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Triglyceride–glucose index, fluid accumulation and subsequent acute respiratory distress syndrome in acute pancreatitis: A two-centre retrospective landmark study

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Abstract

Background

Fluid accumulation may carry different pulmonary risks across metabolic profiles in acute pancreatitis. We examined whether the triglyceride–glucose (TyG) index modified the association between first-day fluid accumulation and subsequent acute respiratory distress syndrome (ARDS).

Methods

We analysed two retrospective hospital cohorts using a 24-hour landmark. Eligible adults had fasting triglyceride and glucose measurements within 24 hours, complete first-day fluid records, and were alive and free of ARDS at the landmark. Fluid accumulation was defined as a net balance of at least 10% of ideal body weight. Multivariable logistic regression assessed its interaction with continuous TyG for ARDS occurring after hour 24 through hour 48, adjusting for centre, age, sex, body mass index, Acute Physiology and Chronic Health Evaluation II score, diabetes and hypertriglyceridaemic aetiology.

Results

Among 2235 source records, 1326 patients met the eligibility criteria; 442 (33.3%) had fluid accumulation and 85 (6.4%) developed subsequent ARDS. The interaction ratio of odds ratios was 2.59 (95% confidence interval [CI] 1.65–4.07) per unit higher TyG. Estimates were similar after adjustment for transfer and fluid indication (2.64; 95% CI 1.69–4.11) and for early physiological measurements (2.51; 95% CI 1.62–3.88). Excluding hypertriglyceridaemic pancreatitis left 891 patients and 58 events, with an interaction estimate of 1.54 (95% CI 0.55–4.27). Post-landmark ARDS incidence was 3.0% in Nanning and 11.3% in Guilin.

Conclusions

Among patients alive and free of recorded ARDS at 24 hours, the odds ratio for subsequent ARDS associated with fluid accumulation increased with TyG. The attenuated estimate after excluding hypertriglyceridaemic pancreatitis suggests that aetiology may contribute to this pattern. Prospective evaluation could clarify whether TyG adds useful information to early fluid and respiratory assessment.

Keywords: Acute pancreatitis; Acute respiratory distress syndrome; Triglyceride–glucose index; Fluid accumulation; Landmark analysis; Effect modification

Background

Fluid resuscitation is a central component of early care in acute pancreatitis (AP) [1,2], yet the volume needed to restore perfusion varies between patients. A prospective cohort associated larger first-day fluid volumes with respiratory insufficiency and persistent organ failure [3]. In the WATERFALL trial, aggressive resuscitation increased fluid overload without improving the primary clinical outcome [4]. A meta-analysis of randomised trials likewise found no advantage for aggressive resuscitation in preventing severe AP; its fluid-overload estimate came from WATERFALL [5]. Current international guidance emphasises repeated reassessment of fluid requirements [6]. Understanding why pulmonary risk differs between patients could help refine that assessment.

The triglyceride–glucose (TyG) index combines fasting triglyceride and glucose concentrations and has been evaluated against the hyperinsulinaemic–euglycaemic clamp as a surrogate for insulin resistance [7]. Higher TyG has been associated with greater AP severity and adverse outcomes [8–10], including acute respiratory distress syndrome (ARDS) [11]. Studies in critically ill patients with AP have also linked TyG to acute respiratory failure [12] and acute

kidney injury [13]. These associations raise a related question: does the relationship between accumulated fluid and ARDS vary across the metabolic profile represented by TyG? Triglycerides contribute both to the index and to AP aetiology, while acute illness and treatment can alter both index components.

The sequence of measurement and outcome is central to this question. Lung injury developing during the first day may alter fluid administration and urine output before a 24-hour balance is complete. We therefore examined TyG and first-day fluid accumulation in two hospital cohorts using a 24-hour landmark. Fasting verification, blood-draw times and three-hourly fluid records defined the exposures; follow-up then captured ARDS arising over the next 24 hours.

Methods

Study design and population

We analysed retrospective clinical cohorts from the First Affiliated Hospital of Guangxi Medical University, Nanning, China (January 2015–December 2025), and Guilin People's Hospital, Guilin, China (January 2020–December 2025). The available dataset contained 2235 records. Reporting followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) framework [14].

AP was diagnosed according to the revised Atlanta classification, requiring at least two of the following: characteristic abdominal pain, pancreatic enzymes at least three times the upper reference limit, and compatible imaging [15]. Eligible patients were adults presenting within 48 hours of symptom onset. Time zero was the first presentation to a participating hospital, including emergency care. Laboratory, fluid and event times were aligned to this origin; transfer and pre-transfer treatment were recorded separately.

The primary analysis used a 24-hour landmark [16]. Eligibility required survival without ARDS through hour 24, verified fasting blood samples collected within the first 24 hours, and complete fluid observations through the landmark. Follow-up for incident ARDS extended from after hour 24 through hour 48. Figure 1 summarises cohort selection and the analysis timeline. Additional file 1 describes record linkage, sequential exclusions and analysis specifications.

