

Timing since last hospitalization for heart failure and risks of cardiovascular death and hospitalization of heart failure

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Declaration of Interest

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Background and purpose

Background: Hospitalization for heart failure (HHF) is associated with high cardiovascular death and HHF risks. Little is known about risks associated with timing since last HHF, “*i.e. months since last hospitalisation for heart failure*”

Purpose: To examine the risk of cardiovascular death and HHF in relation to timing since last HHF in a modern real-world setting on extensive heart failure treatment





Methods

Data sources: Health care registry data from Sweden; full-population, with linked hospital-, prescribed drug- and cause of death register data

Patients: All patients alive **1st January 2018** were included and **identified by a prior HHF** in the nationwide registries

Groups: Patients were grouped according to timing since discharge from last HHF; <1, 1-2, 2-6, 6-12 and >12 months before index

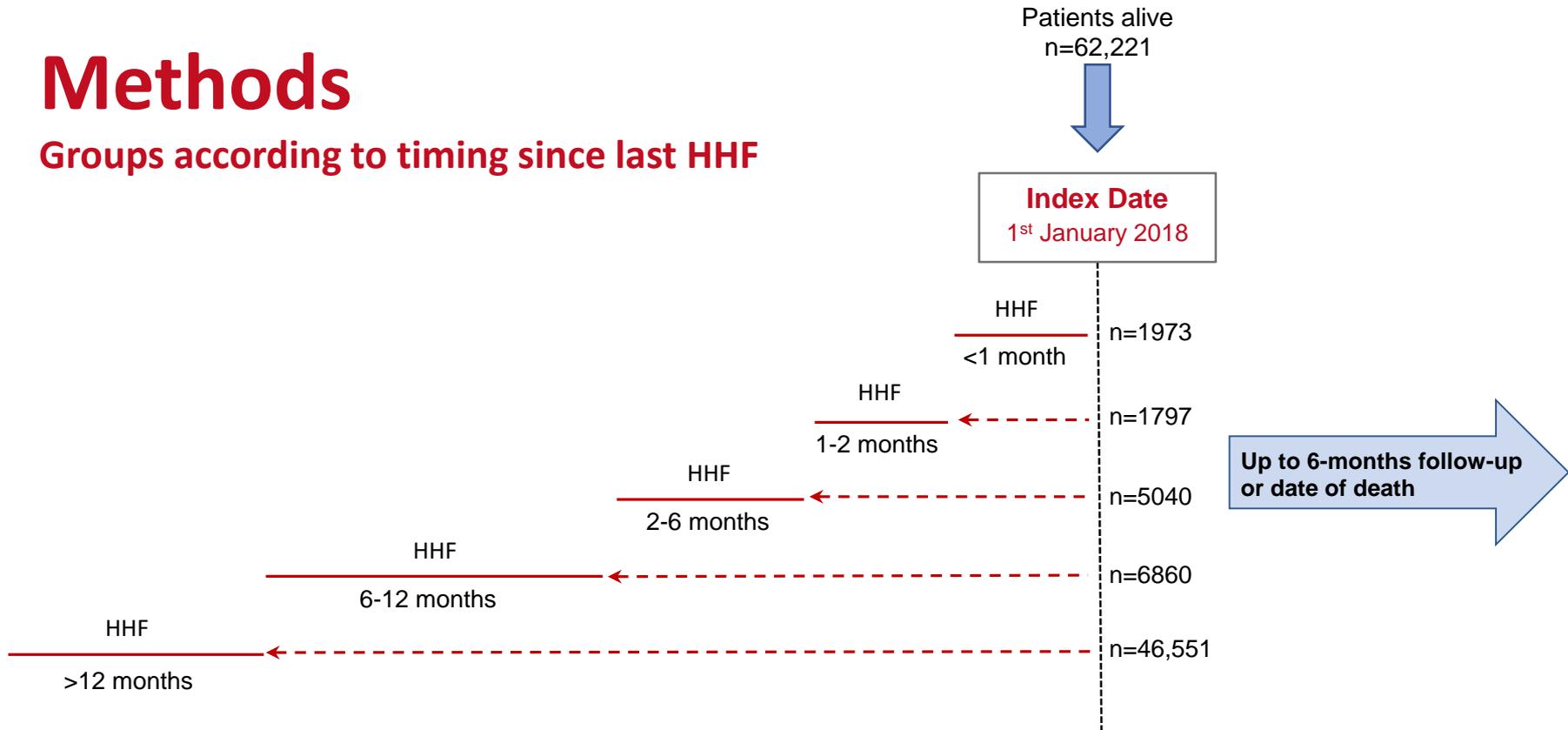
Outcomes: Cardiovascular death, HHF, all-cause death

