For more than a decade there has been considerable interest in the role of QT interval prolongation in the pathogenesis of sudden infant death syndrome. It has been proposed that the QT interval is a surrogate marker for autonomic instability and can be used to identify infants at risk for significant morbidity and mortality, including sudden infant death syndrome. We present the case of an infant that experienced a significant increase in his QTc, as detected by continuous QTc monitoring in the NICU after repositioning from a supine to prone position. This increase from a 413 ± 6 millisecond baseline average to 500 milliseconds was sustained for 2 hours and associated with clinically relevant apnea that ultimately required repositioning of the infant back to the supine position. Repositioning resulted in an immediate decrease of the QTc back to the previous baseline and termination of the apneic events. This case demonstrates an example of how the use of continuous QTc monitoring in the NICU setting may be used to detect QTc-accentuating factors in real time and identify situations that cause perturbations in an infant’s autonomic nervous system. Pediatrics 2013;132:e1690–e1693
The areas in the brainstem that regulate cardiac repolarization are in close proximity to areas that control respiration and temperature, and instability in 1 system may affect other systems. The QT interval, a marker of cardiac repolarization, is highly dependent on autonomic nervous system (ANS) input in the lower brainstem and as such can serve as a surrogate for ANS function and maturation. Over the past decade, many questions have arisen concerning the QT interval and its role in identifying disturbances in the ANS, most notably infants at risk for sudden infant death syndrome (SIDS).2 Recently, continuous QTc monitoring in the NICU has become available and reliable.3 Continuous QTc monitoring in the NICU may help identify situations and infants in which ANS disturbances and instability are present. We demonstrate a case in which continuous QTc monitoring identified marked QTc prolongation and associated apneic episodes in an infant positioned from supine to prone.

CASE

A male infant with no significant family history was found to have a prenatally identified congenital heart defect. After an uneventful delivery at 32 weeks, 5 days estimated gestational age, he was admitted to the NICU wherein a postnatal echocardiogram confirmed congenitally corrected transposition of the great arteries with a single ventricular, left-dominant morphology. The patient was monitored continuously by using the IntelliVue MP70 Neonatal monitor (Philips, Boeblingen, Germany) with continuous QTc monitoring activated, which displays real-time QTc values (calculated by using the Bazett correction formula) that are automatically downloaded to the electronic medical record at 15-minute intervals. The patient was started on prostaglandins, furosemide, and caffeine while awaiting his first palliative heart surgery. Of note, none of these medications have been associated with prolongation of the QT interval.

As of the fourth day of life, the patient remained stable with no occurrence of significant events since birth. Continuous QTc monitoring during the early part of that day showed stable and consistent QTc values averaging 413 ± 6 milliseconds with the patient in the supine position (Fig 1). During this time, there were no apneic episodes or clinical changes requiring significant intervention. Later that morning, the patient was repositioned from a supine to prone position, which correlated with an immediate increase in his QTc to 500 milliseconds. He remained prone for ∼2 hours, during which time his continuous QTc values averaged 495 ± 8 milliseconds. Subsequently, while still prone, he had 4 apneic episodes that required significant nursing intervention. As a result of these episodes, he was repositioned back to the supine position, which precipitated an immediate decrease in his QTc to 412 milliseconds. The QTc remained normal for the remainder of the day.

Subsequent serial 12-lead electrocardiograms (ECGs) documented normal QTc values over the next days and weeks while supine. The remainder of the hospital stay was significant for medical necrotizing enterocolitis, sepsis, and eventual successful modified Blalock-Taussig shunt placement with patent ductus arteriosus ligation. He was discharged on day of life 53 with planned follow-up with cardiology for timing of future surgical interventions.

