Intern Emerg Med (2014) 9:641–647
DOI 10.1007/s11739-013-1006-y

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Prevalence and 1-year prognosis of transient heart failure following coronary revascularization

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Received: 21 June 2013 / Accepted: 7 October 2013 / Published online: 22 October 2013

Abstract The occurrence of heart failure during the whole pre-discharge course of coronary revascularization, as far as its influence on subsequent prognosis, is poorly understood. The present study examined the effect of transient heart failure (THF) developing in the acute and rehabilitative phase on survival after coronary artery bypass graft surgery (CABG) and percutaneous coronary intervention (PCI). Patients in the Italian survey on cardiac rehabilitation and secondary prevention after cardiac revascularization (ICAROS) were analyzed for THF, the latter being defined either as signs and symptoms consistent with decompensation or cardiogenic shock. ICAROS was a prospective, multicenter registry of 1,262 consecutive patients discharged from 62 cardiac rehabilitation (CR) facilities, providing data on risk factors, lifestyle habits, drug treatments, and major cardiovascular events (MACE) during a 1-year follow-up. Records were linked to the official website of the Italian Association of Cardiovascular Prevention and Rehabilitation (GICR-I-ACPR). The overall prevalence of pre-discharge THF was 7.6 %, with 69.8 % of cases in acute wards, 22.9 % during CR, and 7.3 % in both settings. THF affected more frequently patients with chronic cardiac condition (42.7 vs. 30.6 %; $p < 0.05$), age ≥75 years (33.3 vs. 23.1 %; $p < 0.005$), COPD (19.8 vs. 12.3 %; $p < 0.05$), and

For the ICAROS investigators. Members of the ICAROS Study Group are listed in Appendix.

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chronic kidney disease (17.7 vs. 7 %; $p < 0.001$). After discharge, THF patients showed good maintenance rates of RAAS modulators (90.6 %) and beta-blockers (83.3 %), while statin therapy significantly decreased from 81.3 to 64.6 % ($p < 0.05$). The pursuit of secondary prevention targets, as far as self-reported drug adherence, was not different among groups. Patients with THF had increased 1-year mortality (8.3 vs. 1.6 %, $p < 0.001$). Moreover, THF independently predicted adverse outcome with OR for recurrent events (mainly further episodes of decompensation) of 2.4 (CI 1.4–4.3). Patients who experienced THF after coronary revascularization had increased post-discharge mortality and cardiovascular events. Hemodynamic instability, rather than recurrent myocardial ischemia, seems to be linked with worse prognosis.

Keywords Heart failure · Coronary revascularization · Rehabilitation · Prognosis

Introduction

Congestive heart failure (HF) is a common complication during acute cardiac events with a burgeoning body of evidence in the field of acute coronary syndromes (ACS). Approximately 10 % of patients develop HF during hospitalization for ACS, with markedly increased short- and long-term mortality rates as compared with those without HF [1, 2]. Timing of development and resolution of HF also give prognostic information, since ACS patients presenting with HF at index event and persistent at follow-up have significantly worse after-discharge mortality [3].

The occurrence and prognostic value of HF in patients undergoing coronary revascularization, by contrast, remain to be better clarified. Particularly, sparse evidence exists about episodes of transient heart failure (THF) that may occur both early and later after coronary artery bypass surgery (CABG) or percutaneous intervention (PCI), as far as their influence on medium-term outcomes. For this purpose, series of patients undergoing cardiac rehabilitation (CR) programs represent a good model to investigate the occurrence of THF in an extended time window as compared to studies just focused on index hospitalization, as well as the prognostic role of THF after complete stabilization and ultimate referral to primary care.

The aim of this study was to evaluate determinants and 1-year prognosis of THF occurring during the whole in-hospital and rehabilitative course after coronary revascularization in a large cohort of patients admitted to CR at a national level.

