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Metabolic and Nutritional Biomarkers for Cardiovascular Risk Stratification in Beninese Taxi-Motorbike Drivers: Interrelationships Between Homocysteine, Folate, Vitamin B12, TyG Index, and Framingham Risk Score

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Abstract

Background: Higher Framingham Risk Score (FRS) and elevated triglyceride-glucose (TyG) index are well-established markers of cardiovascular disease (CVD) risk. Given the high prevalence of insulin resistance (IR) and dyslipidemia among taxi-motorbike drivers (TMDs) in Cotonou, it is plausible that hyperhomocysteinemia (HHcy) or suboptimal folate and vitamin B12 status may further amplify their cardiovascular risk. However, the relationships between folate, vitamin B12, and homocysteine and established CVD risk markers like the TyG index and FRS have not been systematically investigated within this high-risk occupational group. Therefore, this study aimed to examine the associations of these key nutritional determinants with both the TyG index and FRS among TMDs. **Methods:** In this cross-sectional study of 137 TMDs (mean age 39.2 ± 7.7 years), we collected comprehensive demographic and lifestyle data alongside standardized anthropometric measurements, including BMI and blood pressure. Biochemical assessments encompassed glucose, lipid profiles, creatinine, vitamin B12, folate, and homocysteine levels. Cardiovascular risk was evaluated using risk stratification tools such as the FRS and TyG index. Participants were stratified by TyG cut-off (TyG ≤ 7.73 vs. TyG > 7.73) and by FRS category (<10% vs. ≥10%). HHcy was further classified into moderate and intermediate levels. Statistical analyses included univariate comparisons employing chi-square and Mann-Whitney tests, and

multivariable logistic regression was used to examine associations among metabolic, nutritional, and clinical variables. **Results:** The cohort exhibited a high prevalence of hypertension (47.4%) and markedly elevated homocysteine levels (mean 30.5 ± 18.8 μmol/L), with 88.3% of participants showing HHcy. Plasma folate concentrations declined significantly with increasing homocysteine ($p = 0.006$), strongly linking low folate status to exacerbated HHcy. Participants with elevated FRS were older, hypertensive, and presented with significantly increased triglycerides, TyG index, and homocysteine. Conversely, high TyG index correlated with greater BMI (24.8 vs. 21.9 kg/m^2, $p < 0.001$), elevated blood pressure, pronounced dyslipidemia, lower vitamin B12 levels (376.2 vs. 455.0 pmol/L, $p = 0.002$), and hypertension. Multivariable logistic regression identified BMI (OR = 1.28, $p = 0.001$) and FRS (OR = 1.33, $p = 0.001$) as independent predictors of elevated TyG index; conversely, higher vitamin B12 was protective (OR = 0.98, $p = 0.015$). Increasing age lowered the risk of high TyG (OR = 0.89, $p = 0.025$), while older age (OR = 1.57, $p < 0.001$) and elevated TyG (OR = 8.95, $p = 0.019$) were primary drivers of high FRS risk. **Conclusion:** TMDs in Cotonou face a high burden of hypertension, metabolic dysfunction, and HHcy, with substantial links between adiposity, insulin resistance, and predicted cardiovascular risk. While FRS predominantly reflects age and hypertension-related risk, the TyG index captures modifiable metabolic dysfunction closely linked with adiposity, dyslipidemia, and vitamin B12 status. The TyG index complements traditional risk scores by identifying modifiable metabolic dysfunction and nutritional imbalances, especially in younger individuals. Vitamin B12 offers modest metabolic protection, whereas low folate exacerbates HHcy. Integrating TyG and nutritional biomarkers into occupational health screening could guide targeted interventions to reduce CVD burden in high-risk resource-limited settings.

Keywords

Cardiovascular Disease (CVD), Framingham Risk Score (FRS), Triglyceride-Glucose (TyG) Index, hyperhomocysteinemia (HHcy), Vitamin B12, Cotonou

1. Introduction

Cardiovascular disease (CVD) is a leading cause of morbidity and mortality worldwide, disproportionately affecting populations in low- and middle-income countries (LMICs) [1] [2]. Urban occupational groups, such as taxi-motorbike drivers (TMDs) in Cotonou, are especially vulnerable due to their exposure to elevated levels of traffic-related air pollutants (e.g., benzene, ultrafine particles, and polycyclic aromatic hydrocarbons), and limited access to preventive healthcare.

Previous studies have established that TMDs in Cotonou exhibit clusters of metabolic disturbances, such as hypertension, dyslipidemia, hyperuricemia, and insulin resistance (IR)—factors that together drive up their CVD risk, commonly

estimated using tools like the Framingham Risk Score (FRS) [3] [4] or the triglyceride-glucose (TyG) index, a validated surrogate marker of insulin resistance (IR) [5] [6]. However, the specific cardiometabolic and nutritional determinants influencing their cardiovascular health remain underexplored.

