Clinical Outcomes and Cardiovascular Responses to Different Exercise Training Intensities in Patients With Heart Failure

A Systematic Review and Meta-Analysis

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Objectives
The aim of this study was to establish whether aerobic exercise training intensity produces different effect sizes for fitness, adherence, event rates, mortality rates, and hospitalization rates in patients with heart failure.

Background
Intuitively, greater exercise intensity is considered to result in higher risk for serious events, but intensity may be the primary stimulus for physical adaptation.

Methods
A MEDLINE search (1985 to 2012) was conducted for exercise-based rehabilitation trials in heart failure, using the search terms “exercise training,” “left ventricular dysfunction,” “peak VO2,” “cardio-myopathy,” and “systolic heart dysfunction.” Seventy-four studies were included, producing 76 intervention groups; 9 (11.8%) were high-intensity, 38 (50%) vigorous-intensity, 24 (31.6%) moderate-intensity, and 5 (6.6%) low-intensity groups, providing a total of 3,265 exercising subjects and 2,612 control subjects.

Results
Peak oxygen consumption increased by a mean difference of 3.33 ml · kg⁻¹ · min⁻¹ (95% confidence interval [CI]: 0.53 to 6.13 ml · kg⁻¹ · min⁻¹; p = 0.02) with high-intensity training in exercise groups compared with control groups, equating to a 23% improvement from baseline. For vigorous intensity, the mean difference was 2.27 ml · kg⁻¹ · min⁻¹ (95% CI: 1.70 to 2.84 ml · kg⁻¹ · min⁻¹; p < 0.00001), with an 8% weighted mean; for moderate intensity, the mean difference was 2.17 ml · kg⁻¹ · min⁻¹ (95% CI: 1.34 to 2.99 ml · kg⁻¹ · min⁻¹; p < 0.00001), with a weighted mean of 13%; and for low intensity, the mean difference was 1.04 ml · kg⁻¹ · min⁻¹ (95% CI: –2.50 to 4.57 ml · kg⁻¹ · min⁻¹; p = 0.57), with a weighted mean of 7%. In 123,479 patient-hours of training, not a single death was directly attributable to exercise.

Conclusions
As exercise training intensity rises, so may the magnitude of improvement in cardiorespiratory fitness, accompanied by lower study withdrawal in exercising patients. Total exercise time may be a confounder. (J Am Coll Cardiol HF 2013;1:1-11) © 2013 by the American College of Cardiology Foundation

Meta-analyses have shown exercise training to be beneficial in patients with heart failure in terms of improved cardiorespiratory fitness (1,2). Aerobic exercise probably produces the greatest improvements in peak oxygen consumption (VO2) (2) and left ventricular ejection fraction (3). Endothelial function (4) and serum levels of natriuretic peptides (5) and proinflammatory cytokines (6) are also improved with exercise training. The largest randomized trial of exercise training in heart failure to date, HF-ACTION (Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training), failed to show a survival benefit (7).

The HF-ACTION trial was hindered by poor adherence in those allocated to exercise, which may have led to the intervention groups producing much smaller (4%) improvements in peak VO2 than those expected (15% to 17%) (2). HF-ACTION was designed because moderate-intensity to vigorous-intensity continuous exercise is considered the appropriate exercise intensity for patients with heart failure.

There are perhaps 3 established reasons why vigorous-intensity or moderate-intensity exercise therapy is preferred in people with heart failure, even though a clear mortality benefit has yet to be demonstrated. First, stimulus from vigorous-intensity or moderate-intensity exercise is consid-ered sufficient to stimulate health benefits. Second, intui-tively, one assumes that the risk for serious medical events from vigorous-intensity or moderate-intensity exercise is lower compared with high-intensity exercise for patients...
work in patients with heart failure, which produced unsurpassed clinical improvements in peak VO₂ (46%), considered the best predictor of prognosis. The underlying success of HIIE is attributable to interval exercise allowing rest periods, making it possible for patients with heart failure to perform all exercise at high intensity, possibly the major determinant of adaptation. Moreover, in Wisloff et al.’s work, the comparison (continuous-exercise) group completed similar work, removing ambiguity regarding dose–response relations. In light of the small sample size in Wisloff et al.’s study, some clinicians remain unconvinced of the potential benefits of HIIE and believe that such programs are unsafe and poorly tolerated. Moreover, the exercise session time required to expend the same volume of energy is less for HIIE than for vigorous-intensity or moderate-intensity exercise sessions (9). In addition, less frequent weekly attendance may be required with HIIE. The resultant smaller time commitment is likely to equate to better exercise adherence. For these reasons, high-intensity exercise has been touted as the preferred training prescription for patients with heart failure (10).

