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Original Article

Association between metformin use and handgrip strength in older adult women with type 2 diabetes mellitus in Lima, Peru

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Abstract

Aging is associated with declining muscle strength, which may be exacerbated by type 2 diabetes mellitus (T2DM). Metformin, a widely used antidiabetic drug, could influence muscle-related outcomes, but evidence in older adults remains limited. This study aimed to evaluate the association between metformin use and handgrip strength (HGS) in older adult women with T2DM. This cross-sectional analytical observational study included 114 older adult women (≥60 years) with T2DM recruited from a primary care center. Metformin use was self-reported. HGS was measured using a dynamometer and expressed as absolute values (kg) and normalized for height. Linear regression models were fitted, and β coefficients with 95% confidence intervals (95% CI) were estimated. The mean age was 69.02 years. Overall, 80.7% of participants used at least one antidiabetic medication, and 78.07% used metformin. In adjusted models, metformin use was positively associated with absolute HGS (β=2.51 kg; 95% CI: 0.89–4.12; p=0.003) and height-normalized HGS (β=1.57; 95% CI: 0.52–2.62; p=0.004). Metformin use was positively associated with HGS in older women with T2DM. Longitudinal studies are warranted to clarify the temporal and causal nature of this association.

Keywords: aged, hand strength, type 2 diabetes mellitus, metformin, Peru

Introduction

Type 2 diabetes mellitus (T2DM) is a chronic disease affecting millions of adults worldwide, with a particularly high burden among older populations [1]. In 2021, more than 172 million older adults globally were living with T2DM, and between 1990 and 2021 both prevalence and diabetes-attributable mortality increased steadily, with annual rates of 1.93% and 0.32%, respectively; these trends are projected to continue through 2040 [2]. In Peru, the prevalence of T2DM among older adults has increased in recent years, reaching approximately 14% [3]. Beyond cardiovascular risk, T2DM is associated, both in adults and elderly, with adverse alterations in skeletal muscle, including reduced muscle strength [4, 5], and increased physical disability [6]. At older ages, these manifestations overlap with age-related biological changes, amplifying their functional impact.

Handgrip strength (HGS) is widely recognized as a functional biomarker of aging and is commonly used to assess muscle function in older adults [7]. Lower HGS is associated with a higher risk of physical disability, functional dependence, and mortality [6, 7]. Its decline is influenced by aging, sex, and biological processes related to chronic inflammation, which shape strength trajectories across the life course [8]. In individuals with T2DM, muscle strength declines more markedly than in those without diabetes [9], suggesting that age-related losses may be exacerbated by diabetes-related metabolic disturbances, including oxidative stress,

impaired insulin signaling in skeletal muscle, and the accumulation of advanced glycation end products [10].

Metformin remains the first-line pharmacological therapy for T2DM and is widely prescribed, including among older adults [11]. Because metformin activates the AMP-activated protein kinase (AMPK) pathway, interest has emerged regarding its potential effects on skeletal muscle. In older adults, AMPK activation has been proposed to attenuate mTORC1 signaling, particularly in response to resistance training, potentially impairing anabolic processes such as protein synthesis and muscle adaptation [12]. However, evidence on the association between metformin use and muscle strength remains heterogeneous, with studies reporting positive [13, 14], inverse [15], or null association [16–18], leaving uncertainty regarding its functional impact. In Peru, metformin is the first-line treatment for glycemic control in primary care [19], and a substantial proportion of users are older adult women [3]. Nevertheless, evidence on the association between metformin use and muscle strength in the Peruvian population, particularly among women, is scarce. Therefore, the aim of this study was to evaluate the association between metformin use and handgrip strength in older women with T2DM receiving primary care.

Material and methods

Population and sample

Participants were older adult women attending a primary health care facility located in Lima, the capital city of Peru. Assessments were conducted between July and September 2024 within the context of routine outpatient care.

Eligible participants were women aged ≥60 years with T2DM diagnosis confirmed by medical records, who attended the nutrition service during the study period. Patients with upper-limb amputations, significant motor limitations, or neuromuscular conditions that could interfere with HGS assessment were excluded, as verified during the initial interview.

