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## THE QTc INTERVAL DURATION CLASS AND CLINICAL FEATURES OF PATIENTS WITH PACEMAKERS IN THE ACUTE POSTOPERATIVE PERIOD

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The clinical features of 124 patients (63 men and 61 women) in the acute postoperative period after implantation of the pacemaker (ECS) in the various classes of corrected QTc interval duration of stimulated complexes were investigated. Evaluation was made by sex and age of the patients, chronic forms of ischemic heart disease (CIHD): postinfarction cardiosclerosis, stable angina (I–IV functional classes (FC)); stable angina (I–IV FC), arterial hypertension (AH) — 1–3 degrees and stages (1–4), type of diabetes mellitus (DM), atrial fibrillation (AF) (paroxysmal and persistent, permanent), chronic heart failure (CHF) — stages I–III, I–IV FC; functional indicators before pacemaker implantation and in the acute postoperative period (3–5 days after surgery): QTc interval duration, heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP); ejection fraction (EF) of the left ventricle (LV), anterior-posterior size of the left atrium (LA), end-systolic volume (ESV) and end-diastolic volume (EDV), the thickness of the back wall of the left ventricle (AP LV), the thickness of the interventricular septum (IVS), left ventricular mass (LVM). The patients were divided into 3 classes: class 1 — normal QTc (320–440 ms) — 27 (22 %) patients, class 2 — elongated QTc (> 440 ms) — 97 (78 %) patients. Standard statistical procedures using Microsoft Excel were applied for data processing. The results showed that QTc interval duration of stimulated complexes in the acute postoperative period after pacemaker implantation can be established in a physiological range in 22 % of patients, and in 78 % — it remains longer or even elongated. Elongation associated with a higher incidence and the increase of FC and stages of heart failure, high values of ESV and EDV, mostly in the pacing mode VVI/VVIR and DDD/DDDR. Patients with a pacemaker require more careful monitoring the stimulation parameters as well as ongoing drug therapy.

**KEY WORDS:** pacing, cardiac resynchronisation therapy, electrocardiography, interval QTc

### КЛАС ТРИВАЛОСТІ ІНВАЛУ QTc ТА КЛІНІЧНІ ОСОБЛИВОСТІ ПАЦІЄНТІВ З ІМПЛАНТОВАНИМИ ЕЛЕКТРОКАРДІОСТМУЛЯТОРАМИ В ГОСТРОМУ ПІСЛЯОПЕРАЦІЙНОМУ ПЕРІОДІ

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Досліджені клінічні особливості 124 пацієнтів (63 чоловіків и 61 жінка) в гострому післяопераційному періоді після імплантації електрокардіостимуляторів (ЕКС) в різних класах тривалості коригованого інтервалу QTc стимульованих комплексів. Оцінювали: стать, вік пацієнтів; форми хронічної ішемічної хвороби серця (ХІХС): постінфарктний кардіосклероз, функціональні класи (ФК) стабільної стенокардії (I–IV); стадії артеріальної гіпертензії (АГ) (I–III) ті ступіні АГ (1–3), тип цукрового діабету (ЦД); форми фібриляції передсердь (ФП) (пароксизмальна та персистуюча, постійна); ФК (I–IV) та стадії (I–III) хронічної серцевої недостатності (ХСН); функціональні показники до імплантації ЕКС та в гострому післяопераційному періоді (на 3–5 добу): тривалість коригованого інтервалу QTc, частоту серцевих скорочень (ЧСС), фракцію вигнання (ФВ), кінцево-сістолічний та кінцеводіастолічний об'єми (КСО та КДО) лівого шлуночку (ЛШ), товщину задньої стінки (ЗС) ЛШ, товщину міжшлуночкової перетинки (МШП), масу міокарду лівого шлуночку (ММЛШ), передньо-задній розмір лівого передсердя (ЛП). Пацієнти були розділені на класи: клас 1 — нормального QTc (320–440 мс) — 27 пацієнтів (22 %), клас 2 — подовженого QTc (> 440 мс) — 97 (78 %) пацієнтів. Для обробки даних були використані стандартні статистичні процедури за допомогою Microsoft Excel. Результати показали, що в гострому післяопераційному періоді після імплантації ЕКС у 22 % пацієнтів тривалість інтервалу