Folate and vitamin B12 are crucial micronutrients that regulate DNA synthesis, red blood cell formation, and, importantly, homocysteine metabolism [7]. Deficiencies in these vitamins can result in hyperhomocysteinemia (HHcy), a state linked to oxidative stress, endothelial dysfunction, and heightened CVD risk [8]. Observational and interventional studies in general and clinical populations have shown associations between low levels of these micronutrients and increased cardiovascular morbidity and mortality, although there is variation in results and ongoing debate about causality and the effectiveness of supplementation [8]-[10]. Elevated homocysteine levels may disrupt lipid metabolism, contributing to atherogenic dyslipidemia (characterized by elevated triglycerides and altered cholesterol profiles) while simultaneously promoting visceral fat accumulation—a key driver of metabolic syndrome, IR, and cardiovascular disease pathogenesis [11]. Furthermore, a growing body of work has highlighted the importance of easily accessible composite markers of metabolic risk, such as the triglyceride-glucose (TyG) index, which has demonstrated strong predictive value for both IR and cardiovascular events, often correlating with traditional scores like the FRS in diverse populations. Importantly, previous studies indicated that the TyG index may be particularly valuable for the early identification of individuals at high risk of developing cardiovascular events in ten years, as assessed by the FRS [4] [12]-[14].

Given the high prevalence of IR and dyslipidemia among TMDs, it is plausible that suboptimal folate and vitamin B12 status may further heighten their CVD risk. This may occur either directly through the development of HHcy or indirectly through interactions with air pollution-induced oxidative stress. Despite this substantial cardiometabolic burden and the vulnerability to nutritional deficiencies, the interplay between folate, vitamin B12, homocysteine, and established CVD risk markers—such as the TyG index and FRS—has not yet been systematically explored in this high-risk occupational group of TMDs. This is especially relevant in LMICs, where cost-effective screening and intervention strategies could have a substantial impact. We therefore aimed to examine the associations of nutritional determinants of cardiovascular health (*i.e.*, folate, vitamin B12, and homocysteine) with the TyG index and FRS among TMDs in Cotonou. Such research not only addresses key knowledge gaps for this high-risk group but may also identify actionable nutritional determinants of cardiovascular risk, supporting targeted prevention in occupational health practice.

2. Methods

2.1. Study Design and Population

This cross-sectional study utilized data from a community health initiative targeting taxi-motorbike drivers (TMDs) in Cotonou, Benin—a population with chronic

occupational exposure to traffic-related air pollution (TRAP), including benzene and ultrafine particulate matter [15]. The study involved 137 actively working male TMDs aged ≥18 years who underwent comprehensive health evaluations, as described in detail elsewhere [16] [17]. Eligibility required current professional engagement as a TMD, being an apparently healthy non-smoking man, and having no prior diagnosis of cardiovascular disease or conditions affecting homocysteine or vitamin B12 metabolism. The selection of non-smoking men was intentional to eliminate the confounding effects of tobacco smoke on cardiometabolic parameters, allowing clearer assessment of relationships between the TyG index, FRS, and cardiovascular risk within a TRAP-exposed occupational cohort. Although an a priori power calculation was not performed, the sample size proved sufficient for robust analysis, as evidenced by statistically significant associations detected for key outcomes including vitamin B12 and TyG index in multivariate models. The study protocol was approved by the Benin Environmental Agency in accordance with the Declaration of Helsinki, and all participants provided written informed consent.

2.2. Data Collection and Biochemical Analyses

Trained staff collected data on demographics (age, education level), health-related behaviors (smoking status, alcohol consumption), medical history (hypertension, diabetes, hyperlipidemia, cardiovascular disease, chronic kidney disease, and medications), occupational factors (years driving, daily work hours), and anthropometric measures (height, weight, with BMI calculated as weight (kg)/height (m^2)) using standardized questionnaires. Blood pressure was measured twice in a seated position after five minutes of rest with a calibrated mercury sphygmomanometer; the average of both readings was used. Hypertension was defined as systolic BP ≥140 mmHg, diastolic BP ≥90 mmHg, or self-reported antihypertensive medication use.

Venous blood samples (~5 mL) were collected from each participant following an overnight fast of at least 8 hours. Samples were promptly processed: plasma was separated by centrifugation (3000 rpm, 15 minutes) and stored at −20˚C until analysis. Biochemical analyses—including fasting glucose, creatinine, total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C)—were performed with validated methods on automated clinical analyzers (Roche Diagnostics). Vitamin B12 and folate concentrations were measured using the SimulTRAC-SNB radio-isotope kit (ICN Pharmaceuticals) [18]. Plasma total homocysteine was quantified by high-performance liquid chromatography (HPLC), classifying hyperhomocysteinemia (HHcy) as moderate (15 - 30 μmol/L) or intermediate (30 - 100 μmol/L), following established references [19]. All biochemical analyses were performed at the NGERE Research Unit ("Nutrition-Génétique-Exposition aux risques environnementaux"), Faculty of Medicine, Nancy, France, adhering strictly to manufacturer instructions, rigorous quality control protocols, and standardized international

guidelines to ensure reproducibility and analytical accuracy.