TyG index and fluid balance

TyG was calculated as ln[triglycerides (mg/dL) × glucose (mg/dL)/2] [8,11]. All patients in the primary cohort had a recorded fasting duration of at least eight hours, and both blood samples were collected within the first 24 hours. Hypertriglyceridaemic aetiology was retained from the source AP-cause field without reassignment from the blood sample used to calculate TyG. TyG was analysed continuously and centred at 9.18 for coefficient interpretation. The median-derived split of 9.18 from the earlier single-centre analysis was retained for descriptive comparisons. Fluid balance was reconstructed from eight three-hour intervals as intake minus urine and other recorded output. Cumulative balance was expressed as a percentage of recorded ideal body weight (IBW): net balance in mL/(1000 × IBW in kg) × 100. Fluid accumulation was defined as a balance of at least 10% of IBW. Insensible losses were not estimated, and observations truncated by death were not extrapolated. Sensitivity analyses used a uniform Devine IBW calculation, accumulation thresholds of 5% and 15%, and continuous balance per five percentage points of IBW.

ARDS assessment

Two senior intensive care physicians (associate chief physicians) reviewed the clinical diagnoses using the 2024 global ARDS definition as their clinical framework [17]. Review was unblinded,

and diagnoses were agreed through discussion. The analysis used the recorded ARDS classifications and first onset times.

Available diagnostic information included imaging time, bilateral opacities, arterial oxygenation, respiratory support, positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP), and exclusion of a cardiac explanation. A sensitivity analysis retained ARDS cases with complete records for a selected set of these fields, as specified in Additional file 1.

We also summarised the worst recorded ratio of arterial oxygen tension to inspired oxygen fraction (PaO_2/FiO_2) by hour 48 in bands of >200–300, >100–200 and ≤100 mmHg [18]. Incident ARDS with a worst ratio ≤200 mmHg was a secondary endpoint. These bands describe oxygenation; formal severity staging would also require respiratory support settings at the worst measurement, which were unavailable.

Statistical analysis

Continuous variables are summarised as medians with interquartile ranges and categorical variables as counts and percentages. The primary logistic model included fluid accumulation, continuous TyG, their product term, centre, age, sex, body mass index (BMI), Acute Physiology and Chronic Health Evaluation II (APACHE II) score, diabetes and hypertriglyceridaemic AP aetiology. Centre was a fixed effect, and continuous covariates were entered as linear terms. The interaction was expressed as the ratio of fluid accumulation-associated odds ratios (ORs) per one-unit higher TyG. We calculated 95% confidence intervals (CIs) using type-0 heteroscedasticity-consistent (HC0) covariance.

APACHE II and Bedside Index for Severity in Acute Pancreatitis (BISAP) were the recorded early hospital scores; their component-level assessment times were unavailable. A sensitivity model replaced APACHE II with the first mean arterial pressure, log lactate and log creatinine measured within three hours. Other models added transfer status and the recorded indication for

fluid administration, or systemic inflammatory response syndrome (SIRS) count and log(1 + C-reactive protein).

We included all eligible records. Primary model variables were complete, so no imputation was needed. We assessed estimation stability with 500 bootstrap resamples stratified by centre and a Firth bias-reduced model [19]. To complement the interaction on the odds-ratio scale, we estimated absolute risk contrasts [20]. At each selected TyG quartile, the model predicted risk with and without fluid accumulation for every patient's observed covariate values; predictions were then averaged over the cohort. These secondary contrasts may involve extrapolation in centre–aetiology groups with few or no observations at the selected TyG value. Additional files 1 and 2 provide model specifications, software versions and numerical checks.

Secondary analyses examined AP aetiology, triglyceride concentration, treatment before sampling, fluid definitions, diagnostic-field completeness and centre. An exploratory model also adjusted for first-day crystalloid type and the normal-saline proportion of total crystalloid volume. A six-hour gap analysis retained the first-day exposure window and required survival without ARDS through hour 30 before follow-up began. Earlier landmarks at 3, 6, 12 and 18 hours used blood samples and fluid observations available by each landmark, with adjustment for physiological measurements within three hours. Secondary analyses were exploratory and used no adjustment for multiple comparisons. Three patients who died after hour 24 and by hour 48 without recorded ARDS were counted as noncases for the ARDS endpoint.

Analyses were performed in Python 3.12.14 with statsmodels 0.15.0.

Results

Study population

The source cohorts contained 1537 Nanning records and 698 Guilin records. ARDS was recorded within 48 hours in 325/1537 (21.1%) and 158/698 (22.6%), respectively, giving 483 events overall. Of these events, 242/325 in Nanning and 12/158 in Guilin were recorded within six hours of presentation (Additional file 1, Fig. S1). Case mix also differed: APACHE II scores were below 8 in 53.2% of Nanning records and 44.0% of Guilin records, and at least 15 in 4.0% and 11.7%. Transfers from another hospital accounted for 22.5% and 18.8%, respectively. Table S8 compares the source and landmark cohorts.

Sequential exclusions removed nine records for age or symptom-window criteria, 551 for nonfasting or uncertain fasting status, 93 for missing or out-of-window sampling times, and 256 for ARDS or death by hour 24. The last group comprised 253 ARDS events and three deaths without earlier ARDS. The primary cohort therefore comprised 1326 patients: 778 from Nanning and 548 from Guilin. All had complete first-day fluid observations (Fig. 1A; Additional file 1, Table S1).

Median age was 57 years (interquartile range [IQR] 46–69), and 733 patients (55.3%) were male. Median TyG was 9.14 (IQR 8.54–10.13), and median net fluid balance was 6.4% of IBW (IQR 3.7–10.8). Fluid accumulation was present in 442 patients (33.3%). Hypertriglyceridaemic aetiology was more frequent in Nanning than Guilin (39.3% versus 23.5%), whereas the median APACHE II score was higher in Guilin (8 versus 7). Table 1 presents the characteristics by centre.

