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The Relationship between the TCF7L2 rs7903146 Gene Polymorphism and Anthropometric Parameters and Muscle Mass among Patients with Type 2 Diabetes Mellitus at Puskesmas Waruroyom, Cirebon

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ABSTRACT

Background: Polymorphism of the TCF7L2 gene (rs7903146) is involved in glucose homeostasis and has been strongly associated with type 2 diabetes mellitus (T2DM). However, its relationship with anthropometric characteristics, particularly by glycemic control status, remains unclear.
Subjects and Method: This cross-sectional study included 75 patients with type 2 diabetes mellitus (T2DM) in the working area of Puskesmas Waruroyom, Cirebon. The target population comprised all registered T2DM patients, and total sampling was applied through screening. Subjects were classified into controlled (n = 37; 49.3%) and uncontrolled (n = 38; 50.7%) groups based on glycemic status. TCF7L2 rs7903146 genotypes (CC, CT, TT) were identified, and anthropometric parameters (height, body weight, BMI, waist circumference, and muscle mass) were analyzed using chi-square or Fisher's exact tests, with additional analyses for continuous variables.
Results: The most frequent genotype was CT (69.3%), followed by TT (25.3%) and CC (5.3%). No significant differences were observed in anthropometric parameters across TCF7L2 rs7903146 genotypes in both controlled and uncontrolled groups, including BMI (p= 0.580 and p= 0.830), waist circumference (p= 1.000 and p= 0.760), and muscle mass (p= 1.000 and p= 0.420), respectively.
Conclusion: The TCF7L2 rs7903146 polymorphism was not associated with anthropometric profiles among patients with T2DM, regardless of glycemic control status. This suggests that the influence of TCF7L2 is more strongly related to metabolic regulation through insulin signaling pathways rather than to determinants of body composition.

Keywords: anthropometry, diabetes mellitus, glycemic control, TCF7L2 polymorphism

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BACKGROUND

Type 2 diabetes mellitus (T2DM) is a major global public health problem with a rapidly increasing prevalence. The International Diabetes Federation (IDF) has declared diabetes a global health emergency of the 21st century, driven by unhealthy diet, physical inactivity, and genetic susceptibility. In 2021, approximately 537 million adults aged 20–79 years were living with diabetes worldwide, and this number is projected to increase to 643 million by 2030 and 783 million by 2045 (Magliano and Boyko, 2021). The World Health Organization (WHO) also reported that diabetes caused 1.5 million deaths in 2019, with nearly half occurring in individuals under 70 years of age (World Health Organization, 2023).

Southeast Asia ranks among the regions with the highest burden of T2DM, with a prevalence of 11.3% and a projected increase of 68% by 2045. Indonesia is one of the ten countries with the largest number of people living with diabetes, with cases rising from 10.7 million in 2019 to 19.46 million in 2021. Data from the 2023 Indonesian Health Survey further indicate a persistently high prevalence of T2DM among individuals aged ≥15 years across provinces and districts, highlighting the substantial and widespread impact of the disease at the community level (Ministry of Health of the Republic of Indonesia, 2024).

T2DM is a multifactorial disease resulting from complex interactions between environmental, lifestyle, metabolic, and genetic factors. Genetic predisposition contributes substantially to disease susceptibility, as reflected by familial aggregation and the identification of numerous genetic polymorphisms associated with T2DM risk (Samant et al., 2025; Kreienkamp et al., 2023). In addition to influencing disease onset, genetic variation may also modify metabolic responses to lifestyle factors such as diet and physical activity, suggesting that individual metabolic profiles may differ even under similar environmental exposures (Shin et al., (2022).

Among the identified genetic determinants, the transcription factor 7-like 2 (TCF7L2) gene is considered one of the strongest genetic risk factors for T2DM. This gene regulates insulin secretion and pancreatic β-cell function through the Wnt/β-catenin signaling pathway. The rs7903146 (C>T) polymorphism, particularly the T allele, has been consistently associated with impaired insulin secretion and increased risk of T2DM in diverse populations (Iqbal and Riaz, 2025). Furthermore, emerging evidence suggests that dysregulation of Wnt/β-catenin signaling may also affect adipogenesis and skeletal muscle metabolism, potentially influencing body composition and muscle mass, which are important determinants of metabolic health (Verma et al., 2022).

