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Safety Profile of Low-Dose Risperidone in Critically Ill Children: A Single-Center Retrospective Cohort Study Across General and Cardiac Pediatric Intensive Care Units

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Research Article

Keywords: Risperidone, Pediatric intensive care, Delirium, Congenital heart disease, QTc interval, Antipsychotic safety

Posted Date: November 5th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11418873/v1

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Additional Declarations: No competing interests reported.

Abstract

Purpose

To evaluate the safety profile of low-dose risperidone in critically ill children treated within an institutional multimodal delirium prevention and treatment pathway across general and cardiac pediatric intensive care units (PICU and PCICU).

Methods

Single-center retrospective cohort study of all patients younger than 18 years who received at least one dose of risperidone during a PICU or PCICU admission (January 2015–January 2026). Safety endpoints included corrected QT interval (QTc) change, de novo QTc > 500 ms, hepatic, renal, electrolyte, glucose and thyroid parameters, and neurological adverse events. Paired pre/post comparisons used the Wilcoxon signed-rank test.

Results

A total of 352 patients received risperidone across 7,970 administrations. Median age was 2.8 years (interquartile range [IQR] 0.4–11.2); 35.8% were infants younger than one year. Median dose per administration was 0.19 mg (IQR 0.10–0.37), corresponding to 0.019 mg/kg. Laboratory parameters showed no clinically meaningful hepatotoxicity, renal deterioration, electrolyte instability, or dysglycemia. Paired electrocardiogram data were available for 57 patients (16.2%); no significant QTc change was observed (median ΔQTc + 3.0 ms; p = 0.976). De novo QTc prolongation beyond 500 ms occurred in 1 of 57 patients (1.8%). In-hospital mortality was 14.5%.

Conclusion

Within a structured delirium pathway, low-dose risperidone was not associated with a detectable QTc or laboratory safety signal across general and cardiac pediatric ICU settings, including infants younger than one year. Prospective validation with protocolized monitoring and systematic adverse-event adjudication is required.

What is Known

• Antipsychotics are increasingly used for pediatric ICU delirium, but safety data—particularly QTc and multi-organ laboratory data in children with cardiac disease and in infants—remain limited.

What is New

• In 352 critically ill children, low-dose risperidone within a structured delirium pathway showed no significant QTc or laboratory safety signal across general and cardiac ICUs, including infants younger than one year.

Introduction

Delirium is an acute, fluctuating clinical syndrome characterized by concurrent disturbances in attention, awareness, and baseline cognition, representing a transient yet severe manifestation of acute brain organ dysfunction in critically ill patients [1-3]. In pediatric intensive care units (PICUs), including specialized pediatric cardiac intensive care units (PCICUs), delirium has emerged as a major clinical challenge. A systematic review and meta-analysis by Semple et al. established a pooled prevalence of 34% [1], and a landmark international point-prevalence study documented delirium in 25% of 835 critically ill children across 25 PICUs in five countries, rising to 38% in children hospitalized for six or more days [4-6]. Pediatric delirium is an independent predictor of in-hospital mortality (adjusted OR 4.39; 95% CI 1.96–9.99), prolonged mechanical ventilation, and extended ICU length of stay [6]. Longitudinal data also identify pediatric ICU delirium as a risk factor for neurocognitive sequelae and functional decline, contributing to post-intensive care syndrome in pediatrics (PICS-p) [7, 8].

The pathophysiology of pediatric critical care delirium is multifactorial. A meta-analysis by Zhu et al. quantified key independent risk factors: developmental delay (OR 3.34), mechanical ventilation (OR 4.11), benzodiazepine exposure (OR 5.05), and anticholinergic drug use (OR 5.04) [2]. Young age, cyanotic congenital heart disease, and high illness severity are additional predisposing factors [4-6]. The pathophysiologic cascade involves neuroinflammation, blood–brain barrier disruption, and neurochemical imbalances—most notably dopamine excess, acetylcholine deficiency, and dysregulation of gamma-aminobutyric acid (GABA), serotonin, and melatonin signaling [9, 10].