TyG and the fluid accumulation association

ARDS developed after hour 24 through hour 48 in 85 patients (6.4%): 23/778 in Nanning (3.0%) and 62/548 in Guilin (11.3%). In the primary model, the OR associated with fluid accumulation increased by a factor of 2.59 per unit higher TyG (95% CI 1.65–4.07; interaction P = 0.000035; Table 2). Figure 2A shows the fitted continuous interaction. Model-standardised risk differences associated with accumulation were −3.2 percentage points (95% CI −5.8 to −0.6) at the 25th TyG percentile (8.54), −1.1 (95% CI −3.8 to 1.5) at the median (9.14), and 4.8 (95% CI 1.0–8.6) at the 75th percentile (10.13) (Fig. 2B). The corresponding standardised risks are reported in Additional file 1, Table S4.

Observed ARDS rates by the earlier TyG split are shown in Fig. 2C. At TyG >9.18, ARDS occurred in 13.2% of patients with fluid accumulation and 6.2% without accumulation; the corresponding rates at TyG ≤9.18 were 3.0% and 5.4%. Adjusted accumulation-associated ORs were 2.08 (95% CI 1.12–3.85) and 0.49 (95% CI 0.20–1.18), respectively (Additional file 1, Table S3).

Sensitivity analyses

The interaction estimate was 2.64 (95% CI 1.69–4.11) after adjustment for transfer and fluid indication, and 2.51 (95% CI 1.62–3.88) when timestamped early physiological measurements replaced APACHE II (Fig. 3A). Additional adjustment for crystalloid type and saline fraction yielded 2.58 (95% CI 1.64–4.06). Adjustment for SIRS and C-reactive protein, and exclusion of glucose or insulin administration before sampling, also yielded similar estimates (Additional file 1, Table S2). The bootstrap 95% interval was 1.66–4.40, and the Firth bias-reduced estimate was 2.52.

Excluding hypertriglyceridaemic AP left 891 patients and 58 events, with an interaction estimate of 1.54 (95% CI 0.55–4.27; P = 0.409). Restriction to triglycerides <500 mg/dL (approximately

5.65 mmol/L) yielded 2.71 (95% CI 1.04–7.03). Estimates at accumulation thresholds of 5% and 15% of IBW were 1.40 (95% CI 0.93–2.11) and 4.32 (95% CI 1.16–16.02), respectively. Seventy of the 85 incident ARDS cases had complete records for the selected diagnostic fields. Excluding the other 15 cases yielded an interaction estimate of 2.58 (95% CI 1.57–4.24). The secondary endpoint of incident ARDS with a worst PaO_2/FiO_2 ≤200 mmHg comprised 49 events and yielded an estimate of 2.89 (95% CI 1.76–4.76). Diagnostic completeness and oxygenation distributions are reported in Additional file 1, Tables S5 and S6.

The six-hour gap analysis included 1311 patients and 70 events, with an interaction estimate of 2.33 (95% CI 1.43–3.80). Earlier landmark analyses also yielded positive continuous balance–TyG interaction estimates (Additional file 1, Table S7 and Fig. S2). Separate centre-specific models yielded estimates of 2.83 (95% CI 1.62–4.96) in Guilin and 2.74 (95% CI 1.03–7.32) in Nanning (Fig. 3B). In a joint model allowing centre interactions with accumulation and TyG, the three-way interaction ratio was 0.67 (95% CI 0.25–1.75; P = 0.408; Additional file 1, Table S2).

Discussion

In this two-centre cohort of patients alive and free of recorded ARDS at 24 hours, the odds ratio for ARDS during the next day associated with fluid accumulation increased with TyG. The pattern persisted after accounting for early physiology, transfer, fluid indications and composition, and with a six-hour interval before follow-up. Its attenuation after excluding hypertriglyceridaemic AP suggests a contribution from aetiology. The findings link metabolic variation to the pulmonary risk associated with accumulated fluid, a relationship that may be obscured when either exposure is considered alone.

TyG combines two features of acute AP that have been studied separately: stress hyperglycaemia and elevated triglycerides, both associated with persistent organ failure [21,22]. Although evaluated as an insulin-resistance surrogate [7], TyG during acute illness is likely to reflect

background metabolism as well as the response to illness and treatment. This may help explain its associations with AP severity and ARDS [8–11]. Our analysis extends that perspective by examining how the OR associated with accumulated fluid varies across TyG values. The continuous interaction captures this variation across the metabolic spectrum; the earlier median split of 9.18 provides a descriptive reference.

Lipid-mediated injury offers a plausible biological connection. De Oliveira and colleagues showed that pancreatic triglyceride lipase can hydrolyse visceral adipose triglycerides, generating nonesterified fatty acids and promoting systemic inflammation and organ injury in experimental pancreatitis [23]. Rajalingamgari and colleagues extended this work to circulating triglycerides, combining prospective patient observations with mechanistic experiments [24]. In their rat model, intravascular lipolysis reduced oxygen saturation and produced alveolar wall injury, protein leakage and alveolar fluid accumulation; lipase inhibition attenuated these changes. Lipid-mediated pulmonary injury may increase susceptibility to oedema as fluid accumulates, providing one possible explanation for the interaction observed here.

The aetiological analysis helps locate this signal. Excluding hypertriglyceridaemic AP reduced the interaction estimate to 1.54 (95% CI 0.55–4.27), with 58 events remaining. Part of the pooled signal may arise from this metabolically distinct subgroup, while the wider interval also reflects reduced information. The positive estimate below a measured triglyceride concentration of 500 mg/dL concerns a different population: a contemporaneous laboratory threshold and a recorded aetiological diagnosis capture different aspects of the illness. The source records lacked documentation of a common aetiological adjudication rule across centres, adding uncertainty to the subgroup comparison.

