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Application of the Bogossian formula for evaluation of the QT interval in pacemaker patients with stimulated left bundle branch block

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Abstract

Background The presence of left bundle branch block (LBBB) represents a particular challenge in properly measuring the QT interval. Here we demonstrate the applicability of the "Bogossian formula" in pacemaker patients with LBBB due to apical or nonapical right ventricular (RV) pacing and preserved left ventricular function.

Methods A total of 163 patients with a cardiac one- or two-chamber pacemaker were included in this prospective, multicentre observational study. Twelve-lead ECG recordings were obtained during both intrinsic rhythm and RV pacing with induced LBBB. The QT interval measured during LBBB was corrected using the Bogossian formula to obtain the "modified QT" (QTm). The QTmc interval was calculated with the Bazett formula, and this was compared with the QTc interval during intrinsic rhythm.

Results Eighty-three patients (78 ± 9 years; male $n = 83$) with apical and eighty patients (71 ± 13 years; male $n = 80$) with non-apical RV pacing were included in this study. In the apical group the QTmc was determined to be 444 ± 39 ms in paced rhythm and the QTc interval 413 ± 36 ms in intrinsic rhythm. In the non-apical group these values were 430 ± 34 ms in paced and 416 ± 32 ms in intrinsic rhythm.

Conclusion The Bogossian formula is a reliable tool for QTc interval evaluation in pacemaker patients with LBBB due to apical or non-apical RV pacing. However, an overestimation of 30 ms should be included in the calculation.

Keywords QT formula · Left bundle branch block · QT interval · JT interval · Long QT · Pacemaker

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Introduction

Evaluation of the QTc interval by a 12-lead electrocardiogram is an important and readily available diagnostic screening tool used to identify patients of any age at increased risk for ventricular tachycardia and consequently sudden cardiac death. In addition to being linked to the congenital channelopathies (e.g. primary long QT syndrome), a prolonged QT interval can be secondarily associated with the intake of specific drugs, bradycardia, or hypokalemia [1]. Prolongation of the QT interval is also observed in the presence of bundle branch block. In particular, the left bundle branch block (LBBB) is a common conduction disorder in patients with structural heart disease that is known to be an independent risk factor for all-cause mortality [2, 3]. About 11% of all patients with LBBB show no signs of structural heart disease [2]. In order to more easily identify patients at high risk for ventricular arrhythmias with LBBB due to true prolonged QT duration, the Bogossian formula was recently introduced

(Fig. 1) [3]. This formula ($QT = QT_{LBBB} − 50\% \times QRS_{LBBB}$) was derived by comparing intrinsic QT intervals of patients with narrow QRS with a QT interval in the same patient collective after right ventricular (RV) pacing and induction of a LBBB in the course of an invasive electrophysiological examination [3]. The Bogossian formula was also evaluated in patients with intermittent intrinsic LBBB and in patients who presented initially with a narrow QRS who developed LBBB after transcatheter aortic valve implantation. The formula performed well in these various clinical scenarios [4]. Furthermore, the formula has recently been evaluated in patients with structural heart disease and an implanted cardioverter defibrillator (ICD) [5]. In this specific cohort the formula also proved to be a reliable tool; however, a slight overestimation of the QT interval was inherent and should be noted.

The formula has never been evaluated in a pacemaker patient collective, which usually includes patients with preserved left ventricular function [5, 6]. Functional LBBB due to right ventricular apical- or non-apical pacing is a common finding in pacemaker recipients. Until now, to accurately quantify the QT interval in this patient cohort, it has been necessary to measure the QT interval during intrinsic ventricular rhythm. This requires, first of all, that the investigator has expertise in programming pacemaker devices and that a programmer of the specific pacemaker manufacturer is at hand. Secondly, the patient must have an intrinsic ventricular rhythm of ≥ 30 beats per minute (bpm). Application of the Bogossian formula in this patient collective would help to simplify the measurement of the correct QT interval and to make it easier for non-electrophysiologists.

