1.7; 2.1)]	709 [4.0 (3.7; 4.3)]	1390 [3.0 (2.9, 3.2)]	229 [4.6 (4.0; 5.2)]	144 [3.1 (2.6; 3.6)]	928 [6.45 (6.1; 6.9)]	1301 [5.4 (5.1, 5.7)]	2691 [3.8 (3.7; 4.0)]	< 0.001
	Endocarditis, *n* (%)	139 [1.2 (1.0; 1.5)]	201 [1.2 (1.0; 1.4)]	860 [4.8 (4.5; 5.2)]	1200 [2.6 (2.5, 2.8)]	61 [1.2 (0.9; 1.6)]	70 [1.5 (1.2; 1.9)]	373 [2.6 (2.4; 2.9)]	504 [2.1 (1.9, 2.3)]	1704 [2.4 (2.3; 2.5)]	0.131
Other extra cardiac	Cancer, *n* (%)	996 [8.8 (8.3; 9.3)]	1717 [10.2 (9.7; 10.7)]	2883 [16.2 (15.7; 16.8)]	5596 [12.2 (11.9, 12.5)]	941 [18.7 (17.6; 19.8)]	803 [17.0 (16.0; 18.1)]	3512 [24.5 (23.8; 25.2)]	5256 [21.8 (21.3, 22.3)]	10852 [15.5 (15.2; 15.8)]	< 0.001
	Cushing's syndrome, *n* (%)	8 [0.07 (0.03; 0.1)]	14 [0.1 [0.1; 0.1)]	37 [0.2 (0.2; 0.9)]	59 [0.1 (0.1, 0.2)]	15 [0.3 (0.2; 0.5)]	24 [0.5 (0.3; 0.8)]	58 [0.4 (0.3; 0.5)]	97 [0.4 (0.3, 0.5)]	156 [0.2 (0.2; 0.3)]	< 0.001
	Hyper-aldosteronis, *n* (%)	27 [0.2 (0.2; 0.4)]	23 [0.1 (0.1; 0.2)]	44 [0.3 (0.2; 0.3)]	94 [0.2 (0.2, 0.3)]	19 [0.4 (0.2; 0.6)]	18 [0.4 (0.2; 0.6)]	50 [0.4 (0.3; 0.5)]	87 [0.4 (0.3, 0.4)]	181 [0.3 (0.2; 0.3)]	< 0.002
	Adrenal gland, diseases, *n* (%)	58 [0.5 (0.4; 0.7)]	66 [0.4 (0.3; 0.5)]	129 [0.7 (0.6; 0.9)]	253 [0.6 (0.5, 0.6)]	40 [0.8 (0.6; 1.1)]	54 [1.1 (0.9; 1.5)]	154 [1.1 (0.9; 1.3)]	248 [1.0 (0.9, 1.2)]	501 [0.7 (0.7; 0.8)]	< 0.001

Prognosis of young patients with heart failure

Figure 3A–C illustrates the probability of re-hospitalization for HF (*Figure 3A*) or for any causes (*Figure 3B*) and the probability of death for any causes (*Figure 3C*) within 2 years after the first HF hospitalization. Corresponding estimates are provided in Supplementary material online, *Table S5*. For patients aged 18–50 years, proportions of re-hospitalization for HF were ∼24% and 30% for patients with IHD-related HF and myocarditis–cardiomyopathy diagnoses, respectively, and 31% and 35%, respectively, for patients aged 51–70 years. It remained stable over age group for IHD-related HF and myocarditis–cardiomyopathy, whereas it increased from 15% to 23% over age group for patients with a diagnosis of other-not stated. The proportion of re-hospitalization for any cause was ∼75% and remained stable over age groups and gender. The proportion of deaths in hospital for any cause within 2 years after the first HF hospitalization was high, at ∼10% for patients aged 18–50 years, and it was similar between patients with IHD and myocarditis–cardiomyopathy. Patients with other causes displayed higher all-cause mortality rates, indicating that these patients were likely to have additional extra-cardiac conditions.

