Oxygen uptake kinetics in older patients receiving postacute cardiac rehabilitation: effects of low-intensity aerobic training.

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ORIGINAL RESEARCH ARTICLE

Oxygen Uptake Kinetics in Older Patients Receiving Postacute Cardiac Rehabilitation

Effects of Low-Intensity Aerobic Training

ABSTRACT

Molino-Lova R, Vannetti F, Pasquini G, Paperini A, Zipoli R, Polcaro P, Petrilli M, Cecchi F, Macchi C: Oxygen uptake kinetics in older patients receiving postacute cardiac rehabilitation: Effects of low-intensity aerobic training. Am J Phys Med Rehabil 2010;89:953–960.

Objective: Older patients who receive postacute cardiac rehabilitation improve their physical performance in terms of distance walked at the 6-min walk test. However, the slower and more complicated recovery, along with age-related chronic comorbidities, remarkably limits the intensity of aerobic training, which actually represents the core of cardiac rehabilitation. The aim of this study was to verify whether postacute cardiac rehabilitation also improves the cardiovascular adjustment to exercise, despite low-intensity aerobic training.

Design: Using a portable gas analyzer, we assessed the O_2 uptake kinetics during the 6-min walk test at the beginning and at the end of the rehabilitation in 84 patients aged 65 yrs and above.

Results: All patients significantly improved the distance walked at the 6-min walk test. The comparison of the time constants of O_2 uptake kinetics showed that 40% of patients also significantly improved the hemodynamic response to exercise. This improvement was independently associated with the report of sedentary lifestyle or low-intensity physical activity in the year before surgery and with longer time constants before physical training.

Conclusions: Low-intensity aerobic training improves the cardiovascular adjustment to exercise selectively in patients with physical deconditioning. This confirms the notion that elderly frail patients are those who benefit most from cardiac rehabilitation.

Key Words: Cardiac Rehabilitation, Elderly, Cardiopulmonary Exercise Testing, O_2 Uptake Kinetics

Older patients who have undergone cardiac surgery are commonly referred to medical rehabilitation facilities for postacute inpatient rehabilitation because of their slower and more complicated recovery.[1–3] Current rehabilitation programs are based on a comprehensive geriatric approach, so that physical training, along with aerobic exercises, also includes gentle calisthenic exercises, passive stretching, and specific exercises for balance and coordination.[2–4] However, older patients often show low fitness levels and chronic comorbidities that, in addition to their slower recovery, remarkably limit the intensity of aerobic training, which actually represents the core of cardiac rehabilitation.[5]

The effects of cardiac rehabilitation on older patients' physical performance have been traditionally assessed using the 6-min walk test (6mWT).[6–8] In previous studies, we have shown that older patients who had undergone cardiac surgery increased the distance walked at the 6mWT[2–4] and that patients with poor left ventricular function showed greater relative increases at the end of postacute rehabilitation.[2] However, taking into account the low intensity of aerobic training, it still remains unclear whether the increase of the distance walked at the 6mWT reflects the improvement of the hemodynamic response to exercise, as a result of aerobic training, or it just reflects the improvement of musculoskeletal function, as a result of physical training components other than aerobic exercise.

Assessing the hemodynamic response to exercise during the 6mWT is quite difficult. However, portable systems for breath-by-breath analysis of respiratory gas exchanges are now available, so that cardiopulmonary exercise testing can be performed even on patients walking along a corridor. Among measures provided by cardiopulmonary exercise tests, oxygen (O_2) uptake kinetics has been attracting researchers' attention for a long time, as it accurately describes the rate of change of O_2 uptake during exercise.[9,10] In theory, O_2 uptake depends on both the ability of the cardiovascular system to provide tissues with O_2 and the ability of peripheral tissues to use the delivered O_2.[9–12] Previous studies conducted on healthy individuals have shown that at the onset of submaximal exercise, the increase in cardiac output is faster than the increase in O_2 uptake,[13–15] suggesting that O_2 delivery to skeletal muscles is in excess of their metabolic demands and that, accordingly, O_2 uptake is limited by peripheral O_2 utilization.[11,12] On the contrary, studies conducted on patients with cardiovascular diseases have shown that the increase in cardiac output and the increase in O_2 uptake follow the same course,[16–18] suggesting that O_2 uptake is limited by cardiac output and that, accordingly, O_2 uptake kinetics reflects the progressive adjustment of cardiac output to exercise.[11,12,16–18] Furthermore, in the case of submaximal constant work rate exercises, such as the 6mWT, O_2 uptake kinetics at the onset of the exercise is described by a monoexponential curve, in which the time constant represents the lapse of time needed to achieve 63% of the asymptotic response.[9] Accordingly, the time constant of O_2 uptake kinetics during the 6mWT expresses the promptness of cardiovascular system to adjust to exercise: the shorter the time constant, the faster the adjustment.[11,12,16–18]