Methods

Study patients and ECG analysis

The study conforms to the guiding principles of the Declaration of Helsinki and was approved by the local ethics committees of the various centres. All patients gave informed consent for participation. Consecutive patients with a transvenous pacemaker with an apical or non-apical RV lead who presented with an intrinsic narrow QRS with a duration of less than 120 ms and a heart rate > 30/min were included

in this prospective observational study. All parameters were acquired during routine pacemaker follow-up. In all patients, QRS duration, the intrinsic JT (JT_i) interval, and the intrinsic QT (QT_i) interval were measured in the presence of an intrinsic narrow QRS with VVI 30/min backup stimulation of the pacemaker system. Next, patients underwent RV pacing during the course of RV pacing threshold testing, thereby causing a functional LBBB (Figs. 2, 3), and the same ECG parameters as those measured in intrinsic rhythm were assessed again. The pacing rate during threshold testing was up to 40 bpm above the intrinsic heart rate. The QT interval was always measured in the lead presenting the longest interval, usually V2 or V3, in line with current recommendations [7]. A tangent was applied to the T wave for accurate determination of the QT interval [8]. In all patients, ECG parameters were assessed individually by two independent operators (one experienced electrophysiologist and one trainee) to additionally analyse any potential effects of the level of experience.

Finally, measured values were compared with the corrected QT interval employing the simplified Bogossian formula ($QT = QT_{LBBB} − 50\% \times QRS_{LBBB}$). A deviation of less than 10% of intrinsic QT duration was considered to be acceptable. To exclude potential effects of the heart rate, the Bazett formula was applied before and after employment of the new formula in all patients.

Statistical analysis

Continuous data are displayed as mean $\pm$ standard deviation. Data were analysed by employing a computerized database (Microsoft Excel 2010, Microsoft, Redmond, WA, USA) and were statistically evaluated using SPSS Software Release 23.0.0. The Shapiro–Wilk test was employed to assess normal distribution. Differences between groups were determined by Student's t test. Differences were regarded significant when $p < 0.05$ (two-sided).

Results

RV lead in the apical position

Eighty-three consecutive pacemaker patients with an apical RV lead were included in this study. Table 1 shows the patients' baseline characteristics. The mean age and comorbidities are consistent with a typical pacemaker patient collective.

In the presence of a narrow QRS the mean intrinsic QRS (QRS_i) duration measured by the experienced electrophysiologist was 97 ± 8 ms with a mean JT_i interval of 302 ± 33 ms and a mean QT_i interval of 398 ± 33 ms. The mean intrinsic QTc (QTc_i) interval was 417 ± 34 ms.

Bogossian's formula : $QTm = QT_{LBBB}\text{-}48{,}5\% \times QRS_{LBBB}$
Simplified Bogossian's formula : $QTm = QT_{LBBB} − 50\% \times QRS_{LBBB}$

QTm => „modified QT" (estimated QT by using the Formula)
QT_{LBBB} => QT duration in LBBB
QRS_{LBBB} => QRS duration in LBBB

