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INTRODUCTION

Infertility is defined as failure to achieve pregnancy after twelve or more months of regular unprotected intercourse (1,2). Global prevalence estimates suggest that approximately 72.4 million couples are affected; however, reliable worldwide data remain incomplete (3). Disturbances attributable to the male partner contribute to roughly half of all cases (1,2) and may stem from genetic factors, environmental exposures, comorbid medical

conditions, or pharmacological agents (4). A clinically relevant but often overlooked observation is that infertile men frequently harbor metabolic disturbances—including prediabetes, diabetes mellitus (DM), and metabolic syndrome (MetS)—that detrimentally affect both sperm characteristics and hormonal homeostasis (5-8).

MetS is a clustering of interrelated metabolic abnormalities encompassing visceral adiposity, insulin resistance (IR),

Association of triglyceride-glucose index with serum testosterone and semen parameters in fertile and infertile men

Abstract

Aim: The triglyceride-glucose (TyG) index serves as a practical surrogate measure of insulin resistance (IR), a condition known to exert adverse effects on male reproductive function. This investigation examined how the TyG index relates to serum testosterone concentrations and sperm quality indicators in men with and without fertility impairment.

Materials and Methods: This retrospective study enrolled 302 men who were stratified by their TyG index into two groups: low (TyG < 8.1, n = 78) and high (TyG > 8.1, n = 224). Participants were additionally classified according to fertility status. Reproductive hormones, semen characteristics, and metabolic variables were compared. Statistical evaluation employed Spearman rank correlation and multiple linear regression adjusted for age, body mass index (BMI), and varicocele presence. Receiver operating characteristic (ROC) curve analysis was performed for infertility status and biochemical hypogonadism.

Results: The High-TyG group was significantly older and had higher BMI, fasting glucose, total cholesterol, triglycerides, and low-density lipoprotein cholesterol, alongside lower total testosterone and high-density lipoprotein cholesterol, than the Low-TyG group (all p < .001). Lower testosterone in the High-TyG group was observed among primary and secondary infertile men, but not among fertile men. The TyG index showed significant inverse correlations with total testosterone (ρ = -0.354, p < .001) and non-progressive motility (ρ = -0.338, p < .001). Multivariable regression identified the TyG index as a significant independent predictor of total testosterone (B = -56.26, 95% confidence interval [CI]: -87.52 to -25.00, p < .001). The area under the ROC curve (AUC) was 0.892 (95% CI: 0.855 – 0.928) for infertility status and 0.692 (95% CI: 0.619 – 0.765) for biochemical hypogonadism.

Conclusion: Elevated TyG index co-exists with metabolic disturbances, diminished testosterone, and impaired sperm motility. Given its derivation from standard laboratory measurements, the TyG index may offer a cost-efficient means to flag subfertility risk.

Keywords: Insulin resistance; infertility, male; testosterone; semen analysis; triglycerides

hyperglycaemia, atherogenic dyslipidaemia, and arterial hypertension. Evidence from multiple investigations documents endocrine imbalances and compromised semen quality in men with MetS (9,10). Among the pathophysiological mechanisms involved, IR occupies a central role: hyperinsulinaemia arising from IR suppresses hepatic synthesis of sex hormone-binding globulin (SHBG), thereby lowering bioavailable testosterone (11,12). Beyond this, impaired insulin signalling interferes with steroidogenesis at the level of testicular Leydig cells. Studies employing the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) as a metric of IR severity have linked higher IR scores to reduced testosterone concentrations, smaller semen volumes, and diminished progressive motility (13). Persistent elevation of pro-inflammatory cytokines driven by IR further destabilises the hypothalamic-pituitary-testicular axis, producing a state of functional or metabolic hypogonadism (6). Meta-analytic data confirm significantly lower testosterone and inhibin-B values in men with MetS relative to metabolically healthy controls (10,14).

Despite its status as the reference standard for IR quantification (15), HOMA-IR carries practical limitations stemming from inter-laboratory variability in insulin measurement, technical complexity, and relatively elevated cost (16-18). These shortcomings have motivated interest in alternative IR surrogates that can be derived from routine fasting panels. The triglyceride-glucose (TyG) index, computed from standard fasting glucose and triglyceride measurements, has been validated as a reliable IR proxy owing to its strong concordance with HOMA-IR and fasting insulin across diverse populations (19-23). Given the mechanistic connections between IR, impaired spermatogenesis, suppressed testosterone biosynthesis, and heightened oxidative stress, the TyG index warrants evaluation in the andrology clinic.

Notwithstanding established associations among IR, MetS, and male subfertility, the specific clinical utility of the TyG index in men presenting with fertility concerns has not been thoroughly characterised. Accordingly, the primary objective of this retrospective cross-sectional study was to delineate the relationships among the TyG index, semen quality indicators, reproductive hormone profiles, and lipid parameters across fertile and infertile men.

MATERIALS AND METHODS

Study Population and Patient Assessment

This retrospective study enrolled 302 men who attended the urology outpatient service with concerns regarding fertility. Ethical approval was granted by the Recep Tayyip Erdogan University Non-Interventional Clinical Research Ethics Committee (approval date: 29.05.2025, approval no: 2025/242), following which patient records from January 2025 to April 2025 were retrospectively reviewed and relevant data were extracted at the Andrology Outpatient Clinic of Recep Tayyip Erdogan University Training and Research Hospital. Required sample size was estimated using G*Power (version 3.1, Kiel, Germany),

positing an effect size of 0.40, a two-tailed α of 0.05, and 90% statistical power.

