The American Journal of Surgery xxx (xxxx) xxx

Contents lists available at ScienceDirect

The American Journal of Surgery

journal homepage: www.americanjournalofsurgery.com

Original Research Article

Long-Term effects of physical activity on weight loss, metabolic parameters and blood pressure in subjects undergoing bariatric surgery: A 5-year follow-up study

Diego Moriconi [a,*], Laura Manca [a], Eleni Rebelos [b], Emanuele Guidotti [c], Linda Bonvicini [a], Antonio Troilo [a], Marco Anselmino [d], Monica Nannipieri [a,**]

[a] Department of Clinical and Experimental Medicine, University of Pisa, Italy
[b] Turku PET Centre, University of Turku, Finland
[c] Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy
[d] Bariatric Surgery Unit Ospedale San Raffaele, Gruppo San Donato, Milano, Italy

ARTICLE INFO

Keywords:
Bariatric surgery
Roux-en-Y gastric bypass
Physical activity
Type-2-diabetes

ABSTRACT

Background: bariatric surgery stands as an effective intervention for weight loss and improved metabolic control in obesity, although over time there is a proportion of weight regain and type-2-diabetes (T2D) relapse. Aims: to explore the role of physical activity (PA) after surgery and its impact on metabolic parameters during a 5-year follow-up.

Methods: 148 individuals who underwent bariatric surgery completed scheduled examinations over 5-years. Physical assessments and laboratory tests were conducted pre-surgery and annually thereafter. PA levels were evaluated using the International Physical Activity Questionnaire.

Results: participants were split into the PA group, who engaged in regular physical activity, and No-PA group, who remained sedentary throughout. In T2D individuals before surgery, PA group showed significant reductions in blood pressure and a lower T2D recurrence (6.7 % vs 36 %) compared to No-PA group. In normoglycemic individuals, the PA group led to sustained BMI reduction and improved blood pressure control ($p < 0.001$) compared to No-PA group, for the entire duration of follow-up.

Conclusions: regular PA demonstrated cardio-metabolic benefits post-bariatric surgery. Integrating PA into post-bariatric care could enhance long-term outcomes.

1. Introduction

The coexistence of obesity and type-2-diabetes (T2D), known as diabesity, is becoming increasingly prevalent and exacerbates the burden on healthcare systems.[1]

In obesity management, bariatric surgery is currently considered to be an efficient therapy to obtain long-term weight loss, improvement in glycemic homeostasis and quality of life.[2]

However, although the impact of surgery on weight-decrease and T2D remission is impressive in the first years, studies with long follow-up show progressive weight regain and relapse of T2D over time in a non-negligible percentage of patients.[2,3] For this reason, the management of body weight and T2D following the surgery remains multifaceted and complex, and bariatric surgery should not be seen as a stand-alone solution, but rather as part of an overall health management strategy, in which physical activity (PA) can be considered as an integral component of post-bariatric surgery care to optimize diabetes management, weight control and long-term outcomes.

Engaging in regular exercise not only contributes to weight loss, but also improves cardiometabolic health, systemic blood pressure control, glycemic control and enhances mental well-being in patients with obesity in medical therapy, making it a crucial non-pharmacological intervention also for type-2-diabetes management.[4]

Thus, in the context of bariatric surgery, where physiological changes and metabolic adaptations are significant, PA could have a potential synergistic effect on postoperative outcomes.[5,6]

* Corresponding author. University of Pisa. Via Savi 8-10, 56126, Pisa, Italy.
** Corresponding author. University of Pisa. Via Savi 8-10, 56126, Pisa, Italy.
E-mail address: d.moriconi@ao-pisa.toscana.it (D. Moriconi).

https://doi.org/10.1016/j.amjsurg.2024.04.020
Received 11 March 2024; Received in revised form 5 April 2024; Accepted 23 April 2024

However, the association between PA levels and weight loss post-bariatric surgery, along with the optimal PA intervention strategy to prevent weight regain, remains unclear due to the complexity of PA as a behavior and measurement challenges.[7] Questionnaires are commonly employed to address these challenges due to their cost-effectiveness and ability to capture various PA domains, including occupational, leisure, and domestic activities.[8,9]

The aims of the present study were 1) to investigate the association between PA levels and

postoperative weight loss and maintenance in a cohort of patients who underwent bariatric surgery over five years long term follow-up; 2) to investigate a long-term follow-up impact of PA on metabolic parameters and blood pressure control after bariatric surgery.