Current Society of Critical Care Medicine (SCCM) guidelines recommend universal implementation of multicomponent nonpharmacologic bundles as first-line strategy, incorporating Cornell Assessment of Pediatric Delirium (CAPD) screening, sedation optimization, early mobilization, and sleep hygiene protocols [11-14]. When these strategies prove insufficient to control severe hyperactive delirium—the subtype most likely to require pharmacologic intervention—adjunctive agents including alpha-2 agonists, methadone, and antipsychotics are used [15-17]. First-generation antipsychotics such as haloperidol carry an undesirable adverse effect profile in pediatric cohorts, including extrapyramidal symptoms (EPS) and dose-dependent corrected QT (QTc) interval prolongation [18]. Atypical antipsychotics have therefore been increasingly adopted off-label in critical care settings [3].

Risperidone exhibits combined serotonin (5-HT2A) and dopamine (D2) receptor antagonism with moderate alpha-adrenergic blockade [19]. The prominent 5-HT2A relative to D2 antagonism is theorized to reduce EPS propensity while preserving efficacy against hyperactive delirium symptoms. Adult cardiac surgery trials have demonstrated that low-dose risperidone reduces postoperative delirium incidence and duration [20]. Preliminary pediatric investigations have reported acceptable tolerability with micro-

dosing strategies (0.1–0.25 mg or 0.01–0.04 mg/kg/day), and retrospective PCICU cohorts have noted CAPD score improvements without overt cardiotoxicity [10, 21, 22]. A recent systematic review by Cavagnero et al. identified only 10 pediatric studies involving 283 patients, with risperidone comprising 20% of administered agents, and documented QTc prolongation in 11 cases and dystonia in 7 cases across all antipsychotics, with full resolution in 21 of 22 adverse events after dose adjustment or discontinuation [3].

Despite these observations, systematic safety data evaluating electrocardiographic trajectories and multi-organ laboratory markers in pediatric ICU populations remain sparse. Critically ill children—particularly those undergoing cardiopulmonary bypass for complex congenital heart defects—exhibit shifting fluid volumes, altered hepatic and renal clearance kinetics, and electrolyte instabilities that predispose the myocardium to repolarization abnormalities [21, 23]. Concomitant exposure to QT-prolonging medications such as amiodarone, azole antifungals, or macrolide antibiotics compounds cumulative risk [23, 24].

At Safra Children's Hospital, risperidone is embedded in a structured multimodal delirium prevention and treatment pathway rather than administered as an isolated intervention. This protocolized framework couples CAPD-based surveillance with sedation-weaning protocols, nonpharmacologic environmental optimization, and targeted safety screening including electrocardiograms in high-risk subgroups. The primary objective of the present study was to evaluate the comprehensive safety profile of low-dose risperidone within this institutional framework, utilizing a large single-center cohort spanning both general and cardiac PICU settings. We specifically aimed to characterize QTc interval changes and to assess for signals of hepatotoxicity, acute kidney injury, dysglycemia, electrolyte shifts, and adverse neurological events following drug initiation across a wide pediatric age spectrum.

Materials and methods

Study design and setting

This was a single-center retrospective cohort study conducted in the General PICU and PCICU of Safra Children's Hospital, Sheba Medical Center, Tel HaShomer, Israel, from January 2015 to January 2026. The manuscript was prepared in accordance with STROBE reporting guidelines for observational studies; a completed STROBE checklist is provided as the Supplementary material (Appendix S1, Online Resource 1).

Institutional delirium prevention and treatment pathway

Risperidone exposure occurred within an institutional delirium protocol incorporating CAPD-based monitoring, evaluation of reversible delirium contributors, nonpharmacologic environmental and sleep-oriented strategies, sedative-transition planning, and selective physiologic and electrocardiographic (ECG) monitoring. ECG monitoring was recommended for children with known cardiac disease or

concomitant QT-prolonging medications. The full pathway is described in Supplementary Fig. S1 (Online Resource 1).

Population

All pediatric patients younger than 18 years who received at least one documented dose of risperidone during an ICU admission were eligible for inclusion. Patients were identified through the electronic medication administration record. No exclusion criteria were applied beyond age ≥18 years and absence of risperidone administration. Because all included patients were exposed to risperidone, the study should be interpreted as a safety cohort rather than a comparative effectiveness study.