The aim of this study was to verify whether older patients who receive postacute rehabilitation after cardiac surgery also improve the hemodynamic response to exercise, despite the low intensity of aerobic training. Based on the above considerations, this issue can be addressed by assessing O_2 uptake kinetics during the 6mWT at the beginning and at the end of the rehabilitation and by comparing the time constants of the two tests. If the time constant becomes longer (Fig. 1), then physical training has increased the amplitude of the exponential curve without changing its slope, and hence it has only improved musculoskeletal function. On the contrary, if the time constant becomes shorter (Fig. 2), then physical training has also made steeper the slope of the curve, and hence it has also improved the hemodynamic response to exercise.

METHODS

Study Sample

Participants were enrolled among 213 consecutive patients admitted as inpatients to our rehabilitation center from October 2008 to June 2009 for an intensive postacute 3-wk rehabilitation after cardiac surgery (mean [±SD] time interval between surgery and admission to the rehabilitation center: 7.1 [±2.4] days). All patients aged 65 yrs and above and who had undergone elective cardiac surgery were considered eligible for the study. Patients with cognitive deterioration (corrected Mini-Mental State Examination score < 21) or relevant functional impairment as a result of previous stroke, peripheral artery disease, severe osteoarthritis of weight-bearing joints, or other chronic diseases able "per se" to remarkably limit physical activity were excluded from the study. As recommended by the manufacturer, patients with pacemaker or implantable defibrillator were also excluded, because of possible interferences of the portable gas analyzer with cardiac devices. Finally, patients with postoperative "sequelae," such as chest-wall or diaphragm mobility impairment,

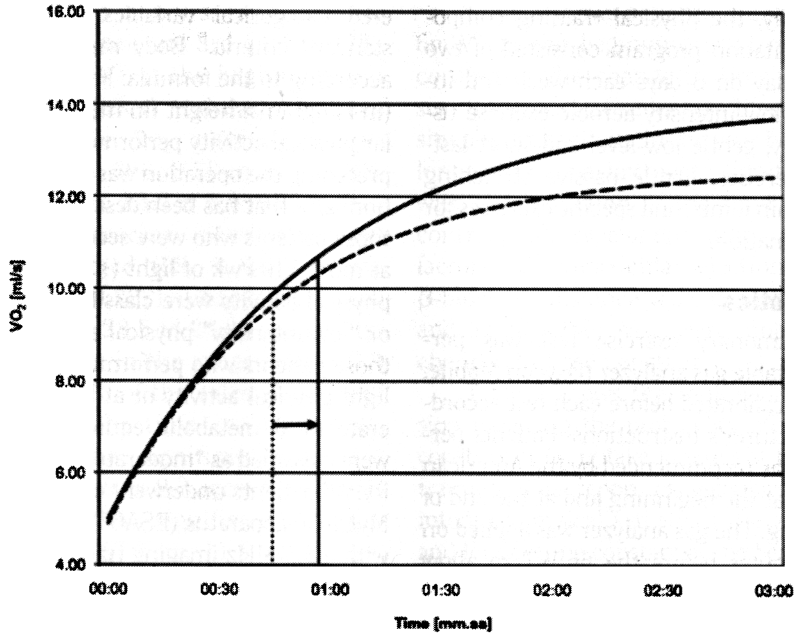

FIGURE 1 *O_2 uptake kinetics during the 6mWT at the beginning (dotted line) and at the end (continuous line) of physical training. The time constant of the test performed at the end of physical training is longer than that of the test performed at the beginning.*

bronchial atelectasias, and posture or walking impairment that were not fixed by intensive individual physiotherapy within the first week after admission, were also excluded to obtain a group of patients fit enough to ensure at least 2 wks of light physical training in the gymnasium.

