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Original Article

QTc prolongation in children following congenital cardiac disease surgery

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Abstract *Introduction:* QTc prolongation has been reported in adults following cardiopulmonary bypass; however, this phenomenon has not been studied in children with congenital cardiac disease. This study's aim was to formally assess QTc in children undergoing cardiac surgery. *Methods:* Pre-operative and post-operative electrocardiograms during hospital stays were prospectively analysed on 107 consecutive patients under 18 years of age undergoing cardiac surgery. QTc was measured manually in leads II, V4, and V5. Measurements of 440 and 480 milliseconds were used to categorise patients. Peri-procedural data included bypass and cross-clamp time, medications, and electrolyte measurements. Outcome data included arrhythmias, length of mechanical ventilation, and hospital stay. Patients with post-operative new bundle branch block or ventricularly paced rhythm were excluded. *Results:* In all, 59 children were included, out of which 26 had new QTc over 440 milliseconds and 6 of 59 had new QTc over 480 milliseconds post-operatively. The mean increase in post-operative QTc was 25 milliseconds, p=0.0001. QTc over 480 was associated with longer cross-clamp time, p=0.003. Other risk factors were not associated with post-operative QTc prolongation. This phenomenon was transient with normalisation occurring in 67% of patients over 60 hours on average. One patient with post-operative QTc over 440 milliseconds developed ventricular tachycardia. There was no correlation between prolonged QTc and duration of mechanical ventilation, or hospital stay. *Conclusion:* A significant number of children undergoing cardiac surgery showed transient QTc prolongation. The precise aetiology of QT prolongation was not discerned, though new QTc over 480 milliseconds was associated with longer cross-clamp time. In this cohort, transient QTc prolongation was not associated with adverse sequela.

Keywords: Electrocardiography; arrhythmias; children; arrhythmias; post-operative

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Prolongation of the QTc is shown to increase the risk of cardiac arrhythmias and sudden cardiac death.[1] Krasner et al[2] reported a transient increase in the QTc among 24 adult patients undergoing elective mitral valve replacement that lasted for 2 days after cardiopulmonary bypass. Of note, in this subset of patients, there was a positive correlation between a prolonged QTc and arrhythmia, specifically ventricular extrasystoles and bigeminy. The pre- to post-operative QTc change was statistically higher in this subgroup. QTc prolongation is seen among some of our children undergoing open heart surgery for the treatment of congenital cardiac disease. However, to our knowledge, no one has performed a detailed characterisation of QTc changes after cardiopulmonary bypass among children with congenital cardiac disease. The primary

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aim of this study was to prospectively determine whether there is a change in QTc on pre- versus post-operative electrocardiograms following surgery for congenital cardiac disease. In addition, a secondary aim was to identify predictor variables that correlate with changes in the QTc. Specifically, we hypothesised that this prolongation may be related to cardiopulmonary bypass time. Finally, we sought to determine whether there is a difference in outcome variables such as incidence of post-operative arrhythmias, length of intensive care unit stay, and length of hospital stay that were associated with perioperative QTc changes.

Methods

Subjects

Routinely performed pre- and post-operative electrocardiograms were prospectively analysed on all patients under 18 years of age undergoing cardiopulmonary bypass for congenital cardiac disease between October, 2006 and June, 2007 at a single centre. This 9-month sampling period was selected based on the availability of the researchers and accessibility of the data. Subjects were excluded from analysis if there was a new bundle branch block, ventricular pacing postoperatively, or an uninterpretable electrocardiogram as these outcomes precluded meaningful pre- and post-operative QTc comparison. For the included patients, serial electrocardiograms in accordance with standard clinical practice were analysed as part of the study during their hospital stay. The pre-operative electrocardiogram was collected at the pre-operative visit while the very first electrocardiogram performed on the day of surgery was deemed to be the post-operative electrocardiogram. None of the patients received antiarrhythmic medications or other agents known to prolong the QT interval in the perioperative period.

Collected data

The primary outcome variable studied was QTc on pre- and post-operative electrocardiograms. Secondary outcome variables including arrhythmia, diminished cardiac function, duration of mechanical ventilation, and length of intensive care unit and hospital stay were also collected. Predictor variables included cardiac diagnosis, specific cardiothoracic procedure with attention to those requiring coronary manipulation, cardiopulmonary bypass time, cross-clamp time, use of modified ultrafiltrate, all perioperative medications, and all perioperative electrolyte measurements. The electrolyte data were obtained in the intensive care unit at the time of the post-operative electrocardiogram.