Sample size was calculated using G*Power version 3.1.9.7, assuming a 5% significance level, 99% statistical power, a beta coefficient of 2.46 for the simple linear regression between metformin use and HGS based on a previous study [14], and a standard deviation of 6 kg [13]. The minimum required sample size was 93 participants. An additional 20% was added to account for potential losses or non-response, resulting in a required sample size of 112 participants. Ultimately, 114 women were recruited. Convenience non-probability sampling was used.

Variables and measures

Outcome variable

The outcome variable was HGS, measured using a hydraulic dynamometer (Jamar; range: 0–90 kg) following international standards [20, 21]. Measurements were performed with participants seated, using the dominant arm flexed at 90°, while exerting maximal isometric force for 5 seconds. Grip width was individually adjusted before testing. Three measurements were obtained with 60-second rest intervals, and the highest value was recorded, in accordance with international recommendations [21]. HGS was analyzed as a continuous variable, expressed in kilograms to reflect absolute strength, and normalized by height squared to obtain a relative measure adjusted for body size.

Exposure variable

The exposure variable was current metformin use, assessed by self-report. This variable was analyzed as a binary categorical variable (yes/no).

Covariates

Sociodemographic characteristics (age, living arrangement, educational level, employment status), clinical variables (presence of comorbidities, medication use), and lifestyle factors (smoking status, alcohol consumption, fruit and vegetable intake, sitting time, and engagement in moderate-intensity physical activity) were collected through direct interview. Anthropometric measurements, including weight, height, and circumferences of the waist, relaxed arm, thigh, and maximum calf, were obtained by an experienced anthropometrist. Waist, arm, and calf circumferences were measured according to the Peruvian technical guidelines for anthropometric nutritional assessment in older adults [22]. Thigh circumference was measured at the midpoint between the inguinal fold and the upper border of the patella. Body mass index (BMI) was calculated as weight (kg)/height^2 (m^2). BMI and waist circumference were categorized for descriptive purposes using cut-off points established by the Peruvian Ministry of Health for older adults [22].

Statistical analysis

Descriptive analyses were performed using absolute frequencies and percentages for categorical variables.

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Continuous variables were summarized using means and standard deviations (SD) or medians and interquartile ranges (IQR), as appropriate. Bivariate comparisons of participant characteristics according to metformin use were conducted using the chi-square test or Fisher's exact test for categorical variables, and the Student's t test or Mann–Whitney U test for continuous variables.

The association between metformin use and HGS was examined using linear regression models. Crude and adjusted beta coefficients (β) with 95% confidence intervals (95% CI) were estimated separately for absolute HGS and height-normalized HGS. Adjusted models included age (years), alcohol consumption (yes/no), engagement in moderate physical activity (yes/no), total sitting time (minutes), waist circumference (cm), insulin use (yes/no), glibenclamide use (yes/no), and use of other antidiabetic medications (yes/no). Additionally, adjusted Cohen's d effect sizes were calculated for the fully adjusted regression models.

All analyses were performed using STATA version 17.0. A two-sided p-value<0.05 was considered statistically significant.

Ethical considerations

This study was approved by the Universidad Nacional Mayor de San Marcos ethics committee (ID: 0128-2025). Authorization was also obtained from the health center administration. Participants were provided with a detailed explanation of the study's purpose, and informed consent was obtained. Ethical standards of the Helsinki Declaration were adhered to [23].

Results

A total of 114 women were analyzed. The mean (SD) age was 69.02 (6.67) years. Regarding demographic characteristics, most participants lived with family members (91.23%) and were not employed (72.81%). In terms of lifestyle factors, the majority were non-smokers (97.37%) and did not consume alcohol (87.72%); only 9.65% met the recommendation of consuming ≥5 servings of fruits and vegetables per day. More than half of the participants were classified as having excess body weight (61.4%), and 96.49% presented abdominal obesity. With respect to clinical characteristics, most participants had at least one comorbidity (81.58%). Among medications used for glycemic control, metformin was the most frequently reported (78.07%). For blood pressure management, angiotensin II receptor blockers (ARBs) were the most commonly used antihypertensive agents (41.33%). Detailed characteristics of the study sample are presented in Table 1.

Bivariate analysis of participant characteristics according to metformin use showed differences between groups in daily sitting time, as well as in absolute and height-normalized handgrip strength. In addition, the presence of dyslipidemia and insulin use were associated with metformin use (Table 2).

