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ORIGINAL ARTICLE

Factors limiting habitual exercise in patients with chronic heart failure: a multicenter prospective cohort study

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Abstract

Physical activity (PA) in the daily life is strongly related to prognosis in patients with or at high risk of heart failure (HF). However, factors limiting habitual exercise and their prognostic impacts remain unknown in HF patients. We sent questionnaires asking factors limiting habitual exercise in the daily life to 8370 patients with Stage A/B/C/D HF in our nationwide registry and received valid responses from 4935 patients (mean age 71.8 years, 71.0% male). Among the 5 components consisting of "busyness", "weak will", "dislike, "socioeconomic reasons" and "diseases" in the questionnaires, "busyness" (34.5%) and "diseases" (34.7%) were the most frequently reported factors limiting habitual exercise, while "socioeconomic reasons" were the least (15.3%). Multiple Cox proportional hazard models indicated that "busyness"and "diseases" were associated with better (hazard ratio (HR) 0.53, 95% confidence interval (CI) 0.39–0.72, $P < 0.001$) and worse prognosis (HR 1.57, 95% CI 1.21–1.98, $P < 0.001$), respectively, while other components were not. Furthermore, it was noted that, while prognostic relevance of "busyness" limiting exercise did not differ by age or sex, negative impact of "diseases" was particularly evident in patients with age < 75 years (P for interaction < 0.01). Factors limiting habitual exercise were associated with "busyness" and "diseases", but not with "weak will", "dislike, or "socioeconomic reasons". While "busyness" was associated with better prognosis regardless of age and sex, "diseases" was associated with worse prognosis in younger populations. Thus, physicians may pay more attentions to the reasons that limit exercise in the daily lives of HF patients rather than the low amount of exercise itself.

Keywords Physical activity · Exercise · Chronic heart failure · Prognosis · Busyness · Diseases

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Introduction

On the premise that the number of heart failure (HF) patients has rapidly increased in the aged society, particularly in Japan, HF has now aroused an emerging concern [1–3]. Physical activity (PA) is recognized as important in patients with HF [4, 5] as well as in general population [6–8], since it has been demonstrated that exercise training in HF patients is associated with reductions in mortality, HF hospitalization, health status, depressive symptoms and their quality of life [9–14]. Furthermore, we and others demonstrated that poor daily PA which was associated with higher risk of HF hospitalization and mortality in patients with HF [15–17], while benefits of higher PA were shown in other studies [18, 19]. However, limited information is available regarding factors that limit habitual exercise in CHF patients. In this study, we thus aimed to elucidate the factors interfering exercise habits and examined their influences on prognosis.

Method

Nationwide registry of HF patients

As a Nationwide registry of HF patients, we successfully enrolled 10,470 CHF patients in Stages A/B/C/D [20] between September 2006 and December 2010 in Japan [17]. The diagnosis of HF was made by attending cardiologists based on the criteria of the Framingham study [21] and the main etiology of HF was determined in each patient. The ethics committees of each institute approved the study protocol and each patient provided a written informed consent. We used an online data collection system (Fujitsu Systems East Limited, Tokyo, Japan) to prospectively collect data from the participating hospitals more than once a year for a median follow-up of 1.84 years: baseline demographic data, medications, comorbidities (previous myocardial infarction (MI) or stroke, dialysis, and atrial fibrillation) and outcomes in terms of death, non-fatal acute MI (AMI), on-fatal stroke and HF hospitalization. In the present study, we primarily employed the definition of metabolic syndrome (MetS) by the Japanese Committee for the Diagnostic Criteria of MetS in April 2005 (the original Japanese criteria), which defined MetS by the presence of 2 or more metabolic abnormalities (dyslipidemia, glucose intolerance and hypertension) in addition to the waist circumference criterion (≥ 85 cm in male and 90 cm in female) [22, 23].

Study design

In 2012, we sent questionnaires asking PA level and factors that limit their habitual exercise to 8370 patients after excluding patients who had been dead or impossible to be followed-up, and obtained responses from 4957 patients. After excluding 22 patients who were in the recuperation periods at medical facilities or at home, 4935 patients were enrolled in this study. The questionnaires consisted of pre-specified 15 items and a free description column: 15 items were automatically, and the answers to the free column were, depending on the contents, categorized into 5 components (busyness, weak will, dislike, socioeconomic reasons and diseases) (Table 1). As for "diseases", Q13 and Q14 intended for patients with an orthopedics disease and those with diseases other than orthopedics disease, including HF and other cardiovascular diseases, respectively. In these patients, we examined the prevalence of these items and components as factors that limited exercise in their daily lives and their impacts on all-cause death, with references to age and sex (< 75 years. vs. ≥ 75 years. and men vs. women).