QTc стимулированных комплексов можно встановити в фізіологічному діапазоні значень та у 78 % — вона продовжує залишатися довгою чи навіть подовжується. Подовження асоціюється з більшою частотою розвитку та збільшенням ФК і стадій ХСН, більшими значеннями КСО и КДО, насамперед в режимах стимуляції VVI/VVIR та DDD/DDDR. Пацієнти з ЕКС потребують більш ретельного контролю як параметрів стимуляції, так і терапії, що проводиться.

**КЛЮЧЕВІ СЛОВА:** електрокардіостимуляція, кардіоресинхронізуюча терапія, електрокардіографія, інтервал QTc

### **КЛАСС ПРОДОЛЖИТЕЛЬНОСТИ ИНТЕРВАЛА QTc И КЛИНИЧЕСКИЕ ОСОБЕННОСТИ ПАЦИЕНТОВ С ИМПЛАНТИРОВАННЫМИ ЭЛЕКТРОКАРДИОСТИМУЛЯТОРАМИ В ОСТРОМ ПОСЛЕОПЕРАЦИОННОМ ПЕРИОДЕ**

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Исследованы клинические особенности 124 пациентов (63 мужчин и 61 женщина) в остром послеоперационном периоде после имплантации электрокардиостимулятора (ЭКС) в различных классах продолжительности скорректированного интервала QTc стимулированных комплексов. Оценивали пол, возраст пациентов; формы хронической ишемической болезни сердца (ХИБС): постинфарктный кардиосклероз, функциональные классы (ФК) стабильной стенокардии (I–IV); стадии артериальной гипертензии (АГ) (I–III) и степени АГ (1–3), тип сахарного диабета (СД); формы фибрилляции предсердий (ФП) (пароксизмальная и персистирующая, постоянная); ФК (I–IV) и стадии (I–III) хронической сердечной недостаточности (ХСН); функциональные показатели до имплантации ЭКС и в остром послеоперационном периоде (на 3–5 сутки): продолжительность скорректированного интервала QTc, частоту сердечных сокращений (ЧСС), фракцию выброса (ФВ), конечно-систолический и конечно-диастолический объемы (КСО и КДО) левого желудочка (ЛЖ), толщину задней стенки (ЗС) ЛЖ, толщину межжелудочковой перегородки (МЖП), массу миокарда левого желудочка (ММЛЖ), переднезадний размер левого предсердия (ЛП). Пациенты были разделены на классы: класс 1 — нормального QTc (320–440 мс) — 27 (22 %) пациентов, класс 2 — удлиненного QTc (> 440 мс) — 97 (78 %) пациентов. Для обработки данных использовались стандартные статистические процедуры с помощью Microsoft Excel. Результаты показали, что в остром послеоперационном периоде после имплантации ЭКС у 22 % пациентов продолжительность интервала QTc стимулированных комплексов удается установить в физиологическом диапазоне значений и у 78 % — она продолжает оставаться дольше или даже удлиняется. Удлинение ассоциируется с большей частотой развития и увеличением ФК и стадий ХСН, большими значениями КСО и КДО, преимущественно в режимах стимуляции VVI/VVIR и DDD/DDDR. Пациенты с ЭКС нуждаются в более тщательном контроле как параметров стимуляции, так и проводимой медикаментозной терапии.

**КЛЮЧЕВЫЕ СЛОВА:** электрокардиостимуляция, кардиоресинхронизирующая терапия, электрокардиография, интервал QTc

Output of corrected QT interval duration (QTc) values beyond physiological scope, so-called qualified shortening and elongation, is an important prognostic factor among patients with sinus rhythm and with implanted pacemakers (PM) [1–3].

However, the possible link of the stimulated QTc interval duration complexes and clinical features of patients with implanted pacemakers in the acute postoperative period is not reported in the literature.