The focus of this work was on aerobic exercise for the following reasons: first, resistance training studies tend not to use peak VO₂ as an outcome measure, and second, there are few isolated resistance training studies to warrant analyses. Moreover, existing resistance training studies seem to be comparisons of 2 or more exercise modalities, with no sedentary comparator groups, rendering comparisons with control groups impossible.

We wished to challenge the opinion that HIIE programs are unsafe and poorly tolerated. We therefore conducted a preliminary, systematic analysis of all clinical randomized controlled trials of aerobic exercise training in patients with heart failure and stratified the trials by exercise intensity according to guidelines (11) (Online Table 1). We aimed to establish whether high-intensity interval training produces larger effect sizes for change in peak VO₂ compared with vigorous-intensity, moderate-intensity, and low-intensity training and a sedentary lifestyle among patients with heart failure. Second, we wished to establish whether exercise intensity or interval training produces better adherence. Third, we examined whether rates of serious events, mortality, and hospitalization were varied with exercise intensity in patients with heart failure.

**Methods**

**Search strategy.** Studies were identified through a MEDLINE search (1985 to 2012), the Cochrane Controlled Trials Registry (1966 to 2012), the Cochrane review “Exercise Based Rehabilitation for Heart Failure” (12), the Cumulative Index to Nursing and Allied Health, SPORTDiscus, and the Science Citation Index. The search strategy included a mix of Medical Subject Headings and free-text terms for key concepts related to exercise training, left ventricular dysfunction, peak VO₂, cardiomyopathy, and systolic heart dysfunction for clinical trials of exercise training in patients with heart failure (Online Table 2). Studies were included if patients exhibited baseline left ventricular ejection fractions < 40%. These searches were limited to prospective randomized or controlled trials and human studies, with no restrictions on publication. Only English-language papers were considered. Reference lists and latest journal editions were scrutinized for new references. Full reports were assessed by 3 reviewers (N.A.S., G.D., and H.I.) for relevance and eligibility. Methodological disagreements were resolved by a fourth reviewer (J.M.).

**Study selection.** Included were randomized controlled designs of exercise training in patients with chronic heart failure with reduced ejection fraction. Studies of patients with heart failure with preserved ejection fraction were excluded because we wished to avoid comparing “apples and oranges,” and patients with heart failure with preserved ejection fraction would have made up a disproportionate (fewer) number of total patients. All included studies were comparisons among groups with different exercise intensities and/or controls. Reviewers categorized the studies into 4 groups on the basis of exercise intensity, described in a recent position statement by Exercise and Sport Science Australia (Online Table 1) (11). All studies were categorized as high, vigorous, moderate, or low exercise intensity on the basis of details provided in the reports. The measures used to classify exercise intensity were percent of heart rate maximum, heart rate reserve, peak VO₂, and Borg score (11).

Records identified 222 reports through database searching (210 records) or reference lists (12 records). Twelve additional records from reference lists were added. Only principal studies, with the most subjects, were included when multiple publications referenced the same dataset. After initial screening, 108 studies were removed, which included overlapping and duplicate reports, duplicate data, abstracts, and irrelevant articles (e.g., editorials and discussion papers). We further excluded 37 studies in which the control groups received additional intervention, nonrelevant studies, studies using inspiratory muscle training and acute exercise responses, and non-English reports. Three studies were excluded because the authors failed to provide missing data, leaving 74 studies for analysis (Online Fig. 1).
Outcomes measures. We recorded the following: peak VO₂ (baseline and after exercise), training frequency, intensity, duration per session, length of program, participant completion rates, mortality, adverse medical events, and hospitalizations.

Data synthesis. We calculated patient-hours of exercise training and percent change in peak VO₂, and we conducted a composite analysis of mortality and hospitalization.

Assessment of study quality. We assessed study quality using the Physiotherapy Evidence Database (PEDro) scale (13) with slight modification, because subject blinding is unlikely in exercise training studies and no mark is awarded for eligibility criteria, so the maximum possible PEDro score was 8 (Online Table 3).