Statistical analysis

Continuous variables are expressed as mean ± standard errors (SE), and categorical variables as counts and percentages. Comparisons between two groups were conducted with Welch's *t* test for continuous variables and the Fisher's exact test for categorical variables. In the multiple analysis for events, the Cox regression hazard model was utilized with the covariates including age, sex (other than in each sex group), body mass index (BMI), B-type natriuretic peptide (BNP), left ventricular ejection fraction (LVEF) assessed with echocardiography, systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate. $P < 0.05$ and P value for interaction < 0.10 were considered to be statistically significant. Statistical analyses were performed using the statistical computing software R version 3.4.1 (http://www.r-project.org).

Results

Patient characteristics

The baseline characteristics of the patients are shown in Table 2. Among the 4935 consecutive patients with Stages A/B/C/D HF, 3503 (70.9%) were males and 1432 (29.1%) were females. As compared with females, male patients were characterized by younger age, higher body mass index,

Table 1 Questionnaires asking factors limiting patients' habitual exercise

Questionnaire	
Please choose among below items which is the factor Interfering your exercise you think	
Busyness	
Q1.	Enough amount of exercise in the daily life (no need of extra exercise)
Q2.	Do not have time
Weak will	
Q3.	Lack of habits for exercise
Q4.	Do not have a strong will for exercise and give up easily
Q5.	Do not know how to exercise
Dislike	
Q6.	Not at ease with exercise
Q7.	Not good at exercise
Q8.	Dislike exercising
Socioeconomic reasons	
Q9.	Do not have fellow(s) to exercise together
Q10.	Lack of place for exercise
Q11.	Too far from the place for exercise
Q12.	Economic reason
Diseases	
Q13.	Orthopedic diseases (leg pain, back pain, etc.)
Q14.	Diseases other than orthopedic disease (name of disease:)
Q15.	Attending physicians forbid or do not allow or do not recommend exercise
(*) Other	
	Other reason ( )

higher diastolic blood pressure, lower heart rate, longer waist circumference, higher levels of triglyceride and glucose, and lower levels of total cholesterol, HDL cholesterol, LDL cholesterol, LVEF and BNP. In addition, males had higher prevalence of MetS, hypertension, diabetes, dyslipidemia and ischemic heart disease and lower prevalence of hypertensive heart disease and cardiomyopathy. As compared with 2222 patients (45.0%) with age ≥ 75 years, the remaining 2713 patients (55.0%) with age < 75 years had higher prevalence of males. The younger patients were characterized by higher BMI and DBP, lower SBP, higher levels of triglyceride, total cholesterol and LDL cholesterol, decreased levels of BNP and LVEF, higher prevalence of dyslipidemia and cardiomyopathy, which mainly consisted of dilated, hypertrophic and restrictive cardiomyopathies, and lower prevalence of hypertension, ischemic heart disease and valvular heart disease.

Frequency of components and items limiting habitual exercise in HF patients

Figure 1 shows the frequency of the answer "yes" for each component and item in the questionnaire. In overall patients, the most frequent component was "diseases" (34.7%), indicating that diseases could interfere exercise regardless of orthopedic diseases or not. "busyness" was also frequently pointed out as a component limiting exercise (34.5%). Items in "socioeconomic reasons" were generally less frequently adopted as reasons limiting exercise; in particular, Q12 "economic reason" was the least frequent item (1.6%). Furthermore, and items related to place for exercise had relatively low frequency (e,g, Q10; 6.0%, Q11; 5.1%).

Frequency of components and items by age and sex

Figure 2a, b indicates the frequency of the answer "yes" for each component and item limiting exercise by age and sex. "busyness" was the most frequently adopted component in < 75 years (38.8%) and male (36.1%). On the other hand, "diseases" was the more frequent in ≥ 75 years (42.8%) and female (43.5%). Q1 "enough amount of exercise in the daily life" was the most frequently adopted item in < 75 years and in males. In the elder and female group, Q13 "orthopedic diseases" and Q14 "diseases other than orthopedic disease" had higher frequency. Among items in "dislike", Q7 and Q8 were more frequent in females, while Q6 was more frequent in males, as well as in patients aged < 75 years.