Fig. 1 Bogossian formula

Fig. 2 **a** p.a. thoraxic X-ray with apically located pacemaker RV lead; **b** same patient with lateral X-ray; **c** 12-lead ECG intrinsic rhythm (60 bpm) (50 mm/s); **d** 12-lead ECG bipolar pacing with apical RV lead position (85 bpm) (50 mm/s)
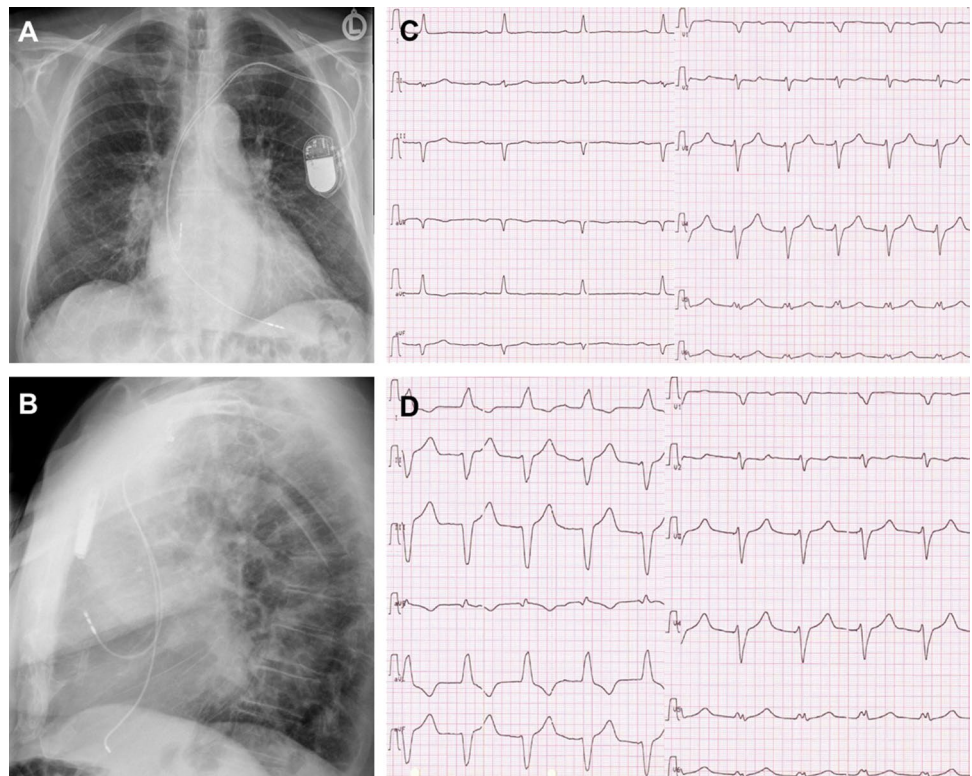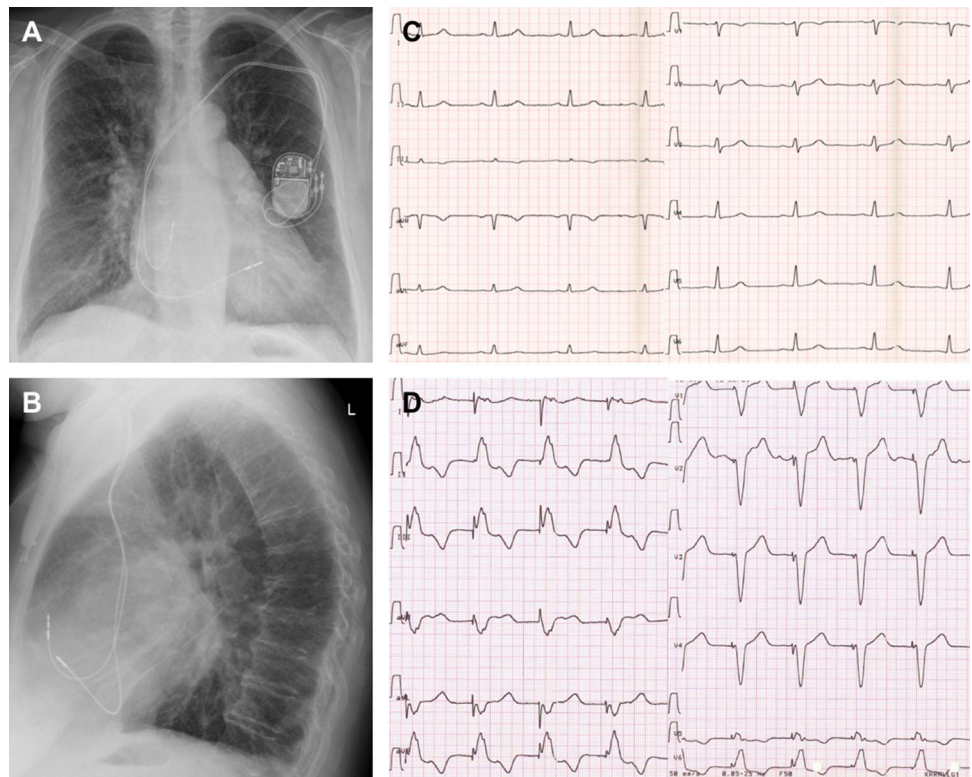

Fig. 3 **a** p.a. thoraxic X-ray with septally located pacemaker RV lead; **b** same patient with lateral X-ray **C** 12-lead ECG intrinsic rhythm (76 bpm) (50 mm/s); **d** 12-lead ECG bipolar pacing with non-apical RV lead position (100 bpm) (50 mm/s)

No significant difference was observed for values measured by the trainee: QRS_i duration: 97 ± 8 ms; JT_i interval 298 ± 33 ms; QT_i interval 394 ± 34 ms; QTc_i interval 409 ± 36 ms. During apical RV pacing and LBBB the intervals assessed by the experienced electrophysiologist were: QRS_{LBBB} duration 171 ± 18 ms, JT_{LBBB} interval

Table 1 Baseline characteristics of patients with RV apical or non-apical pacemaker lead placement