2.3. Cardiovascular Risk Assessment Markers

2.3.1. Framingham Risk Score (FRS)

The 10-year cardiovascular disease (CVD) risk for each participant was estimated using the sex-specific Framingham Risk Score (FRS), which combines age, total cholesterol, HDL cholesterol, systolic blood pressure, smoking status, and antihypertensive treatment according to established formulas and point-based tables consistent with validated Framingham algorithms [3]. Individual data for sex, age (categorized in five-year intervals), SBP, lipid profile, and smoking status (excluded here, thus assigned zero points) were weighted and summed to generate each participant's 10-year CVD risk score. Diabetes also contributed zero points due to exclusion criteria. Based on widely accepted prognostic thresholds, participants were categorized according to their 10-year CVD risk as low (<10%), intermediate (10% - 20%), or high (>20%). For analytical purposes, the intermediate and high-risk groups were combined into a single category (FRS ≥10%) to enhance statistical power and facilitate comparison of elevated-risk profiles against the low-risk reference group. Elevation in the FRS has been consistently shown to predict long-term cardiovascular outcomes across diverse populations, supporting its use for risk stratification in epidemiologic studies and clinical assessments.

2.3.2. Triglyceride-Glucose (TyG) Index

The TyG index was calculated using the formula: TyG = ln [fasting triglycerides (mg/dL) × fasting glucose (mg/dL)/2]. This index serves as a simple surrogate marker of insulin resistance and is increasingly recognized for its predictive value in cardiometabolic risk assessment. In this high-risk cohort of TMDs, the optimal threshold for elevated TyG was determined to be 7.73, based on receiver operating characteristic (ROC) curve analysis optimized to identify individuals at increased 10-year cardiovascular risk (*i.e.*, Framingham Risk Score ≥ 10%) [20]. Participants with a TyG index above 7.73 were classified as having high TyG, indicating greater metabolic risk, while those at or below the threshold were considered low TyG.

2.4. Statistical Analysis

Descriptive statistics for continuous variables are presented as mean ± standard deviation (SD) or median with interquartile range (IQR); categorical variables are shown as counts and percentages. Group comparisons were performed using the Chi-square test for categorical variables and the Mann-Whitney U test for continuous variables. Univariate analyses were conducted to assess differences in cardiometabolic and nutritional factors across homocysteine categories, FRS strata, and TyG index groups. Multivariable logistic regression models were developed with elevated TyG index (>7.73) and high FRS (≥10%) as dependent variables. Independent variables included age, BMI, folate, vitamin B12, and homocysteine levels. Results are reported as adjusted odds ratios (aORs) with 95% confidence intervals (CIs). A two-sided p value <0.05 was considered statistically significant.

Analyses were performed using IBM SPSS statistical software (version 27).

3. Results

3.1. Cardiometabolic and Nutritional Determinants in the Study Cohort

The study cohort of 137 TMDs demonstrated a concerning cardiometabolic risk profile (Table 1). The mean (SD) age was 39.2 (7.7) years, with elevated blood pressure (systolic: 134.2 (18.6) mmHg; diastolic: 84.8 (13.0) mmHg and a high prevalence of hypertension (47.4%). Notably, homocysteine levels were markedly elevated: 30.5 (18.8) µmol/L, while vitamin B12 413.0 (159.3) pmol/L and folate 6.6 (1.9) nmol/L levels were generally adequate. The mean 10-year CVD risk was 6.8 (5.0%), with maximum risk reaching 25.3% in high-risk individuals (Table 1).

Table 1. Cardiometabolic and nutritional determinants in the study cohort.

Variables	Mean (SD)	95%CI	Median	IQR	Min	Max
Age (year)	39.2 (7.7)	38.0 - 40.6	39	34.0 - 44.0	22	59
BMI (Kg/m²)	23.5 (3.8)	22.9 - 24.2	23.1	21.0 - 25.7	17.5	37.2
SBP (mmHg)	134.2 (18.6)	131.2 - 137.5	130	120.0 - 150	100	190
DBP (mmHg)	84.8 (13.0)	82.7 - 87.1	80	80.0 - 90.0	60	120
Creatinine (mg/L)	11.5 (1.3)	11.4 - 11.8	11.6	10.5 - 12.3	8.2	15
Glucose (mmol/L)	4.2 (0.6)	4.1 - 4.3	4.3	3.9 - 4.6	2.3	6.4
TC (mmol/L)	4.3 (0.9)	4.1 - 4.5	4.4	3.6 - 4.9	1.9	7.7
TG (mmol/L)	0.8 (0.4)	0.7 - 0.9	0.7	0.5 - 1.0	0.3	2.9
HDL (mmol/L)	1.3 (0.4)	1.3 - 1.4	1.3	1.1 - 1.6	0.2	3.4
LDL (mmol/L)	2.6 (0.8)	2.4 - 2.7	2.5	2.0 - 3.0	1	5
TyG index	7.8 (0.5)	7.7 - 7.9	7.8	7.5 - 8.1	6.8	9
10-year CVD risk (%)	6.8 (5.0)	6.0 - 7.7	5.6	3.3 - 7.9	1.4	25.3
Folate (nmol/L)	6.6 (1.9)	6.3 - 6.9	6.5	5.3 - 8.2	2.6	25.9
Vitamin B12 (pmol/L)	413.0 (159.3)	383.8 - 437.2	387.5	316.0 - 498.8	146	1020
Homocysteine (µmol/L)	30.5 (18.8)	26.8 - 32.4	23.4	16.9 - 35.6	9.3	96.2
	n/N (%)	**95%CI**				
Alcohol (>= 1 drink/day)	54/137 (39.4)	31.4 - 47.9				
Hypertension	65/137 (47.4)	39.1 - 56.0				

BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; TC: Total cholesterol; TG: Triglycerides; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; TyG: Triglyceride-glucose index; CI: confidence interval; IQR: Interquartile range. Values are reported as mean (standard deviation) or median with IQR: interquartile range.