Event rates: Patients were followed for up to 6 months. Risks were presented by cumulative incidence and multiple adjusted Cox regressions, using patients with **>12 months since last HHF as reference**



Methods

Groups according to timing since last HHF



Patients grouped according to time since last HHF discharge date. Baseline captured at index date 1st of January 2018; patients were followed up to 6 months or death. Stippled lines represents HHF free period.

HHF, hospitalization for heart failure



Baseline

Mean age 75-78 yrs
Previous HHF 28-50%
Previous MI 33-38%
Previous AF 58-66%
CKD 22-34%
Diabetes 28-32%
RAASi 77-82%
Beta-blocker 83-89%

Group <1 month: elderly and more often men, IHD, stroke, AF, CKD, DM.

In general well treated with RAASi and Beta-blocker. Low use of novel treatments.

	<1 month	1-2 months	2-6 months	6-12 months	>12 months
Number of patients, n (%)	1973 (3)	1797 (3)	5040 (8)	6860 (11)	46,551 (75)
Heart failure history, >1 HHF	997 (50.5)	866 (48.2)	2251 (44.7)	2702 (39.4)	12827 (27.6)
Length of stay last HHF, days (SD)	5.6 (5.1)	5.8 (5.3)	5.5 (4.9)	5.5 (5.2)	4.7 (5.2)
Age, years (SD)	78.2 (11.2)	78.5 (11.4)	78.0 (11.5)	78.2 (11.4)	75.6 (12.4)
Sex, women (%)	833 (42.2)	795 (44.2)	2187 (43.4)	3088 (45.0)	20238 (43.5)
Coronary ischemic disease, n (%)	1107 (56.1)	1008 (56.1)	2766 (54.9)	3682 (53.7)	23736 (51.0)
Myocardial infarction	756 (38.3)	662 (36.8)	1820 (36.1)	2379 (34.7)	15529 (33.4)
Coronary revascularization	270 (13.7)	246 (13.7)	610 (12.1)	827 (12.1)	5395 (11.6)
Unstable angina	592 (30.0)	505 (28.1)	1321 (26.2)	1743 (25.4)	11546 (24.8)
Angina pectoris	800 (40.5)	700 (39.0)	1919 (38.1)	2521 (36.7)	17037 (36.6)
Stroke, n (%)	372 (18.9)	334 (18.6)	929 (18.4)	1235 (18.0)	7883 (16.9)
Atrial fibrillation/flutter, n (%)	1312 (66.5)	1204 (67.0)	3294 (65.4)	4545 (66.3)	27041 (58.1)
Peripheral artery disease, n (%)	228 (11.6)	197 (11.0)	497 (9.9)	674 (9.8)	4082 (8.8)
Chronic kidney disease, n (%)	672 (34.1)	557 (31.0)	1508 (29.9)	1901 (27.7)	10160 (21.8)
Diabetes, n (%)	631 (32.0)	543 (30.2)	1527 (30.3)	1988 (29.0)	12840 (27.6)
Heart failure treatment, n (%)	1948 (98.7)	1789 (99.6)	5023 (99.7)	6829 (99.5)	44607 (95.8)
RAAS inhibitor	1620 (82.1)	1518 (84.5)	4210 (83.5)	5740 (83.7)	35675 (76.6)
Beta-blocker	1763 (89.4)	1606 (89.4)	4539 (90.1)	6167 (89.9)	38500 (82.7)
Loop-diuretics	1758 (89.1)	1636 (91.0)	4623 (91.7)	6212 (90.6)	30023 (64.5)
MRA	960 (48.7)	878 (48.9)	2565 (50.9)	3409 (49.7)	15956 (34.3)
Sacubitril-valsartan	92 (4.7)	75 (4.2)	212 (4.2)	234 (3.4)	642 (1.4)
Digitalis	312 (15.8)	279 (15.5)	759 (15.1)	1094 (15.9)	6209 (13.3)
Device therapy*	459 (23.3)	436 (24.3)	1091 (21.6)	1557 (22.7)	10508 (22.6)
Low dose aspirin, n (%)	679 (34.4)	612 (34.1)	1747 (34.7)	2190 (31.9)	14121 (30.3)
Statins, n (%)	1046 (53.0)	887 (49.4)	2527 (50.1)	3337 (48.6)	22488 (48.3)
Nitrates, n (%)	588 (29.8)	538 (29.9)	1542 (30.6)	1937 (28.2)	9519 (20.4)
Warfarin, n (%)	610 (30.9)	565 (31.4)	1495 (29.7)	2015 (29.4)	14116 (30.3)
Receptor P2Y12 antagonists, n (%)	230 (11.7)	217 (12.1)	615 (12.2)	773 (11.3)	2735 (5.9)
Glucose lowering drugs, n (%)	580 (29.4)	472 (26.3)	1382 (27.4)	1783 (26.0)	11212 (24.1)