Table 2 Baseline characteristics of patients

	Orverall ($N=4935$)	Patients < 75 ($N=2713$)	Patients ≥ 75 ($N=2222$)	P value	Male ($N=3503$)	Female ($N=1432$)	P value
Sex; Male (%)	3503 (70.9%)	2028 (74.8%)	1475 (66.4%)	< 0.001	–	–	–
Age (years)	71.8 ± 0.2	64.4 ± 8.6	80.7 ± 4.3	< 0.001	71.1 ± 0.2	73.2 ± 0.3	< 0.001
Body mass index (kg/m^2)	24.2 ± 0.1	24.3 ± 3.4	23.9 ± 3.4	< 0.001	24.4 ± 0.1	23.5 ± 0.1	< 0.001
Systolic blood pressure (mmHg)	128.1 ± 0.3	126.3 ± 17.9	130.4 ± 17.6	< 0.001	128.1 ± 0.3	128.3 ± 0.5	0.723
Diastolic blood pressure (mmHg)	74.1 ± 0.2	75 ± 11.4	73 ± 11.1	< 0.001	74.7 ± 0.2	72.6 ± 0.3	< 0.001
Heart rate (beats/min)	70.0 ± 0.2	69.9 ± 13.3	70.1 ± 13.7	0.586	69.4 ± 0.2	71.5 ± 0.4	< 0.001
Waist (cm)	86.2 ± 0.1	86.3 ± 9.3	86.2 ± 9.1	0.646	87.6 ± 0.1	82.8 ± 0.3	< 0.001
Triglyceride (mg/dl)	132.2 ± 1.8	142.3 ± 104.3	120.5 ± 61.6	< 0.001	137.4 ± 1.6	120.7 ± 1.8	< 0.001
Total cholesterol (mg/dl)	184.7 ± 0.7	186.4 ± 35.5	182.6 ± 33.7	< 0.001	181.0 ± 0.6	193.7 ± 1.0	< 0.001
HDL-cholesterol (mg/dl)	52.3 ± 0.3	52.5 ± 15.0	52.9 ± 14.9	0.425	50.8 ± 0.3	57.3 ± 0.4	< 0.001
LDL-cholesterol (mg/dl)	105.6 ± 0.7	106.6 ± 30.2	104.3 ± 27.8	0.017	103.7 ± 0.6	110.2 ± 0.9	< 0.001
Glucose (mg/dl)	115.2 ± 0.7	114.8 ± 34.0	115.6 ± 34.5	0.393	117.0 ± 0.6	110.6 ± 0.9	< 0.001
Brain natriuretic peptide (pg/ml)	54.2 (23.1/131.0)	43.6 (18.5/112.0)	65.7 (30.8/154.0)	< 0.001	49.6 (20.7/119.0)	65.4 (29.6/153.0)	< 0.001
Left ventricular ejection fraction (%)	62.5 ± 0.2	61.2 ± 13.8	63.9 ± 13.1	< 0.001	61.2 ± 0.2	65.4 ± 0.4	< 0.001
Metabolic syndrome (%)	2182 (46.0%)	1224 (47.0%)	958 (44.7%)	0.128	1874 (55.7%)	308 (22.3%)	< 0.001
Hypertension (%)	4014 (81.9%)	2105 (77.6%)	1909 (86.0%)	< 0.001	2891 (82.6%)	1123 (78.5%)	0.001
Diabetes (%)	1432 (28.6%)	791 (29.2%)	640 (28.8%)	0.777	1085 (31.0%)	346 (24.2%)	< 0.001
Dyslipidemia (%)	3860 (78.3%)	2158 (79.6%)	1702 (76.6%)	0.011	2779 (79.4%)	1081 (75.6%)	0.004
Ischemic heart disease (%)	2682 (54.5%)	1410 (52.0%)	1272 (57.2%)	< 0.001	2120 (60.5%)	562 (39.2%)	< 0.001
Hypertensive heart disease (%)	449 (9.1%)	242 (8.9%)	207 (9.3%)	0.654	297 (8.5%)	152 (10.6%)	0.019
Valvular heart disease (%)	887 (18.0%)	426 (15.7%)	461 (20.7%)	< 0.001	500 (14.3%)	387 (27.0%)	< 0.001
Cardiomyopathy (%)	674 (13.7%)	440 (16.2%)	234 (10.5%)	< 0.001	473 (13.5%)	201 (14.0%)	0.616
NYHA classes (%)				< 0.001			< 0.001
I	2608 (51.4%)	1596 (57.9%)	1089 (56.6%)		1982 (56.6%)	676 (47.2%)	
II	2123 (44.2%)	1074 (39.6%)	1049 (41.1%)		1439 (41.1%)	684 (47.8%)	
III	140 (4.1%)	59 (2.2%)	81 (3.6%)		70 (2%)	70 (4.9%)	
VI	9 (0.4%)	7 (0.3%)	2 (0.1%)		8 (0.2%)	1 (0.1%)	