2. Materials and methods

Single-center, 5-years observational study, involving 192 consecutive subjects with morbid obesity (body mass index $\geq$35 kg/m^2) and sedentary lifestyle underwent Roux-en-Y gastric bypass (RYGB) between 2015 and 2017.

Of 192 patients admitted to surgery, 148 patients have completed all the scheduled medical examinations for the first 5 years and have been included in the study.

Thirty-two subjects were excluded due to loss of follow-up and the remaining twelve fell within the exclusion criteria.

The exclusion criteria were severe medical conditions (malignancies, liver cirrhosis, end-stage kidney disease), history of type 1 diabetes, previous bariatric surgery or pregnancy.

2.1. Anthropometric and clinical characteristics

Height, weight, systemic blood pressure were recorded pre-surgery, peripheral blood samples were obtained for determination of routine blood chemistry.

All patients were evaluated at 2 and 12 months in the first year, and then every 12 months for the following 5 years. At each follow-up visit, all physical examinations and laboratory tests performed before surgery were repeated.

During each visit, according to guidelines,[10] it was stressed the importance of performing at least 150 min of moderate-intensity aerobic physical activity and two to three sessions of muscle-strengthening activities exercise per week.

Furthermore, PA levels were evaluated using the International Physical Activity Questionnaire every six months with a telephone interview.

2.2. International Physical Activity Questionnaire (IPAQ)

PA participation at baseline, every six months with phone interview and during the annual follow up visits was evaluated using the *International Physical Activity Questionnaire* (IPAQ).[9,11]

In particular, the long and short version of IPAQ are a translation of the English version available on the site https://sites.google.com/view/ipaq/home. In the short version, seven questions on PA provide information on vigorous and moderate intensity physical activity, time spent on walking and on sedentary activity while in the long version 27 questions are administered in order to obtain information on physical activity related to five different domains: “job”, “transportation”, “housework, house maintenance, and caring for family”, “recreation, sport, and leisure-time” and “time spent sitting”. The amount of PA in the questionnaire is expressed in minutes per day and days per week.

From the type, frequency, amount and duration of each session of physical activity, the baseline metabolic equivalents of tasks (MET) were calculated according to the Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ) available on the site https://sites.google.com/view/ipaq/home and using the proposition of Ainsworth et al.[12] According to the guidelines, participants are usually classified into three categories: *Low*, composed by individuals who do not meet criteria for categories *moderate* or *high* and consequently are considered low/inactive; *Moderate*, composed by individuals doing 3 or more days of vigorous intensity activity of at least 20 min per day OR 5 or more days of moderate-intensity activity or walking of at least 30 min per day OR 5 or more days of any combination of walking, moderate-intensity or vigorous intensity activities achieving a minimum of at least 600 MET-min/week of total physical activity; *High*, in which individuals do vigorous-intensity activity on at least 3 days and accumulating at least 1500 MET-minutes/week of total physical activity OR 7 or more days of any combination of walking, moderate-intensity or vigorous-intensity activities achieving a minimum total physical activity of at least 3000 MET-minutes/week. The physical activity intensity levels was considered as moderate if between 3 and 6 METs and vigorous if $>$ 6 METs.

Since 70.2 % of our participants did not reach 600 METs/week during the 5-year follow-up (336 $\pm$ 112), while the 29.8 % exceeded 1000 METs/week (1211 $\pm$ 221), and no participants fell within the range between 600 and 1000 METs/week, we divided the population into two groups, No-PA and PA, respectively, for further analysis.

2.3. Statistical analysis

Shapiro-Wilk test was applied to check for normality. Gaussian distributed variables were expressed as mean and standard deviation (SD); otherwise, median and interquartile range (IR) were used for quantitative variables, while categorical data were expressed as frequency.

To evaluate the impact of physical activity on BMI, glycemia, glycated hemoglobin, total cholesterol, LDL and HDL, triglycerides, systolic and diastolic blood pressure, eGFR evolution, in a 5-year follow-up, we conducted independent linear mixed-effects models. Each model has been performed on the sample subdivided into two subgroups: patients with or without type 2 diabetes. The variables were included as fixed effects in the model and each patient as random effect. When appropriate, two additional models, adding as an effect fix the BMI or drugs, respectively, were built.

Comparisons between groups of categorical variables were carried out with the Chi Square test while, for numerical variables, Mann-Whitney test or Wilcoxon test was used, based on the distribution of the variables.