Methods

Study population

The study included patients within 2 months after CABG or PCI, completing a CR program. Exclusion criteria were the following: combined valvular and coronary surgery for pre-operative detection of asymptomatic coronary artery disease; unfavorable short-term prognosis at 1 year for any reason (e.g., cancer); refusal of the informed consent to participate in the survey. Web-based electronic case report forms (e-CRF), accessible in a dedicated section of the Italian Association of Cardiovascular Prevention and Rehabilitation (GICR-IACPR) website were used for data entry. The e-CFR form collected data in relation to patients' comorbidities, global risk profile, and treatment (related to index event and rehabilitation phase), also providing follow-up for major adverse cardiovascular events, therapies, and lifestyle changes. The study did not involve any intervention that was not part of the clinical practice routinely adopted by each participating facility. The Ethics Committee of each center approved the protocol.

Study design

The Italian survey on cardiac rehabilitation and secondary prevention after cardiac revascularization (ICAROS) was a prospective, longitudinal, multicenter registry recruiting consecutive patients discharged from 62 in- or out-of hospital CR facilities in a 4 weeks period between 17th November and 15th December 2008 [4]. The geographical countrywide distribution (Northern Italy 61 %, Central Italy 23 %, and Southern Italy 16 %) as well as the proportion of inpatient to outpatient settings (77 and 23 % respectively) did not differ significantly from the global national network.

Definitions

Heart failure was clinically defined either as signs and symptoms consistent with that diagnosis (principally breathlessness and signs of fluid retention) resulting in treatment with loop diuretics, or patients suffering from cardiogenic shock or pulmonary oedema. Cardiogenic shock was defined as an arterial pressure <100 mmHg because of low cardiac output requiring inotropic therapy or an intra-aortic balloon pump. Use of loop diuretics for the treatment of hypertension or renal failure was not included in the definition of HF. Evidence of left ventricular systolic dysfunction was not required for a diagnosis of HF, as far as the blood concentration of natriuretic peptides or documentation of pulmonary venous congestion in a chest X-ray study. The

resolution of HF before the end of the CR program, defined as the withdrawal of diuretics without the recurrence of symptoms, identified THF cases.

One year after hospital discharge, information on secondary prevention targets, pharmacological treatment, and adverse events were collected through a structured interview according to a standard relational model provided by the study protocol. Drug therapy adherence was evaluated using the Morisky simplified self-report measure [5]. Targets for secondary prevention were as follows: body mass index 20–25; waist circumference, male <102 cm, female <88 cm; systolic blood pressure 140 mmHg (130 mmHg among diabetics and patients with chronic kidney disease), diastolic blood pressure 90 mmHg (80 mmHg); total cholesterol <=175 mg/dl; LDL cholesterol <100 mg/ml (80 in diabetics); HDL cholesterol >40, fasting glucose <110 mg/dl; hemoglobin A1c = <7 %.

Clinical events considered at the 1-year follow-up were death from any cause, acute coronary syndrome, coronary revascularization, decompensated heart failure, and stroke.

Statistical analysis

Patients were grouped according to the presence or absence of THF, and clinical variables available were compared between groups. Categorical variables were tested using either the χ^2 or the Fisher exact test, where appropriate and continuous variables were tested with the two-tailed Student t test, with a $p \leq 0.05$ considered significant. In order to evaluate the attributable risk of THF on adverse outcomes, selected variables shown to be significantly associated with at least one event during follow-up at univariate analysis and were tested in a model of binary logistic regression analysis using SPSS version 13.0 Software

Table 1 Characteristics of the study population at the end of the rehabilitative phase according to the presence of transient heart failure after coronary revascularization

