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Baseline levels and longitudinal trajectories of the combined TyG-AIP index and their association with the Risk of Frailty in Older Adults

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Abstract

Background

Frailty is a critical health issue in aging populations, and metabolic dysfunction is considered an important driving factor. This study aimed to investigate the associations of baseline levels and longitudinal trajectories of the combined triglyceride-glucose (TyG) index and atherogenic index of plasma (AIP) (TyG-AIP) with the risk of incident frailty in middle-aged and older adults.

Methods

Based on the prospective Kunshan Aging Electronic Health Cohort (KARE), this study included 30,524 community-dwelling permanent residents aged ≥ 60 years. Using continuous annual physical examination data from 2018 to 2021, latent class growth modeling (LCGM) was applied to identify longitudinal TyG-AIP trajectories. With incident frailty assessed by the electronic frailty index (eFI) from 2022 to 2024 as the primary outcome, Cox proportional hazards regression and restricted cubic splines (RCS) were used to analyze the associations and dose-response relationships.

Results

During follow-up, 6,069 participants developed incident frailty. The composite TyG-AIP exhibited a significant positive association and a nonlinear dose-response relationship with the risk of incident frailty. Compared with the lowest tertile (T1) of baseline TyG-AIP, participants in the highest tertile (T3) had a 22% increased risk of incident frailty (HR = 1.22, 95% CI: 1.14–1.30). LCGM identified three stable trajectory groups (low-, moderate-, and high-stable). Compared with the low-stable group, the high-stable group presented the highest frailty risk (HR = 1.35, 95% CI: 1.25–1.45). In the joint classification of AIP and TyG, the low AIP/high TyG group (Class 2) had the highest frailty risk (HR = 1.45).

Conclusions

Both higher baseline TyG-AIP levels and persistently elevated longitudinal trajectories were independently associated with an increased risk of incident frailty in middle-aged and older adults. Longitudinal metabolic trajectories provide more comprehensive risk information than a single baseline measurement, supporting TyG-AIP as a practical tool for identifying individuals at high risk of frailty in primary care settings.

Introduction

With global population aging and increasing life expectancy, maintaining functional reserve rather than merely prolonging survival has become a central goal of geriatric medicine and public health[1]. Frailty is

one of the most clinically significant age-related conditions because it reflects increased vulnerability to stressors and predicts a range of adverse outcomes, including falls, disability, hospitalization, and mortality[2, 3]. Frailty is distinct from chronological age, multimorbidity, and disability; rather, it represents a multidimensional decline in physiological reserves across multiple organ systems. Current frailty research is primarily based on two complementary conceptual models. The frailty phenotype model defines frailty as a clinical syndrome characterized by exhaustion, slowness, weakness, low physical activity, and unintentional weight loss[2], whereas the deficit accumulation model conceptualizes frailty as a continuous process resulting from the accumulation of health deficits across multiple systems[4]. In recent years, the electronic frailty index (eFI), which is based on the deficit accumulation model, has been increasingly applied in community-based settings because it quantifies vulnerability on a continuous scale and can be derived from routinely collected electronic health data[4–6].

Among the biological processes implicated in frailty, metabolic dysfunction has received increasing attention. Evidence suggests that insulin resistance (IR) and glucolipotoxicity may contribute to mitochondrial dysfunction, oxidative stress, endothelial injury, and impaired cellular energy metabolism. At the organ level, these disturbances may manifest as skeletal muscle anabolic resistance and vascular dysfunction, ultimately reducing the body's ability to maintain homeostasis in response to physiological stress and accelerating the development and progression of frailty[7–10]. These metabolic abnormalities are particularly relevant from a clinical perspective because they are common, potentially modifiable, and amenable to standardized assessment using routinely available laboratory parameters. They may therefore represent practical targets for risk stratification in older populations.

The triglyceride-glucose (TyG) index is an easily accessible surrogate IR marker and has demonstrated good concordance with the euglycemic-hyperinsulinemic clamp, a reference method for assessing insulin sensitivity[11–14]. Compared with more complex measures of IR, the TyG index is inexpensive, readily available, and straightforward to calculate, making it suitable for epidemiological surveys and clinical application in resource-limited settings[15]. Higher TyG values have been associated with an increased risk of metabolic syndrome, diabetes mellitus (DM), hypertension (HTN), and cardiovascular disease[13, 16–19]. The atherogenic index of plasma (AIP) reflects atherogenic dyslipidemia and adverse alterations in the lipoprotein profile[20]. Higher AIP values have also been associated with HTN, DM, coronary heart disease (CHD), and carotid atherosclerosis across diverse populations[21–26]. Although TyG and AIP provide complementary information on glucose-insulin metabolism and atherogenic lipid abnormalities, respectively, they are biologically interconnected and may capture two related but heterogeneous dimensions of cardiometabolic dysfunction[12, 13, 27]. Therefore, integrating these two indices may provide a more comprehensive measure of metabolic burden than either index alone. This may be particularly relevant in older adults, in whom frailty is likely to reflect the cumulative effects of chronic, multisystem metabolic stress rather than an isolated metabolic abnormality[28].

However, several important knowledge gaps remain. First, previous studies examining metabolic dysfunction in relation to frailty have largely focused on overt DM, metabolic syndrome, or individual

metabolic biomarkers[29, 30], whereas the joint contribution of IR-related abnormalities and atherogenic dyslipidemia to frailty remains insufficiently characterized. Second, most existing studies have relied on a single baseline measurement of metabolic status. Because frailty is a dynamic process and metabolic abnormalities may persist or evolve over time, a single measurement may inadequately capture long-term exposure and may obscure clinically relevant heterogeneity in metabolic trajectories. Repeated assessments may therefore provide a more informative characterization of cumulative or persistent metabolic burden. Third, evidence from large community-based Chinese cohorts incorporating repeated biochemical measurements and prospective assessment of incident frailty remains limited. This evidence gap is particularly important, as metabolic indicators derived from routine health examinations could provide inexpensive and scalable tools for identifying individuals at elevated frailty risk and informing population-based prevention strategies.

To address these gaps, this study used data from the Kunshan Aging Electronic Health Cohort to investigate the associations of both baseline levels and long-term trajectories of the combined TyG-AIP index with subsequent risk of frailty. By integrating annual repeated laboratory measurements, latent class growth modeling (LCGM), and incident frailty assessed using the eFI, we aimed to determine whether a higher baseline TyG-AIP burden and persistently elevated longitudinal trajectories were associated with an increased incident frailty risk, independent of major demographic and lifestyle factors. The study further explored the dose-response relationship between TyG-AIP and frailty and evaluated the robustness of the associations across clinically relevant subgroups and sensitivity analyses.

Methods

Study design and population

This study used physical examination data from the Kunshan Aging Electronic Health Cohort (KARE), a prospective community-based cohort, collected between January 2018 and December 2024. KARE is a large, community-based cohort established to include permanent residents aged ≥ 60 years across all subdistricts and townships of Kunshan City, China. Participants underwent annual physical examinations, including standardized anthropometric measurements and blood biochemical testing, while demographic characteristics, lifestyle factors, and health-related information were collected using standardized questionnaires. A total of 133,022 individuals were initially identified from the KARE database. Participants were sequentially excluded according to the following criteria: (1) absence of baseline data in 2018 (n = 57,713); (2) age < 60 years (n = 7,627); (3) missing data or extreme outliers for key biochemical variables, including fasting blood glucose (FBG), triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C) (missing data, n = 11,844; extreme outliers, n = 705); (4) occurrence of frailty or death during the exposure assessment period (2018–2021) (n = 3,768); (5) loss to follow-up (n = 8,923); and (6) fewer than four TyG-AIP measurements during the study period (n = 11,918). Ultimately, 30,524 participants were included in the final analysis. The study was approved by the Ethics Committee of the First People's Hospital of Kunshan (2023-03-014-H01-K01), and written informed consent was

obtained from all participants at enrollment into the prospective KARE cohort.. The participant selection process is illustrated in Fig. 1.

Definition and assessment of TyG-AIP

The TyG index was calculated as a surrogate measure of IR using fasting TG and FBG concentrations:

$TyG = \ln [TG\ (mg/dL) \times FBG\ (mg/dL) / 2]$[14].

The AIP was calculated as the base-10 logarithm of the ratio of TG to HDL-C:

$AIP = \log_{10} [TG\ (mg/dL) / HDL\text{-}C\ (mg/dL)]$[31].