The study sample was represented by 88 patients, 61 men and 27 women. The Institutional Review Board of the Don Gnocchi Foundation approved the study protocol, and all enrolled patients signed their informed consent form to be included in the study.

Rehabilitation Program

A detailed description of the rehabilitation program performed in our center has been reported

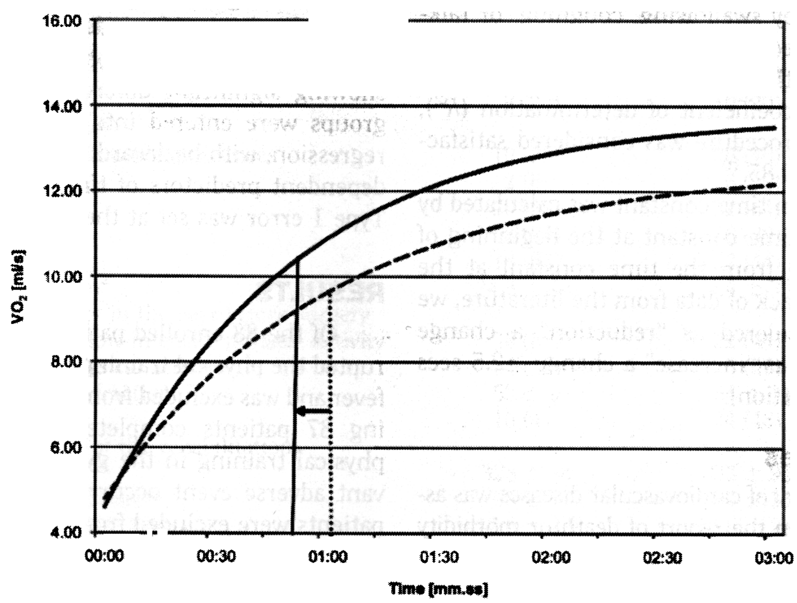

FIGURE 2 *O_2 uptake kinetics during the 6mWT at the beginning (dotted line) and at the end (continuous line) of physical training. The time constant of the test performed at the end of physical training is shorter than that of the test performed at the beginning.*

elsewhere.[2–4] Briefly, the physical training component of the rehabilitation program consisted of two 1-hr sessions per day on 5 days each week and included 20 mins of low-intensity aerobic exercise using cycle ergometry, gentle low-level and short-lasting calisthenic exercises, gentle passive stretching involving all the main joints, and specific exercises for balance and coordination.

O_2 Uptake Kinetics

The cardiopulmonary exercise test was performed using a portable gas analyzer (Oxycon Mobile, Jaeger, Germany), calibrated before each test according to the manufacturer's instructions. Patients performed the 6mWT as recommended by the American Thoracic Society,[6] at the beginning and at the end of the physical training. The gas analyzer was applied on patients a few minutes before the 6mWT to allow patients' adjustment to the mask.

According to Whipp and Wasserman,[9] O_2 uptake kinetics of submaximal constant work rate exercises is described by the monoexponential curve:

$$\dot{V}O_2(t) = \dot{V}O_{2\,\text{baseline}} + (\dot{V}O_{2\,\text{steady-state}} - \dot{V}O_{2\,\text{baseline}})(1 - e^{-\frac{t}{\tau}})$$

where τ is the time constant of the curve, expressed in seconds. Baseline $\dot{V}o_2$ was calculated as the average $\dot{V}o_2$ of the last minute of rest before the 6mWT. Steady-state $\dot{V}o_2$ was calculated as the average $\dot{V}o_2$ of the last 3 mins of the test. The time constant of the curve was calculated by fitting $\dot{V}o_2$ data to the monoexponential model using the nonlinear least squares method (MATLAB 7.0 software, MathWorks, Natick, MA). Occasional errant breaths, caused by swallowing, coughing, or talking, were removed from the data set. The "goodness of fit" for the monoexponential model was assessed by the coefficient of determination (R^2), and the fitting procedure was considered satisfactory if R^2 was ≥ 0.85.[10]

The change in time constant was calculated by subtracting the time constant at the beginning of physical training from the time constant at the end. Because of lack of data from the literature, we empirically considered as "reduction" a change <-2.5 secs and as "increase" a change >2.5 secs (see "Results" section).