	Overall (n = 1,262)		No THF (n = 1,166)		THF (n = 96)		p^
	n	%	n	%	n	%	
Age ≥75 years	301	23.8	269	23.1	32	33.3	0.023
Male/female	1,000/262	79.2/20.8	925/241	79.3/20.7	75/21	78.1/21.9	0.779
CABG	873	69.2	814	69.8	59	61.5	0.088
PCI	389	30.8	352	30.2	37	38.5	0.088
Previous history of ACS or CHF	398	31.5	357	30.6	41	42.7	0.014
Impaired systolic function[a]	364	29.5	332	29.0	32	35.2	0.259
LVEF 30–49 %	329	26.7	301	26.3	28	30.8	0.417
LVEF <30 %	35	2.8	31	2.7	4	4.4	0.540
<5 years education	188	14.9	172	14.8	16	16.7	0.612
Living alone	157	12.4	141	12.1	16	16.7	0.192
Smoking habit: current smokers	239	18.9	223	19.1	16	16.7	0.555
Smoking habit: past smokers (>1 year)	535	42.4	491	42.1	44	45.8	0.478
Hypertension	925	73.3	858	73.6 %	67	69.8 %	0.419
Hypercholesterolemia/use of statins	845	67	787	67.5	58	60.4	0.156
Family history of early CHD	578	45.8	538	46.1	40	41.7	0.398
BMI ≥25	240	19.0	215	18.4	25	26.0	0.068
Diabetes mellitus	372	29.4	339	29.1	33	34.4	0.396
Metabolic syndrome (according to the NCEP ATP III criteria)	322	25.5	304	26.1	18	18.8	0.114
PAD	215	17	193	16.6	22	22.9	0.111
COPD	163	12.9	144	12.3	19	19.8	0.037
CKD (≥stage II)	99	20.7	82	7.0	17	17.7	0.000
Gastrointestinal disease	128	10.1	123	10.5	5	5.2	0.096
Prior stroke	46	3.6	42	3.6	4	4.2	0.777

THF transient heart failure, *CABG* coronary artery bypass graft, *PCI* percutaneous coronary intervention, *ACS* acute coronary syndrome, *CHF* chronic heart failure, *CHD* chronic heart disease, *BMI* body mass index, *PAD* peripheral arterial disease, *COPD* chronic obstructive pulmonary disease, *CKD* chronic kidney disease

^*p* value of selected variables among THF patients in relation to the non-THF group at univariate analysis

[a] 1,234 patients evaluated (1,143 THF, 91 no THF)

Table 2 Therapy at the end of cardiac rehabilitation after coronary revascularization according to the presence of transient heart failure

	No HF ($n = 1,166$)		HF ($n = 96$)		p^
	n	%	n	%	
ACE inhibitors	750	65.1	68	71.6	0.202
Angiotensin-renin blockers	143	12.4	10	10.5	0.590
Beta-blockers	928	80.6	77	81.1	0.906
Statins	1011	86.7	78	81.3	0.135
Calcium channel blockers	181	15.5	11	11.5	0.286
Nitrates	147	12.8	14	14.7	0.581
Diuretics (potassium sparring)	130	11.3	35	36.8	0.000
Diuretics (non-potassium sparring)	415	36.0	75	78.9	0.000
Insulin	110	9.5	17	17.9	0.010
Oral antidiabetics	176	15.3	8	8.4	0.070
Omega-3 fatty acids	286	24.8	22	23.2	0.717
Amiodarone	150	13.0	17	17.9	0.180
Anticoagulants	189	16.2	31	32.3	0.000
Antiaggregants	1072	91.9	87	90.6	0.651

^p value of selected variables among THF patients in relation to the non-THF group at univariate analysis

Table 3 Major cardiovascular events after 1 year according to the occurrence of transient HF after cardiac revascularization

	Overall ($n = 1,262$)		No HF ($n = 1,166$)		HF ($n = 96$)		p^
	n	%	n	%	n	%	
Death	27	2.1	19	1.6	8	8.3	0.000
Acute coronary syndrome	8	0.6	7	0.6	1	1.0	0.600
Coronary revascularization	38	3.0	36	3.1	2	2.1	0.580
Decompensated heart failure	38	3.0	28	2.4	10	10.4	0.000
Stroke	4	0.3	4	0.3	0	0	0.565
Total	115	9.1	94	8.1	21	21.9	0.000

^p value of selected variables among THF patients in relation to the non-THF group at univariate analysis

Package (SPSS Inc., Chicago, IL, USA), to determine the independent characteristics associated with poor prognosis. Kaplan–Meier curves were generated to illustrate patients' overall survival from events and in relevant subgroups. Kaplan–Meier curves were compared by the log-rank test, while hazard ratios (HRs) and 95 % CI were calculated by Cox regression analysis.

