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The role of short- and long-term electrocardiography in the additional assessment of severity and prognosis in patients with non-high risk acute pulmonary embolism

Rola krótko- i długoterminowej rejestracji elektrokardiograficznej w dodatkowej ocenie ciężkości i rokowania u pacjentów z ostrą zatorowością płucną niewysokiego ryzyka

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Abstract

Introduction. In acute pulmonary embolism (APE), various abnormalities are reported in short- and long-term electrocardiographic monitoring. However, their importance in determining the severity and prognosis of APE is not well understood.

Materials and methods. Patients with confirmed non-high-risk APE were included in the study. Immediately after admission, standard examinations along with 12-lead electrocardiogram (ECG), echocardiography, cardiac troponin and NT-proBNP concentration and 24-hour Holter monitoring with assessment of heart rate variability were performed.

Results. Of the 204 patients, 197 were finally examined, aged 59 years (Q1–Q3: 44–73), and 54% were women. According to recent guidelines 59 (30%) patients were classified into low risk of early mortality, 66 (34%) into intermediate-low, and 72 (36%) into intermediate-high categories. Significant differences in the ECG evaluation were revealed between the groups of patients with low, intermediate-low and intermediate-high risk APE for the following parameters: S1Q3T3 patterns ($p = 0.02$), limb leads voltage < 5 mm ($p = 0.02$), inverted T waves in V1–V4 ($p = 0.0002$), ST-segment depression in V1–V4 ($p = 0.04$), as well as for ECG without abnormalities ($p = 0.0005$). Moreover, in examined groups, significant differences were noted for most of the Holter-derived cardiac autonomic tone parameters.

Conclusions. The authors confirmed the potentially important role of electrocardiography in managing patients with newly diagnosed APE. The present results suggest the potential usefulness of these methods in an indirect estimation of the severity of APE, which may be useful before biomarkers or echocardiography results are available. Observed was also more impaired cardiac autonomic tone, along with increasing severity of APE. These findings indicate the need for further evaluation to determine the clinical significance of the study results.

Keywords: acute pulmonary embolism, electrocardiography, Holter monitoring, heart rate variability, early mortality risk

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Introduction

Despite continuous improvement in diagnostic and therapeutic capabilities, venous thromboembolism with its most prominent manifestation i.e. acute pulmonary embolism (APE), remains the third most frequent acute cardiovascular event, with an annual incidence of 100–200 per 100,000 population [1]. Various patterns in the 12-lead electrocardiogram (ECG) are recognized to be associated with APE, however, their role in managing patients with APE has not been elucidated yet [2]. On the other hand, data on 24-hour Holter monitoring or other long-term electrocardiography monitoring in the assessment of the clinical status and prognosis of patients with APE is sparse, thus limiting its practical application.

Therefore, this study was performed to assess the usability of short- and long-term electrocardiography in determining the clinical status and evaluating the prognosis of patients with APE. In the previous study, the authors proved a significant association between a more severe clinical presentation of APE and impaired heart rate variability (HRV) parameters, obtained during 24-hour Holter monitoring [3]. In the current study, the focus was on determining the role of different types of electrocardiographic methods in assessing the clinical severity and short-term prognosis of patients with APE. To the authors' knowledge, such a complex electrocardiographic approach in the early stages of APE, which includes both a standard 12-lead ECG and sophisticated 24-hour Holter monitoring with HRV analysis, is completely novel and has not been previously presented in the literature.

Materials and methods

Study population

A prospective, single-centre, cross-sectional observational study was conducted over 9 years. At baseline, adult patients admitted to the study intensive cardiac care unit due to APE were enrolled. Each APE diagnosis was confirmed by diagnostic imaging, mainly computed tomography pulmonary angiogram (CTPA). According to protocol, detailed clinical assessment along with laboratory tests (including NTproBNP and cardiac troponin levels) and 12-lead ECG were done at admission, while transthoracic echocardiography and 24-h Holter monitoring were performed within the first 24 hours (in few cases within the initial 48 hours).