P values $<$ 0.05 were considered significant. Statistical analysis was performed using Stata and R statistical packages, for Mac OSX.

3. Results

3.1. baseline characteristics of the sample

The 148 subjects included in this 5-year follow-up study were divided before surgery into two groups based on the glycaemic status.

Among seventy-six subjects affected by type-2-diabetes (T2D) before surgery, 15 performed regular physical activity (PA) and 61 were sedentary (No-PA) throughout the follow-up period. The participants exhibited comparable characteristics in terms of diabetes duration, age, BMI, blood pressure levels, as well as glycaemic control, lipid levels, and renal function. The only difference at baseline was a higher prevalence of males in the PA group (Table 1).

Seventy-two participants were not affected by T2D before surgery, 29 of which performed physical activity (PA) and 43 not (No-PA). In the No-PA group, individuals were older, with slightly lower eGFR and higher diastolic blood pressure and fasting blood glucose values than the PA group. There were no differences in BMI, gender and lipid profile between groups (Table 1).

Table 1
Baseline characteristics of participants before bariatric surgery.

Parameters	Individuals with T2D		Individuals without T2D	
	PA	No-PA	PA	No-PA
Numbers of patients	15	61	29	43
Age, years	54 ± 9	56 ± 7	45 ± 10	51 ± 12*
Gender, F(%)	6 (40)	47 (77)*	24 (83)	30 (70)
BMI, kg/m^2	46.0 ± 6.1	46.2 ± 6.0	43.2 ± 5.7	45.3 ± 7.4
Hypertension, n(%)	11 (73 %)	48 (79 %)	6 (21 %)	21 (49 %)*
SBP, mmHg	137 ± 6	139 ± 12	131 ± 12	135 ± 13
DBP, mmHg	84 ± 6	84 ± 8	79 ± 9	83 ± 10*
Fasting glucose, mg/dl	124 ± 35	135 ± 61	83 ± 12	90 ± 11*
HbA1c, %	7.0 ± 1.1	7.3 ± 1.6	5.7 ± 0.3	5.8 ± 0.4
Diabetes duration	3.8 ± 2.1	3.3 ± 2.5	–	–
eGFR (EPI), ml/min/ 1.73m^2	96 ± 16	87 ± 20	108 ± 13	100 ± 17*
Dyslipidemia, n(%)	9 (60)	41 (67)	9 (31)	13 (30)
Tot Cholesterol, mg/dl	188 ± 46	199 ± 39	179 ± 38	175 ± 31
LDL, mg/dl	122 ± 35	125 ± 34	114 ± 29	126 ± 26
HDL, mg/dl	46 ± 11	44 ± 12	49 ± 12	52 ± 13
Triglycerides, mg/dl	138 ± 45	177 ± 73	129 ± 53	125 ± 40

Continuous variables with a normal distribution were compared between PA and No-PA by the Student T test, while the not-normally distributed variables by the Mann-Whitney *U* test.
The statistical tests were applied separately within the group of individuals with and without T2D: Statistically significant differences ($p < 0.05$) are expressed as *.
Abbreviations: T2D, type-2-diabetes; SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; BMI, body mass index.

3.2. *effect of exercise on metabolic outcomes from 1 to 5 years of follow-up*

In the T2D cohort (76 pts), hypertension prevalence was 62 % in the No-PA group at the end of 5-year follow-up, compared to 33 % in the PA group (15 pts), *p=0.043* (Table 4).

Using linear mixed model, we found a significant effect of PA on both SBP and DBP ($p < 0.001$) (Fig. 1, **2**) during 5-years follow up. Furthermore, when we performed a post hoc analysis, after dividing the T2D subjects into PA and No-PA group, the PA individuals showed lower values of systemic blood pressure in all time points considered ($p < 0.001$) (Figs. 1 and 2). This result remained significant also when accounting for the need of anti-hypertensive treatment. Concerning the other parameters analysed, there was no effect of physical activity on BMI and kidney function (Fig. 3, Table 2).

Analysing the lipid profile, LDL was lower in the PA group both in the first and third year, similarly to the triglycerides, whose levels were significantly lower in the first and fifth year in PA group compared to no-PA group (Table 2). However, using a linear mixed model test, we did not find any effect of physical activity on HDL, LDL and triglycerides. The statin use increased similarly of 13 % and 12 % from the first to the fifth year of follow up, in the no-PA and PA groups respectively, without difference (Table 4).

