ESC HEART FAILURE
ESC Heart Failure 2023; **10**: 264–273
Published online 5 October 2022 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.14179

ORIGINAL ARTICLE

Risk of death associated with incident heart failure in patients with known or suspected chronic coronary syndrome

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Abstract

Aims Traditional adverse events in chronic coronary syndrome (CCS) include atherothrombotic events but usually exclude heart failure (HF). Data are scarce about how new-onset HF modifies mortality risk. We aimed to determine the incidence of HF and compare its long-term mortality risk with myocardial infarction (MI) and stroke in patients with known or suspected CCS.

Methods We prospectively evaluated 5811 consecutive HF-free patients submitted to vasodilator stress cardiac magnetic resonance (CMR) for known or suspected CCS. Ischaemic burden and left ventricular ejection fraction were assessed by CMR. HF included outpatient diagnosis or acute HF hospitalization. The mortality risk for the incident events and their cross-comparisons were evaluated using a Markov illness–death model with transition-specific survival models.

Results The mean age was 55 ± 11 years, and 38.9% were female. At a median follow-up of 5.44 (IQR = 2.53–8.55) years, 591 deaths were registered (1.79 per 100 P-Y). The rates of new-onset HF were higher compared with MI and stroke [1.02, 0.62, and 0.51, respectively ($P < 0.05$)]. The adjusted association between new-onset HF, MI, and stroke, and subsequent mortality was time dependent. The risk increased almost linearly for HF and became significant by the third year. By Year 10, the mortality risk attributable to new-onset HF was more than 2.5-fold (HR: 2.68, 95% CI = 1.74–4.12). For MI, there was a significant increase in mortality risk up to the second year, followed by a monotonic decrease. For stroke, the mortality risk increased for the entire follow-up but became significant by the third year. A cross-comparison among incident endpoints HF outnumbers risk for those with MI by the sixth year ($HR_{year6.3}$: 1.88, 95% CI = 1.03–3.43). There was no difference in mortality risk between incident HF and stroke.

Conclusions In patients with CCS, long-term rates of incident HF were higher than MI and stroke. Patients with new-onset HF showed a higher risk of long-term mortality.

Keywords Cardiac magnetic resonance; Coronary artery disease; Heart failure; Chronic coronary syndrome

Received: 23 June 2022; Revised: 21 August 2022; Accepted: 15 September 2022
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Introduction

In patients with coronary artery disease (CAD), especially in those with chronic coronary syndromes (CCS), most prognostic studies have focused on the risk of mortality, myocardial infarction (MI), or revascularization.[1,2] Some recent studies have also pointed out a significantly increased risk of incident heart failure (HF) in patients with CCS.[3,4] However, in this

setting, little is known about the impact of new-onset HF patients on the risk of mortality compared with traditional atherosclerotic events.

This study evaluated the impact of new-onset HF diagnosis on the risk of all-cause death in a cohort of patients who underwent vasodilator stress cardiac magnetic resonance (CMR) imaging due to chest pain. Additionally, in this same population, we aimed to compare the risk of mortality attributable to incident HF with the mortality risk in those with spontaneous MI and stroke.

Methods

Study design

This is a retrospective analysis based on a large prospective registry that included 6675 consecutive outpatients referred for vasodilator stress CMR due to known or suspected CCS from 2001 to 2016 in a single healthcare department of Valencia, Spain. Baseline characteristics and CMR data were prospectively recorded and immediately entered into the predefined database. The physician in charge of the patient had full access to all CMR parameters, and their management was left to their discretion. After excluding cases with incomplete baseline data, those lost to follow-up, incomplete CMR study, insufficient image quality, and prior diagnosis of HF or cardiomyopathy, 5899 patients were included in this analysis. Additionally, 88 patients were excluded due to insufficient/ambiguous data for HF at the time of CMR assessment; thus, the final sample included 5811 patients (*Figure 1*).

This registry was carried out following the Declaration of Helsinki, and all patients provided signed consent. In September 2018, the local ethics committee authorized a retrospective update of the occurrence of all-cause mortality.

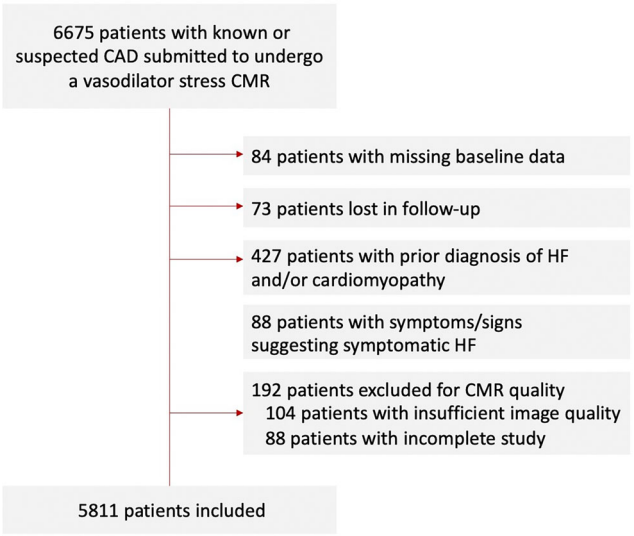
This work is part of a line of research in which the same registry has been used to analyse the implications of stress CMR in risk stratification and decision-making in patients with stable ischaemic heart disease.[5,6]

CMR data analysis

Technical aspects related to CMR studies are presented elsewhere.[5,7] Images were examined using customized software (Syngo, Siemens, Erlangen, Germany).