3.2. Cardiometabolic and Nutritional Determinants Stratified by Homocysteine Categories

Among the 137 TMDs, HHcy was highly prevalent, with 88.3% exhibiting moderate levels (15 - 30 μmol/L) or intermediate elevations (30 - 100 μmol/L). Only 11.7% had normal homocysteine concentrations (<15 μmol/L). Despite this gradient in homocysteine levels, most traditional cardiometabolic parameters—including age, BMI, blood pressure, fasting glucose, lipid profiles, TyG index, and estimated 10-year cardiovascular risk—did not show statistically significant differences across homocysteine categories (Table 2). The exception was for creatinine, which was significantly higher in the moderate HHcy group compared to the normal group (11.7 vs. 10.9 mg/L, p = 0.025). Importantly, an inverse relationship was observed between plasma folate concentrations and homocysteine levels, with folate significantly decreasing from moderate to intermediate HHcy groups (8.6 to 6.2 nmol/L, p = 0.006) and a similar trend between individuals with normal homocysteine levels and those with intermediate HHcy (p = 0.026), reflecting folate's critical role in homocysteine metabolism. Vitamin B12 levels, while trending lower with increasing homocysteine, did not differ significantly across groups (Table 2).

Table 2. Cardiometabolic and nutritional determinants stratified by homocysteine categories in taxi-motorbike drivers.

	Homocysteine classes								
	Normal (<15 μM)		Moderate HHcy (15 - 30 μM)		Intermediate HHcy (30 - 100 μM)		*P-Value**		
n (%)	16 (11.7)		75 (54.7)		46 (33.6)				
Variables	**Mean (SD)**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Normal vs moderate**	**Normal vs intermediate**	**Moderate vs intermediate**
Age (years)	37.7 (7.3)	34.7 - 40.7	38.8 (7.9)	37.2 - 40.4	40.8 (7.7)	38.8 - 42.9	NS	NS	NS
BMI (Kg/m²)	24.7 (4.4)	22.9 - 26.5	23.6 (3.9)	22.8 - 24.4	23.8 (3.7)	22.7 - 24.8	NS	NS	NS
SBP (mmHg)	129.5 (13.8)	121.5 - 137.5	132.3 (18.1)	128.3 - 136.4	139.2 (19.9)	133.2 - 145.2	NS	NS	NS
DBP (mmHg)	84.3 (11.6)	77.6 - 90.9	83.9 (11.9)	81.2 - 86.5	86.7 (15.2)	82.1 - 91.2	NS	NS	NS
Creatinine (mg/L)	10.9 (1.2)	10.4 - 11.4	11.7 (1.3)	11.4 - 11.9	11.5 (1.3)	11.2 - 11.9	0.025	NS	NS
Glucose (mmol/L)	4.4 (0.5)	4.2 - 4.7	4.2 (0.6)	4.1 - 4.4	4.1 (0.6)	3.9 - 4.3	NS	NS	NS
TC (mmol/L)	4.3 (1.0)	3.8 - 4.8	4.3 (0.9)	4.1 - 4.5	4.3 (1.0)	4.0 - 4.6	NS	NS	NS

Continued

TG (mmol/L)	0.9 (0.6)	0.6 - 1.2	0.8 (0.3)	0.7 - 0.9	0.8 (0.4)	0.7 - 0.9	NS	NS	NS
HDL (mmol/L)	1.2 (0.4)	1.0 - 1.4	1.3 (0.3)	1.3 - 1.4	1.4 (0.5)	1.3 - 1.5	NS	NS	NS
LDL (mmol/L)	2.7 (0.7)	2.3 - 3.1	2.6 (0.7)	2.4 - 2.8	2.6 (0.8)	2.5 - 2.7	NS	NS	NS
TyG index	7.8 (0.6)	7.5 - 8.2	7.8 (0.5)	7.7 - 7.9	7.8 (0.5)	7.7 - 7.9	NS	NS	NS
Framingham 10-year CVD risk (%)	5.0 (3.3)	3.2 - 6.9	6.5 (4.9)	5.3 - 7.6	8.0 (5.5)	6. - 9.6	NS	NS	NS
Folate (nmol/L)	8.6 (3.6)	7.1 - 10.1	7.1 (2.7)	6.6 - 7.7	6.2 (2.2)	5.6 - 6.8	NS	0.026	0.006
Vitamin B12 (pmol/L)	455.2 (158.7)	389.7 - 520.7	420.9 (175.4)	384.7 - 457.3	412.3 (149.8)	371.9 - 452.8	NS	NS	NS
Homocysteine (μM)	13.8 (1.0)	13.2 - 14.3	21.3 (4.1)	20.3 - 22.2	50.9 (20.7)	44.7 - 57.0	0.105	<0.001	<0.001

HHcy: Hyperhomocysteinemia; BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; TC: Total cholesterol; TG: Triglycerides; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; TyG: Triglyceride-glucose index; CI: confidence interval; IQR: Interquartile range. NS denotes nonsignificant p value. Values are reported as mean (standard deviation) along with the 95% CI.