Because TyG and AIP are calculated on different numerical scales, min–max normalization was applied to the AIP values to rescale them to a range of 0–1 before constructing the composite TyG-AIP index. The TyG-AIP index was subsequently derived by integrating the TyG index with the normalized AIP according to the prespecified composite formula Higher TyG-AIP values indicated a greater combined burden of IR-related metabolic dysfunction and atherogenic dyslipidemia.

Assessment of longitudinal changes in TyG-AIP

To characterize longitudinal patterns of TyG-AIP from 2018 to 2021, annual physical examination data collected over four consecutive years were used to construct a repeated-measures dataset. Participants were required to have complete blood laboratory data at at least one time point in each of the four consecutive years. LCGM was used to identify distinct longitudinal trajectories of TyG-AIP and to classify participants into relatively homogeneous subgroups according to their baseline levels and changes over time. Models containing one to five latent classes were sequentially fitted, and both linear and quadratic time functions were considered to allow for different patterns of change. Missing longitudinal observations were handled using full-information maximum likelihood, thereby allowing participants with incomplete repeated measurements to contribute the available information to model estimation. The optimal trajectory classes were determined based on statistical fit indices, class size, model convergence, and clinical interpretability. The identified trajectory groups were then characterized according to their baseline TyG-AIP levels and longitudinal changing patterns.

Assessment of frailty

The primary outcome of this study was incident frailty, defined as the first transition to the frailty state during the outcome observation period from January 2022 to December 2024 among participants who were free of frailty throughout the exposure assessment period (January 2018 to December 2021). Frailty was assessed using eFI, which was constructed according to the cumulative deficit model proposed by Rockwood et al. The eFI comprised 26 health deficits derived from electronic health records

and covered multiple domains, including physical function, chronic diseases, nutritional status, cognition, and sensory function. The eFI was calculated as:

eFI = number of deficits present/total number of assessed deficits

The resulting score ranged from 0 to 1, with higher values indicating greater frailty severity (Supplementary Table S1). Based on commonly used frailty index thresholds[6, 32] and validation studies in Chinese older populations[33], participants were classified as healthy (eFI ≤ 0.10), pre-frail (0.10 < eFI < 0.25), or frail (eFI ≥ 0.25). For the primary analysis, incident frailty was defined as the first occurrence of an eFI ≥ 0.25 during the outcome observation period.

Covariates

Potential confounding variables were assessed primarily at baseline in 2018. Demographic characteristics included age, sex, and educational level. Education was categorized as low (primary school or below, including illiteracy), middle (middle school, high school, or vocational school), or high (college, undergraduate, or above). Anthropometric and blood pressure (BP) measurements were obtained during standardized physical examinations conducted by trained nurses. Height, weight, and body mass index (BMI) were recorded. BP was measured in the seated position, and the mean of three measurements was recorded. HTN was defined as systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, current use of antihypertensive medication, or self-reported physician-diagnosed HTN. Lifestyle characteristics included alcohol consumption, smoking, and physical activity. Current smoking was defined as an average consumption of ≥ 1 cigarette per day. Alcohol consumption was defined as drinking at least once per week in the past year.. Physical activity was assessed based on moderate-intensity exercise lasting ≥ 30 minutes per session and categorized according to frequency as daily, frequent (1–3 times/week), occasional (< 1 time/week), or never. Medication use was recorded for antihypertensive, glucose-lowering, and lipid-lowering medications and was categorized as yes/no. In sensitivity analyses, medication use was alternatively defined as self-reported use of at least one glucose-lowering or antihypertensive medication at baseline. Laboratory measurements were obtained from fasting venous blood samples. Lipid parameters, including total cholesterol, TG, and HDL-C, were measured using standard enzymatic methods, while FBG was measured using the glucose oxidase method. Comorbidities were determined using information from electronic health records, medication histories, and self-reported medical histories. DM was defined as FBG ≥ 7.0 mmol/L, glycated hemoglobin ≥ 6.5%, current use of glucose-lowering medication, or self-reported physician-diagnosed DM. A history of CHD or stroke was determined based on documented clinical diagnoses in electronic health records.

Statistical analysis

All statistical analyses were performed using R 4.3.1. The proportion of missing values for each covariate was < 10%. Missing covariate data were handled using multiple imputation by chained

equations (MICE), generating 10 imputed datasets. Descriptive and regression analyses were performed across the imputed datasets, and estimates were pooled according to Rubin's rules.

Continuous variables' distribution was assessed using the Shapiro–Wilk test in conjunction with Q–Q plots. Normally distributed continuous variables were summarized as mean ± standard deviation (SD), whereas skewed continuous variables as median (interquartile range, IQR). Categorical variables were summarized as frequencies and percentages. Participants were categorized into tertiles of baseline TyG-AIP (T1–T3, from lowest to highest). Participants were further categorized into four classes according to the median values of baseline AIP and TyG: low AIP/low TyG (Class 1), low AIP/high TyG (Class 2), high AIP/low TyG (Class 3), and high AIP/high TyG (Class 4). Baseline characteristics were compared using one-way ANOVA for normally distributed continuous variables, the Kruskal–Wallis test for skewed continuous variables, and the chi-square test for categorical variables, as appropriate.

LCGM was used to identify heterogeneous longitudinal trajectories of TyG-AIP from 2018 to 2021. LCGM is based on finite mixture models, which assume that the study population comprises unobserved subgroups with distinct longitudinal trajectories that can be described using polynomial functions of time. Unlike traditional clustering methods, LCGM allows for missing measurements in individuals and handles missing data *via* full-information maximum likelihood to maximize sample retention, with model parameters estimated using the expectation-maximization algorithm. In this study, models containing one to five latent classes were sequentially fitted, and both linear and quadratic time terms were evaluated. Model selection was based on multiple criteria, including the Bayesian Information Criterion (BIC) and Akaike Information Criterion (AIC), entropy, the bootstrap likelihood ratio test (BLRT), the Lo–Mendell–Rubin likelihood ratio test (LMR-LRT), class size, model convergence, and clinical interpretability. Lower AIC and BIC values indicated better model fit, whereas an entropy value > 0.70 indicated acceptable classification quality. A significant LMR-LRT or BLRT ($P < 0.05$) was considered evidence that the k-class model provided a better fit than the corresponding (k − 1)-class model. Each trajectory class was required to contain at least 5% of the study population, and models were required to converge within 1,000 iterations. Individual participants were assigned to the trajectory class for which they had the highest posterior probability. Based on these criteria, a three-class trajectory solution was selected as the optimal model. The resulting trajectory groups were then used as the primary longitudinal exposure in Cox proportional hazards models.

Cox regression models were used to estimate the associations of baseline TyG-AIP, analyzed both continuously and by tertiles, and longitudinal TyG-AIP trajectory groups with incident frailty. Follow-up commenced on January 1, 2022, after completion of the exposure assessment period, and continued until the first occurrence of frailty, death, loss to follow-up, or the end of follow-up on December 31, 2024, whichever occurred first. Because the outcome (frailty) was assessed based on the eFI, and HTN, DM, and CHD are components of the eFI outcome measure (Supplementary Table S1), these conditions were not included as covariates in the primary multivariable model to minimize potential overadjustment and outcome-component overlap. Two Cox regression models were specified. Model 1 was unadjusted, whereas Model 2 was adjusted for sex, age, drinking status, smoking status, total cholesterol, and LDL-C.

Multicollinearity among covariates was assessed using the criterion VIF > 10. The proportional hazards assumption was assessed using Schoenfeld residuals (all P > 0.05). Kaplan–Meier curves were generated to illustrate the cumulative incidence of frailty across TyG-AIP trajectory groups, and between-group differences were assessed using the log-rank test. Restricted cubic spline (RCS) functions were incorporated into Cox proportional hazards models to examine potential nonlinear dose–response associations between baseline TyG-AIP and incident frailty. TyG-AIP was modeled as a continuous exposure, with covariate adjustment identical to that used in the main multivariable analysis. Four knots were placed at the 5th, 35th, 65th, and 95th percentiles of the TyG-AIP distribution, with the median value used as the reference. Predicted HRs and corresponding 95% CIs were estimated across 200 equally spaced points spanning the 1st to 99th percentiles of the TyG-AIP distribution. Continuous covariates were fixed at their medians and categorical covariates at their modal values for prediction. The overall association and departure from linearity were assessed using Wald tests for the corresponding spline terms.

