Asociatia Romana de Balneologie

Research article

Effects of Physical Activity on Patients With Diabetes Type 2: A Systematic Review

Bojan Bjelica ¹, Nikola Aksović ², Saša Bubanj ³, Milan Zelenović ¹, Mima Stanković ³, Lazar Pajović ¹, Ilma Čaprić ⁴, Oliver Radenković ⁴, Izet Kahrović ⁴, Benin Murić ⁴, Raid Mekić ⁴, Omer Špirtović ⁴, Vladan Milić ⁴, Emir Bilalović ⁵, Tatiana Dobrescu ⁶

Citation: Bjelica B., Aksović N., Bubanj S., Zelenović M., Stanković M., Pajović L., Čaprić I., Radenković O., IKahrović I., Murić B., Mekić R., Špirtović O., Milić V., Bilalović E., Dobrescu T. - Effects of Physical Activity on Patients With Diabetes Type 2: A Systematic Review Balneo and PRM Research Journal 2024, 15(3): 719

Academic Editor(s): Constantin Munteanu

Reviewer Officer: Viorela Bembea

Production Officer: Camil Filimon

Received: 10.06.2024 Published: 25.09.2024

Reviewers:

Mihai Hoteteu Elena Amaricăi

Publisher's Note: Balneo and PRM Research Journal stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

(cc) BY-NC-ND

Copyright: © 2024 by the authors. Submitted for open-access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://crea-tivecommons.org/licenses/by/4.0/).

- Faculty of Physical Education and Sport, University of East Sarajevo, 71420 Pale, Bosnia and Herzegovina (vipbjelica@gmail.com; milan-zeleni13@gmail.com; lazar.pajovic@yahoo.com);
- 2 Faculty of Sport and Physical Education, University of Priština–Kosovska Mitrovica, 38218 Leposavić, Serbia (kokir87np@gmail.com);
- 3 Faculty of Sport and Physical Education, University of Niš, 18000 Niš, Serbia (bubanjsale@gmail.com; mima.stankovic974@gmail.com);
- 4 Department of Biomedical Science, State University of Novi Pazar, 36300 Novi Pazar, Serbia (icapric@np.ac.rs; oradenkovic@np.ac.rs; ikahrovic@np.ac.rs; bmuric@np.ac.rs; rmekic@np.ac.rs; ospirtovic@np.ac.rs; vmilic@np.ac.rs);
- 5 Department of Internal Medicine, Medical Centre Novi Pazar, 36300 Novi Pazar, Serbia (emirbilalovic8@gmail.com);
- 6 Department of Physical Education and Sport Performance, Vasile Alecsandri University, 600115 Bacau, Romania (tatiana.dobrescu@ub.ro).
 - * Correspondence: mima.stankovic974@gmail.com

Abstract: The aim of the research was to collect and to examine the positive effects of various physical activity (PA) programs on individuals with type 2 diabetes mellitus (T2DM). This included a combination of aerobic exercises and resistance training, with varying intensities, in order to compare which approach yielded better outcomes for T2DM management; This systematic review was conducted in line with PRISMA guidelines, focusing on the period from 1991 to 2024. Studies included in this review involved both experimental procedures and questionnaire-based surveys to assess the impact of PA on T2DM patients. The primary outcome was the effect of PA on T2DM, with secondary outcomes including changes in blood pressure, cholesterol levels, and glycemic control; A total of 23 studies, encompassing 1752 participants (515 men, 546 women, and 691 unspecified), met the inclusion criteria. The studies highlighted the positive effects of exercise, such as improvements in glycemic control, insulin sensitivity, and lipid profiles. Most studies recommended a combination of aerobic and resistance exercises performed 3-4 times per week for 30-60 minutes per session; This systematic review confirms that regular PA is instrumental in managing T2DM. Health care providers should integrate PA programs into treatment plans for T2DM patients to optimize glycemic control and overall health outcomes.

Keywords: DM type 2, intensity, exercise, insulin, glycemic, obesity

1. Introduction

About 442 million people worldwide live with diabetes, and type 2 diabetes mellitus (T2DM) accounts for 90% of the total percentage [1]. T2DM represents a set of metabolic changes with different etiologies characterized by chronic hyperglycemia associated with changes in glucose, lipid, and protein metabolism due to insulin deficiencies [2]. Risk factors for developing T2DM include obesity, physical inactivity, smoking, and age. Diabetes is more common among certain ethnic and racial minorities. The majority of people suffering from T2DM do not exercise any type of physical activity (PA), so the daily values of energy consumption are significantly lower compared to people without the presence of any disease [3,4]. Lack of PA and a sedentary lifestyle represent separate risk factors for the development of cardiovascular diseases as well as increased mortality rates in patients with T2DM [5,6]. With today's increasing risk factors, the promotion of

PA is one of the basic priorities of public health [2]. PA is one of the most important therapeutic steps in the treatment of people suffering from T2DM [7,8,9] and one of the best types of non-pharmacological treatment [10]. Regular physical exercise is an effective tool in improving glycemia, reducing insulin resistance and stimulating insulin secretion [7]. Previous research has shown that aerobic exercise has the best effects compared to other forms of PA. The best type of aerobic activity implies activity that lasts constantly and has a low intensity. This type of activity includes walking, running, cycling, swimming, etc. The exercises themselves are the result of increased activity of the cardiopulmonary system and greater endurance capacity [11]. During exercise, the need for energy consumption increases. The most effective intensity of aerobic activities depends on the individual characteristics of the patient with T2DM, but it is recommended that it be from 55% to 85% of the maximum heart rate [12]. Recent trends in physical activity have introduced promising approaches such as high-intensity interval training (HIIT) and technology-assisted exercise programs. HIIT, which involves short bursts of intense exercise followed by recovery periods, may offer more effective improvements in glycemic control compared to traditional moderate-intensity exercise. Additionally, technology-assisted programs like fitness trackers and mobile apps can enhance engagement and adherence to exercise routines, potentially leading to better management of T2DM.

The aim of the research was to collect and to examine the positive effects of various PA programs on individuals with T2DM. To realize the set aim, the following tasks were performed:

- Searching electronic databases;
- Review and translation of collected literature;

2. Materials and Methods

The systematic review of the papers was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) standards [13].

2.1 Search Strategy

The electronic search of papers included the following search databases: MEDLINE, Google Scholar, PubMed and other relevant literature that could answer the set problem. The papers published in the period 1991-2024 were analyzed. The search was performed using a combination of keywords, primarily related to T2DM and aerobic activities. The keywords used to search the databases are: "intensity", "exercise", "insulin", "glycemic", "obesity". For the purposes of the research, a descriptive method was used.

2.2 Criteria for inclusion

Study type: Longitudinal and transversal studies were analyzed and included for further analysis.

Sample of participants: The study included men and women with an average age of 50.9 years, regardless of lifestyle (active and sedentary population) and health status.

Type of intervention: Papers in which an experimental procedure was used, as well as papers where information was obtained based on filling out a questionnaire, were included.

Type of outcome: The primary outcome of the search was the effects of PA on T2DM after implementation of a program; while the secondary result was information obtained based on the statements of T2DM patients based on questionnaires (obese, normally fed), data on blood pressure, cholesterol, insulin, glycemic control, and the like.

The search for relevant research was conducted by B.B. The language of the research was not a criterion for the selection of studies. The age limit of participants (50.9) was considered because this age group is most exposed to the negative effects of T2DM, and physical activity is an exceptionally necessary and effective means for controlling T2DM compared to medication.

2.3 Criteria for exclusion

- Duplicates;
- Conference abstracts;
- It was a systematic review research;
- Inappropriate frame of analysis in the period between 1991-2024 years;
- These were people who did not suffer from T2DM.

Selection criteria were carefully defined to include longitudinal and cross-sectional studies with rigorous methodologies. Although a meta-analysis was not performed, the study critically assessed the quality of the included research and noted that dietary interventions, when combined with physical activity, often contributed to better outcomes in managing T2DM. The review also acknowledged potential limitations such as variability in sample sizes and study designs.

3. Results

The procedure of collection, analysis and elimination of the found papers is shown in Figure 1. After a general search of the source databases, 317 potential researches were identified. After deleting duplicate papers based on titles and analyzed abstracts and other reasons, 81 papers remained. Based on the other criteria, 58 papers were excluded, and 23 researches that were included in the systematic review met the set criteria and conditions.

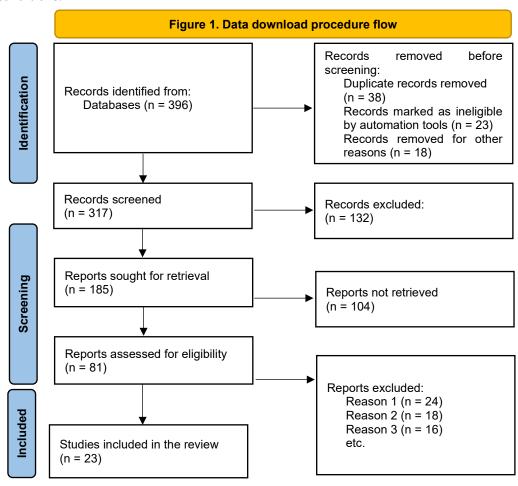


Figure 1. Flow chart diagram of the study selection.



Table 1. Systematic review of the effects of various PA programs on individuals with T2DM.