Electrocardiogram data

QTc was measured in all leads and corrected using Bazett's formula.[3] In cases where the end of the T-wave was ambiguous, the point in which the steepest slope of the descending limb of the T-wave bisects the isoelectric line was used to establish the termination of the T-wave.[4] Lead II QTc measurements were utilised for analysis when the electrocardiogram signal was interpretable. Otherwise, QTc measurements from leads V4 or V5 were used. Measurement of the QRS duration was also obtained pre- and post-operative intervention to ensure that changes in the QTc were not secondary to changes in QRS duration.[5,6] For any patient with an increase in post-operative QRS duration, the measured QT interval was adjusted to account for the change in QRS duration as follows:

$$\text{QT-adjusted} = \text{QT measured} - \Delta\text{QRS duration}$$

where ΔQRS duration = post-operative QRS duration − pre-operative QRS duration in milliseconds. The adjusted QT interval is then corrected for rate using Bazett's formula as described above. Despite patients with the new right bundle branch block being excluded from the primary analysis, for completeness, the JTc was measured on the pre- and post-operative electrocardiograms performed on these patients and compared using 360 milliseconds as the upper limits of normal.[5] The final measured electrocardiogram variable was change in ST segment elevation or depression. Any post-operative ST segment change that was greater than 2 millivolts was considered significant. To minimise bias, the observer performing the electrocardiographic measurements was blinded to the study date and therefore unaware of which electrocardiogram was performed pre- or postoperatively.

Statistics

The rates of QTc prolongation before and after surgery were compared using McNemar's test. All categorical risk factors for QTc prolongation were

Table 1. Reason for excluded patients.

New right bundle branch block	33
Atrioventricular canal repair	12
Ventricular septal defect repair	12
Tetralogy of Fallot repair	5
Other	4
New left bundle branch block	3
Intraoperative decision for no cardiopulmonary bypass	4
Uninterpretable T-waves for QTc	3
Post-operative ventricular pacing	3
Missing post-operative electrocardiogram	2
Total number of patients in the excluded group	48

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Table 2. Patient demographics.

	Post-operative QTc <440 ms	Post-operative QTc between 440 and 480 ms	Post-perative QTc >480 ms	p-value
Number of patients	33	20	6	–
Number of females*	14 (42)	15 (75)	3 (50)	0.07
Age in years**	2.4 ± 3.1	2.0 ± 3.6	3.0 ± 6.5	0.83
Septal defects*	6 (18)	8 (40)	2 (33)	0.18
Single ventricle*	16 (48)	9 (45)	0 (0)	0.08
Tetralogy of Fallot	3	0	0	–
Complete transposition	3	0	1	–

Data are presented as numbers and percentages (in parentheses) or mean ± standard deviation
Comparison were made using the Freeman–Halton test* and ANOVA test**

compared using Fisher's exact test. When multiple comparisons of categorical risk factors were necessary, the Freeman–Halton test was implemented. A Student's *t*-test was used to compare continuous data sets when the variances were similar, whereas the unequal *t*-test with Satterthwaite's adjusted degrees of freedom was used for continuous data comparison with unequal variances. Pre- and post-change scores in QTc, JTc, and QRS duration were assessed using paired *t*-test. The percentage of patients with JTc greater than 360 milliseconds was compared pre- and postoperatively using Fisher's exact test. This JTc value represents two standard deviations above the mean.[5] A subset of the study patients was randomly selected and the QTc measurement was obtained by a separate blinded observer. A Pearson's correlation coefficient was established between the two observers' measurements and the percentage of agreement. The two observers' QTc measurements were highly correlated with an R^2 of 0.85 and p-value of less than 0.0001 with an inter-observer difference of 5.9%.

Change in p-values of less than 0.05 was considered to be statistically significant. All statistical calculations were performed using SAS Enterprise Guide 4.2 and SAS 9.2 (SAS Institute Inc., Cary, North Carolina, United States of America).

Results

Subject characteristics

A total of 107 consecutive patients meeting initial inclusion criteria were enrolled during the study period. We excluded 48 patients from the analysis due to one or more exclusion criteria as shown in Table 1. QTc analysis was performed on the remaining 59 patients as shown in Tables 2 and 3 that form the basis of this study. Table 2 provides a synopsis of the demographic data using comparisons of the patients with new QTc prolongation to those without new QTc prolongation. Septal defects and single ventricles constituted 41 out of the 59 patients, and therefore statistical comparisons were made for these groups. However, no particular lesion was associated with new QTc prolongation. None of the single ventricle patients had QTc prolongation greater than 480 milliseconds. A somewhat larger proportion of females was noted in patients with post-operative QTc between 440 and 480 milliseconds; however, this did not achieve statistical significance. The age of the patients in each subgroup was not different.

QTc measurements

The pre- and post-operative measurements of QTc were symmetrical, approximately normally distributed, but contained a few outliers (Fig 1).

The average of all post-operative QTc measurements was 25 milliseconds longer than the pre-operative values. The 95% confidence limit measured 15–36 milliseconds with a p-value of less than 0.0001. The average pre- and post-operative QTc measurements were 432 and 457 milliseconds, respectively. There were 26 of 59 patients (44%) who had new QTc prolongation greater than 440 milliseconds; 6 of 59 patients (10%) had new post-operative QTc prolongation greater than 480 milliseconds. The principal diagnosis and procedure for the six patients with new QTc prolongation greater than 480 milliseconds are noted in Table 4. Patient 5 listed in this table had a low potassium level; however, the follow-up electrocardiogram showed a QTc of 493 milliseconds despite electrolyte correction. Only one patient, patient 2, had a procedure involving coronary manipulation. Despite Figure 2 showing that some of the children's QTc values regressed to the mean, a larger proportion of patients had QTc prolongation postoperatively (75%) compared to those with QTc prolongation preoperatively (38%). These differences in proportions reached statistical significance given a p-value less than 0.001. Figure 3 shows the proportions of QTc measurements pre- and postoperatively.