Subgroup analyses were conducted to evaluate the consistency of the associations across clinically relevant strata. Participants were stratified according to age (60–<70, 70–<80, and ≥ 80 years), sex, BMI (< 24, 24–<28, and ≥ 28 kg/m²), use of glucose-lowering or antihypertensive medications, DM status, HTN status, history of stroke, and history of cardiovascular disease. Baseline TyG-AIP tertiles and longitudinal TyG-AIP trajectory groups were evaluated separately as exposure variables within each subgroup. Statistical interactions were assessed using likelihood ratio tests comparing models with and without the corresponding exposure-by-subgroup interaction term.

Several sensitivity analyses were performed to assess the robustness of the primary findings. First, antihypertensive, glucose-lowering, and lipid-lowering medication use was additionally included as covariates in the multivariable models. Second, the primary analyses were repeated after excluding participants who developed frailty or died within the first two years of the outcome follow-up period. All tests were two-sided, and P < 0.05 was considered statistically significant. For prespecified multiple-comparison analyses, the Bonferroni method was used to adjust the significance threshold.

Results

Baseline characteristics of participants according to baseline TyG-AIP tertiles

A total of 30,524 participants from the KARE cohort were included in the final analysis, among whom 6,069 developed incident frailty. Participants were categorized into tertiles based on baseline TyG-AIP (T1, lowest; T2, middle; T3, highest). Baseline characteristics across the three groups are presented in Table 1. Except for the prevalence of stroke history (P = 0.995), all baseline characteristics differed significantly across TyG-AIP tertiles (all P < 0.001). Participants in T3 were younger and had a higher proportion of females, whereas the proportions of smokers and drinkers were lower. Participants in the higher TyG-AIP tertiles also had higher BMI, FBG, TC, LDL-C, and BP, but lower HDL-C levels. Moreover,

the median TyG index increased progressively from 6.60 in T1 to 7.63 in T3, while the median AIP increased from − 0.27 to 0.27. Regarding comorbidities and medication use, the cardiometabolic comorbidities' prevalence also increased across TyG-AIP tertiles. The DM prevalence increased from 13.6% in T1 to 29.5% in T3, HTN from 59.2% to 75.4%, and CHD from 3.9% to 4.9%. Similarly, the proportions of participants receiving glucose-lowering, antihypertensive, and lipid-lowering medications were highest in T3, at 18.3%, 70.7%, and 20.7%, respectively. In the baseline joint classification of TyG and AIP, participants in T1 were predominantly classified as having low TyG (95.9%) and low AIP (100%), whereas those in T3 were predominantly classified as having high TyG (98.3%) and high AIP (100%).

Table 1
Baseline characteristics by TyG-AIP tertile

Characteristic	Total	T1	T2	T3	P *value* [c]
Age,years [a]	73.48 ± 6.83	74.15 ± 6.94	73.6 ± 6.74	72.69 ± 6.72	< 0.001
Female sex	16259(53.3%)	4971(48.8%)	5460(53.7%)	5828(57.3%)	< 0.001
Current smoking	7646(25%)	2697(26.5%)	2543(25%)	2406(23.7%)	< 0.001
Current drinking	6458(21.2%)	2434(23.9%)	2070(20.3%)	1954(19.2%)	< 0.001
Education level					
Low level	19066(62.5%)	6650(65.3%)	6412(63%)	6004(59%)	< 0.001
Middle level	11067(36.3%)	3390(33.3%)	3640(35.8%)	4037(39.7%)	< 0.001
High level	391(1.3%)	138(1.4%)	124(1.2%)	129(1.3%)	< 0.001
Exercise					
1	11263(36.9%)	3613(35.5%)	3753(36.9%)	3897(38.3%)	< 0.001
2	1381(4.5%)	378(3.7%)	457(4.5%)	546(5.4%)	< 0.001
3	1337(4.4%)	407(4%)	440(4.3%)	490(4.8%)	< 0.001
4	16543(54.2%)	5780(56.8%)	5526(54.3%)	5237(51.5%)	< 0.001
BMI,kg/m²[a]	24.28 ± 3.25	23.1 ± 3.12	24.37 ± 3.15	25.36 ± 3.07	< 0.001
TG,mg/dl [b]	115.14(79.71-159.43)	70.86(62-88.57)	115.14(97.43-132.85)	186(159.43-239.14)	< 0.001
TC,mg/dl [a]	182.11 ± 34.99	177 ± 33.39	182.36 ± 34.75	186.96 ± 36.08	< 0.001
LDL-C,mg/dl [a]	103.03 ± 30.4	96.1 ± 27.89	106.73 ± 29.6	106.27 ± 32.35	< 0.001
HDL-C,mg/dl [a]	53 ± 14.07	63.6 ± 14.41	51.6 ± 10.69	43.79 ± 8.55	< 0.001

Characteristic	Total	T1	T2	T3	P *value* [c]
FBG,mg/dl [a]	104.75 ± 24.19	100.52 ± 19.42	103.71 ± 22.92	110.02 ± 28.39	< 0.001
SBP,mmHg [a]	138.28 ± 18.71	135.98 ± 18.77	138.45 ± 18.73	140.4 ± 18.37	< 0.001
DBP,mmHg [a]	80.52 ± 10.73	79.11 ± 10.78	80.58 ± 10.6	81.87 ± 10.62	< 0.001
UA,mg/dl [b]	5.25(4.42–6.22)	4.93(4.15–5.82)	5.25(4.42–6.17)	5.63(4.76–6.63)	< 0.001
ALT,U/L [b]	17(14–23)	16(13–21)	17(13–22)	19(15–25)	< 0.001
AST,U/L [b]	20(17–24)	20.9(18–24)	20(17–24)	20.05(17–25)	< 0.001
eFI score [a]	0.1 ± 0.05	0.09 ± 0.05	0.1 ± 0.05	0.1 ± 0.05	< 0.001
AIP [b]	0(-0.19-0.19)	-0.27(-0.38–0.19)	0(-0.07-0.05)	0.27(0.19–0.39)	< 0.001
TyG index [b]	7.07(6.72–7.45)	6.6(6.4–6.78)	7.05(6.9–7.22)	7.63(7.4–7.89)	< 0.001
Diabetes	6398(21%)	1383(13.6%)	2019(19.8%)	2996(29.5%)	< 0.001
Stroke	2456(8%)	820(8.1%)	820(8.1%)	816(8%)	0.995
CHD	1298(4.3%)	402(3.9%)	402(4%)	494(4.9%)	0.001
Hypertension	20684(67.8%)	6025(59.2%)	6986(68.7%)	7673(75.4%)	< 0.001
Anti-HTN med	20875(68.4%)	6631(65.2%)	7050(69.3%)	7194(70.7%)	< 0.001
Anti-DM med	4532(14.8%)	1213(11.9%)	1457(14.3%)	1862(18.3%)	< 0.001
Lipid-lowering med	5865(19.2%)	1850(18.2%)	1906(18.7%)	2109(20.7%)	< 0.001
TyG					
low	15186(49.8%)	9762(95.9%)	5252(51.6%)	172(1.7%)	< 0.001
high	15338(50.2%)	416(4.1%)	4924(48.4%)	9998(98.3%)	< 0.001

Characteristic	Total	T1	T2	T3	P *value* *c*
AIP					
low	14958(49%)	10178(100%)	4780(47%)	0(0%)	< 0.001
high	15566(51%)	0(0%)	5396(53%)	10170(100%)	< 0.001
TyG&AIP					
Class1	12678(41.5%)	9762(95.9%)	2916(28.7%)	0(0%)	< 0.001
Class2	2280(7.5%)	416(4.1%)	1864(18.3%)	0(0%)	< 0.001
Class3	2508(8.2%)	0(0%)	2336(23%)	172(1.7%)	< 0.001
Class4	13058(42.8%)	0(0%)	3060(30.1%)	9998(98.3%)	< 0.001

a Data are mean ± SD; *b* Data are median (IQR); *c* One-way ANOVA, Pearson's Chi-square, Kruskal-Wallis rank sum test; AIP, the atherogenic index of plasma; Anti-HTN agents, antihypertensive agents; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; CHD, coronary heart disease; Glucose-lowering agents, glucose-lowering medications; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; Lipid-lowering agents, lipid-lowering medications; TC, total cholesterol; SBP, systolic blood pressure; TG, triglyceride; TyG-AIP, TyG × Z ~ AIP~; TyG index, triglyceride–glucose index; UA, uric acid. Class1, low AIP and low TyG; Class2, low AIP and high TyG; Class3, high AIP and low TyG; Class4, high AIP and high TyG.