**Aims:** to evaluate the link between the classes of stimulated QTc interval duration under different modes of permanent cardiac pacing

with the clinical features of patients in the acute postoperative period.

### **MATERIALS AND METHODS**

124 patients aged  $68 \pm 8$  (M  $\pm$  sd) (61 — female, 63 — male) were examined in the department of ultrasound and instrumental diagnostics with miniinvasive interventions of SI «Zaycev V. T. Institute of General and Urgent Surgery of NAMS of Ukraine», among them — 29 patients has sinus node dysfunction (SND), 78 patients — atrio-ventricular block (AVB) (57 — III degree, 16 — II degree, 5 — I degree), 40 — atrial fibrillation (AF), 7 —

dilated cardiomyopathy (DCMP). All patients were underwent permanent pacing therapy from 2006 to 2012 in modes: DDD (25 patients) and DDDR (42 patients), among them 29 patients with mainly atrial pacing (more than 90 %), VVI (36 patients), VVIR (12 patients), cardiac resynchronization therapy (CRT) (9 patients).

Evaluation was made by sex and age of the patients, chronic forms of ischemic heart disease (CIHD) — postinfarction atherosclerosis, stable angina (I–IV functional classes (FC)) [4]; stable angina (I–IV functional classes (FC)), arterial hypertension (AH) — 1–3 degrees and stages (1–4), type of diabetes mellitus (DM), atrial fibrillation (AF) (paroxysmal, persistent and permanent), chronic heart failure (CHF) — stages I–III, I–IV (FC) [4]; functional indicators before pacemaker implantation and in the acute postoperative period (3–5 days after surgery): QTc interval duration, heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP); figures echocardiography: ejection fraction (EF) of the left ventricle (LV), anterior-posterior size of the left atrium (LA), end-systolic volume (ESV) and end-diastolic volume (EDV), the thickness of the back wall of the left ventricle (AP LV), the thickness of the interventricular septum (IVS), left ventricular mass (LVM).

To measure the duration of the QT interval and heart rate of the patients before and after pacemaker implantation (3–5 days after surgery) were recorded on a computer ECG electrocardiograph «Cardiolab+» (HAI-Medica). The stimulated QTc interval duration was measured after the removal of the stimulus artifact in three consecutive complexes of the Q wave to the beginning of the descending segment of the return of the T wave in leads to the contour II, V5, and V6 with choosing of a maximum value. The corrected QT interval duration (QTc) of the patients with spontaneous rhythm and pacing was calculated by the Bazett formula:  $QTc = QT / (RR \wedge 0,5)$ . For patients with AF, QTc was calculated using the formula  $QTc = QT + 0,154 \times (1000 - RR)$  Farmingem study for patients with atrial fibrillation [12], the measurement accuracy — 0,5 ms. SBP and DBP were measured by tonometer Microlife BP AG1-20 Korotkov method, the measurement accuracy — 1 mm Hg.

Echocardiography was conducted by the ultrasound machine Siemens Cypress and Toshiba Applio 400. RA, LA, RV sizes, end-systolic size (ESS), end-diastolic size (EDS)

and AP LV, IVS thickness was measured. EDV and ESV were calculated by the method of Simpson. LVEF was calculated using the formula  $LVEF = (EDV - ESV) / EDV * 100 \%$ . Left ventricular mass (LVM) was calculated according to the formula Devereux:  $LVM = 1,04 * ((AP \text{ LV} + IVS + ESS)^3 - ESS^3) - 13,6$  [2]. The measurement accuracy was 0,5 mm. For the calculation of ejection fraction (EF) using the formula  $PV = SV / EDV$  [5].