Statistical analyses. RevMan version 5.1 software (The Nordic Cochrane Centre, Copenhagen, Denmark) was used to construct forest plots. Continuous data are reported as mean ± standard deviation. RevMan enabled calculation of postintervention change from baseline for the standard deviation, using change in mean values, number of subjects, and p value or, preferably, the 95% confidence interval (CIs).

In many cases in which exact p values were not provided, we used default values (e.g., p < 0.05 became p = 0.049). Mean differences (MDs) from baseline in these data were analyzed. For dichotomous data such as difference between exercise and control participants for mortality, chi-square analyses were performed. Because hospitalizations decrease as deaths increase, we also calculated a composite end point of death or hospitalization.

We used a 5% level of significance and a 95% CI to report changes in outcome measures. Egger plots were produced to identify sources of publication bias (14) (Online Figs. 2 to 5).

We analyzed baseline versus postintervention change in peak VO₂ for exercise intensity categories. We also conducted subanalyses of high-intensity studies that did and did not use interval breaks in training protocols. The largest exercise training study in patients with heart failure to date is HF-ACTION (7), which contributed about 50% of all existing patient data and may have skewed the vigorous-intensity data analysis, so we also conducted a subanalysis of vigorous data minus HF-ACTION data. Pearson’s correlation coefficients were calculated for total hours versus percent change in peak VO₂ and also weekly exercise time for percent change in peak VO₂.

Results

Included studies. Seventy-four studies met the selection criteria, with 2 studies including 2 training intervention groups (Online Table 3). Of these, 9 (11.8%) were high-intensity, 38 (50%) vigorous-intensity, 24 (31.6%) moderate-intensity, and 5 (6.6%) low-intensity groups, providing a total of 3,263 exercising subjects and 2,612 control subjects, totaling 5,877 participants. Of these, 241 patients completed high-intensity, 2,215 vigorous-intensity, 672 moderate-intensity, and 137 low-intensity training. Total patient-hours of exercise training reported were 123,479, which consisted of 7,223 for high-intensity groups, 84,655 for vigorous-intensity groups, 26,908 for moderate-intensity groups, and 4,693 for low-intensity groups.

Exercise training parameters. Program length for high-intensity training varied from 8 to 16 weeks and frequency from 2 to 4 sessions weekly. Three high-intensity studies used interval training exclusively, 1 used only continuous training, and 5 used both interval and continuous training, in which the intensity level was based on progressive increases from 80% heart rate reserve. Exercise training at high intensity ranged from 30 to 60 min/session, from 8 to 16 weeks, and from 90 to 426 minutes (mean 166 minutes) weekly. Exercise duration with vigorous-intensity, moderate-intensity, and low-intensity training ranged from 15 to 60 minutes, program duration from 4 to 52 weeks, and frequency from 2 to 7 days weekly. Vigorous-intensity study duration ranged from 4 to 52 weeks, 45 to 200 minutes weekly (mean 114 minutes); moderate-intensity studies from 8 to 52 weeks, 60 to 360 minutes weekly (mean 141 minutes); and low-intensity studies from 8 to 26 weeks, 30 to 120 minutes weekly (mean 96 minutes).

Outcome Measures. CHANGE IN PEAK VO₂. Baseline peak VO₂ was 17.5 ± 3.4, 15.0 ± 1.7, 16.3 ± 0.6, and 15.5 ± 0.4 ml · kg⁻¹ · min⁻¹ in high-intensity, vigorous-intensity, moderate-intensity, and low-intensity studies, respectively. Of 8 high-intensity studies, data from 3 studies showed that the MD for peak VO₂ was 3.33 ml · kg⁻¹ · min⁻¹ (95% CI: 0.53 to 6.13 ml · kg⁻¹ · min⁻¹; p = 0.02) with high-intensity exercise groups compared with control groups (Fig. 1). The weighted mean percent change in peak VO₂ in high-intensity training was 23%. In our subanalyses (supplementary subanalyses 1 and 2) of high-intensity training, the 2 studies that used interval training reported that the MD of peak VO₂ was 3.28 ml · kg⁻¹ · min⁻¹ (95% CI: −1.01 to 7.57 ml · kg⁻¹ · min⁻¹; p = 0.13). In the 1 study that used continuous high-intensity training, the MD of peak VO₂ was 3.94 ml · kg⁻¹ · min⁻¹ (95% CI: 0.61 to 7.27 ml · kg⁻¹ · min⁻¹; p = 0.02).