Identification of longitudinal TyG-AIP trajectories

Longitudinal TyG-AIP trajectories from 2018 to 2021 were analyzed using LCGM. Based on the comprehensive model selection criteria detailed in the Statistical analysis section, a 3-class model was ultimately identified as optimal.

The three trajectory groups were characterized as low-stable, moderate-stable, and high-stable trajectories (Fig. 2). Trajectory 1 (low-stable) comprised 12,077 participants (39.6%) and was characterized by consistently low TyG-AIP levels with little change over time. Trajectory 2 (moderate-stable) comprised 13,843 participants (45.4%) and represented the largest group, with moderately elevated but relatively stable TyG-AIP levels throughout the exposure period. Trajectory 3 (high-stable) comprised 4,604 participants (15.1%) and was characterized by the highest TyG-AIP levels at baseline and persistently elevated levels throughout the exposure period. The average posterior probability of

class assignment exceeded 0.70 for all three trajectory groups, indicating acceptable classification quality.

Baseline characteristics according to longitudinal TyG-AIP trajectories

According to the three longitudinal TyG-AIP trajectory groups identified by LCGM, baseline characteristics are presented in Supplementary Table S2. Except for the prevalence of stroke history (P = 0.995), all baseline characteristics differed significantly among the three trajectory groups (all P < 0.001).

Participants in Trajectory 3 were younger and had a higher proportion of females, whereas the proportions of current smokers and current drinkers were lower than those in the other trajectory groups. Trajectory 3 also had the highest baseline BMI, systolic blood pressure, FBG, TG, and uric acid levels, as well as relatively higher liver enzyme levels and the lowest HDL-C levels. The median baseline TyG index and AIP were also highest in Trajectory 3, at 7.63 and 0.27, respectively. The prevalence of DM, HTN, and CHD was highest in Trajectory 3, as were the proportions of participants using glucose-lowering, antihypertensive, and lipid-lowering medications. Participants in Trajectory 1 generally had the lowest levels of these cardiometabolic characteristics. Cross-tabulation of the baseline joint TyG-AIP classes (Class 1–Class 4) and longitudinal trajectory groups showed significant correspondence between baseline metabolic status and longitudinal patterns. Among participants in Trajectory 3, 97.7% were classified in the baseline Class 4 (high TyG/high AIP), whereas 83.1% of participants in Trajectory 1 belonged to the baseline Class 1 (low TyG/low AIP).

Associations of baseline indices and longitudinal trajectories with incident frailty

Cox regression analyses demonstrated positive associations between baseline metabolic indices and incident frailty risk (Table 2; Fig. 3). After potential confounding factors' adjustment, each 1-unit increase in TyG and AIP was associated with a 35% and 31% higher incident frailty risk, respectively (both P < 0.001). When categorized into binary groups, high TyG participants had a higher frailty risk than those with low TyG (HR = 1.27[1.20–1.34]), as did high AIP participants compared with low AIP (HR = 1.09[1.04–1.15]).

In the combined classification of AIP and TyG, with Class 1 as the reference, Class 2 had the highest risk of incident frailty (HR = 1.45 [1.32–1.60]), followed by Class 4 (HR = 1.22 [1.15–1.29]). Class 3 was not significantly different from the reference group. When baseline TyG-AIP was categorized into tertiles, participants in T3 had a 22% higher incident frailty risk than those in T1 (HR = 1.22[1.14–1.30]).

Longitudinal TyG-AIP trajectories were also significantly associated with incident frailty. Compared with the low-stable trajectory (Trajectory 1), the adjusted HR was 1.10 (1.04–1.17) for the moderate-stable trajectory (Trajectory 2) and 1.35 (1.25–1.45) for the high-stable trajectory (Trajectory 3). A significant trend across the three trajectory groups was observed (P < 0.001).

Table 2
Associations of metabolic indices with frailty

Exposure	Level	N(%)	Model 1 HR(95%CI)	P	Model2 HR(95%CI)	P
TyG	Per 1 unit increase	-	1.25(1.19–1.31)	< 0.001	1.35(1.29–1.42)	< 0.001
AIP	Per 1 unit increase	-	1.24(1.13–1.36)	< 0.001	1.31(1.19–1.44)	< 0.001
TYG.D2	Low	15186(49.8%)	1.00		1.00	
	High	15338(50.2%)	1.21(1.15–1.28)	< 0.001	1.27(1.20–1.34)	< 0.001
AIP.D2	Low	14958(49.0%)	1.00		1.00	
	High	15566(51.0%)	1.08(1.03–1.14)	0.002	1.09(1.04–1.15)	< 0.001
TyG&AIP	Class1	12678(41.5%)	1.00		1.00	
	Class2	2280(7.5%)	1.38(1.25–1.51)	< 0.001	1.45(1.32–1.60)	< 0.001
	Class3	2508(8.2%)	0.97(0.87–1.07)	0.487	0.91(0.82-1.00)	0.056
	Class4	13058(42.8%)	1.18(1.11–1.24)	< 0.001	1.22(1.15–1.29)	< 0.001
TyG-AIP	T1	10178(33.3%)	1.00		1.00	
	T2	10176(33.3%)	1.09(1.02–1.16)	0.008	1.07(1.01–1.15)	0.029
	T3	10170(33.3%)	1.18(1.11–1.26)	< 0.001	1.22(1.14–1.30)	< 0.001
TyG-AIP Trajectory	Trajectory 1	12077(39.6%)	1.00		1.00	
	Trajectory 2	13843(45.4%)	1.11(1.05–1.17)	< 0.001	1.10(1.04–1.17)	< 0.001
	Trajectory 3	4604(15.1%)	1.28(1.19–1.38)	< 0.001	1.35(1.25–1.45)	< 0.001

Note. Each model cell shows HR (95% CI) and the model P value. N (%) is the comparison-group denominator in the supplied Cox output; Model 1: no covariates were adjusted; Model 2: adjusted for age, sex, smoking, drinking, total cholesterol, and LDL-C. Missing covariate handling follows the source analysis table and was not reinterpreted in this display-review rebuild. AIP, atherogenic index of plasma; CI, confidence interval; HR, hazard ratio; LDL-C, low-density lipoprotein cholesterol; TyG, triglyceride-glucose index.

Figure 3. Adjusted associations with frailty. The forest plot shows Model 2 hazard ratio estimates for metabolic indices and grouped exposure definitions. Points show estimates and horizontal lines show 95% confidence intervals; the vertical reference line marks a hazard ratio (HR) of 1.00.

Model 2 adjusted for sex, age, drinking, smoking, total cholesterol, and LDL-C. This is an adjusted association summary and should be interpreted within the locked Cox model sequence. AIP, atherogenic index of plasma; LDL-C, low-density lipoprotein cholesterol; TyG, triglyceride-glucose index; HDL-C, high-density lipoprotein cholesterol.

Dose-response relationships of TyG-AIP, AIP, and TyG for incident frailty

RCS analyses demonstrated significant nonlinear dose-response associations of baseline TyG, AIP, and TyG-AIP with the risk of incident frailty (Fig. 4). For TyG, the overall association was significant ($P < 0.001$), with evidence of nonlinearity ($P = 0.0002$). Significant overall and nonlinear associations were also observed for AIP and TyG-AIP (both $P < 0.001$).

TyG-AIP, triglyceride glucose-atherogenic index of plasma; AIP, the atherogenic index of plasma; TyG index, triglyceride-glucose index; 95% CIs, 95% confidence intervals.

Cumulative incidence of frailty: Kaplan–Meier curves

Kaplan–Meier analyses demonstrated significant differences in the cumulative incidence of frailty across all metabolic groupings (log-rank $P < 0.001$ for all comparisons; Supplementary Figure S1; Supplementary Table S3). For individual baseline metabolic indicators (Supplementary Figure S1A), participants with high TyG or high AIP had higher cumulative incidences of frailty than those in the respective low-level groups. In the joint TyG-AIP classification (Supplementary Figure S1B), cumulative frailty incidence differed significantly among the four groups over follow-up. When participants were categorized according to baseline TyG-AIP tertiles (Supplementary Figure S1C), a graded separation of the cumulative incidence curves was observed, with the highest incidence in T3. Similarly, cumulative frailty incidence differed significantly across the three longitudinal TyG-AIP trajectory groups (Supplementary Figure S1D). Participants in the high-stable trajectory (Trajectory 3) had the highest cumulative incidence throughout follow-up, whereas those in the low-stable trajectory (Trajectory 1) had the lowest cumulative incidence.