Fluid studies provide a complementary clinical context. WATERFALL showed the risk of fluid overload with aggressive early resuscitation in AP [4]. In established acute lung injury, the Fluid

and Catheter Treatment Trial (FACTT) found more ventilator-free days with conservative fluid management, without a statistically significant mortality difference [25]. A secondary FACTT analysis suggested differing responses across ARDS subphenotypes [26]; a recent multicentre cohort also described heterogeneous associations between early fluid intake and mortality across severe-AP subtypes [27]. Our cohort examines an earlier stage, before recorded ARDS at 24 hours, and measures net accumulation, which combines administered fluid with physiological retention. TyG may help characterise metabolic variation in this setting.

The centre contrast becomes clearer across cohort selection. Post-landmark ARDS incidence was 3.0% in Nanning and 11.3% in Guilin; the proportions with ARDS within 48 hours in the source cohorts were 21.1% and 22.6%. Nanning contributed more ARDS cases in absolute terms and a larger proportion of patients with low APACHE II scores; Guilin had a larger proportion with high scores. A large regional referral hospital may receive severely ill transfers while also treating many patients with less physiological disturbance. That broader case mix could lower its median score.

Recorded event timing further changed the populations remaining at risk. In Nanning, 242 of 325 ARDS cases were recorded within six hours of presentation, compared with 12 of 158 in Guilin. Later presentation in the illness course could place more events before the landmark, particularly among transfers. Diagnostic assessment and recording may also contribute, consistent with the ascertainment variability documented in LUNG SAFE [28]. The higher subsequent incidence in Guilin may therefore reflect selection after early events, case mix and ascertainment. Centre-specific interaction estimates pointed in the same direction, although Nanning's 23 events and the wide between-centre interval leave clinically relevant heterogeneity plausible.

At low TyG, the fitted association also depends on how risk is estimated. The standardised risk difference at the 25th percentile was −3.2 percentage points (95% CI −5.8 to −0.6). Fixing TyG

at the 25th percentile for the full cohort, including centre–aetiology groups with higher observed values, relies partly on extrapolation and the linear interaction assumption. The binary lower-TyG estimate had a wide interval and only seven events among patients with accumulation. These features favour treating the inverse pattern as a model-dependent observation, rather than a basis for increasing fluid administration.

Small randomised AP trials found lower inflammatory markers with lactated Ringer's solution than with saline [29,30]. Adjustment for crystalloid type and saline fraction changed our estimate little. Fluid indications evolve, however: hypoperfusion prompts resuscitation, while lung injury and impaired urine output may precede recorded ARDS. The landmark, early-physiology and six-hour gap analyses address parts of this sequence; pre-transfer treatment and first-day changes may still confound the association. Most metabolic samples followed hospital fluid initiation, so TyG often represents the early treated state.

ARDS ascertainment relied on retrospective records reviewed by two physicians through unblinded consensus. Blood-gas timestamps were unavailable. The records documented exclusion of a cardiac explanation but did not separately establish the contribution of fluid overload to pulmonary oedema. Misclassification between ARDS and hydrostatic oedema may therefore influence the association. The analysis retaining the 70 cases with complete selected diagnostic fields and all noncases yielded a similar estimate; some global-definition elements and noncase classifications remained unverified. Most incident cases initially received noninvasive support. Formal staging at worst oxygenation also requires the corresponding support settings [17]. Fasting and sampling-time requirements selected the cohort, particularly in Nanning. The full screening denominator was unavailable, and de-identification prevented independent checks of repeat admissions or cross-centre transfers. With 85 events and 11 model coefficients, smaller-subgroup estimates were imprecise and estimates varied across fluid thresholds;

secondary comparisons remain exploratory. Counting three deaths without recorded ARDS as noncases may also affect the endpoint estimate.

The clinical question is whether TyG adds useful information to the repeated assessment of perfusion, volume status and organ function recommended in AP guidance [2,6]. Prospective cohorts could combine pretreatment metabolic samples and three-hourly fluid records with haemodynamic and respiratory assessments at 3, 6, 12 and 24 hours. Consistent aetiological classification and ARDS review, with synchronised imaging, blood gases and support settings, would improve comparability. Serial fatty-acid and pulmonary injury measurements could test the proposed mechanism. Demonstrating added clinical value in this setting would provide a rationale for testing a TyG-informed fluid strategy in a trial.

Conclusions

Among patients with AP who were alive and free of recorded ARDS at 24 hours, the odds ratio for ARDS over the next day associated with fluid accumulation increased with TyG. This pattern may partly reflect hypertriglyceridaemic aetiology and differences in the patients remaining at risk after the first day. Prospective evaluation should establish whether TyG adds useful information to early fluid and respiratory assessment.

List of abbreviations

AP, acute pancreatitis; APACHE II, Acute Physiology and Chronic Health Evaluation II; ARDS, acute respiratory distress syndrome; BISAP, Bedside Index for Severity in Acute Pancreatitis; BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; HC0, type-0 heteroscedasticity-consistent covariance; FACTT, Fluid and Catheter Treatment Trial; CPAP, continuous positive airway pressure; FiO_2, fraction of inspired oxygen; IBW, ideal body weight; IQR, interquartile range; MAP, mean arterial pressure; OR, odds ratio; PaO_2, arterial oxygen

tension; PEEP, positive end-expiratory pressure; SIRS, systemic inflammatory response syndrome; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; TyG, triglyceride–glucose.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. Protocol approval was issued by the Medical Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (approval No. 2025-E0947, 15 November 2025) and the Medical Ethics Committee of Guilin People's Hospital (approval No. 2026-164KY, 23 July 2026). Informed consent to participate was obtained at both centres. The study extracts used sequential research identifiers and contained no hospital identifiers.