Despite extensive studies on the metabolic implications of TCF7L2 polymorphisms, evidence regarding their association with anthropometric parameters and muscle mass among patients with T2DM in Indonesia remains limited, especially in primary healthcare settings where most patients receive routine care. Moreover, glycemic control status may modify the relationship between genetic factors and physical characteristics, yet this aspect has received little attention in previous studies.

Therefore, this study aimed to analyze the association between TCF7L2 rs7903146 polymorphism and anthropometric parameters and muscle mass among patients with T2DM at Puskesmas Waruroyom, Cirebon, while considering glycemic control status. The findings are expected to contribute to a better understanding of the interaction between genetic factors and physical characteristics in T2DM patients at the primary care level.

SUBJECTS AND METHOD

1. Study Design

This was an analytical observational study with a cross-sectional design conducted to examine the association between TCF7L2 rs7903146 gene polymorphism and anthropometric parameters and muscle mass among patients with type 2 diabetes mellitus (T2DM) in the working area of Puskesmas Waruroyom, Cirebon.

2. Population and Sample

The study population was all registered T2DM patients residing in 12 villages within the working area of Puskesmas Waruroyom, Cirebon. Subjects were selected using total sampling through a screening process. Inclusion criteria were age ≥18 years, registered as a T2DM patient at Puskesmas Waruroyom, having a family history of T2DM, random blood glucose ≥200 mg/dL, and willingness to participate. Exclusion criteria included incomplete clinical data and the presence of diabetes-related complications.

A total of 75 eligible patients met the criteria and were included in the analysis. No formal sample size calculation was performed due to the limited size of the accessible population in this primary healthcare setting; therefore, this study was exploratory and may have limited statistical power to detect small or moderate associations.

3. Study Variables

The independent variable was TCF7L2 rs7903146 gene polymorphism (CC, CT, TT). The dependent variables were anthropometric parameters (height, body weight, body mass index, waist circumference) and muscle mass. Glycemic control status (controlled vs uncontrolled) was used as a stratification variable.

4. Operational Definition of Variables

TCF7L2 rs7903146 polymorphism was defined as the genetic variation identified through PCR-RFLP analysis and classified into CC, CT, and TT genotypes.

Height was measured in centimeters using a stadiometer, while body weight was measured in kilograms using a digital scale.

Body mass index (BMI) was calculated as body weight in kilograms divided by height in meters squared (kg/m²).

Waist circumference was measured in centimeters at the midpoint between the lowest rib and the iliac crest using a non-elastic measuring tape.

Muscle mass was estimated in kilograms using bioelectrical impedance analysis (BIA) according to the manufacturer's protocol.

Glycemic control status was determined based on glycated hemoglobin (HbA1c) values obtained from medical records, with controlled diabetes defined as HbA1c <7% and uncontrolled diabetes defined as HbA1c ≥7%.

5. Study Instruments

Anthropometric measurements were performed by trained health personnel using a stadiometer (accuracy 0.1 cm) and a digital scale (accuracy 0.1 kg). Waist circumference was measured using a non-elastic measuring tape, and muscle mass was assessed using bioelectrical impedance analysis (BIA) according to the manufacturer's instructions.

Genomic DNA was extracted from venous blood samples collected in EDTA using a spin column method (Tiangen DNA/RNA Extraction Kit). Genotyping of TCF7L2 rs7903146 was conducted using polymerase chain reaction–restriction fragment length polymorphism (PCR-RFLP). PCR amplification used forward primer 5′-GACTCTGCAGTGAGGCCCTA-3′ and reverse primer 5′-ACGTTGCAGTTGCCTTTCTT-3′ under the following conditions: initial denaturation at 95°C for 5 minutes; 35 cycles of denaturation at 95°C for 30 seconds, annealing at 60°C for 30 seconds, and extension at 72°C for 30 seconds; followed by final extension at 72°C for 9 minutes. PCR products were digested using RsaI restriction enzyme. Fragment patterns were CC (176 bp and 25 bp), TT (201 bp), and CT (201 bp, 176 bp, and 25 bp), and were visualized using 2% agarose gel electrophoresis under ultraviolet transillumination.

6. Data analysis

Univariate analysis was used to describe the characteristics of study participants. Bivariate analysis was performed to assess the association between TCF7L2 genotypes and anthropometric variables using chi-square test or Fisher's exact test for categorical variables, and ANOVA, Kruskal–Wallis test, or Spearman correlation for continuous variables, depending on data distribution. Statistical significance was set at $p < 0.05$. Stratified analysis by glycemic control status was conducted to explore potential effect modification.