Prognostic impacts of factors limiting exercise

During the follow-up period of 1.84 ± 0.4 years, 319 patients (24.5%) died. Figure 3 shows the forest plots of adjusted HR and 95% CI by components and items for all-cause death in overall patients. Among the components limiting habitual exercise, multiple Cox proportional hazard models indicated that "busyness" and "diseases" were associated with better and worse prognosis, respectively. Among the items, it was noted that Q1 "enough amount of exercise in the daily life" was associated with better prognosis, while Q14 "diseases other than orthopedic diseases" was associated with worse prognosis. None of the items in "weak will", "dislike" or "socioeconomic reasons" were associated with prognosis.

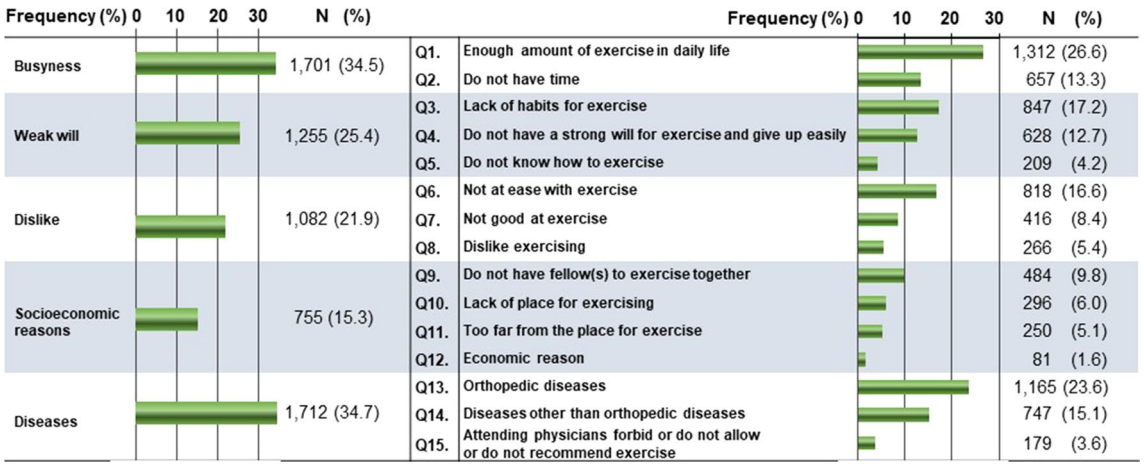

Fig. 1 The frequency of the answer "yes" for each item in overall patients. Items were sorted in the order of frequency

Prognostic impacts of factors limiting exercise by age and sex

Figure 4a, b shows the associations between components and items for all-cause death by age and sex. Among components limiting exercise, "busyness" was comparably associated with better prognosis by age and sex (*P* for interaction 0.44 and 0.77, respectively), while "diseases" was associated with worse prognosis in < 75 years and male groups. It was noted that all the prognostic impacts of Q1 and Q14, both of which were significant in the overall population, did not differ by age and sex. In contrast, negative impacts of diseases were particularly evident in patients with age < 75 years group (*P* for interaction < 0.01), but did not differ by sex (*P* for interaction 0.32). In addition, "weak will" was associated with better prognosis in younger group, but not in elder group (*P* for interaction = 0.03). Among the items, those with different prognostic impacts by subgroups were all categorized in the component "diseases" except for Q4 by age: negative impacts of Q14 and Q15 "attending physicians do not allow or recommend exercise" were more evident in younger age group (*P* for interaction = 0.04 and 0.08, respectively). Among "weak will" items, Q4 "do not have a strong will for exercise and give up easily" had negative impacts in elder group (*P* for interaction = 0.03).

Discussion

This is the first study to elucidate reasons by which HF patients are kept aside from exercise and their prognostic relevance in the daily lives. The present study demonstrated that factors limiting habitual exercise were most frequently related with "busyness" and "diseases" in HF patients, each of which were positively and negatively associated with prognosis, respectively.