3.7 Subgroup analyses

Subgroup analyses were conducted to evaluate the consistency of the associations between TyG-AIP and incident frailty across clinically relevant subgroups. Longitudinal TyG-AIP trajectory groups were evaluated in Model 1, whereas baseline TyG-AIP tertiles were evaluated in Model 2. Analyses were stratified by age (60–<70, 70–<80, and ≥ 80 years), sex, BMI (< 24, 24–<28, and ≥ 28 kg/m²), use of glucose-lowering or antihypertensive medications, DM history, stroke history, CHD history, and HTN history. Trajectory 1 and T1 were used as the respective reference groups. Forest plots present the HRs

and 95% CIs for the highest-risk categories (Trajectory 3 and T3), together with the corresponding P values for interaction (Supplementary Figures S2 and S3). Stratified models were adjusted for sex, age, drinking status, smoking status, total cholesterol, and LDL-C, consistent with Model 2 of the primary analysis, except where the stratifying variable was included.

For baseline TyG-AIP tertiles, T3 was generally associated with a higher risk of incident frailty across the examined subgroups (Supplementary Figure S2). The association reached statistical significance among participants aged 60–<70 years (HR = 1.31) and 70–<80 years (HR = 1.22), whereas the association was not statistically significant among those aged ≥ 80 years (HR = 1.11, P = 0.133). Similarly, T3 was significantly associated with higher frailty risk among participants with BMI ≥ 28 kg/m² (HR = 1.22), whereas the associations did not reach statistical significance in the BMI < 24 kg/m² and 24–<28 kg/m² groups. Among all examined subgroup variables, only HTN showed a borderline statistically significant interaction (P = 0.049); no significant interactions were observed for the other stratification variables (all P > 0.05).

For longitudinal TyG-AIP trajectories, Trajectory 3 was associated with a higher incident frailty risk across most subgroups (Supplementary Figure S3). The adjusted HRs for Trajectory 3 were 1.39, 1.37, and 1.20 among participants aged 60–<70, 70–<80, and ≥ 80 years, respectively. In BMI-stratified analyses, the strongest association was observed among participants with BMI ≥ 28 kg/m² (HR = 1.34), whereas the association did not reach statistical significance among those with BMI < 24 kg/m². No statistically significant interactions were found between longitudinal TyG-AIP trajectories and any of the examined subgroup variables (all P > 0.05), supporting the overall consistency of the association across subgroups.

Sensitivity analyses

To validate the statistical robustness of the main findings and assess the potential impact of medication use, as well as reverse causality, on effect estimates, two prespecified sensitivity analyses were conducted.

First, additional adjustment was performed for glucose-lowering and lipid-lowering medication use on the basis of the primary multivariable model. After additional adjustment, the effect estimates were slightly attenuated, but the principal associations remained statistically significant. Compared with T1, participants in T3 had a higher incident frailty risk (HR = 1.16[1.09–1.24], P < 0.001). In the joint TyG-AIP classification, both Class 2 (HR = 1.28[1.16–1.41], P < 0.001) and Class 4 (HR = 1.15[1.09–1.22], P < 0.001) remained associated with higher frailty risk than Class 1. For longitudinal trajectories, Trajectory 3 remained significantly associated with incident frailty (HR = 1.27[1.18–1.37], P < 0.001), with a significant increasing trend across trajectory groups (Supplementary Table S4).

Second, to reduce the potential influence of reverse causality, participants who developed frailty during the first two years of outcome follow-up were excluded, and the multivariable Cox regression analyses were repeated among the remaining 23,360 participants. The associations were largely unchanged. In

the combined TyG-AIP classification, both Class 2 and Class 4 remained associated with a higher incident frailty risk compared with Class 1. For baseline TyG-AIP, participants in T3 continued to have an elevated frailty risk (HR = 1.20[1.07–1.34], P = 0.001). Similarly, Trajectory 3 remained significantly associated with incident frailty (HR = 1.33[1.17–1.51], P < 0.001) (Supplementary Table S5).

Discussion

In this community-based Chinese population of older adults, higher metabolic burden, reflected by baseline TyG, AIP, and the combined TyG-AIP index, was associated with a higher incident frailty risk. Longitudinal trajectory analyses further showed that participants with persistently high TyG-AIP levels during the exposure period had the most significant risk of subsequently developing frailty. These associations were supported by nonlinear dose-response analyses and remained materially consistent across multiple sensitivity analyses. These findings suggest that chronic adverse glucolipid metabolic status is not merely cross-sectionally coexistent with frailty, but more likely reflects a sustained cumulative biological process that progressively elevates the risk of frailty over time through long-term impairment of multisystem homeostatic reserve.

Our findings are generally consistent with previous evidence linking metabolic dysfunction to frailty. At the level of individual indicators, several cohort studies have reported positive associations between the TyG index and incident frailty. A study based on the CHARLS (n = 6,003; 7-year follow-up) reported that each 1-unit increase in TyG was associated with an 18% higher incident frailty risk (HR = 1.18), while participants in an elevated TyG trajectory group also had a higher frailty risk (HR = 1.30) [34]. Another study involving 8,510 participants reported a J-shaped association between TyG and the frailty index, with each 1-unit increase in TyG above 9.10 associated with a significantly higher frailty risk (HR = 1.67) [35]. Evidence regarding AIP is comparatively limited but broadly consistent with our findings. A cross-sectional analysis of the U.S. NHANES identified a significant nonlinear association between AIP and frailty, with participants in the highest AIP quartile having a higher prevalence of frailty (OR = 1.73) [29]. A longitudinal CHARLS study reported that cumulative AIP exposure was positively associated with frailty and that frailty partially mediated the association between cumulative AIP exposure and cardiovascular disease[36]. Together with these findings, our results support the relevance of both IR-related and atherogenic lipid abnormalities to frailty risk.

An important finding of this study was observed in the joint classification of TyG and AIP. Contrary to a simple additive pattern, participants in Class 2 had the highest observed frailty risk, whereas those in Class 4 showed a more modest association. This finding should be interpreted cautiously. One possible explanation is that the frailty-related signal associated with glucose-insulin dysregulation may be stronger than that associated with atherogenic dyslipidemia in this population. IR may contribute to skeletal muscle anabolic resistance, impaired mitochondrial energy metabolism, oxidative stress, and reduced metabolic flexibility, all of which could compromise physiological reserve and increase susceptibility to frailty[13, 37].Another possibility is that the lipid abnormalities reflected by AIP might be

partly influenced by medication use, dietary changes, or survivor bias in older populations. Moreover, the longitudinal evidence linking AIP to frailty remains relatively limited[29]. Therefore, the stronger association observed for Class 2 should not be interpreted as evidence that atherogenic dyslipidemia is irrelevant. Rather, it may indicate that glucose-insulin dysregulation represents a particularly prominent component of the metabolic pathway linking cardiometabolic dysfunction to frailty in this population.

