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ORIGINAL ARTICLE

# The influence of physical activity performed at 20-40 years of age on cardiovascular outcomes in medical patients aged 65-75

*L'influenza sugli eventi cardiovascolari dell'attività fisica svolta fra i 20 e i 40 anni di età, in pazienti di 65-75 anni*

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## KEYWORDS

Cardiovascular events;  
Diabetes;  
Exercise.

## Summary

**Introduction:** Several studies show that physical activity can reduce the risk of cardiovascular disease, but the vast majority of these focus on the short- to intermediate-term benefits or refer to very specific populations. This observational study was conducted to determine whether physical activity performed during the third or fourth decade of life influences the occurrence of cardiovascular events in patients aged 65-75 years.

**Materials and methods:** We studied a cohort of 2191 unselected patients admitted to Internal Medicine Departments. Data were collected on the patients' medical history and their physical

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activity level when they were 20 to 40 years old. For the latter purpose, we used a specific questionnaire to assess the levels of physical activity related to the patients' job, daily life, leisure time, and sports.

**Results:** Almost half (44.2%) of the patients we evaluated reported moderate-intense physical activity when they were 20-40 years old. Around one third (35.8%) of the patients had experienced at least one major cardiovascular event, and there was a slight trend towards fewer cardiovascular events in patients with histories of physical activity (mean risk reduction: 4%, multivariate analysis). More evident benefits were observed in the subgroup of patients with diabetes, where cardiovascular outcomes were much better in patients who had been physically active than in those with sedentary life-styles (mean risk reduction: 24%).

**Conclusions:** Given its design, our study may have underestimated the cardiovascular benefits of physical activity. Nonetheless, our results suggest that moderate-intense exercise during young adulthood may have limited beneficial effects on cardiovascular disease in old age, except in specific high-risk populations (diabetic patients). More evident benefits are probably associated with regular physical activity throughout life.

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## Introduction

In the last few decades, several studies [1–9] have demonstrated that physical activity, as with other modifiable life-style factors, can reduce the risk of cardiovascular disease and all-cause mortality. Compared to the large number of reports documenting benefits in the short-term (1-5 years), there are few studies evaluating the long-term effects of physical activities, and the majority of these refer to selected populations performing specific types of exercise. A favorable long-term outcome of physical activity was first reported by Morgan [10] in a group of oarsmen, who demonstrated a mean life-expectancy two years longer than the general population. Paffenbarger et al. [6] documented a lower rate of death from all causes and from coronary heart disease in Harvard College alumni who had performed physical activity, and a reduced risk for coronary heart disease and type 2 diabetes was reported by Kujala et al. [11] in male Finnish athletes participating in international endurance competitions. More recently, running in middle and old age appeared to be associated with reduced disability in later life and improved survival in a 21-year longitudinal study [12].

The aim of our study was to evaluate whether physical activity performed in the third or fourth decade of life as part of work, daily life, leisure time and sports, is associated with favorable effects in terms of reduced cardiovascular morbidity in old age.

## Materials and methods

During the period of February – April 2007, 51 Italian Departments of Internal Medicine (IM) took part in this observational study. Data were collected under the scientific coordination of the Istituto Superiore di Sanità (ISS – the leading technical and scientific public body of the *Italian National Health Service*) and the FADOI (*Italian Federation of Internal Medicine*) Research Department.

The study aimed to evaluate whether a relevant physical activity performed during the third or fourth decade of life could influence the occurrence of cardiovascular events in consecutive patients, aged 65-75 years, admitted for any

cause to IM Departments. Patients who had experienced a major cardiovascular event before the age of 40 and those with predicted poor compliance for the study procedures (e.g. severe cognitive impairment) were excluded from the study.

At hospital admission, demographic and vital parameters, medical history, and information regarding physical activity performed between the ages of 20 and 40 years were collected for each patient. Specifically, patients answered a specific questionnaire assessing the level of physical activity performed as part of work, daily life, leisure time and sports. For each decade (third and fourth), patients were asked to define the type of job (sedentary / requiring only technical ability / requiring moderate or vigorous physical activity), if they regularly used a bike and for what duration each time ( $\leq 30$  / 31-60 / 61-90 /  $> 90$  minutes), and if they performed a sport as part of leisure time, or at competitive level.

Patients were classified as experiencing a relevant physical activity if they reported at least one of the following:

- job requiring vigorous physical activity
- regular use of a bike for more than 90 minutes a day
- sport at a competitive level.