The first survey for the factors limiting habitual exercise in patients with HF

In the present study, we sought to elucidate factors which play key roles in avoidance of exercise in the daily life of HF patients. To date, many studies have demonstrated a close relationship between daily PA and prognosis in patients with HF [15–17, 19]. However, few studies have examined exercise-limiting factors and their influence on prognosis. Thus, this study has a clinical significance as the first survey to elucidate factors by which HF patients consider to be kept aside from exercise in their daily lives, and furthermore, their prognostic relevance. The present study clearly indicated that "busyness" and "diseases" were the key factors that kept patients away from exercise in the daily lives, while "weak will", "dislike", or "socioeconomic reasons" were not. Furthermore, the exercise-limiting reasons related with prognosis were also "busyness" and "diseases", but not "weak will", "dislike", or "socioeconomic reasons". Thus, the results indicated that physicians may pay more attentions to the reasons that limit exercise in the daily lives of HF patients rather than the low amount of exercise itself.

Busyness

In our study, we found that patients who adopted "busyness" as factors limiting habitual exercise were more than one-third of the whole and had better prognosis. Most importantly, the item Q1 as well as Q2, a previously reported exercise interfering factor [24], was associated with better prognosis regardless of age and sex. In a past study, it was also reported that moderate PA in the occupational time