	RV apical ($n=83$)	RV non-apical ($n=80$)	P value
Age (years)	78 ± 9	71 ± 13	0.0001
Male (%)	51	51	1
BMI (kg/m^2)	26 ± 4	27 ± 5	0.16
LVEF (%)	62 ± 5	60 ± 8	0.06
Diabetes (n, %)	23%	33%	0.22
Coronary artery disease (%)	32%	33%	0.86
Renal dysfunction (%)	16%	15%	1
Cardiac rhythm (%)			
Sinus rhythm	59%	78%	0.01
Atrial fibrillation	41%	22%	0.01
Pacemaker device (%)			
Single-chamber	23%	13%	0.16
Dual-chamber	77%	87%	0.16
Implantation site (%)			
Right pectoral	40%	4%	0.0001
Left pectoral	60%	96%	0.001

Data given as means $\pm$ SD

BMI body mass index, *LVEF* left ventricular ejection fraction, *RV* right ventricular

Table 2 Pooled mean values (trainee and expert) of ECG parameters for patients with apical or non-apical lead placement and for all patients in cohort

	RV apical	RV non-apical	P value	All patients
Heart rate$_i$ (bpm)	67 ± 15	68 ± 12	0.64	67 ± 14
Heart rate$_{LBBB}$ (bpm)	88 ± 15	85 ± 12	0.16	86 ± 14
QRS$_i$ (ms)	97 ± 8	96 ± 8	0.43	97 ± 8
QRS$_{LBBB}$ (ms)	171 ± 18	156 ± 18	<0.001	164 ± 18
JT$_i$ (ms)	300 ± 33	297 ± 30	0.55	299 ± 32
JT$_{LBBB}$ (ms)	284 ± 29	285 ± 29	0.83	285 ± 29
QT$_i$ (ms)	396 ± 33	393 ± 30	0.55	395 ± 32
QT$_{LBBB}$ (ms)	454 ± 30	441 ± 30	<0.01	448 ± 30
QTc$_i$ (ms)	413 ± 36	416 ± 32	0.58	415 ± 34
QTmc (ms)	444 ± 39	430 ± 34	<0.05	447 ± 37
ΔQTc (ms)	31 ± 31	14 ± 24	<0.01	23 ± 28

RV lead in the non-apical position

Eighty consecutive pacemaker patients with a RV lead in the non-apical position were included in this study. Patients with a non-apical RV lead were younger (71 ± 13 years vs. 79 ± 9 years; $p<0.001$) and had a lower prevalence of atrial fibrillation (22 vs. 41%; $p=0.01$) than those with an apical lead. Nevertheless, ECG measurements were comparable to those obtained in patients with an apical RV lead. Here, mean QRS$_i$ duration measured by the experienced electrophysiologist was 96 ± 8 ms, resulting in a JT$_i$ interval of 298 ± 30 ms and a QT$_i$ interval of 394 ± 30 ms. No significant differences were observed for values assessed by the trainee: QRS$_i$ duration: 96 ± 8 ms, JT$_i$ interval 297 ± 31 ms, QT$_i$ interval 393 ± 31 ms. During RV pacing the following intervals were measured by the experienced electrophysiologist and the trainee, respectively: QRS$_{LBBB}$ duration 156 ± 18 ms (vs. 156 ± 18 ms), JT$_{LSB}$ interval 285 ± 29 ms (vs. 285 ± 29 ms), QT$_{LBBB}$ interval 441 ± 30 ms (vs. 442 ± 31 ms), QTc$_{LBBB}$ interval 522 ± 41 ms (vs. 524 ± 43 ms).

After use of the Bogossian formula the corrected QT interval was 363 ± 28 ms for values obtained by both the electrophysiologist and the trainee. Heart rate correction by Bazett's formula led to modified QTc intervals of 429 ± 34 ms for values obtained by the experienced electrophysiologist and 430 ± 35 ms for those measured by the trainee. The pooled mean values of the two examiners for the ECG measurements in the non-apical position are listed in Table 2.

As mentioned above for patients with apical leads, the difference between corrected intrinsic QTc$_i$ interval and corrected modified QTc interval in LBBB was more marked when heart rate correction by the Bazett formula was performed before application of the Bogossian formula (QTc$_m$ 447 ± 34 ms vs. QTc$_i$ 416 ± 32 ms).

280 ± 28 ms, QT$_{LBBB}$ interval 451 ± 29 ms. These measurements led to a QTc$_{LBBB}$ interval of 544 ± 46 ms that was prolonged compared with that of intrinsic rhythm, as anticipated. Again, the values measured by the trainee did not vary significantly from these values: QRS$_{LBBB}$ duration 171 ± 18 ms, JT$_{LBBB}$ interval 287 ± 29 ms, QT$_{LBBB}$ interval 456 ± 32 ms, QTc$_{LBBB}$ interval 551 ± 52 ms.