Concerning glycemic profile, we observed lower HbA1c values in the PA compared to No-PA group at each follow-up period, although there was no significant impact of physical activity using linear mixed model (Table 2). However, T2D recurrence progressively increased in the no-PA group from 23 % to 36 % (Table 4), while no individual developed relapse at 5 years in PA group, with the prevalence of diabetes remaining stable (6.7 %), p=0.034.

In individuals without T2D, we found a significant effect of PA on BMI ($p < 0.001$), with the median BMI further decreasing from the first to the fifth year of follow-up by −1.6 kg/m^2 [−3.3 to 0.9], while in the No-PA group it gradually increased by 0.6 kg/m^2 [−1.4 to 2.1] (Fig. 3).

Concerning blood pressure control, 8 patients (19 %) in the No-PA group exhibited hypertension after the first year of follow-up. Subsequently, an additional 4 patients experienced a recurrence of hypertension at the end of the 5-years of follow-up period, resulting in an overall prevalence of 28 %. In contrast, among PA group, the prevalence of hypertension in the first year after surgery was 6.9 %, and it remained stable until the end of the 5-years follow-up.

Using linear mixed model, we found a significant effect of PA on systemic blood, SBP and DBP ($p < 0.001$, for both). When we performed a post hoc analysis, after dividing the patients into PA and No-PA group, the PA individuals showed lower values of systemic blood pressure, at each time points considered ($p < 0.001$, for both) (Figs. 1 and 2). The difference about the blood pressure levels remained significant also when accounting for the anti-hypertensive treatment used.

On the contrary, there were no effect of physical activity on kidney function as well as on lipid profile (HDL, LDL, triglycerides), with statin use increasing from 9 % to 26 % in the no-PA group and from 3 % to 10 % in the PA group (Tables 3 and 4) during 5-years of FU.

In terms of glycemic control, physical activity showed no impact on fasting glucose and HbA1c values (Table 3).

4. Discussion

The main results of this study are: i) moderate physical activity has superior impact on weight reduction/maintaining in patients without T2D compared to inactivity; ii) moderate physical activity has a major effect on systemic blood pressure, resulting in reduced medication, for

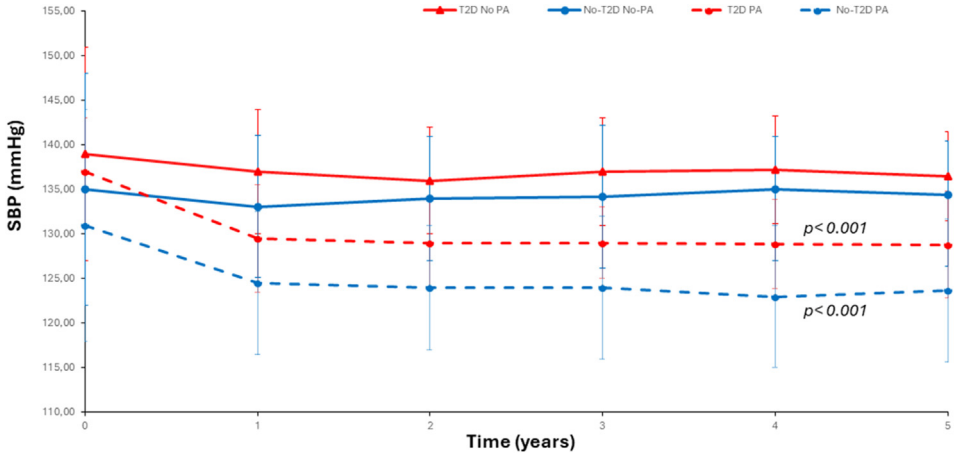

Fig. 1. Shows the trajectories of systolic blood pressure (SBP). The solid red line and the dashed red line represent, respectively, PA and No-PA subjects with T2D. The solid blue line and the dashed blue line represent, respectively, PA and No-PA subjects without T2D. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