The study was approved by the Ethics Committees of the *Istituto Superiore di Sanità* and of all participating centers, and informed consent was obtained from all patients.

## Statistical analysis

The association between physical activity performed in the third and fourth decade and cardiovascular outcome measured between ages 65-75 was evaluated in the overall study population by means of a multivariable logistic regression analysis. Cardiovascular events considered as study outcomes were cerebrovascular disease (stroke or transient ischemic attack), coronary heart disease, peripheral arterial disease, history of thromboendarterectomy, coronary or peripheral revascularization, and known abdominal aneurism. Covariates for the multivariable analysis included gender, smoking habit (present or past), diabetes, hypertension and dyslipidemia. Patients were defined as affected with diabetes, hypertension or dyslipidemia if they were receiving specific

treatments for these and/or were given these diagnoses upon hospital admission.

Subsequently, a further multivariable logistic regression analysis was performed to assess whether physical activity could influence the occurrence of cardiovascular events in the subgroup of diabetic patients.

Odds Ratios (ORs) and 95% CIs were reported with 2-tailed probability values. A  $p$  value  $\leq 0.05$  was considered statistically significant.

Statistical analysis was carried-out using SAS<sup>®</sup> software, version 9.1.3.

## Results

### Study population

A total of 2191 patients were included in the study, and their characteristics are detailed in Table 1. Around half of the patients (44.2%) were considered as having performed physical activity when they were 20-40 years old. A major cardiovascular event had occurred in 35.8% of patients. A diagnosis of diabetes was present in one-third of patients (33.3%).

### Physical activity and cardiovascular outcome

Table 2 and Figure 1 report the results of two multivariable analyses concerning the overall study population and the subgroup of patients with diabetes, respectively. In these analyses, the occurrence of cardiovascular events was related to physical activity performed at age 20-40 and to other potential prognostic factors. As far as the overall study population is concerned, a slight trend towards a decrease in the incidence of cardiovascular events was reported in patients performing physical activity (mean risk reduction of around 4%). A stronger trend towards improved cardiovascular outcomes (though not statistically significant) was demonstrated by the subgroup of diabetic patients who were physically active as compared to sedentary diabetics (mean risk reduction of around 24%). In both the total patient population and the diabetics, male gender, hypertension and dyslipidemia were associated with a significantly increased incidence of major cardiovascular events. Smoking was significantly associated with worse cardiovascular outcomes

**Table 1** Characteristics of patients.

Characteristics	
Age	
Mean $\pm$ SD	71.6 $\pm$ 3.1
Male gender (%)	54.6
Physical activity at 20-40 yrs (%)	44.2
Patients experiencing	
CV events (%)	35.8
Smoking* (%)	53.8
Diabetes (%)	33.3
Dyslipidemia (%)	34.2
Hypertension (%)	61.9

\* at present or in the past.

**Table 2** Multivariable logistic regression analysis for the occurrence of cardiovascular events in the overall study population. OR = Odds Ratio; CI = Confidence Intervals.

Variable	Effect	OR	95% CI	p value
Physical activity	Yes vs No	0.96	0.79 – 1.17	0.71
Gender	Male vs Female	1.53	1.22 – 1.92	0.0002
Smoking	Yes vs No	1.76	1.41 – 2.19	< 0.0001
Diabetes	Yes vs No	1.37	1.13 – 1.67	0.0017
Hypertension	Yes vs No	1.84	1.51 – 2.24	< 0.0001
Dyslipidemia	Yes vs No	1.76	1.45 – 2.14	< 0.0001

in the general study population and with a near-to-significant increase in cardiovascular events in the subgroup of diabetics.