Of 38 vigorous-intensity intervention groups, 26 measured change in peak VO₂ with vigorous-intensity training compared with control, which was greater in the training groups (MD 2.27 ml · kg⁻¹ · min⁻¹; 95% CI: 1.10 to 3.45 ml · kg⁻¹ · min⁻¹; p < 0.00001), with an 8% weighted mean percent change (Fig. 2) compared with control. The subanalysis of vigorous-intensity data minus HF-ACTION data showed that peak VO₂ increased by 2.46 ml · kg⁻¹ · min⁻¹ (95% CI: 1.80 to 3.13 ml · kg⁻¹ · min⁻¹; p < 0.00001), or a weighted mean of 16% (supplementary subanalysis 3).

Of 24 moderate-intensity intervention groups, 18 reported peak VO₂ in exercising participants compared with controls (MD 2.17 ml · kg⁻¹ · min⁻¹; 95% CI: 1.34 to 2.99 ml · kg⁻¹ · min⁻¹; p < 0.00001; Fig. 3), with a weighted mean percent change in peak VO₂ of 13%.
Of 5 studies of low-intensity exercise, 2 reported peak VO$_2$ and demonstrated no significant changes (MD 1.04 ml · kg$^{-1}$ · min$^{-1}$; 95% CI: -2.50 to 4.57 ml · kg$^{-1}$ · min$^{-1}$; $p = 0.57$) between exercise and control groups, although the weighted mean percent increase in peak VO$_2$ was 7% (Fig. 4). All exercise and control group data can be seen in Figure 5.

Total exercise training time for each study and also weekly exercise time in minutes for all groups are reported in Online Table 3. No correlation was found between peak VO$_2$ change and total or weekly exercise time, except for weekly exercise time for low-intensity studies ($r = 0.93$).

**Adverse events.** All high-intensity and low-intensity groups reported adverse events (deaths, hospitalizations,...)
and cardiovascular events; Online Table 4). All but 6 studies (12%) reported these data in vigorous-intensity studies; in moderate-intensity studies, all but 4 (15%) reported events. The PEDro scores of studies that did not report adverse events were 6, except for 1 vigorous-intensity study scoring 5 and 1 moderate-intensity study scoring 4 (Online Table 4). One (12.5%) high-intensity, 8 (16%) vigorous-intensity, 4 (15%) moderate-intensity, and no low-intensity studies failed to report withdrawal. These studies all achieved PEDro scores of 6, except for 2 vigorous-intensity studies that each scored 5 and 2 moderate-intensity studies that scored 8 and 5 (Online Table 5).

There was a significantly lower withdrawal ratio in high-intensity training compared with control groups (log-rank chi-square = 5.73, p < 0.05). There were no significant differences for death (log-rank chi-square = 2.02, p > 0.05) or cardiac events (log-rank chi-square = 0.23, p > 0.05) in high-intensity studies. There were no hospital admissions or deaths reported in any high-intensity exercise groups; there were 2 deaths in nonexercise control groups.

There was no significant difference between vigorous-intensity training and control groups for withdrawal (110 in exercise vs. 109 in control arms, log-rank chi-square = 0.47, p > 0.05), death, exercise and control arms (205 vs. 221, respectively, log-rank chi-square = 3.83, p > 0.05), or cardiac events between vigorous-intensity training and control arms (7 exercise events vs. 5 control, log-rank chi-square = 0.01, p > 0.05). Hospitalization was significantly lower in vigorous-intensity training groups (739 in exercise...
vs. 771 for control arms; log-rank chi-square = 13.31, p < 0.05). The relative risk for hospitalization was 13.5% lower in vigorous-intensity exercise versus control groups (relative risk: 0.86; 95% CI: 0.80 to 0.95; p = 0.001). The composite end point of death or hospitalization yielded a relative risk of 0.86 (95% CI: 0.79 to 0.94; p = 0.001). When HF-ACTION data were removed from analyses, only mortality remained statistically significant. There were 16 exercise and 23 control deaths, so vigorous exercise training appears to have reduced mortality risk (log-rank chi-square = 4.636, p < 0.05). Overall, no deaths were directly attributable to exercise training in 123,479 patient-hours.