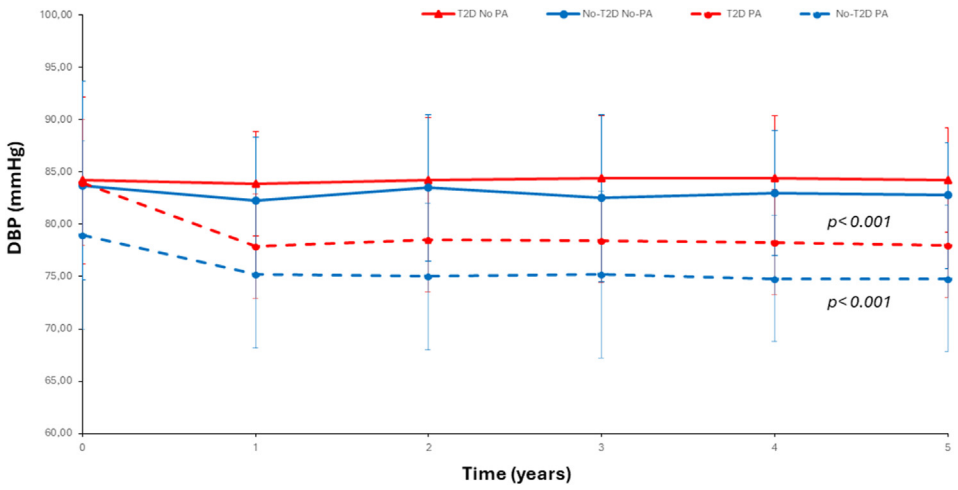

Fig. 2. Shows the trajectories of diastolic blood pressure (DBP). The solid red line and the dashed red line represent, respectively, PA and No-PA subjects with T2D. The solid blue line and the dashed blue line represent, respectively, PA and No-PA subjects without T2D. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

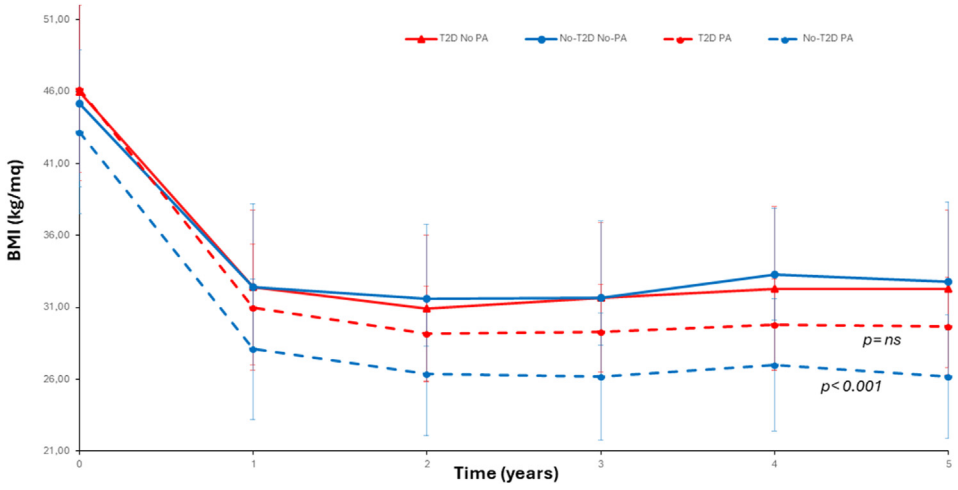

Fig. 3. Shows the trajectories of body mass index (BMI). The solid red line and the dashed red line represent, respectively, PA and No-PA subjects with T2D. The solid blue line and the dashed blue line represent, respectively, PA and No-PA subjects without T2D. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

both T2D and no-T2D individuals; iii) there are no impact of moderate physical activity on glycated hemoglobin levels during the 5 years, but we observe a significant increase in the recurrence of T2D in sedentary subjects.

Currently, there is a notable absence of evidence-based physical activity (PA) guidelines tailored for individuals who have undergone bariatric surgery. Various organizations, such as the American Society for Metabolic and Bariatric Surgery (ASMBS) and the American Heart Association (AHA), have put forth recommendations regarding PA for these individuals.[13]

These guidelines advocate for postoperative patients to engage in a health-promoting lifestyle, including a minimum of 30 min of daily exercise.[14] However, it is to acknowledge the limited availability of empirical data upon which to construct PA guidelines designed for bariatric surgery patients. The American College of Sports Medicine (ACSM) recommends that individuals with obesity participate in at least 150 min/week of moderate-intensity aerobic PA to elicit modest reductions in body weight and reduce associated chronic disease risk factors. However, greater weight loss and enhanced prevention of weight regained seems to be obtained with doses of moderate intensity PA that approximate 250–300 min/week (approximately 2000 kcal/week).[15]

A clinical trial indicated that a short-term (6-months) exercise program did not lead to additional weight loss after RYGB, with weight loss of 22.0 *vs* 22.8 kg for conventional treatment and the exercise program, respectively.[16]

Furthermore, Shah et al.,[17] demonstrated that a high-volume exercise regimen (>2000 kcal·wk−1 at 60%–70 % of VO2 max) post-bariatric surgery had no discernible effect on body weight and waist circumference compared to a control group. In our opinion, in those short-term follow up studies, the absence of a discernible exercise-induced effect on weight loss is likely attributed to the significant impact of the surgery itself, being the studies carried out in the first months after surgery.