Regression analyses showed a positive association between metformin use and HGS, both in absolute and height-normalized forms. In the adjusted model, metformin users exhibited, on average, 2.51 kg higher absolute HGS than non-users (95% CI: 0.89–4.12; p=0.003). Similarly, metformin users showed 1.57 kg/m^2 higher normalized HGS compared with non-users (95% CI: 0.52–2.62; p=0.004) (Table 3). The adjusted effect size (Cohen's d) for the fully adjusted models was 0.76 (95% CI: 0.28–1.24) for absolute HGS and 0.73 (95% CI: 0.25–1.21) for height-normalized HGS.

Discussion

The present study aimed to evaluate the association between metformin use and handgrip strength in older women with type 2 diabetes mellitus receiving care at a primary health care center. Our findings show that metformin use was independently associated with higher absolute and height-normalized handgrip strength after adjustment for sociodemographic, anthropometric, clinical, and lifestyle factors. The magnitude of these associations was moderate, as reflected by adjusted effect sizes, supporting the robustness of the observed relationship.

Evidence regarding the association between metformin use and muscle strength in older adults with T2DM remains mixed. In line with our findings, previous observational studies have reported positive associations between metformin use and muscle-related outcomes. A cohort study conducted in the United States found that metformin use was associated with higher muscle strength (β=1.51; 95% CI: 0.06–2.95) [14], while a cross-sectional study in a Chinese population reported a lower likelihood of sarcopenia among metformin users (OR=0.51; 95% CI: 0.29–0.90) [13]. However, these results contrast with findings from studies using other methodological approaches. A Mendelian randomization study identified an inverse association between genetically proxied metformin exposure and

Table 1: Sample characteristics of participants (n=114).

Characteristics	n (%)
Sociodemographics	
Age (years), mean (SD)	69.02 (6.67)
Living arrangement	
Alone	10 (8.77)
With family members	104 (91.23)
Educational level	
None	22 (19.30)
Primary	53 (46.49)
Secondary	37 (32.46)
Technical/college	2 (1.75)
Employment status	
No	83 (72.81)
Yes	31 (27.19)
Lifestyle	
Smoking status	
No	111 (97.37)
Yes	3 (2.63)
Alcohol consumption	
No	100 (87.72)
Yes	14 (12.28)
≥5 servings of fruits and vegetables/day	
No	103 (90.35)
Yes	11 (9.65)
Moderate physical activity	
No	64 (56.14)
Yes	50 (43.86)
Sitting time (min/day), median (p25; p75)	187.5 (120; 300)
Anthropometric characteristics	
Excess body weight	
No	44 (38.60)
Yes	70 (61.40)
Abdominal obesity	
No	4 (3.51)
Yes	110 (96.49)
BMI(kg/m^2), mean (SD)	30.09 (5.21)
Waist circumference (cm), mean (SD)	97.99 (10.91)
Waist-to-height ratio, mean (SD)	0.66 (0.08)
Arm circumference (cm), mean (SD)	32.07 (4.11)

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Table 1: Continued.

Characteristics	n (%)
Thigh circumference (cm), mean (SD)	46.67 (5.30)
Calf circumference (cm), mean (SD)	35.15 (3.50)
Clinical characteristics	
Comorbidities	
No	21 (18.42)
Yes	93 (81.58)
Hypertension	
No	51 (44.74)
Yes	63 (55.26)
Dyslipidemia	
No	78 (68.42)
Yes	36 (31.58)
Other comorbidities	
No	64 (56.14)
Yes	50 (43.86)
Medication use	
Antidiabetic medications	
No	22 (19.30)
Yes	92 (80.70)
Insulin	
No	102 (89.47)
Yes	12 (10.53)
Metformin	
No	25 (21.93)
Yes	89 (78.07)
Glibenclamide	
No	104 (91.23)
Yes	10 (8.77)
Antihypertensive medications	
No	53 (46.49)
Yes	61 (53.51)
ARBs	
No	67 (58.77)
Yes	47 (41.23)
ACEi	
No	106 (92.98)
Yes	8 (7.02)

Note: SD – Standard deviation; ARBs – Angiotensin II receptor blockers; ACEi – Angiotensin-converting enzyme inhibitors.