Data collection

Data were retrieved using the MDClone ADAMS platform. Variables included demographics, ICU setting, primary diagnosis, surgical procedure, respiratory support at risperidone initiation, concomitant medications (opioids, benzodiazepines, dexmedetomidine, ketamine, corticosteroids, and other QT-prolonging agents), risperidone dose and cumulative exposure, CAPD documentation when available, and clinical outcomes. Safety data included 12-lead ECGs with QTc (Bazett's formula), liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT]), renal function (creatinine), electrolytes (potassium), glucose, thyroid-stimulating hormone (TSH), and documented neurological adverse events.

Safety definitions

QTc safety endpoints were defined a priori as absolute QTc values >450 ms and >500 ms, de novo QTc >500 ms among patients without baseline QTc >500 ms, and individual QTc changes exceeding +30 ms or +60 ms. Laboratory endpoints included clinically meaningful changes in AST, ALT, creatinine, potassium, glucose, and TSH after risperidone initiation. Neurological adverse events included documented seizures, EPS, dystonia, neuroleptic malignant syndrome, or clinician-documented suspected drug reactions.

Statistical analysis

Continuous variables are reported as median (IQR) and mean ± standard deviation (SD). Categorical variables are reported as count and percentage. The Wilcoxon signed-rank test was used for paired pre/post comparisons; the Mann–Whitney U test for unpaired group comparisons (PICU vs. PCICU). Event rates for rare safety endpoints are reported descriptively, with emphasis on absolute counts and clinical interpretation. A two-tailed p-value <0.05 was considered statistically significant; for the creatinine comparison, where statistical significance was expected on the basis of large sample size, effect size and clinical magnitude are emphasized over the p-value alone. Confidence intervals (CIs) for proportions are exact binomial CIs. All analyses were performed using Python 3.12 (SciPy 1.11). Where P values are reported without confidence intervals, effect size is provided in the text.

Results

Patient characteristics and clinical outcomes

A total of 352 unique pediatric patients received risperidone during the study period across 7,970 individual administrations. The cohort comprised 210 males (59.7%) and 142 females (40.3%), with a median age of 2.8 years (IQR 0.4–11.2; range 0.01–18.0). Infants younger than one year represented the largest age stratum (n = 126, 35.8%), consistent with the high proportion of neonates and infants admitted after congenital cardiac surgery. Most patients (64.2%, n = 226) were admitted to the general PICU; 35.8% (n = 126) were cared for in the PCICU. At risperidone initiation, 52.0% of patients were invasively ventilated via endotracheal tube, underscoring illness severity. In-hospital mortality was 14.5% overall (51/352), with 13.3% in the PICU and 16.7% in the PCICU, consistent with the acuity and complexity of the cohort; causal attribution to risperidone was not assessable in this retrospective design. Median ICU length of stay (LOS) was 22.2 days (IQR 13.0–43.0), with PCICU patients having longer ICU stays than general PICU patients (31.7 vs. 18.6 days; $p < 0.001$). Complete baseline characteristics and clinical outcomes are presented in Supplementary Table S1 (Online Resource 1).

Risperidone dosing characteristics

The median number of administrations per patient was 11.5 (IQR 6–24; maximum 335). Overall median dose per administration was 0.19 mg (IQR 0.10–0.37 mg), corresponding to 0.019 mg/kg (IQR 0.012–0.028). Absolute doses increased with age and weight, whereas weight-normalized doses remained within a narrow range across age strata, suggesting systematic weight-based titration. Median cumulative dose was 2.0 mg (IQR 0.9–5.5 mg). Full dosing data stratified by age group are presented in Table 1.

Laboratory safety parameters

Laboratory parameters were assessed in the 48-hour window preceding and the 72-hour window following risperidone initiation. AST and ALT did not show clinically meaningful deterioration. Potassium remained stable (3.58 to 3.60 mEq/L; $p = 0.229$) with no signal of drug-associated electrolyte disturbance, and glucose was unchanged (114.6 to 114.4 mg/dL [6.36 to 6.35 mmol/L]; $p = 0.854$). Serum creatinine decreased after initiation (median 0.37 to 0.31 mg/dL [32.7 to 27.4 µmol/L]; $p < 0.001$), but the magnitude was clinically small (median $\Delta = -0.03$ mg/dL [−2.7 µmol/L]) and most plausibly reflects evolving ICU physiology, fluid balance, and recovery rather than a direct pharmacological effect. TSH showed a non-significant trend toward elevation (2.01 to 2.68 mIU/L; $p = 0.063$), a biologically plausible finding limited by sparse thyroid testing. Laboratory safety data are summarized in Table 2.