Left ventricular end-diastolic and end-systolic volume indexes and left ventricular ejection fraction (LVEF) were quantified in cine images. Ischaemia was visually defined, using the 17-segment model, as the presence of a segmental perfusion deficit (PD), determined as a persistent delay (in at least three consecutive temporal images, in comparison with other segments in the same slice) during the first pass of contrast through the myocardium after vasodilator infusion. The ischaemic burden was defined as the number of segments that showed post-stress PD. The presence of stress-induced PD was ruled out in segments exhibiting transmural late gadolinium enhancement (LGE) and segments with simultaneous PD and non-transmural LGE in which the extent of PD did not clearly exceed the extent of LGE. The ischaemic burden was also analysed as a continuous variable and dichotomized as non-extensive ($\leq$5 segments) and extensive ($>$5 segments with PD). This cut-off value was derived from this same series of patients based on its ability to predict all-cause death in

Figure 1 Flow chart. CAD, coronary artery disease; CMR, cardiac magnetic resonance; HF, heart failure.



the entire population.[7,8] LGE extent was visually defined as the number of segments with LGE. Inter and intra-observer variability for all parameters used in the present registry were <5% and have been previously reported.[7]

CMR-related revascularization

CMR-related revascularization was identified as those procedures [either coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI)] performed within 3 months following the index vasodilator stress CMR study, as long as no hospital admission for cardiovascular indications had taken place during that period of time (in this case, patients were censored upon readmission).

Affected vessels were defined as those with >2 mm diameter and at least one stenosis >50%. The presence of multivessel disease (regarded as two or more affected vessels and/or left main stem disease) was used throughout as a proxy for extensive angiographic coronary disease. In addition, the proximal left anterior descending or left main disease was also registered.

Endpoint and follow-up

The clinical endpoints were all-cause mortality (terminal event), and intermediate endpoints [new-onset HF, spontaneous acute myocardial infarction (AMI), and stroke] were registered during follow-up. New-onset HF included a new diagnosis of HF at the outpatient level according to current ESC guidelines or hospitalization for acute HF (AHF).[9] AHF hospitalization was defined as any unplanned in-hospital stay with symptoms and signs of HF longer than 24 h requiring intravenous therapy. Acute coronary syndrome (Killip >I) was not considered as admission for AHF. AMI was defined following the fourth definition of MI.[10] Stroke was defined as the presence of a focal deficit associated with neurological involvement in imaging tests. Additionally, non-CMR-related revascularization was also registered. Follow-up was carried out centrally from October 2018 to November 2018 by four cardiologists authorized by the local ethics committee using the unified electronic regional health system registry.

Statistical analysis

Continuous variables are described by means ± standard deviation (SD) or medians [interquartile range (IQR)] when appropriate. Discrete variables are summarized as percentages. At baseline, the comparisons of means, medians, and frequencies were carried out using *t*-test, Wilcoxon–Mann–Whitney test, and chi-square test, respectively.

A parametric multi-state survival model[11] was used to estimate crude and adjusted mortality rates according to groups characterized by having a new HF episode, AMI, or stroke during the follow-up. By comparing these adjusted rates, we were able to rank the mortality risk among these three incident events. Each intermediate endpoint was tested for time-dependent effect using a likelihood ratio test. These three intermediate endpoints were modelled with a time interaction using restricted cubic splines with two degrees of freedom. All regression models included as covariates age, sex, hypertension, dyslipidaemia, diabetes, current smoking, prior history of ischaemic heart disease, prior history of stroke/transient ischaemic attack (TIA), prior coronary revascularization, undergoing coronary revascularization at follow-up, and the following CMR parameters: LVEF, number of ischaemic segments, and number of segments with necrosis.

A two-sided *P*-value of <0.05 was the threshold used for significance in all analyses. Stata 16.1 was used for data preparation and statistical analysis. The multistate package within Stata was used for the multistate analysis (https://www.mjcrowther.co.uk/software/multistate/).

Results

Baseline characteristics

Table 1 summarizes the baseline clinical characteristics of patients who did and did not develop HF during follow-up. Patients with new-onset HF were older, were more frequently women, and had a greater burden of cardiovascular risk factors, prior history of coronary heart disease, and left bundle branch block. Regarding CMR parameters, patients with incident HF exhibited lower LVEF and more segments with ischaemia and necrosis. These patients also showed higher rates of MI, stroke, and coronary revascularization during the follow-up (*Table 1*).