Consent for publication

Not applicable. No identifiable individual patient details or clinical images are presented.

Availability of data and materials

Aggregate results and figure source values are provided in the article and its additional files. De-identified participant-level data and analysis code are available from the corresponding authors on reasonable request, subject to institutional approval and applicable ethics and privacy requirements.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

ZW, GL and TL designed the study, analysed and interpreted the data, and drafted the manuscript. KZ, WM, YG, HS, BZ, DW, JL, GP and ZH collected and curated the clinical data. WW and ZJ supervised the study, contributed to its design, and critically revised the manuscript. All authors read and approved the final manuscript.

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Registration

The original project is listed in the Chinese Clinical Trial Registry as ChiCTR2600122934, registered on 20 April 2026. The clinical observation periods preceded registration; the current two-centre landmark analysis was specified subsequently.

Additional files

Additional file 1 (.docx). Supplementary methods and results. Detailed analysis definitions, Tables S1–S8 and Figs. S1 and S2.

Additional file 2 (.xlsx). Statistical results. Model specifications, coefficients, exact P values, recorded diagnostic fields, cohort counts, fluid-composition summaries, TyG support ranges and figure source values.

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Figure legends

Figure 1 Cohort selection and analysis timeline

A, Sequential selection of records from Nanning and Guilin. Eligible adults presented within 48 hours of symptom onset, had verified fasting and both metabolic blood samples collected within 24 hours, and were alive and free of ARDS at hour 24. All had complete first-day fluid observations. B, Measurement and follow-up windows from first hospital presentation. Primary follow-up extended from after hour 24 through hour 48. The six-hour gap analysis used the same first-day exposure and required survival without ARDS through hour 30 before follow-up began. ARDS, acute respiratory distress syndrome.

Figure 2 TyG and the association between fluid accumulation and subsequent ARDS

A, Adjusted fluid accumulation-associated ORs across continuous TyG. Shading shows pointwise HC0 95% CIs over the fifth to 95th TyG percentiles; rug marks show observed values. B, Model-standardised risk differences at the 25th, 50th and 75th TyG percentiles, expressed as accumulation minus no accumulation in percentage points. Low-TyG contrasts partly extrapolate beyond the observed centre–aetiology ranges. Points, error bars and labels show estimates and delta-method HC0 95% CIs. Panels A and B use the primary interaction model, adjusted for centre, age, sex, BMI, APACHE II, diabetes and hypertriglyceridaemic aetiology; standardisation averages over the covariate distribution of all 1326 patients. C, Observed ARDS proportions using the earlier median-derived TyG split of 9.18; these groups differ from the fixed TyG values used in panel B. Points and error bars show proportions and Wilson 95% CIs; labels give events/patients. Fluid accumulation was a net 24-hour balance ≥10% of IBW. ARDS

occurred after hour 24 through hour 48. APACHE II, Acute Physiology and Chronic Health Evaluation II; ARDS, acute respiratory distress syndrome; BMI, body mass index; CI, confidence interval; HC0, type-0 heteroscedasticity-consistent covariance; IBW, ideal body weight; OR, odds ratio; TyG, triglyceride–glucose index.

Figure 3 Sensitivity analyses and comparison between centres

A, Primary and selected secondary fluid accumulation–TyG interaction estimates, grouped by the question addressed. Points and error bars show ratios of ORs per unit higher TyG and HC0 95% CIs; counts are events/patients. Models use the primary adjustment set unless specified otherwise. Early physiological measurements replace APACHE II with mean arterial pressure, log lactate and log creatinine recorded within three hours. B, Centre-specific interaction estimates alongside observed ARDS incidence after hour 24 through hour 48. Models use the primary covariates with the centre term omitted. In a separate joint model, the three-way centre interaction ratio was 0.67 (95% CI 0.25–1.75). AP, acute pancreatitis; APACHE II, Acute Physiology and Chronic Health Evaluation II; CI, confidence interval; HC0, type-0 heteroscedasticity-consistent covariance; P/F, PaO_2/FiO_2; IBW, ideal body weight; OR, odds ratio; TyG, triglyceride–glucose index. Full secondary results are provided in Additional files 1 and 2.