Other Variables

Family history of cardiovascular diseases was ascertained based on the report of death or morbidity for angina, myocardial infarction, stroke, or peripheral artery disease in one or both parents, or in one or more siblings, younger than 65 yrs. Modifiable cardiovascular risk factors, such as smoking habit, hypertension, diabetes, and dyslipidemia, were considered categorical variables and ascertained using standard criteria.[5] Body mass index was calculated according to the formula: body mass index = weight (in kilograms)/height (in meters).[2] The level of regular physical activity performed by patients in the year preceding the operation was assessed by using a questionnaire that has been described elsewhere.[3] Briefly, those patients who were sedentary or who performed at most 4 hrs/wk of light (<3 metabolic equivalents) physical activity were classified as sedentary lifestyle or "low-intensity" physical activity. On the contrary, those patients who performed more than 4 hrs/wk of light physical activity or at least 1–2 hrs/wk of moderate (3–6 metabolic equivalents) physical activity were classified as "moderate-intensity" physical activity. All patients underwent echocardiography, using a MyLab30 apparatus (ESAOTE, Genoa, Italy) equipped with a 2.5-MHz imaging transducer, and left ventricular ejection fraction was assessed using standardized criteria.[19] Information on medications was gathered from medical records, and the use of β-blockers was considered as a categorical variable.[20]

Statistics

Statistical analysis was performed using the STATA 7.0 software (Stata Corporation, College Station, TX). Continuous variables are presented as mean ± SD. Categorical variables are presented as absolute value and percentage. Differences between the 6mWT at the beginning and at the end of the physical training were tested using the paired Student's t test. Differences in general characteristics and in the 6mWT at the beginning of physical training between patients who showed a reduction and those who showed an increase in the time constant of O_2 uptake kinetics were tested by using the Student's t test for independent samples or the Pearson χ^2 test, as appropriate. Finally, variables showing significant differences between the two groups were entered into a multivariate logistic regression, with backward selection, to identify independent predictors of time constant reduction. Type 1 error was set at the two-sided 0.05 level.

RESULTS

Of the 88 enrolled patients, one patient interrupted the physical training for few days because of fever and was excluded from the study. The remaining 87 patients completed the scheduled 2-wk physical training in the gymnasium, and no relevant adverse event occurred. Furthermore, three patients were excluded from the study because the coefficient of determination (R^2) of the fitting procedure for time constant calculation was <85%, either at the beginning or at the end of the physical training. The final study sample was represented by 84 patients, 58 men (69%) and 26 women (31%), with mean age ± SD, 71 ± 6 yrs; range, 65–84; median, 69; 1st quartile, 66; and 3rd quartile, 78.

Comparing the 6mWT at the beginning and at the end of the physical training, distance walked and steady-state $\dot{V}O_2$ significantly increased (331 ± 93 m *vs.* 390 ± 79 m, $P < 0.001$ and 12.6 ± 2.7 ml/sec *vs.* 13.9 ± 3.3 ml/sec, $P < 0.001$, respectively), whereas maximum heart rate remained unchanged (99 ± 16 bpm *vs.* 101 ± 17 bpm; $P = 0.222$). Changes in time constant ranged from −28.5 to 28.2 secs, and no patient showed a change in the range from −2.9 to 2.6 secs (~0% ± 10% of the extreme values). In 34 patients (40%), the time constant of O_2 uptake kinetics became significantly shorter (61.8 ± 12.1 secs *vs.* 51.9 ± 9.3 secs; $P < 0.001$) and in 50 patients (60%) significantly longer (47.2 ± 13.5 secs *vs.* 57.6 ± 11.5 secs; $P < 0.001$). There was no significant difference in the increase of the distance walked and of the steady-state $\dot{V}O_2$ between patients who showed a reduction and those who showed an increase in the time constant (57 ± 42 m *vs.* 61 ± 44 m, $P = 0.717$ and 1.4 ± 1.8 ml/sec *vs.* 1.3 ± 1.9 ml/sec, $P = 0.883$, respectively).