Incidence of HF, MI, and stroke along the follow-up

At a median follow-up of 5.44 (2.53–8.55) years, 314 (5.40%), 192 (3.30%), and 159 (2.74%) developed a new-onset HF, AMI, and stroke, respectively. Incident HF included 162 patients with de novo hospitalization for AHF and 152 patients with an ambulatory diagnosis. The median LVEF at the diagnosis of incident HF was 48% (IQR 35–60%). Natriuretic peptides were available in 121 de novo hospitalizations for AHF (74.7%). The median NT-proBNP in these patients at admission was 3359 pg/mL (1650–7999). The rates (per 100 person-years) of new-onset HF were higher than those found for AMI (1.02 vs. 0.62, $P < 0.001$) and stroke (1.02 vs. 0.51, $P < 0.001$).

Table 1 Baseline characteristics across incident HF

Variables	Total *N* = 5811	No incident HF *N* = 5497 (94.6)	New onset HF *N* = 314 (5.4)	*P* value
Demographics, anthropometry, and medical history				
Age, years	65 (54–76)	65 (54–76)	71 (61–81)	<0.001
Female, *n* (%)	2258 (38.9)	2104 (38.3)	154 (49.0)	<0.001
Weight, kg	77.4 (63.4-91.4)	77.4 (63.3–91.5)	77.4 (63.7–91.1)	0.944
Height, m	1.65 (1.55–1.75)	1.65 (1.55–1.75)	1.62 (1.53–1.71)	<0.001
BSA, m^2	1.88 (1.67–2.09)	1.88 (1.67–2.09)	1.86 (1.66–2.06)	0.231
BMI, kg/m^2	28.7 (20.8–36.6)	28.6 (20.6–36.6)	29.4 (24.6–34.2)	0.091
Hypertension, *n* (%)	3785 (65.1)	3554 (64.7)	231 (73.6)	0.001
Dyslipidaemia, *n* (%)	3339 (57.5)	3150 (57.3)	189 (60.2)	0.314
Diabetes mellitus, *n* (%)	1643 (28.3)	1490 (27.1)	153 (48.7)	<0.001
Current smoker, *n* (%)	1031 (17.7)	995 (18.1)	36 (11.5)	0.003
Family history of CHD, *n* (%)	309 (5.3)	296 (5.4)	13 (4.1)	0.339
Prior history of CHD, *n* (%)	2180 (37.5)	2044 (37.2)	136 (43.3)	0.029
Prior history of AMI, *n* (%)	1054 (18.1)	1000 (18.2)	54 (17.2)	0.657
Prior history of CPA, *n* (%)	1067 (18.4)	1011 (18.4)	56 (17.8)	0.804
Prior history of CABG, *n* (%)	371 (6.4)	340 (6.2)	31 (9.9)	0.009
Prior history of coronary revascularization, *n* (%)	1381 (23.8)	1297 (23.6)	84 (26.8)	0.201
Prior history of CVA/TIA, *n* (%)	144 (2.5)	134 (2.4)	10 (3.2)	0.408
ECG—left bundle branch block, *n* (%)	316 (5.4)	290 (5.3)	26 (8.3)	0.022
CMR parameters				
LVEF <50%, *n* (%)	732 (12.6)	641 (11.7)	91 (29.0)	<0.001
LVEF, %	64 (53–75)	64 (53–75)	59 (46–72)	<0.001
Presence of necrosis, *n* (%)	1897 (32.64)	1772 (32.24)	125 (39.81)	0.005
Presence of inducible ischaemia, *n* (%)	2474 (42.57)	2306 (41.95)	168 (53.50)	<0.001
Segments with ischaemia, *n* (%)				<0.001
0–1	3529 (60.7)	3377 (61.4)	152 (48.4)	
2–5	1411 (24.3)	1326 (24.1)	85 (27.1)	
6–8	590 (10.1)	544 (9.9)	46 (14.6)	
>8	281 (4.8)	250 (4.6)	31 (9.9)	
Clinical outcomes				
Angiography during the follow-up, *n* (%)	1296 (22.3)	1187 (21.6)	109 (34.7)	<0.001
PCI during the follow-up, *n* (%)	686 (11.8)	619 (11.3)	67 (21.3)	<0.001
CABG during the follow-up, *n* (%)	226 (3.9)	197 (3.6)	29 (9.2)	<0.001
Coronary revascularization–elective (yes), *n* (%)	525 (9.0)	483 (8.8)	42 (13.4)	0.006
Death, *n* (%)	591 (10.2)	501 (9.1)	90 (28.7)	<0.001
New-onset acute MI, *n* (%)	192 (3.3)	146 (2.7)	46 (14.6)	<0.001
New-onset CVA, *n* (%)	159 (2.7)	134 (2.4)	25 (8.0)	<0.001
Coronary revascularization during follow-up, *n* (%)	889 (15.3)	800 (14.6)	89 (28.3)	<0.001
Coronary revascularization—elective, *n* (%)	525 (9.0)	483 (8.8)	42 (13.4)	0.006

AMI, acute myocardial infarction; BMI, body mass index; BSA, body surface area; CABG, coronary artery bypass graft; CHD, coronary heart disease; CMR, cardiac magnetic resonance; CPA, cardiopulmonary arrest; CVA, cerebrovascular accident; HF, heart failure; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; TIA, transient ischaemic attack.
Values expressed as mean (SD) and median (percentile 25% to percentile 75%). Categorical variables are presented as percentages.