Participants were allocated to two strata according to their TyG index: a Low-TyG group (TyG index < 8.1 , $n = 78$) and a High-TyG group (TyG index > 8.1 , $n = 224$). Each stratum was then divided by reproductive status into three subgroups—fertile, primary infertility (defined as inability to achieve conception after twelve months of regular unprotected intercourse with a partner of established fertility), and secondary infertility (defined as inability to conceive again after a prior natural conception, following at least twelve months of unprotected intercourse).

Fertility diagnoses were established by specialist urologists using the criteria of the World Health Organization (WHO) Laboratory Manual for the Examination and Processing of Human Semen (24). Consistent with WHO guidance, when an initial semen analysis yielded out-of-reference-range values, a confirmatory second sample was requested. Fertile controls were men who had fathered at least one child by natural conception within the preceding two years, verified through hospital registry documentation. Patients with established causes of infertility—including hormonal disorders, obstructive aetiology, chromosomal or genetic anomalies (e.g., Klinefelter syndrome, Y-chromosome microdeletions), or DM irrespective of glycaemic control, as well as those on antidiabetic therapy—were excluded to minimise confounding. All participants underwent a structured medical history review, a comprehensive general examination incorporating genital assessment, and recording of anthropometric data. Body mass index (BMI) was derived from weight in kilograms divided by height in metres squared. Varicocele was assessed by physical examination and confirmed using scrotal Doppler ultrasonography; a diagnosis was established when pampiniform venous diameter exceeded 3.0 mm with documented retrograde venous flow.

Blood Sample Collection and Biochemical Analysis

Fasting venous blood was drawn between 09:00 and 11:00 h following a minimum 12-hour fast. Biochemical parameters, fasting glucose, triglycerides (TG), total cholesterol, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C), were quantified on a Beckman Coulter AU5800 automated chemistry analyser (Brea, CA, USA) in accordance with standardised operating procedures. Reproductive hormones—follicle-stimulating hormone (FSH), luteinizing hormone (LH), total testosterone (tT), and estradiol (E2)—were measured by chemiluminescent immunoassay on a Siemens ADVIA Centaur XPT platform (Forchheim, Germany), in conformance with the manufacturer's instructions. Instrument calibration and internal quality-control procedures were performed daily per manufacturers' protocols. The TyG index was derived using the following formula:

$$\text{TyG index} = \ln [\text{fasting triglycerides (mg/dL)} \times \text{fasting glucose (mg/dL)} / 2]$$

A threshold value of 8.1 was applied to classify IR status, consistent with prior validation studies (25). Hypogonadism was operationally defined as a tT concentration below 300 ng/dL in accordance with established guidelines (26).

Semen Analysis

Semen specimens were obtained by masturbation following an abstinence interval of 2–7 days, conforming to WHO Laboratory Manual recommendations (24). After complete liquefaction at room temperature for approximately 30 minutes, samples were maintained at 37 °C throughout evaluation to protect sperm viability. Assessed ejaculate parameters included volume (mL), total sperm count (millions per ejaculate), total progressive motility (%), non-progressive motility (%), immotility (%), and morphology (%). Motility analysis was conducted manually using phase-contrast microscopy (Olympus BX43; Hachiōji, Tokyo, Japan) at 400× magnification. Each sample was assessed independently by two experienced laboratory personnel who were blinded to clinical data; discrepancies were resolved by consensus.

Statistical Analysis

Analyses were conducted using IBM SPSS Statistics version 23.0 (IBM Corp., Armonk, NY, USA) and OriginPro 2026 (OriginLab Corporation, Northampton, MA, USA). Data quality was verified by screening for missing values and univariate outliers using box plots. Distribution normality was assessed with the Shapiro-Wilk test. Between-group comparisons of continuous non-normally distributed variables were performed with the Mann-Whitney U test; categorical variables were evaluated by Chi-square analysis. Associations among continuous variables were quantified using Spearman rank correlation (ρ), interpreted as weak (0 – 0.3), moderate (0.3 – 0.7), or strong (> 0.7). Continuous data are reported as median (Q1 – Q3) and categorical data as frequency and percentage. To probe the independent contribution of the TyG index to tT variance, a multiple linear regression model was constructed incorporating age, BMI, and varicocele as covariates. Multicollinearity was evaluated through variance inflation factor (VIF) values and collinearity diagnostics.

To validate the TyG index threshold of 8.1 within our study population, receiver operating characteristic (ROC) curve analysis was performed using infertility status (fertile = 0; infertile = 1, combining primary and secondary infertility) as the state variable, with the primary aim of confirming the discriminatory capacity of the grouping strategy rather than proposing the TyG index as a diagnostic test for infertility per se. A second ROC curve analysis was conducted with biochemical hypogonadism (total testosterone < 300 ng/dL = 1; ≥ 300 ng/dL = 0) as the outcome variable, to evaluate the clinical utility of the TyG index as a metabolic screening marker for androgen deficiency. For each analysis, the area under the curve (AUC) and its 95% confidence interval were

calculated to quantify discriminatory performance. The optimal cut-off was defined as the threshold at which sensitivity and specificity were most closely balanced. The diagnostic performance of the pre-specified literature-derived threshold of 8.1 was additionally reported for comparison. A two-tailed $p < .05$ was the threshold for statistical significance. Figures were generated with OriginPro 2026 (OriginLab Corporation, Northampton, MA, USA).