Table 1 shows patients' characteristics and the 6mWT at the beginning of physical training, according to the change in time constant. Female sex, the report of sedentary lifestyle or low-intensity physical activity in the year before surgery, and longer time constant were significantly associated with the reduction of the time constant. On the contrary, age, type of operation, cardiovascular risk factors, left ventricular ejection fraction, use of β-blockers, distance walked, maximum heart rate, and steady-state $\dot{V}O_2$ were not associated with changes in time constant.

Table 2 shows the multivariate logistic regression modeling the probability of reducing the time constant of O_2 uptake kinetics at the end of physical training. The report of sedentary lifestyle or low-intensity physical activity in the year before surgery and longer time constant at the beginning of physical training remained independent predictors, while female sex was removed by backward selection.

DISCUSSION

This study was aimed at verifying whether older patients who receive postacute rehabilitation after cardiac surgery also improve the hemody-

TABLE 1 Patients' characteristics and 6mWT at the beginning of physical training according to the change in time constant ($n = 84$)

	Time Constant: Reduction [n = 34 (40%)]	Time Constant: Increase [n = 50 (60%)]	P^a
Demographics			
Age, yrs	71.0 ± 6.7	71.4 ± 5.6	0.711
Female sex	18 (53)	8 (16)	<0.001
Operation			
Coronary artery bypass graft	14 (41)	20 (40)	
Valve repair/replacement	12 (35)	20 (40)	0.886
Combined procedures	8 (24)	10 (20)	
Cardiovascular risk factors			
Family history of cardiovascular diseases	10 (29)	20 (40)	0.320
Current smokers	2 (6)	6 (12)	0.348
Hypertension	20 (59)	32 (64)	0.632
Diabetes	8 (24)	16 (32)	0.399
Dyslipidemia	18 (53)	22 (44)	0.421
Body mass index, kg/m^2	24.8 ± 4.0	24.4 ± 3.0	0.625
Reported physical activity in the year before surgery			
Sedentary lifestyle or low-intensity physical activity	30 (88)	22 (44)	<0.001
Moderate-intensity physical activity	4 (12)	28 (56)	
Left ventricular ejection fraction, %	53 ± 9	54 ± 11	0.825
Use of β-blockers	16 (47)	24 (48)	0.932
6mWT at the beginning of the rehabilitation			
Distance walked, m	328 ± 94	333 ± 93	0.802
Maximum heart rate, bpm	98 ± 17	99 ± 15	0.697
Steady-state $\dot{V}O_2$, ml/sec	12.6 ± 2.9	12.6 ± 2.6	0.918
Time constant, secs	61.8 ± 11.9	47.2 ± 13.3	<0.001

Values are presented as n (%) or mean ± SD.
[a]From Student's t test or Pearson's χ^2 test, as appropriate.
6mWT, 6-min walk test.

TABLE 2 Multivariate logistic regression modeling the probability of reducing the time constant of O_2 uptake kinetics at the end of physical training

Time Constant Reduction	Odds Ratio (95% Confidence Interval)	*P*
Sedentary lifestyle or low-intensity physical activity in the year before surgery (Y/N)	11.6 (2.7–49.3)	<0.001
Longer time constant at the beginning of physical training (Y/N)[a]	27.3 (6.9–108.3)	<0.001

Final model: number of observations = 84; χ^2 of the logistic regression = 50.2; hypothesis 0 probability according to $\chi^2 < 0.001$; coefficient of determination for logistic regression, according to Nagelkerke = 0.443. The initial model also included female sex that was removed by backward selection ($P = 0.147$).

[a]The time constant was dichotomized according to the median value in the whole group (51.5 secs).

namic response to exercise, despite low-intensity aerobic training. As expected, all patients improved their physical performance in terms of distance walked at the 6mWT. Interestingly, 40% of patients also reduced the time constants of O_2 uptake kinetics, suggesting that the low-intensity aerobic training had also improved the hemodynamic response to exercise in these patients.