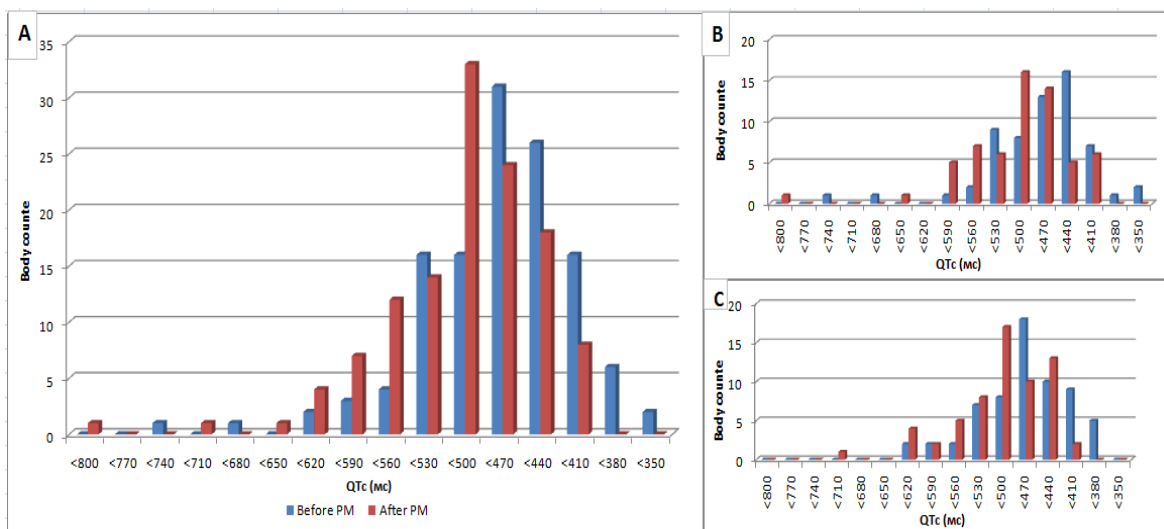
The patients with pacemakers were divided into 3 classes of stimulated QTc interval duration: Class 1 — normal (in the physiological range of values) — 320–439 ms, Class 2 — (qualified) an elongated QTc — > 440 ms, and Class 3 — (qualified) shortened the QTc — < 320 ms [10]. Values and/or frequency of clinical signs in the classes were estimated in the total sample, and electrophysiological parameters, moreover, a separate group with mainly atrial pacing.

The data were processed after formation the Microsoft Excel and Statistica base. For statistical evaluation of the results, the parametric criteria (mean — M, standard deviation — sd) and nonparametric ones (absolute (n, number) and relative (percentage of (p, %) and the mean percentage error (sP), the criterion  $\chi^2$ ) units) were used. The probability of differences between groups was determined using a non-parametric U — Mann-Whitney test. The expected result is determined by levels of reliability  $p < 0,01$  and  $p < 0,05$ .

## RESULTS AND DISCUSSION

Distribution of QTc interval duration in the studied group of patients before pacemaker implantation was close to normal with the mode in the physiological range. Ventricular stimulation did not change its shape, but moved stimulated QTc interval duration to higher values (Fig. 1A). Sex differences were not found (Fig. 1B, C).

There are a 27 (22 %) patients in class 1 (male — 16, female — 11, in the stimulation mode DDD / DDDR — 11 patients (41 %), VVI/VVIR — 16 patients (59 %), patients with mainly atrial pacing — 10 (37 %)) and 97 patients (78 %) in class 2 (male — 47, female — 50, in the stimulation mode DDD/DDDR — 56 patients (58 %), VVI/VVIR — 32 patients (33 %), CRT — 9 patients (9 %)), patients with mainly atrial pacing — 19 (20 %)). In class 3, there was not a single patient. Average duration of the QTc interval in class 1 patients has not