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Table 3. Study patients' diagnosis, procedure, cardiopulmonary bypass/cross-clamp time, and pre- and post-operative QTc measurements.

Patient	Age	Gender	Diagnosis	Procedure	Bypass time (min)	Cross-clamp time (min)	Pre-QTc (ms)	Post-QTc (ms)
1	0.3	Female	Tricuspid atresia	Bidirectional Glenn	73	0	412	456
2	1.4	Male	Tricuspid atresia	Lateral tunnel Fontan	133	0	392	400
3	1.8	Female	Tricuspid atresia	Lateral tunnel Fontan	136	0	404	467
4	0.0	Male	Total anomalous pulmonary veins	Pulmonary venous return repair	142	69	432	494
5	5.2	Male	Sinus venosus atrial septal defect	Atrial septal defect repair	77	27	465	468
6	0.0	Male	Complete transposition of great vessels	Arterial switch repair	186	66	389	389
7	0.0	Male	Complete transposition of great vessels	Arterial switch repair	175	76	400	481
8	6.5	Male	Secundum atrial septal defect	Atrial septal defect repair	37	16	428	444
9	0.0	Female	Truncus, interrupted aortic arch type B	Truncus and arch repair	194	74	412	454
10	0.7	Male	Unbalanced canal, hypoplastic right ventricle	Bidirectional Glenn	90	0	388	417
11	6.5	Male	Unbalanced canal, hypoplastic left ventricle	Fontan fenestration revision	55	21	485	450
12	1.9	Male	Pulmonary atresia, intact ventricular septum	Lateral tunnel Fontan	78	13	408	452
13	3.9	Male	Primum atrial septal defect, cleft mitral valve	Atrial septal defect, cleft repair	59	43	465	490
14	5.6	Male	Tricuspid regurgitation, severe	Tricuspid valve replacement	128	48	519	453
15	0.3	Female	Primum atrial septal defect, cleft mitral valve	Atrial septal defect, cleft repair	79	39	494	439
16	6.3	Female	Hypoplastic left heart syndrome	Lateral tunnel Fontan	84	0	454	454
17	2.0	Female	Mitral regurgitation, canal repair	Mitral valve repair	78	31	444	467
18	0.2	Female	Aortopulmonary window	Aortopulmonary window repair	61	19	438	457
19	0.3	Male	Hypoplastic left heart syndrome	Bidirectional Glenn	71	0	473	474
20	0.4	Female	Pulmonary atresia, intact ventricular septum	Bidirectional Glenn	244	53	433	448
21	11.5	Female	Aortic regurgitation	Aortic replacement, Cox maze III	264	125	633	546
22	11.2	Female	Pulmonary regurgitation, tetralogy of Fallot	Right ventricle pulmonary conduit	76	0	464	476
23	0.5	Male	Double outlet right ventricle, hypoplastic left ventricle	Bidirectional Glenn	111	0	405	432
24	6.4	Female	Pulmonary regurgitation, tetralogy of Fallot	Right ventricle pulmonary conduit	150	0	468	551
25	0.5	Male	Complete atrioventricular canal, subaortic stenosis	Canal repair and subaortic resection	269	115	463	569
26	0.0	Female	Truncus arteriosus	Truncus repair	184	66	288	459
27	0.2	Female	Membranous ventricular septal defect	Ventricular septal defect repair	122	52	406	494
28	1.3	Female	Tetraology of Fallot with pulmonary atresia	Blalock–Tausig Shunt	163	46	447	412
29	0.5	Male	Unbalanced canal, hypoplastic left ventricle	Bidirectional Glenn	93	12	457	401
30	0.0	Male	Sinus venosus atrial septal defect	Sinus venosus atrial septal defect repair	135	33	417	446
31	16.3	Male	Right ventricular myxoma	Right ventricular myxoma resection	100	42	431	504
32	9.2	Female	Supracristal ventricular septal defect, subaortic membrane	Ventricular septal defect, membrane repair	113	75	426	478
33	13.8	Male	Severe aortic regurgitation	Aortic valve replacement	91	64	431	457
34	0.3	Male	Unbalanced canal, hypoplastic left ventricle	Bidirectional Glenn	104	0	406	460
35	0.3	Female	Balanced canal	Complete canal repair	96	46	384	459
36	2.2	Female	Tricuspid atresia	Bidirectional Glenn	143	29	452	417
37	2.0	Female	Hypoplastic left heart syndrome	Lateral tunnel Fontan	135	63	413	454
38	0.6	Female	Double inlet left ventricle, pulmonary stenosis	Bidirectional Glenn	94	36	384	462
39	0.5	Female	Double outlet right ventricle, left outflow tract obstruction	Bidirectional Glenn	67	0	416	448
40	1.2	Female	Apical ventricular septal defect	Pulmonary arterioplasty, septal device	94	0	376	447
41	0.4	Female	Double outlet right ventricle, pulmonary/mitral atresia	Bidirectional Glenn	91	0	377	417
42	0.3	Female	Tricuspid atresia	Bidirectional Glenn	72	0	389	459