RESULTS

Comparison of Fertility Status and Clinical Parameters by TyG Index

Men in the High-TyG group were significantly older, heavier, and had higher BMI than those in the Low-TyG group (all $p < .001$), while height, smoking, and alcohol use did not differ between groups ($p > .05$). Varicocele prevalence was significantly higher in the Low-TyG group ($p < .001$). The High-TyG group demonstrated a markedly adverse metabolic profile, with significantly elevated fasting glucose, total cholesterol, triglycerides, and LDL-C, alongside lower HDL-C (all $p < .001$). Total testosterone was also significantly reduced in the High-TyG group ($p < .001$), whereas FSH, LH, and E2 were comparable between groups ($p > .05$). Regarding semen parameters, ejaculate volume, total sperm count, and total progressive motility did not differ significantly (all $p > .05$). However, non-progressive motility was significantly lower ($p < .001$), and both immotility and morphology showed significant differences in the High-TyG group (both $p < .05$). Notably, the High-TyG group contained a markedly smaller proportion of fertile men (7.6% vs. 52.6%) and substantially higher rates of primary infertility (67.0% vs. 29.5%) (all $p < .001$) (Table 1).

Fertile Men Stratified by TyG Index

Among fertile men, age did not differ between groups ($p > .05$), whereas BMI was significantly higher in the High-TyG subgroup ($p < .001$). Semen volume and total sperm count were comparable (both $p > .05$); however, the High-TyG group showed significantly lower total progressive motility and morphology, alongside significantly higher immotility (all $p < .001$). Non-progressive motility was also significantly reduced in the High-TyG group ($p < .001$). Regarding hormonal parameters, FSH, LH, E2, and total testosterone did not differ significantly between groups (all $p > .05$). Metabolically, fasting glucose was comparable between groups ($p > .05$), whereas total cholesterol and triglycerides (both $p < .001$) and LDL-C ($p < .01$) were significantly elevated, and HDL-C was significantly reduced ($p < .01$) in the High-TyG group (Table 2).

Primary Infertile Men Stratified by TyG Index

Among men with primary infertility, age did not differ between groups ($p > .05$), while BMI was significantly higher in the

High-TyG subgroup ($p < .05$). Most semen parameters — including volume, total sperm count, total progressive motility, immotility, and morphology — were comparable between groups (all $p > .05$). Non-progressive motility, however, was significantly lower in the High-TyG group ($p < .001$). Hormonally, FSH, LH, and E2 did not differ significantly (all $p > .05$), whereas total testosterone was significantly reduced in the High-TyG group ($p < .01$). Metabolically, fasting glucose, total cholesterol, and triglycerides were all significantly elevated in the High-TyG group ($p < .01$, $p < .01$, and $p < .001$, respectively), and HDL-C was significantly lower ($p < .05$). LDL-C did not reach statistical significance in this subgroup ($p > .05$) (Table 3).

Secondary Infertile Men Stratified by TyG Index

Among men with secondary infertility, age, BMI, and all semen parameters — including volume, total sperm count, total progressive motility, non-progressive motility, immotility, and morphology were comparable between groups (all $p > .05$). Similarly, FSH, LH, and E2 did not differ significantly (all $p > .05$), whereas total testosterone was significantly lower in the High-TyG group ($p < .05$). Metabolically, fasting glucose, total cholesterol, and LDL-C were significantly elevated in the High-TyG group ($p < .01$, $p < .01$, and $p < .05$, respectively), with triglycerides showing the most pronounced difference (all $p < .001$). HDL-C did not reach statistical significance in this subgroup ($p > .05$) (Table 4).

Table 1. Comparison of clinical and reproductive parameters between low and high TyG index groups