3.3. Cardiometabolic and Nutritional Determinants Stratified by Framingham Risk Score and TyG Index Categories (Univariate Analysis)

The study cohort demonstrated significant differences in cardiovascular and metabolic profiles when stratified by FRS categories. Participants with intermediate/high FRS (≥10%) were older (48.9 vs. 36.7 years, $p < 0.001$) and exhibited higher systolic (149.1 vs. 130.3 mmHg) and diastolic blood pressure (93.9 vs. 82.3 mmHg, both $p < 0.001$). Hypertension prevalence was nearly twice as high in the intermediate/high FRS group (75.0% vs. 40.4%, $p = 0.001$) (Table 3). While lipid profiles (total cholesterol, LDL-C) did not differ significantly, triglycerides were elevated in the higher-risk group (1.0 vs. 0.8 mmol/L, $p = 0.005$), aligning with their marginally higher TyG index (8.0 vs. 7.8, $p = 0.008$). Homocysteine levels were also elevated in the intermediate/high FRS group (35.6 vs. 29.1 μmol/L, $p = 0.049$), suggesting a potential link between HHcy and long-term CVD risk. Notably, folates and vitamin B12 showed no association with FRS categories ($p > 0.1$) (Table 3).

When stratified by TyG index using the cut-off of 7.73, TMDs with elevated TyG demonstrated a more pronounced metabolic disturbance: higher BMI (24.8 vs. 21.9 kg/m^2, $p < 0.001$), elevated blood pressure (SBP 139.1 vs. 128.5 mmHg,

DBP 87.4 vs. 81.5 mmHg, both $p < 0.01$), and worsened lipid profiles including higher triglycerides (1.0 vs. 0.5 mmol/L, $p < 0.001$), total cholesterol, and LDL-C (Table 3). They also had a greater prevalence of hypertension (58.1% vs. 34.9%, $p = 0.007$) and significantly lower vitamin B12 levels (376.2 vs. 455.0 pmol/L, $p = 0.002$). The TyG-high group's increased cardiovascular risk was also reflected in elevated FRS (8.2% vs. 5.1%, $p < 0.001$). Folate and homocysteine levels did not differ significantly by TyG strata (Table 3).

Table 3. Cardiometabolic and nutritional determinants stratified by Framingham Risk Score and TyG Index categories.

	Low FRS (n = 109)	Intermediate or High FRS (n = 28)	Low TyG < 7.73 (n = 63)	High TyG > 7.73 (n = 74)	P value (FRS)	P value (TyG)
Age (Years)	36.7 (6.1)	48.9 (5.0)	37.8 (7.8)	40.3 (7.4)	<0.001	0.097
BMI (Kg/m²)	23.2 (3.8)	24.2 (3.8)	21.9 (2.6)	24.8 (4.2)	0.186	<0.001
SBP (mmHg)	130.3 (16.4)	149.1 (19.6)	128.5 (15.8)	139.1 (19.6)	<0.001	0.001
DBP (mmHg)	82.3 (11.7)	93.9 (14.0)	81.5 (12.4)	87.4 (13.0)	<0.001	0.005
Glucose (mmol/L)	4.2 (0.6)	4.2 (0.7)	4.0 (0.5)	4.4 (0.6)	0.94	<0.001
TC (mmol/L)	4.2 (0.9)	4.6 (1.2)	4.0 (0.9)	4.5 (0.9)	0.162	0.001
TG (mmol/L)	0.8 (0.3)	1.0 (0.5)	0.5 (0.1)	1.0 (0.4)	0.005	<0.001
HDL (mmol/L)	1.4 (0.4)	1.3 (0.4)	1.4 (0.3)	1.3 (0.4)	0.062	0.021
LDL (mmol/L)	2.5 (0.7)	2.9 (1.0)	2.4 (0.7)	2.7 (0.8)	0.068	0.002
TyG index	7.8 (0.4)	8.0 (0.5)	7.4 (0.2)	8.1 (0.3)	0.008	<0.001
FRS (%)	4.7 (2.1)	15.1 (4.2)	5.1 (3.5)	8.2 (5.7)	<0.001	<0.001
Folates (nmol/L)	6.7 (1.9)	6.2 (2.1)	6.7 (2.1)	6.5 (1.7)	0.171	0.439
Vitamin B12 (pmol/L)	418.8 (168.1)	390.8 (119.6)	455.0 (163.2)	376.2 (147.3)	0.778	0.002
Homocysteine (µmol/L)	29.1 (19.3)	35.6 (18.8)	29.1 (21.1)	31.6 (17.7)	0.049	0.093
	n (%)	**n (%)**	**n (%)**	**n (%)**	**P value (FRS)**	**P value (TyG)**
Hypertension, n (%)	44 (40.4)	21 (75.0)	22 (34.9)	43 (58.1)	0.001	0.007
Alcohol use, n (%)	42 (38.5)	12 (42.9)	21 (33.3)	33 (44.6)	0.702	0.203

BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; TC: Total cholesterol; TG: Triglycerides; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; TyG: Triglyceride-glucose index; FRS: Framingham Risk Score. The optimal TyG index cut-off value of 7.73 was derived from receiver operating characteristic (ROC) curve analysis for predicting intermediate/high cardiovascular risk. The 10-year cardiovascular disease (CVD) risk, calculated using the Framingham Risk Score (FRS), was categorized as low risk (FRS <10%) or intermediate/high risk (FRS ≥10%). Values are reported as mean (standard deviation).