Afterwards, the prognosis of APE was determined according to recent European Society of Cardiology (ESC) guidelines [4]. In terms of the present data analysis, a retrospective assignment to risk categories defined in the 2019 ESC Guidelines for the Management of APE was done. Patients with symptoms of haemodynamic instability were classified as high-risk and were not included in the study. Patients were treated according to contemporary ESC guidelines. No deaths were observed in the non-high-risk APE study population during hospitalization.

At enrolment, all patients gave their informed consent to participate in the study. This study was conducted in accordance with the amended Declaration of Helsinki and approved by the local ethics board.

Echocardiography, 12lead electrocardiography, and 24-hour Holter monitoring

Transthoracic echocardiography was performed using a Philips iE33 ultrasound system (Philips Medical System, Andover, MA, USA) with a 2.53.5 MHz transducer. Patients were examined in the left lateral position. All standard dimensions, valve morphology and function, left ventricular ejection fraction (LVEF), and all required right heart parameters were evaluated by experienced experts in echocardiography and assessed according to the current American and European recommendations [5]. Emphasis on right ventricle (RV) parameters was placed, including RV, AcT, TAPSE, RVSP and IVC (full explanation of abbreviations in the footnote to Table 1).

Standard 12-lead ECG was obtained using an ECGdevice (Philips, Page Trim III, NL) at 25 mm/second paper speed. Careful analysis of electrocardiograms was performed before reviewing the APE diagnosis by qualified cardiologists or trained students, according to guidelines based on the American Heart Association, the American College of Cardiology Foundation and the Heart Rhythm Society Recommendations for the Standardization and Interpretation of the Electrocardiogram, published in six parts in 2007–2009. The focus was on the presence of signs which are well known to be associated with right ventricular overload in APE: tachycardia > 100 bpm, right axis deviation, right bundle branch block (RBBB), qR pattern in V1 lead, S1Q3T3 and S1S2S3 patterns, notches S waves in V1–V2 leads, P pulmonale occurrence, limb leads voltage < 5 mm, inverted T-waves in V1–V4 leads, ST-segment depression in V1–V4 leads, ST-segment elevation in aVR and/or V1 leads and supraventricular arrhythmias (SVA in ECG). SVA was a merged group which included supraventricular ectopic beats, supraventricular tachycardia, and atrial fibrillation (AF) or flutter (Table 2).

Performed was also 24-hour Holter monitoring with HRV analysis using 3-channel digitized recordings (Lifecard CF, Spacelabs Healthcare, Snoqualmie, WA, USA). Qualified specialist performed routine evaluations of heart rates and various arrhythmias using careful manual review and filtering algorithms (Sentinel Impresario, Spacelabs Healthcare, USA). In addition, time-domain HRV analysis was done and indices representing both sympathetic and parasympathetic function of the cardiac autonomic nervous system (cANS) were calculated. The following 4 indices were included in the study: SDNN, SDANN, RMSSD, and triangular index (full explanation of abbreviations in the footnote

Table 1. Patient characteristics by severity of acute pulmonary embolism (APE) category on admission: general characteristics, echocardiographic parameters and cardiac biomarkers.