Parameters	TyG index < 8.1 (n = 78) Median (Q1 – Q3) / % (n)	TyG index > 8.1 (n = 224) Median (Q1 – Q3) / % (n)	p (Mann-Whitney U / Chi-Square)
TyG index	7.94 (7.8 – 8.04)	8.72 (8.51 – 9.05)	$p < .001^a$
Fertile men, % (n)	52.6% (41)	7.6% (17)	$p < .001^b$
Primary infertile, % (n)	29.5% (23)	67.0% (150)	
Secondary infertile, % (n)	17.9% (14)	25.4% (57)	
Age (Years)	29 (23.7 – 32)	33 (28 – 38)	$p < .001^a$
Height (cm)	176 (172 – 180.2)	175 (170 – 180)	$p > .05^a$
Weight (kg)	73 (68 – 86)	82.5 (76 – 90)	$p < .001^a$
BMI (kg/m ²)	23.1 (21.1 – 25.6)	27 (25.1 – 29.3)	$p < .001^a$
Smoking, Yes, % (n)	75.6% (59)	78.1% (175)	$p > .05^b$
Alcohol, Yes, % (n)	43.6% (34)	43.8% (98)	$p > .05^b$
Varicocele, Yes, % (n)	66.7% (52)	43.8% (98)	$p < .001^b$
Semen volume (mL)	3.63 (2.7 – 5.1)	3.56 (2.7 – 5)	$p > .05^a$
Total sperm count $\times 10^6$	148.7 (57.9 – 240.7)	127.1 (47.9 – 253.7)	$p > .05^a$
Total progressive motility (%)	38 (32 – 45)	38 (30 – 45.7)	$p > .05^a$
Non-progressive motility (%)	5.5 (4 – 7)	4 (2 – 5)	$p < .001^a$
Immotility (%)	56 (48 – 62)	58 (50 – 66)	$p < .05^a$
Morphology (%)	3 (1 – 5)	3 (1 – 4)	$p < .05^a$
FSH (mIU/mL)	3.41 (2.1 – 5.56)	3.38 (2.38 – 5.7)	$p > .05^a$
LH (mIU/mL)	3.50 (2.57 – 4.75)	3.78 (2.71 – 4.92)	$p > .05^a$
E2 (pg/mL)	30.5 (24.3 – 37.1)	28.7 (22.7 – 35)	$p > .05^a$
tT (ng/dL)	490.5 (395.2 – 585.5)	396.2 (298.6 – 510.9)	$p < .001^a$
Glucose (mg/dL)	85 (80 – 91)	93 (87 – 100)	$p < .001^a$
Cholesterol (mg/dL)	169.5 (142.8 – 195.8)	208 (178.5 – 234)	$p < .001^a$
TG (mg/dL)	64 (52 – 73.25)	132 (110 – 187.5)	$p < .001^a$
HDL (mg/dL)	49.3 (44.6 – 55)	44.8 (38.3 – 49.4)	$p < .001^a$
LDL (mg/dL)	107.8 (83.9 – 133.8)	134.9 (109.2 – 158.4)	$p < .001^a$

^aMann-Whitney U, ^bChi-square Abbreviations: BMI, Body Mass Index; FSH, Follicle-Stimulating Hormone; LH, Luteinizing Hormone; tT, Total Testosterone; E2, Estradiol; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein; TG, Triglycerides; TyG, Triglyceride–Glucose Index.

Table 2. Comparison of Clinical, Semen, and Hormonal Parameters in Fertile Men by TyG Index

Parameters	TyG index < 8.1 (Fertile, n = 41) Median (Q1 – Q3)	TyG index > 8.1 (Fertile, n = 17) Median (Q1 – Q3)	p (Mann-Whitney U)
Age (Years)	25 (21 – 29)	28 (26 – 29.5)	p > .05
BMI (kg/m ²)	22.2 (20.9 – 24)	25.3 (23.3 – 27.3)	p < .001
Semen volume (mL)	3.5 (2.58 – 5.64)	4.13 (2.8 – 4.9)	p > .05
Total sperm count	177.9 (83.3 – 285.6)	165.2 (79.8 – 342.9)	p > .05
Total progressive motility (%)	38 (33 – 45)	26 (21 – 33)	p < .001
Non-progressive motility (%)	6 (5 – 7)	3 (2 – 4)	p < .001
Immotility (%)	56 (48 – 62)	72 (63.5 – 76)	p < .001
Morphology (%)	3 (1.5 – 5)	1 (0.5 – 2)	p < .001
FSH (mIU/mL)	3.20 (1.92 – 5.01)	3.04 (1.97 – 6.14)	p > .05
LH (mIU/mL)	3.35 (2.69 – 4.91)	3.78 (2.82 – 5.28)	p > .05
E2 (pg/mL)	31.1 (27.2 – 38.4)	29 (18.5 – 33)	p > .05
tT (ng/dL)	496.8 (389.0 – 589.1)	537.7 (466.8 – 783.0)	p > .05
Glucose (mg/dL)	84 (78.5 – 89.5)	86 (80 – 90)	p > .05
Cholesterol (mg/dL)	163 (137 – 185.5)	206 (179 – 224.5)	p < .001
TG (mg/dL)	60 (46 – 73.5)	108 (95 – 114)	p < .001
HDL (mg/dL)	49 (46.1 – 54.1)	40.8 (38.5 – 47.6)	p < .01
LDL (mg/dL)	99.2 (76.7 – 122.1)	140.9 (101.3 – 165.8)	p < .01

Abbreviations: BMI, Body Mass Index; FSH, Follicle-Stimulating Hormone; LH, Luteinizing Hormone; tT, Total Testosterone; E2, Estradiol; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein; TG, Triglycerides; TyG, Triglyceride–Glucose Index.

Table 3. Comparison of Clinical, Hormonal, and Semen Parameters in Primary Infertile Men by TyG Index