Reference	Population	Grouping	Treatment	Protocol		The results
Segal et al. (1991) [21]	♂ 25-40 yo T2DM	G1=10 G2=10 G3=6 NA <2y	G1 - normally fed- G2 - obese G3-DM2 BER, 70%	TT - 12 w, 4h p/w 70 min.	INS, GK, BIA, Calorimetry, VO2max	KSF-27%↑everyone. GK-G1= 5.33 t, 0.39 mg kg; G2= 9.07 t 0.49 and 8.91 - + 0.60 mg; G3= 3.86 t 0.44 and 3.49 t 0.21 GKI-22%↓INSr =G2, G3 x FA=VO2max+, INS/INSr -
Yamanouchi et al. (1995) [22]	ී 23-59yo T2DM	G1=10; G2=14 NA	G1 - 10,000 st/pd on flat ground, followed by a pedometer. 19 200 +/- 2100 st/pd + diet G2 – SA 4,500 +/- 290 st/pd + diet	TT – 6/8 w, number st/pd Movement INS 720 to 790 pmol / l.	BW, GK infusion, Metabolic clearance, Pedometer	BW-G1=4.2 \downarrow G2=7.8 \downarrow Blood GK before G1=0.8 \downarrow G2=0.9 \downarrow Blood GK after G1=0.6 \downarrow G2=0.8 \downarrow INSp before G1=34 \downarrow G2=57 \downarrow INSp after G1=13 \uparrow G2=51 \downarrow FA=BW+INS+
Ligtenberg et al. (1997) [23]	∂ ♀ 55- 75yo T2DM	G1=30(♂20, ♀10) G2=28 (♂18, ♀10)	G1 - 60-80% of VO2max at BER, TGY, CHL	TT – 14 w, 3 p/w Measurement 6/12/26	INS, HbAlc, CHL, LDL, HDL, VO2max, TGY, APT AI, APT B	HbAlc/6w G2=0.2 ¹ 2w/ G2=0.2 ² 6w/ G2=0.3 ¹ Total CHL/6w G2=0.1 ¹ 2w/ G2=0.3 ² 6w/ G1/G2=0.0 LDL/6w G2=0.1 ¹ 2w/ G2=0.1 ² 6w/ G1/G2=0.0 ¹ HDL/6w G1=0.03 ¹ 2w/ G1=0.04 ² 6w/ G2=0.01 ¹ Total TGY/6w G2=0, 3 ¹ 2w/ G2=0. 4 ² 6w/ G1/G2=0.0 APT AI 6w/ G1/G2=0.0 ¹ 2w/ G1=0. 1 ² 6w/ G1=0.1 ¹ APT B /6w G2=0.0 3 ¹ 12w/ G2=0.03 ² 6w/ G2=0.0 3 ⁵ FA=CHL+, TGY+ INS-
Tuomilehto et al. (2001) [24]	♂♀55yo T2DM	G1=265; G2=257 ♀350 ♂172	G1 - diet G2 – exercise+advice for fat intake, UH, PT, fiber intake, FA	TT – 3.2 y Measurement 1/2/3	BW,Change in plasma GK, Change in serum INS (mg/ml),CHL, High- density lipoprotein, CHL, TGY, SP, DP	BW-G1=3.4↓Change in plasma GK-G1=3.1↑Change in serum INS (mg/ml) G1=3.0↑ CHL-G1=2.0↓Highdensity lipoprotein CHL G1=1.0↑TGY G1=17.0↑Systolic p. G1=4.0↑Diastolic p. G1=2.0↑FA= BW +, DM2 +
Maiorana et al. (2001) [25]	♂♀52yo T2DM	♀1 4 ♂2	G1 - Trainers+ BER 70% - 85. Load always kept between 55% - 65% G2 - untrained	TT – 8 w, frequency /	HB, CHL, LDL, HDL, TGY, GK, HB, Fasting blood GK (mmolzl), MAP (mm Hg), Resting HR (beats/min)	CHL-G1/G2=0.0 LDL-G1=0.1↑HDL-G1=0.1↑TGY-G1=0.5↑Glycated HB G1=0.6↓Fasting blood GK (mmolzl) G1=2.2↓MAP (mm Hg) G1=2.0↑Resting HR (beats/min) G1=4.0↓FA= HB + Fasting blood GK +

Ishii et al. (2001) [26]	♂ ⊊56- 57.9 T2DM	G1=23 (9♀, 14♂); G2=27(11♀, 16♂)	G1 – WK + BER 50%. G2 - diet			BW (kg) G1=2.8 \downarrow G2=2.5 \downarrow Body fat (%) G1=2.3 \downarrow G2=1.5 \downarrow Ventilatory threshold (mL/kg/min)= G1=1.4 \uparrow G2=x Fasting INSp (pmol/L)= G1=8.9 \downarrow G2=4.7 \downarrow Cortisol (mmol/L)= G1=0.12 \downarrow G2=0.11 \downarrow Urinary 17-OHCS excretion (mg/m2/d)= G1=0.5 \downarrow G2=0.5 \downarrow FA= Leptin in serum, BW+, Fasting plasma INS (pmol/L) +
Castaneda et al. (2002) [27]	♂ ♀ 66 +/- 8 T2DM	62 (40♂ 22♀) Randomized EG and KG	G1 - pneumatic training, 60-80%, G2 - SA	TT - 16 w, 3 p/w	Plasma GK, HB concentrations (%), Muscle glycogen stores (mmol GK/kg muscle), Serum TGY concentrations (mmol/l), HDL, LDL	Plasma GK HB concentrations (%)= $G1=1.1\downarrow G2=0.1\downarrow Muscle$ glycogen stores (mmol GK/kg muscle) = $G1=18.8\uparrow G2=14.2\downarrow Serum$ TGY concentrations (mmol/l)= $G1=0.21\downarrow G2=0.11\uparrow HDL$ $G1=0.07\downarrow G2=0.01\uparrow LDL$ $G1=0.24\downarrow G2=0.34\uparrow FA=HB$ +, glycogen +, BW +
Loimaala et al. (2003) [28]	♀53.3 +/- 5.1 T2DM	G1=24♀ G2=25♀	G1 - Running, WK 65– 75%, session 8 resistance exercises 10-12 repetitions 70–80% - 2 months G2- SA	TT - 12 w 2 p/w	VO2max (ml/kgl/min), HbA1c, BRS (ms/mmHg), GK	VO2max (ml/kgl/min) G1=1.9 \uparrow G2=0.8 \downarrow HbA1c G1=0.6 \downarrow G2=0.3 \uparrow BRS (ms/mmHg) G1=1.8 \uparrow G2=1.1 \downarrow FA= Baroreflex sensitivity+, GK control +, muscle strength +
Čizmić et al. (2003) [29]	♀ 47+/- 1.2 T2DM	G1=10♀ G2=10♀	G1 - WK on the tape 5x35min. 45-75% G2-no activity+diet	TT – 14 w, 10 sessions	VO2max, INS, M component (ml/kgl/min), INS mU/l, Basal insulinemia	Hyperinsulin plateau G1= 12.7% \downarrow G2= 2.91% \uparrow INS G1= 13.7 \downarrow G2= 19.19 \downarrow Basal insulinemia G1= 17.05 \downarrow G2= 14.41 \downarrow FA=aerobic capacity + INS +
Kirk et al. (2003) [30]	♂♀57.6± 7.9 T2DM	35♂35♀ G1=35♂♀, G2=35♂♀	G1 - Transtheoretical exercise model, questionnaire	TT - 6 months, monitored every 7 days	HbA1c, Lipid profile, Fibrinogen, HDL, LDL BP, BMI, VO2max	VO2max= $G1=30.8 \uparrow G2=185.8 \downarrow HbA1c=G1=0.31 \downarrow G2=0.37 \uparrow HDL$ $=G1=0.05 \uparrow G2=0.03 \uparrow LDL=G1=$ $0.10 \downarrow G2=0.01 \uparrow TGY \text{ (mmol/l)}=$ $G1=0.20 \downarrow G2=0.07 \downarrow \text{Fibrinogen (mg/dl)}=$ $G1=3.59 \downarrow G2=21.53 \uparrow$ FA= INS Control +, Patient Health +, Fibrogen +, Blood Pressure +
Yokoyama et al. (2004) [14]	♂♀53.0±1 2.2 T2DM	23(6♂ 17♀) G1=7♂♀ G2=8♂♀ G3=8♂♀	EG – BER 40x5, 40–60% + WK, recommendations 10,000 st/pd, 50%	TT – 3 w	BF %, FPG (mmol/l), HbA1c (%), TGY (mmol/l), HDL (mmol/l)	BF %=G1=45.0 G2=41.9 G3=37.4 FPG (mmol/l)= G1=7.7 G2=7.9 G3=7.8 HbA1c (%)=G1=8.1 G2=8.5 G3=9.0 TGY (mmol/l)= G1 =1.13 G2=1.29 G3=1.56

						HDL (mmol/l)= G1=1.32 G2=1.11 G3=1.19 FA= INSr+, Reduction of arterial stiffness +
Araiza et al. (2006) [31]	♂♀52±20. 1 T2DM	G1=15♂♀ G2=15♂♀	G1 - 10000 st/pd followed by a pedometer G2-SA	TT - 6 w, 5 p/w	BF %, HbA1C (%), GK (mg/dL), INS (lU/mL), TGY (mg/dL), HDL(mg/dL), LDLC(mg/dL)	BF %= G1=0.6 \downarrow G2=0.1 \uparrow HbA1C (%)=G1=0.2 \uparrow G2=0.1 \uparrow GK-(mg/dL)= G1=1.3 \downarrow G2=2.1 \downarrow INS (IU/mL)= G1=2.0 \downarrow G2=0.3 \downarrow TGY (mg/dL))= G1=23.8 \downarrow G2=9.5 \uparrow HDL (mg/dL)= G1=3.9 \uparrow G2=0.9 \uparrow LDLC(mg/dL))= G1=9.2 \uparrow G2=12.9 \downarrow FA=Plasminogen activator inhibitor +, Therapeutic effects +
Brooks et al. (2006) [32]	♂55 +/- 6 T2DM	62♂ G1=31♂ G2=31♂	G1 - trainers, upper back, chest press, leg press, knee extension and flexion 3x8 repetitions 60- 80% G2-SA	TT - 16 a, 3 p/w x35min	GK, HB Concentrations (%), GK (mmol/L), INS (pmol/L), Adiponectin (µg/mL)	GK HB Concentrations (%) =G1=1.1 \downarrow G2=0.5 \uparrow GK (mmol/L) = G1=0.9 \downarrow G2=0.4 \downarrow INS (pmol/L)= G1=16.0 \downarrow G2=6.0 \uparrow Adiponectin (μ g/mL)=G1=1.3 \downarrow G2=0.4 \uparrow FA=MK +, DM2r+
Manders et al. (2010) [17]	♂57 +/- 2 T2DM	G1=∂9	G1 - 3 x, 60 min at low intensity LI 35%, 30 min at high intensity 70% HI,	TT - Monitoring parameters after a 24-hour period from the start of exercise	GK (mmol/L), Hyperglycemia (%24h)	G1=GK (mmol/L)=LI 1.6↓G1=Blood GK 24h= LI+HI 0.8↓G1=Hyperglycemia (%24h) NI 35%↓G1=Hyperglycemia (%24h) LI 49.7%↓G1=Hyperglycemia (%24h) HI 18.6%↓G1=FA= reduction of hyperglycemia + LI +
Yavari et al. (2010) [33]	♂52.5±20 T2DM	65♂ G1=35♂ G2=30♂	G1 – aerobic training, 50- 80% VO2max G2–SA	TT - 16 w, 3 p/w 90 min	GK HB A1c, BMI, BP	GK HB A1c = G1=0.73↓G2=0.28↑ FA= GK HB A1c+
Bello et al. (2011) [34]	ී46.22 ± 9.79 T2DM	්18 G1=9∂ G2=9∂	BER 50%-75% 10–20W after 3 min. + 5–10W WHOQoL-BREF	TT – 8 w, 3 p/w, 30 min	Fasting blood sugar (mmol/L), GK HB (%), High-density lipoproteins (mmol/L), Low-density lipoproteins (mmol/L), QOL (%)	Fasting blood sugar (mmol/L)= $G1=0.35\downarrow G2=0.48\downarrow GK$ Hemoglobin (%)= $G1=0.18\uparrow G2=0.18\downarrow High$ -density lipoproteins (mmol/L)= $G1=0.12\uparrow G2=0.08\uparrow Low$ -density lipoproteins (mmol/L)= $G1=0.03\downarrow G2=0.11\downarrow Quality$ of life (%)= $G1=4.21\uparrow G2=2.84\downarrow FA=GK+$, Lipoprotein
Moura et al. (2014) [35]	♂51.1 ± 8.2 T2DM	්8 ්G1/G1.1	G1/G1.1 – VO2max consumption 50 - 60%	TT – 8 w, 3 p/w, 30 – 60 min	BF %, BW (kg), A1C (%), FPG (mg/dL), Peak VO2 (ml.kg.min-1)	BF %= G1/G1.1 =1.0 \downarrow Fat mass (kg) = G1/G1.1 =1.2 \downarrow A1C (%)= G1/G1.1 = 0.6 \downarrow FPG (mg/dL)= G1/G1.1 =15.5 \downarrow Peak VO2 (ml.kg.min-1)= G1/G1.1 =3.8 \uparrow FA= VO2max +, reduced dose of drugs +