Tables

Table 1 Clinical characteristics of the 24 hour landmark cohort

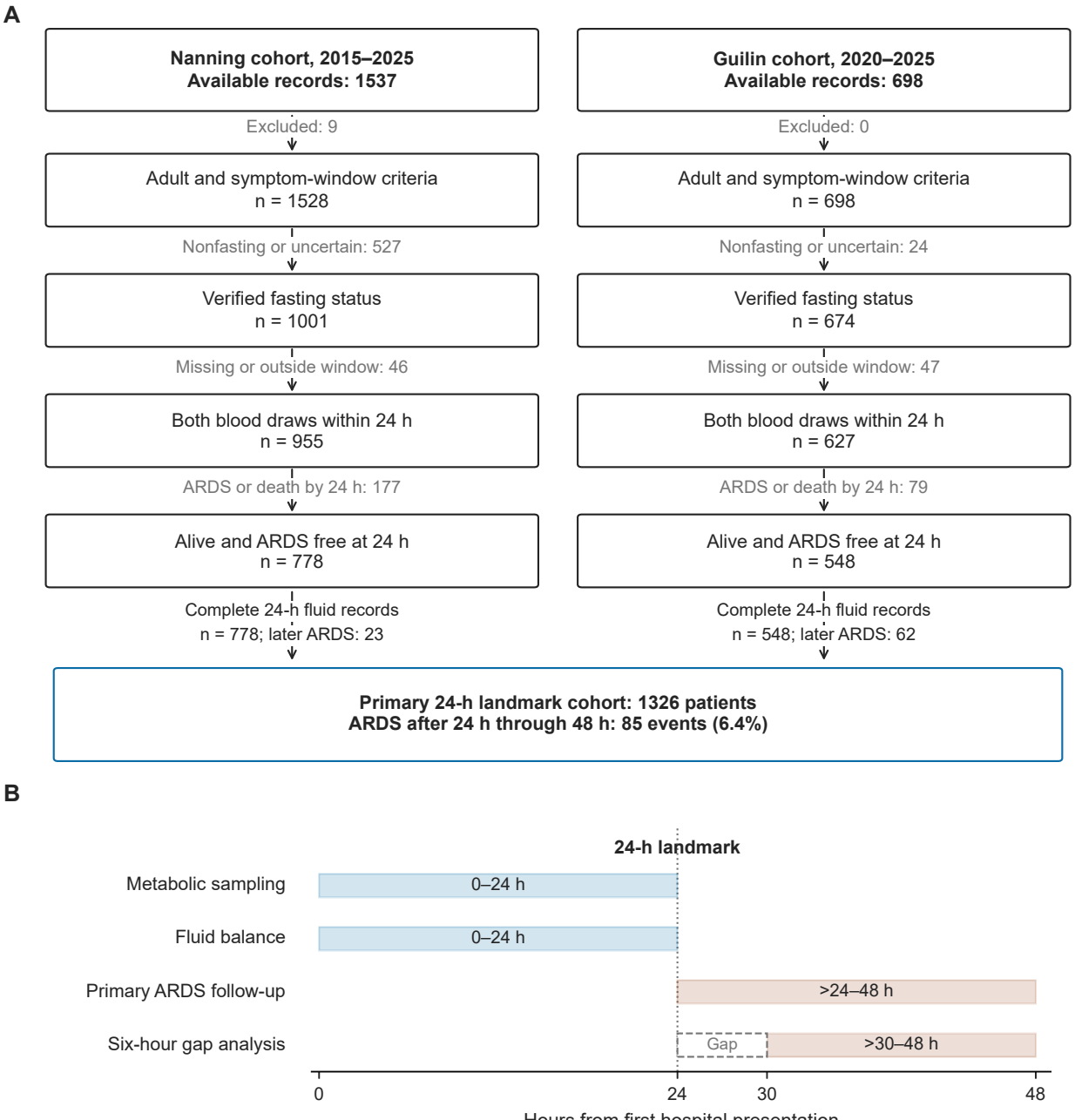
Characteristic	All n = 1326	Nanning n = 778	Guilin n = 548
Age, years	57 (46–69)	58 (45–70)	57 (47–67)
Male sex, n/N (%)	733/1326 (55.3)	438/778 (56.3)	295/548 (53.8)
Body mass index, kg/m²	24.2 (21.6–26.8)	23.9 (21.2–26.8)	24.6 (22.3–27.0)
Diabetes, n/N (%)	263/1326 (19.8)	157/778 (20.2)	106/548 (19.3)
Hypertriglyceridaemic aetiology, n/N (%)	435/1326 (32.8)	306/778 (39.3)	129/548 (23.5)
Transferred from another hospital, n/N (%)	258/1326 (19.5)	161/778 (20.7)	97/548 (17.7)
Recorded APACHE II score	7 (4–10)	7 (4–9)	8 (5–11)
Recorded BISAP score	2 (1–2)	1 (1–2)	2 (1–2)
SIRS criteria count	2 (1–3)	3 (0–3)	2 (1–3)
C-reactive protein, mg/L	60.1 (36.7–100.1)	78.6 (52.7–120.8)	40.5 (25.6–63.4)
First mean arterial pressure, mmHg	88 (80–95)	87 (81–94)	88 (79–96)
First lactate, mmol/L	1.4 (1.0–1.9)	1.3 (0.9–1.7)	1.6 (1.1–2.1)
First creatinine, μmol/L	75 (57–97)	70 (55–90)	82 (60–103)
Triglycerides, mmol/L	1.39 (0.80–3.46)	1.32 (0.73–3.57)	1.51 (0.96–3.21)
Glucose, mmol/L	8.60 (7.37–9.86)	8.98 (7.80–10.24)	7.99 (6.83–9.27)
TyG index	9.14 (8.54–10.13)	9.14 (8.48–10.23)	9.17 (8.67–10.01)
Last of the two blood draws, hours	1.50 (0.75–2.50)	1.25 (0.75–2.00)	2.00 (0.75–6.00)
24-hour fluid intake, mL	5436 (3728–7670)	5032 (3030–7542)	5762 (4525–7840)
24-hour urine output, mL	1316 (1019–1597)	1251 (954–1526)	1416 (1147–1703)
24-hour other output, mL	180 (122–244)	182 (121–242)	173 (124–250)
24-hour net fluid balance, mL	3773 (2185–6307)	3458 (1505–6426)	4131 (2784–6174)
24-hour net fluid balance, % IBW	6.4 (3.7–10.8)	5.7 (2.5–10.9)	7.1 (4.8–10.4)
Fluid accumulation ≥10% IBW, n/N (%)	442/1326 (33.3)	292/778 (37.5)	150/548 (27.4)
ARDS after 24 through 48 hours, n/N (%)	85/1326 (6.4)	23/778 (3.0)	62/548 (11.3)