Table 3. *Continued*

Patient	Age	Gender	Diagnosis	Procedure	Bypass time (min)	Cross-clamp time (min)	Pre-QTc (ms)	Post-QTc (ms)
43	0.0	Male	Complete transposition of great vessels	Arterial switch repair	240	106	343	379
44	0.4	Female	Unbalanced canal, hypoplastic left ventricle	Bidirectional Glenn	148	0	414	412
45	0.4	Female	Perimembranous ventricular septal defect	Ventricular septal defect repair	103	46	377	447
46	1.1	Male	Anomalous left coronary artery from pulmonary artery	Anomalous coronary artery repair	136	69	457	518
47	0.4	Female	Ventricular septal defect	Ventricular septal defect repair	89	47	432	494
48	0.4	Male	Double inlet left ventricle, pulmonary stenosis	Bidirectional Glenn	116	0	462	447
49	2.3	Male	Primum atrial septal defect, cleft mitral valve	Atrial septal defect and cleft repair	74	37	446	453
50	0.4	Female	Hypoplastic left heart syndrome	Bidirectional Glenn	116	0	420	457
51	0.3	Female	Balanced atrioventricular canal	Complete atrioventricular canal repair	146	8	429	454
52	1.1	Male	Double outlet right ventricle, right outflow tract obstruction	Right ventricle pulmonary conduit	166	0	463	477
53	2.6	Male	Double inlet left ventricle, pulmonary stenosis	Extracardiac Fontan	102	0	454	443
54	3.6	Male	Hypoplastic left heart syndrome	Pulmonary arterioplasty	124	64	407	406
55	0.8	Female	Hypoplastid left heart syndrome	Right ventricle pulmonary conduit	340	0	443	469
56	0.7	Male	Unbalanced canal, hypoplastic left ventricle	Unifocalisation, Blalock–Taussig shunt	100	0	428	438
57	0.4	Female	Complete transposition of great vessels	Arterial switch repair	238	129	453	432
58	0.3	Female	Hypoplastic left heart syndrome	Bidirectional Glenn	159	0	367	428
59	1.2	Female	Truncus arteriosus	Right ventricle pulmonary conduit	176	80	438	515

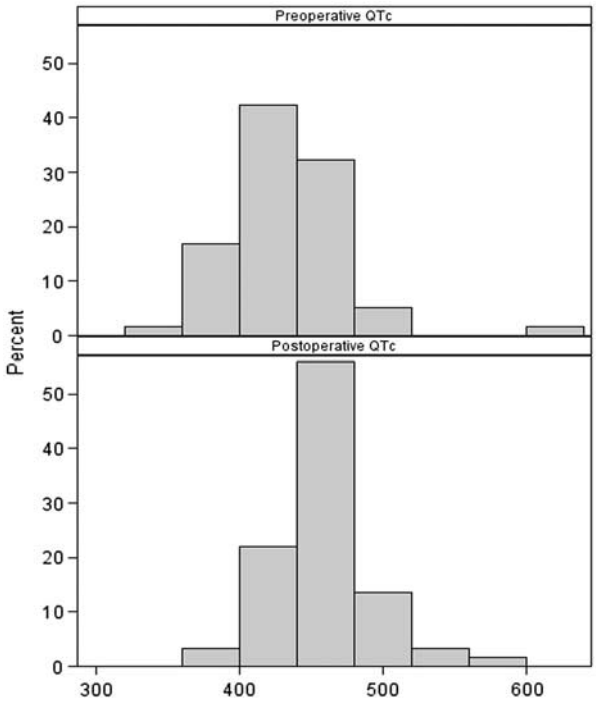

Figure 1.
Histograms of pre- and post-operative QTc values show an approximate normal distribution. Comparison of values were made with a paired Student's t*-test.*

QRS duration and ST segment changes

There was no significant difference between pre- and post-operative QRS duration with a p-value of 0.12 in the study cohort. A total of 11 patients had an increase in the QRS duration postoperatively with a range of 10–30 milliseconds. After correcting for changes in the QRS duration, three patients initially characterised as having post-operative QTc greater than 440 milliseconds now had adjusted QTc values in the normal range. None of the patients with QTc measurements greater than 480 milliseconds were affected by adjusting for QRS duration. The ST segments were depressed by 2 or more millivolts in only six patients. The average post-operative QTc for these patients – 463 milliseconds – was not significantly different from those without ST segment changes – 456 milliseconds with a p-value of 0.76.

JTc measurements

The largest group of patients were excluded from the study on the basis of the new right bundle branch block. For completeness, an analysis of JTc measurements before and after surgery was performed on this group of 33 patients who were otherwise excluded from the analysis. The mean JTc for the group was 320 milliseconds preoperatively and 370 milliseconds postoperatively. This 50-millisecond difference was statistically significant with a p-value of 0.0001.