The corrected QT interval derived from the Bogossian formula was 366 ± 27 ms for values obtained by the electrophysiologist and 371 ± 30 ms for values obtained by the trainee. After correction for heart rate by application of the Bazett formula, the modified QTc intervals were 440 ± 36 ms as measured by the experienced electrophysiologist and 447 ± 41 ms as measured by the trainee. Table 2 shows the mean values of the pooled ECG measurements of both examiners.

It is worth mentioning that the difference between the true intrinsic QT interval in the presence of a narrow QRS and the corrected QT interval with LBBB was more distinct when heart rate correction by the Bazett formula was performed before employing the Bogossian formula (QTc$_m$ 470 ± 39 ms vs. QTc$_i$ 413 ± 36 ms). This is why it is recommended to apply the Bazett formula only after assessment of the adjusted QT interval.

Deviation of the intrinsic QTc from the modified QTc during LBBB and heart rate regression

Intrinsic QTc intervals were compared with the values obtained for the modified QTc interval during paced LBBB after use of the Bogossian formula. An accepted deviation of 30 ms (according to 7.6% of intrinsic QTc_i) reached a significant value in the equivalent paired t-test (Table 3). The regression analysis revealed a linear relationship between the deviation of the intrinsic QTc from the modified QTc and the difference between the intrinsic heart rate and paced heart rate (Fig. 4). A fast heart rate resulted in an increasing difference between intrinsic and modified QTc.

Discussion

The implication of a long QT interval for cardiovascular risk stratification has been demonstrated in large populations [9, 10]. A bundle brunch block is commonly associated with an extended QTc interval. However, the QT interval, which is easily overestimated, is the result of a prolongation of depolarisation and not of repolarisation [3]. In the past, it was suggested that the JT interval may be measured in patients

with LBBB as an alternative method of risk stratification in the presence of LBBB [11]. A different approach in pacemaker recipients is the subtraction of 50 ms of the QTc_{LBBB} as a rule of thumb, leading to reasonable values at a paced rate of 66 bpm (± 16 ms). Higher paced rates lead to a relevant overestimation of up to 81 ms [12]. A specific RV lead position-dependent QTc measurement was not conducted.

Recently, the Bogossian formula was evaluated in a heart failure patient collective with transvenous ICDs. The formula delivered acceptable results in comparing the true QT interval in a narrow QRS with the corrected QT interval in LBBB, although the formula led to a slight overestimation of the true QT interval (± 25 ms) in this patient cohort [13]. Since chronic heart failure is known to be associated with a prolonged repolarization period as a result of complex electrical remodelling and a downregulation of cardiac potassium currents, we sought to investigate the Bogossian formula in a pacemaker patient collective with normal left ventricular function [14–16].

Right ventricular lead position and operator dependency

The localization of the RV pacing lead profoundly influences the morphology of the QRS complex and thus the ensuing repolarization period. Results from our previous studies showed no significant differences between values obtained from right ventricular apical pacing and from pacing in the right ventricular outflow tract [3, 13]. In the present study that included patients with preserved ejection fraction, the results for QTc adjustment were similar to those observed in the heart failure patient collective studied previously [13].

Table 3 Accepted deviation of the mean, ΔQTc

Accepted deviation [ΔQTc = QTmc − QTci]	ΔQTc as percentage of QTci	P value
20 ms	5.1%	0.9492
30 ms	7.6%	<0.001