Cardiac safety: QTc interval analysis

Pre-treatment QTc data were available for 90 patients (25.6%), post-treatment data for 63 patients (17.9%), and paired pre/post measurements for 57 patients (16.2%) (Table 3). ECG data coverage was limited primarily by historical documentation architecture: retrievable ECG images and structured QTc

fields became routinely available in the electronic health record mainly in the later years of the study, whereas earlier ECG tracings were often stored as paper records or summarized in clinical notes without extractable QTc values. Missing QTc data therefore reflect incomplete retrievable documentation rather than definitive absence of ECG monitoring, though era and clinical subgroup selection may contribute (Supplementary Table S2, Online Resource 1).

The median pre-treatment QTc was 447.0 ms (IQR 423.2–477.5; mean 454.1 ± 44.6 ms) (Fig. 1). Baseline QTc values were frequently elevated, with 42.2% of patients (38/90) exceeding 450 ms and 13.3% (12/90) exceeding 500 ms, reflecting the burden of cardiac disease, postoperative physiology, electrolyte vulnerability, and concomitant QT-prolonging medications in this population. In the paired analysis (n = 57), the median ΔQTc was +3.0 ms (IQR −35.0 to +28.0 ms; mean −2.6 ± 42.9 ms), with no statistically significant change (Wilcoxon signed-rank test, p = 0.976) (Fig. 2). De novo QTc prolongation beyond 500 ms occurred in 1 of 57 paired patients (1.8%; exact 95% CI 0.04–9.4%). Clinically significant prolongation (ΔQTc > +30 ms) occurred in 13 patients (22.8%), with a comparable proportion demonstrating clinically significant shortening (ΔQTc < −30 ms; 15 patients, 26.3%), indicating bidirectional variability without a systematic rightward shift. These findings do not support a detectable QTc-prolonging effect among patients with paired ECG documentation, but they do not exclude rare arrhythmic risk or risk in unmonitored patients.

Discussion

Principal findings

In this single-center cohort of 352 critically ill children exposed to 7,970 risperidone administrations, low-dose risperidone was not associated with a detectable signal of QTc prolongation or clinically meaningful laboratory toxicity among patients with available monitoring data. The cohort was high-acuity, with more than half of patients invasively ventilated at treatment initiation and substantial representation from both the general PICU and PCICU. The principal safety finding was the absence of a systematic QTc increase in the paired ECG subgroup, despite a high prevalence of baseline QTc prolongation and substantial competing risk factors for repolarization abnormalities. This aligns with systematic review evidence demonstrating that risperidone shows minimal to no significant QTc prolongation in pediatric populations, and meta-analytic data showing only modest QTc increases (+1.68 ms) that did not translate to clinically significant prolongation or increased incidence of pathological QTc values compared with placebo [25, 26].

Institutional protocol and clinical context

These findings should be interpreted within the clinical framework in which risperidone was used. At our institution, risperidone is embedded in a multimodal delirium pathway that includes CAPD-based monitoring, evaluation of reversible causes, nonpharmacologic strategies, sedative-transition planning, and selective ECG monitoring. The observed safety profile therefore reflects low-dose risperidone under monitored ICU conditions rather than unstructured antipsychotic prescribing. The protocolized approach

also explains the dosing pattern observed: absolute doses increased with age and weight, while weight-normalized doses remained relatively consistent across age groups, concordant with age-stratified starting doses and daily maximum dose recommendations. Recent naturalistic cohort data suggest that risk-based rather than universal ECG screening may be appropriate in pediatric patients receiving antipsychotics, particularly given that QTc prolongation in otherwise healthy youth appears uncommon and typically mild [27].