Discussion

In this nationwide study conducted in France using data from 2013 to 2018, we found that HF was rare in patients aged < 50 years (4.7%), but HF incidence progressively increased in young men and particularly in those aged 36–50 years. In these patients, IHD was the most frequently reported cause of HF, and its incidence increased over the study period. This result suggests that IHD-related HF is increasing and is progressively affecting younger patients. Concordantly, we found that young HF patients frequently presented with multiple comorbidities, including high rates of traditional risk factors for IHD. The proportion of re-hospitalization (for HF or for any cause) within 2 years after the first HF event was high for the entire study population (∼25% for HF and 75% for any causes) regardless of the primary aetiology and age group, indicating a population at poor prognosis. In-hospital mortality rates also were high (roughly 10%). The strength of our study is the large patient cohort that included the entire French population hospitalized for HF from 2011 to 18 (1 486 877 patients regardless of age). Patients from 18 to 70 years old were followed over a median of 73 months before and 58 months after first HF event.

Previous data from Sweden, the USA, and Australia have shown that HF admissions levelled off and eventually declined during the last two decades.[3,4,18,19] This is in line with the overall trend observed in our study in France, indicating a worldwide tendency.[2] However, we found that epidemiological trends in France depended on age, with increasing HF incidence in the young male population. This confirms and expands the progressive increase in HF incidence in young patients previously reported in Sweden.[3] By analysing the associated diagnostic codes, we found that this increase in young men was likely linked to an increase of ischaemic HF. We found that IHD-related HF was one of the most prevalent causes of HF in men > 40 years old and women > 45 years old but not in younger patients with very premature HF, who were more likely to present with cardiomyopathies. The higher likelihood of observing IHD-related HF in young men is supported by observations from others countries. In the USA, more than 200,000 30–54-year-old patients were hospitalized every year with a diagnosis of acute myocardial infarction,[19] and men had the highest incidence rate across all age groups.[20] Similar results were reported in the UK, where the prevalence of acute myocardial infarction reach 0.5% in men and 0.18% in women aged 35–44 years.[21]

The progressive increase of IHD at younger age can be linked to the overall increase of inactivity, atherothrombosis risk factors, and related comorbidities.[22] Smoking, hypertension, dyslipidaemia, diabetes, and obesity are classical risk factors leading to atherosclerosis and coronary artery disease and were frequently observed in our patients (notably in those with IHD-related HF) as compared to the known incidences in healthy French people of the same age. In addition, even if we cannot ensure a direct causality link with the increase of IHD, we found a significant increase over the study period in the rates of smokers and obesity suggesting that preventive efforts should be particularly strengthened regarding these two major risk factors. The CONSTANCES study, a general prospective population-based cohort with 200 000 French adults aged 18–69 years at inception, reported that 12.5% and 10.3% of French women and men, respectively, aged 18–49 years presented with obesity (BMI > 30 $kg.m^{-2}$), whereas 22.9% were obese in our population.[14] According to the French national ESTABAN study, the expected rate of arterial hypertension among the young men (18–34, 53–44, and 45–54 years old) should be 11.7%, 17%, and 36.6% respectively.[16] Moreover, the prevalence of arterial hypertension is significantly lower among young women (18–34, 53–44, and 45–54 years old), at 1.5%, 9.1%, and 21.1%, respectively.[16] The expected rate of dyslipidaemia (e.g. hypercholesterolaemia) among the French population (47.3 ± 14.6 years old) should be 23.3% (27.8% for men and 19.0% for women) according the ESTABAN study,[15] but it exceeded 30% in young HF patients with IHD. Finally, the number of diabetic patients (type 1 or 2) among our population was much higher than anticipated by the French Health Insurance agency (Système national d'information inter-régimes de l'assurance maladie, Sniiram), as only 2.5% of the young French population present with diabetes.[17,23]

In our study, young French patients with IHD-related HF also presented with significantly higher rates of risk factors. A recent study reported important age differences in the effect of traditional risk factors on the development of future HF. Specifically, risk factors for HF carried a stronger relative risk among young people compared to older people.[12] These results have to be interpreted in line with the dramatic increase in the prevalence of metabolic diseases with cardiac consequences in young people.[22] Our data likely suggest a progressive increase in the prevalence of IHD-related HF in younger patients.

The incidence of HF in young patients can also be influenced by socio-economic factors that were not investigated in our study. Recent studies have reported that HF patients in low-middle-income countries were younger than patients in high-income countries.[2,24] A recent study in the U.S. showed that nearly half of young patients with HF reside in zip codes in the lowest quartile of national household income.[4] Additional analyses will be now be needed to better define the relations between HF incidence, HF risk factors and socio-economic factors in young vs. older patients.