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Table 4. Diagnosis and procedure for patients with new QTc prolongation >480 ms.

Patient	Diagnosis	Procedure	Calcium level	Magnesium level	Potassium level
1	Total anomalous pulmonary venous return, infracardiac	Total anomalous pulmonary venous return repair	12.4	1.9	3.0
2	Complete transposition of the great vessels with intact ventricular septum	Arterial switch procedure with atrial septal defect repair	9.6	NA	3.1
3	Perimembranous ventricular septal defect	Ventricular septal defect repair	8.4	2.1	3.4
4	Right ventricular myxoma	Resection of right ventricular myxoma	9.2	2.2	3.8
5	Double outlet right ventricle with subaortic ventricular septal defect	Ventricular septal defect repair with baffle closure	11	3.4	2.7
6	Hypoplastic left heart syndrome	Right ventricle to pulmonary artery conduit revision	11.3	3.2	3.4

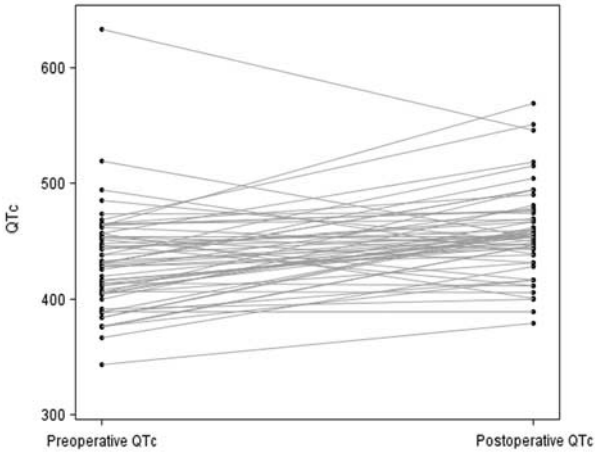

Figure 2.
The QTc scores regress to the mean, exemplified by the larger scatter in values in the baseline compared to the final measurements.

Of the 33 patients who were excluded due to the new right bundle branch block, 16 had a JTc greater than 360 milliseconds postoperatively, whereas only 4 of the 33 patients had a JTc greater than 360 milliseconds preoperatively. The p-value for this comparison measured 0.0029.

Outcomes

Of the 26 study patients with new post-operative QTc prolongation, the majority (67%) normalised their QTc within an average of 60 hours after the first post-operative electrocardiogram. Of the six patients with new post-operative QTc prolongation greater than 480 milliseconds, only one had normalised by the time of discharge. In the remaining five patients, serial post-operative electrocardiograms showed QTc measurements trending downwards but still ranged 452–464 milliseconds at the time of discharge. None of the patients with QTc prolongation greater than 480 milliseconds had post-operative arrhythmia. There was one patient with QTc prolongation greater than 440 milliseconds who had one episode of non-sustained

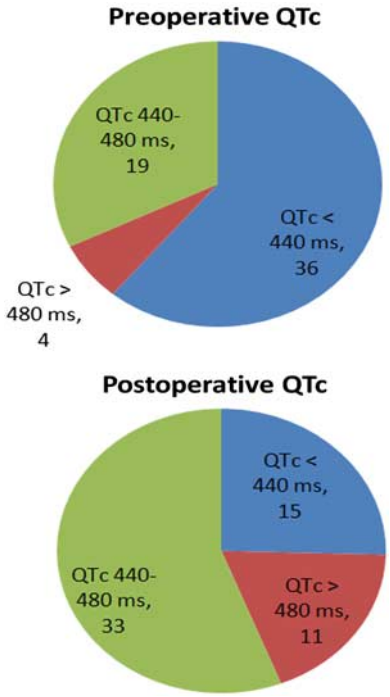

Figure 3.
Pre- and post-operative count of patients with QTc values that are normal, between 440 and 480, and greater than 480 milliseconds. Proportions were compared using McNemar's test.

ventricular tachycardia in the early post-operative period that did not require therapy. This patient had an aortic valve replacement and was noted to have mild to moderately depressed systolic ventricular function by echocardiogram. Patient 21 had a pre-operative history of atrial fibrillation; however, she had no post-operative arrhythmia. Of note, the pre-operative QTc measured greater than 600 milliseconds in this patient. None of the patients had a pre-operative history of ventricular arrhythmia. Patients with QTc prolongation did not have a prolonged intubation time, intensive care unit level of care, or hospital stay when compared to patients with normal QTc values postoperatively.