All-cause mortality following new-onset HF, MI, and stroke

A total of 591 deaths (10.17%) were reported during the follow-up, which means a rate of 1.79 per 100 person-years. The mortality rates along the follow-up were higher in those with new-onset HF, MI, and stroke.

Incident HF

After multivariate adjustments, death rates remained higher in those with new-onset HF than in those without incident HF (*Figure 2A*). Their comparison showed that the mortality risk of those with HF was greater over the follow-up, becoming significant by Year 3.7 (HR: 1.55, 95% CI = 1.09–2.19) and thereafter (*Figure 2B*). By Year 10, the mortality risk attributable to new-onset HF was more than 2.5-fold (HR: 2.68, 95% CI = 1.74–4.12) (*Figure 2B*). The mortality risk was earlier and greater when HF was newly diagnosed during hospitalization for AHF vs. ambulatory HF diagnosis (*Figure 3*). In fact, at 5.2 years, admitted patients showed an almost 2.4-fold increased risk of death (HR: 2.38, 95% CI = 1.63–3.46). At this same time point, the ambulatory diagnosis was not significantly associated with the risk of death (HR: 1.53, 95% CI = 0.96–2.43). In a sensitivity analysis, only adjudicating as hospitalization for AHF those with available high levels of NTproBNP and using the same set of covariates in the model, incident HF remained associated with a higher risk of mortality after the third year (*Figure S1*). Likewise, further sensitivity

Figure 2 All-cause mortality among patients with or without new-onset HF. (A) All-cause mortality rates in those with and without new-onset HF. (B) All-cause mortality risk in those with vs. without new-onset HF. HF, heart failure.

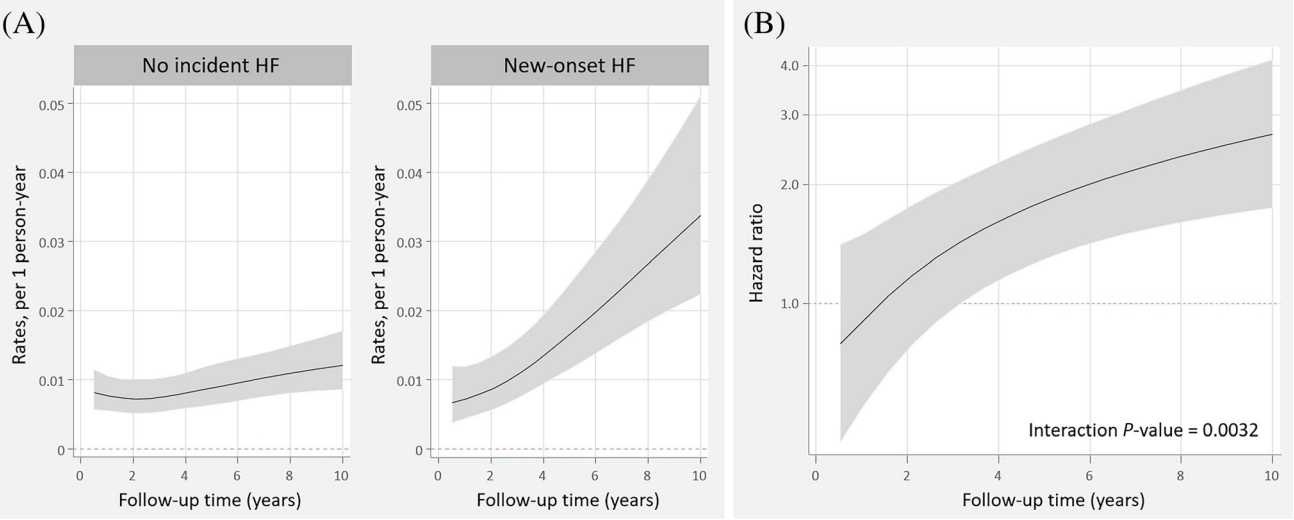
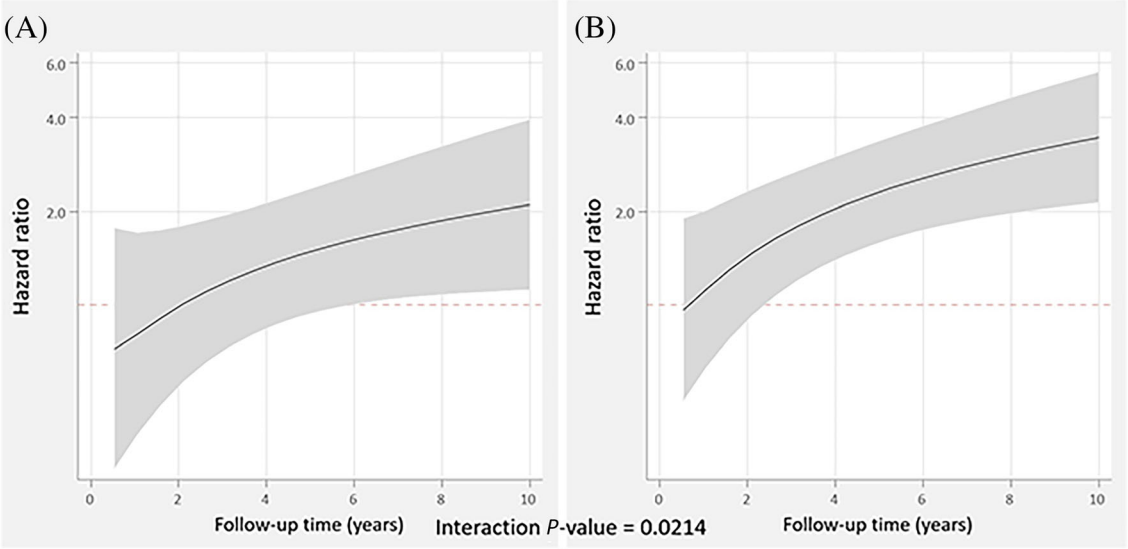


