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QT-RR REGRESSION LINES DURING VALSALVA MANOEUVRE IN YOUNG HEALTHY WOMEN ARE DIFFERENT FROM RESTING CONDITIONS

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Abstract

The aim of the study was to find out alterations of QT-RR and QT-HR regression lines during all phases of the Valsalva manoeuvre toward resting normal ventilation (RNV) in Slovak young healthy women. The electrocardiogram of 28 healthy women (18-24 years) was registered during RNV (control) and during 4 phases of VM (20 s at 40 mmHg = 5.33 kPa) in the daytime (9:00 to 17:00). The relation between QT and RR intervals compared to RNV was expressed by manually measured alterations of QT, RR, QTc intervals (paired t-test), and by linear regression QT = a + b.HR or QT = a + b.RR. Compared to RNV, the heart rate, RR interval, QT and QTc values altered significantly ($p < 0.001$) during all phases of VM; the course of regression lines was different from resting conditions as well. The independence between the duration of QT and RR intervals was the most distinct in phase 4. In conclusion, QT, RR, QTc intervals and regression lines QT = a + b.HR or QT = a + b.RR are significantly different from RNV during VM.

Key words

Electrocardiography, Valsalva manoeuvre, QT interval, Heart rate, Regression lines

Abbreviations used

HR, Heart rate; QT, Measured QT interval; QTc, Corrected QT interval (Bazett's formula); RNV, Resting normal ventilation; RR, Electrocardiographic RR interval; VM, Valsalva manoeuvre

INTRODUCTION

The Valsalva manoeuvre was proposed by the Italian physician Valsalva in 1704 as a way for expulsion of pus from the middle ear. In the 19th century it was found that it had expressed cardiovascular effects as well. In the typical course it has 4 phases (*1*). Its influence on the electrical stability of the heart has been intensively studied and applied (*1*) since the 20th century.

The duration of the QT interval of the electrocardiogram (electrical systole) is one of the indicators of electrical stability of the heart. The QT interval is generally considered to be dependent on the heart rate (HR), its duration decreases with increasing HR (*Table 1*). For mathematical processing of the results and their graphic demonstration within the range of normal heart rates it is sufficiently reliable to use regression lines. In an attempt to remove or diminish its dependence on the HR, numerous formulae were proposed for calculation of the corrected (HR-independent) QT interval (QTc) (*2, 3*), and many others (*4*). All formulae can be divided mathematically into nine groups (4). They are dependent on QT-RR relation and have some limitations.

In our previous study (*5*) it was demonstrated that several types of pulmonary ventilation alterations and the Valsalva manoeuvre were able to alter the dependence of QT interval on the heart rate. The aim of the present study was to find out alterations of QT-RR regression lines during all four phases of the Valsalva manoeuvre toward resting normal ventilation in Slovak young healthy women.

MATERIALS AND METHODS

Twenty-eight young healthy non-obese non-smoking female volunteers (18–24 years) were studied. They had negative results of preventive medical examination, their history was without any serious disease, their cardiac and pulmonary auscultation findings or blood pressure were within the normal range of values. The non-obese women were chosen because a more expressive obesity decreases parasympathetic activity and increases sympathetic predominance. They were not suffering from anorexia nervosa, either. Obesity prolongs the QTc interval and increases the catecholamine level (*6*), and anorexia nervosa increases QT dispersion (*7*), i.e., both act proarrhythmically. Our volunteers refrained from alcohol for 24 hours and from coffee, tea, cola drinks or heavy meals for 6 hours before examination. Vigorous physical activity was avoided on the day of the study.

Our young volunteers were examined during resting normal ventilation (RNV = control values) and during total VM in the recumbent position with head tilted up by 60 degrees. The basal recordings (RNV = control phase) were obtained after at least 5 minutes of rest, breathing frequency was controlled at 12–14 cycles/minute. The VM was performed by using a mouthpiece connected to a manometer; an expiration pressure of 40 mmHg (5.33 kPa) was sustained for 20 seconds.