Ruffino et al. (2017) [36]	♂55±5 T2DM	ి16 ిG1/G1.1	G1/G1.1- 40-55%	TT - 8 w REHIT; WK 8 w	BW (kg), VO2max (L·min- 1), Glucose (mM), Insulin (mU·L-1), TG (mM), LDL, HDL, Plasma ALT (U/L)	BW (kg)= G1/G1.1 REHIT =0.3↑VO2max (L·min-1)= G1/G1.1 REHIT =0.19↑Glucose (mM)= G1/G1.1 REHIT =x Insulin (mU·L-1)= G1/G1.1 REHIT =0.1↑ Triglycerides (mM)= G1/G1.1 REHIT =0.1↓LDL= G1/G1.1 REHIT =0.3↑HDL= G1/G1.1 REHIT =0.1↑ Plasma ALT (U/L)= G1/G1.1 REHIT =x BW (kg)= G1/G1.1 WK =0.2↑VO2max (L·min-1)= G1/G1.1 WK =0.2↑Glucose (mM)= G1/G1.1 WK =x Insulin (mU·L 1)= G1/G1.1WK =4.0↑Triglycerides (mM)= G1/G1.1WK =0.1↓LDL= G1/G1.1 WK=0.2↓HDL= G1/G1.1 WK =x Plasma ALT (U/L)= G1/G1.1 WK =1.0↑FA=Aerobic a. +, INS -, GK -
Najafipour et al. (2017) [37]	57.2±8.3 T2DM	♂♀65 G1=♂♀30 G2=♂♀30	Treadmill, elliptical or BER, 50-80%	TT - 8 y, 3 p/w, 40-50 min 16/52/3y/6y	BMI, HbA1c, Post-VO2 max	BMI=G1/16m=0.58 \downarrow G1/52m=1.2 \downarrow G1/4y=1.58 \downarrow G1/6y =1.84 \downarrow BMI=G2/16m=0.05 \uparrow G2/52m=0.88 \uparrow G2/4y=1.03 \uparrow G2/6y=1.83 \uparrow HbA1c=G1/16m=0.73 \downarrow G1/52m=1.31 \downarrow G1/4y=1.13 \downarrow G1/6y=1.84 \downarrow HbA1c=G2/16m=0.28 \uparrow G2/52m=0.15 \uparrow G2/4y=0.02 \uparrow G2/6y=0.3 9 \uparrow Post-VO2 max G1=12.97 \uparrow , G2=12.97 \downarrow FA=BMI +, HbAlc +, VO2max +
Magalhães et al. (2019) [38]	58.4±1.1 T2DM	♂♀80 G1=♂♀27 G2=♂♀28 G3=♂♀25	G1=KG; G2=T moderate continuous training; G3=high intensity interval training 40-60%/up to 90%	TT - 1y, 3 p/w	SBP (mmHg), DBP (mmHg), CF PWV (m/s), CD PWV (m/s), CR PWV (m/s), VO2peak (ml/kg/min)	SBP (mmHg)=G1=5.9 \downarrow G2=4.7 \downarrow G3=7.1 \downarrow DBP (mmHg)=G1=2.7 \downarrow G2=3.0 \downarrow G3=5.7 \downarrow CF PWV (m/s)=G1=0.9 \uparrow G2=1.0 \uparrow G3=0.7 \uparrow CD PWV (m/s)=G1=1.3 \uparrow G2=0.2 \downarrow G3=1.1 \downarrow CR PWV (m/s)=G1=0.1 \uparrow G2=0.6 \downarrow G3=1.2 \downarrow VO2peak (ml/kg/min)=G1=1.1 \downarrow G2=1.1 \uparrow G3=1.0 \downarrow
Verboven et al. (2020) [39]	57 ± 3 T2DM	ੋਂ 29 G1=ਹੈ 15 G2=ਹੈ 14	G1 - 15 (final 12) FA before breakfast G2-14 (final 13) FA after breakfast 25 min. st/pd room, 25min. bike at 65%	TT - 12 w, 3 p/w	BW, kg, VO2 peak, ml*min1, VO2 peak, ml*min-1*kg-1 (FFM), HbA1c, %, LDL mg*dl-1, HDL mg*dl-1, GK, mg*dl -1, INS, mIU*L-1	BW, kg=G1=0.5 \downarrow G2=0.7 \downarrow VO2 peak, ml*min-1=G1=18.0 \uparrow G2=186.0 \uparrow VO2 peak, ml*min-1*kg-1 (FFM)=G1=0.2 \uparrow G2=3.0 \uparrow HbA1c,%=G1=0.3 \downarrow G2=0.3 \uparrow LDL cholesterol, mg*dl-1=G1=3.0 \uparrow G2=2.0 \downarrow HDL cholesterol, mg*dl-1=G1=1.0 \uparrow G2=1.0 \uparrow GK mg*dl-1=G1=7.0 \downarrow G2=6.0 \downarrow INS, mIU*L-1=G1=1.4 \uparrow G2=2.1 \downarrow FA=HbA1c+, VO2+
Ahmad et al. (2021)	49±2 T2DM/x T2DM	♂♀300 G1=150 G2=150	G1/G1 – High PA, Moderate PA, Low PA	TT – 6m	FBS, MET, IPAQ-S	FBS ≥ 126mg/dl ; High PA 3.19 (0.69-14.74), Moderate PA 3.84 (1.18-12.42), Low PA 18.01 (6.45- 50.26)

Г1	E 1
LI	J.

Eshete et al. (2023) [16]	45±50 T2DM	♂♀216 G1=108 G2=108	G1- vigorous intensive work-related; walking or bicycle 10 min.; brisk walking 30 min.= 150 min of moderate-intensity aerobic exercise; G2-usual care by the healthcare provide	TT – 6m, 30-50 min., 3-5 p/w	GK, GKc, FBS	FBS/G1=18.96 mg/dl↓; FBS/G2=2.04 mg/dl↑
------------------------------------	---------------	---------------------------	--	---------------------------------	--------------	---

[♂] male gender; ♀ female gender; G1/G2 group one/group two; T2DM diabetes mellitus-type 2; BIA body composition; st steps; pd per day; BW body weight; CHL cholesterol; TGY triacylglycerols; QOL quality of life; SA standard activity; APT Apolipoprotein; BER bicycle ergometer; WK walking; BF body fat; NA no activity; AQ survey questionnaire; KSF cardiorespiratory fitness; HB hemoglobin; MK metabolic control; DM2r reducing the risk of type 2 diabetes; GK glucose, GKl glucose in the liver; INS insulin; INSr insulin resistance; INSp insulin in plasma; TT protocol;SBPsystolic pressure; DBP diastolic pressure; BP blood pressure; IW interview; FBS fasting blood sugar



The total number of participants included in this study was 1752 of the participant, of which it is 515 male participants, 546 of the female sex, while code 691 participants did not present a clear number of men and women in the frame studies. The average duration of experimental treatments, excluding longitudinal studies, lasted 15.7 weeks, the shortest in the research [14], lasting three weeks, and the longest in the papers for 24 weeks [15,16]. In the author's study [17], certain parameters were monitored after a 24-hour period from the start of exercise. Within the research, the Table 1 shows three papers that were of great importance due to the subjective assessment of subjects suffering from T2DM [18,19,20]. The a forementioned research used survey questionnaires as an experimental procedure. In the study, the influence of factors such as age, gender, and the presence of comorbidities on the effectiveness of physical activity (PA) in managing T2DM was considered. Older individuals and those with additional health issues may exhibit varying responses to PA due to physiological changes and the complexity of their health conditions. Gender also plays a significant role in the variability of responses to different types of exercise, which can impact diabetes management outcomes. The analysis indicated that tailoring PA to individual characteristics could enhance results, highlighting the need for personalized exercise programs. Additionally, the study emphasized the importance of further research to better understand how these factors affect PA effectiveness and to optimize treatment strategies for T2DM patients.

4. Discussion

In the majority of studies, exercise protocols and forms of exercise and their effects on T2DM patients were presented. As the content of experimental programs, a combination of weight-bearing exercises and aerobic programs such as walking or running is most often used. Changes in the level of glycemia, insulin, changes in LDL and quality of life based on indirect indicators are evident [40,41,42]. The weekly training frequency was 3-4 times, which corresponds to the guidelines for regular PA [43], while the duration was between 30-60 minutes, which corresponds to the laws of aerobic work [44,45]. Within the program that was implemented in home conditions, in addition to the use of additional load, in most studies the diet is advised.

4.1 Mechanisms of action of PA on patients with T2DM

PA plays a key role in increasing insulin sensitivity, which significantly contributes to the control of blood glucose levels [46]. Insulin sensitivity refers to the ability of cells in the body to efficiently respond to insulin and transfer glucose from the blood into the cells. Increased sensitivity to insulin results in better regulation of blood glucose levels and a reduction in the risk of developing T2DM [47]. PA has several positive effects on insulin sensitivity, including increasing muscle mass, activating insulin receptors, and reducing adipose tissue [48]. During exercise, the muscles use glucose as fuel, thus reducing the level of glucose in the blood. This increases the need for glucose and promotes increased sensitivity to insulin. The activity promotes the activation of insulin receptors on the cells, facilitating the entry of glucose into the cells and reducing blood glucose levels [44]. Regular PA also helps reduce fat deposits, especially visceral adipose tissue, which is associated with insulin resistance [49,50]. PA plays a key role as a strategy for controlling blood glucose levels. It contributes to the regulation of blood glucose levels by promoting the entry of glucose into muscle cells and reducing insulin resistance. In addition, regular PA can significantly reduce the risk of developing T2DM, contributing to increased sensitivity to insulin and better control of blood glucose levels.

PA has a significant impact on metabolism, including energy consumption and the burning of glucose as fuel. When we exercise, muscles use energy in the form of ATP (adenosine triphosphate) to do work. Depending on the intensity of exercise, muscles use different energy sources. During low-intensity exercise, the body uses mostly fatty acids from fat. However, during high-intensity exercise, glucose becomes the main source of energy [50]. This adaptation enables the efficient use of available energy sources according to the body's needs during exercise.