7. Research Ethics

Ethical approval was obtained from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Swadaya Gunung Jati (No. 105/EC/FKUGJ/X/-2025). All participants received information regarding study objectives, procedures, risks, and benefits, and provided written informed consent prior to participation. Confidentiality of participant data was maintained throughout the study.

RESULTS

1. Sample Characteristics

A total of 75 participants diagnosed with T2DM participated in this study. Participants were recruited from the working area of Puskesmas Waruroyom, with a relatively balanced distribution between the controlled (49.3%) and uncontrolled (50.7%) diabetes mellitus groups. Regarding anthropometric indicators, the majority of participants were classified as having class I obesity (34.7%) and class II obesity (16.0%). This pattern was observed in both groups, with class I obesity identified in 40.5% of participants with controlled T2DM and 30.6% of those with uncontrolled T2DM.

The normal body mass index category accounted for 26.7% of the research population, with an equal distribution between the two groups. Muscle mass was predominantly within the normal category (82.7%), both among participants with controlled (83.8%) and uncontrolled (86.1%) diabetes mellitus. Most participants also had a normal waist circumference (70.7%), with comparable proportions between the controlled (73.0%) and uncontrolled (72.2%) groups (see Table 1).

Genetic analysis of the TCF7L2 rs7903146 polymorphism showed that the CT genotype was the most prevalent (69.3%), with comparable proportions in the controlled (73.0%) and uncontrolled (65.8%) groups. The TT genotype was identified in 25.3% of participants, while the CC genotype was the least prevalent (5.3%) (see Table 1).

Table 1. Participant Characteristics (n=75)

Variables	Total	%	Controlled (n=37)		Uncontrolled (n=38)	
			N	%	N	%
Body Mass Index						
Underweight	5	6.7	2	5.4	3	8.3
Normal	20	26.7	10	27.0	10	27.8
Overweight	10	13.3	4	10.8	6	16.7
Class I Obesity	26	34.7	15	40.5	11	30.6
Class II Obesity	12	16.0	6	16.2	6	16.7
Empty data	2	2.7	0	0	2	5.6
Muscle Mass						
Low (<25)	1	1.3	0	0	1	2.8
Normal (25–39)	62	82.7	31	83.8	31	86.1
High (>39)	12	16.0	6	16.2	6	16.7
Waist Circumference						
Normal (<90 cm)	53	70.7	27	73.0	26	72.2
Central obesity (≥90 cm)	21	28.0	10	27.0	11	30.6
Missing data	1	1.3	0	0	1	2.8
Polymorphism						
CC Genotype	4	5.3	1	2.7	3	7.9
CT Genotype	52	69.3	27	73.0	25	65.8
TT genotype	19	25.3	9	24.3	10	26.3

Figure 1. Electrophoresis Visualization

Identification of the TCF7L2 rs7903146 polymorphism was performed using PCR. Visualization of the amplification results is presented in Figure 1, which shows DNA band patterns corresponding to the CC, CT, and TT genotypes.

Electrophoresis visualization in Figure 1 indicates that the CT heterozygous genotype was the most frequently encountered pattern, characterized by the presence of bands at approximately 201 bp and 176 bp in most sample lanes. Some samples showed a single band at approximately 201 bp corresponding to the TT genotype, while the CC genotype was identified based on complete fragment classification in all samples.

Participant characteristics demonstrated a relatively homogeneous anthropometric profile and body composition, with a predominance of obesity, particularly class I and class II obesity, and muscle mass within the normal range. The distribution of TCF7L2 genotypes, dominated by the CT genotype, reflects genetic variation consistent with findings from previous population-based studies. These findings provide the basis for further analysis of the relationship between TCF7L2 gene polymorphisms and anthropometric parameters among patients with T2DM (see Table 2).