From the theoretical framework of frailty as a multisystem functional decline, the observed association between the TyG-AIP index and incident frailty is biologically plausible. TyG captures IR-related metabolic dysfunction, whereas AIP reflects an atherogenic lipid profile, representing complementary but interconnected dimensions of cardiometabolic dysregulation. These processes are not biologically independent. IR may contribute to the development of atherogenic dyslipidemia through a sequence linking impaired insulin signaling to increased lipid flux and lipotoxicity[13, 38]. Impaired insulin-mediated suppression of adipose tissue lipolysis increases the release of free fatty acids (FFAs) and may increase hepatic glucose production[13, 38, 39]. Increased hepatic FFA availability promotes the synthesis and secretion of TG-rich very-low-density lipoprotein (VLDL), contributing to hypertriglyceridemia[39]. Elevated VLDL may subsequently increase cholesteryl ester transfer protein (CETP)-mediated lipid exchange, resulting in TG enrichment of HDL particles and their accelerated catabolism, thereby contributing to lower HDL-C concentrations[40, 41]. This sequence provides a plausible biological basis for the high-TG/low-HDL-C pattern captured by AIP. IR may also affect skeletal muscle and vascular function through multiple pathways, including impaired glucose uptake, increased proteolysis, mitochondrial dysfunction, oxidative stress, and chronic inflammation[37, 42, 43]. These disturbances may contribute to anabolic resistance, reduced muscle function, and impaired physiological stress responses. Meanwhile, the atherogenic lipid abnormalities reflected by AIP[40, 44], including elevated TG and low HDL-C and their association with small dense LDL particles, may promote endothelial dysfunction and atherosclerotic vascular injury, potentially compromising cerebral and peripheral perfusion and contributing to physical manifestations such as slowed gait and reduced physical activity, and cognitive manifestations relevant to frailty[29, 45]. When IR and atherogenic dyslipidemia coexist, these pathways may converge on a broader metabolic environment characterized by glucolipotoxicity, oxidative stress, impaired nitric oxide bioavailability, and chronic low-grade inflammation[39, 46, 47]. Thus, the combined TyG-AIP index may provide a broader representation of interconnected metabolic stress than either indicator alone.

A further strength of this study is the extension of metabolic exposure assessment from a single baseline measurement to longitudinal repeated observations. Frailty is inherently dynamic and reflects the progressive accumulation of health deficits over time[4, 5], while metabolic abnormalities may similarly persist or change throughout the aging process. A single TyG-AIP measurement may be influenced by short-term variation, including recent dietary intake, medication changes, or transient illness. Repeated measurements may better characterize persistent metabolic status and reduce the influence of short-term fluctuations. Consistent with this interpretation, the highly stable TyG-AIP trajectory was more strongly associated with incident frailty than the highest baseline TyG-AIP tertile (HR = 1.35 vs. HR = 1.22). The trajectory associations also remained relatively consistent across the

examined subgroups. The LCGM analysis further indicated that TyG-AIP patterns in this population were characterized predominantly by stable rather than markedly changing trajectories, comprising low-, moderate-, and high-stable groups. This finding suggests substantial persistence of metabolic status during the four-year exposure period. Individuals in the high-stable group maintained comparatively high TyG-AIP levels over time and subsequently experienced the highest incident frailty risk. Although this pattern is compatible with the hypothesis that persistent metabolic dysregulation may be more informative for frailty risk than a single measurement, it should not be interpreted as direct evidence of cumulative biological damage because this study did not directly measure cumulative metabolic injury or mechanistic biomarkers. Our findings are also broadly consistent with previous longitudinal evidence. Yuan et al. identified three relatively stable TyG trajectories in a Chinese urban older population and reported a higher frailty risk among participants in the high-stable trajectory (OR = 2.17, 95% CI: 1.01–3.88)[48]. In our study, no statistically significant interactions were observed between TyG-AIP trajectory groups and the examined subgroup variables (all $P > 0.05$), whereas baseline TyG-AIP showed a borderline interaction with HTN status ($P = 0.049$). Although this finding should be interpreted cautiously given the multiple subgroup comparisons, it raises the possibility that repeated exposure assessment may provide more stable risk estimates across heterogeneous older populations than a single baseline measurement[35]. Further longitudinal studies with longer follow-up and repeated metabolic assessments are needed to determine whether persistent TyG-AIP exposure improves risk prediction beyond baseline metabolic status.

Several limitations should be acknowledged. First, this study was based on routinely collected electronic health examination records from a community-based cohort. Because variable selection and measurement were determined by the original data collection procedures, measurement error, information bias, and residual confounding cannot be completely excluded. Second, direct measurements of insulin, inflammatory mediators, dietary quality, body composition, and other mechanistic factors were unavailable. Therefore, although the observed associations are biologically plausible, the underlying pathways linking TyG-AIP to frailty could not be directly examined. Third, several clinically relevant variables, including DM and HTN, were not included as covariates in the primary models because they are themselves represented among the deficits contributing to the eFI. BMI was also not included in the primary multivariable models. Although this approach was intended to minimize overadjustment and overlap with the outcome definition, residual confounding by these factors cannot be completely excluded and should be considered when interpreting the effect estimates. Fourth, the study population was derived from a single community-based Chinese cohort, and the requirement for repeated TyG-AIP measurements may have preferentially selected participants who remained engaged with routine health examinations and survived throughout the exposure assessment period. This potential healthy-survivor or selection effect may limit the generalizability of the findings to populations with less frequent health monitoring, different healthcare access, or different ethnic and socioeconomic characteristics. Finally, the longitudinal trajectories identified in this study were predominantly stable patterns rather than marked increasing or decreasing trajectories. The four-year exposure period may therefore have been insufficient to capture longer-term metabolic deterioration or improvement. Longer

follow-up with more frequent measurements will be needed to determine whether changes in TyG-AIP over extended periods, including metabolic worsening and improvement, are associated with different magnitudes of frailty risk. These limitations also warrant caution in interpreting the biological implications of our findings. The observed association between persistent TyG-AIP elevation and frailty is compatible with the deficit accumulation framework, in which multiple chronic and subclinical insults may contribute over time to declining physiological reserve[4, 5]. However, this study did not directly measure cumulative biological damage or establish a critical threshold beyond which frailty accelerates. Thus, the observed longitudinal association should be regarded as supportive of, rather than definitive evidence for, this theoretical framework.

Despite these limitations, this study has several important strengths. First, it included a large community-based sample of 30,524 participants, providing substantial statistical power to investigate the association between metabolic status and incident frailty. Second, annual biochemical measurements enabled the assessment of longitudinal TyG-AIP patterns rather than relying only on a single baseline measurement. Third, the use of LCGM identified clinically interpretable subgroups of persistent metabolic status. Fourth, the study focused on incident rather than prevalent frailty, thereby establishing a clearer temporal sequence between metabolic exposure and subsequent frailty onset. Finally, the consistency of the findings across multiple sensitivity analyses and clinically relevant subgroups strengthens the overall robustness of the observed associations.

From a clinical and public health perspective, TyG and AIP are inexpensive, routinely available, and readily calculated from standard laboratory measurements. They may therefore have potential as scalable markers for frailty risk stratification in community settings, particularly where comprehensive geriatric assessment is not routinely available. The potential value of TyG-AIP lies not in replacing comprehensive geriatric assessment, but in helping identify individuals who may benefit from more detailed assessment and early preventive interventions. Participants with persistently high TyG-AIP levels may represent a group warranting closer monitoring of physical function, nutritional status, and other frailty-related domains. The longitudinal findings also suggest that repeated metabolic assessments may provide clinically useful information beyond a single measurement. Because TyG-AIP can be derived from routine health examinations, incorporating its longitudinal pattern into existing health-monitoring systems may offer a feasible approach to identifying individuals with persistently adverse metabolic profiles. However, whether trajectory-based TyG-AIP assessment improves discrimination or clinical decision-making beyond conventional risk factors remains to be established in prospective validation studies.

Conclusions

In summary, higher TyG-AIP levels were associated with an increased incident frailty risk among middle-aged and older adults in this community-based Chinese cohort. Participants with persistently high TyG-AIP levels over the exposure period had a particularly elevated risk, suggesting that longitudinal metabolic status may provide additional information beyond a single baseline measurement. These

findings support the potential utility of routinely available glucolipid biomarkers for identifying individuals at increased frailty risk. Further prospective studies should validate these results in diverse populations, determine whether TyG-AIP trajectories improve frailty risk prediction beyond established clinical factors, and investigate whether integrating longitudinal TyG-AIP patterns with inflammatory, nutritional, body-composition, and functional measures can improve the early identification and prevention of frailty.

Declarations

Ethics approval and consent to participate

The experimental protocol was established, according to the ethical guidelines of the Helsinki Declaration and was approved by the ethics committee of the Kunshan Hospital Affiliated to Jiangsu University. Informed consent of all participants has been obtained (2023-03-014-H01-K01).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Author Contribution

D.N. Yan and F. Wu analyzed the data and drafted the original manuscript. J. Shao and Y. Cheng were responsible for data provision and data management. Y. Pan, K. Lu, and K.X. Zhou contributed to the study design and methodology. D.N. Yan, F. Wu, Y.J. Li, and J.L. Zhang provided support in data curation and statistical analysis. Y. Pan conceptualized the study, supervised the project, and critically revised the manuscript. All authors reviewed and approved the final manuscript.