In addition, regular PA increases muscle mass and muscle metabolism, contributing to increased calorie consumption even at rest. Muscle is a metabolically active tissue that consumes energy even while we are at rest, which contributes to the total caloric expenditure during the day [51]. Increased muscle mass improves metabolism, which facilitates weight maintenance and glucose metabolism. In addition, PA increases insulin sensitivity, which contributes to better control of blood glucose levels. Increased sensitivity to insulin facilitates the entry of glucose into cells, thus reducing the risk of developing insulin resistance and T2DM [48]. Through PA, the body achieves a better balance between energy intake and consumption. This process is critical for maintaining body weight and preventing obesity, a common risk factor for developing T2DM [52].

PA plays a key role in reducing insulin resistance, which can significantly reduce the risk of developing T2DM [53]. According to Ahmad and associates [15], we can conclude that PA reduces the risk of T2DM, which strongly emphasizes the importance of promoting PA to reduce the prevalence of T2DM. In addition, it has been shown that a PA enhancement program increases patient compliance and glycemic control significantly [16]. Endurance exercise training in the fasting or nourished condition has the same effectiveness in reducing fat mass, increasing fat oxidation capacity, increasing cardiorespiratory fitness and HDL concentrations, and lowering the risk of hypoglycemia in male T2DM [39]. Insulin resistance is a condition in which cells in the body do not respond effectively to insulin and do not absorb glucose from the blood to use it as a source of energy. PA stimulates greater energy consumption and increases muscle mass, which directly affects the reduction of insulin resistance. Activity helps with better weight management and reduction of visceral fat, which is associated with insulin resistance [54]. Increased sensitivity to insulin enables the body to respond more effectively to insulin and better regulate blood glucose levels. Studies have shown that regular PA can reduce the risk of developing T2DM by around 40-50%. Activity increases insulin sensitivity, stimulates metabolism, and helps maintain a healthy body weight, which are key factors in the prevention of T2DM [55,56]. In addition, PA can contribute to better functioning of the pancreas, which produces insulin. Regular exercise has been linked to improved function of the insulinproducing beta cells of the pancreas. This is important because damaged beta cells are associated with the development of T2DM [48,57].

4.2 Positive metabolic effects of PA combined with nutrition on patients with T2DM

PA and proper nutrition have a significant synergistic effect on the control of blood glucose levels, especially in people with diabetes or a predisposition to the development of T2DM. This combination contributes to better regulation of glycemia and can significantly affect the long-term state of health [58]. Regular PA increases insulin sensitivity, which facilitates glucose uptake into cells and lowers blood glucose levels [59]. PA also helps maintain a healthy body weight and reduce visceral fat, which is important for controlling insulin resistance. Proper nutrition with a focus on balanced consumption of carbohydrates, proteins and healthy fats contributes to a stable level of glucose in the blood during the day. The synergistic effect of PA and proper nutrition lies in their ability to jointly influence glucose regulation [60]. Exercise improves the absorption of glucose in muscles during and after activity, while proper nutrition provides an adequate source of fuel for muscle cells and prevents a sudden rise in glucose levels after a meal [61]. Research has shown that the combination of

regular PA and proper nutrition can significantly improve glycemic control, reduce the need for medication, improve lipid profile and blood pressure, and reduce the risk of developing diabetes complications [24,48,50,62-65].

Regular exercise plays a key role in maintaining a healthy body weight and reducing the risk of obesity [66]. The combination of cardiovascular exercises, strength and flexibility contributes to increased calorie consumption and improves muscle mass, which helps to control body weight. PA stimulates metabolism and calorie expenditure, which can lead to the loss of extra pounds and maintenance of optimal body weight [52]. Adequate nutrition plays a key role in controlling blood sugar levels. Consumption of healthy foods with a low glycemic index, a balanced intake of carbohydrates, proteins and healthy fats, and control of sugar intake have a significant effect on blood glucose levels. A controlled diet prevents a sudden rise in blood sugar, thereby maintaining stable glycemia and reducing the risk of T2DM [67,68].

Research has shown that the combination of regular exercise and adapted diet is very effective in controlling body weight and blood glucose levels. PA promotes calorie burning, while proper nutrition ensures adequate nutritional intake. The synergistic effect of this combination helps maintain a healthy body weight and optimal glycemia [69,70]. Continuous PA and proper nutrition have long-term health benefits. Maintaining a healthy weight reduces the risk of a variety of chronic diseases, including heart disease, T2DM, and osteoarthritis. At the same time, an adapted diet low in saturated fat and rich in fiber has a favorable effect on glucose metabolism and insulin sensitivity [71,72].

PA has a significant impact on the lipid profile, blood pressure and other risk factors for heart disease in patients with T2DM. Regular exercise leads to increased sensitivity to insulin, weight loss, improvement of lipid metabolism and reduction of blood pressure. These positive effects help control and reduce the risk of heart disease in people with T2DM [73]. Regarding the lipid profile, regular PA leads to an increase in the level of "good" HDL cholesterol and a decrease in the level of "bad" LDL cholesterol, thereby reducing the risk of atherosclerosis and heart disease [74]. In addition, exercise contributes to the reduction of triglycerides in the blood, which is also important for heart health [75].

When it comes to blood pressure, regular exercise can reduce high blood pressure (hypertension), which is a common problem in people with T2DM. PA strengthens the heart, improves circulation, and reduces strain on blood vessels, thereby lowering blood pressure [76]. Nutrition also plays a key role in controlling the lipid profile and blood pressure in people with T2DM. Dietary recommendations include reducing the intake of saturated fat, trans fat and cholesterol, and increasing the intake of fiber and omega-3 fatty acids [77].

4.3 Main Findings of the Research

The results of the systematic review show that regular physical activity (PA) has a significant positive impact on glycemic control and overall health in patients with type 2 diabetes mellitus (T2DM). The most commonly used forms of exercise in experimental programs include a combination of aerobic exercises, such as walking or running, and resistance exercises. These programs have demonstrated improvements in glycemia levels, insulin sensitivity, reductions in LDL cholesterol, and enhanced quality of life for patients. The recommended frequency of exercise was 3-4 times per week, with a duration of 30 to 60 minutes per session, aligning with the guidelines for regular physical activity and the principles of aerobic work.

Furthermore, PA has been shown to significantly increase insulin sensitivity, which is crucial for regulating blood sugar levels. In most studies, the combination of exercise with a recommended diet further contributed to better control of glucose levels and a reduction in the need for medication. The studies also indicated that programs incorporating a combination of endurance, strength, and flexibility exercises

improve cardiorespiratory fitness, reduce body fat, and increase levels of "good" HDL cholesterol. Finally, it was found that regular PA is effective in lowering blood pressure and other cardiovascular risk factors, which is highly significant for individuals with T2DM.

4.4 Limitations of the study

The research has certain limitations due to the extensive organization of the results of the different studies according to the types of exercises used, such as resistance training, aerobic exercises, high-intensity interval training, and continuous moderate-intensity training. The possibility of refining and separating the program would give readers a better insight into the effects of different approaches to exercise.

To enhance the discussion, it's essential to compare the findings with existing guidelines and literature on physical activity (PA) for T2DM patients. While current guidelines align with the study's focus on combining aerobic and resistance exercises, implementing these programs in practice faces challenges such as patient adherence, accessibility to exercise facilities, and socio-economic barriers. Future research should explore strategies to improve adherence, such as digital health tools or wearable fitness devices, and investigate the long-term effects of PA interventions. These approaches could help tailor programs to patient needs and overcome barriers to effective implementation.

5. Conclusion

Diabetes mellitus is a leading chronic disease closely linked to lifestyle factors such as inactivity and diet. PA is a highly effective supplementary treatment for T2DM, improving cardiovascular health, aiding weight loss, lowering blood pressure, and enhancing the lipid profile. Regular, individually tailored moderate-intensity exercise increases insulin sensitivity, helps regulate blood glucose levels, manages body weight and blood pressure, raises HDL cholesterol, and reduces LDL cholesterol, thus delaying complications. Additionally, exercise provides significant psychological benefits, including improved mood, increased self-confidence, reduced dependence on medication, and better cognitive function, enhancing the overall quality of life. Personalized PA plans, developed in consultation with healthcare professionals, are essential for safely integrating exercise into the management of T2DM, benefiting both physical and mental health. To effectively integrate PA into clinical practice for T2DM management, healthcare providers should prioritize the development of personalized exercise plans tailored to each patient's needs, capabilities, and preferences. Collaborating with fitness professionals can further ensure that exercise programs are safe, effective, and sustainable. Additionally, ongoing patient education and support are crucial for promoting long-term adherence to PA and optimizing its benefits.

Author Contributions: Conceptualization, B.B., N.A., and S.B.; methodology, N.A. and B.B.; software, M.Z. and M.S.; investigation, N.A and S.B.; writing—original draft preparation, B.B., O.R., I.K., B.M., I.Č., V.M., T.D., and E.B..; writing—review and editing, S.B. and T.D.; supervision, N.A., R.M., and V.M.; All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflicts of interest.

highlighted both by qualitative parameters: bone micro architecture. the disposition of bone trabeculae and by quantitative ones represented by bone mineral density (BMD) and the decrease in the number of trabeculae [1]. The consequence of the decrease in bone strength is the increase in bone fragility and the risk of fractures. BMD is a quantitative parameter of bone composition and has age-dependent dynamics: it increases from childhood until the age of 25-30 years, when it is maximum. Then it goes through a plateau until 45-50 years. after which it starts to decrease by 0 .5-1% per

year. The decrease in BMD is more pronounced in post menopausal state. when due to the fall in estrogen levels. bone mineralization suddenly decreases and. consequently. a drop in BMD greater than 1% may occur [2, 3].

In order to evaluate the degree of bone mineralization. the T score is used. It represents the comparison between the patient's BMD and the ideal BMD i.e. the average of young people aged 25-30. When the bone capital is maximum, this score is expressed in standard deviation (SD) from the average. The diagnosis of osteoporosis is made in a patient with a T-score lower than - 2.5 SD or in a patient with a T-score higher than - 2.5 SD but presenting a fragility fracture [4]. Osteoporosis is also called the "silent disease" it does not have specific symptomatology patients are not aware of the presence of the condition until a fracture accompanied by pain occurs. The name "silent" disease also refers to the fact that osteoporosis has received limited attention despite its serious physical and psychosocial consequences [5]. Vertebral fractures are the most common type of fracture in osteoporosis.

These fractures are due. first of all. to the fact that osteoporotic vertebrae have a lower bone mass. which means that the stress distribution is on a smaller surface than in a normal vertebra; resulting in higher local stresses and an increased risk of fracture. Secondly. the osteoporotic vertebrae also present an altered micro architecture. an aspect that contributes to the production of vertebral fractures. The narrowing of the dorsal vertebral bodies leads to the severe rounded back ("the dowager's hump"). the decrease in height and hunching of the patients. with the protrusion and reduction of the abdomen, with ileus and consecutive postprandial bloating and also the reduction of the ribcage volume, with consecutive dyspnea [6].