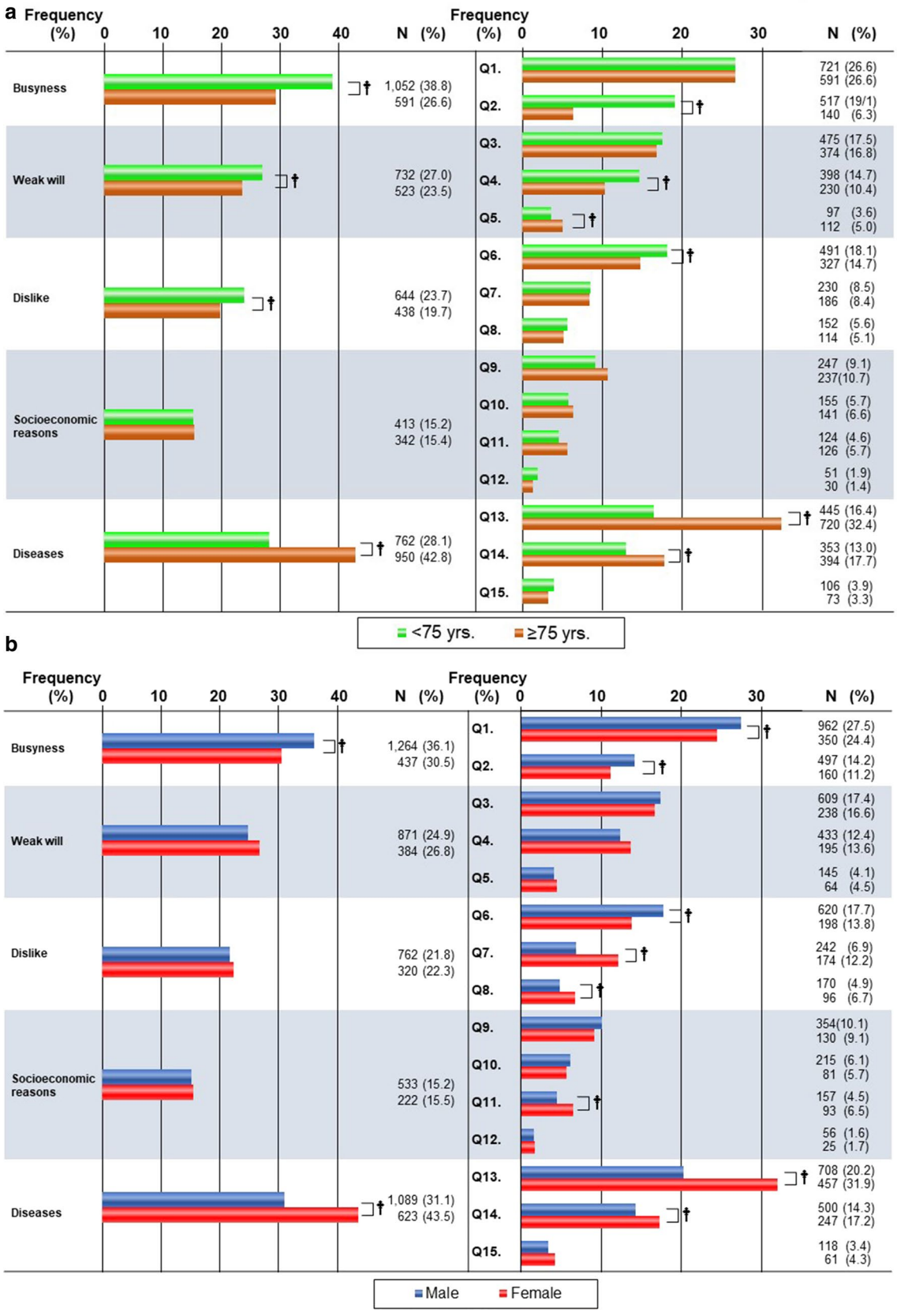

Fig. 2 The frequency of the answer "yes" for each item by **a** age (< 75 years, vs. and ≥ 75 years) and **b** sex (male vs. female). Items were sorted in the order of frequency in overall patients. †$P < 0.001$. *HF* heart failure

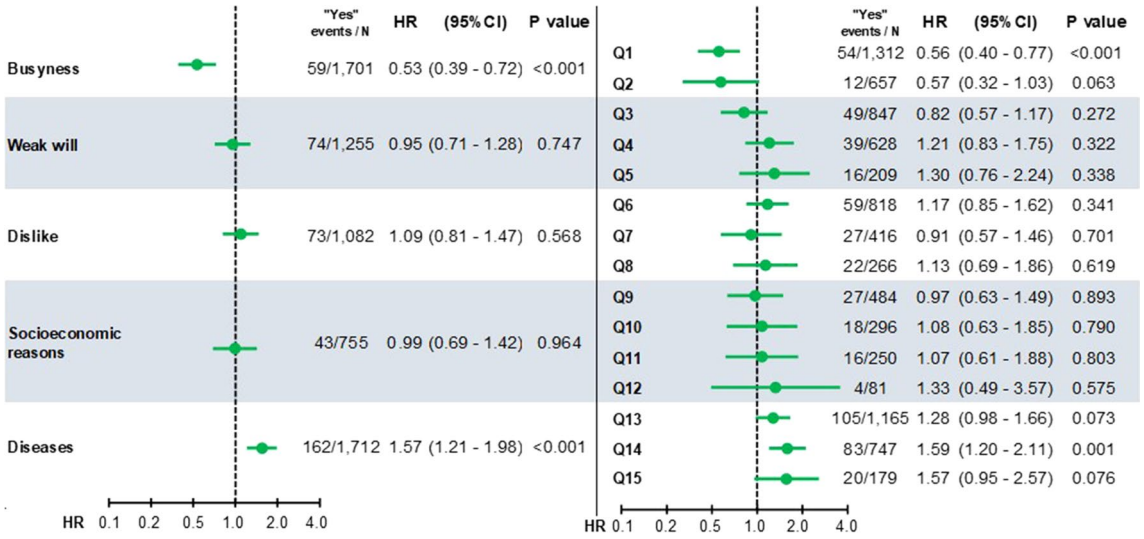

Fig. 3 Forest plots of adjusted hazard ratio (HR) and 95% confidence interval (95% CI) for all-cause death in overall patients adjusted with age, sex, BMI, BNP, LVEF, systolic blood pressure, diastolic blood pressure and heart rate. *BMI* body mass index, *BNP* B-type natriuretic peptide, *LVEF* left ventricular ejection fraction

was related with reduction of the cardiovascular risk as like the appropriate activity in the leisure time [25]. Thus, if the amount of exercise in their daily life is felt enough and adequate, patients may have better prognosis even without additional habitual exercise. It should be effective to continue performing appropriate PA between work hours, not only leisure time.

Diseases

Orthopedic diseases also appear to be important factors which keep HF patients away from exercise. The rate of patients who felt their orthopedic diseases as exercise-limiting factors were relatively high, especially in females and those with age ≥ 75 years, while prognostic impact of the orthopedic factor as an exercise-limiting factor was not significant regardless of age and sex.

Q14 was the item that we should pay more attention to, because it was adopted with a relatively high frequency as an exercise-limiting factor and strongly related to worse prognosis. Among the specific descriptions for Q14, cardiovascular diseases accounted for almost 50% (Table 3). Although it was unclear whether cardiovascular diseases were attributable to the unfavorable prognostic impact of Q14 as exercise-limiting diseases, it should be examined whether and how cardiac rehabilitation programs can be implemented to those who were not motivated for exercise because of cardiovascular diseases. In addition, when their diseases becomes the factors limiting exercise in the HF patients not in old age, because the factors may have stronger worse influence possibly, we should pay more attention for instruction of their rehabilitation for HF.