We also found that young HF patients had a poor prognosis that was comparable to that observed in older patients, with a high rate of re-hospitalizations in the 2 years following HF diagnosis. HF is known to be associated with the highest 30-day readmission rate (around 20%–25%) regardless of the primary aetiology.[25–27] Gender also seems to have an impact on re-hospitalization among the elderly. In one study, women older than 60 years had a 2.5 times greater risk for rehospitalization than men.[28] However, in our study the observed proportion of re-hospitalization was similar between men and women younger than 50 years. Additionally, some studies found that patients with HF

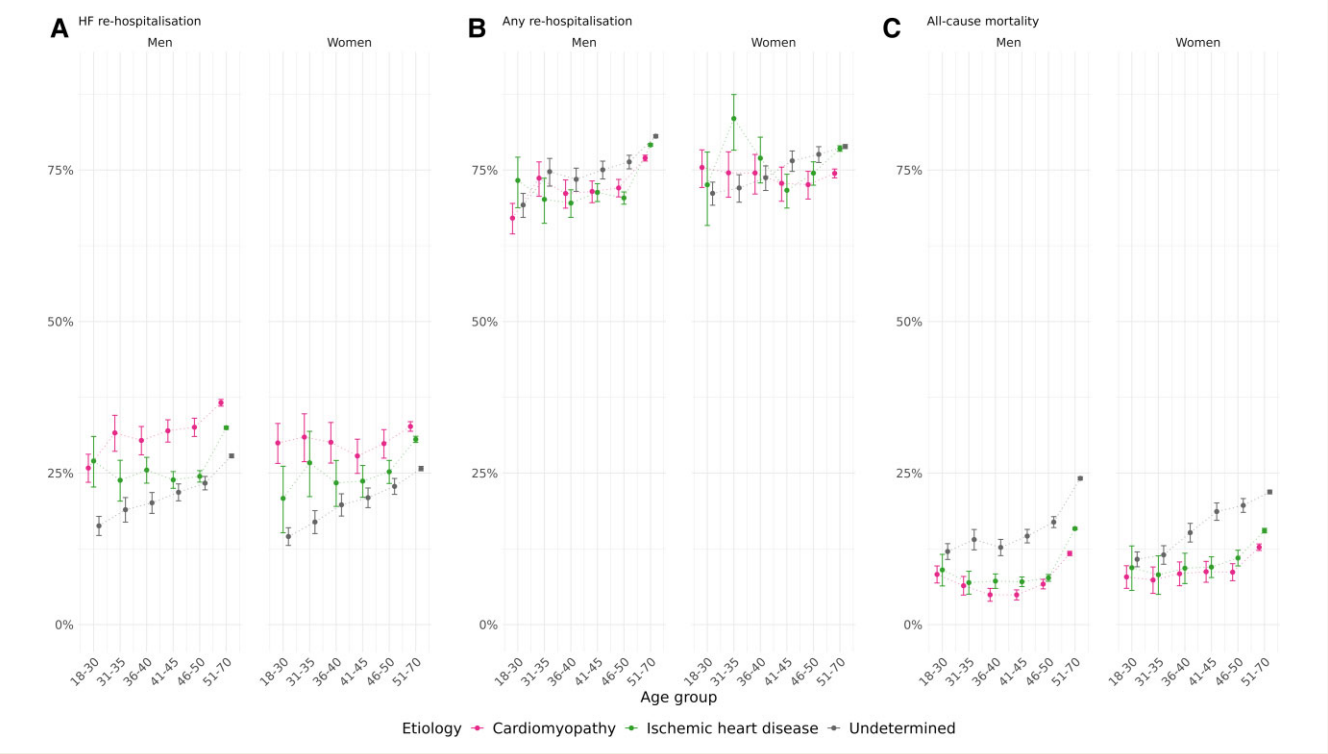


Figure 3 According to age group, gender, and the primary aetiology (categories myocarditis–cardiomyopathy, ischaemic heart disease, and other-not stated): (*A*) Observed proportion of re-hospitalization for heart failure within 2 years after the first heart failure event. (*B*) Observed proportion of any re-hospitalization within 2 years after the first heart failure event. (*C*) Observed proportion of death within 2 years after the first heart failure event.

presented with significant comorbidities and reported that 45% of re-hospitalizations were non-cardiovascular related,[29,30] which is in line with our results. Patients who were readmitted had more peripheral vascular disease, diabetes, and stroke when compared with HF patients who were not readmitted after their index hospitalization.[30] These studies indicate that comorbid conditions may be significant predictors of repeat hospitalization of HF patients.