Figure 3 All-cause mortality risk in those with new-onset HF requiring hospitalization vs. those with ambulatory HF diagnosis. (A) New-onset HF requiring hospitalization. (B) Ambulatory HF diagnosis. HF, heart failure.



analyses also showed a positive association between incident HF and subsequent mortality in those with angiographic evidence of epicardial CAD at baseline (*Figure S2*).

CMR-LVEF assessed at baseline was independently associated with the risk of new-onset HF (Supplementary file 3a). However, under this same multivariate adjustment, the number of segments with transmural necrosis and the number of segments with ischaemia were not associated with the risk of new-onset HF (*Figure S3B* and *S3C*).

Incident MI

Patients with incident AMI showed an increased adjusted mortality rate, particularly during the first 2 years after the event and levelling-off afterwards (*Figure 4A*). The ratio of these two rates showed that those with incident MI had a sizable increase in mortality early after the event, but the risk decreased over the follow-up and became non-significant after the sixth year (*Figure 4B*).

Figure 4 All-cause mortality among patients with or without incident AMI. (A) All-cause mortality rates in those with and without incident AMI. (B) All-cause mortality risk in those with vs. without incident AMI. AMI, acute myocardial infarction.

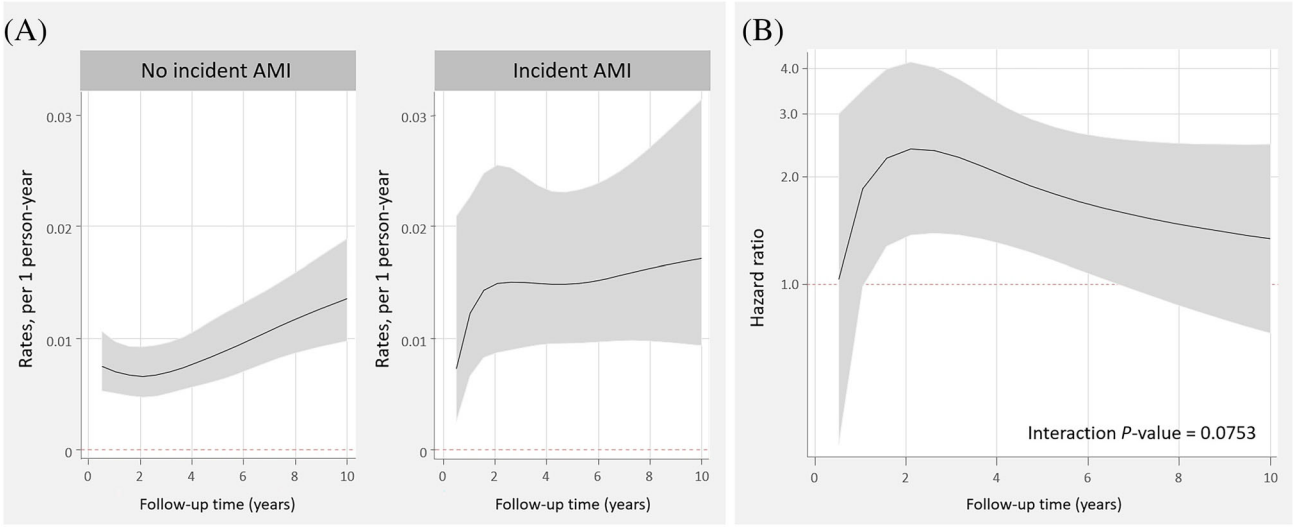
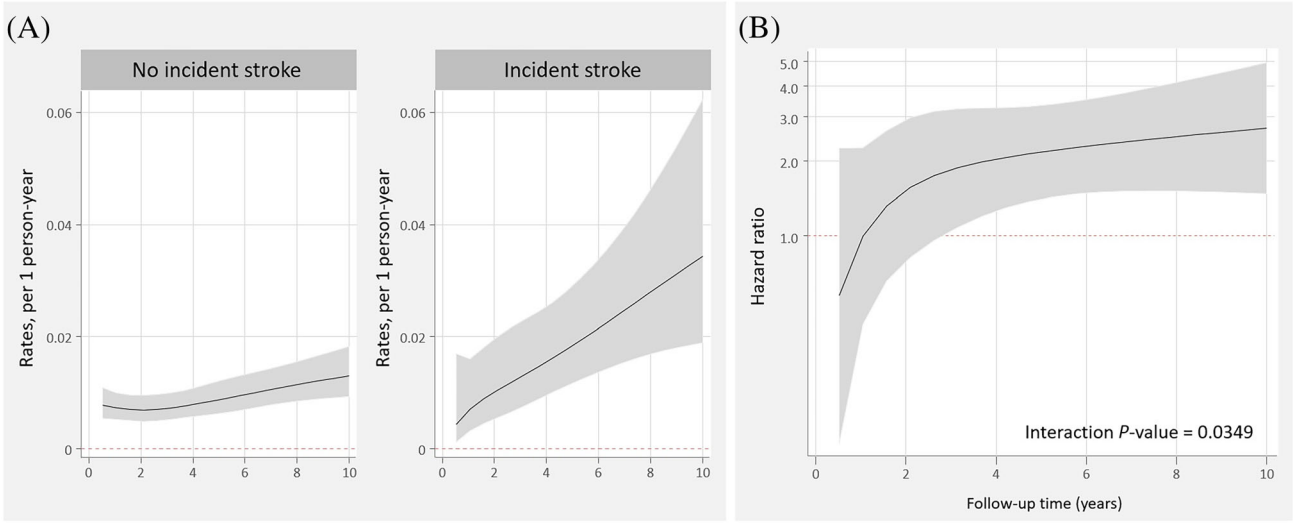


Figure 5 All-cause mortality among patients with or without incident stroke. (A) All-cause mortality rates in those with and without incident stroke. (B) All-cause mortality risk in those with vs. without incident stroke.



Incident stroke

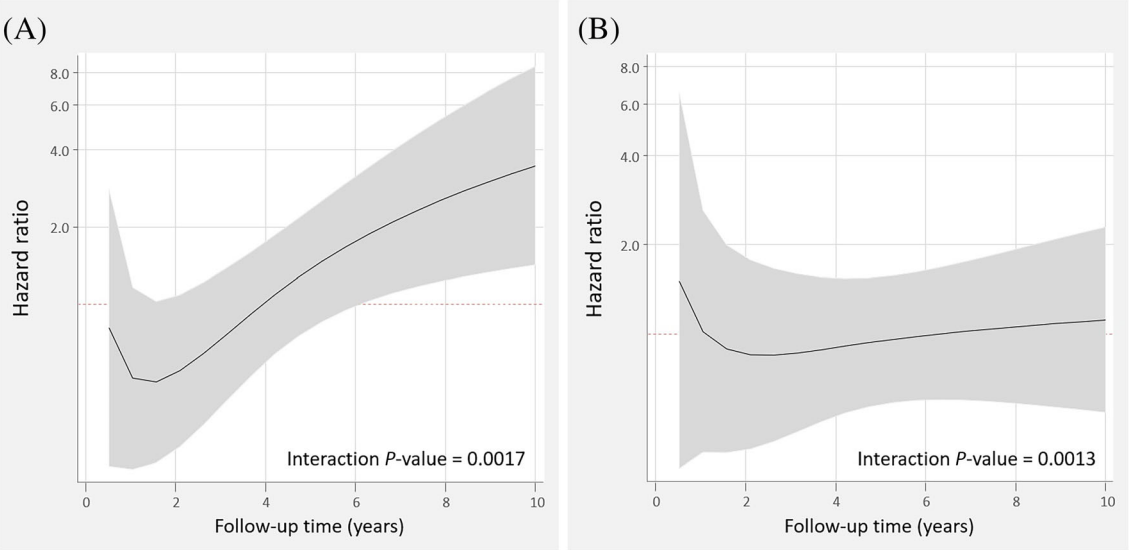
We found a sustained higher risk of mortality over the follow-up in those with incident stroke (*Figure 5A*). Their comparison showed that the mortality risk was higher in those with incident stroke than in their counterpart and became significant slightly after the third year and thereafter (*Figure 5B*). Indeed, the HR at Year 3.2 was 1.87 (95% CI = 1.08–3.23).