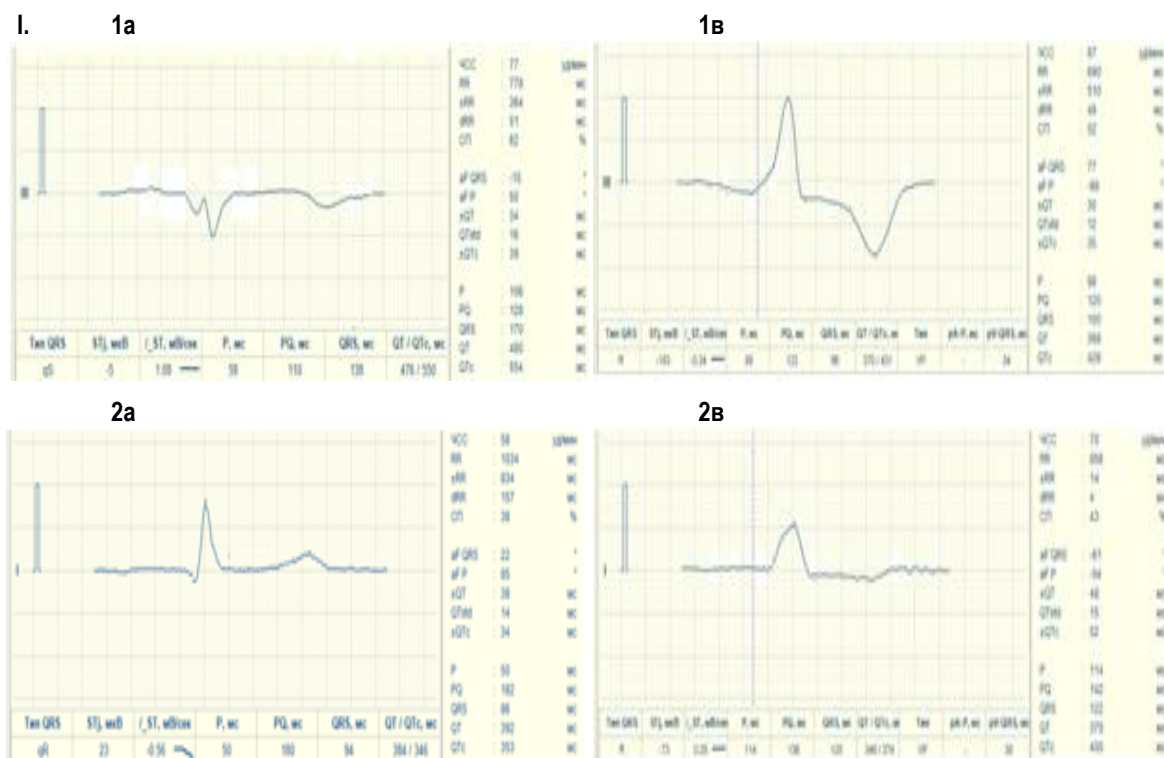


**Fig. 1. Distribution of QTc interval duration before and after (stimulated) pacemaker implantation in the studied group of patients, including those of female (B) and male (C) sex**

changed (from  $420 \pm 53$  ms, to  $419 \pm 14$  ms) and class 2 patients — lengthened (from  $460 \pm 48$  ms to  $506 \pm 42$  ms), but neither in the first nor the second did not reflect the essence of individual patient.

QTc interval duration before and after pacemaker implantation in acute postoperative period in 15 (56%) patients of class 1 was within the physiological range of values and in

12 (44%) — initially extended and shortened to class 1 after pacemaker implantation. QTc interval before and after pacemaker implantation was lengthened in 61 (63%) patients of class 2, and in 36 (37%) — extending from physiological values to class 2 after pacemaker implantation. Individual changes in the QTc interval duration in response to the pacing for classes 1, 2, and transitions between them are shown in Fig. 2.



