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Age, Sex and Benefits from Exercise Training in Diastolic Heart Failure

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Background

Our trial Exercise Training in Diastolic Heart Failure-Pilot (Ex-DHF-P) (Edelmann et al. 2011) showed that exercise interventions have the potential to improve functional capacity, diastolic function, physical quality of life and psychological well-being. Question remaining: Which patients respond best to exercise treatment?

Aim

To investigate which factors moderate benefits from exercise training.

Methods

The multicenter, prospective RCT Ex-DHF-P tested a **12-week supervised endurance/resistance training** (N=44) against usual care (N=20).
Collective: 64 symptomatic outpatients (age 47-77 years, 42% male) with diagnosed DHF of which the **44 intervention patients are presently analyzed**.
Assessment: echocardiography/tissue Doppler: **E/e'**, cardiopulmonary exercise testing: **peak oxygen uptake** (pVO_2), **6-minute walk test** (6MWT), Short Form-36 Health Survey (SF-36): **subjective physical function**, Patient Health Questionnaire (PHQ) and Hospital Anxiety and Depression Scale (HADS): **depressive symptoms and/or anxiety**.
Statistical analyses: **multiple linear regression analyses** (dependent variables: improvement in physiological/psychological parameters among intervention patients, independent variables: age and sex, adjustments: corresponding baseline values of dependent variables); bivariate analyses using **t-tests**; **effect size calculations** (Cohen's d) for parameter change from baseline to follow-up.

Descriptive Results

Intervention group characteristics at baseline, after 12 weeks of exercise training and their absolute change are displayed in **Table 1**.

Table 1: Characteristics at Baseline and Follow-up and their absolute Change

Parameter	**Baseline** ± SD	**Follow-up** ± SD	**Change** (95% CI)
Peak VO_2 [ml/min/kg]	16.1 ± 4.9	18.7 ± 5.4	2.6 (1.8 – 3.4)
6-Minute Walk Distance [m]	545 ± 86	569 ± 88	24 (10 – 38)
E/e'	12.8 ± 3.2	10.5 ± 2.5	-2.3 (-1.6 – -3.0)
Left Atrial Volume Index [ml/m²]	27.9 ± 7.6	24.3 ± 6.5	-3.7 (-4.9 – -2.4)
Subjective Physical Function	65 ± 22	79 ± 19	14 (8 – 19)
Depressive Symptoms	6.6 ± 5.8	5.1 ± 5.1	-1.5 (2.4 – 0.5)
Anxiety	5.9 ± 4.1	4.7 ± 4.3	-1.2 (2.0 – 0.5)

Results

Age did not moderate any of the training benefits in E/e', left atrial volume index, pVO_2, 6MWT, SF-36, PHQ or HADS in t-tests split at the median age of 67 years. Above that, regression analyses for all target parameters were independent of age on a continuous scale. **Table 2** displays effect sizes for both age groups and the excess in effect size for age ≥ 67 years.

Table 2: Cohen's d Age < 67 and ≥ 67 Years and its Difference

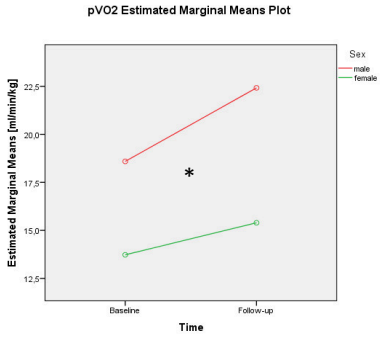
Parameter	**47-66 Years**	**67-77 Years**	**Difference**
Peak VO_2 [ml/min/kg]	0.45	0.58	0.13
6-Minute Walk Distance [m]	0.12	0.19	0.07
E/e'	-0.61	-0.86	0.25
Left Atrial Volume Index [ml/m²]	-0.45	-0.60	0.15
Subjective Physical Function	0.41	0.79	0.38
Depressive Symptoms	-0.31	-0.44	0.13
Anxiety	-0.24	-0.37	0.13

Diagram 1 exemplarily displays improvement in pVO_2 in the intervention group according to age split at the median.

Differential training effects were seen between the sexes: in men increase in pVO_2 (p=.008, **Cohen's d=.75 versus .48**) and 6MWT (p=.043, **Cohen's d=.41 versus -.07**) were greater than in women. The observed sex difference persisted for both pVO_2 (p=.001) and 6MWT (p=.007) after adjustment for corresponding baseline levels in multiple regression analyses. Training effects in all other parameters did not significantly differ between the sexes. Only a trend toward greater improvement was detected for SF-36, PHQ and HADS in women versus men. **Diagram 2** displays the differential increase in pVO_2 in men versus women.

Diagram 1

Diagram 2



Summary → Conclusions

1. In DHF patients 47-77 years old age does not moderate exercise training benefits in functional capacity, diastolic function, subjective physical function or psychological well-being. **The data demonstrate that elderly DHF patients can benefit from exercise training as much as younger patients.** → If this important finding will be confirmed in our Ex-DHF main study then exercise training is an excellent treatment option for both young and elderly DHF patients.
2. **Differential effects were seen in men versus women in terms of stronger increase in submaximal and maximal exercise capacity independent of different baseline levels**. For all other parameters no differential effects were seen → Future research should clarify the observed sex differences and investigate if specific exercise interventions for female patients with DHF are needed.

Discussion

- Some studies in heart failure suggest inefficacy of exercise training in elderly patients ↔ Our findings demonstrate: exercise training can be effective in elderly DHF patients and reveal no significant differences in efficacy in an age range of 3 decades (47-77 years). Applicability to a broad age range yields high clinical significance particularly in DHF.
- The high prevalence of DHF in women calls for sex dependent evaluation of treatment regimes. Our analysis is the first to systematically do so and reveals differential increase in maximal and submaximal exercise capacity. It could be argued that differential increase is due to differences in training protocol adherence between both sexes but as all other somatic and psychological parameters improved equally well in both sexes we suspect other underlying mechanisms which have to be clarified in future.

Disclosures: Nothing to disclose.

Limitations

- The examined collective of 44 patients is suboptimal in size. The independence of training benefits from age might in part be due to statistical insignificance because of the small sample size → Prospective investigation is warranted to provide precise delineation of age dependent outcomes. Yet, our study is presently the biggest of its kind and presented effect sizes add weight to the hypothesis.
- The Ex-DHF-P Study shows beneficial effects of a 12-week training. However, time trajectories are uncertain. Achieved effects might either reverse, reach steady state or increase with longer training duration depending on the identified moderators.

Literature: Edelmann F et al. Exercise training improves exercise capacity and diastolic function in patients with heart failure with preserved ejection fraction: results of the Ex-DHF (Exercise training in Diastolic Heart Failure) pilot study. J Am Coll Cardiol 2011;58:1780–91.

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