REVIEW

THE AMERICAN JOURNAL of MEDICINE®

The ciprofloxacin QTc alarm: What every hospitalist needs to know

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ABSTRACT

Fluoroquinolones are widely used antibiotics, however, concerns about QTc prolongation often limit their use in inpatient care. Ciprofloxacin, despite demonstrating minimal QTc effects and the lowest arrhythmic risk within its class, is frequently avoided due to non-specific electronic medical record warnings. This perspective reviews pharmacologic and real-world data to understand the real QTc risk, emphasizing ciprofloxacin's favorable cardiac safety profile. Aligning evidence with clinical practice may reduce unnecessary hospitalization, avoid prolonged intravenous therapy, and support safer transitions to oral antibiotics.

 • The American Journal of Medicine (2026) 139:988–990

KEYWORDS: Fluoroquinolones; QTc prolongation; Drug-induced arrhythmia; Ciprofloxacin; Antibiotic safety

Terminology and Definitions: In accordance with the Sex and Gender Equity in Research (SAGER) guidelines, this article distinguishes between "sex" and "gender." Sex refers to biological attributes such as chromosomes, hormones, and physiological features (e.g., cardiac ion channel expression). Gender refers to the socially constructed identities and roles of individuals. Given that QTc prolongation is primarily driven by biological mechanisms, the term "sex" is used throughout this review when discussing physiological differences and clinical risk thresholds. When citing previous research, we have retained the authors' original terminology but interpreted findings within this biological framework.

Fluoroquinolones remain among the most frequently prescribed classes of antibiotics worldwide. Their broad-spectrum antimicrobial activity, excellent oral bioavailability, and reliable tissue penetration make them attractive options in both inpatient and outpatient settings. Despite these advantages, uncertainty persists among clinicians regarding their cardiovascular safety profile, particularly concerns related to QTc prolongation and potential arrhythmic risk.

Among the fluoroquinolones, ciprofloxacin is often the only feasible oral option for common inpatient infections such as complicated urinary tract infections, intra-abdominal infections, select bloodstream infections, and osteomyelitis. In many cases, it represents the key step that allows transition from intravenous therapy to discharge. Yet, in routine practice, ciprofloxacin prescriptions are increasingly abandoned—not because of clinical contraindications, but because of electronic medical record (EMR) warning boxes related to QTc prolongation. These alerts, often triggered by modest baseline QTc values or concomitant medications, create uncertainty and frequently lead clinicians to avoid oral therapy altogether. The result is a familiar inpatient scenario: prolonged hospitalization, continued intravenous antibiotics, additional monitoring, increased cost, and greater exposure to hospital-acquired complications. While fluoroquinolones as a class have been associated with QTc prolongation and rare arrhythmias, not all agents carry the same risk. Ciprofloxacin demonstrated minimal QTc effects and the lowest arrhythmic risk among fluoroquinolones. However, EMR systems do not differentiate between agents, treatment durations, or patient-specific risk profiles,

Credit Authorship Contribution Statement: Zeynep Naz Efe: Conceptualization, Data curation, Formal analysis, Investigation, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing. **Mir A. Husain:** Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – review & editing.

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0002-9343/
https://doi.org/10.1016/j.amjmed.2026.03.020

often applying class-level warnings in a uniform manner. This perspective aims to reframe the conversation for hospitalists by focusing on ciprofloxacin's real-world cardiac safety, contextualizing QTc risk, and highlighting when EMR warnings should prompt caution—and when they may inadvertently delay care. By aligning pharmacologic data with everyday inpatient decision-making, we seek to reduce unnecessary hesitation, avoid preventable hospital days, and promote safer, more efficient transitions to oral therapy.

CLINICAL SIGNIFICANCE

- Ciprofloxacin has the lowest arrhythmic risk in its class, typically prolonging QTc by only 2-3 ms.
- Non-specific EMR alerts often cause clinicians to avoid ciprofloxacin unnecessarily, delaying hospital discharges.
- Serious arrhythmias (Torsades de Pointes) are extremely rare, usually occurring only in high-risk patients with multiple comorbidities.
- Recognizing ciprofloxacin's safety can reduce costs, length of stay and IV-related complications.