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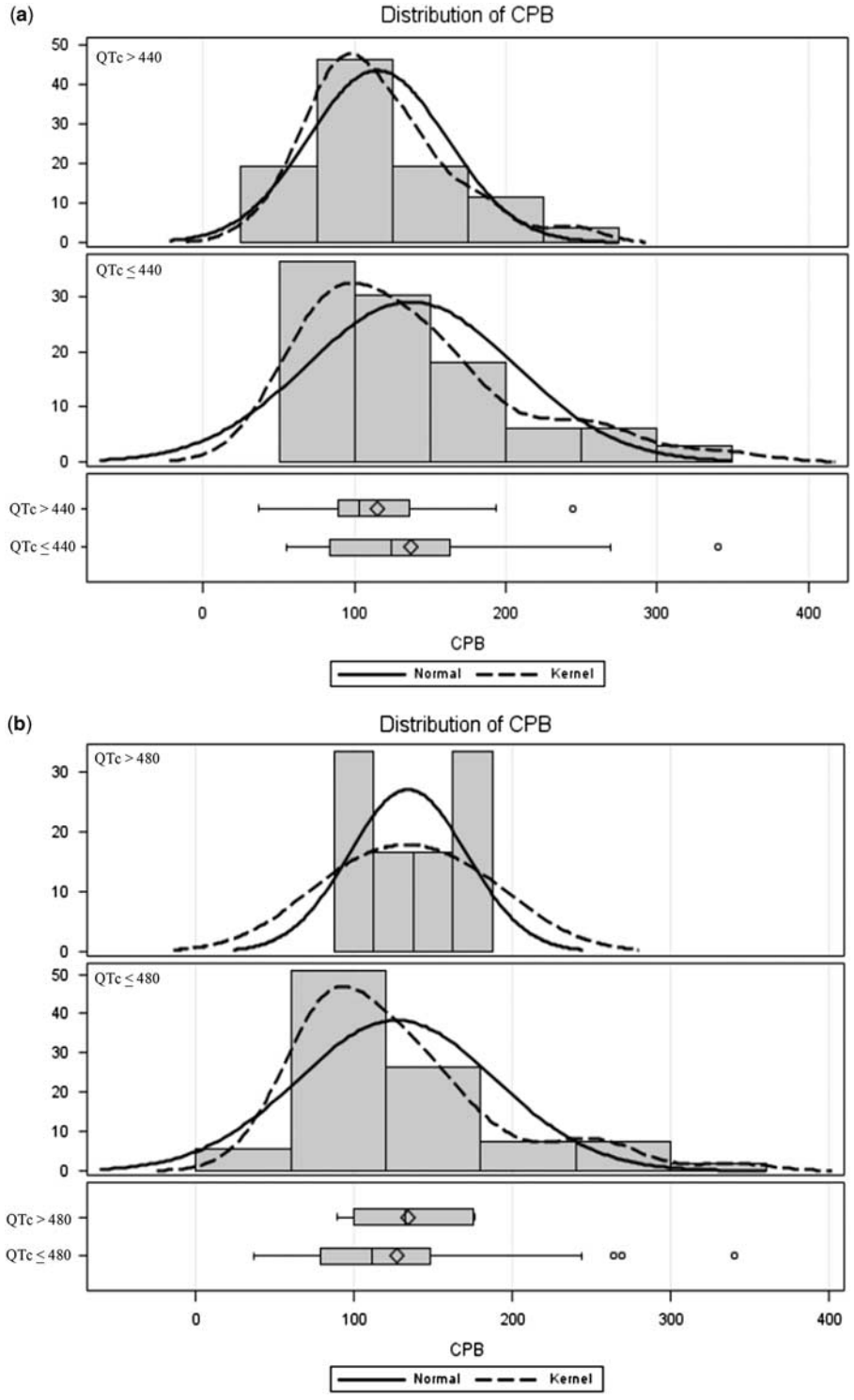

Figure 4.
*(**a**) Cardiopulmonary bypass time versus presence of QTc prolongation greater than 440 milliseconds. (**b**) Cardiopulmonary bypass time versus presence of QTc prolongation greater than 480 milliseconds. Comparison made with Student's* t*-test and unequal* t*-test with Satterthwaite's adjusted degrees of freedom.*

Risk factors for post-operative QTc prolongation

The mean cross-clamp and cardiopulmonary bypass time for patients with new QTc measurements over 480 milliseconds were 61 and 134 minutes, respectively.

These patients had, on average, 30 minutes more cross-clamp time than those with QTc measurements less than 480 milliseconds with a p-value of less than 0.003. The cardiopulmonary bypass time