Interpretation of QTc findings

QTc safety is the most clinically relevant concern for antipsychotic use in the PCICU population because congenital heart disease, postoperative physiology, electrolyte disturbance, autonomic instability, and concomitant QT-prolonging medications all influence repolarization. The paired ECG analysis did not demonstrate systematic QTc prolongation after risperidone initiation; however, ECG availability was incomplete and influenced by the historical evolution of electronic ECG storage. The QTc results should therefore be framed as reassuring monitored-subgroup data rather than definitive evidence of absence of risk across the entire exposed cohort. Prospective pediatric studies have similarly reported that risperidone treatment produces statistically significant but clinically modest QTc increases (mean 3.8 ms) remaining below pathological thresholds in most patients [28]. Emerging evidence suggests that additional repolarization parameters—including QT dispersion, Tp-e interval, and frontal QRS-T angle—may provide more comprehensive proarrhythmic risk assessment beyond QTc alone [29]. Individual risk factors, including baseline cardiac disease, electrolyte abnormalities, genetic arrhythmia predisposition, and concomitant QT-prolonging medications, necessitate personalized risk stratification [25, 30].

Laboratory and neurological safety

Routine laboratory measures did not demonstrate a clinically meaningful signal of hepatotoxicity, renal deterioration, potassium instability, or dysglycemia after risperidone initiation. The statistically significant creatinine decline was small in absolute magnitude and is more plausibly explained by changing ICU physiology than by a drug effect. Thyroid and endocrine outcomes were incompletely measured and should be considered exploratory. While prolactin elevation is a well-documented adverse effect of risperidone in pediatric populations, its clinical significance in the acute ICU setting remains uncertain and was not systematically evaluated in this cohort [30]. Documented seizures were uncommon (3.1%), but causality could not be determined without systematic adjudication of timing, baseline neurological disease, electrolyte status, and concomitant medications. The short-term nature of ICU risperidone exposure likely limited the emergence of metabolic complications—weight gain, dyslipidemia, and insulin resistance—that are more prominent with chronic outpatient use and demonstrate dose-dependent relationships emerging within the first 3–6 months of treatment [31, 32].

Relationship to existing pediatric critical care evidence

The findings are consistent with the limited pediatric critical care literature suggesting that risperidone and other atypical antipsychotics may be used in selected ICU patients without a large QTc signal.

Existing studies remain small, heterogeneous, and largely retrospective, and most focus on delirium treatment rather than prevention. The present cohort contributes the largest single-center safety experience across both general and cardiac pediatric ICU settings, but does not establish delirium prevention or treatment efficacy. The broader pediatric psychiatry literature demonstrates risperidone efficacy for disruptive behaviors in children with intellectual disability and neuropsychiatric conditions, though these populations differ substantially from critically ill children in baseline medical complexity, concomitant medications, and physiologic instability [33].

Strengths and limitations

Strengths include the relatively large pediatric critical care cohort, inclusion of both PICU and PCICU populations, detailed medication administration data, patient-level dosing summaries, and paired pre/post safety assessment for multiple laboratory domains. The large infant subgroup is clinically important because infants and children after congenital heart surgery are underrepresented in delirium pharmacotherapy studies. Limitations include the retrospective single-center design limiting causal inference and generalizability; the absence of an untreated or alternative-treatment control group; incomplete ECG data (paired QTc available for only 16.2%); reliance on clinical documentation rather than prospective adjudication for neurological adverse events; inability to assess CAPD-based delirium prevention efficacy across all study years; and the absence of systematic prolactin, lipid, and longitudinal weight data.

Conclusion

Low-dose risperidone used within an institutional multimodal delirium prevention and treatment pathway in this high-acuity pediatric PICU and PCICU cohort was not associated with a detectable QTc or laboratory safety signal among patients with available monitoring data. Across both general and cardiac pediatric ICU settings, risperidone demonstrated an acceptable safety profile characterized by no significant drug-induced QTc prolongation, stable hepatic and renal function, and a low rate of adverse neurological events. These data support the safety feasibility of risperidone as a pharmacologic strategy for delirium prevention in critically ill children, including those with underlying cardiac disease and including infants younger than one year — a population historically underrepresented in delirium pharmacotherapy studies — who constituted the largest single age stratum (35.8%) and tolerated low-dose risperidone without a disproportionate safety signal. The results must be interpreted in the context of retrospective design, incomplete retrievable ECG documentation, absence of a control group, and lack of systematic adverse-event adjudication. Prospective validation should combine protocolized delirium screening, protocol-adherence measurement, systematic ECG monitoring, and clinically meaningful delirium and safety outcomes.