DISCUSSION

The case of this infant with transient, marked QT prolongation and apnea associated with positional change illustrates how dynamic changes in this index of cardiac repolarization might provide a noninvasive barometer of autonomic health. In 1998, Schwartz et al published a groundbreaking article demonstrating an increased frequency of QT prolongation among infants who subsequently died of SIDS.2 The authors included a recommendation for routine newborn ECG screening in an attempt to identify infants with significant QT prolongation as possible candidates for medical prophylaxis. These findings and subsequent recommendations sparked immediate debate in which many opposing arguments centered on a previous study that did not demonstrate this correlation.4 This debate led many to revisit the literature regarding SIDS and its possible pathophysiologic origins as a terminal respiratory event as opposed to death resulting from a cardiac arrhythmia.5–10 What was lost during the debate was the idea that QT prolongation may be a marker of vulnerable infants with autonomic instability rather than denoting the nature or mechanism of the terminal event itself.7 It is well known that the brainstem is the major regulatory site for respiration, cardiovascular function, sleep, and arousal and that dysfunction in any 1 of these areas influences the other regulatory systems.1 Our case demonstrates how the use of continuous QTc monitoring in the NICU setting can detect this complex interplay and possibly be used as a sensitive marker of autonomic instability.

In our infant, simple repositioning was associated with a dramatic increase in QTc values with subsequent clinical instability as demonstrated by repeated apneic episodes. Although it cannot be proven from a single case report, we speculate that in this case, prone positioning precipitated autonomic dysregulation and apnea that were demonstrated by the transient and almost immediate rise in the infant’s continuous QTc readings. Regardless, it is obvious that positional changes induced in this infant a vulnerable state that was relieved with repositioning back to the supine position. Previous studies have investigated the role of sleep position on QTc values and have found virtually no or little difference.
among healthy infants.\textsuperscript{11,12} The correlation of these events with the dramatic changes in the QTc of our infant is both fascinating and provocative.

The infant in our study had 3 normal ECGs during his early life. However, continuous QTc monitoring demonstrated an acute and dramatic change that correlated with clinically relevant deterioration. Although determining causation and the exact mechanism of this phenomenon is impossible at this time, the QTc served as a noninvasive barometer of the patient’s ANS. Autonomic stressors are often cumulative and only result in clinical significance in an infant at critical times of autonomic or clinical vulnerability. The goal is to use the QTc to be able to detect these vulnerable states in an attempt to intervene or investigate a possible cause earlier than has been previously able.

Currently there are many QTc-inciting factors in neonates. The use of the standard 12-lead ECG has demonstrated QT prolongation in the setting of various electrolyte derangements and drug administration.\textsuperscript{13} Enhanced use of continuous QTc monitoring in the NICU setting may alert us to other relevant QTc altering situations. Is there an association between sepsis and QTc values that might suggest acute QTc changes as a possible marker? Does exposure to hypoxia alter the QTc in neonates, a finding already demonstrated in mice?\textsuperscript{14} Can the severity and clinical relevance of gastroesophageal reflux be better understood by the effect it has on the QTc? These are a few of the many questions that may be explored with continuous QTc monitoring.

Inherent to the proposed use of continuous QTc monitoring in the NICU is the unique challenge that neonates present in measuring such intervals and which correction formula should be used.\textsuperscript{15} It is well known that high heart rates, low-amplitude T waves, artifact secondary to crying, respirations, and caregiver interventions makes interpreting the QTc in neonates difficult and often unreliable.\textsuperscript{13,16} The monitors used in our NICU are designed to account for these difficulties and use a signal averaging and filter-based algorithm to measure the QTc more accurately and provide more stable trends.\textsuperscript{3,17} Its use has been demonstrated previously to reliably and accurately measure QTc values compared with a cardiologist.\textsuperscript{5}

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure1.png}
\caption{QTc values and their association with infant position and apneic episodes.}
\end{figure}
CONCLUSIONS
With the clinical availability of continuous QTc monitoring, QTc-accentuating factors now may be gleaned in real time and infants with perturbations in their ANS might be identified. It remains to be determined whether continuous QTc monitoring will become the next vital sign.

REFERENCES
QTc Interval Prolongation and Severe Apneas Associated With a Change in Infant Positioning

Marc A. Ellsworth, Timothy J. Ulrich, William A. Carey, Christopher E. Colby and Michael J. Ackerman

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