Parameters	TyG Index < 8.1 (Primary infertility, n = 23) Median (Q1 – Q3)	TyG Index > 8.1 (Primary infertility, n = 150) Median (Q1 – Q3)	p (Mann-Whitney U)
Age (Years)	30 (28 – 31)	32 (28 – 37)	p > .05
BMI (kg/m ²)	24.69 (23.1 – 27.7)	26.9 (25 – 29.3)	p < .05
Semen volume (mL)	3.64 (2.78 – 4.57)	3.55 (2.69 – 5.06)	p > .05
Total sperm count (×10 ⁶)	155.3 (16.3 – 213.5)	120.9 (43.4 – 255.7)	p > .05
Total progressive motility (%)	38 (34 – 41)	39 (32 – 47)	p > .05
Non-progressive motility (%)	6 (4 – 7)	4 (2 – 5)	p < .001
Immotility (%)	58 (52 – 62)	57.5 (50 – 64)	p > .05
Morphology (%)	4 (1 – 6)	3 (0.75 – 4)	p > .05
FSH (mIU/mL)	2.69 (1.77 – 5.34)	3.35 (2.39 – 5.51)	p > .05
LH (mIU/mL)	3.36 (2.46 – 4.52)	3.82 (2.58 – 4.91)	p > .05
E2 (pg/mL)	25.6 (20.5 – 32.4)	28.2 (22.5 – 36.2)	p > .05
tT (ng/dL)	481 (396.1 – 584.8)	395 (301.3 – 482.1)	p < .01
Glucose (mg/dL)	86 (83 – 94)	93 (87 – 100)	p < .01
Cholesterol (mg/dL)	174 (160 – 200)	207 (176 – 231.7)	p < .01
TG (mg/dL)	69 (63 – 75)	135.5 (115.7 – 189.7)	p < .001
HDL (mg/dL)	49.8 (42.6 – 53.4)	44.7 (38.4 – 49.1)	p < .05
LDL (mg/dL)	112.7 (97.6 – 140.4)	134.2 (107.1 – 155.1)	p > .05

Abbreviations: BMI, Body Mass Index; FSH, Follicle-Stimulating Hormone; LH, Luteinizing Hormone; tT, Total Testosterone; E2, Estradiol; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein; TG, Triglycerides; TyG, Triglyceride–Glucose Index.

Table 4. Comparison of Clinical, Hormonal, and Semen Parameters in Secondary Infertile Men by TyG Index

Parameters	TyG Index < 8.1 (Secondary infertility, n = 14) Median (Q1 – Q3)	TyG Index > 8.1 (Secondary infertility, n = 57) Median (Q1 – Q3)	P (Mann-Whitney U)
Age (Years)	38 (31.5 – 40.5)	38 (35 – 42)	p > .05
BMI (kg/m ²)	26.6 (20.8 – 28.5)	27.7 (25.9 – 29.7)	p > .05
Semen volume (mL)	4.21 (2.68 – 5.38)	3.6 (2.57 – 4.55)	p > .05
Total sperm count (×10 ⁶)	81.8 (51.4 – 186.9)	128.7 (70.6 – 241)	p > .05
Total progressive motility (%)	41 (31 – 50)	38 (29 – 44)	p > .05
Non-progressive motility (%)	4.5 (3 – 6)	4 (2 – 5.5)	p > .05
Immotility (%)	54 (44 – 64)	58 (50 – 66)	p > .05
Morphology (%)	2 (0 – 4)	3 (1 – 4)	p > .05
FSH (mUI/mL)	6.04 (3.52 – 9.32)	3.8 (2.73 – 5.81)	p > .05
LH (mUI/mL)	4.32 (2.79 – 5.13)	3.7 (2.9 – 4.87)	p > .05
E2 (pg/mL)	31.3 (19.6 – 35.6)	31 (25.2 – 34.6)	p > .05
tT (ng/dL)	493.4 (390.6 – 552.4)	338.5 (286.1 – 480.1)	p < .05
Glucose (mg/dL)	85.5 (81.2 – 92)	97 (90 – 109)	p < .01
Cholesterol (mg/dL)	178 (150 – 195)	214 (183 – 246)	p < .01
TG (mg/dL)	62 (51.2 – 70)	134 (111 – 228)	p < .001
HDL (mg/dL)	52 (41.5 – 56.6)	45.7 (39.1 – 51.1)	p > .05
LDL (mg/dL)	123.1 (84.1 – 137.8)	137.4 (113.7 – 160.1)	p < .05

Abbreviations: BMI, Body Mass Index; FSH, Follicle-Stimulating Hormone; LH, Luteinizing Hormone; tT, Total Testosterone; E2, Estradiol; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein; TG, Triglycerides; TyG, Triglyceride–Glucose Index.

Correlation Between TyG Index and Metabolic, Hormonal, and Semen Parameters

Spearman correlation analysis revealed that TyG index was significantly and positively correlated with BMI ($\rho = 0.459$, $p < .001$), and significantly and negatively correlated with total testosterone ($\rho = -0.341$, $p < .001$) and non-progressive motility ($r = -0.337$, $p < .001$). In contrast, TyG index showed no significant correlation with total sperm count, total progressive motility, immotility, morphology, or FSH (all $p > .05$) (Figure 1).

Multiple Linear Regression Analysis

To examine the independent contribution of the TyG index to serum testosterone variance, a multiple linear regression model was constructed with age, BMI, and varicocele status as covariates. The overall model reached statistical significance ($F(4, 297) = 14.65$, $p < .001$) and explained approximately 15.3% of the variance in total testosterone (Adjusted $R^2 = 0.154$). Both BMI ($B = -9.48$, 95% CI: -13.98 to -4.98, $p < .001$) and TyG index ($B = -56.26$, 95% CI: -87.52 to -25.00, $p < .001$) emerged as significant independent predictors of total testosterone, each demonstrating a significant inverse association. Age ($B = -0.095$, 95% CI: -2.77 to 2.58, $p = .945$) and varicocele status ($B = -0.012$, 95% CI: -34.17 to 34.15, $p > .99$) were not independently associated with testosterone levels. No multicollinearity was

detected, as all VIF values remained below 1.5. The inverse relationship between total testosterone and TyG index is illustrated in Figure 2 as a scatter plot with a fitted regression line.