Hence, investigations with long-term follow-up period, could better clarify if, after surgery, a moderate/high level of physical activity can exert more influence on weight loss and weight-regain. This is because, over time, the impact of bariatric surgery tends to diminish after about 18 months,[1] underscoring the importance of sustained lifestyle measures in further weight maintenance.

We noticed that physical activity had a remarkable effect in maintaining body weight over a period of 5-years in subjects without T2D. This observation aligns with the findings of recent research, including a randomized controlled trial (RCT) and a retrospective 5-year follow-up

Table 2
Glycometabolic characteristics and kidney function in PA and No-PA individuals with T2D, during the 5-years of follow-up period.

Parameters	Pre-surgery	1st year	3rd year	5th year
Glycemia (mg/dl)				
No-PA	135 ± 61	105 ± 18	101 ± 26	107 ± 22
PA	124 ± 35	99 ± 31	86 ± 10*	90 ± 11
HbA1c (%)				
No-PA	7.3 ± 1.6	6.1 ± 0.8	6.0 ± 0.9	6.1 ± 1.1
PA	7.0 ± 1.1	5.5 ± 0.4*	5.4 ± 0.3*	5.6 ± 0.5*
Tot Cholesterol (mg/dl)				
No-PA	199 ± 39	184 ± 40	184 ± 35	182 ± 38
PA	188 ± 46	152 ± 29*	154 ± 39*	159 ± 27*
LDL Cholesterol (mg/dl)				
No-PA	125 ± 34	110 ± 35	105 ± 25	105 ± 33
PA	122 ± 35	87 ± 23*	83 ± 23*	86 ± 25
HDL Cholesterol (mg/dl)				
No-PA	44 ± 12	57 ± 15	63 ± 17	62 ± 20
PA	46 ± 11	53 ± 18	66 ± 18	59 ± 11
Tryglicerides (mg/dl)				
No-PA	177 ± 73	126 ± 66	108 ± 39	116 ± 48
PA	138 ± 45	95 ± 33*	96 ± 32	73 ± 25*
eGFR (ml/min/1.73m^2)				
No-PA	87 ± 20	94 ± 16	93 ± 15	89 ± 18
PA	96 ± 16	102 ± 13	101 ± 11	97 ± 16*

The comparison was conducted annually using the Mann-Whitney test.
*$p < 0.05$ PA vs No-PA group.
Abbreviations: PA, physical activity; T2D, type-2-diabetes; eGFR, estimated glomerular filtration rate.

Table 3
Glucometabolic characteristics and kidney function in PA and No-PA individuals without T2D during the 5-years of follow up period.

Parameters	Pre-surgery	1st year	3rd year	5th year
Glycemia (mg/dl)				
No-PA	90 ± 11	87 ± 14	90 ± 10	88 ± 10
PA	83 ± 12	86 ± 9	84 ± 10	87 ± 7
HbA1c (%)				
No-PA	5.8 ± 0.4	5.4 ± 0.3	5.3 ± 0.3	5.3 ± 0.2
PA	5.7 ± 0.3	5.4 ± 0.3	5.3 ± 0.3	5.3 ± 0.3
Tot Cholesterol (mg/dl)				
No-PA	175 ± 31	175 ± 31	190 ± 25	191 ± 28
PA	179 ± 38	179 ± 38	179 ± 34	178 ± 35
LDL Cholesterol (mg/dl)				
No-PA	126 ± 26	101 ± 21	114 ± 26	109 ± 23
PA	114 ± 29	107 ± 27	99 ± 27	99 ± 20
HDL Cholesterol (mg/dl)				
No-PA	52 ± 13	58 ± 17	64 ± 11	67 ± 16
PA	49 ± 12	55 ± 18	68 ± 16	68 ± 15
Tryglicerides (mg/dl)				
No-PA	125 ± 40	107 ± 47	97 ± 37	95 ± 54
PA	129 ± 53	119 ± 59	84 ± 32*	104 ± 43
eGFR (ml/min/1.73m^2)				
No-PA	100 ± 17	103 ± 13	97 ± 17	97 ± 13
PA	108 ± 13	107 ± 14	101 ± 16	101 ± 15