The electrocardiogram in Frank leads (X, Y, Z) and standard limb leads (I, II, III) was recorded by a Chiracard 600T (Chirana) device continuously during RNV and VM at a paper speed of 100 mm/s, calibration 1 mV = 1.5 cm; the T-P interval was defined as the isoelectric baseline. The QT interval was measured from the earliest onset of the QRS complex in any lead to the latest end of the T wave in any lead, defined as return to the baseline. The measured QT and the preceding RR intervals were always measured during the total VM manually. An excellent agreement was demonstrated between manual and automated measurements (*8*). The division into 4 phases of VM was made according to changes of the heart rate. The values obtained from five consecutive beats were averaged for every phase of VM. If a U wave was present, the end of the T wave was measured according to the principles described by *Lepeschkin and Surawicz (9*). The values of QTc over 440 ms were considered pathological (*10*). The measurements were performed in the daytime (9:00 to 17:00), i.e., within a period of higher QT variability (*11*). The QTc interval was calculated from 5 consecutive beats according to the Bazett's formula (*2*) QTc = QT/square root of the preceding RR interval. The group "Total VM" was created as the average result from all four phases of VM. The relationship between the measured QT and its corresponding RR interval at rest and in every phase of VM was expressed by simple linear regression according to the formula QT = a + b.RR or QT = a + b.HR.

QT interval dispersion was not measured since QT dispersion measured from the body surface was not a reliable index of repolarisation dispersion in the ventricular myocardium (*12, 13*). The investigation conforms to the principles outlined in the Declaration of Helsinki.

Table 1
The range of physiological values of QT interval in men and women in dependence on heart rate (according to the American Heart Association) in seconds (17)

Heart rate	Lower border	Mean value		Upper border	
		Men + children	Women	Men + children	Women
40	0.42	0.45	0.46	0.49	0.50
43	0.39	0.44	0.45	0.48	0.49
46	0.38	0.43	0.44	0.47	0.48
48	0.37	0.42	0.43	0.46	0.47
50	0.36	0.41	0.43	0.45	0.46
52	0.35	0.41	0.42	0.45	0.46
55	0.34	0.40	0.41	0.44	0.45
57	0.34	0.39	0.40	0.43	0.44
60	0.33	0.39	0.40	0.42	0.43
63	0.32	0.38	0.39	0.41	0.42
67	0.31	0.37	0.38	0.40	0.41
71	0.31	0.36	0.37	0.38	0.41
75	0.30	0.35	0.36	0.38	0.39
80	0.29	0.34	0.35	0.37	0.38
86	0.28	0.33	0.34	0.36	0.37
93	0.28	0.32	0.33	0.35	0.36
100	0.27	0.31	0.32	0.34	0.35
109	0.26	0.30	0.31	0.33	0.33
120	0.25	0.28	0.29	0.31	0.32
133	0.24	0.27	0.28	0.29	0.30
150	0.23	0.25	0.26	0.28	0.28
172	0.22	0.23	0.24	0.26	0.26

The numerical data were expressed as arithmetic mean ± one SD. Descriptive statistics of the electrocardiographic parameters was calculated by the Microsoft Excel programme in Microsoft Office 97. One volunteer was excluded during regression processing as an extreme value and the regression lines were constructed of the results of 27 persons. Statistical significance of the ECG differences was tested by the paired t-test, of regression line differences against normal ventilation by the line parallelism test.

RESULTS

a) Normal ventilation at rest (RNV = control group):

During RNV no extrasystoles occurred in young healthy women. The RR, heart rate (HR), measured QT, and QTc intervals were within normal electrocardiographic values (*Table 2*). The average QTc intervals were normal (under 440 ms) in all persons. The relation between QT and RR intervals was individual; the same duration of QT occurred with different RR. Durations of studied parameters at rest were considered 100 % and compared with alterations during VM. The equations of the regression lines are in *Table 3,* their course is in *Figs 1 and 2.*

b) The first phase of VM:

No extrasystoles occurred in the first phase of VM. The duration of QT and RR intervals shortened (because of tachycardia), but not proportionally; the QT interval was more stable. This phase was the most variable for RR intervals since the highest value of SD occurred here. Compared to RNV the HR, RR, QT, and QTc intervals were significantly different ($p < 0.001$; *Table 2*), their average values were the smallest compared to RNV. The course of the regression lines was significantly ($p < 0.01$) different from RNV (*Figs 1 and 2, Table 3*).

c) The second phase of VM:

No extrasystoles occurred here. This phase was the most variable (the highest value of SD) for the QT interval. The RR, QT, QTc intervals and HR were significantly different ($p < 0.001$) compared to RNV. The normal duration of the average QTc intervals (under 440 ms) was in 8 volunteers (28.57 %) only. The course of the regression lines was significantly ($p < 0.01$) different from RNV (*Figs 1 and 2, Table 3*).

d) The third phase of VM:

No extrasystoles occurred here. Compared to RNV the HR, RR, QT and QTc intervals were significantly different ($p < 0.001$); the maximum differences compared to RNV of all VM phases occurred here. The duration of the average QTc intervals was below 440 ms in 5 persons (17.86 %) only. The course of the regression lines was significantly ($p < 0.01$) different from RNV (*Table 3, Figs 1 and 2*).