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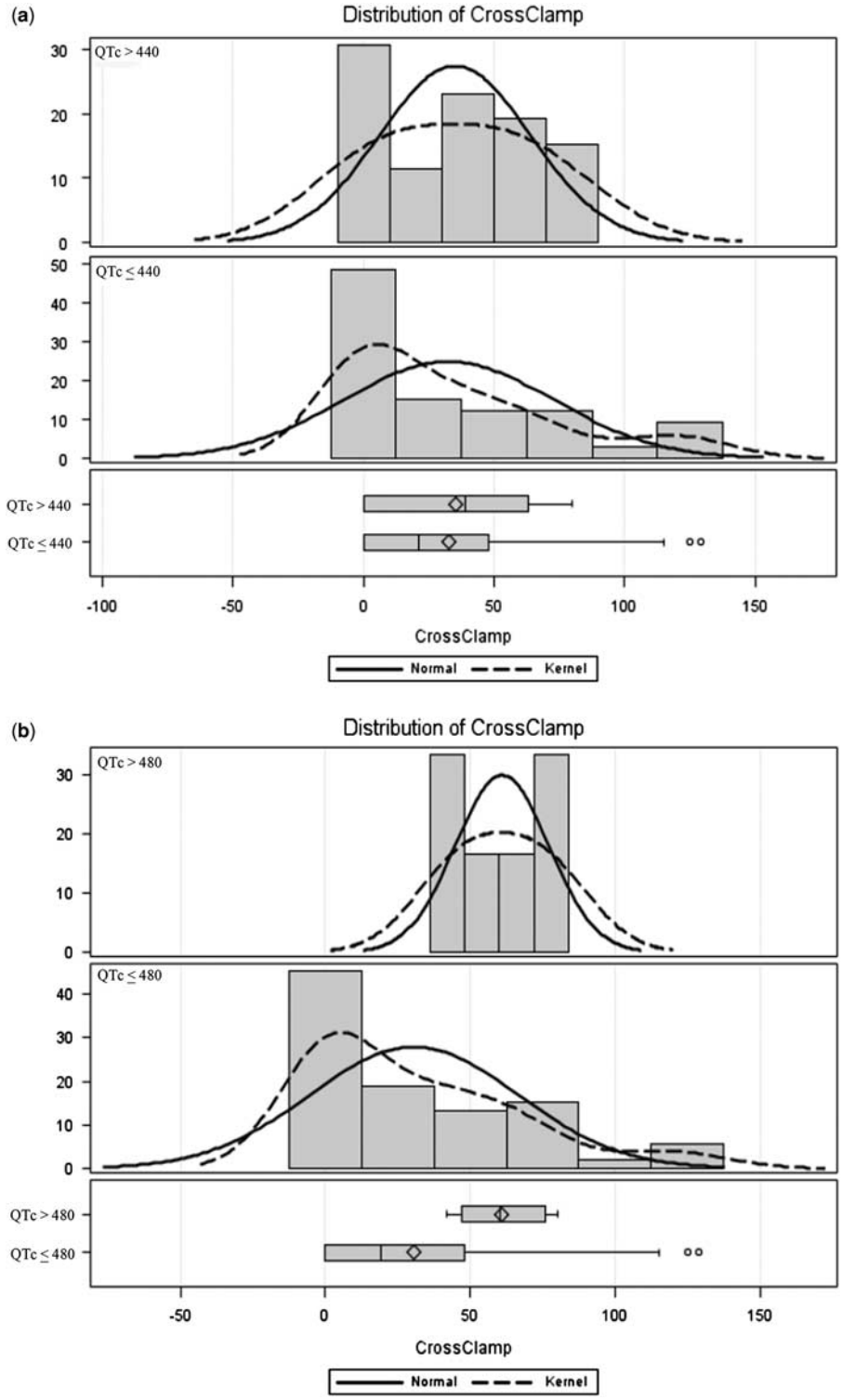

Figure 5.
*(**a**) Cross-clamp time versus presence of QTc prolongation greater than 440 milliseconds. (**b**) Cross-clamp time versus presence of QTc prolongation greater than 480 milliseconds. This comparison was noted to be statistically significant with a p-value of 0.003. Comparison made with Student's* t*-test and unequal* t*-test with Satterthwaite's adjusted degrees of freedom.*

was 7 minutes longer in those patients with new QTc prolongation greater than 480 milliseconds; however, this difference did not achieve statistical significance with a p-value less than 0.78 (Figs 4 and 5). Cross-clamp time was not statistically different when comparing patients with and without

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Table 5. Risk factors for new post-operative QTc prolongation.

	QTc >440 ms			QTc >480 ms		
Risk factor	**Yes**	**No**	**p-value**	**Yes**	**No**	**p-value**
Glycopyrrolate*						
Yes	4 (50)	4	0.72	1 (13)	7	1.00
No	21 (43)	28		5 (10)	44	
Hypokalemia*						
Yes	21 (49)	22	0.26	5 (12)	38	1.00
No	5 (31)	11		1 (6)	15	
Diminished ventricular systolic function*						
Yes	4 (80)	1	0.16	1 (20)	4	0.43
No	22 (42)	31		5 (9)	48	
Coronary artery manipulation*						
Yes	2 (29)	5	0.45	1 (14)	6	0.55
No	24 (46)	28		5 (10)	47	
Modified ultrafiltrate*						
Yes	22 (43)	29	1.00	5 (10)	46	0.50
No	3 (50)	3		1 (17)	5	
Anaesthetic type**						
Sevoflurane						
Yes	7 (44)	9	0.48	1 (6)	15	0.21
Isoflurane						
Yes	8 (36)	14		2 (9)	20	
Isoflurane/sevoflurane						
Yes	9 (56)	7		2 (13)	14	
Ketamine/fentanyl						
Yes	1 (100)	0		1 (100)	0	

Data are presented as numbers and percentages (in parentheses)
Comparison made using the Fisher's exact test* and Freeman–Halton test**
Two patients were missing glycopyrrolate data. One patient had no post-operative echocardiogram to assess ventricular function

Table 6. Electrolyte levels for patients with and without new post-operative QTc prolongation.