There were 45 patient withdrawals in moderate-intensity exercise groups compared with 30 in control groups (log-rank chi-square = 0.06, p > 0.05). There were no deaths in exercise training groups and 3 deaths in control groups in moderate-intensity training studies (chi-square = 2.62, p > 0.05) and 1 cardiac event in exercise groups versus 4 in control groups (log-rank chi-square = 2.81, p > 0.05). There was no significant difference in hospital admissions between moderate-intensity training (39 exercise vs. 37 control) (log-rank chi-square = 3.48, p > 0.05).

There was no significant difference between low-intensity training (34 vs. 24) and control withdrawals (chi-square = 0.83, p > 0.05), deaths (3 exercise vs. 2 controls; log-rank chi-square = 0.01, p > 0.05), cardiac events (1 in each group; chi-square = 0.41, p > 0.05), or hospital admissions (0 exercise vs. 3 control; log-rank chi-square = 1.56, p > 0.05).

Study quality. The median PEDro score was 6 for all intensity categories high-intensity studies; median PEDro score for high-intensity studies was 7. Funnel (Egger) plots (Online Figs. 2 to 5) of the analysis showed minimal evidence of publication bias, although 17% of vigorous-intensity studies fell outside the funnel plots.

Discussion

Our meta-analysis is the first to stratify heart failure exercise studies by activity intensity. The findings indicate that the magnitude of gain in cardiorespiratory fitness is greater with increasing exercise intensity and appears to be unrelated to baseline fitness level or exercise volume. Moreover, high and vigorous exercise intensities do not appear to increase the risk for study withdrawal, death, adverse events, and hospitalization. Intuition suggests that higher exercise intensity equates to a higher risk for serious health events in these patients, but the data presented question this.

Change in peak VO₂. A previous study established a strong prognostic relationship between peak VO₂ and mortality (15). The largest improvements in peak VO₂ were observed with high-intensity exercise training, and there may be a linear decrease in effect size with decreasing exercise intensity. Moreover, in 2 studies using high-intensity interval training, the MD for change in peak VO₂ was lower than in the 1 study that used continuous high-intensity training, which supports previous work (8,16,17). Of note is that studies of continuous exercise training used a greater volume (duration) of exercise and multiple daily sessions. The 2 low-intensity studies actually produced better peak VO₂ results for control participants. Both low-intensity exercise and control groups produced improvements in cardiorespiratory fitness, although this must be attributed to medical interventions such as optimizing medications and is unlikely to be explained by baseline fitness levels, as these showed no appreciable relationship with exercise intensity, with the exception of 4 low-intensity studies.

The majority of exercise training studies to date have used vigorous-intensity programs, and although the percent change appears to be less than in high-intensity studies, an 8% improvement is likely to be clinically significant and to offer patients relief from breathlessness and reduced risk for adverse events, hospitalization, and death. For thoroughness, we conducted a subanalysis of vigorous data by removing the HF-ACTION data (7), which contributed >50% of the patients in the vigorous-intensity analysis. Percent change in peak VO₂ was improved to 16% by removing HF-ACTION data (7). Likely explanations are as follows: 1) the study was conducted across 85 centers on 2 continents, and consistent administration must have been challenging; 2) more than one-third of the patients randomized to exercise failed to reach their exercise intervention targets; and 3) the HF-ACTION investigators reported that almost one-third of participants randomized to sedentary control crossed over to exercise (7). Vigorous-intensity exercise programs are likely to elicit changes in peak VO₂ of about 16%, similar to previously reported effect sizes (2), but sufficient supervision is required to ensure exercise adherence.

A previous meta-analysis showed that aerobic exercise training yields small but measurable benefits in cardiac function (3), but we suspect that these changes do not account for all of the improvements in peak VO₂; we therefore acknowledge that some changes are due to improved endothelial function (4) and perhaps improved...
oxygen extraction and utilization within mitochondria. An individual patient analysis of studies reporting these data would be required to avoid speculation.

**Study withdrawal, deaths, adverse events, and hospitalization.** There were no obvious differences in PEDro scores and hence study quality between those studies that did and did not report events and withdrawals. In terms of examining study withdrawal, adverse events, deaths, and hospitalization, it appears that there exist sufficient event data to conduct meaningful analyses only for vigorous-intensity studies. There were no significant differences for withdrawal, death, and cardiac events between the training and control arms in vigorous-intensity studies. There was, however, a significant difference in hospital admissions, as the relative risk for hospitalization was 15% lower in vigorous-intensity exercise versus control participants, which equates to an absolute risk reduction for hospital admission of 6%. However, as deaths increase, intuitively, hospitalizations are reduced; therefore, it is appropriate to use a composite end point of combined deaths and hospitalizations. These data have implications for the cost-effectiveness of clinical services, as clear data exist for the use of vigorous-intensity training, while insufficient data currently exist to evaluate the efficacy of high-intensity exercise, although results to date are promising. Medical centers may consider weighing the cost of delivering an exercise program versus the cost of an average-duration hospital stay for heart failure.