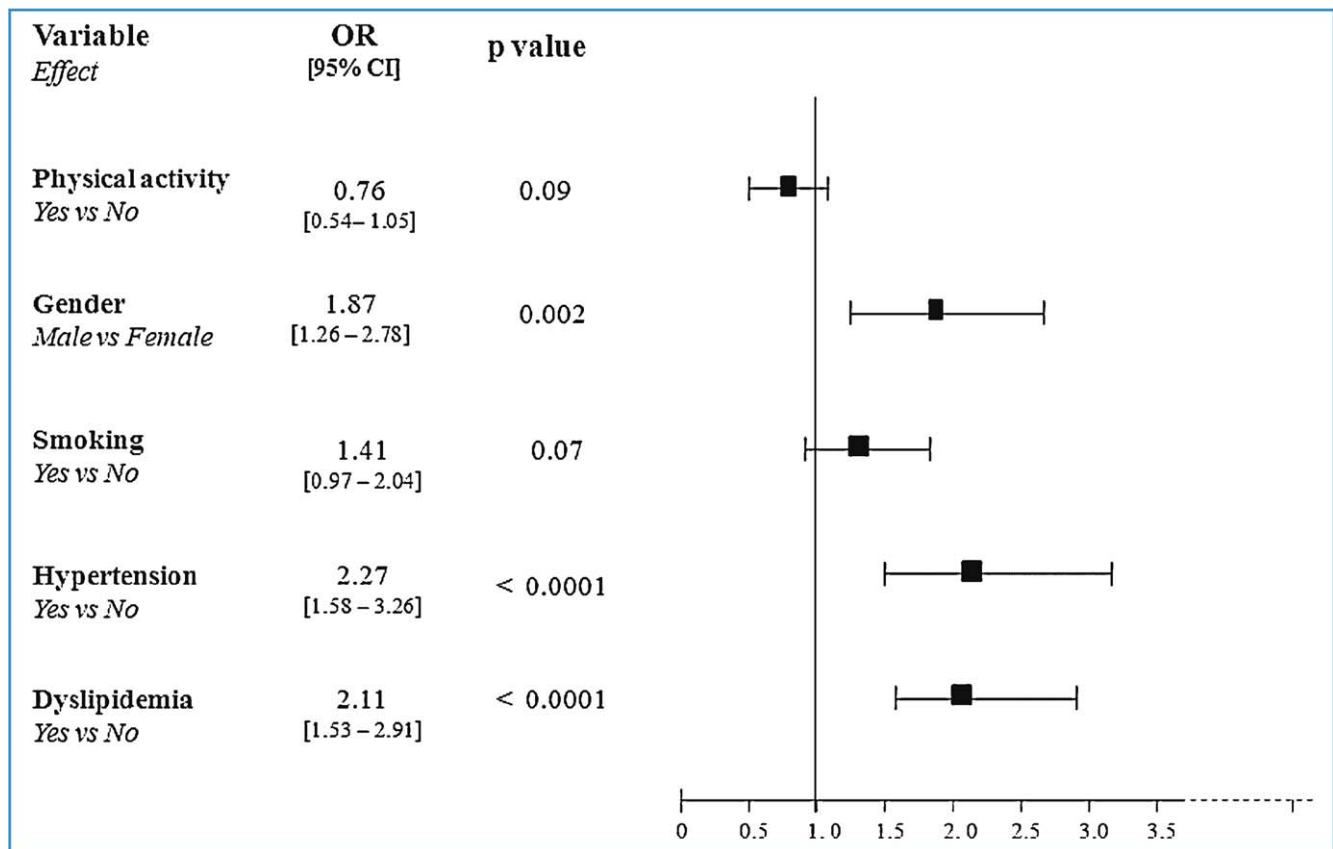
## Discussion

A large number of prospective population studies [13–17] have found beneficial effects of physical activity on rates of cardiovascular disease and all-cause mortality; this evidence is of major importance to public health because physical inactivity is highly prevalent in contemporary society and is a potentially modifiable factor [18].

Few data, however, are available concerning the long-term effects of physical activity, and the data that is available refers to specific populations and activities (in the majority of cases, athletes and competitive sports). The aim of our study was to address this gap by evaluating, in a population of patients aged 65-75 years, whether overall physical activity (both work and leisure related) performed between 20-40 years of age, could lead to a reduced risk of subsequent major cardiovascular events.

In our study, no clear benefit in cardiovascular outcome was seen in the overall population of patients participating in physical activity as young adults. This finding adds to the heterogeneous data reported to date on this issue. Namely, in the study by Kujala et al. [11], athletes participating in international competitions for endurance sports demonstrated a reduced risk of coronary heart disease, diabetes and disability in old age, but the same results were not found in subjects performing strength-based sports. Furthermore, Paffenbarger et al. [6] reported a reduced mortality in Harvard College alumni who had been physically active, and in the group of individuals who discontinued physical activity, long-term morbidity and mortality were higher than in those individuals who continued with lifelong activity. These earlier results support the concept that continuity of physical activity is of particular value in improving health, and the results from our study, though indirectly, seem to support this hypothesis. Indeed, we have not collected systematic information on the physical activities of our patients after the fourth decade of life, but it is plausible that the majority of them experienced a more sedentary lifestyle in the following decades [19–21], particularly after retirement; this activity change may have reduced the positive influence of physical activity performed when they were younger.