Abbreviations

ALT

alanine aminotransferase
AST
aspartate aminotransferase
CAPD
Cornell Assessment of Pediatric Delirium
CI
confidence interval
ECG
electrocardiogram
EPS
extrapyramidal symptoms
GABA
gamma-aminobutyric acid
ICU
intensive care unit
IQR
interquartile range
LOS
length of stay
PCICU
pediatric cardiac intensive care unit
PICS-p
post-intensive care syndrome in pediatrics
PICU
pediatric intensive care unit
QTc
corrected QT interval
SCCM
Society of Critical Care Medicine
SD
standard deviation
TSH
thyroid-stimulating hormone

Statements and Declarations

Acknowledgments: The authors thank the nursing and medical staff of the PICU and PCICU at the Edmond and Lily Safra Children's Hospital for their commitment to structured delirium prevention and treatment pathways.

Funding. The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Competing interests. The authors have no relevant financial or non-financial interests to disclose.

Ethics approval. This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Institutional Review Board (Helsinki Ethics Committee) of Sheba Medical Center, Tel HaShomer, Israel (4 August 2025; No. 1500-24-SMC).

Consent to participate. The requirement for informed consent was waived by the Institutional Review Board (Helsinki Ethics Committee) of Sheba Medical Center given the retrospective, observational design without direct patient contact or additional interventions.

Consent to publish. Not applicable. The manuscript does not contain any individual person's identifying data, images, or videos.

Data availability. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author contributions. All authors contributed to the study conception and design. Data collection and analysis were performed by Evyatar Hubara. The first draft of the manuscript was written by Evyatar Hubara, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Use of AI tools. Artificial intelligence–assisted tools were used for language editing only. All content was verified by the authors, who accept full responsibility for the accuracy, analysis, and conclusions of this work.

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Tables

Table 1. *Risperidone dosing characteristics stratified by age group (n = 352).*

Age Group	n	Dose/admin (mg) Median (IQR)	Dose/admin (mg) Mean ± SD	Dose/kg (mg/kg) Median (IQR)	Cumulative (mg) Median (IQR)
< 1 year	126	0.07 (0.05–0.10)	0.07 ± 0.04	0.018 (0.012–0.025)	0.9 (0.4–1.8)
1–5 years	94	0.19 (0.14–0.25)	0.21 ± 0.10	0.016 (0.010–0.021)	2.0 (1.0–4.9)
5–12 years	53	0.36 (0.22–0.64)	0.41 ± 0.27	0.020 (0.009–0.027)	3.3 (1.0–7.2)
12–18 years	79	0.50 (0.35–0.88)	0.62 ± 0.50	0.025 (0.007–0.021)	4.7 (1.7–12.3)
Overall	**352**	**0.19 (0.10–0.37)**	**0.27 ± 0.31**	**0.019 (0.012–0.028)**	**2.0 (0.9–5.5)**

Doses originally recorded in micrograms were converted to milligrams. Dose/admin = mean dose per individual administration. Dose/kg = weight-normalised dose per administration. Cumulative = total dose across all administrations during hospitalisation.

Table 2. *Laboratory safety parameters before and after risperidone initiation.*

Parameter	n (pre)	Pre-treatment Median (IQR)	n (post)	Post-treatment Median (IQR)	Pairs	p-value
AST (U/L)	316	39.4 (26.8–68.3)	312	38.3 (28.0–66.3)	305	0.059
ALT (U/L)	314	22.0 (12.2–44.3)	311	22.5 (12.7–51.0)	303	0.689
Creatinine (mg/dL) [µmol/L]	341	0.37 (0.24–0.52) [32.7 (21.2–46.0)]	335	0.31 (0.24–0.48) [27.4 (21.2–42.4)]	328	**< 0.001**
Potassium (mEq/L)	335	3.58 (3.30–3.98)	332	3.60 (3.35–3.94)	329	0.229
Glucose (mg/dL) [mmol/L]	328	114.6 (102.2–129.0) [6.36 (5.68–7.17)]	322	114.4 (101.8–129.6) [6.35 (5.66–7.20)]	316	0.854
TSH (mIU/L)	112	2.01 (0.62–4.25)	59	2.68 (1.22–7.61)	53	0.063