Regarding proportion of death within 2 years after the first HF event, 2-year mortality data among young adults with HF are scarce. In line with our results, 1-year case fatality rates after a first HF hospitalization in a New South Wales, Australia, study were 13% in the 45–49-year-old age group.[31] The Swedish National Registry reported rates of 11%–12% for those aged 18–54 years, which is high but lower than that of older patients.[3] More recently, a Canadian study reported a 5-year mortality rate of 28% among patients aged 20–44 years.[32] We found concordant results in our study, and all of these reports highlight the important role of surveillance in the immediate post-discharge period. Practitioners should be warned of high re-hospitalization and mortality risks in young HF patients, and strict monitoring should be recommended.

Our study illustrates the need for better identification and prevention of HF in the young population. Our results suggest that many cases are related to modifiable risk factors, including smoking, obesity, dyslipidaemia, diabetes, and hypertension, as observed in young patients with first myocardial infarction.[33] Additional analyses on the temporal trends of HF risk factors further identify growing rates of smoking habits and obesity, suggesting a growing contribution of these two factors, even if the causality link would remain to be demonstrated. Currently, screening for these traditional risk factors is not proposed for young patients in France (and in other countries). Our data indicate that the associated cause leading to HF was not identified before the first HF hospitalization for many young patients. Therefore, efforts to detect, prevent, and treat cardiovascular risk factors in young patients (beginning at 36 years old in men and 40 years old in women) should be recommended to efficiently limit incident HF. Reciprocally, some young patients had IHD or myocarditis–cardiomyopathy diagnostic codes before the first HF event. Our study highlights the need for a specific monitoring of these young patients in order to decrease the transition to HF.

Our study had some limitations. First, it was performed using medico-administrative databases, and the use of discharge diagnosis codes could result in underestimation of relevant data. More particularly, diagnoses that do not require significant medical care might not be coded. Therefore, we cannot exclude that associated diagnoses and risk factors are underestimated, while HF requiring significant medical treatment is not likely to be underestimated. This will result in higher rates for associated diagnoses and risk factors than the observed ones that were already high is such a population of young adults. Second, we used hospital admission rates and not true incidence. However, the French medical care organization ensures that all young adults having a first episode of HF will be referred to a reference hospital and the PMSI database is likely exhaustive for HF diagnoses. Third, the coding practices might have change over time, but if this occurred, the resulting bias would not be influenced by ages or genders, thus limiting the risk. Fourth, the database does not provide indications on medications, HF classification, or left ventricular ejection fraction. However,

most of young patients with HF present with aetiologies associated with reduced ejection fraction[34] which has well-established management guidelines. Fifth, in order to identify patients with a new HF diagnosis, we excluded patients with a HF diagnosis in the 2 years before the first HF event; however, patients could have had an older HF diagnosis. However, we show that this limitation was minor based on the high tendency of re-hospitalization for HF in the early stage after first hospitalization for HF.

In conclusion, the increase of HF incidence in young adults (< 50 years old) documented in our study differs from the general trend noted in older patients. Among the young population, men seemed to be more vulnerable to premature HF than women. We found that myocarditis–cardiomyopathy and IHD were major causes of HF admission, with inverse probability trends according to age group. In the young population, and especially in young men, ischaemic HF was the predominant form of HF, and our data suggest that it is progressively increasing. The young adults hospitalized for premature HF also presented with high rates of major modifiable risk factors for ischaemic HF, including obesity, dyslipidaemia, smoking, hypertension, and diabetes. The observed proportion of re-hospitalization for HF or from any cause within 2 years after the first HF event is alarming. Although the cause of the increased incidence of HF among the young population is not fully known, it may reflect true epidemiological changes linked to increased prevalence of cardio-metabolic risk factors in young people. This study highlights the need for a specific care pathway for HF patients under 50 years old. Strategies for the prevention of HF risk factors should be strongly considered for patients under 50 years old.

Supplementary data

Supplementary data is available at *European Heart Journal* online.

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Data availability

This study was performed using the PMSI (Programme de Médicalisation des Systèmes d'Information) French national database and restrictions apply to the availability of these data, which were used under license for this study.

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