Table 2. Relationship between TCF7L2 Genotype and Anthropometric Characteristics and Muscle Mass Based on Glycemic Control Status

Variables	Controlled						p	Uncontrolled						p
	CC		CT		TT			CC		CT		TT		
	N	%	N	%	N	%		N	%	N	%	N	%	
BMI														
Underweight	0	0	1	3.7	1	11.1	0.58	0	0	2	8.0	1	10.0	0.83
Normal	1	100	7	25.9	2	22.2		2	66.7	7	28.0	1	10.0	
Overweight	0	0	2	7.4	2	22.2		1	33.3	3	12.0	2	20.0	
Obesity Class I	0	0	13	48.1	2	22.2		0	0	8	32.0	3	30.0	
Obesity Class II	0	0	4	14.8	2	22.2		0	0	4	16.0	2	20.0	
Missing data	0	0	0	0	0	0		0	0	1	4.0	1	10.0	
Waist Circumference														
Normal (<90 cm)	1	100	19	70.4	7	77.8	1.00	3	100	16	64.0	7	70.0	0.76
Central obesity (≥90 cm)	0	0	8	29.6	2	22.2		0	0	8	32.0	3	30.0	
Missing data	0	0	0	0	0	0		0	0	1	0	0	0	
Muscle Mass														
Low (<25)	0	0	0	0	0	0	1.00	0	0	0	0	1	10.0	0.42
Normal (25–39)	1	100	23	85.2	7	77.8		2	66.7	21	84.0	8	80.0	
High (>39)	0	0	4	14.8	2	22.2		1	33.3	4	16.0	1	10.0	

Note: a Monte Carlo test. Fisher's exact test. *Statistically significant ($p < 0.05$).
N = frequency; % = percentage.

Table 2 shows that there was no significant association between TCF7L2 genotypes (CC, CT, and TT) and body mass index, waist circumference, or muscle mass either among participants with controlled and uncontrolled T2DM (all $p > 0.05$). In both groups, the CT genotype was the most frequently observed, particularly in the class I obesity category (48.1% among participants with controlled T2DM and 32.0% among participants with uncontrolled T2DM). Most participants also had normal waist circumference, especially those with the CT genotype (70.4% among participants with controlled T2DM and 64.0% among participants with uncontrolled T2DM). Normal muscle mass predominated across all genotypes, with the

highest proportion observed in the CT genotype (85.2% among participants with controlled T2DM and 84.0% among participants with uncontrolled T2DM). These findings indicate that the TCF7L2 rs7903146 polymorphism is not associated with anthropometric characteristics or muscle mass, regardless of glycemic control status.

Spearman correlation analysis showed weak correlations between TCF7L2 genotype and continuous anthropometric variables. In the controlled group, the correlation coefficients (effect sizes) were p= 0.139 for height and p= 0.118 for body weight, with non-significant p-values (p = 0.413 and p = 0.487, respectively; n = 37). In the uncontrolled group, the correlation coefficients were p= −0.094 for height and p= 0.075 for body weight, also with non-significant p-values (p= 0.573 and p= 0.656, respectively; n = 38) (see Table 3). All correlation coefficients indicated very weak associations between genotype and anthropometric measurements.

Table 3. Analysis of the Relationship between TCF7L2 Gene Polymorphisms and Height and Body Weight Using the Spearman Correlation Test Based on Glycemic Control Status

Variables		Height	Body Weight
Controlled			
Polymorphism	Correlation Coefficient	0.139	0.118
	p	0.413	0.487
	N	37	37
Uncontrolled			
Polymorphism	Correlation Coefficient	-0.094	0.075
	p	0.573	0.656
	N	38	38

Note: a Spearman correlation test (p). Sig. (2-tailed) = p-value (two-tailed).
*Statistically significant (p < 0.05). N = number of subjects

DISCUSSION

This study examined the association between the TCF7L2 rs7903146 polymorphism and anthropometric indicators and muscle mass among patients with T2DM stratified by glycemic control status. Overall, no significant associations were observed between genotype and body mass index, waist circumference, or muscle mass, supporting the hypothesis that TCF7L2 primarily affects metabolic regulation rather than body composition.

The CT genotype was the most prevalent variant in both controlled and uncontrolled T2DM groups, indicating that this genotype represents the dominant background polymorphism in this population. Similar genotype distributions have been reported in Asian cohorts, where CT is frequently observed in both healthy individuals and those with metabolic disorders (Guan *et al.*, 2023). This suggests that genotype frequency alone may not explain variability in anthropometric outcomes.