	QTc >440 ms			QTc >480 ms		
Electrolyte	**Yes**	**No**	**p-value**	**Yes**	**No**	**p-value**
Potassium	3.2 ± 0.3	3.4 ± 0.7	0.20	3.1 ± 0.4	3.4 ± 0.6	0.25
Calcium	11.4 ± 1.2	11.6 ± 2.1	0.70	10.6 ± 1.2	11.6 ± 1.7	0.10
Magnesium	2.6 ± 0.5	2.7 ± 0.5	1.00	2.7 ± 0.6	2.6 ± 0.5	0.69

Data are presented as mean ± standard deviation

new QTc prolongation greater than 440 milliseconds; the actual average cross-clamp time measured 35 versus 32 minutes, respectively, with a p-value of less than 0.78. Similarly, cardiopulmonary bypass time was also not significantly different between these patients with and without new QTc measurements greater than 440 milliseconds; the average cardiopulmonary bypass time measurements were 115 versus 137 minutes, respectively, with a p-value of less than 0.15 as shown in Figures 4 and 5.

The mean cross-clamp time for all included patients measured 33.6 minutes with a standard deviation of 4.6. There were four patients who had a cross-clamp time greater than 2 standard deviations above the mean. After excluding these four patients, the remaining 55 had a pre-operative QTc of 428 milliseconds and a post-operative QTc of 455 milliseconds. This 27-millisecond difference was statistically significant with a p-value of less than 0.001. Thus, when controlling for excessively high cross-clamp time, the QTc remains increased postoperatively.

Additional variables including medications, electrolyte abnormalities, and ventricular dysfunction were investigated to determine any statistical associations with a new QTc prolongation. None of these variables achieved statistical significance (see Tables 5 and 6). There were seven patients who had procedures that required a form of coronary artery manipulation. These operations were an arterial switch procedure for four patients, an aortic

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valve replacement for two patients, and an anomalous left coronary artery repair for one patient. Table 3 again describes the procedures for the included patients. None of these procedures had a statistical association with new QTc prolongation of either greater than 440 or 480 milliseconds as shown in Tables 5 and 6.

Discussion

Transient prolongation of the QTc indeed occurs in a proportion of children after cardiothoracic surgery for congenital cardiac disease. A subset of patients develop QTc prolongation greater than 480 milliseconds. Despite not being shown in this study, it is generally believed that this degree of prolongation may put patients at risk for ventricular arrhythmias.[7,8] Like Krasner et al's study,[2] our study shows that in the majority of our patients, this phenomena is transient in nature. Significant QT prolongation was associated with longer cross-clamp time. Despite the precise aetiology of this phenomenon being unknown, one may speculate that this association of higher cross-clamp time with new QTc prolongation greater than 480 milliseconds is related to transient ischaemia during the surgical intervention. The hypothesis that QTc prolongation may be related to the length of ischaemia is in keeping with other studies that have shown transient prolongation of QTc during myocardial infarction and balloon coronary angioplasty in adult patients.[9,10] In addition, there are case reports of patients presenting with QT prolongation during myocardial ischaemia that resolved after a coronary intervention.[11,12] Interestingly, our study did not show an association between those procedures requiring direct coronary artery manipulation and QT prolongation. Other factors may influence the QTc prolongation as the QTc increase was still noted when controlling for patients with very high cross-clamp times.

Our study is underpowered to definitively determine the frequency of adverse events related to this transient QT prolongation, but our anecdotal experience and the results of this study suggest that this phenomenon does not pose a significant risk to the majority of patients because of its transient nature and the highly monitored environment of the post-operative setting.

In individuals in whom QT prolongation persists at hospital discharge, careful follow-up with repeat electrocardiography seems prudent to document normalisation of the QT interval. In those patients whose corrected QT interval remains prolonged, formal assessment by a cardiologist experienced in the diagnosis and management of long QT syndrome is warranted.

Limitations

Our study is limited by the fact that electrocardiograms were obtained based on clinical indications rather than study design, despite the prospective nature of the trial. In addition, since only one electrocardiogram was obtained per day, the time to normalisation could be overestimated in this study. The study exclusion criteria also created a potential selection bias in that patients with certain congenital cardiovascular lesions were eliminated from the study in greater numbers than others. For example, patients with ventricular septal defect, complete atrioventricular canal, and tetralogy of Fallot tended to be excluded in greater numbers due to the new right bundle branch block patterns frequently incurred during these procedures. In a *post hoc* analysis, these excluded patients had a prolongation in JTc after surgery. Finally, this study did not address follow-up after discharge from the hospital, and nor did it assess for genetic abnormalities that may predispose certain individuals to longer QT intervals.

Conclusion

A modest transient increase in the QTc is seen in the majority of children undergoing operative intervention for the treatment of congenital cardiac disease. In almost half of the patients (44%), this QTc prolongation exceeded the normal value of 440 milliseconds. More significant QTc prolongation with QTc values in excess of 480 milliseconds was seen in 10% of the study population. The precise aetiology of QTc prolongation in this setting is unknown; however, it appears to be associated with longer cross-clamp times. Fortunately, in this cohort, the observed QTc prolongation was transient and not associated with clinical adverse outcomes.

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