Pharmacologic studies have shown that in some circumstances fluoroquinolones prolong the QT interval primarily through blockade of high human Ether-à-go-go-Related Gene (hERG)-encoded myocardial potassium channels, reducing the delayed rectifier potassium (IKr) current and delaying ventricular repolarization. This effect may predispose to torsades de pointes in the presence of reduced repolarization reserve, electrolyte disturbances, or concomitant QT-prolonging medications.[1] In clinical practice, the QT interval represents the time from the start of ventricular depolarization to the end of repolarization and is corrected for heart rate as the QTc to allow meaningful comparisons across patients and ECGs. A QTc interval is generally considered prolonged when it exceeds sex-specific normal values (typically > 450 ms for males and > 460 ms for females), and QTc > 500 ms or an increase > 60 ms from baseline are thresholds often associated with higher risk of torsades de pointes.[2] Even when fluoroquinolones exhibit modest QTc prolongation in some pharmacologic studies, this does not universally translate into clinically significant arrhythmias in all patients, particularly during short courses of therapy (eg, 7-14 days) without additional risk factors. Real world data suggest that while QTc prolongation is measurable, the absolute incidence of torsades attributable to typical fluoroquinolone use remains low outside high-risk clinical scenarios.[3] It is important to underscore that the QTc prolongation effect varies among individual fluoroquinolones due to differences in IKr channel inhibition. Agents with stronger IKr inhibition, such as moxifloxacin, are associated with mean QTc increases of approximately 10 ms in healthy subjects, whereas ciprofloxacin is associated with minimal or negligible QTc changes, often < 2−3 ms. These changes remain well below thresholds typically associated with torsades de pointes in patients without additional risk factors. The marked differences in IKr IC_{50} values reported by Anderson et al[4] ranging from 0.23 μM for sparfloxacin and 0.75 μM for moxifloxacin to > 25 gt; 25 μM for gatifloxacin and grepafloxacin, support the observed clinical heterogeneity in QTc effects across the class. Although moxifloxacin blocks the IKr channel and has been linked to torsades de pointes, this complication is extremely rare, occurring in fewer than 1 in 100,000 patients. In other words, generalized to all fluoroquinolone reported incidence rates are approximately 0.2−2.7 cases per million prescriptions.[5] However, among this class, ciprofloxacin appears to carry the lowest arrhythmic risk. As it increases QTc by less than 10 milliseconds compared with placebo, indicating a low risk of clinically significant QT prolongation.[6] In other words, we can say that in real life, ciprofloxacin remains a very safe choice and can be used without significant hesitation.

One of the most common real-life scenarios for this situation is when EMR systems generate warning boxes while attempting to prescribe medications associated with QTc prolongation. For instance, large multicenter studies have shown that ciprofloxacin is associated with only a 2-3 millisecond prolongation of the QT interval. If a patient's QTc interval exceeds even 450 milliseconds, we will still receive this notification, which sometimes leads physicians to unnecessarily avoid prescribing ciprofloxacin. Statistically, even if a patient experiences a 3-millisecond QTc prolongation (which is rare), it remains significantly below the 500-millisecond threshold, which is considered dangerous.

Large observational studies suggest that the risk of serious cardiac events associated with fluoroquinolones is context-dependent and patient-specific. In a cohort study by Assimon et al, comparing respiratory fluoroquinolones (levofloxacin or moxifloxacin) with amoxicillin-based regimens, use of respiratory fluoroquinolones was associated with a higher 5-day risk of sudden cardiac death (SCD) among 264,968 in-center hemodialysis patients.[1] In contrast, several large-scale real-world studies examining ciprofloxacin specifically have reported reassuring cardiac safety profiles. A large bi-national cohort study including more than 900,000 matched treatment courses, of which 82.6% involved ciprofloxacin, found no increased risk of serious arrhythmia compared with penicillin V during current use (rate ratio 0.85; 95% CI, 0.61-1.18). The absolute risk difference was −13 cases per 1,000,000 fluoroquinolone courses, effectively excluding even small increases in arrhythmic risk in the general population.[7] Taken together, these findings suggest that fluoroquinolone-associated arrhythmic risk is not uniform across agents or patients. In individuals with known susceptibility, such as female sex, advanced age, marked bradycardia, concomitant use with another QTc prolonging drugs, or renal failure, selection of

agents with lower QT liability, such as ciprofloxacin, along with closer clinical and electrocardiographic monitoring, appears prudent. Notably, the majority of available safety data derive from short treatment durations (approximately 7-14 days), and robust evidence guiding the cardiac safety of longer-term fluoroquinolone therapy remains limited.

For hospitalists, the decision to prescribe ciprofloxacin is rarely theoretical—it is a practical choice made at the bedside, often determining whether a patient remains hospitalized or goes home. While fluoroquinolones can prolong the QTc interval, clinically significant torsades de pointes is rare, and the risk is not uniform across the class. Among available agents, ciprofloxacin consistently demonstrates minimal QTc prolongation and the most favorable cardiac safety profile. EMR warning systems, though well-intentioned, frequently lack nuance. By issuing non-discriminatory QTc alerts, they may inadvertently discourage appropriate oral therapy and contribute to prolonged hospital stays, unnecessary intravenous antibiotics, and increased healthcare costs. In attempting to prevent rare adverse events, we may instead expose patients to more common and predictable harms. A patient-centered approach and preferentially selecting lower-risk agents-such as ciprofloxacin-allows hospitalists to use this antibiotic safely and effectively. Reconsidering how we interpret QTc warnings is not about minimizing risk; it is about placing risk in context. Doing so can facilitate timely discharge, reduce unnecessary inpatient care, and ultimately improve outcomes, goals that lie at the heart of hospital medicine.

Funding sources

The authors declare that no funding was received for this work.

Data access and author contribution statement

All authors confirm that they had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors participated in the drafting and critical revision of the manuscript.

Declaration of competing interest

All authors report no relevant financial or non-financial conflicts of interest related to this work.

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