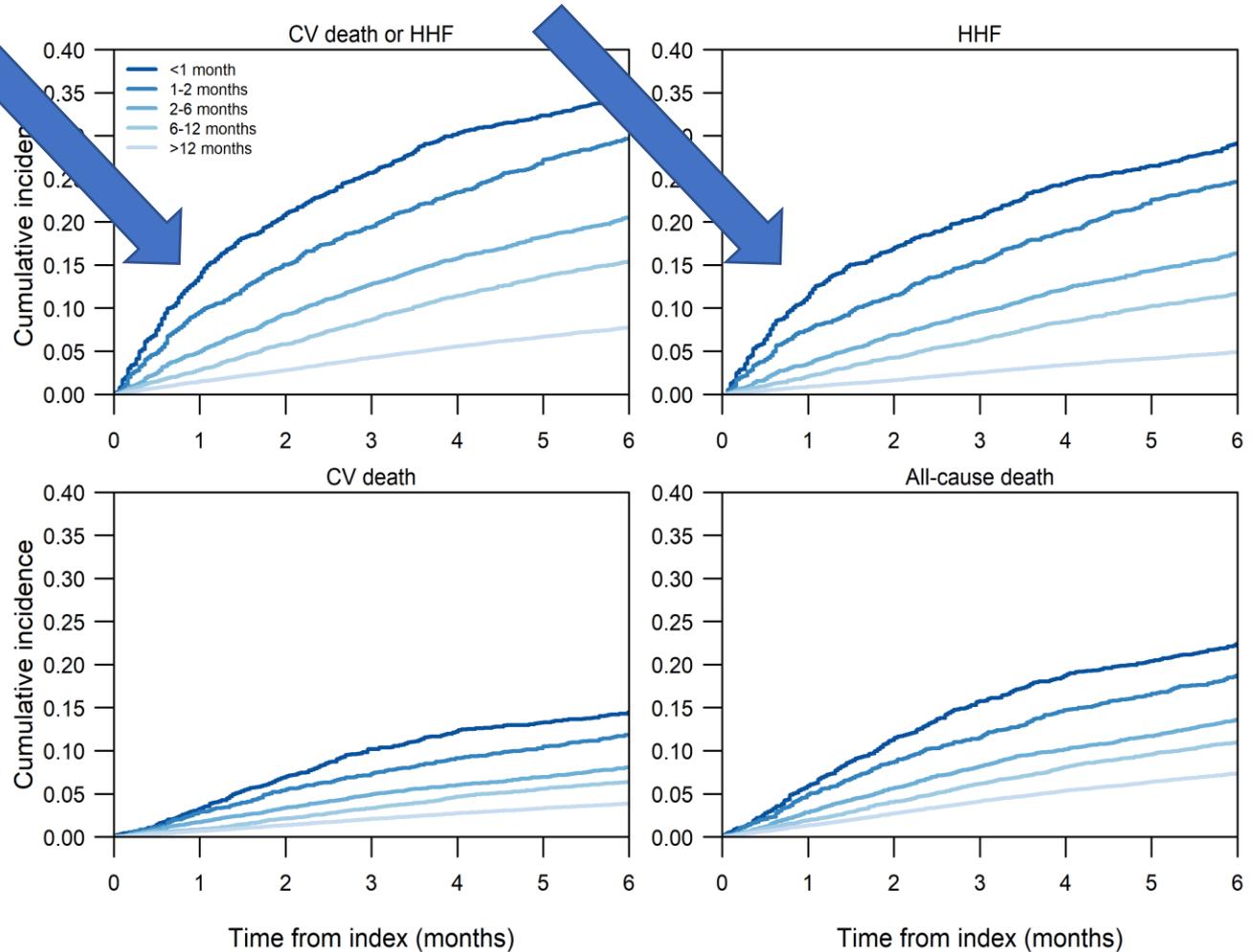
HHF, hospitalization for heart failure

*Device therapy includes both implantable cardioverter-defibrillator or cardiac resynchronization therapy.

Incidence of events

Faster onset of events -
HHF or CV-death/HHF -
in the group with recent
hospitalization for HF

Event-rates compared to trials	CV death or HHF	HHF	CV death