A more evident improvement in cardiovascular outcome was documented in our study in the subgroup of diabetic



**Figure 1** Multivariable logistic regression analysis for the occurrence of cardiovascular events in the subgroup of patients with diabetes. OR = Odds Ratio; CI = Confidence Intervals.

patients who had performed a relevant physical activity when they were 20-40 years old compared to diabetics who were sedentary at the same age. This finding, though not statistically significant, seems to be worth noting because it is consistent with the known beneficial effects of physical activity on glucose metabolism and with the concept of exercise as a cornerstone of diabetes management, along with diet and medication [22–24]. A reduced morbidity in diabetics who performed relevant physical activity may also be related to the previously described positive effects of regular exercise on the overall metabolic risk profile and to changes in inflammatory and coagulation markers as well as platelet reactivity [25–27]. Our study highlights that these benefits may be lifelong.

Over the years, various expert groups, based on the best evidence available, have formulated different physical activity dosing recommendations and guidelines. It is plausible that there is a minimum dose of physical activity required to obtain health benefits, that these benefits increase with increasing dose, and that beyond a certain level of activity, adverse effects (e.g., musculoskeletal injuries [28], sudden death [29]) outweigh the benefits. The minimum effective dose, dose-response curve and maximum safe dose of physical activity are not well understood, however, and indications of the type, intensity, duration and frequency of physical activity are not easy to synthesize across studies since investigators have assessed and classified them in a number of different ways [30,31]. Considering these

uncertainties and the difficulties associated with retrospective data collection, we chose to dichotomize patients by considering whether they performed at least one relevant physical activity including vigorous work, the regular use of a bike for more than 90 minutes a day, and a competitive sport. This simplified approach, which selected patients were engaged in a high level of physical activity, was in our opinion, consistent with the exploratory nature of our study and with the aim of identifying the possible long-term benefits of physical activity.

Although the size and the long follow-up strengthen its validity, our study may have some potential limitations worth discussing. First, retrospective collection of data through questionnaires may limit their accuracy and could be subject to recall bias and misclassification. Our choice was to collect a limited set of pivotal information and to avoid ambiguous questions as well as more sophisticated items, which might be difficult to remember. As a consequence, we may have omitted some variables, such as dietary habits, potentially altering the results. Moreover, because we focused on exercise during the third and fourth decades of life, we cannot exclude the possible influence of later physical activity. However, because we adjusted our results for gender, smoking, hypertension, diabetes and dyslipidemia, we are confident that we have considered the most relevant prognostic factors for cardiovascular outcome in our cohort.

Furthermore, to classify patients on the basis of their physical activity, we considered both intentional exercise

and activities of daily living. This approach is different from the one used by contemporary recommendations, which generally focus exclusively on intentional physical activity; this inclusion seemed salient for the social environment in Italy between 1950 and 1970. In addition, in our classification, we mixed aerobic and muscle-strengthening activity, but this combination may be confounding or inappropriate. However, recent guidelines support the benefits of and recommend both types of exercise [32]. More specifically, muscle-strengthening activity has been reported to promote the development and maintenance of metabolically active lean muscle mass, which is particularly important for glucose metabolism [32], and this may have contributed to the clear trend towards reduced cardiovascular morbidity in physically active versus sedentary diabetics in our cohort.

Finally, due to the study design, we cannot exclude the possibility that our study population represents a selected cohort compared to the general population of Italy in the period between 1950 and 1970. It is also plausible that our population, composed of patients requiring medical assistance but omitting people who died before our survey was conducted, underestimates the potential long-term benefits of physical activity.

In conclusion, the results from our study in medical patients suggest that moderate-intensity physical activity performed during young adulthood may have limited beneficial effects on cardiovascular disease in old age, particularly when a specific high-risk population (e.g. diabetic patients) showing a clear trend towards a better outcome is excluded. Most likely, and in agreement with previous data, regular lifelong physical activity is crucial to reap more significant benefits. Considering that our data is preliminary, we hope that future studies of adequate design can further assess this issue.

## Conflict of interest statement

The authors have no conflict of interest to declare.

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## Appendix A

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