Wilcoxon signed-rank test on all available paired observations. Pre = 48-h average before first dose; Post = 72-h average after first dose. Creatinine p-value reflects 328 paired observations; statistical significance driven by large sample size rather than clinical magnitude (median Δ = −0.03 mg/dL [−2.7 µmol/L]). AST = aspartate aminotransferase; ALT = alanine aminotransferase; TSH = thyroid-stimulating hormone; SI units provided in brackets.

Table 3. *QTc interval parameters before and after risperidone initiation.*

QTc Parameter	Value
ECG Data Coverage	
Pre-treatment QTc available	90/352 (25.6%)
Post-treatment QTc available	63/352 (17.9%)
Paired measurements available	57/352 (16.2%)
Pre-treatment QTc (n = 90)	
Median (IQR), ms	447.0 (423.2–477.5)
Mean ± SD, ms	454.1 ± 44.6
QTc > 450 ms	38/90 (42.2%)
QTc > 500 ms	12/90 (13.3%)
Paired ΔQTc Analysis (n = 57)	
ΔQTc — median (IQR), ms	+3.0 (−35.0 to +28.0)
ΔQTc — mean ± SD, ms	−2.6 ± 42.9
ΔQTc > +30 ms	13/57 (22.8%)
ΔQTc < −30 ms	15/57 (26.3%)
New QTc > 500 ms (de novo)	1/57 (1.8%)
Wilcoxon signed-rank test, p	*0.976*
QTc by ICU Setting	
PICU — pre-treatment (n = 38)	443.0 (420.8–475.8)
PICU — post-treatment (n = 20)	432.0 (421.8–440.5)
PCICU — pre-treatment (n = 52)	448.0 (428.8–479.2)
PCICU — post-treatment (n = 43)	448.0 (428.5–470.0)

QTc intervals measured or corrected using Bazett's formula. Pre-treatment ECG: most recent within 48 h before first risperidone dose. Post-treatment ECG: first available within 72 h after first dose. Clinically significant ΔQTc threshold: ±30 ms. High-risk prolongation threshold: >500 ms. Wilcoxon signed-rank test applied to 57 paired observations. Supplementary Table S2 (missing data and data-quality considerations) is provided in Online Resource 1. All QTc values are expressed in milliseconds (ms).