3.4. Determinants of Elevated TyG Index (>7.73) and High FRS (>10%)

The logistic regression analysis identified several key determinants associated with an elevated TyG index or FRS. Higher BMI significantly increased the odds of an elevated TyG index, with each unit increase in BMI raising the risk by 28% (OR = 1.28; 95% CI: 1.11 - 1.47; p = 0.001; Table 4), underscoring the central role of adiposity in metabolic dysfunction. Similarly, higher FRS was strongly associated with elevated TyG, where each unit increase in FRS corresponded to a 33% increase in odds (OR = 1.33; 95% CI: 1.11 - 1.58; p = 0.001), reaffirming the link between global cardiovascular risk and insulin resistance. Conversely, vitamin B12 demonstrated protective effect against elevated TyG index, though clinically modest; a higher vitamin B12 levels slightly reduced the likelihood of elevated TyG (OR = 0.98; 95% CI: 0.98 - 0.99; p = 0.015; Table 4). Unexpectedly, increasing age was associated with an 11% reduction in the odds of a high TyG index (OR = 0.89; 95% CI: 0.81 - 0.98; p = 0.025), suggesting that within the studied cohort, younger individuals were more likely to exhibit elevated TyG, potentially reflecting early metabolic changes.

As anticipated, older age was a powerful driver of high FRS, with the odds increasing by 57% for each additional year of age (OR = 1.57, 95% CI: 1.31 - 1.89, p < 0.001). Most notably, an elevated TyG index (>7.73) was the strongest metabolic predictor, associated with a nearly 9-fold increase in the odds of having a high FRS (OR = 8.95, 95% CI: 1.43 - 36.18, p = 0.019). Elevated homocysteine levels showed a positive trend towards association with high FRS, but this did not reach formal statistical significance (OR = 1.03, 95% CI: 0.99 - 1.06, p = 0.069; Table 4).

Table 4. Multivariable logistic regression analysis of predictors for elevated TyG Index (>7.73) in TMDs.

Dependent determinant	Residual determinant	OR	95% CI	P value
TyG > 7.73	Age	0.89	0.81 - 0.98	0.025
	BMI	1.28	1.11 - 1.47	0.001
	FRS	1.33	1.11 - 1.58	0.001
	Vitamin B12	0.99	0.98 - 0.99	0.015
FRS ≥ 10%	Age	1.57	1.31 - 1.89	<0.001
	TyG>7.73	8.95	1.43 - 36.18	0.019
	Homocysteine	1.03	0.99 - 1.06	0.069

TyG: triglyceride-glucose index; BMI: Body mass index; FRS: Framingham Risk Score; OR: odd ratio; CI: confidence interval.

4. Discussion

This study provides one of the most comprehensive assessments to date of the

interplay between nutritional and metabolic risk factors among TMDs in Cotonou. The findings highlight three critical public health concerns: 1) An alarmingly high prevalence of hypertension and HHcy; 2) The TyG index's superior sensitivity over traditional risk factors in identifying metabolic dysfunction in this young cohort (underscoring early cardiometabolic deterioration within this high-risk occupational group); 3) the complex interplay between adiposity, micronutrient status, and cardiovascular risk.

4.1. Nutritional and Metabolic Determinants of Cardiovascular Risk in TMDs

The study cohort exhibited a cardiovascular risk profile remarkable for its mean age of 39 years, characterized most notably by an exceptionally high prevalence of HHcy approaching 90%. This widespread elevation likely stems from multifactorial origins including dietary patterns, occupation-related environmental exposures, and potential genetic predispositions such as MTHFR polymorphisms. It is important to clarify that the role of genetic factors in this cohort remains speculative, as genetic testing was not conducted in this study. Despite this pronounced metabolic abnormality, stratification of HHcy into moderate and intermediate levels revealed few significant differences in traditional cardiometabolic markers including BMI, blood pressure, glucose, lipid profiles, and TyG index across these categories. The elevated serum creatinine observed in the moderate HHcy group suggests potential early renal involvement that could worsen cardiovascular prognosis if unaddressed.

While the direct association between HHcy and FRS was weak in multivariate analysis (OR = 1.03, 95% CI: 0.99 - 1.06; p = 0.069), the significantly higher homocysteine levels in participants with elevated FRS (p = 0.049) warrant clinical attention given HHcy's established role in endothelial dysfunction and atherothrombosis [21] [22]. This apparent paradox may reflect the overwhelming predominance of HHcy in this cohort—with only 11.7% (n = 16) exhibiting normal homocysteine levels—which renders binary classification (present vs. absent) impractical for risk stratification and may attenuate measurable effects on cardiovascular risk.