Table 2: Diagnostic accuracy of anthropometric index tests for hypercholesterolemia and elevated plasma triglycerides, stratified by sex.

Characteristics	Metformin use		p*
	No (n=25) n (%)	Yes (n=89) n (%)	
Sociodemographic characteristics			
Age (years), mean (SD)	69.76 (7.79)	68.82 (6.36)	0.536 ¶
Living arrangement			
Alone	3 (30.00)	7 (70.00)	0.455 ‡
With family members	22 (21.15)	82 (78.85)	
Educational level			
None	5 (22.73)	17 (77.27)	
Primary	10 (18.87)	43 (81.43)	0.599 ‡
Secondary	9 (24.32)	28 (75.68)	
Technical/college	1 (50.00)	1 (50.00)	
Employment status			
No	22 (26.51)	61 (73.49)	0.053
Yes	3 (9.68)	28 (90.32)	
Lifestyle			
Smoking status			
No	24 (21.62)	87 (78.38)	0.528 ‡
Yes	1 (33.33)	2 (66.67)	
Alcohol consumption			
No	24 (24.00)	76 (76.00)	0.298 ‡
Yes	1 (7.14)	13 (92.86)	
≥5 servings of fruits and vegetables/day			
No	21 (20.39)	82 (79.61)	0.254 ‡
Yes	4 (36.36)	7 (63.64)	
Moderate physical activity			
No	17 (26.56)	47 (73.44)	0.254 ‡
Yes	8 (16.00)	42 (84.00)	
Sitting time (min/day), median (p25; p75)	240 (180; 375)	180 (120; 285)	0.020 £
Anthropometric characteristics			
Excess body weight			
No	1 (25.00)	3 (75.00)	1.00
Yes	24 (21.82)	86 (78.18)	
Abdominal obesity			
No	11 (25.00)	33 (75.00)	0.530 ‡
Yes	14 (20.00)	56 (80.00)	
BMI (kg/m^2), mean (SD)	30.1 (4.88)	30.09 (5.33)	0.989 ¶
Waist circumference (cm), mean (SD)	98.01 (11.43)	97.98 (10.83)	0.990 ¶

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Table 2: Continued.

Characteristics	Metformin use		
	No (n=25)	Yes (n=89)	p*
	n (%)	n (%)	
Waist-to-height ratio, mean (SD)	0.67 (0.08)	0.66 (0.08)	0.676¶
Arm circumference (cm), mean (SD)	32.4 (3.81)	31.97 (4.21)	0.644¶
Thigh circumference (cm), mean (SD)	46.66 (5.74)	46.68 (5.21)	0.984¶
Calf circumference (cm), mean (SD)	34.8 (3.34)	35.25 (3.56)	0.571¶
Clinical characteristics			
Comorbidities			
No	7 (33.33)	14 (66.67)	0.240‡
Yes	18 (19.35)	75 (80.65)	
Hypertension			
No	13 (25.49)	38 (74.51)	0.408
Yes	12 (19.05)	51 (80.95)	
Dyslipidemia			
No	22 (28.21)	56 (71.79)	0.017
Yes	3 (8.33)	33 (91.67)	
Other comorbidities			
No	13 (20.31)	51 (79.69)	0.637
Yes	12 (24.00)	38 (76.00)	
HGS (kg), mean (SD)	17.44 (3.51)	19.78 (3.42)	0.003¶
Height-normalized HGS (kg/m^2), mean (SD)	11.83 (2.28)	13.29 (2.20)	0.005¶
Medication use			
Insulin			
No	19 (18.63)	83 (81.37)	0.023‡
Yes	6 (50.00)	6 (50.00)	
Glibenclamide			
No	23 (22.12)	81 (77.88)	1.00‡
Yes	2 (20.00)	8 (80.00)	
Antihipertensive medications			
No	13 (24.53)	40 (75.47)	0.532
Yes	12 (19.67)	49 (80.33)	
ARBs			
No	13 (19.40)	54 (80.60)	0.436‡
Yes	12 (25.53)	35 (74.47)	
ACEi			
No	25 (23.58)	81 (76.42)	0.197
Yes	0 (0.00)	8 (100.00)	

Note: SD – Standard deviation; HGS – Handgrip strength; ARBs – Angiotensin II receptor blockers; ACEi – Angiotensin-converting enzyme inhibitors. * – Analyzed using the chi-square test unless otherwise specified; £ – Analyzed using the Mann–Whitney U test; ¶ – Analyzed using the Student's t test; ‡ – Analyzed using Fisher's exact test.