Results

Among 1,262 patients included in the survey, 96 (7.6 %) presented THF as a complication of coronary revascularization with 67 (69.8 %) cases emerging during residence on acute wards, 22 (22.9 %) during CR, and the remaining 7 (7.3 %) in both settings. The prevalence of THF was not different between the CABG and the PCI group [83 (9.5 %) vs. 26 (6.7 %) cases, respectively, $p = 0.112$]. Patients with a previous history of heart failure or acute coronary syndrome (42.7 vs. 30.6 %, $p < 0.005$), age ≥75 years (33.3 %), COPD (19.8 %), and chronic kidney disease (17.7 %) were significantly more represented in the THF group (Table 1). At multivariate analysis, previous history of heart failure or acute coronary syndrome [odds ratio (OR) 1.683, 95 % confidence interval (CI) 1.097–2.581, $p < 0.05$] and chronic kidney disease [odds ratio (OR) 2.490, 95 % confidence interval (CI) 1.391–4.455, $p < 0.01$] independently predicted the occurrence of THF. Patients with and without THF showed a similar prevalence of impaired systolic function [32 (35.2 %) and 332 (29 %) cases, respectively, $p = 0.259$]. At discharge (Table 2), THF patients were prescribed more diuretics (78.9 % non-potassium sparring, 36.8 % potassium sparring diuretics), insulin (17.9 %), and anticoagulants (32.3 %) as compared to patients without THF.

Globally, 30 patients (2.3 %) were lost to follow-up and 68 (5.3 %) withdrew their consent during the course of the survey. During the follow-up, THF patients maintained similar rates of ongoing therapies with cardioprotective drugs as compared to controls [antithrombotics 71 (91 %) vs. 987 (94.2 %) cases, $p = 0.259$; ACE inhibitors 67 (69.8 %) vs. 767 (65.8 %) cases, $p = 0.425$; Angiotensin-renin blockers 20 (20.8 %) vs. 213 (18.3 %) cases, $p = 0.533$; beta-blockers 80 (83.3 %) vs. 956 (82 %) cases, $p = 0.741$), with the exception of statins (62 (64.6 %) vs. 958 (82.2 %) cases, $p < 0.001$]. Only 24 (2.2 %) patients—all in the non-THF group—had Morisky scores suggesting a high likelihood of non-adherence, without significant difference ($p = 0.257$).

Patients with THF after coronary revascularization displayed increased mortality (8.3 vs. 1.6 %, $p < 0.001$) and a significantly higher incidence of adverse events (21.9 vs. 8.1 %, $p < 0.001$) during the 1-year follow-up (Table 3). Additional and repeated episodes of decompensated heart failure (10.4 vs. 2.4 %, $p < 0.001$) were the most frequent events.

After adjusting for variables shown to be significantly associated with at least one event during follow-up at univariate analysis (Table 4), THF independently predicted adverse outcomes at multivariate analysis with OR for recurrent events of 2.4 (CI 1.4–4.3). Kaplan–Meier analysis showed worsened prognosis among THF patients, with hazard ratio for death and cardiovascular events of 3.0 (95 % CI, 1.8–4.8) (Fig. 1).