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Data Availability

The health care data used in this study were retrieved from the primary medical center in Kunshan and anonymized for privacy purposes. Summary data that support the findings of this study may be requested from the corresponding author at [py97183@163.com].

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Figures

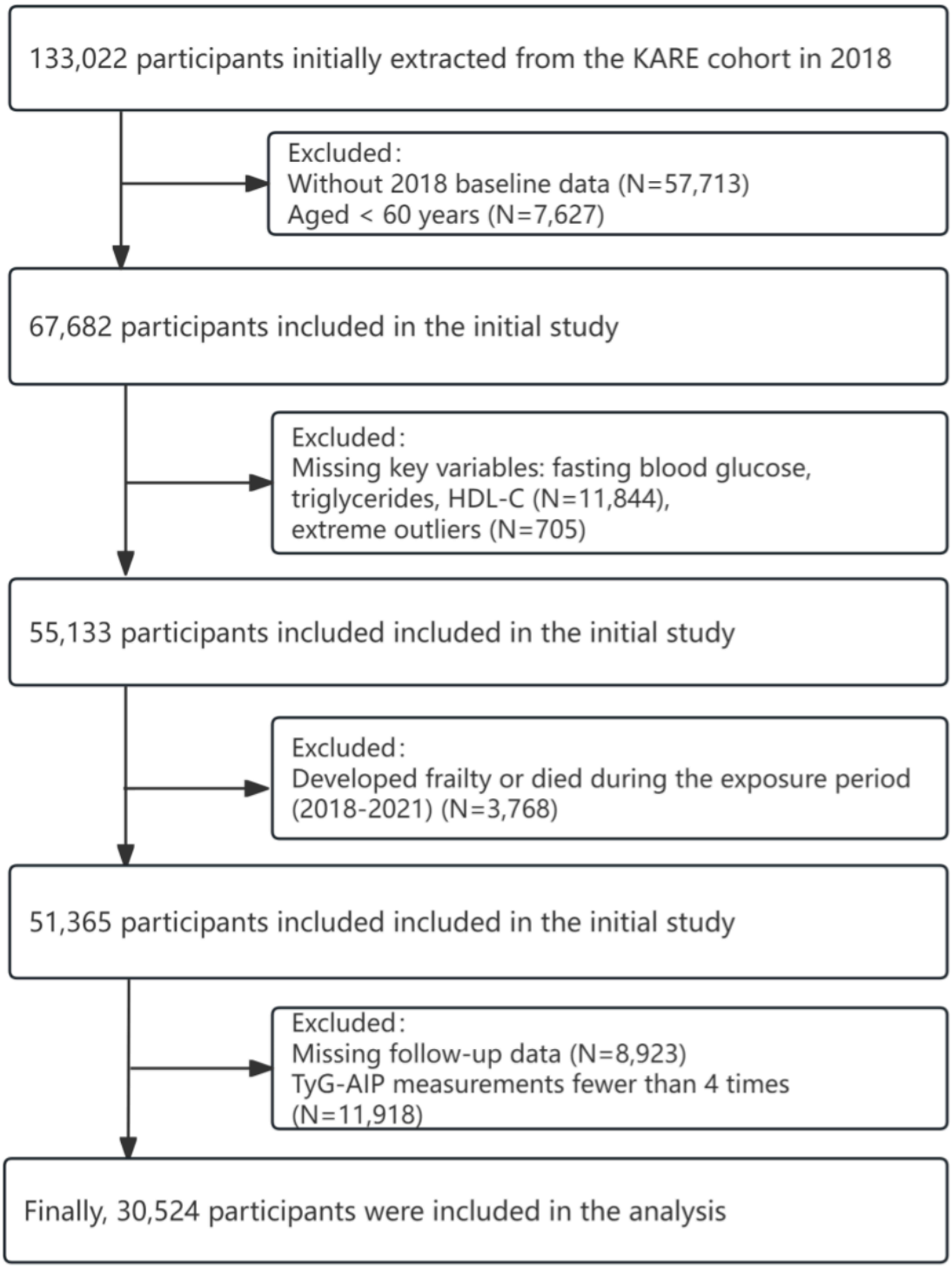


Figure 1

Flowchart of Participant Inclusion and Exclusion.