Risk of death across HF status: A cross-comparison among incident endpoints

Incident HF vs. incident AMI

As shown in *Figure 6A*, we found that by Year 6, those with HF outnumber in risk those who had suffered an AMI ($HR_{year6.3}$: 1.88, 95% CI = 1.03–3.43). However, we did not find significant differences between them before the sixth year (*Figure 6*).

Figure 6 All-cause mortality risk in those with incident HF vs. incident AMI. (A) Incident HF. (B) Incident AMI. AMI, acute myocardial infarction; HF, heart failure.



Incident AHF (HF with hospital admission) vs. incident MI

When comparing the subset of patients with HF diagnosed during an episode of admission for AHF with those with an MI event, we found that those with an index hospitalization for AHF showed an increased risk of death that becomes significant by 5.5 years ($HR_{year5.8}$: 1.87, 95% CI = 1.04–3.34) and after that, as shown in *Figure 6*.

Incident HF vs. incident stroke

During the entire follow-up, the mortality risk associated with incident HF did not significantly differ among those with incident stroke.

Discussion

The current findings indicate that new-onset HF is a frequent clinical adverse event in patients with known or suspected CCS. Indeed, the long-term incidence of new-onset HF was more frequent than traditional atherosclerotic events such as MI and stroke. Furthermore, new-onset HF resulted in an increased risk of long-term mortality. This excess of risk was comparable with the harmful effect found with stroke. Compared with MI, patients with new-onset HF exhibited a higher mortality risk in a more prolonged follow-up.

Heart failure as a 'major' endpoint in CCS

Classically, the main clinical events evaluated in patients with CAD have been cardiovascular mortality, non-fatal MI, stroke, and unplanned revascularization, in several cases grouped in major adverse cardiovascular events. Indeed, these endpoints have been the primary endpoints in contemporary and large randomized clinical trials,[12,13,14] and only the ISCHEMIA trial has included HF-events in the composite primary endpoint.[15,16] Additionally, in the last decade, some studies have focused on evaluating the risk of HF, the factors associated with it, and how HF modifies the natural history of CAD, especially following an acute MI.[17,18,19] In the setting of CCS, the evidence is more scarce, but a number of risk factors, including older age, women, hypertension, diabetes, medical therapy, and revascularization, have been associated with an increased risk of HF.[4] More recently, some authors have pointed out the relevance of HF as a frequent adverse event in patients with CCS. For instance, in a substudy of CORONOR registry[20] that included 3871 patients with stable CAD and free of HF, the authors found that these patients were frequently hospitalized for HF, and most HF hospitalizations were not preceded by an incident MI (>90% of the cases). In this study, the 5-year cumulative incidences of hospitalization were higher for HF vs. MI (5.7% vs. 4.2% P = 0.011), especially after the third year of follow-up.[20] Similarly, in a large international, observational, contemporary cohort of CCS patients (CLARIFY registry) that included 32 703 patients in 45 countries (15.1% had prior HF), the 5-year rates of hospitalization for HF were 5.4% compared with 2.8% and 1.1% for non-fatal MI and 1.1% for fatal MI.[21] In the current study, we included not only hospitalizations but also ambulatory diagnoses of HF. Similarly, in both large observational studies, we found HF is a relevant adverse event in patients with known or suspected CCS. In the ISCHEMIA trial, 4% had a prior history of HF, and 5-year rates of hospitalization for HF were higher in the invasive vs. conservative revascularize-

tion strategy (2.8% vs. 1.6%).[15] Differences in the HF rates among the studies rely on different risk profiles, HF-event definitions, and adjudication. Further studies in CCS should better define the epidemiology of HF, homogenize the definition, and systematically include HF events within the efficacy endpoint of trials.

Incident HF and mortality risk in CCS

There is well-documented evidence supporting the harmful role of new atherosclerotic events on the risk of mortality.[22] However, how incident HF modifies the course of the disease remains less well evaluated. From a theoretical point of view, it seems logical to postulate that new-onset HF leads to an increased risk of death.[23,24] However, the magnitude of this risk, the temporal trend, and a formal comparison with traditional endpoints in CCS such as MI and stroke remain elusive. In the CORONOR registry, hospitalization for HF was an independent and powerful predictor of mortality (adjusted hazard ratio 5.97, 95% confidence interval 4.55–7.83; $P < 0.001$), irrespective of LVEF.[20]

The current study confirmed that incident HF in patients with known or suspected CCS was associated with a significantly higher risk of death, and these estimates become more pronounced in more prolonged follow-up. More interestingly, after performing a thorough multivariate adjustment, we found that the risk of mortality attributable to incident HF was comparable with that reported for MI and stroke. According to our findings, we envision a differential temporal effect on mortality. Those with MI will show an increased risk the first years after the event. Conversely, HF events will result in a sustained and more extended effect on the risk of death. These findings are consistent with the temporal trends in survival widely described in the literature for both conditions.[25,26,27] According to the current results, in the case of stroke, it seems to behave similarly to new-onset HF. Accordingly, some authors report a higher long-term risk of death after stroke than following MI.[28]