e) The fourth phase of VM:

No extrasystoles occurred here. The heart rate was the most variable in this phase (the highest value of SD), fast alterations of RR intervals from one cardiac cycle to another accompanied with small QT alterations were present here. Compared to RNV the HR, RR, QT and QTc intervals were highly significantly different ($p < 0.001$). The duration of the average QTc intervals was below 440 ms in 11 per-

Table 2
Electrocardiographic parameters during Valsalva manoeuvre (mean ± one SD) in young healthy women (n = 28) with statistical significance compared to RNV

Period	HR [beat/min]	***RR [ms]***	***QT [ms]***	***QTc [ms]***
RNV (control)	77.04 ± 9.07	791.3 ± 116.0	364.4 ± 26.5	410.7 ± 13.1
VM phase 1	98.1 ± 17.4 p < .001	635.6 ± 144.2 p < .001	346.1 ± 29.1 p < .001	437.8 ± 25.6 p < .001
VM phase 2	108.8 ± 23.8 p < .001	579.3 ± 135.7 p < .001	342.5 ± 31.8 p < .001	455.1 ± 32.0 p < .001
VM phase 3	118.0 ± 25.6 p < .001	534.2 ± 127.1 p < .001	335.0 ± 29.2 p < .001	463.5 ± 30.9 p < .001
VM phase 4	112.3 ± 28.2 p < .001	563.5 ± 126.2 p < .001	337.7 ± 28.6 p < .001	454.2 ± 37.3 p < .001
VM all phases	112.6 ± 24.2 p < .001	557.9 ± 125.8 p < .001	340.3 ± 27.8 p < .001	460.7 ± 32.7 p < .001

HR – heart rate, QT – measured QT interval, QTc – corrected QT interval according to the Bazett's formula, RNV – resting normal ventilation

sons (39.29 %) only. The course of the regression lines was significantly ($p < 0.01$) different from RNV (*Table 3, Figs 1 and 2*).

f) The total VM (all four phases together):

During the total VM no extrasystoles occurred. All the parameters measured were significantly different ($p < 0.001$) from RNV. The duration of the average QTc interval was under 440 ms in 5 women (17.86 %) only. The course of the regression lines was significantly ($p < 0.01$) different from RNV (*Figs. 1 and 2, Table 3*).

The results of all studied parameters are shown in three tables and two figures. Compared to RNV the heart rate, RR interval, QT and QTc values altered significantly during all phases of VM (*Table 2*), the course of the regression lines during VM was different ($p < 0.01$) from resting conditions as well (*Table 3, Figs. 1 and 2*). This means that the decrease in QT interval duration was markedly slower with increasing heart rate than at rest (*Fig. 2*). The differences among regression lines within all phases of VM are insignificant, i.e., all these lines are parallel. The independence between the duration of QT and RR intervals was the most distinct in phase 4 of the manoeuvre.

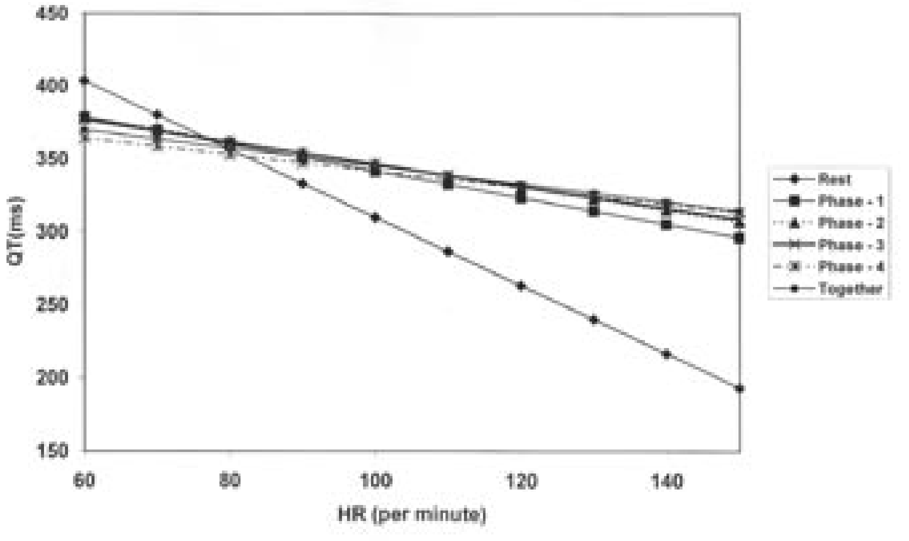

Fig. 1
The course of regression lines QT = a + b.RR during Valsalva manoeuvre in young healthy women (n = 27). Together – total Valsalva manoeuvre