Substantial evidence indicates that the T allele of rs7903146 is strongly associated with impaired insulin secretion and β-cell dysfunction, independent of obesity status (Cropano et al., 2020; Zeini; et al., 2024). These metabolic effects may occur before clinically detectable changes in body composition, which may explain why indi-

viduals carrying the T allele develop T2DM across a wide range of BMI categories. Therefore, TCF7L2-related diabetes risk appears to be mediated mainly through insulin signaling pathways rather than through adiposity.

Although some population-specific studies have suggested possible associations between the C allele and obesity-related traits, these findings have not been consistently observed across larger or multi-ethnic cohorts. In line with previous reports, the present study did not identify a consistent relationship between either allele and BMI or waist circumference (Noordam et al., 2018; Cropano et al., 2020). Moreover, the wide BMI distribution observed among TT genotype carriers, ranging from underweight to obesity, further supports the concept that the T allele contributes to diabetes susceptibility primarily via impaired insulin secretion rather than excess body weight (Bride et al., 2021). This pattern is consistent with the "lean diabetes" phenotype frequently reported in Asian populations.

The lack of association between TCF7L2 polymorphism and waist circumference in both glycemic control groups is also consistent with previous studies reporting stronger associations of TCF7L2 variants with hyperglycemia and dyslipidemia than with central obesity (Gunavathy et al., 2023; Elhourch et al., 2021). These findings reinforce the classification of TCF7L2 as a metabolic susceptibility gene rather than an obesity-related gene.

Muscle mass did not differ significantly across genotypes, and most participants exhibited normal muscle mass regardless of genetic variation. This suggests that TCF7L2 does not directly influence skeletal muscle composition. Prior studies have similarly reported that TCF7L2 effects are more prominent in biochemical and metabolic pathways than in structural body components (Younus et al., 2024; Lu et al., 2025). In patients with uncontrolled T2DM, reduced muscle mass is more likely attributable to chronic hyperglycemia, inflammation, and reduced physical activity rather than to genetic variation alone (Perry et al., 2016).

Correlation analysis also showed very weak and non-significant relationships between TCF7L2 genotype and height or body weight. This supports the understanding that physical growth and body size are largely influenced by polygenic and environmental factors rather than by single metabolic-risk genes such as TCF7L2 (Li et al., 2020). Additionally, some studies suggest that TCF7L2 risk alleles may exert neutral or even protective effects on body weight through mechanisms related to relative insulin deficiency (del Bosque-Plata et al., 2021)

Taken together, these findings indicate that TCF7L2 rs7903146 plays a limited role in determining anthropometric profiles but remains clinically relevant for metabolic risk stratification in patients with T2DM. Genetic screening of TCF7L2 may therefore be more informative for identifying individuals at risk of impaired insulin secretion rather than for predicting nutritional status or body composition in primary healthcare settings.

This study demonstrates that the TCF7L2 rs7903146 polymorphism is not significantly associated with anthropometric parameters, including body mass index, waist circumference, muscle mass, height, and body weight, among patients with T2DM, regardless of glycemic control status. No significant association was

observed between TCF7L2 genotype and indicators of general or central obesity. These findings support the role of TCF7L2 primarily as a metabolic risk gene influencing glucose homeostasis and β-cell function rather than body composition or adiposity.

From a practical perspective, these results suggest that routine anthropometric measurements in primary healthcare settings, such as body mass index and waist circumference, remain essential for nutritional assessment and lifestyle counseling but may not reflect underlying genetic susceptibility related to TCF7L2. Therefore, prevention and management strategies for T2DM in primary care should continue to emphasize lifestyle modification, including diet and physical activity, irrespective of TCF7L2 genetic status.

This study has several limitations. The relatively small sample size and single-center design may limit generalizability and statistical power to detect small genetic effects. Important confounding factors, including dietary intake, physical activity, duration of diabetes, and medication use, were not fully controlled and may influence anthropometric outcomes. In addition, the absence of a healthy control group prevents assessment of the role of rs7903146 in diabetes susceptibility. Future studies with larger, multi-center samples and inclusion of non-diabetic controls are recommended to better clarify genotype–phenotype relationships.

Future studies are recommended to include larger and more diverse populations, as well as healthy control groups, to better clarify the role of TCF7L2 polymorphisms in T2DM susceptibility. Further research should also explore interactions between genetic variants, dietary patterns, physical activity, and other metabolic biomarkers to provide a more comprehensive understanding of personalized risk profiles and to support the development of precision-based prevention strategies for T2DM.

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CONFLICT OF INTEREST

There was no conflict of interest in this study.

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