The complete cure of osteoporosis is still a challenge. The specialized treatment of osteoporosis includes both drug therapy (DT) and physical therapy (PT). DT improves the evolution of the pathology. but does not cure the disease. Skeletal damage resumes sooner or later when a drug is discontinued. and problems that interfere with the effectiveness of DT in clinical practice. such as poor adherence to therapy and safety in long-term treatment. also arise.

Physical therapy is of great importance in patients with osteoporosis because it contributes to improving the quality of life (QoL) and increasing their level of independence and functionality. The physical therapy (PT) and occupational therapy (OT) are essential rehabilitation methods. because they have no adverse effects and can be performed for an indefinite period [7, 8]. PT has a very important role because. according to studies. it can not only prevent osteoporosis. but even improve it when it has set in [9, 10]. In patients with osteoporosis (OP). the PT program learned in the hospital must be followed by the patients after discharge. at least four times a week. The level of exercise intensity at the beginning of the program depends on the physical capacity of the patients and their intensity is increased by increasing the number of repetitions and resistance to movement [11].

Also. OT is of particular importance. having as main objectives the increase of body stability and the reduction of the risk of falling [12]. Within the OT. are included both the adaptive changes and the development of specific strategies that the patient with osteoporosis must respect. Currently. in everyday medical practice there is no standard protocol for rehabilitation: as far as PT is concerned, there are only objectives that the exercises should pursue and OT is considered to be a recovery method that could only improve the quality of life in patients with osteoporosis.

The main objective of this study was to highlight the effectiveness of the association of drug therapy with physiotherapy and occupational therapy. versus only specific drug therapy. in patients with osteoporosis. on a period of one year. We also propose the implementation of therapeutic approach that will help establish a standard protocol regarding the detection and treatment of primary osteoporosis.

2. Results

The data analysis involves the intergroup and within group comparison of study group and control group. The comparison analysis of initial values aims to observe whether or not the groups are homogeneous before the treatment. The final values allowed us to compare the effectiveness of the two types of treatment followed in the study: only specific medication for osteoporosis versus medication associated with a rehabilitation program. The comparison between initial and final values for each group. we highlighted the therapeutic impact on the parameters studied.

In order to describe the characteristics of the two groups. the following parameters were taken into account: gender. age and the environment of origin (table 1). From the point of view of the characteristics, there are no significant differences between the two groups (p>0.05).

Demographic cl	naracteristics	Mean ± SD	p
A == (=======)	Group A	61.85 ± 5.40	- 0.241
Age (years)	Group B	63.40 ± 6.50	
C 1	Group A	F/B: 61.10%/ 39.90%	0.752
Gender	Group B	F/B: 60.84%/ 39.16%	0.753
Engineers	Group A	U/R: 67.23%/ 32.77%	0.220
Environment	Group B	U/R: 65.71%/ 34.29%	0.329

Table 1. Demographic characteristics of the study group (n=46) and control group (n=48).

Group A= study group (drug therapy. physical therapy. occupational therapy). Group B = control group (only drug therapy) p= statistical significance. SD=standard deviation.

The initial comparison between the two groups. showed that there are no significant differences regarding the different sections of the Qualeffo score and the T score (p > 0.05) (table 2). This aspect highlights the fact that study group and control group were homogeneous at the beginning of the treatment in terms of quality of life and bone mineral density.

Table 2. Baseline scores comparison of Qualeffo test sections and T score between the group A (n=46) and group B (n=48).

Parameter	Group A	Group B	p	95% CI
Qualeffo-pain	15.61 ± 2.7	16.32 ± 3.38	0.3001	-1.223/0.690
Qualeffo-daily activities	10.89 ± 1.71	10.3488 ± 1.212	0.0958	-2.783/0.450
Qualeffo- daily activities	13.71 ± 2.22	14.55 ± 2.38	0.1038	-2.852/0.391
Qualeffo-mobility	23.35 ± 2.54	22.86 ± 2.74	0.3984	-1.120/0.980
Qualeffo-leisure time	18.77 ± 3	19.63 ± 3.1	0.2065	-1.852/0.591
Qualeffo-health status	9.82 ± 1.27	9.30 ± 1.24	0.0664	-2.413/0.510
Qualeffo-mental health	19.89 ± 3.37	20.81 ± 2.55	0.1668	-1.653/0.274
Qualeffo-total	112.09 ± 14.75	114.78 ± 14.22	0.4031	-1.346/0.570
T score	-3.175 ± 0.364	-3.183 ± 0.370	0.752	-1.546/0.380

Group A= study group (drug therapy. physical therapy. occupational therapy). Group B= control group (only drug therapy) p= statistical significance.

The homogeneity of the 2 groups allowed the evaluation of the difference in therapeutic efficiency during one year. between the association of medication for osteoporosis associated with rehabilitation intervention compared to only drug therapy. in terms of quality of life and bone mineral density. Intergroup analysis of the final Qualeffo test scores found that there are statistically significant differences (p < 0.05) both between the total Qualeffo values and for the section values: pain. daily activities. leisure activities and mental function. In study group. Qualeffo total score and the sections mentioned above have significantly higher values compared to the values at control group. No statistical differences were found between the two groups for the sections: household chores. mobility and state of health (p > 0.05) (table 3).

Table 3. Intragroup and intergroup analysis of Qualeffo sections scores and T score (IC 95%).

	Group A (n=46)		Group 1	B (n=48)	Inter-	Effect	Group A		Group B	
	(mean	±SD)	(mean	± SD)	action	size	changes		changes	
	Baseline	Post	Baseline	Post	p	p	p	95% CI Lower/Upper	p	95% CI Lower/Upper
Qf-P	15.61±2.7	13.58±3.85	16.32±3.38	15.27±3.6	0.0436	0.076	< 0.001	3.862/5.158	< 0.001	4.115/6.228
Qf-DA	10.89±1.71	8.71±2.37	10.34±1.21	9.79±1.45	0.0147	0.046	< 0.001	4.965/6.169	< 0.001	6.115/8.239-
Qf-HC	13.71±2.22	12.51±3.5	14.55±2.38	13.55±2.59	0.1261	0.003	< 0.001	7.996/11.671	<0.001	6.889/10.981
Qf-M	23.35±2.54	21.05±5.04	22.86±2.74	21.88±3.75	0.3962	0.002	< 0.001	8.291/10.963	0.001	9.341/11.233
Qf-Lt	18.77±3	16.65±3.95	20.55±4.84	19.63±3.1	0.0003	0.457	< 0.001	6.837/9.143	0.1645	6.727/7.297
Qf-HS	9.82±1.27	8.28±1.94	9.3±1.24	7.95±1.78	0.4276	0.002	< 0.001	5.167/7.563	<0.001	6.237/8.303
Qf-MH	19.89±3.37	18.41±4.05	20.81±2.55	20.09±3.23	< 0.005	0.376	< 0.001	8.117/9.996	0.001	9.156/10.796
Qf-T	112.09±14.75	99.24±22.96	114.78±14.22	108.27±16.45	< 0.005	0.296	< 0.001	14.347/19.613	0.012	15.347/17.293
T score	-3.175±0.364	-3.182±0.375	-3.183±0.370	-3.200±0.449	0.221	0.006	0.863	-1.781/-0.685	0.471	-1.901/-0.545

Group A= study group (drug therapy. physical therapy. occupational therapy). Group B = control group (only drug therapy) p= statistical significance. Qf-P= Qualeffo-Pain. Qf-DA=Qualeffo- Daily activities. Qf-HC=Qualeffo-Home Chores. QF-M=Qualeffo-Mobility. Qualeffo- Leasure time. Qf-HS=Qualeffo- Heatph Status. Qf-MH= Qualeffo-Mental Health. Qf-T = Qualeffo total score. CI = confidence interval.

The intergroup analysis of the final scores, showed significant differences in quality of life between subjects from study group versus subjects from control group. This improvement was achieved by reducing pain, making it easier to carry out daily and leisure activities, as well as by increasing confidence in one's own state of well-being. Regarding the Qualeffo test values, in study group, we observed statistically significant differences between the final and initial scores for Qualeffo test sections and also for the total Qualeffo score (p < 0.001).

In control group, there are also statistically significant differences between the final and initial scores in all sections of the Qualeffo test (p < 0.001), except for the free time activities section (p > 0.05). Analysing the evolution of the total Qualeffo score during the study, we found a statistically significant change (p=0.012, <0.05). Comparison between initial and final values of the T score, in the two groups, it was found that there were no significant differences statistically between study and control group. Compared to the initial values, in both subjects from study and control group, the T score decreased insignificantly at the final assessment (-3.175 vs -3.182 p=0.863, respectively -3.183 vs -3.200 p=0.471), as can be seen in table III. Comparison between groups showed that both at the initial and at the final evaluation, the T score was insignificantly higher in study group compared to control group (-3.175 vs -3.183 with p=0.752 respectively -3.182 vs -3.200 with p=0.387).

After one year of treatment, comparing the differences regarding the decrease in height of the patients from the two groups, we found the existence of a statistically significant difference (independent t-Student test: p=0.014 < 0.05) in favor of the patients from control group, who does not comply with rehabilitation at home (table 4).

Tabel 4. Final comparison regarding the decreasing in height between the study group (n-46) and control group (n=48).

Decrease in height	Group A Mean ± SD	Group B Mean ± SD	р	Effect size
Final	1.019 ± 0.342	1.683 ± 0.782	0.014	0.242

G

Group A= study group (drug therapy. physical therapy. occupational therapy). Group B = control group (only drug therapy) p= statistical significance

3. Discussion

Osteoporosis is perceived by patients as a disease that can lead to severe functional limitations or even disability; this disease affects different aspects of personal life with a variety of unwanted effects such as: chronic pain. reduced physical capacity. limited social activity. decreased good mood or even depression. According to Bianchi [13] patients diagnosed with osteoporosis have a great fear of losing their functional and social independence. The consequence is a decrease in quality of life, this aspect is observed even in the absence of fragility fractures. It is known that, in patients with osteoporosis. chronic pains do not only cause postural changes. they also limit the activities of everyday life. induce depressive states. decrease physical capacity and overall QoL [14]. In patients study group, we observed, after one year of specific medication associated with rehabilitation program. a significant decrease in pain. compared to patients from control group. The results of our study highlight the positive impact of Pt and OT on the quality of life (for sections pain. daily activities. leisure activities and mental function and for total Qualeffo). Our results are consistent with the results of other specialized studies that also support that a specific physical exercise program performed regularly will cause an increase of the quality of life in patients with primary osteoporosis [15, 16].

According to studies [17] the improvement of chronic pain from osteoporosis is naturally followed by the easier performance of daily and leisure activities. as well as an increase in self-confidence. The fact that the mobility, household chores and health status sections do not show statistically significant changes in patients from study group compared to control, can be explained by the fact that in study group there is a predominance of patients from an urban environment and older than 60 years, with an increased degree of sedentarism and with an associated pathology.