Other reasons

"Socioeconomic reasons" had relatively less frequency than other exercise-limiting components. It was noted that the economic reason was the least frequently adopted item as an exercise-limiting factor, indicating that financial supports may not likely increase PA of HF patients. Importantly, lack of or poor accessibility to the places to exercise was not the major reasons to distance HF patients from exercise. "weak will" and "dislike" were reported as exercise-limiting factors with intermediate frequencies, which did not seem to have impacts on prognosis in overall patients and mostly in subgroup populations. It was noted that, however, Q4 was associated with poor prognosis particularly in the older patients, indicating that supports to motivate exercise could be beneficial particularly for the elderly HF patients.

Study limitations

Several limitations should be mentioned for the present study. First, we did not define habitual exercise in the questionnaire and PA was just determined based on the patient declarations, which may require careful interpretation of our results. Second, relatively low response rates for the questionnaire might have biased the findings. Third, our study population included HF patients in Stage D or with NYHA IV, who had less chance to participate in a long-term physical activity, and those who were older and

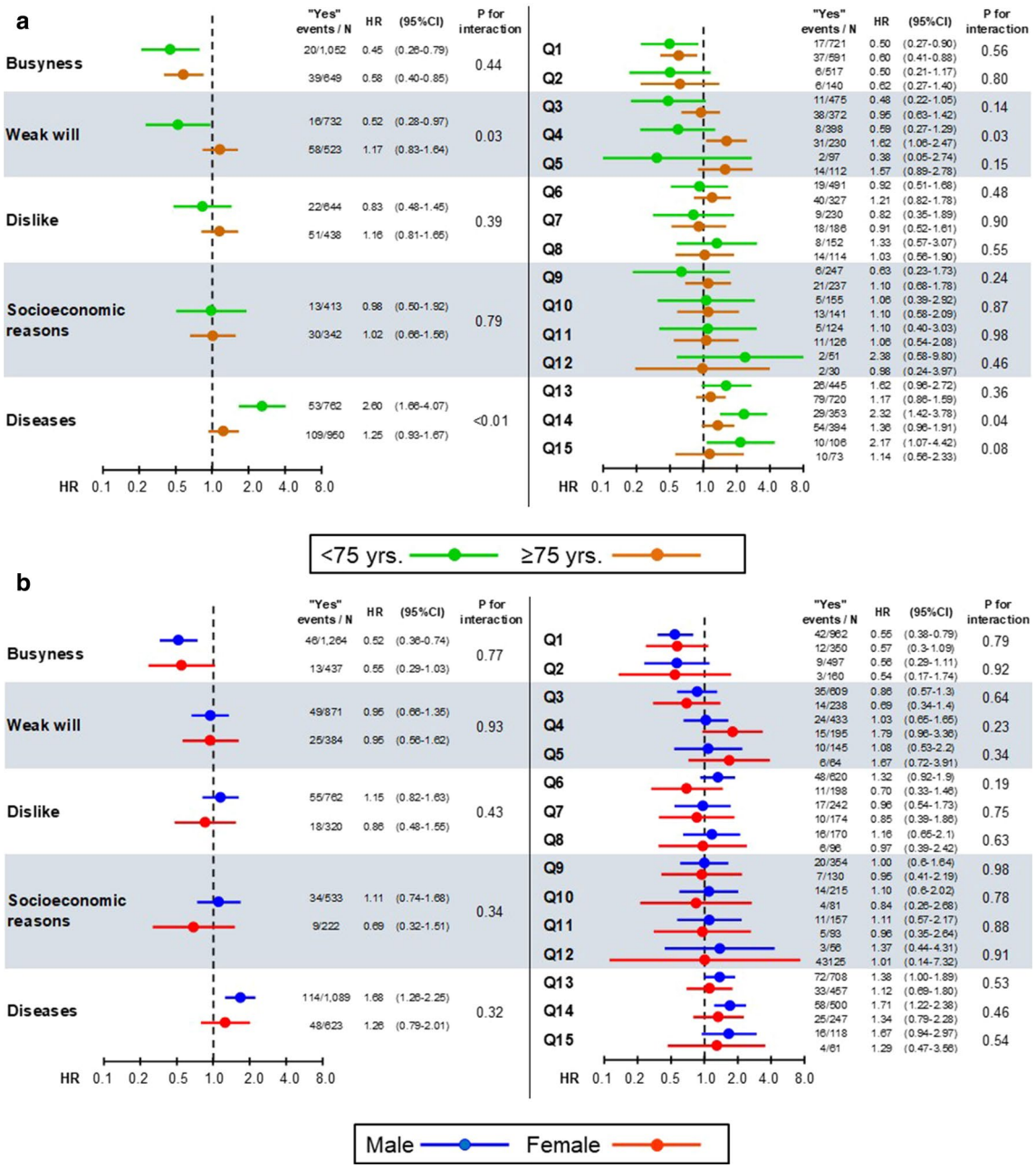

Fig. 4 Forest plots of adjusted hazard ratio (HR) and 95% confidence interval (95% CI) for all-cause death by **a** age (< 75 years, vs. and ≥ 75 years) and **b** sex (male vs. female) adjusted with sex (excluding **b**), age, BMI, BNP, LVEF, systolic blood pressure, diastolic blood pressure and heart rate. *BMI* body mass index, *BNP* B-type natriuretic peptide, *LVEF* left ventricular ejection fraction

had more preserved LVEF as compared with the previous reports [15, 16, 18, 19]. Fourth, beneficial impacts of exercise are still controversial in patients in HF. Finally, unlike the previous reports, a recent meta-analysis failed to show benefits of exercise trainings in patients with HF [26]. Thus, further examinations are warranted to confirm our results in HF patients with different conditions.

Conclusions