To the best of our knowledge, this finding has never been reported before, so that direct comparisons with the existing literature are impossible. In our patients, the improvement of the hemodynamic response to exercise was significantly associated with the report of sedentary lifestyle or low-intensity physical activity in the year before surgery, suggesting that the low-intensity aerobic training included in current rehabilitation programs had improved the cardiovascular adjustment to exercise selectively in patients with physical deconditioning. Actually, the notion that patients with physical deconditioning are those who benefit most from cardiac rehabilitation is not new. In a previous article, we have, in fact, reported that among older patients receiving postacute rehabilitation after cardiac surgery, patients with poor left ventricular function were those who showed greater relative increases of the distance walked at the 6mWT.[2] Furthermore, this notion is also supported by the significant association that we found between the improvement of the hemodynamic response to exercise and longer time constant of O_2 uptake kinetics at the beginning of physical training. Previous studies have, in fact, shown that patients with physical deconditioning as a result of chronic heart failure show time constants of the same magnitude, ~60 secs.[11,15,16] Surprisingly, the improvement of the hemodynamic response to exercise was not associated with left ventricular ejection fraction, which actually was normal or, at most, moderately depressed in all patients. This confirms the notion that aerobic training has favorable effects on peripheral hemodynamic variables, such as endothelial function and arteriolar resistances,[12,21] and suggests that these effects are more relevant in patients with physical deconditioning. Furthermore, the improvement of the hemodynamic response to exercise was not associated with the distance walked during the 6mWT at the beginning of physical training. This suggests that the 6mWT performed in the immediate postacute phase after cardiac surgery reflects patients' current physical condition, but it is not able to capture retrospectively the degree of patients' physical deconditioning before the operation.

Finally, 60% of our patients increased the time constant of O_2 uptake kinetics. This was the consequence of the increase of the steady-state $\dot{V}O_2$ in the absence of a concomitant improvement of the hemodynamic response to exercise. For these patients, most of whom reported a more active lifestyle in the year before surgery and showed shorter time constants before training, it is reasonable to hypothesize that the intensity of aerobic training, limited by patients' current physical condition, was actually not enough to improve the hemodynamic response to exercise.

This study provides an interesting insight into the pathophysiology of exercise in older patients receiving postacute cardiac rehabilitation. However, some inherent limitations that might restrict the extension of the results of this study to all cardiac patients need to be considered. First, to obtain a group of patients fit enough to ensure at least 2 wks of physical training, we introduced a wide series of exclusion criteria, so that our patients represent a selected sample of patients who receive postacute rehabilitation after cardiac surgery. This may explain, for instance, the fact that left ventricular ejection fraction was normal or, at most, moderately depressed in all patients, which, unluckily, does not happen in everyday clinical practice. Second, patients enrolled in this study were all postsurgical older patients receiving inpatient postacute rehabilitation, so our results cannot be directly extended to younger patients, to patients attending outpatient cardiac rehabilitation, which traditionally begins 4–6 wks after the acute event, and to patients receiving cardiac rehabilitation for clinical conditions other than cardiac surgery.

In conclusion, our findings show that current programs for older patients receiving postacute rehabilitation after cardiac surgery improve the hemodynamic response to exercise selectively in patients with physical deconditioning. This confirms the notion that patients with physical deconditioning are those who benefit most from cardiac rehabilitation. Obviously, it cannot be proposed in everyday clinical practice to perform a cardiopulmonary exercise test for evaluating the time constant of O_2 uptake kinetics before physical training. However, an accurate assessment of the physical activity level in the year before surgery might be a useful tool to identify those patients who will improve their hemodynamic response to exercise and those who will not.

Future studies should confirm our results on a broader scale and investigate the effects of low-intensity physical training on the hemodynamic response to exercise in patients with poor left ventricular function. Furthermore, future studies should also verify whether a cautious increase of the intensity of aerobic training might also improve the cardiovascular adjustment to exercise in those patients who report moderate-intensity physical activity in the year before surgery. Finally, future studies conducted on larger samples might show that other factors, not found to significantly correlate with change in time constant in this study, are also able to affect the improvement of the hemodynamic response to exercise. This might help in better identifying patients who would benefit most from cardiac rehabilitation.

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