In our study, the benefits of rehabilitation on the quality of life for people with osteoporosis were highlighted by analysing individuals over the course of a year. In study group, after one year of treatment, we observed a strongly statistically significant improvement (p < 0.001) in all sections of the Qualeffo score. Also, the total Qualeffo score presented a strongly statistically significant improvement. Compared to control group, in the free time activities section, we did not find a statistically significant change and the total Qualeffo score showed only a statistically significant improvement. A superior improvement in the quality of life for patients from study group, compared with control group, is therefore observed.

The decrease in height with age is a natural phenomenon. but a significant loss in height is a warning sign for a potential diagnosis of osteoporosis [7, 18]. In the elderly, there are two major causes that cause the decrease in height. The first is represented by

the degenerative changes of the intervertebral discs. With age. they lose their elasticity. dehydrate. they compress becoming less tall. The other major cause of the decrease in height with age consists of vertebral fractures due to osteoporosis. which are accompanied by pain in the spine and kyphotic changes of the spine [19, 20]. In patients with osteoporosis, height loss may indicate a vertebral fracture, the accuracy of height information is relevant to clinical practice [21]. Mumtaz considers that the periodic monitoring of the height at the PO is mandatory, it can highlight early the occurrence of osteoporotic fractures [22]. A significant decrease in height also has a diagnostic value, raising the suspicion of osteoporosis, especially in the absence of clinical symptoms.

In order to get a clearer picture of the impact that PT and OT have on people with osteoporosis. we compared the decreasing in height between the two groups. We also compared the patient's height at the beginning and at the end of the study. The results highlight the impact of PT and OT on bone fracture's fragility. The patients from study group. due to the fact that they followed a daily home rehabilitation program. showed a smaller decrease in height and therefore a more correct body posture compared to the control group.

The result of the study is in agreement with other studies [23, 24] which highlight the benefits of PT and OT for correcting the body posture in patients with osteoporosis.

Specific physical exercises have an important role in increasing bone strength. this being highlighted by the fact that lack of physical activity is followed by a decrease in BMD and thinning of the cortical bone in the diaphysis area [25]. In order to have an osteogenic effect, physical exercises must cause muscle contractions intense enough to cause dynamic stresses on the bone [26]. In the specialized literature, there is no consensus regarding the effectiveness of the combination of physical therapy and drug therapy on BMD in patients with osteoporosis. Lespessailles claims that research studies on the effects of this association in animals have more promising results compared to human studies that have mixed results [27].

Comparison analysis between groups. shows that, from the point of view of bone mineral density, there is no significant difference neither between the baseline scores, nor between the final scores of the two groups. According to our results, confirmed by other studies [28, 29] in primary osteoporosis drug therapy and rehabilitation will not cause a statistically significant improvement in BMD compared to only specific medication. At the end of the study, lower values are recorded compared to the beginning of the study, but there is no significant difference in any of the two groups. Thus, in the study group an average bone loss of 0.22% was found during the study and in control group, an 0.53% average bone loss of was found. Therefore PT and OT has a limiting effect on BMD reduction, an aspect that was also highlighted by Korpelainen in his study [30].

An explanation in this regard is the fact that if medication for osteoporosis has an antiresorptive effect preventing bone resorption by osteoclasts. PT and OT has an osteogenic effect on osteoblasts and osteocytes. However, the osteogenic effect of PT and OT is inversely related to age, i.e. the older the patient, the more limited is the effect of rehabilitation exercises due to cellular changes following senescence: the number and activity of osteoblasts and osteoclasts decreases. It turns out that physical therapy in primary osteoporosis has only a braking effect on the decrease in BMD.

Zehnacker claims that the duration of exercise program should be at least one year to cause changes in BMD. The duration of PT is important, because the total time of formation of a basic multicellular unit for bone is 4-6 months, the duration of specific physical exercises to be effective on BMD should be at least 2-3 times longer than this period, i.e. 12 - 18 months [31].

This study was limited by the relatively small number of patients and the short duration of the study. Our findings may stimulate further research with longer follow-up periods and larger patient groups.

4. Materials and Methods

Based on subjective and objective anamnestic criteria. a number of 94 patients admitted to the Rehabilitation Hospital in Băile Felix. aged between 56-69 years and who expressed their written consent to participate. were taken into the study. Initially. there were 100 participants. but 6 were excluded during the research. for various reasons. Our study took place over two years. between April 2022 and June 2024.

The inclusion criteria in the clinical study were: hospitalization at the Rehabilitation Hospital in Băile-Felix. the diagnosis of primary osteoporosis confirmed by DEXA. the compliance with the recommended medication during the study; the following of a 2 weeks rehabilitation treatment; the compliance with the initial and final assessment.

The exclusion criteria were: the refuse to participate; the alteration of the patient's general condition during the study regardless of the cause; any type of infectious complications. neoplasms. debilitating co-morbidities or mental illnesses; body mass index (BMI) < 20 kg/m2. a BMI < 20 kg/m2 is a significant risk factor in osteoporosis [32]; the presence of a TM for osteoporosis prior to our study.

All the 94 patients in our study followed a two weeks rehabilitation program at the Clinical Rehabilitation Hospital in Băile Felix. consisting of drug therapy and physical therapy. The medication used was: medication for osteoporosis; Ca / vitamin D supplements and pain killers and drugs necessary for pathologies that can cause imbalance in walking and static. if needed.

The rehabilitation therapy included for all study subjects specific physical exercises; analgesic electrotherapy (TENS; aquatic therapy) and occupational therapy. including measures to prevent falls and increase postural stability.

Characteristic for patient with osteoporosis. is that the rehabilitation program. including PT and TO. must not be interrupted once the patient is discharged. It must be continued at home for the entire life. From medical discipline reasons. some of the patients from this study did not respected this indication. Therefore, according to this criteria, the study subjects were divided into two groups:

- 1. the study group (group A) 46 subjects with osteoporosis medication. who followed continuous PT. OT for one year;
- 2. the control group (group B) 48 subjects with osteoporosis medication who did not followed the above mentioned rehabilitation program.

Assessment tools

In order to highlight the therapeutic efficiency of the medication for osteoporosis associated with rehabilitation exercises versus only drug therapy. in the treatment of osteoporosis, we followed. in both the two groups of subjects included in the study. the evolution of the following parameters. over the course of one year:

- the decrease in patient's height during the study the assessment was carried out using a standard thalometer, common for all patients;
- the T score value expressing BMD. obtained by DEXA examination at admission and after 1 year of treatment;
- the value of the Quallefo test. a useful tool in the overall assessment of osteoporosis patients. through which their quality of life is evaluated [33]; the Qualeffo test includes 41 questions divided into 7 sections (pain. daily activities. daily activities. mobility. leisure time. health status. mental health).

Intervention

After discharged. all the patients from study group performed 5 weekly PT and OT sessions at home. monitored by the physiotherapists and volunteer doctors from this study.

PT was structured as follows: warm-up (5 to 7 min). exercise program (30 to 35 min). and recovery (5 min). The OT sessions were adapted individually according to each patient.

All PT exercises were aerobic and their intensity level. at the beginning of the program, depended on the physical capacity of each individual patient. The benefits of PT exercises on the skeleton are limited to the stimulated anatomical area. Therefore, special importance was given to exercises to stimulate bone remodeling in the forearm, hip and lumbar spine, the areas most susceptible to osteoporotic fractures. In this sense, exercises with small weights were performed for the flexor and supinator-pronator muscles of the seated fist. Also, exercises with bags attached to the ankles for hip flexion and abduction from standing and sitting with support from the back of a chair.

The goal was to improve balance and tone the muscles of the lower limbs. especially the quadriceps. The exercises to strengthen the abdominal and paravertebral muscles were performed only from the supine and ventral positions. Exercises to improve balance also included improving proprioception and the function of the vestibular system. The necessary exercises for the re-education of abdominal and diaphragmatic breathing were also carried out. Exercises and activities involving excessive flexion of the thoracic and lumbar spine were avoided because it increases the risk of vertebral compression fractures.

Within the OT a safe ADL improvement program was initiated. including transfers. sitting and standing. household activities. pedaling and gardening. Also, within the OT adaptive changes were made at home and the workplace to avoid falls and injuries: the elimination of thresholds. obstacles and slippery surfaces. the installation of support bars.

Statistical analysis

For data analysis. we used the Statistical Package for Evaluation in Social Sciences (SPSS) version 15.0. issued by IBM SPSS Statistic. Oradea. Romania. For the quantitative analysis of numerical variables. we used mean and standard deviation. and for categorical variables we used percentage and mean. We analysed the normality of data distribution using the Kolmogorov-Smirnov test. For the intergroup analysis of baseline values. we used the Independent samples T-test because we had a normal distribution of the data (Kolmogorov–Smirnov test. $p \ge 0.05$). The chi-square test for homogeneity was performed to explore whether the frequency counts were identically distributed between the two patient groups. with respect to gender and environment. To test whether there was a significant difference between the two groups for baseline and final outcomes. we used one-way ANOVA between patients. as we had a normal distribution of data (Kolmogorov-Smirnov test. $p \ge 0.05$). For the pretest - post-test analysis of the two groups. we used one-way ANOVA with repeated measures. To measure effect size for both between-subjects one-way ANOVA and repeated-measures one-way ANOVA. partial Eta squared was used. Overall. 95% confidence intervals (CI) were reported as appropriate.

5. Conclusions

Patients with osteoporosis. who during one year. undertakes drug therapy with physiotherapy and occupational therapy. compared to those who only take medication for osteoporosis. have the following advantages: the quality of life and mental tone improvement. and significant decrease in pain; slowing down the decrease in height.

with postural improvement; slowing down the decrease in bone mineral density: PT and OT have a braking effect on the decrease in bone mineral density.

Our study proposes a therapeutic protocol for PO that includes: annual monitoring of patients' height; the inclusion of occupational therapy within the rehabilitation management; compliance with an individual program adapted by a physiotherapist performed 5 times a week.

Author Contributions: Conceptualization. F.M.; methodology. F.M. and N.P.; software. D.C.; validation. D.I. and R.S.; formal analysis. D.C.; investigation. F.M. and I.A.; resources. F.M. and R.S.; data curation. F.M. and A.B.I.; writing—original draft preparation. I.A. and A.B.I.; writing—review and editing. D.C., I.A., R.S. and D.I.; visualization. D.C.; supervision. R.S.; project administration. N.P. and R.S. All authors have read and agreed to the published version of the manuscript. All authors have equal contribution to this article.

Funding: This research received no external funding

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki. and approved by the Institutional Ethics Committee of Rehabilitation Hospital in Băile Felix (opinion no. 3881/02.04.2024).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The datasets either used. analyzed. or both. during the current study are available from the corresponding authors on reasonable requests.