Fig. 4 Fit Plot showing the regression of the delta (between intrinsic QTc and modified QTc_{LBBB}) in relation to the difference between the intrinsic heart rate and the paced heart rate during threshold measurement
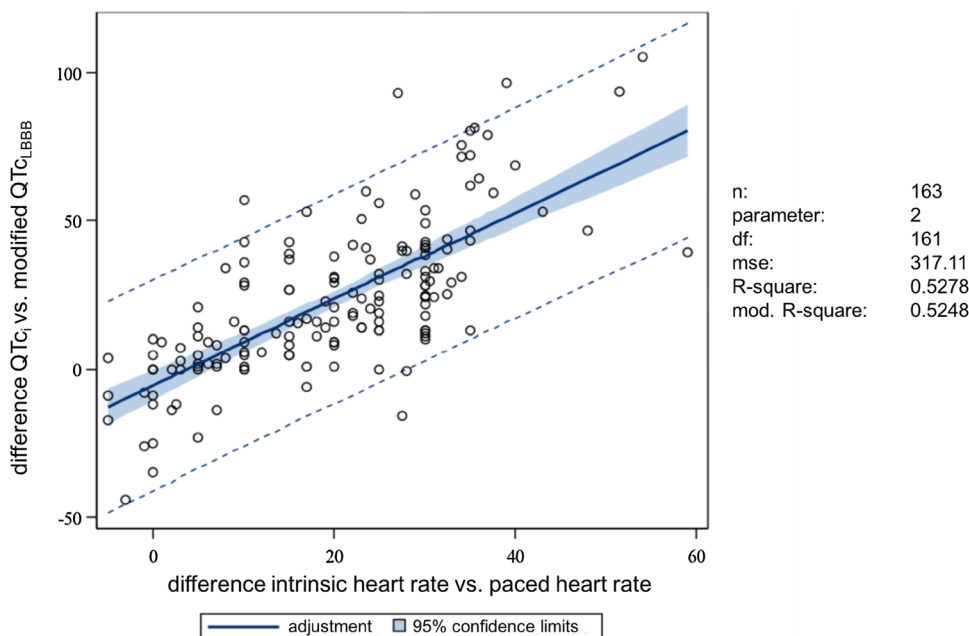
Interestingly, in the pacemaker patient cohort a reduced width of QRS complexes was associated with non-apical RV lead position. In the literature, data concerning QRS width and the position of the RV lead are contradictory [17, 18]. In particular, pacing in the high RV outflow tract leads to broad QRS complexes with a width that is similar to that obtained in the apical pacing position. In our experience, QRS complexes can be expected to be rather narrow only if the lead is in absolute proximity to the sound intrinsic cardiac conduction system, which we have usually observed to be mid-septal. Although a non-apical RV lead position results in an improved calculation of QTc with significantly less deviation to the true QTc_i, our results suggest that the Bogossian formula can be effectively applied in pacemaker patients independent of the position of the RV lead.

Accurate analysis of ECG parameters is essential for precise determination of the QT interval. The aspect of investigator-dependant divergent results is also addressed in the current recommendations for ECG interpretation [7]. In the present study, ECG parameters were assessed by two independent operators. No significant differences were observed between the experienced electrophysiologist and the trainee. This applied for all measured values as well as for calculation of the corrected QT interval employing the Bogossian formula. These findings underline the fact that general analysis of ECG parameters can and needs to be standardized and that the Bogossian formula can easily be applied by any physician.

Systematic deviation of the corrected QT interval

In the present study, a slight systematic overestimation of the true QT interval by the Bogossian formula was observed in almost all individuals, which is comparable to our recent findings in heart failure patients. The corrected QT interval was about 25 ± 21 ms longer than QTc_i. This phenomenon was detected in all patients independent of RV lead position. Of note, these results are consistent with well-known divergences reported for heart rate-dependant QT correction using Bazett's or Fridericia's formula where deviations of up to 15% are considered to be acceptable [7]. Of note, the Bogossian formula for correction of the QT interval in the presence of LBBB displayed a mean deviation of only 5.5% (from the mean intrinsic QTc interval). In the present study, the deviation of the QTc_i from the modified QTc was driven mainly by an increasing alteration between intrinsic heart rate and stimulated heart rate during threshold measurement (Fig. 4). The fact that the Bogossian formula tends to slightly overestimate the true QT interval may be regarded as a kind of safety margin for risk assessment during therapy with QT-prolonging drugs. On the other hand in cases with borderline QTc prolongation, bearing a marginal QTc overestimation

in mind, unnecessary discontinuation of medication should be avoided.

Limitations

LBBB induced by RV pacing features differences compared to intrinsic LBBB regarding the ventricular activation pattern. This may contribute to the deviation observed between the intrinsic and modified QTc interval.

Conclusion

The Bogossian formula is a simple and reliable tool that can be used in routine clinical practice for QTc interval evaluation in pacemaker patients with LBBB due to apical or non-apical right ventricular pacing. The observed overestimation of the QTc interval of approximately 15 ms (for non-apical pacing) and 30 ms (for apical pacing) should be taken into consideration when using the Bogossian formula in pacemaker recipients.

Complinace with ethical standards

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