**Vigorous-intensity and high-intensity exercise in patients with heart failure.** Current data available on high-intensity exercise are limited; however, this type of exercise appears not to increase the risk for death and may actually show a trend toward a mortality reduction. Abundant data from vigorous-intensity studies appear to support the notion that exercise at vigorous and high intensities appears to be well tolerated, especially in studies using rest intervals rather than a continuous approach. We suggest that rest intervals will improve exercise adherence, as the opportunity to recover between work bouts offers relief. High-intensity exercise programs may require shorter session duration and lower frequency because the volume of work is completed more rapidly, meaning that participants demonstrate better adherence.

**Study limitations.** The major limitation of this study is that only limited high-intensity and low-intensity data exist, and the majority of data were generated from vigorous-intensity studies. Within the vigorous-intensity classification, HF-ACTION (7), because of the study sample size, may have skewed this analysis, so a subanalysis was conducted. Despite classifying the studies according to intensity, other variations in the exercise prescriptions vary slightly, such as study duration and weekly exercise volume.

In terms of study quality, PEDro scores for high-intensity studies ranged from 5 to 8, which may indicate that these studies reported their findings most comprehensively, and the range for low-intensity studies was only 5 to 6, which may indicate the lowest quality of reporting. Better study quality in high-intensity studies warrants consideration for using this type of exercise prescription. PEDro scores for all vigorous-intensity and moderate-intensity studies ranged from 4 to 8. A possible benchmark is HF-ACTION, which scored 6, suggesting that PEDro scores < 6 indicate suboptimal reporting.

Meta-analysis of continuous data is problematic; we adjusted for baseline differences in primary outcomes between allocation groups by measuring preintervention versus postintervention change. Often we were able to accurately calculate change in standard deviation, but in cases in which exact p values were not provided in study reports, we used default values (e.g., p < 0.05 or p < 0.001) in our calculations, which may have introduced errors.

Our funnel plots (Online Figs. 2 to 5) appear to suggest nonminimal publication bias for vigorous-intensity, moderate-intensity, and low-intensity studies. We suspect that unpublished datasets with perhaps less convincing results exist for these exercise training categories, and if this analysis included these datasets, our findings would strengthen our assertion that high-intensity training is most beneficial to patients with heart failure.

Finally, we acknowledge that factors related to volume of exercise may explain some of the outcomes reported. For example, study duration may have been longer in high-intensity training studies, and longer periods of training may have yielded better results (1). Our findings suggest that high-intensity exercise may be superior despite relatively shorter periods of training.

**Clinical implications.** In summary, if one adopts the previously suggested premise that in patients with chronic disease, the risk for exercise-induced adverse events is less than the risk of adopting a sedentary lifestyle, then exercise training is warranted. Although we have not established a clear mortality benefit for any exercise intensity category, previous work suggests that clinical benefits are more likely with the greatest changes in cardiorespiratory fitness (15). In fact, a small volume of data from low-intensity exercise studies suggest that low-intensity exercise is not beneficial and may actually be detrimental to cardiorespiratory fitness compared with sedentary controls. Our data may show a relationship between increasing cardiorespiratory fitness and increasing exercise intensity. Increasing exercise intensity does not appear to elicit increased risk for study withdrawal, death, cardiac events, and hospitalization, which appear to be reduced with vigorous intensity intervention. To date, there exist 123,479 patient-hours of exercise training conducted in research studies, and not a single death while a patient was exercising has been reported.

**Conclusions**

As exercise training intensity increases, so may the magnitude of improvement in cardiorespiratory fitness, although...
time spent exercising should also be considered. As exercise intensity increases, study withdrawal in exercising patients appears to decrease. Higher intensity exercise does not appear to result in lower exercise adherence or increased mortality rates compared with other exercise intensities.

**REFERENCES**


**Key Words:** cardiorespiratory fitness • exercise intensity • heart failure • hospitalization • mortality.

**APPENDIX**

For supplementary figures and tables, please see the online version of this article.