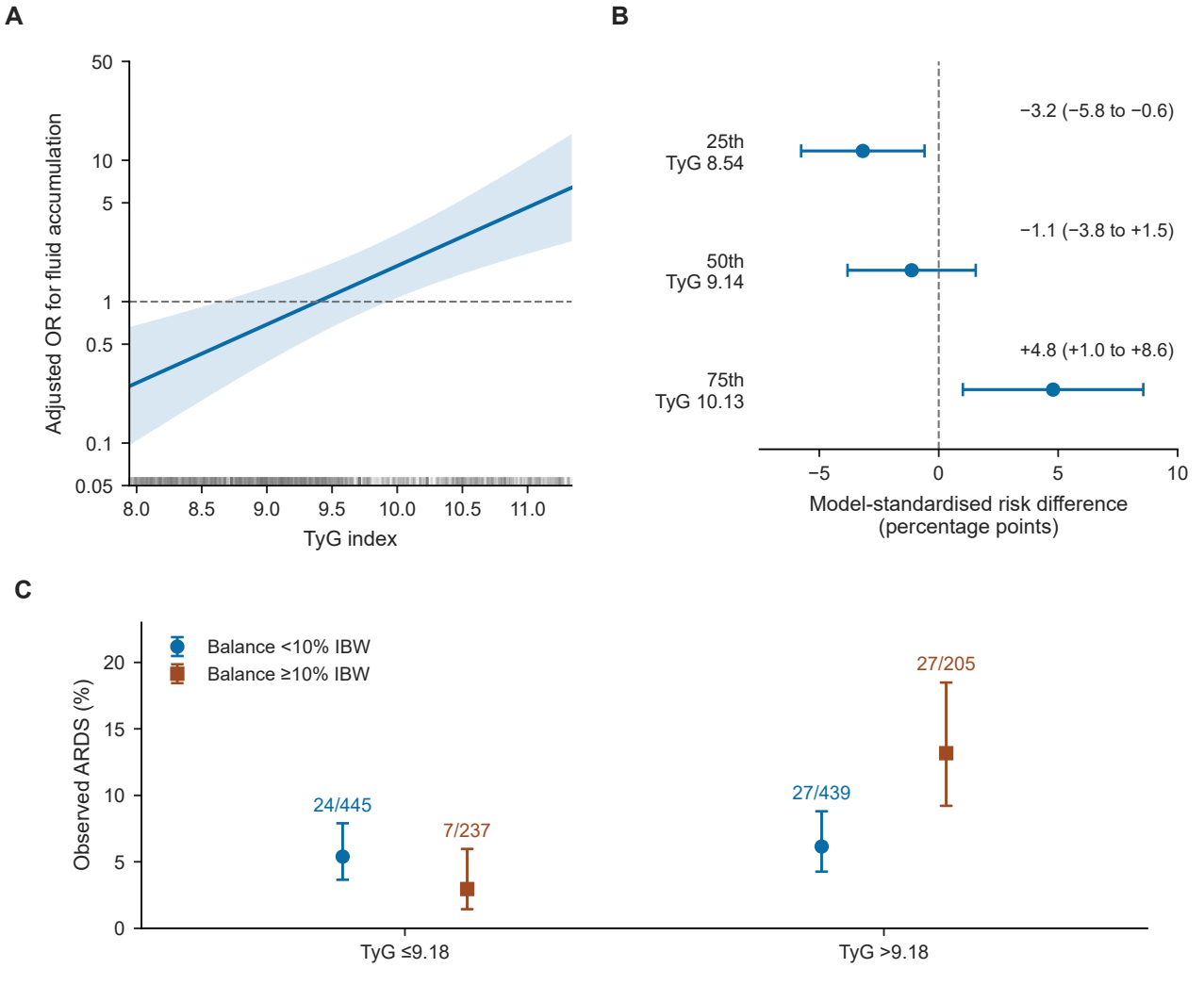
Values are median (interquartile range) or n/N (%). Laboratory concentrations are in SI units; TyG uses concentrations converted to mg/dL. First physiological measurements were recorded within three hours; APACHE II and BISAP are recorded early hospital scores. All listed variables were complete. IBW, ideal body weight; SIRS, systemic inflammatory response syndrome; TyG, triglyceride–glucose index. ARDS occurred after hour 24 through hour 48. APACHE II, Acute Physiology and Chronic Health Evaluation II; ARDS, acute respiratory distress syndrome; BISAP, Bedside Index for Severity in Acute Pancreatitis; BMI, body mass index.