<1 month	91	74	32
>12 months	16	10	8
DAPA-HF, placebo	16	10	8
EMPEROR-R, placebo	21	16	8

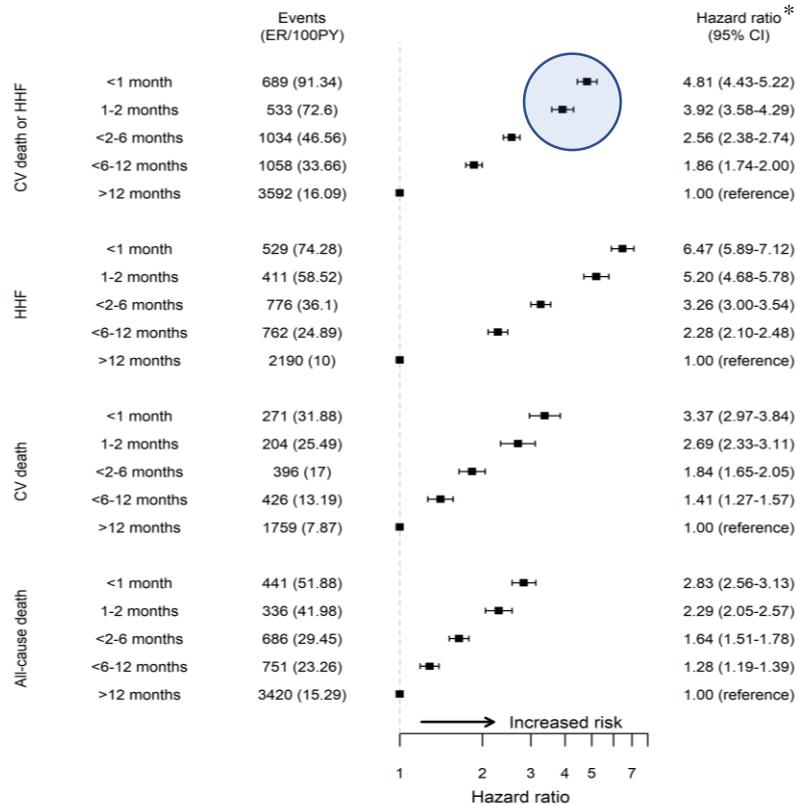


Cumulative incidence of cardiovascular (CV) death, hospitalization of heart failure (HHF) and total mortality after the index date 1st of January 2018, in groups allocated according to timing from last HHF discharge date prior to index.