ROC Curve Analyses

ROC curve analysis using infertility status as the state variable yielded an AUC of 0.892 (95% CI: 0.855 – 0.928; $p < 0.001$; Figure 3), confirming that the TyG index effectively captures the metabolic divergence between fertile and infertile men and supporting the validity of the TyG > 8.1 grouping strategy within our cohort. The software-identified optimal cut-off was 8.34 (sensitivity: 77.5%; specificity: 77.6%). At the pre-specified 8.1 threshold, sensitivity was 84.8% and specificity was 70.7%, confirming the applicability of this cut-off in our population.

In the clinically focused analysis targeting biochemical hypogonadism (total testosterone < 300 ng/dL), the TyG index yielded an AUC of 0.692 (95% CI: 0.619 – 0.765; $p < 0.001$; Figure 4), reflecting moderate discriminatory performance. The optimal cut-off was 8.70 (sensitivity: 65.1%; specificity: 64.9%). At the 8.1 threshold, sensitivity reached 88.9% with a specificity of 29.7%, a trade-off consistent with the lower cut-off value and appropriate for a metabolic screening context where maximising sensitivity is clinically prioritised.

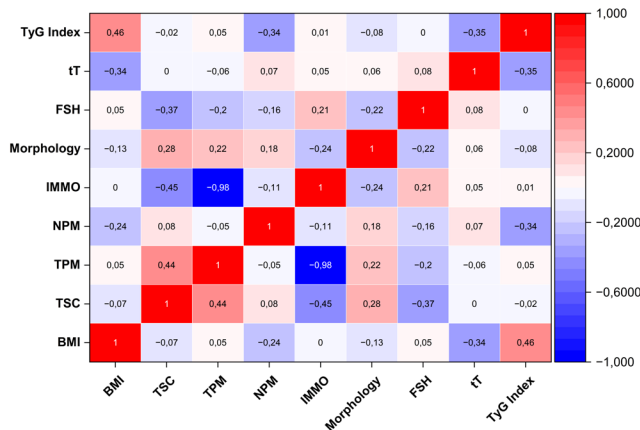


Figure 1. Spearman correlation heatmap of TyG index with clinical, hormonal, and semen parameters.

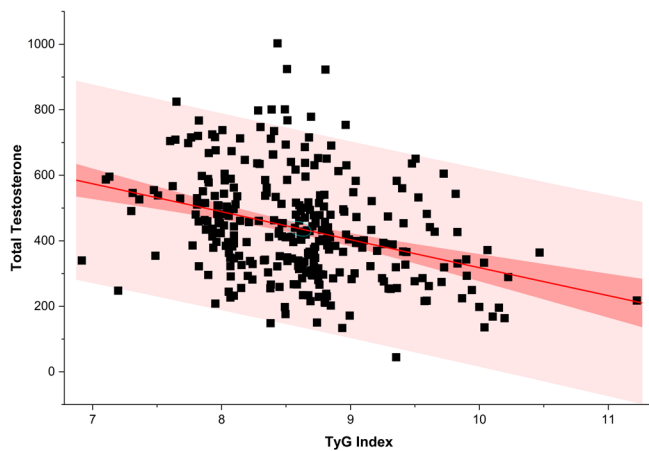


Figure 2. Scatter plot with fitted linear regression line illustrating the inverse relationship between serum total testosterone (ng/dL) and the TyG index.

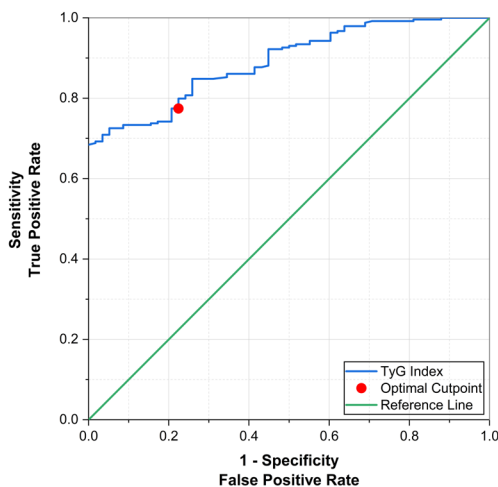


Figure 3. ROC curve illustrating the capacity of the TyG index to discriminate infertile men (primary and secondary infertility combined, $n = 244$) from fertile controls ($n = 58$), presented to validate the metabolic divergence captured by the TyG > 8.1 grouping strategy. AUC = 0.892 (95% CI: 0.855 – 0.928; $p < 0.001$). The red dot indicates the software-identified optimal cut-off (TyG = 8.34; sensitivity: 77.5%; specificity: 77.6%).