In the daily lives of HF patients, habitual exercise was associated with busyness and chronic disease (especially orthopedic disease), but not with others including socioeconomic reasons. Since factors limiting exercise and their prognostic impacts differed by age and sex, supports to implement exercise in HF patients should be applied

Table 3 Contents of answers to Q14 and (*) other reason

Q14. Disease other than orthopedics disease	(Total $N=747$)
Cardiovascular disease	416
Cranial nerve disease (other than dementia)	63
Rheumatic disease, systemic lupus erythematosus	20
Renal disease or dialysis	17
Respiratory tract disease (other than lung cancer)	16
Diabetes	14
Sensory organ disease (visual or hearing disorder)	14
Malignancy including cancer	13
Digestive organ disease (other than digestive organ cancer)	11
Dementia	11
Muscle disease	7
Orthopedic disease (*no check in Q13)	4
Blood disease (other than leukemia)	3
Other diseases	26
No description	111
(*) other reason	(Total $N=551$)
Physical reason	287
Reason of lifestyle	137
Reason of intention to exercise	27
Enough amount of routine exercise inhibit (*no check in Q1)	36
Lack of knowledge about exercise (*no check in Q5)	3
Lack of fellows (*no check in Q9)	3
Unclassifiable reason	7
None in particular or no description	61

on an individual basis, with consideration of clinical backgrounds.

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Compliance with ethical standards

Conflict of interest The Department of Evidence-based Cardiovascular Medicine, Tohoku University Graduate School of Medicine is supported in part by unrestricted research grants from Daiichi Sankyo Co., Ltd. (Tokyo, Japan), Bayer Yakuhin, Ltd. (Osaka, Japan), Kyowa Hakko Kirin Co., Ltd. (Tokyo, Japan), Kowa Pharmaceutical Co., Ltd. (Tokyo, Japan), Novartis Pharma K.K. (Tokyo, Japan), Dainippon Sumitomo Pharma, Co., Ltd. (Osaka, Japan), Nippon Boehringer Ingelheim Co., Ltd. (Tokyo, Japan), Astellas Pharma (Tokyo, Japan), AstraZeneca (Osaka, Japan), Chugai Pharmaceutical (Tokyo, Japan), GlaxoSmithKline (Tokyo, Japan), Mitsubishi Tanabe Pharma (Osaka, Japan), Mochida Pharmaceutical (Tokyo, Japan), MSD (Tokyo, Japan), Otsuka Pharmaceutical (Tokyo, Japan), Shionogi (Osaka, Japan) and Takeda Pharmaceutical (Tokyo, Japan). H.S. has received lecture fees from Bayer Yakuhin, Ltd. (Osaka, Japan), Daiichi Sankyo Co., Ltd. (Tokyo, Japan) and Novartis Pharma K.K. (Tokyo, Japan).

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