Table 4 Univariate and multivariate analysis of conditions associated to adverse events during the 1-year follow-up

Variable	Univariate analysis					Multivariate analysis		
	No event (1,147)		Event (115)		p^			p^^
	n	%	*n*	%		OR	95 % CI	
Transient HF	94	8.1	21	21.9	0.000	2.451	1.403–4.282	0.002
Infective complications	24	2.1	7	6.1	0.008	2.750	1.096–6.899	0.031
PCI vs. CABG	335	29.2	54	47.0	0.000	2.256	1.515–3.360	0.000
Diabetes	326	28.4	46	40.0	0.000	1.385	1.126–1.704	0.002
Age ≥75 years	264	23.0	37	32.2	0.028	1.525	0.992–2.346	0.055
Transient renal failure	43	3.7	10	8.7	0.012	1.690	0.731–3.910	0.220
Chronic renal failure	84	7.3	15	13.0	0.030	1.318	0.668–2.599	0.425
Male sex	910	79.3	90	78.3	0.786			
Atrial fibrillation during the acute phase	230	20.1	25	21.7	0.668			
Postoperative stroke	4	0.3	1	0.9	0.397			
Perioperative acute coronary syndrome	49	4.3	8	7.0	0.186			
Severe postoperative anemia	116	10.1	17	14.8	0.120			
Smoking habit	488	42.5	47	40.9	0.418			
Hypertension	841	73.3	84	73.0	0.949			
Hypercholesterolemia	774	67.5	71	61.7	0.212			
Metabolic syndrome	285	24.8	37	32.2	0.086			
BMI ≥25	213	18.6	27	23.5	0.201			
Limited physical activity	866	75.5	88	76.5	0.808			
Living alone	71	6.2	9	7.8 %	0.492			
Poorness	80	7.0	12	10.4	0.174			
<5 years scholarity	164	14.3	24	20.9	0.059			
Chronic atrial fibrillation	27	2.4	5	4.3	0.195			
Peripheral arterial disease	191	16.7	24	20.9	0.251			
COPD	147	12.8	16	13.9	0.738			
Chronic renal failure	84	7.3	15	13.0	0.668			
Gastric disease	119	10.4	9	7.8	0.388			
Cancer	60	5.2	6	5.2	0.995			
Orthopedic disease	117	10.2	18	15.7	0.071			
Hepatic disease	14	1.2	3	2.6	0.218			

^p value of selected variables among THF patients in relation to the non-THF group at univariate analysis

^^p value of selected variables among THF patients for independent association to any adverse outcome during follow-up

Discussion

This study provided an evidence that THF episodes are not rare after coronary revascularization and carry higher risk of death and readmission for congestive heart failure in the medium term.

According to our data, about one out of ten patients develop THF after PCI or CABG. However, since we evaluated patients who actively recovered from THF and did not include those transferred to acute wards during the rehabilitative course, as well as those who died before referral or during CR, the prevalence of THF after coronary revascularization may even be underestimated. Up to one-third of all episodes were found during CR, and about 10 % of those who presented THF in acute wards relapsed during CR, thus suggesting that several acute HF syndromes attributable to coronary revascularization are currently detected after the index hospitalization, during the rehabilitative course or in primary care for those not attending CR. Although our study provided a large time window for THF detection at baseline (with a mean coverage of 43 days after coronary revascularization) it is possible that an extended observation period would be able to capture additional late-onset THF cases.

Myocardial injury, neurohormonal abnormalities, and endothelial dysfunction were involved to explain HF