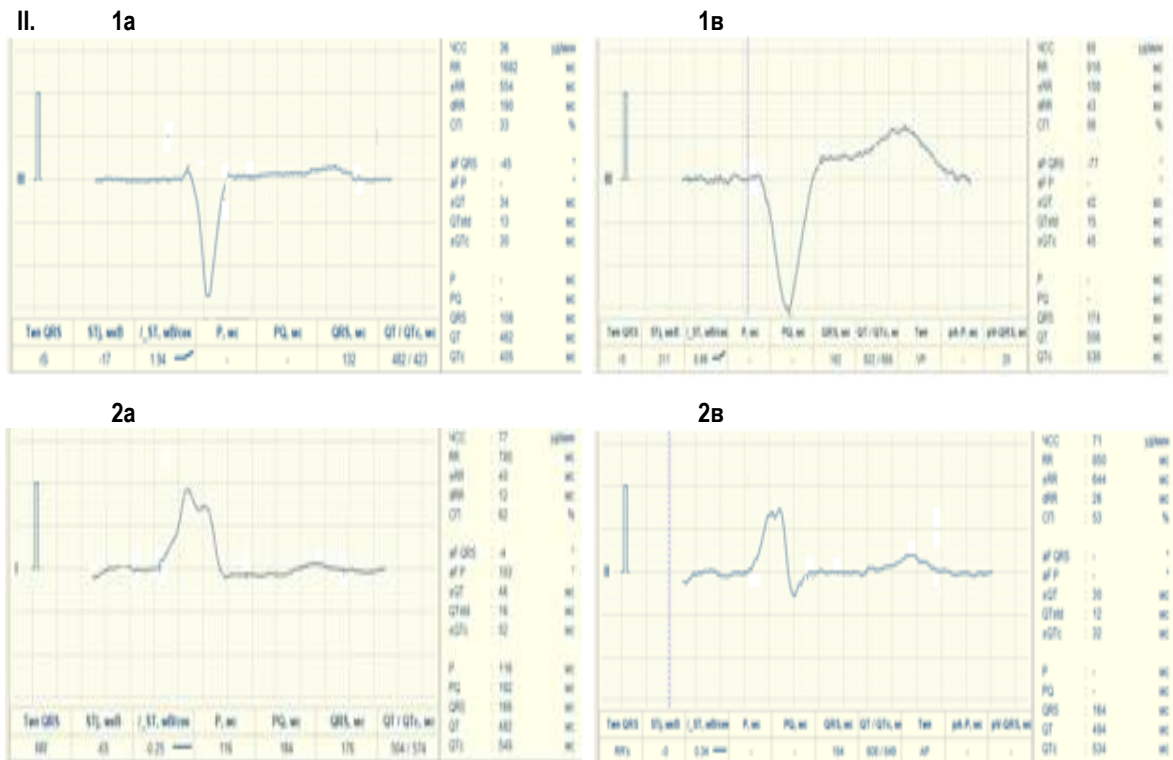


Fig. 2. Individual changes in the QTc interval duration of the in patients' response to the pacing

Legend:

I — class 1:

1 — shortening initially extended to normal QTc, 2 — changes within class 1;

II — class 2:

1 — elongation initially normal to lengthened QTc, 2 — changes within class 2;

a — before pacemaker implantation, b — after pacemaker implantation

QTc interval duration in patients with mainly atrial pacing was similar to that of the total sample before and after pacing in classes (in the class 1:  $421 \pm 35$  ms before and  $412 \pm 12$  ms after stimulation vs  $420 \pm 53$  and  $419 \pm 14$  ms in the total sample ( $p > 0,05$ ); in

the class 2:  $432 \pm 57$  ms and  $505 \text{ ms} \pm 39$  vs  $460 \pm 48$  and  $506 \pm 42$  ( $p > 0,05$ ), respectively).

Clinical features of patients with pacemakers are presented in the classes of stimulated QTc interval duration in the acute postoperative period in Table 1.

Table 1

Clinical features of patients with pacemakers in the classes of stimulated QTc interval duration in the acute postoperative period (% ± p)

Clinical features		All off patients, the proportion of total (n, % ± p)	Class of stimulated QTc interval duration			
			Class 1	Class 2		
Sex (n, % ± p)	Male	63, (51 ± 4)	25 ± 5	75 ± 5		
	Female	61, (49 ± 4)	18 ± 5	82 ± 5		
Age (M ± sd, years)		124	68 ± 7	68 ± 9		
Diseases	CIHD	Postinfarction cardiosclerosis (n, %±p)	16, (13 ± 3)	7 ± 5	14 ± 4	
		Stable angina (n, % ± p)	Total	49, (40 ± 4)	48 ± 10**	37 ± 5
			FC I	13, (27 ± 6)	38 ± 13	22 ± 7
			FC II	22, (45 ± 7)	62 ± 13*	39 ± 8*
			FC III	11, (22 ± 6)	—	31 ± 8*
FC IV	3, (6 ± 3)	—	8 ± 5			