Acknowledgments: In this section, you can acknowledge any support given which is not covered by the author contribution or funding sections. This may include administrative and technical support, or donations in kind (e.g. materials used for experiments).

Conflicts of Interest: The authors declare no conflict of interest.

References

- 1. Huffman F.G.; Vaccaro J.A. Physical activity, type 2 diabetes, and ethnicity: recent findings and implications. American Journal of Lifestyle Medicine, 2012, 7, 104–114. https://doi.org/10.1177/1559827612469337
- 2. World Health Organization. Diet and physical activity: a public health priority. 2016.
- 3. Balducci S.; D'Errico V.; Haxhi J, Sacchetti M.; Orlando G.; Cardelli P. Italian Diabetes, Exercise Study 2 (IDES-2) Investigators et al. Effect of a behavioral intervention strategy on sustained change in physical activity and sedentary behavior in patients with type 2 diabetes: the IDES 2 randomized clinical trial. JAMA, 2019, 321, 880–890. https://doi.org/10.1001/jama.2019.0922
- 4. Amanat S.; Ghahri S.; Dianatinasab A.; Fararouei M.; Dianatinasab M. Exercise and Type 2 Diabetes. Adv Exp Med Biol., 2020, 1228, 91–105. https://doi.org/10.1007/978-981-15-1792-1_6
- 5. La Sala L.; Pontiroli A.E. Prevention of Diabetes and Cardiovascular Disease in Obesity. Int J Mol Sci., 2020 21, 8178. https://doi.org/10.3390/ijms21218178
- 6. Cocchi C.; Coppi F.; Farinetti A.; Mattioli AV. Cardiovascular disease prevention and therapy in women with Type 2 diabetes. Future Cardiol., 2021, 17, 487–496. https://doi.org/10.2217/fca-2021-0011
- 7. Hamasaki H. Daily physical activity and type 2 diabetes: A review. World J Diabetes., 2016, 7, 243–251. https://doi.org/10.4239/wjd.v7.i12.243
- 8. Advika T.S.; Idiculla J.; Kumari S.J. Exercise in patients with Type 2 diabetes: Facilitators and barriers A qualitative study. J Family Med Prim Care., 2017, 6, 288–292. https://doi.org/10.4103/2249-4863.219998
- 9. Mohamed B.A.; Mahfouz M.S.; Badr M.F. Physical activity and its associated factors in females with type 2 diabetes in Riyadh Saudi Arabia. PLoS One, 2020, 15, e0239905. https://doi.org/10.1371/journal.pone.0239905
- 10. Colberg S.R. Exercise as Medicine for Diabetes: Prescribing Appropriate Activities and Avoiding Potential Pitfalls: Preface. Diabetes Spectr., 2015, 28, 10-13. https://doi.org/10.2337/diaspect.28.1.10
- 11. Klimek M.; Knap J.; Reda M.; Masternak M. Physical activity in prevention and treatment of type 2 diabetes mellitus. J Educ Health Sport., 2019, 9, 1175-1181. http://dx.doi.org/10.5281/zenodo.3464935
- 12. Achten J.; Jeukendrup A.E. Optimizing fat oxidation through exercise and diet. Nutrition, 2004, 20, 716-726. https://doi.org/10.1016/j.nut.2004.04.005
- 13. Page M.J; McKenzie J.E; Bossuyt P.M; et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ., 2021, 372:n71. https://doi.org/10.1136/bmj.n71

- 14. Yokoyama H.; Emoto M.; Fujiwara S.; Motoyama K.; Morioka T.; Koyama H.; Shoji T.; Inaba M.; Nishizawa Y. Short-term aerobic exercise improves arterial stiffness in type 2 diabetes. Diabetes Res Clin Pract., 2004, 65, 85-93. https://doi.org/10.1016/j.diabres.2003.12.005
- Ahmad I.; Aung M.N.; Ueno S.; Khin E.T.; Latt T.S.; Moolphate S.; Yuasa M. Physical Activity of Type 2
 Diabetes Mellitus Patients and Non-Diabetes Participants in Yangon, Myanmar: A Case-Control Study
 Applying the International Physical Activity Questionnaires (IPAQ-S). Diabetes Metab Syndr Obes., 2021,
 14, 1729-1739. https://doi.org/10.2147/DMSO.S291468
- Eshete A.; Mohammed S.; Shine S.; Eshetie Y.; Assefa Y.; Tadesse N. Effect of physical activity promotion program on adherence to physical exercise among patients with type II diabetes in North Shoa Zone Amhara region: a quasi-experimental study. BMC Public Health, 2023, 23, 709. https://doi.org/10.1186/s12889-023-15642-7
- 17. Manders R.J.; Van Dijk J.W.; Van Loon L.J. Low-intensity exercise reduces the prevalence of hyperglycemia in type 2 diabetes. Med Sci Sports Exerc., 2010, 42, 219-225. https://doi.org/10.1249/mss.0b013e3181b3b16d
- 18. Antić S.; Lazarević G.; Đinđić B.; Jovanović V. Assessment of physical activity in patients with diabetes mellitus type 2. Acta Medica Medianae, 2003, 42, 5-10.
- 19. Bosić-Živanović D.; Medić-Stojanoska M.; Kovačev-Zavišić B. Quality of life of patients with type 2 diabetes mellitus. Clinic for endocrinology, diabetes and diseases. Vojnosanit Pregl., 2012, 69, 858-863. https://doi.org/10.2298/vsp1210858b
- 20. Radaš J.; Furjan-Mandić G.; Ružić L. Differences in physical activity between men and women with diabetes mellitus. Croat Sports Med J., 2012, 27, 24-27.
- Segal K.R.; Edano A.; Abalos A.; Albu J.; Blando L.; Tomas M.B.; Pi-Sunyer F.X. Effect of exercise training on insulin sensitivity and glucose metabolism in lean, obese, and diabetic men. J Appl Physiol., 1991, 71, 2402-2411. https://doi.org/10.1152/jappl.1991.71.6.2402
- 22. Yamanouchi K.; Shinozaki T.; Chikada K.; Nishikawa T.; Ito K.; Shimizu S.; Ozawa N.; Suzuki Y.; Maeno H.; Kato K. Daily walking combined with diet therapy is a useful means for obese NIDDM patients not only to reduce body weight but also to improve insulin sensitivity. Diabetes Care, 1995, 18, 775-778. https://doi.org/10.2337/diacare.18.6.775
- 23. Ligtenberg P.C.; Hoekstra J.B.; Bol E.; Zonderland M.L.; Erkelens D.W. Effects of physical training on metabolic control in elderly type 2 diabetes mellitus patients. Clin Sci., 1997, 93, 127-135. https://doi.org/10.1042/cs0930127
- 24. Tuomilehto J.; Lindström J.; Eriksson J.G.; Valle T.T.; Hämäläinen H.; Ilanne-Parikka P.; Uusitupa M. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med., 2001, 344, 1343-1350. https://doi.org/10.1056/NEJM200105033441801
- 25. Maiorana A.; O'Driscoll G.; Cheetham C.; Dembo L.; Stanton K.; Goodman C.; Taylor R.; Green D. The effect of combined aerobic and resistance exercise training on vascular function in type 2 diabetes. J Am Coll of Cardiol., 2001, 38, 860-866. https://doi.org/10.1016/S0735-1097(01)01439-5
- 26. Ishii T.; Yamakita T.; Yamagami K.; Yamamoto T.; Miyamoto M.; Kawasaki K.; Hosoi M.; Yoshioka K.; Sato T.; Tanaka S.; Fujii S. Effect of exercise training on serum leptin levels in type 2 diabetic patients. Metabolism., 2001, 50, 1136-1140. https://doi.org/10.1053/meta.2001.26745
- 27. Castaneda C.; Layne J.E.; Munoz-Orians L.; Gordon P.L.; Walsmith J.; Foldvari M.; Roubenoff R.; Tucker K.L.; Nelson M.E. A randomized controlled trial of resistance exercise training to improve glycemic control in older adults with type 2 diabetes. Diabetes Care, 2002, 25, 2335-2341. https://doi.org/10.2337/diacare.25.12.2335
- 28. Loimaala A.; Huikuri H.V.; Koobi T.; Rinne M.; Nenonen A.; Vuori I. Exercise training improves baroreflex sensitivity in type 2 diabetes. Diabetes, 2003, 52, 1837-1842. https://doi.org/10.2337/diabetes.52.7.1837
- Čizmić M.; Životić-Vanović M.; Živanić S.; Dragojević R. Effects of a two-week program of individually dosed physical activity on insulin resistance in obese insulin-independent diabetics. Military medical examination. Vojnosanit Pregl., 2003, 60, 683-690. https://doi.org/10.2298/VSP0306683C
- 30. Kirk A.; Mutrie N.; MacIntyre P.; Fisher M. Increasing physical activity in people with type 2 diabetes. Diabetes Care, 2003, 26, 1186-1192. https://doi.org/10.2337/diacare.26.4.1186
- 31. Araiza P.; Hewes, H.; Gashetewa, C.; Vella, C.A.; Burge, M.R. Efficacy of a pedometer-based physical activity program on parameters of diabetes control in type 2 diabetes mellitus. Metabolism., 2006, 55, 1382-1387. https://doi.org/10.1016/j.metabol.2006.06.009
- 32. Brooks N.; Layne J.E.; Gordon P.L.; Roubenoff R.; Nelson M.E.; Castaneda-Sceppa C. Strength training improves muscle quality and insulin sensitivity in Hispanic older adults with type 2 diabetes. Int J Med Sci., 2006, 14, 19-27. https://doi.org/10.7150%2Fijms.4.19
- 33. Yavari A.; Hajiyev A.M. Naghizadeh F. The effect of aerobic exercise on glycosylated hemoglobin values in type 2 diabetes patients. J Sports Med Phys Fitness, 2010, 50, 501-505.