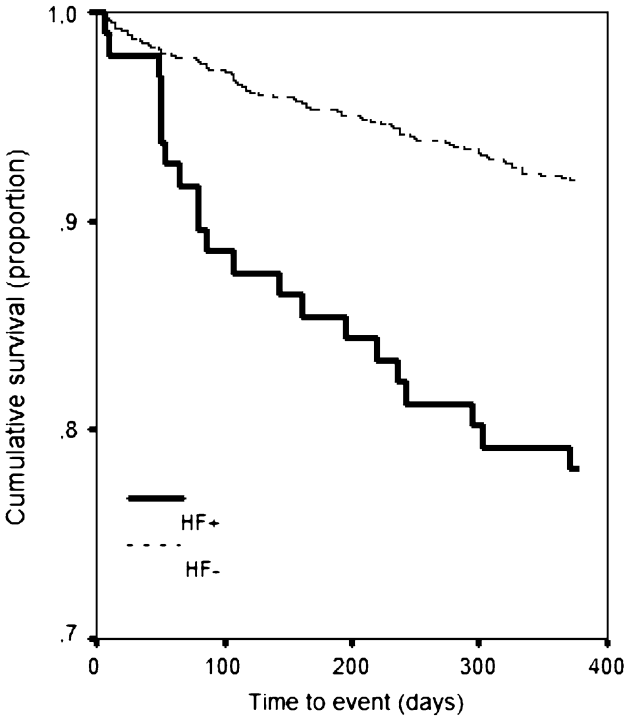

Fig. 1 Kaplan–Meier curves showing prognosis among patients following coronary revascularization with and without transient heart failure in the acute and/or rehabilitative ward

episodes in patients with underlying coronary artery disease [6], and also in our series THF occurred more frequently among revascularized patients with a previous history of HF or acute coronary syndromes. However, THF was not associated to higher degrees of systolic dysfunction at baseline, confirming previous reports after ACS indicating that the majority of patients presenting HF as a complication have preserved LVEF [7]. The elderly, diabetes, COPD, and chronic kidney disease were conditions at increased risk for THF. Advanced age predicted the development of THF also in the GRACE registry [2], which included a large unselected population after ACS. Concomitant COPD may induce hemoglobin desaturation, hypo/hypercapnia, and further worsening of right-ventricular function [8], and all these mechanisms could facilitate the occurrence of THF. In our series, COPD was not powerful enough to predict the adverse outcome in the medium term after coronary revascularization, as was the case for THF, thus not confirming previous experiences in the field of primary angioplasty [9].

As is known, chronic heart failure has been independently associated with increased adverse events both in-hospital and in the long-term among patients undergoing CABG [10, 11] and PCI [12–14]. In this survey, transient acute decompensation also marked a significant turning point in the disease course after coronary revascularization, with about five times higher mortality and three times higher incidence of adverse events during the 1-year follow-up as compared to the non-THF population. Repeated episodes of HF constituted the most frequent event during follow-up, suggesting that secondary prevention strategies after CABG or PCI should actually be tailored both on restenosis and hemodynamic instability. In our series, THF patients did not display significant gaps in cardioprotective pharmacotherapy (with the exception of statins) and drug adherence during follow-up as compared to non-THF patients, and consequently special attention after discharge should also be paid to the fluid retention.

Cardiac surgery patients generally have a direct referral pathway to CR in Italy, but unfortunately this is not the case of PCI patients. Consequently, our study population appeared representative of all patients discharged from cardiac surgery units, while after PCI conclusions can be generalized only on patients with in-hospital complications, persistent clinical instability, or serious concomitant diseases, who actually constitute major referral groups to CR [15]. Another selection bias might be related to the amount of ACS-driven interventions (about 60 % in the ICAROS registry), giving caution on extending our estimated prevalence of THF to other populations characterized by different levels of primary or elective revascularizations. As a further study limitation, the study was not able to evaluate the effect of pre-operative thrombolysis on THF, as far as to provide the number of deaths directly attributable to episodes of acute decompensated heart failure, and consequently the negative prognostic effect of THF on mortality cannot be linked to specific events. The definition of THF we adopted was pragmatically based both on diagnosis and treatment of congestive symptoms deriving from water retention, without other strict instrumental or laboratory requirements, to appreciate the prognostic role of this condition as usually detected and reported in the real life. Similarly, precise information about timing of THF onset (i.e., days from the index event) was not collected, and consequently THF during the acute and rehabilitative phase after coronary revascularization should be considered as an easily detectable dichotomous (yes/no) variable, helping to identify patients at higher risk of poor prognosis.

In conclusion, THF is a valuable prognostic marker after coronary revascularization. Given its role for risk stratification, it should be actively treated during the hospitalization period, and accurately reported at discharge.

Acknowledgments ICAROS was supported by IFB STRODER with an unrestricted research grant.

Conflict of interest None.

Appendix: ICAROS Study Group

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