Continuation of table 1

Arterial hypertension (n, % ± p)	Total		102, (82 ± 3)	85 ± 7	81 ± 4	
	Stage	I	5, (5 ± 2)	4 ± 4	5 ± 2	
		II	56, (55 ± 5)	57 ± 10*	54 ± 6*	
		III	39, (40 ± 5)	39 ± 10	41 ± 6	
	Degree	1	39, (40 ± 5)	43 ± 10*	41 ± 6*	
		2	27, (26 ± 4)	17 ± 8	29 ± 5	
		3	13, (13 ± 3)	9 ± 6	10 ± 3	
	Diabetes mellitus (n, % ± p)	Total		17, (14 ± 3)	4 ± 4	16 ± 4**
		Type 1		1, (6 ± 6)	—	6 ± 6
		Type 2		16, (94 ± 6)	100	94 ± 6*
Clinical syndromes	Atrial fibrillation (n, % ± p)	Total		40, (32 ± 4)	41 ± 9**	30 ± 5
		Paroxysmal and persistent		22, (55 ± 8)	64 ± 15*	52 ± 9
		Permanent		18, (45 ± 8)	36 ± 15	48 ± 9
	CHF (n, % ± p)	Total		92, (74 ± 4)	67 ± 9	76 ± 4**
		FC	I	9, (10 ± 3)	22 ± 10	7 ± 3
			II	42, (46 ± 5)	44 ± 12*	46 ± 6*
			III	35, (38 ± 5)	33 ± 11	39 ± 6
			IV	6, (6 ± 2)	—	8 ± 3
		Stage	I	11, (12 ± 3)	17 ± 9	11 ± 4
			IIA	55, (60 ± 5)	72 ± 11*	55 ± 6*
IIB			24, (26 ± 4)	6 ± 5	31 ± 5	
III	2, (2 ± 1)		—	3 ± 2		

Comment :

p — average percentage error, M — mean value, sd — standard deviation;

\* p < 0,05 — between the values in the classes after pacemaker implantation,

\*\* p < 0,05 — a class of values before and after pacemaker implantation

Age, sex, the proportion of patients with postinfarction cardiosclerosis, AH, the ratio of the degrees and stages of hypertension (prevalence of stage II, and 1 degree) in classes 1 and 2 were not statistically different. Stable angina was more frequent in the class 1 (p < 0,05), which was dominated by patients with FC II. In class 2 equally often met II and III angina. Patients with III and IV FC stable angina were represented only in class 2.

The amount of patients with type 2 diabetes in the 1 was smaller than in class 2 (p < 0,05). Diabetes mellitus type 1 was observed only 1 patient in Class 2.

AF was more frequent in class 1 than in class 2 (p < 0,05). In class 1 prevailed over paroxysmal and persistent AF constant (p < 0,05), in class 2 statistically significant differences in their frequencies were not. CHF was observed more frequently in class 2 (p < 0,05). In both classes of patients with FC II and stage IIA CHF are prevail (p < 0,05), III and IV CHF stage was more frequent in class 2.

Functional performance in the classes of stimulated QTc interval duration before pacemaker implantation and in the acute postoperative period are shown in Table 2.

The average heart rate after pacemaker implantation in both classes was established more than before to 7 1/min in class 1 and 13 1/min in class 2.

Systolic and diastolic blood pressure, ejection fraction, antero-posterior size of the LA, the thickness of the IVS and AP LV, and average LVM did not differ significantly in classes of patients, and in each of them before and after pacemaker implantation, except for the mean value of ESV and EDV, which were larger before pacemaker implantation, and have a direct correlation with the QTc interval duration (p < 0,05).

Distribution of the QTc interval within adults was close to normal [6]. Our data regarding it among patients with bradyarrhythmia before and after pacemaker implantation are new.