HR (95% CI) for event

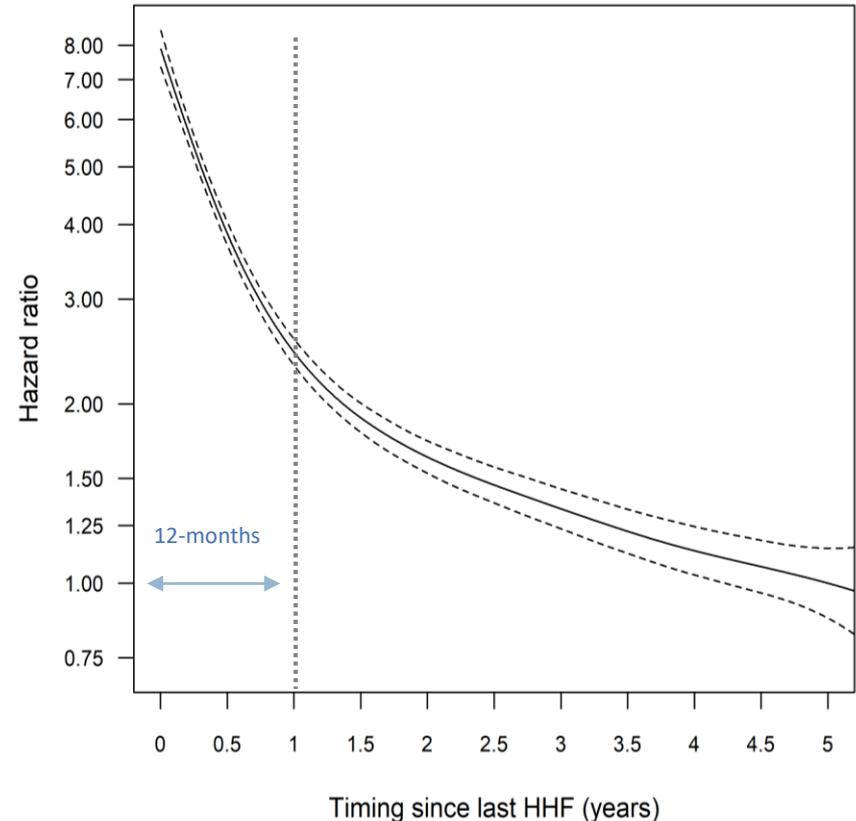
Outcome risks in groups allocated according to timing from last HHF discharge date



Spline curve

HR for event of HHF by time since HHF

Cubic spline curve illustrates that HHF risk is higher if short timing from last HHF



*Adjusted for age, sex, history of diabetes, coronary ischemic heart- and chronic kidney disease

HHF, hospitalization for heart failure





Summary

Cumulative CV-death or HHF incidence increased early (within 1-month) during follow-up, especially in patients with less than 1-month since last HHF; and was particularly steep compared to that seen in randomized clinical trials

Real-world patients with short time since last HHF were at very high risk of serious events; much higher compared to that seen in randomized clinical trials

While risks are known to be high after HHF discharge, our data support that “*the timing since last HHF*” could be a useful, easily accessible risk stratifying variable in the clinical setting to identify patients with a strong need for fast effective preventive treatments

Limitations

The method was conditioned on patients having survived up to the index date in order to contribute with follow-up data, inherently impacting relative risk comparisons

Lack of information on laboratory measurements or clinical data on heart failure severity, *e.g.* functional NYHA class, ejection fraction, pro-BNP





Conclusion

In a modern real-world clinical setting, cardiovascular death and heart failure risks were especially high in patients immediately post HHF discharge and subsequently declining over time

This supports an urgent and prompt need for effective treatment strategies to be instituted early after hospitalisation for heart failure, in order to prevent early severe events, with limited acceptance for treatment inertia