Concurrently, the high prevalence of hypertension (47.4%) and adiposity-driven insulin resistance (as captured by the TyG index) highlights a population experiencing rapid epidemiological transition characterized by traditional cardiovascular risk factors compounded by unique occupational exposures. Rather than HHcy alone, it is likely that the convergence of multiple factors—including chronic inflammation, traffic-related particulate matter exposure, and psychosocial stress—collectively drives cardiovascular risk pathogenesis among TMDs. Future larger, well-powered studies should explore whether alternative stratification approaches or combined risk factor assessments might better capture clinically relevant risk differences in similar hyperhomocysteinemic populations.

Vitamin B12, although not significantly different across groups, trended lower

with higher homocysteine and was inversely associated with an elevated TyG index, indicating a protective effect against metabolic dysfunction. Importantly, the strong inverse correlation between folate and homocysteine ($p = 0.006$) reinforces the integrity of the one-carbon metabolism pathway in this population and suggests that low folate intake is a key modifiable driver of HHcy, consistent with established literature [23].

Building on these nutritional insights, our findings suggest potential intervention opportunities. In our study, vitamin B12 emerged as a modest but statistically significant, protective factor against elevated TyG, highlighting potential benefits of addressing micronutrient deficiencies or optimizing nutritional status as part of cardiometabolic risk management. Emerging research reveals a complex interplay between low vitamin B12 status, insulin resistance, and dyslipidemia. Specifically, vitamin B12 deficiency has been independently linked to elevated triglycerides, potentially mediated through impaired mitochondrial fatty acid oxidation and disturbances in one-carbon metabolism that worsen both dyslipidemia and insulin resistance [24] [25]. In line with these findings, our recent work in TMDs demonstrated a protective effect of adequate vitamin B12 status against insulin resistance [17]. The relationship between HHcy and the TyG index appears more nuanced and context-dependent: although HHcy often coexists with B12 or folate deficiencies, its association with TyG is inconsistent in this study. While some studies show significant interaction effects—where HHcy may potentially eclipse TyG's predictive value for cardiovascular events [26]—others suggest a predictive relationship where elevated TyG index precedes the development of HHcy, particularly in individuals with dyslipidemia. A longitudinal study by Xiong *et al.* [27] involving 1,018 Chinese male bus drivers found that higher TyG levels significantly predicted incident HHcy (OR = 1.47; 95% CI: 1.11 - 1.94), particularly in those with elevated LDL-C, further highlighting the metabolic-lipid-nutrient intersection.

Notably, while folate primarily influences homocysteine regulation rather than TyG index levels, the paucity of longitudinal and mechanistic studies limits firm conclusions. Nonetheless, clinical trials indicate that vitamin B12 supplementation can improve glycemic control and insulin resistance, particularly in type 2 diabetes patients [28]. Collectively, these data support incorporating TyG and nutritional biomarkers—especially vitamin B12 and homocysteine—into cardiovascular risk assessments for high-risk occupational populations, emphasizing the importance of targeted nutritional and metabolic interventions to mitigate cardiovascular disease burden.

4.2. Complementary Roles of the TyG Index and FRS in Cardiovascular Risk Stratification

A central finding of this study is the demonstration of the complementary roles of the TyG index and the FRS. Stratification analyses revealed that the FRS, heavily weighted by age and blood pressure, effectively identified older TMDs with estab-

lished risk factor accumulation, as shown by significantly elevated blood pressure and hypertension prevalence in the intermediate/high-risk group (FRS ≥10%), a finding consistent with global and regional epidemiological trends that confirm these as critical determinants of cardiovascular [29] [30]. However, this age dependence represents a key limitation for this young workforce, as the FRS may underestimate risk in younger individuals with metabolic syndrome. Critically, CVDs in Sub-Saharan Africa disproportionately affect younger populations, occurring approximately two decades earlier than in high-income countries [30]. Therefore, integrating the TyG index with the FRS may provide a more accurate and sensitive assessment of cardiovascular risk in younger individuals within this high-risk occupational group.

In contrast, the TyG index alone proved to be a powerful tool for identifying metabolic dysfunction irrespective of age, consistent with previous reports [31] [32]. Its strong associations with BMI, blood pressure, dyslipidemia, and lower vitamin B12 levels capture the core features of adiposity-driven insulin resistance. The most compelling evidence of its utility is its staggering association with high FRS—TMDs with an elevated TyG index had a nine-fold increased odds of being in the high-risk FRS category. This suggests the TyG index identifies the metabolic "engine" driving the future risk that the FRS calculates. On the other hand, this finding demonstrates the TyG index's exceptional ability to identify individuals within this cohort who have accrued significant risk based on the traditional FRS algorithm, aligning with prior studies reports in hypertensive patients [4] or among patients with type 2 diabetes patients [13] [33]. However, this observation requires cautious interpretation due to wide confidence intervals (95% CI: 1.43 - 36.18) and limited sample size, which may affect the precision of this effect estimate.