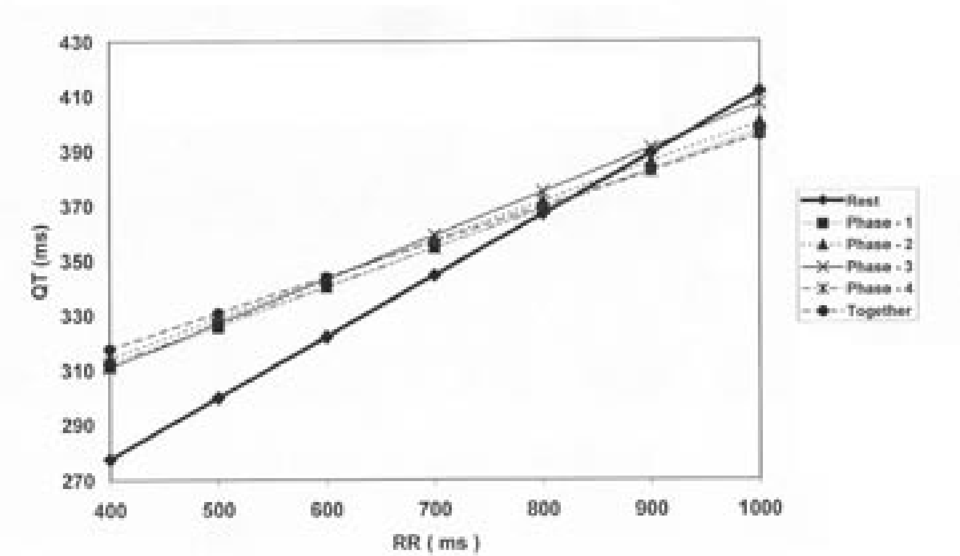

Fig. 2
The course of regression lines QT = a + b.HR during Valsalva manoeuvre in young healthy women (n = 27). Together – total Valsalva manoeuvre

Table 3
Regression lines QT = a + b.RR and QT = a + b.HR during Valsalva manoeuvre (VM) in young healthy women (n = 27). Test of parallelism compared to resting NV

Phase	Regression lines [ms]	Test of parallelism
Resting NV	QT = 188.3421 + 0.2232. RR	----
	QT = 543.4409 – 2.3336. HR	----
VM – phase 1	QT = 253.5964 + 0.1444. RR	$p < .01$
	QT = 433.4451 – 0.9134. HR	$p < .01$
VM – phase 2	QT = 257.2295 + 0.1434. RR	$p < .01$
	QT = 425.7548 – 0.7899. HR	$p < .01$
VM – phase 3	QT = 247.3489 + 0.1613. RR	$p < .01$
	QT = 421.8731 – 0.7532. HR	$p < .01$
VM – phase 4	QT = 256.6295 + 0.1399. RR	$p < .01$
	QT = 398.253 – 0.5627. HR	$p < .01$
All 4 phases of VM together	QT = 266.0046 + 0.1296. RR	$p < .01$
	QT = 406.6245 – 0.6117. HR	$p < .01$

NV – normal ventilation, HR – heart rate

DISCUSSION

The ventricular repolarisation is inhomogeneous, its differences exist between the left and the right ventricle, between the epicardium, mid-myocardium (M cells), and endocardium, and between the cardiac base and the apex. These differences (increased or decreased) are influenced by various physiological, pharmacological, and pathological interventions (*14*), such as autonomic tone, hypoxia, ischaemia, cardiac hypertrophy, temperature, drugs or ionic imbalance. It was demonstrated that the QT-RR relationship pattern varied significantly already among healthy individuals but their intraindividual stability was observed as well (*15*). Statistical significance of the QT interval differences is also dependent on the mode of QT expression (measured QT, corrected QT or QT together with its heart rate – *16*).

We studied the female gender only since it is considered to be a risk factor for ventricular arrhythmias. Clinical and experimental observations suggest the existence of true differences in the electrophysiological properties between the sexes (*17, Table 1, 18*). Oestrogen has an impact on the electrophysiological properties of the heart. The progestin-oestrogen replacement therapy significantly reduces ventricular QT-dispersion compared to the control group, while only oestrogen replacement therapy significantly prolongs QTc-intervals without affecting QT-dispersion (*19*). At physiological resting heart rates, the spatial ST-T vector voltage time trajectory is steeper in men than in women (*20*). Since the QT and RR intervals alter with increased or decreased heart rates, many formulae for QT correction (removing the rate dependence) were introduced within the last 80 years. The Bazett's formula for QTc calculation merely diminishes but does not remove the rate dependence (*Table 2*).