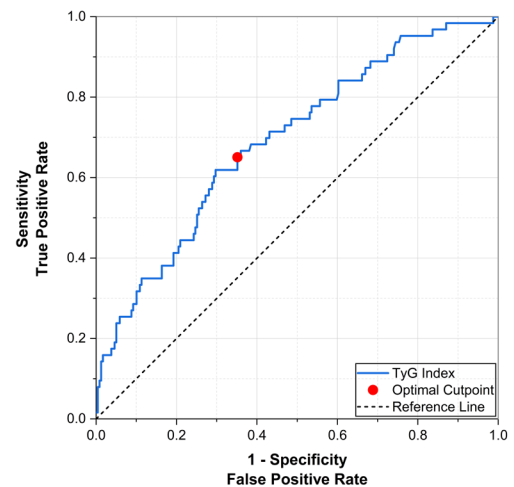


Figure 4. ROC curve for the TyG index as a metabolic screening marker for biochemical hypogonadism (total testosterone < 300 ng/dL). AUC = 0.692 (95% CI: 0.619 – 0.765; $p < 0.001$). The red dot indicates the software-identified optimal cut-off (TyG = 8.70; sensitivity: 65.1%; specificity: 64.9%). At the pre-specified threshold of 8.1, sensitivity was 88.9% and specificity was 29.7%.

DISCUSSION

The present study demonstrated that men with an elevated TyG index (> 8.1), a widely used surrogate marker of IR, exhibit measurable reproductive impairment, particularly with regard to testosterone concentrations. Higher TyG values corresponded to significantly lower tT levels in the overall cohort and in both primary and secondary infertile men, whereas no such difference was observed among fertile men. While ejaculate volume, total sperm count, and total progressive motility did not differ significantly in the overall cohort, non-progressive motility and morphology were significantly impaired in the High-TyG group, and immotility was significantly elevated. Subgroup analyses further revealed meaningful differences in sperm motility and morphology among fertile men with elevated TyG. Spearman correlation analysis confirmed a significant inverse relationship between TyG index and both total testosterone and non-progressive motility. Critically, multiple linear regression analysis identified the TyG index as a significant independent predictor of total testosterone, independent of age, BMI, and varicocele status. These findings suggest that progressive metabolic deterioration may adversely affect male reproductive function, though causal inference awaits prospective confirmation. A notable practical strength of the present study is the use of the TyG index, which is derived solely from fasting glucose and triglyceride values routinely obtained in standard metabolic panels, unlike HOMA-IR, which additionally requires an insulin assay with associated methodological variability and cost. Our study thereby addresses a clinically underrepresented area in andrology by demonstrating the potential utility of the TyG index as an accessible metabolic risk stratification tool in men presenting with fertility concerns..

Several prior investigations support and contextualise the present findings. Belladelli et al. conducted a cross-sectional study in primary infertile men and documented that those with

TyG > 8.1 had significantly lower testosterone, reduced sperm concentration, and elevated sperm DNA fragmentation rates (25). A comprehensive meta-analysis incorporating data from 2,923 infertile men and 14,062 healthy controls demonstrated that MetS was consistently associated with lower testosterone and inhibin-B concentrations, worse overall semen quality, and increased sperm DNA fragmentation (10). Salvio et al. emphasised that MetS impairs male reproductive function through endocrine and inflammatory pathways that extend beyond its well-recognised cardiometabolic consequences (27). The absence of significant overall cohort-level differences in total sperm count and progressive motility is consistent with findings reported by Ventimiglia et al., who examined 1,337 infertile men and found no meaningful differences in fundamental semen parameters between those with and without MetS, attributing this to the inherently multifactorial aetiology of male infertility (28). Notably, however, subgroup analyses in the present study revealed that fertile men with a high TyG index exhibited significantly lower total progressive motility, lower non-progressive motility, higher immotility, and worse morphology compared to their low-TyG counterparts, suggesting that TyG-associated metabolic burden may exert subtle but detectable effects on sperm function even in men who have achieved natural conception.

The biological mechanisms linking IR to male reproductive impairment are multifaceted. At the gonadal level, disrupted insulin signalling at testicular Leydig cell receptors directly compromises steroidogenic enzyme activity, resulting in reduced androgen synthesis (12-14). At the systemic level, visceral adiposity characteristic of MetS drives chronic low-grade inflammation, with pro-inflammatory cytokines and adipokines released from hypertrophied adipose tissue impairing both local testicular function and central hypothalamic-pituitary regulation (29-31). Inflammatory mediators associated with MetS attenuate gonadotropin-releasing hormone (GnRH) secretion by disrupting the hypothalamic kisspeptin-GnRH neuroendocrine network, leading to secondary suppression of LH and FSH and ultimately contributing to functional hypogonadism (32,33). Consistent with this mechanism, a trend toward lower FSH was observed in the High-TyG secondary infertile subgroup compared to Low-TyG counterparts (3.8 vs. 6.04 mIU/mL, $p = .058$), although this difference did not reach statistical significance, likely reflecting limited statistical power owing to the markedly unequal subgroup sizes (Low-TyG: $n = 14$; High-TyG: $n = 57$). Nonetheless, this pattern supports a centrally mediated suppression of gonadotropin secretion rather than a primary spermatogenic failure, given that men with secondary infertility have demonstrated prior natural conception and thus retain residual spermatogenic capacity. Additionally, the excess generation of reactive oxygen species inherent to MetS inflicts oxidative damage on spermatogenic cells, compromising sperm DNA integrity and motility (34-36). The convergence of these pathways provides a mechanistic basis for the TyG index—as a composite marker of the underlying metabolic milieu—to reflect reproductive risk in clinical settings.