The comparison was conducted annually using the Mann-Whitney test.
*$p < 0.05$ PA vs No-PA group.
Abbreviations: PA, physical activity; T2D, type-2-diabetes; eGFR, estimated glomerular filtration rate.

study.[18,19]

On the contrary, in the present study, the impact of physical activity on weight loss appears to be less pronounced in individuals with T2D. Our research team previously established that, after bariatric surgery, individuals with T2D tend to experience comparatively smaller weight loss outcomes in contrast to those without diabetes.[20]

The reason why the impact of physical activity is less pronounced in T2D after surgery is not entirely clear. Hypotheses propose different endocrinological mechanisms in these individuals, such as diminished GLP-1 response, altered adipokine secretion, or greater suppression of resting energy expenditure.[21,22]

Table 4
Anti-hypertensive, anti-diabetic and anti-lipidemic treatment individuals with and without T2D during the 5-years of follow-up period.

Medications	Pre-surgery	1st year	3rd year	5th year
With T2D				
Anti-lipemic agents, n(%)				
No-PA	41 (67.2)	21 (34.4)	27 (44.3)	28 (45.9)
PA	9 (60.0)	4 (26.7)	4 (26.7)	6 (40.0)
Anti-diabetic agents, n(%)				
No-PA	18 (29.5)	14 (22.9)	18 (29.5)	22 (36.1)
PA	2 (13.3)	1 (6.7)	1 (6.7)	1 (6.7)
Anti-Hypertensive agents, n(%)				
No-PA	48 (78.7)	34 (55.7)	37 (60.7)	38 (62.3)
PA	11 (73.3)	4 (26.7)	5 (33.3)	5 (33.3)
Without ***T2D***				
Anti-lipemic agents, n(%)				
No-PA	13 (30.2)	4 (9.3)	10 (23.2)	12 (25.6)
PA	9 (31.0)	1 (3.4)	1 (3.4)	3 (10.3)
Anti-diabetic agents, n(%)				
No-PA	0 (0)	0 (0)	0 (0)	1 (2.3)
PA	0 (0)	0 (0)	0 (0)	0 (0)
Anti-Hypertensive agents, n(%)				
No-PA	21 (48.8)	8 (18.6)	12 (27.9)	12 (27.9)
PA	6 (20.7)	2 (6.9)	2 (6.9)	2 (6.9)

An overall reduction of both systolic and diastolic blood pressure values was observed for all 5-years of follow-up, in the physical activity group, both diabetic and non-diabetic; this remained significant even after adjustment for BMI. The effectiveness of physical activity on reducing systolic blood pressure has been previously reported after exercise training, although the effect of exercise was not specifically assessed in subjects underwent bariatric surgery.[23]

While in earlier studies it has been demonstrated that exercise yields greater effects when combined with weight loss,[24] there are distinct mechanisms brought about by exercise that, independently

from weight loss, contribute to reducing blood pressure. Specifically, modifications in body composition, as a decrease in visceral adipose tissue and ectopic fat, have a positive impact on the inflammatory and metabolic profile of overweight and obese individuals, resulting in beneficial effects on blood pressure regulation.[25]

In our cohort of patients the effect of physical activity on the lipid profile is rather marginal. In particular, there is no impact of physical activity on either triglycerides or HDL cholesterol. In fact, over time, we assisted a substantial stability in the triglycerides level after surgery and an increase in HDL values starting from the second year of follow up both in T2D and normoglycemic patients, without a significant impact of physical activity.

Many studies showed a significant positive impact of aerobic exercise on HDL-cholesterol but no effects either on LDL or on triglycerides.[26]

Kodama et al.[27] found that exclusive physical activity, without medications or diet intervention, increased HDL levels by 2.53 mg/dL, achieved through aerobic exercise at 5.3 MET intensity (equivalent to 64.8 % of maximal aerobic capacity).

A plausible explanation of the lack of physical activity impact on HDL cholesterol levels in the present study, is the overshadowing effect of bariatric surgery, which demonstrates an even more substantial influence on HDL over time.[28]

Furthermore, it was not observed a significant impact of physical activity over time on LDL-cholesterol levels and statin use, although patients who performed exercise tended to have lower LDL levels, both in T2D and non-diabetic groups.