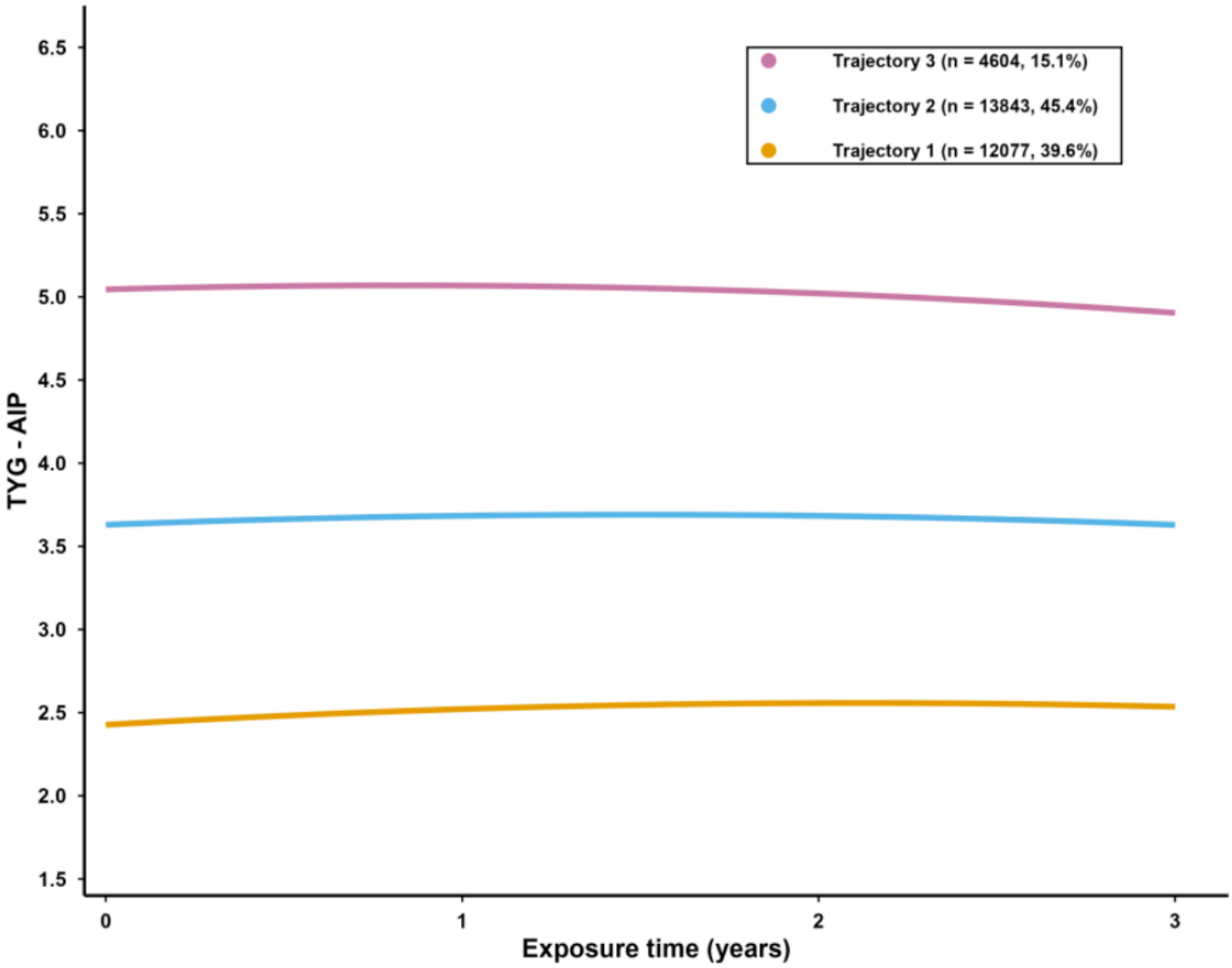


Figure 2

Trajectory patterns of TyG-AIP

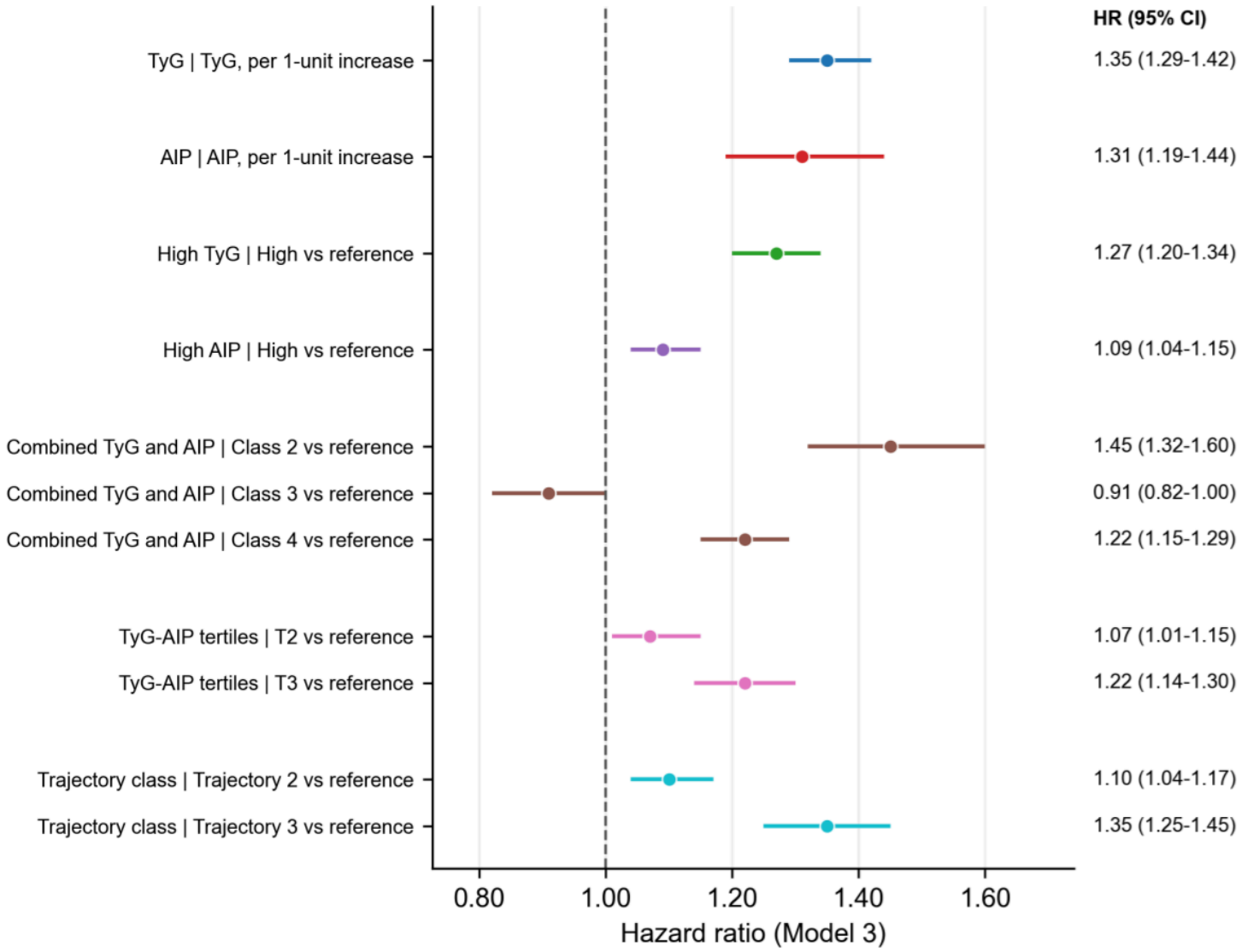


Figure 3

Adjusted associations with frailty. The forest plot shows Model 2 hazard ratio estimates for metabolic indices and grouped exposure definitions. Points show estimates and horizontal lines show 95% confidence intervals; the vertical reference line marks a hazard ratio (HR) of 1.00.

Model 2 adjusted for sex, age, drinking, smoking, total cholesterol, and LDL-C. This is an adjusted association summary and should be interpreted within the locked Cox model sequence. AIP, atherogenic index of plasma; LDL-C, low-density lipoprotein cholesterol; TyG, triglyceride-glucose index; HDL-C, high-density lipoprotein cholesterol.

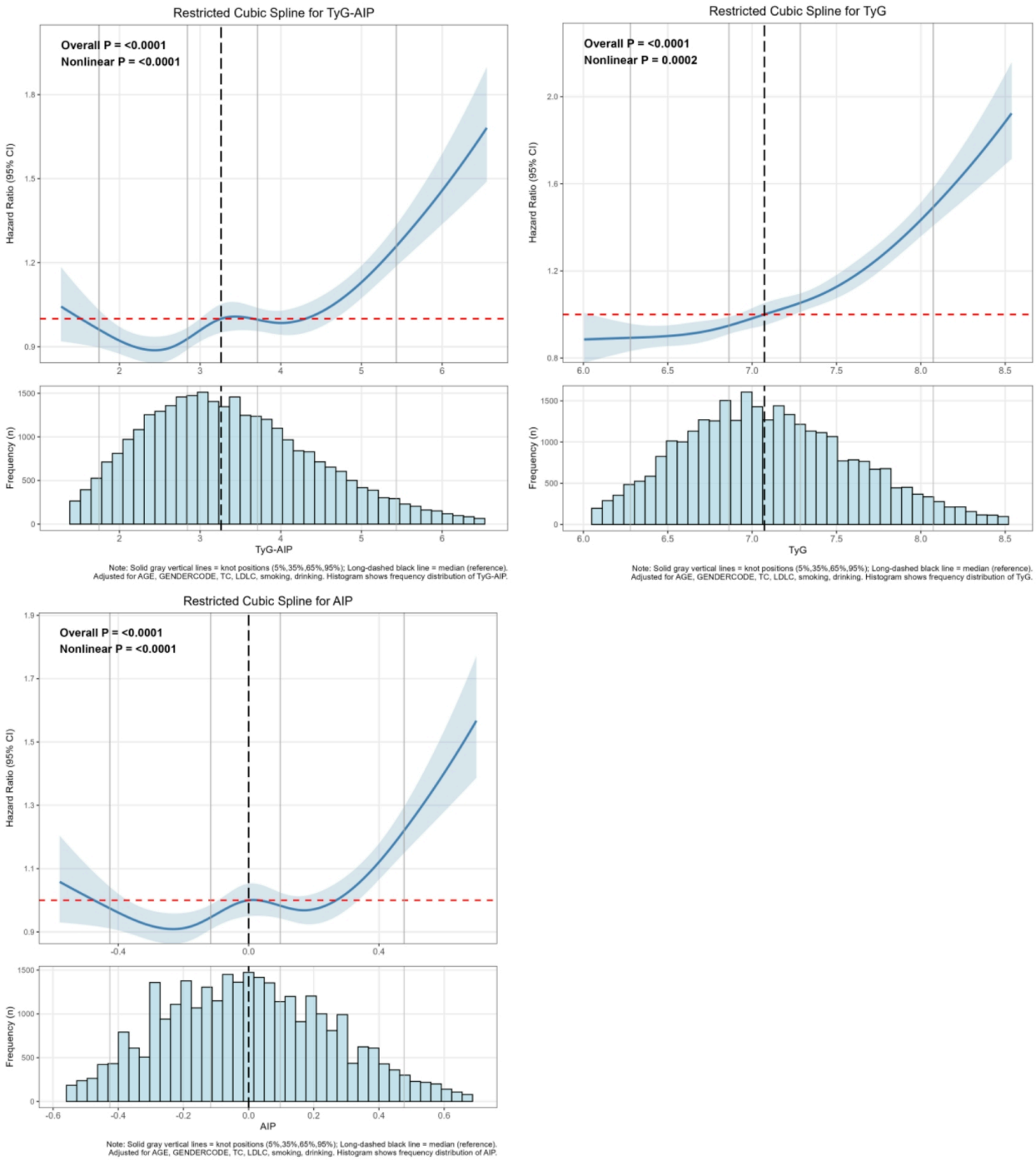


Figure 4

RCS analysis of the associations among TyG-AIP, AIP, TyG, and the increased frailty risk. Model adjusted for sex, age, drinking, smoking, LDL-C, and TC.

TyG-AIP, triglyceride glucose-atherogenic index of plasma; AIP, the atherogenic index of plasma; TyG index, triglyceride-glucose index; 95% CIs, 95% confidence intervals.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryTablesandFigures.docx