Figures

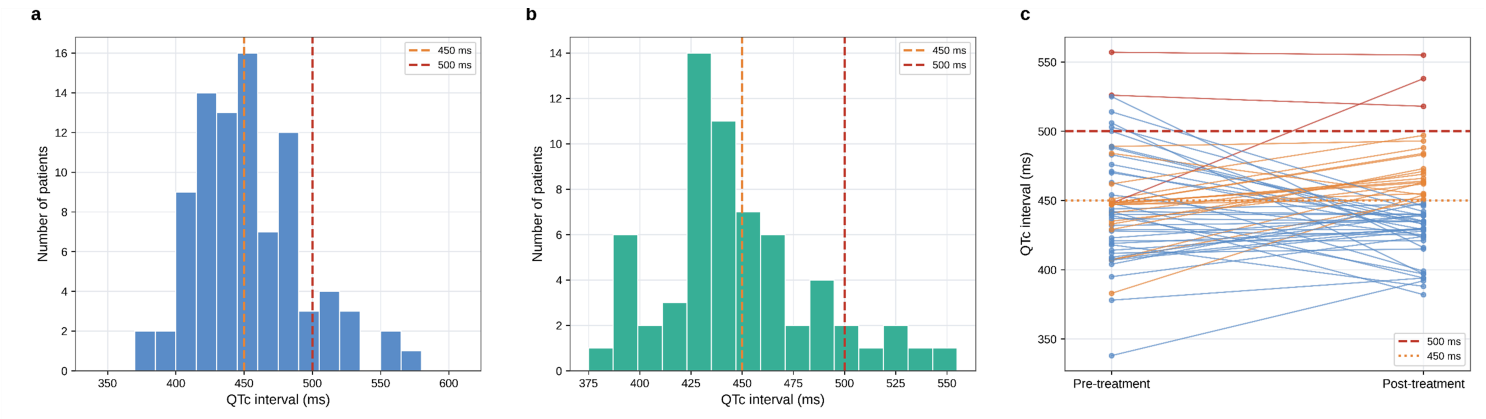


Figure 1

Pre-treatment QTc distribution, post-treatment QTc distribution, and individual paired trajectories (n = 57). a Pre-treatment QTc histogram (n = 90); dashed reference lines at 450 ms and 500 ms. b Post-treatment QTc histogram (n = 63). c Paired QTc trajectories; red lines indicate patients whose post-treatment QTc exceeded 500 ms, orange lines post-treatment QTc 450–500 ms, and blue lines post-treatment QTc <450 ms. Connecting lines show individual patient change direction and magnitude. QTc corrected QT interval, IQR interquartile range

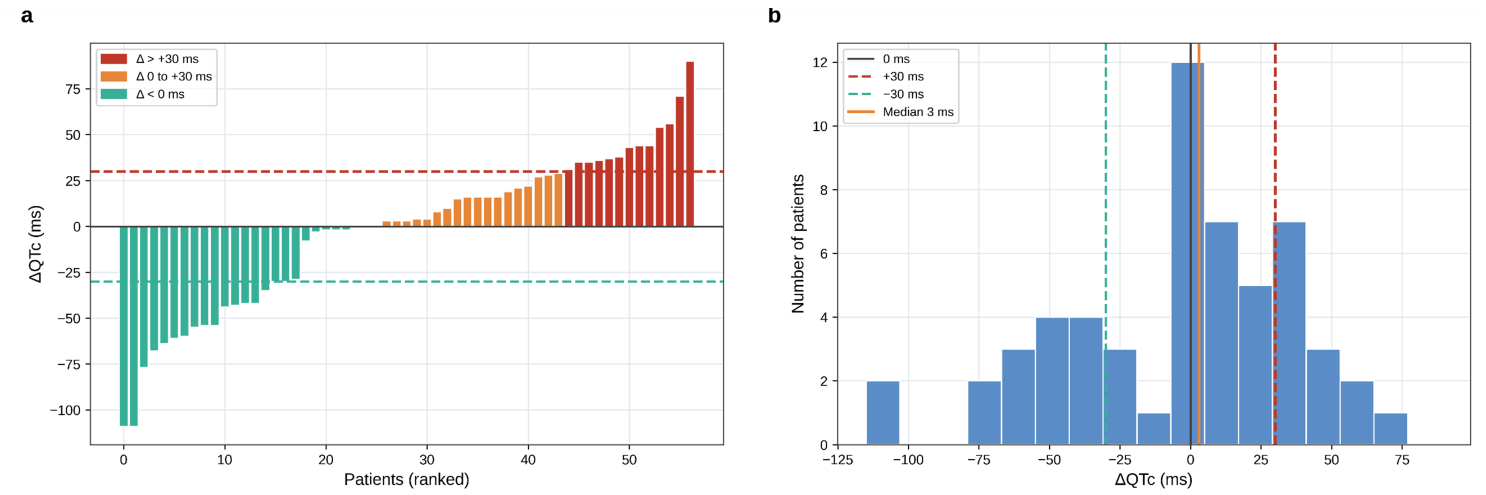


Figure 2

Individual ΔQTc values (waterfall plot) and distribution across 57 paired patients. a Waterfall plot of individual ΔQTc values ranked in ascending order; red bars indicate ΔQTc > +30 ms (clinically significant prolongation), teal bars ΔQTc < −30 ms (clinically significant shortening), and orange bars ΔQTc within 0 to +30 ms. b Distribution histogram of ΔQTc centred around zero (median +3 ms) with no systematic rightward shift. ΔQTc change in corrected QT interval from pre-treatment to post-treatment value

Supplementary Files

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

- SupplementaryEJP.docx