In the present study confirmed the individuality of the QTc interval duration reactions to stimulation with shortening and lengthening among some other patients after pacemaker implantation. Prochnau at al. [7] were observed QTc interval shortening among patients with CRT and Medina-Ravell VA at al. [8] — its elongation among patients with biventricular

Table 2

**Functional performance in the classes of stimulated QTc interval duration  
in the acute postoperative period before and after pacemaker implantation (M ± sd)**

Functional performance		Class of stimulated QTc interval duration			
		Class 1		Class 2	
		Before pacing	Paced	Before pacing	Paced
HR (M±sd, 1/min)		61 ± 11	68 ± 6**	58 ± 16	71 ± 9**
BP	SBP (M ± sd, mm Hg)	143 ± 19	137 ± 17	145 ± 15	145 ± 17
	DBP (M ± sd, mm Hg)	83 ± 10	82 ± 10	84 ± 11	84 ± 10
Figures echocardiography	EF (M ± sd, %)	45 ± 8	52 ± 9	41 ± 10	51 ± 13
	LA (M ± sd, sm)	4,6 ± 0,5	4,4 ± 0,5	4,7 ± 0,6	4,5 ± 0,7
	ESV (M ± sd, ml)	62 ± 27*	41 ± 32**	109 ± 35*	87 ± 55**
	EDV (M ± sd, ml)	170 ± 31*	149 ± 36**	226 ± 42*	179 ± 60**
	AP LV (M ± sd, sm)	1,23 ± 0,1	1,23 ± 0,11	1,2 ± 0,16	1,19 ± 1,15
	IVS (M ± sd, sm)	1,22 ± 0,15	1,23 ± 0,13	1,2 ± 0,14	1,2 ± 0,18
	LVM (M ± sd, g)	331 ± 63	337 ± 71	341 ± 90	331 ± 86

*Comment :*

M — mean value, sd — standart deviation;

\* p < 0,05 — between the values in the classes,

\*\* p < 0,05 — a class values before and after pacemaker implantation

pacing, which was associated with an unfavorable increase in transmural dispersion of repolarization.

The possibility of lengthening the duration of the QTc interval with a qualified going beyond the physiological range of values was shown in all studied modes of stimulation performed by us, unlike J.A. Chiladakis et al. [9]. The probable reason for this is the large amount of patients with baseline repolarization disorders and borderline QTc values before pacemaker implantation among some patients [10], a few CRT implantations for economic reasons, as well as the selection of sub-optimal stimulation parameters and drug therapy.

We also found that the duration of the QTc interval among patients with SND after pacemaker implantation with mainly atrial pacing is similar to that among patients with other modes of stimulation.

A large proportion of heart failure, higher stage and CHF FC, FC stable angina, higher EDV and ESV among patients with impaired repolarization and a prolonged QTc interval were identified by us, as T. Ishikawa at al. [11]. As for the greater incidence of type 2 diabetes mellitus in the class of QTc prolongation in patients with a pacemaker, such data in the literature was not found.

Taking into consideration that the lengthening of the QTc interval associated high risk of acute cardiovascular events up to sudden car-

diac death [7, 12, 13], these results require a dedicated research.

Patients with a qualified lengthening of the QTc interval after pacemaker implantation for permanent pacing in the acute postoperative period require more attention and in optimization of its parameters, and in therapeutic management.

## CONCLUSIONS

1. Pacemaker implantation in all modes of stimulation has a modifying effect on the QTc interval duration in the acute postoperative period, with 22 % of patients in the physiological range of values, and in 78 % — it continues to be long or even elongates.

2. Prolongation of stimulated QTc interval duration associated with the increase in FC and stages of heart failure, high values of CSR and EDV, mainly in VVI/VVIR and DDD/DDDR modes of stimulation.

3. Patients require more careful monitoring of the stimulation parameters and ongoing drug therapy, because of the potential for permanent pacemaker lengthening of the QTc interval.

## PROSPECTS FOR FURTHER RESEARCH

It seems appropriate to investigate the relationship changes of the QTc interval duration among patients with implanted pacemaker due to the stimulation parameters and characteristics of ongoing drug therapy.

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