Table 2 Primary interaction model for subsequent ARDS

Model term	Adjusted estimate (95% CI)	P value
Nanning versus Guilin centre	0.31 (0.17–0.56)	0.000117
Fluid accumulation at TyG = 9.18	0.82 (0.46–1.45)	0.493
TyG, per unit, without accumulation	0.98 (0.66–1.45)	0.902
Age, per year	0.99 (0.97–1.00)	0.111
Male versus female sex	0.89 (0.56–1.42)	0.624
BMI, per kg/m²	1.03 (0.97–1.10)	0.276
Recorded APACHE II, per point	1.17 (1.10–1.24)	2.29e-07
Diabetes	1.61 (0.96–2.71)	0.074
Hypertriglyceridaemic aetiology	0.62 (0.24–1.62)	0.325
Accumulation × TyG interaction*	2.59 (1.65–4.07)	0.000035

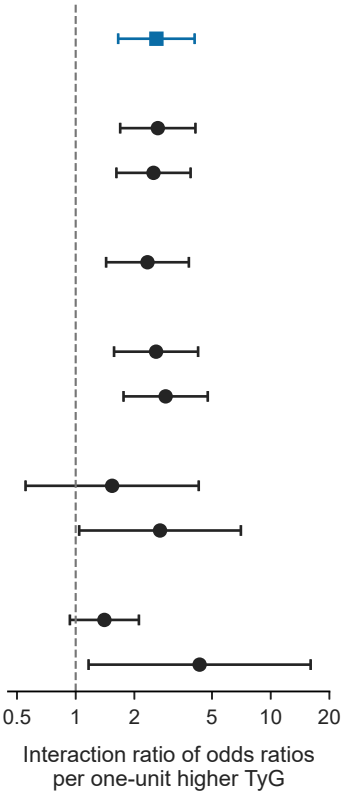
n = 1326; ARDS events = 85. Estimates use one multivariable logistic model and HC0 covariance. *The interaction estimate is a ratio of accumulation-associated odds ratios per one-unit higher TyG; other rows are conditional odds ratios. Accumulation denotes net 24-hour balance ≥10% of recorded IBW. TyG is centred at 9.18 solely for coefficient interpretation. The intercept is omitted here but retained in Additional file 2. The likelihood-ratio interaction P value was 0.000047. APACHE II, Acute Physiology and Chronic Health Evaluation II; ARDS, acute respiratory distress syndrome; BMI, body mass index; CI, confidence interval; HC0, type-0 heteroscedasticity-consistent covariance; IBW, ideal body weight; OR, odds ratio; TyG, triglyceride–glucose index.


A
Nanning cohort, 2015–2025
Available records: 1537
Excluded: 9
Adult and symptom-window criteria
n = 1528
Nonfasting or uncertain: 527
Verified fasting status
n = 1001
Missing or outside window: 46
Both blood draws within 24 h
n = 955
ARDS or death by 24 h: 177
Alive and ARDS free at 24 h
n = 778
Complete 24-h fluid records
n = 778; later ARDS: 23
Guilin cohort, 2020–2025
Available records: 698
Excluded: 0
Adult and symptom-window criteria
n = 698
Nonfasting or uncertain: 24
Verified fasting status
n = 674
Missing or outside window: 47
Both blood draws within 24 h
n = 627
ARDS or death by 24 h: 79
Alive and ARDS free at 24 h
n = 548
Complete 24-h fluid records
n = 548; later ARDS: 62
Primary 24-h landmark cohort: 1326 patients
ARDS after 24 h through 48 h: 85 events (6.4%)
B
24-h landmark
Metabolic sampling
0–24 h
Fluid balance
0–24 h
Primary ARDS follow-up
>24–48 h
Six-hour gap analysis
Gap
>30–48 h
0
24
30
48
Hours from first hospital presentation


A
Adjusted OR for fluid accumulation
50
10
5
1
0.5
0.1
0.05
8.0
8.5
9.0
9.5
10.0
10.5
11.0
TyG index
B
25th
TyG 8.54
−3.2 (−5.8 to −0.6)
50th
TyG 9.14
−1.1 (−3.8 to +1.5)
75th
TyG 10.13
+4.8 (+1.0 to +8.6)
−5
0
5
10
Model-standardised risk difference
(percentage points)
C
Balance <10% IBW
Balance ≥10% IBW
Observed ARDS (%)
20
15
10
5
0
24/445
7/237
27/439
27/205
TyG ≤9.18
TyG >9.18

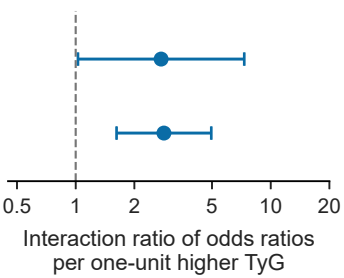
A

Analysis	Events / n	Ratio of ORs (95% CI)
Primary analysis	85/1326	2.59 (1.65–4.07)
Confounding		
Add transfer and fluid indication	85/1326	2.64 (1.69–4.11)
Use early physiological measurements	85/1326	2.51 (1.62–3.88)
Timing		
Six-hour gap before follow-up	70/1311	2.33 (1.43–3.80)
ARDS definition		
Complete recorded fields	70/1311	2.58 (1.57–4.24)
ARDS with worst P/F ≤200 mmHg	49/1326	2.89 (1.76–4.76)
Metabolic aetiology		
Exclude hypertriglyceridaemic AP	58/891	1.54 (0.55–4.27)
Triglycerides <5.65 mmol/L	65/1082	2.71 (1.04–7.03)
Fluid accumulation definition		
Accumulation threshold 5% IBW	85/1326	1.40 (0.93–2.11)
Accumulation threshold 15% IBW	85/1326	4.32 (1.16–16.02)



B

Centre	Events / n	ARDS (%)	Ratio of ORs (95% CI)
Nanning	23/778	3.0%	2.74 (1.03–7.32)
Guilin	62/548	11.3%	2.83 (1.62–4.96)



Supplementary Files

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- 02Additionalfile1Supplementarymaterial.docx