More extensive, controlled studies are required to better define the mortality risk attributable to incident HF and compare the long-term survival impact of incident MI and stroke vs. HF in CCS. Additionally, it is required to unravel the pathophysiological role of myocardial ischaemia in the occurrence of incident HF in these patients. Firstly, we found a significant association between the number of segments with myocardial ischaemia and the risk of HF in the univariate but not in the multivariable assessment. We have previously observed that CMR-derived LVEF represents the most robust CMR index for predicting events in patients with ischaemic heart disease[29]; inclusion of this potent index in the adjustment for predicting incident HF probably attenuated the prognostic role of myocardial ischaemia. Secondly, the association between the ischaemic burden and incident HF may be confounded by the use of more aggressive medical and interventional therapies during follow-up in those with more extensive ischaemia. Controlled studies, out of the scope of the present study, would be required to define the effect of specific therapeutic strategies based on the extent of ischaemic burden for modifying the risk of incident HF in CCS patients. Finally, specifically designed studies would be necessary to better understand the role exerted by microvascular dysfunction in this field.

Clinical implications

Current findings pointed out that incident HF is a frequent complication in patients with known or suspected CCS. In addition, new-onset HF dramatically changed the natural history of the syndrome. Thus, efforts to improve CCS management should (i) increase the awareness of HF as a frequent complication in CCS, (ii) promote early HF detection, and (iii) evaluate the impact of different treatment strategies on the risk of HF events.

Study limitations

The current study has several limitations that should be addressed. First, this is an observational study in which unmeasured confounders might be playing a role. For example, in this registry, we did not register data about the medical treatment of the patients or coronary anatomy in all patients. Second, indices of microvascular dysfunction or data about fractional flow reserve or instantaneous wave-free ratio were not recorded. They could have contributed to increasing the understanding of the pathophysiology of the link between CCS and HF. Third, data about natriuretic peptides at baseline were not available. Additionally, data about natriuretic peptides were not available in all patients with new-incident HF. Lastly, angiographic data were available in a small subset of patients. Thus, we cannot unravel the contribution of the extension of CAD on the risk of HF.

Conclusions

In patients with CCS, long-term rates of incident HF were higher than MI and stroke. New-onset HF was associated with an increased risk of death. Compared with MI, patients with new-onset HF had a lower mortality risk during the first years; however, HF patients showed a higher risk in the long term. Compared with acute stroke, HF had a similar chronological pattern in terms of effects on mortality.

Conflict of interest

No conflicts of interest.

Funding

This work was supported by 'Instituto de Salud Carlos III' (PI20/00637; postgraduate contracts FI18/00320 to C.R.N. and CM21/00175 to V.M.G.) and 'Fondos Europeos de Desarrollo Regional FEDER' (CIBERCV16/11/00486 and CIBERCV16/11/00420), by Conselleria de Educación–Generalitat Valenciana (PROMETEO/2021/008), Sociedad Española de Cardiología (grant SEC/FEC-INV-CLI 21/024). J. G. acknowledges financial support from the 'Agencia Estatal de Investigación' (FJC2020-043981-I/AEI/10.13039/501100011033) and Centro de Investigación Biomédica en Red en Bioingeniería, Biomateriales y Nanomedicina (CIBER) Cardiovascular grants (16/11/00420 and 16/11/00403). There are no relationships with industry.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. All-cause mortality among patients with new-onset heart failure. Subanalysis only including acute heart failure in which N-terminal prohormone of brain natriuretic peptide were available and >125 pg/ml at the time of heart failure diagnosis.
Follow-up time truncated at 10 years.
Estimates adjusted for age, sex, hypertension, dyslipidemia, diabetes, current smoking, prior history of ischemic heart disease, prior history of stroke/transient ischemic attack, prior coronary revascularization, undergoing coronary revascularization at follow-up, and the following CMR parameters: LVEF, number of ischemic segments, and number of segments with necrosis.
CMR: cardiac magnetic resonance; LVEF: left ventricular ejection fraction.

Figure S2. All-cause mortality among patients with new-onset heart failure. Subanalysis only including patients with angiographic evidence of epicardial coronary artery disease at baseline.
Follow-up time truncated at 10 years.
Estimates Adjusted for age, sex, hypertension, dyslipidemia, diabetes, current smoking, prior history of ischemic heart disease, prior history of stroke/transient ischemic attack, prior coronary revascularization, undergoing coronary revascularization at follow-up, and the following CMR parameters: LVEF, number of ischemic segments, and number of segments with necrosis.
CMR: cardiac magnetic resonance; LVEF: left ventricular ejection fraction.

Figure S3. CMR-parameters and risk of new-onset HF
CMR: cardiac magnetic resonance; HF: heart failure

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