The impact of exercise on LDL levels is characterized by inconsistency, and some studies even yielded entirely contradictory results.[26,29] These divergent outcomes across studies could potentially be attributed to fluctuations in individuals' body weight. In fact, some studies showed that engaging in aerobic exercise did not lead to notable alterations in blood LDL levels unless there was concurrent weight change during this period.

In the present study, even after correcting the mixed model by inserting BMI as a fixed effect, we did not find a significant impact of physical activity on LDL.

However, we did not measure the subfractions of LDL, therefore we cannot evaluate the effect on that portion of smaller and denser LDL which are correlated with an increase in cardiovascular events.

As regards the glycemic profile, we did not find a significant impact of physical activity on HbA1c over the time among non-diabetic patients, although significantly lower fasting glucose levels were found in subjects who practiced exercise.

In T2D there were slightly higher blood glucose levels in participants who did not engage in physical activity during the long-term follow-up, suggesting reduced insulin sensitivity compared to active individuals. However, the study lacked plasma insulin measurements, limiting insights into insulin sensitivity.

A single-blind randomized trial in normoglycemic patients described that moderate exercise following RYGB provided additional improvements in insulin sensitivity in the first 6-months.[16] However, in this short follow-up study, insulin resistance showed improvement despite of equivalent weight loss, as weight loss depended on bariatric surgery in the first months and not on physical activity, which could contribute to the reduced fasting glucose that we observe in the third, fourth and fifth years.

In T2D group we assisted to a progressive increase in the relapse of diabetes in sedentary patients from 25 to 33 % after the first year from surgery, while in the PA group the prevalence remained unchanged over time, suggesting that engaging in PA may be more effective in preventing recurrences of T2D, reducing the necessity of medications.

Additionally, resistance training has also shown benefits in glycemic control, insulin resistance, and fat mass reduction in non-bariatric individuals with T2D, in metanalysis including short-medium follow-up studies[30]; our results seem to be able to extend the observations to the bariatric population.

The present study has limitations that should be addressed. First, it should be recognized that, although higher levels of PA were associated with improvement in metabolic parameters it is plausible that other factors may also contribute. Individuals who engage in regular physical activity may inherently possess healthier lifestyle habits, such as better food choices, and may have higher levels of motivation or self-discipline. Therefore, although the observed correlation between physical activity and favorable outcomes is noteworthy, establishing causality requires further investigation that future research may focus on.

Secondly, self-reported activity levels present potential limitations and recall bias. While the International Physical Activity Questionnaire (IPAQ) is a validated tool widely accepted across diverse populations, including those undergoing bariatric surgery, it's crucial to acknowledge the absence of a definitive gold-standard objective method for assessing physical activity in real-life settings. Additionally, although efforts were made to ensure consistency in questionnaire administration, independent assessments of inter-rater reliability were not performed in this study. While self-reported questionnaires are commonly used due to their practicality, the use of objective measures such as accelerometry could provide more precise estimates of physical activity. However, logistical constraints and participant burden often limit their feasibility in long-term follow-up studies involving large cohorts.

Finally, extending the follow-up period beyond 5 years encompassing a larger cohort and other bariatric procedures will provide crucial insights into the enduring effects of physical activity in association with bariatric surgery, including weight loss maintenance, glycemic control, blood pressure management and the impact on major adverse cardiovascular events (MACE), chronic kidney disease (CKD) development and end-stage renal disease (ESRD). This future research will allow for a comprehensive examination of the role of physical activity in mitigating long-term health risks and optimizing patient outcomes, thereby informing tailored interventions and refining post-bariatric surgery guidelines.

In conclusion, incorporating moderate physical activity into the post-bariatric surgery lifestyle is crucial for optimizing metabolic health in individuals with or without T2D. Exercise supports weight loss and maintenance and blood pressure control, providing a range of additional health benefits that are vital for long-term well-being in patients who underwent bariatric surgery.

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

CRediT authorship contribution statement

Diego Moriconi: Writing – original draft, Conceptualization. **Laura Manca:** Methodology, Formal analysis. **Eleni Rebelos:** Writing – original draft, Investigation. **Emanuele Guidotti:** Writing – original draft, Methodology, Investigation. **Linda Bonvicini:** Investigation. **Antonio Troilo:** Investigation, Data curation. **Marco Anselmino:** Investigation. **Monica Nannipieri:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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