Table 3: Association between metformin use and handgrip strength.

	Absolute handgrip strength (kg)			
	Crude model		Adjusted model*	
	β (95% CI)	p	β (95% CI)	p
Metformin use				
No	Reference		Reference	
Yes	2.34 (0.80; 3.88)	0.003	2.51 (0.89; 4.12)	0.003
	Height-normalized handgrip strength (kg/m²)			
	Crude model		Adjusted model*	
	β (95% CI)	p	β (95% CI)	p
Metformin use				
No	Reference		Reference	
Yes	1.46 (0.46; 2.45)	0.005	1.57 (0.52; 2.62)	0.004

Note: * – Adjusted for age (years), educational level, alcohol consumption, moderate physical activity, total sitting time, waist circumference, insulin use, glibenclamide use, and use of other antidiabetic medications.

normal muscle strength (OR=0.64; 95% CI: 0.45–0.91) [15], suggesting that associations observed in observational studies may be influenced by residual confounding or prescribing context. Similarly, a cross-sectional study conducted in women with T2DM in the United Kingdom found no statistically significant association between metformin use and normal muscle strength (OR=1.12; 95% CI: 1.00–1.26 ; p=0.056) [18]. Furthermore, randomized controlled trials in older adults with T2DM have not demonstrated consistent improvements in HGS associated with metformin use [16, 17]. Taken together, this heterogeneity indicates that the relationship between metformin and muscle function is not uniform and may depend on study design, exposure duration, outcome definition, and baseline characteristics of the population studied. Importantly, most available evidence derives from high-income countries and mixed-sex samples, whereas studies focusing exclusively on women remain scarce and show less consistent results. In this context, our study contributes novel evidence from a Latin American primary care setting, focusing specifically on older women—a population that is underrepresented in the literature.

From a biological perspective, plausible mechanisms may underlie the positive association observed in this study. Metformin exerts its primary metabolic effects through activation of the AMP-activated protein kinase (AMPK) pathway, which has been associated with improved insulin sensitivity and modulation of low-grade chronic inflammation [24, 25]. These processes are relevant in the pathophysiology of T2DM and may indirectly support skeletal muscle function through reductions in oxidative stress, systemic inflammation, and accumulation of advanced glycation end products [10]. Nevertheless, these potential benefits must be interpreted cautiously, as AMPK activation may also attenuate anabolic signaling mediated by mTORC1, particularly in older adults [12]. The balance between favorable metabolic effects and possible inhibition of anabolic pathways may partially explain the variability of findings reported across studies.

The present findings have relevant clinical implications for primary care, where a substantial proportion of T2DM management in older adults takes place. In Peru, the prevalence of T2DM among older adults reached approximately 14% in 2024 [3], with higher prevalence among women. Current clinical practice guidelines recommend metformin as first-line pharmacological therapy for T2DM in primary care [19]; however, functional outcomes are not routinely assessed during follow-up. Our results highlight the importance of considering muscle function, in addition to glycemic control, in the clinical management of older women with T2DM. HGS assessment is a simple, low-cost, and feasible tool that could be incorporated into routine practice to aid in early identification of individuals at risk of functional decline [7].

This study has limitations that should be acknowledged. Its cross-sectional design precludes causal inference. The sample consisted exclusively of women from

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a single primary care facility, limiting generalizability to men or other health care settings. The use of convenience sampling introduces the possibility of selection bias. Although regression models were adjusted for relevant covariates, residual confounding by unmeasured factors—such as dietary intake or body composition assessed using direct methods—cannot be excluded. Additionally, metformin use was self-reported, and information on treatment duration or cumulative dose was unavailable, which may influence the observed associations.

Conclusion

This study showed a positive association between metformin use and both absolute and height-normalized handgrip strength in older women with type 2 diabetes mellitus. These findings highlight the need for longitudinal studies to evaluate the long-term impact of metformin on muscle function in this population.

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Conflict of interest

The authors declare no conflict of interest.

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