From a clinical utility standpoint, the TyG index is particularly well-suited for large-scale screening because it requires no additional laboratory tests beyond those already included in routine metabolic panels (37). Belladelli et al. reported a significant positive correlation between the TyG index and HOMA-IR in infertile men (Spearman $\rho = 0.46$, $p < .001$), supporting its validity as a reliable IR surrogate in this population (25). Furthermore, multiple independent investigations indicate that the TyG index equals or surpasses HOMA-IR in predicting incident metabolic disease. A large prospective study demonstrated a superior AUC for the TyG index over HOMA-IR in predicting type 2 diabetes (0.784 vs. 0.728) (38), and comparable or superior diagnostic accuracy for MetS identification has been reported across diverse populations (39).

In the present study, ROC curve analysis was not employed to position the TyG index as a diagnostic test for infertility; rather, the infertility-based ROC analysis (AUC = 0.892) was performed to confirm that the TyG > 8.1 grouping strategy adequately captures the metabolic divergence between fertile and infertile men in our population, thereby validating the study's analytical framework. The locally derived optimal cut-off of 8.34 closely approximated the literature-derived threshold of 8.1 (sensitivity 84.8%, specificity 70.7%), supporting the appropriateness of this pre-specified value in our cohort.

The more clinically pertinent ROC analysis concerned biochemical hypogonadism, where the TyG index demonstrated moderate discriminatory performance (AUC = 0.692). At the 8.1 threshold, sensitivity for identifying men with total testosterone below 300 ng/dL reached 88.9%, at the cost of specificity (29.7%) — a trade-off that is not only expected at a lower cut-off value but is also clinically acceptable when the TyG index is applied as an inexpensive metabolic screening parameter rather than a confirmatory test. In this context, high sensitivity ensures that men with androgen deficiency driven by underlying insulin resistance are not missed, with confirmatory serum testosterone measurement serving as the definitive diagnostic step. These findings support integrating the TyG index into the preliminary metabolic workup of men presenting with reproductive concerns, particularly in resource-limited settings where more complex indices of insulin resistance are unavailable.

The present findings carry practical clinical implications. Incorporating the TyG index into the routine evaluation of men attending infertility clinics may offer an inexpensive and rapid means of identifying underlying IR or MetS, pending validation in larger prospective cohorts. Men with elevated TyG indices may benefit from structured lifestyle interventions encompassing dietary modification, increased physical activity, and weight management, as well as pharmacological approaches including insulin-sensitising agents such as metformin, all of which have been shown to favourably influence cardiometabolic health and may secondarily improve hormonal profiles and sperm parameters (27). Bariatric surgery in severely obese hypogonadal men has additionally been reported to elevate tT levels, suggesting

broader reproductive benefits from weight loss (40). Emerging pharmacological agents including glucagon-like peptide-1 (GLP-1) receptor agonists and sodium-glucose cotransporter-2 (SGLT2) inhibitors represent promising adjunctive options given their established efficacy in reducing IR and visceral adiposity; however, dedicated prospective studies examining their direct effects on male reproductive endpoints are currently lacking and are warranted.

Future research should prioritise longitudinal and intervention-based study designs to establish causal directionality between TyG-defined IR and male reproductive dysfunction. Prospective trials specifically evaluating reproductive outcomes following IR-targeted interventions are needed to translate the present cross-sectional associations into actionable clinical evidence. Expanding the panel of assessed biomarkers to include adipokines such as adiponectin and leptin, visceral adiposity indices, inflammatory cytokines, oxidative stress markers, and direct insulin measurements would provide a more comprehensive characterisation of the metabolic-reproductive interface. Finally, multicentre studies enrolling larger and more demographically diverse populations are warranted to validate the external applicability of TyG index-based findings in broader reproductive health contexts.

CONCLUSION

This study highlights the meaningful role of insulin resistance and metabolic dysfunction in male reproductive impairment. The TyG index, calculated from standard fasting laboratory parameters, emerges as a practical and accessible tool that can identify men at metabolic risk with implications for fertility. Its independently confirmed inverse association with testosterone, demonstrated by multiple linear regression, combined with its correlations with non-progressive motility and its advantages over HOMA-IR in simplicity and cost, suggests its potential utility as a complementary measure in reproductive health assessments, subject to validation in larger and more diverse populations. Addressing the underlying metabolic disturbances through targeted interventions warrants consideration as part of a holistic management strategy for male infertility, particularly in men with an elevated TyG index.

Limitations

The retrospective design precludes definitive causal inference regarding the relationship between TyG index and infertility; longitudinal data are required to confirm whether IR is causally antecedent to reproductive dysfunction or whether both conditions share common aetiological determinants. The relatively limited number of fertile controls constrains generalisability, and the single-institution setting may not be representative of broader populations. The absence of direct insulin measurements and HOMA-IR data restricts formal validation of TyG as an IR surrogate within this cohort. Inflammatory and oxidative stress biomarkers—both mechanistically relevant to IR-associated infertility—were not measured. Finally, the retrospective nature

of data collection precluded systematic recording of dietary habits, physical activity levels, and medication use, all of which could exert independent effects on reproductive outcomes.

Conflict of Interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

The authors declare that there is no financial support.

Ethical Approval

This study was approved by the Recep Tayyip Erdogan University Non-Interventional Clinical Research Ethics Committee (Protocol no: 2025/242; Approval date: 29 May 2025).

Informed Consent

Due to the retrospective design of the study, data were obtained from medical records; general consent for the use of anonymized data for research purposes was obtained from all patients at the time of hospital admission.

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