These recent results prove our previous ones (*5*) that the Valsalva manoeuvre decreases the dependence of the QT interval on the heart rate. This means that QT duration shortens more slowly with increasing heart rate during the Valsalva manoeuvre. The insignificant differences among the regression lines in all four phases of the Valsalva manoeuvre are probably produced by not very different QT, RR, and QTc values in every phase of the manoeuvre (*Table 2*). At the present time it is generally accepted that alterations of the QT dependence on the heart rate are produced by altered autonomic nervous activity.

There are two different morphologically and functionally autonomic innervations of the heart. The vagus nerves supply predominantly the atria and the conductive system of the heart and influence mostly the cardiac HR or RR intervals and conduction velocity in the atria. The chronotropic parasympathetic influence (RR interval or heart rate) is realised mainly through the right vagus nerve (*21*) acting predominantly on the sinus node. A vagus nerve stimulation exerts only minimum effects on ventricular functions. In ventricles the sympathetic nerves influence the QT interval duration, excitability, and contractility. A recent study (*22*) shows the heterogeneity of sympathetic innervation in various kinds of pathological conditions in the normal human heart – the inferoposterior region shows distinctly less sympathetic innervation than the anterior region.

The effect of autonomic nerves on the heart and QT interval is complex but the cardiac autonomic blockade in the ganglia prolongs the QTc interval (*23*). Parasympathetic postganglionic acetylcholine is removed very rapidly from the muscarinic receptors by acetylcholine esterase and alterations of the RR interval are substantially different already from beat to beat (fast cardiac control). The sympathetic postganglionic noradrenaline is metabolised longer (slow cardiac control), most of its amount is reuptaken, and QT duration is not substantially altered within several cardiac cycles (*24)*. The simultaneous slow and fast controls of the heart are the cause of the obtained results during the Valsalva manoeuvre: QT is relatively stable but RR alters very markedly, or sometimes one parameter is shortened and the other prolonged.

However, the RR interval duration is not a result of the quantity of sympathetic or parasympathetic activity. There is no physiological evidence that the levels of sympathetic and vagal nerve fluctuations are balanced (*25*). Already in the first half of the twentieth century the different branches of the cardiac plexus were named according to their main function (acceleratory, slowing or strengthening nerves). Thus, the cardiac autonomic nerves were divided according to their function.

In conclusion, unequal alterations in QT interval duration within VM can be produced by a relatively slow adaptation of the QT interval to changes in the heart rate (*24, 26*). Beat-to-beat adaptation of the QT interval is therefore not always parallel with RR alterations. In women but not in men there are also race differences in the QRS interval, P and QRS wave axes but not in the QT interval (27). Dispersion of the QT interval and other ECG variables of dispersion of ventricular repolarisation are independent on the heart rate.

A c k n o w l e d g e m e n t

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REGRESNÉ PRIAMKY QT-RR POČAS VALSALVOVHO POKUSU U MLADÝCH ZDRAVÝCH ŽIEN SÚ ODLIŠNÉ OPROTI POKOJOVÝM PODMIENKAM

S ú h r n

Cieľom práce bolo zistiť zmeny regresných priamok QT-RR a QT-HR počas všetkých fáz Valsalvovho pokusu (VP) oproti pokojnému dýchaniu (NVP) u slovenských mladých zdravých žien. Elektrokardiogram 28 zdravých žien (18–24 rokov) bol registrovaný počas NVP (kontrola) a počas 4 fáz VP (20 s pri 40 mmHg = 5.33 kPa) počas dňa (9:00 až 17:00). Vzťah QT-RR voči NVP bol vyjadrený pomocou manuálne meraných zmien intervalov QT, RR a QTc (párový t-test) a regresnými priamkami QT = a + b.RR aj QT = a + b.HR. Srdcová frekvencia, intervaly QT, RR a QTc boli oproti NVP signifikantne odlišné ($p < 0.001$) počas všetkých fáz VP, priebeh regresných priamok bol tiež odlišný ($p < 0.01$). Nezávislosť medzi trvaním QT a RR intervalov bola najzreteľnejšia vo fáze 4. Záverom konštatujeme, že intervaly QT, RR, QTc a regresné priamky QT = a + b.HR aj QT = a + b.RR sú počas VP signifikantne odlišné od NVP.

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