The strong association between the TyG index and BMI underscores that it primarily reflects adiposity-driven metabolic dysregulation, specifically insulin resistance and atherogenic dyslipidemia, in this population. This is a crucial finding for TMDs, a group prone to sedentary behaviors and dietary challenges. The unexpected inverse association between age and TyG index may reflect early metabolic deterioration in younger TMDs. This phenomenon could be driven by occupational and lifestyle factors unique to these individuals, such as irregular meal patterns, reliance on energy-dense roadside foods, or greater stressful work intensity, all of which can accelerate the development of insulin resistance and dyslipidemia at a younger age. Thus, younger TMDs may be particularly vulnerable to premature metabolic risk, underscoring the need for targeted preventive interventions early in their careers.

The elevated triglycerides and TyG index observed in the higher FRS group align with the role of insulin resistance and dyslipidemia as important cardiovascular risk contributors. Furthermore, the modestly higher homocysteine in this group suggests its potential additive role in cardiovascular pathogenesis, although folate and vitamin B12 levels did not differ by FRS category. Together, these findings illustrate that while the FRS captures the burden of age and hypertension, the

TyG index reflects underlying metabolic dysfunction, making them complementary tools for comprehensive risk assessment in this occupational cohort.

4.3. Public Health Implications and Future Directions

The findings have substantial public health implications, particularly for LMICs where occupational exposure to air pollution and limited access to healthcare contribute to premature cardiovascular morbidity and mortality. Notably, this study highlights a critical convergence of metabolic dysfunction and nutritional vulnerability in Benin's TMDs. The population demonstrates an alarming triad of hypertension, insulin resistance, and hyperhomocysteinemia, establishing them as a cardiovascular high-risk group. These findings support implementing a two-tiered screening approach combining: 1) practical metabolic indices (TyG index and Framingham Risk Score) with 2) targeted biochemical markers (homocysteine and vitamin B12) for identifying high-risk individuals who would benefit from targeted interventions.

Particularly in resource-constrained settings, the TyG index offers distinct advantages as a screening tool, requiring only routine lipid and glucose tests while demonstrating superior feasibility compared to complex IR measures like HOMA-IR. Its strong association with FRS, adiposity, and vitamin B12 status in our cohort underscores its value for detecting metabolic dysfunction and guiding potential nutritional interventions. This integrated screening model could transform occupational health programs by enabling early identification of TMDs requiring targeted interventions, from weight management to micronutrient supplementation, while informing broader policy changes to mitigate environmental and work-related risk factors.

4.4. Study Strengths and Limitations

This study has several notable strengths, including its focus on an understudied, high-risk occupational cohort and its comprehensive phenotyping incorporating biochemical, nutritional, and cardiovascular risk assessments. However, several limitations must be acknowledged. The cross-sectional design precludes causal inferences regarding the observed relationships between metabolic markers, nutritional factors, and cardiovascular risk. Additionally, residual confounding by unmeasured variables—such as detailed dietary patterns, physical activity levels, and genetic factors (e.g., MTHFR variants)—cannot be excluded. We therefore recommend that future research directly investigate the prevalence and functional impact of MTHFR and other relevant genetic variants in this population to better understand their contribution to hyperhomocysteinemia and cardiovascular risk.

The relatively small sample size and exclusion of smokers, while methodologically necessary, may affect the generalizability of our findings. Importantly, the exclusion of smokers, though methodologically necessary for this investigation, may restrict the generalizability of our findings to the broader driver population, where smoking is a common and influential risk factor. Smoking interacts com-

plexly with metabolic and cardiovascular risk, and its omission may underestimate risk profiles and mask potential effect modifications. Thus, extrapolation to all urban transport workers should be made cautiously.

Despite these limitations, the results likely extend to other urban transport workers in LMICs who face similar occupational exposures. Future longitudinal studies are needed to establish temporal relationships and determine whether elevated TyG index and nutritional imbalances predict incident cardiovascular events in this population. Additionally, intervention studies are warranted to evaluate whether targeted strategies—such as vitamin B12 supplementation or dietary modifications—can directly improve metabolic parameters and reduce cardiovascular risk. These findings underscore the need for scalable, context-specific public health interventions to protect metabolic health in high-risk occupational populations across LMICs.

5. Conclusion

This study reveals a high burden of cardiometabolic risk factors among TMDs, characterized by hypertension and prevalent HHcy. Two distinct risk pathways emerged for long-term (FRS) versus immediate (TyG) CVD risk in TMDs: 1) Framingham Risk Score was driven primarily by age and hypertension, with homocysteine as a secondary contributor; 2) TyG index captured modifiable metabolic dysfunction, presenting itself as an actionable screening target closely associated with obesity, dyslipidemia, and hypertension. Notably, an elevated TyG index was linked to lower vitamin B12 levels, highlighting a potential role for vitamin B12 optimization in mitigating IR and reducing CVD risk. The high prevalence of HHcy—especially in the context of declining folate status—further highlights the need to address micronutrient sufficiency as part of broader CVD prevention strategies. These findings underline the importance of integrating easily obtained metabolic indices such as the TyG index with targeted nutritional screening in occupational health programs, especially within resource-constrained settings including Benin. Implementation of dual screening approaches can facilitate early identification and personalized interventions, potentially reducing the burden of CVD among high-risk urban workers.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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