- 34. Bello A.I.; Owusu-Boakye E.; Adegoke B.O.; Adjei D.N. Effects of aerobic exercise on selected physiological parameters and quality of life in patients with type 2 diabetes mellitus. Int J Gen Med., 2011, 4, 723-727. https://doi.org/10.2147/IJGM.S16717
- 35. Moura B.P.; Amorim P.R.S.; Silva B.P.P.; Franceschini S.C.C.; Reis J.S.; Mar J.C.B. Effect of a short-term exercise program on glycemic control measured by fructosamine test in type 2 diabetes patients. Diabetol Metab Syndr., 2014, 6. https://doi.org/10.1186/1758-5996-6-16
- 36. Ruffino J.S.; Songsorn P.; Haggett M.; Edmonds D.; Robinson A.M.; Thompson D.; Vollaard N.B.A comparison of the health benefits of reduced-exertion high-intensity interval training (REHIT) and moderate-intensity walking in type 2 diabetes patients. Appl Physiol Nutr Metab., 2017, 42, 202-208. https://doi.org/10.1139/apnm-2016-0497
- 37. Najafipour F.; Mobasseri M.; Yavari A.; Nadrian H.; Aliasgarzadeh A.; Abbasi M.N.; Mitra N.; Gharamaleki J.H.; Sadra V. Effect of regular exercise training on changes in HbA1c, BMI and VO2 max among patients with type 2 diabetes mellitus: an 8-year trial. BMJ Open Diab Res Care, 2017, 5, 1-8. https://doi.org/10.1136%2Fbmjdrc-2017-000414
- 38. Magalhães J.P.; Melo X.; Correia I.R.; Ribeiro R.T.; Raposo J.; Dores H.; Bicho M.; Sardinha L.B. Effects of combined training with different intensities on vascular health in patients with type 2 diabetes: a 1-year randomized controlled trial. Cardiovasc Diabetol., 2019, 18, 34. https://doi.org/10.1186/s12933-019-0840-2
- 39. Verboven K.; Wens I.; Vandenabeele F.; Stevens A.N.; Celie B.; Lapauw B.; Dendale P.; Van Loon L.J.C.; Calders P.; Hansen D. Impact of Exercise-Nutritional State Interactions in Patients with Type 2 Diabetes. Med Sci Sports Exerc., 2020, 52, 720-728.https://doi.org/10.1249/MSS.0000000000002165
- 40. Liu Y.; Liu S.X.; Cai Y.; Xie K.L.; Zhang W.L.; Zheng F. Effects of combined aerobic and resistance training on the glycolipid metabolism and inflammation levels in type 2 diabetes mellitus. J Phys Ther Sci., 2015, 27, 2365–2371. https://doi.org/10.1589/jpts.27.2365
- 41. Kirwan J.P.; Sacks J.; Nieuwoudt S. The essential role of exercise in the management of type 2 diabetes. Cleve Clin J Med., 2017, 84, S15–S21. https://doi.org/10.3949/ccjm.84.s1.03
- 42. Carbone S.; Del Buono M.G.; Ozemek C.; Lavie C.J. Obesity, risk of diabetes and role of physical activity, exercise training and cardiorespiratory fitness. Prog Cardiovasc Dis., 2019, 62, 327–333. https://doi.org/10.1016/j.pcad.2019.08.004
- 43. Eckstrom E.; Neukam S.; Kalin L.; Wright J. Physical Activity and Healthy Aging. Clin Geriatr Med., 2020, 36, 671–683. https://doi.org/10.1016/j.cger.2020.06.009
- 44. Hargreaves M.; Spriet L.L. Skeletal muscle energy metabolism during exercise. Nat Metab., 2020, 2, 817–828. https://doi.org/10.1038/s42255-020-0251-4
- 45. Kramer A. An Overview of the Beneficial Effects of Exercise on Health and Performance. Adv Exp Med Biol., 2020, 1228, 3–22. https://doi.org/10.1007/978-981-15-1792-1_1
- 46. Lin Y.; Fan R.; Hao Z.; Li J.; Yang X.; Zhang Y.; Xia Y. The Association Between Physical Activity and Insulin Level Under Different Levels of Lipid Indices and Serum Uric Acid. Front Physiol., 2022, 13, 809669. https://doi.org/10.3389/fphys.2022.809669
- 47. American Diabetes Association. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2021. Diabetes Care, 2021, 44, S15-S33. https://doi.org/10.2337/dc21-S002
- 48. Colberg S.R.; Sigal R.J.; Fernhall B.; Regensteiner J.G.; Blissmer B.J.; Rubin R.R.; ... Braun B. Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement. Diabetes Care, 2010, 33, e147–e167. https://doi.org/10.2337/dc10-9990
- 49. Ross R.; Janssen I.; Dawson J.; et al. Exercise-induced reduction in obesity and insulin resistance in women: a randomized controlled trial. Obes Res., 2004, 12, 789-798. https://doi.org/10.1038/oby.2004.95
- 50. Hawley J.A.; Lessard S.J. Exercise training-induced improvements in insulin action. Acta Physiol., 2008, 192, 127-135. https://doi.org/10.1111/j.1748-1716.2007.01783.x
- 51. Leibel R.L.; Rosenbaum M.; Hirsch J. Changes in energy expenditure resulting from altered body weight. N Engl J Med., 1995, 332, 621-628. https://doi.org/10.1056/NEJM199503093321001
- 52. Donnelly J.E.; Blair S.N.; Jakicic J.M.; Manore M.M.; Rankin J.W.; Smith B.K.; Appropriate Physical Activity Intervention Strategies for Weight Loss and Prevention of Weight Regain for Adults. Med Sci Sports Exerc., 2009, 41, 459-471. https://doi.org/10.1249/MSS.0b013e3181949333
- 53. Hill M.A.; Yang Y.; Zhang L.; Sun Z.; Jia G.; Parrish A.R.; Sowers J.R. Insulin resistance, cardiovascular stiffening and cardiovascular disease. Metabolism., 2021, 119, 154766. https://doi.org/10.1016/j.metabol.2021.154766
- 54. Adeva M.M.; Calviño J.; Souto G.; Donapetry C. Insulin resistance and the metabolism of branched-chain amino acids in humans. Amino Acids, 2012, 43, 171–181. https://doi.org/10.1007/s00726-011-1088-7
- 55. Hu F.B.; Sigal R.J.; Rich-Edwards J.W.; et al. Walking compared with vigorous physical activity and risk of type 2 diabetes in women: a prospective study. JAMA, 1999, 282, 1433-1439. https://doi.org/10.1001/jama.282.15.1433

- 56. Knowler W.C.; Barrett-Connor E.; Fowler S.E.; et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med., 2002, 346, 393-403. https://doi.org/10.1056/NEJMoa012512
- 57. Perseghin G.; Lattuada G.; De Cobelli F.; et al. Habitual physical activity is associated with intrahepatic fat content in humans. Diabetes Care, 2003, 26, 1473-1478. https://doi.org/10.2337/dc06-2032
- 58. Sharma S.; Mandal A.; Kant R.; Jachak S.; Jagzape M. Is Cinnamon Efficacious for Glycaemic Control in Type-2 Diabetes Mellitus?. JPMA. J Pak Med Assoc., 2020, 70, 2065–2069.
- 59. Emerson S.R.; Haub M.D.; Teeman C.S.; Kurti S.P.; Rosenkranz S.K. Summation of blood glucose and TAG to characterise the 'metabolic load index'. Br J Nutr., 2016, 116, 1553–1563. https://doi.org/10.1017/S0007114516003585
- 60. Poggiogalle E.; Jamshed H.; Peterson C.M. Circadian regulation of glucose, lipid, and energy metabolism in humans. Metabolism., 2018, 84, 11–27. https://doi.org/10.1016/j.metabol.2017.11.017
- 61. Lennerz B.; Lennerz J.K. Food Addiction, High-Glycemic-Index Carbohydrates, and Obesity. Clin Chem., 2018, 64, 64–71. https://doi.org/10.1373/clinchem.2017.273532
- 62. Pan X.R.; Li G.W.; Hu Y.H.; Wang J.X.; Yang W.Y.; An Z.X.; ... Howard B.V. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and Diabetes Study. Diabetes Care, 1997, 20, 537-544. https://doi.org/10.2337/diacare.20.4.537
- 63. Diabetes Prevention Program Research Group (DPRG). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med., 2002, 346, 393-403. https://doi.org/10.1056/NEJMoa012512
- 64. Shai I.; Schwarzfuchs D.; Henkin Y.; Shahar D. R.; Witkow S.; Greenberg I.; ... Stampfer M.J. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. N Engl J Med., 2008, 359, 229-241. https://doi.org/10.1056/NEJMoa0708681
- 65. American Diabetes Association. Nutrition therapy for adults with diabetes or prediabetes: a consensus report. Diabetes Care, 2019, 42, 731-754. https://doi.org/10.2337%2Fdci19-0014
- 66. Swift D.L.; McGee J.E.; Earnest C.P.; Carlisle E.; Nygard M.; Johannsen N.M. The Effects of Exer Colberg cise and Physical Activity on Weight Loss and Maintenance. Prog Cardiovasc Dis., 2018, 61, 206–213. https://doi.org/10.1016/j.pcad.2018.07.014
- 67. Jenkins D.J.; Kendall C.W.; Augustin L.S.; Franceschi S.; Hamidi M.; Marchie A.; ... Axelsen M. Glycemic index: overview of implications in health and disease. Am J Clin Nutr., 2002, 76, 266S-273S. https://doi.org/10.1093/ajcn/76/1.266S
- 68. Evert A.B.; Dennison M.; Gardner C.D.; Garvey W.T.; Lau K.H.K.; MacLeod J.; ... Yancy W.S. Nutrition therapy for adults with diabetes or prediabetes: a consensus report. Diabetes Care, 2019, 42, 731-754. https://doi.org/10.2337/dci19-0014
- 69. Lean M.E.; Leslie W.S.; Barnes A. C.; Brosnahan N.; Thom G.; McCombie L.; ... Taylor R. Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. Lancet, 2018, 391, 541-551. https://doi.org/10.1016/S0140-6736(17)33102-1
- 70. Look AHEAD Research Group. Eight-year weight losses with an intensive lifestyle intervention: the Look AHEAD study. Obesity, 2014, 22, 5-13. https://doi.org/10.1002/oby.20662
- Mann J. I.; De Leeuw I.; Hermansen K.; Karamanos B.; Karlström B.; Katsilambros N.; ... Laakso M. Evidence-based nutritional approaches to the treatment and prevention of diabetes mellitus. Nutr Metab Cardiovasc Dis., 2004, 14, 373-394. https://doi.org/10.1016/s0939-4753(04)80028-0
- 72. Ginter E.; Simko V. Type 2 diabetes mellitus, pandemic in 21st century. Adv Exp Med Biol., 2013, 771, 42-50. https://doi.org/10.1007/978-1-4614-5441-0_6
- 73. Boule N.G.; Haddad E.; Kenny G.P.; Wells G.A.; Sigal R.J. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. JAMA, 2001, 286, 1218-1227. https://doi.org/10.1001/jama.286.10.1218
- 74. Kodama S.; Tanaka S.; Saito K.; Shu M.; Sone Y.; Onitake F.; ... Yamada N. Effect of aerobic exercise training on serum levels of high-density lipoprotein cholesterol: a meta-analysis. Arch Intern Med., 2007, 167, 999-1008. https://doi.org/10.1001/archinte.167.10.999
- 75. Leon A.S.; Sanchez O.A. Response of blood lipids to exercise training alone or combined with dietary intervention. Med Sci Sports Exerc., 2001, 33, S502-515. https://doi.org/10.1097/00005768-200106001-00021
- 76. Whelton S.P.; Chin A.; Xin X.; He J. Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. Ann Intern Med., 2002, 136, 493-503. https://doi.org/10.7326/0003-4819-136-7-200204020-00006
- 77. American Diabetes Association. Lifestyle management: Standards of Medical Care in Diabetes-2019. Diabetes Care, 2019, 42, S46-S60. https://doi.org/10.2337/dc19-s005