Characteristic	All APE patients (n = 197)	Low-risk APE (n = 59)	Intermediate low-risk APE (n = 66)	Intermediate high-risk APE (n = 72)	p-value
General characteristics					
Age (years)*	59 (44–73)	52 (3173)	59 (44–70)	61 (49–74)	0.12[KW]
Females (no., %)	106 (54%)	31 (53%)	35 (53%)	40 (56%)	0.91[F]
Systolic blood pressure [mmHg]*	130 (120–140)	130 (117–140)	132 (128–140)	127 (120–138)	0.03[KW]
Pairwise comparison[CI]		A, B	B	A	
Echocardiographic parameters of right ventricular overload					
RV [mm]	37.0 ± 6.8	32.9 ± 4.9	34.9 ± 5.0	42.3 ± 6.2	< 0.000001[A]
Pairwise comparisons[FLSD]		A	B	C	
AcT [ms]	83 ± 29	106 ± 24	87 ± 27	61 ± 16	< 0.01[A]
Pairwise comparisons[FLSD]		C	B	A	
TAPSE [mm]	21.0 ± 4.4	23.7 ± 3.2	21.6 ± 3.8	18.1 ± 4.1	< 0.000001[A]
Pairwise comparisons[FLSD]		C	B	A	
RVSP [mmHg]	42.4 ± 21.1	26.3 ± 6.8	44.7 ± 26.3	53.5 ± 14.7	< 0.000001[A]
Pairwise comparisons[FLSD]		A	B	C	
IVC [mm]	15.7 ± 4.1	13.9 ± 2.9	15.4 ± 3.9	17.4 ± 4.4	0.000004[A]
Pairwise comparisons[FLSD]		A	B	C	
Biomarkers of right ventricular overload					
Abnormal cTn (no., %) **	134 (68.0%)	0 (0%)	62 (95.5%)	72 (100%)	-
NT-proBNP [pg/mL]	1465 ± 2051	153 ± 110	1668 ± 1568	2355 ± 2660	< 0.000001[A]
Pairwise comparisons[FLSD]		A	B	C	

*value expressed as median with interquartile range; **abnormal cTn — at least one elevated cardiac troponin T or cardiac troponin level, regardless of whether it was performed in the study or another centre, and also regardless of the laboratory method. Test of significance, p-value: KW-Kruskal-Wallis one-way Analysis of Variance, F — chi-square or Fisher's exact test, A — one way ANOVA for independent groups. *Pairwise comparisons*: CI — Test POST-HOC Conover-Iman, FLSD — Test POST-HOC Fisher's LSD: similar letters = insignificant difference, different letters = significant difference. AcT — pulmonary velocity acceleration time; cTn — cardiac troponin; IVC — inferior vena cava diameter; NT-proBNP — N-terminal-pro-B-type-natiuretic-peptide level; RV — right ventricle diameter; RVSP — right ventricular systolic pressure; TAPSE — tricuspid annulus plane systolic excursion

to Table 3). The choice of the subsequent parameters is considered sufficient for time-domain HRV analysis due to their strict correlation with other parameters [6].

Statistical analysis

IBM SPSS Statistics (version: *28.0.1.0[142]*) and PQStat (version: *1.8.6.*) were used to perform statistical analyses and to prepare all the visualizations. The Shapiro–Wilk test was used to examine if a variable was normally distributed. All the numerical values, which did not have a normal distribution, are presented as median and the first and third quartiles (Q_1–Q_3). Values characterized by a normal distribution are presented as means and standard deviations, while qualitative variables are presented as raw numbers and percentages. P-values below 0.05 are considered statistically significant. For interval scale variables that do not meet the condition of normal distribution and for all variables not characterized by a normal distribution the Kruskal–Wallis one-way Analysis of Variance test was used, while for quantitative variables with normal distribution, the one-way ANOVA test was employed. For nominal or independent variables the chi-square/ /Fisher's exact test was used. For variables characterized by a normal distribution, the POST-HOC Fisher's LSD, while for variables with a non-normal distribution, the POST--HOC Conover–Iman tests were performed. To estimate the relationship between the parameters, correlation coefficients were calculated. For quantitative variables, Spearman's rank correlation coefficient was used, while for the correlation of qualitative and quantitative variables, the eta correlation was used.

Table 2. Patient characteristics by acute pulmonary embolism (APE) severity category on admission: 12lead electrocardiographic features and its various abnormalities.

Characteristic	All APE patients (n = 197)	Low-risk APE (n = 59)	Intermediatelow--risk APE (n = 66)	Intermediatehigh risk APE (n = 72)	p-value
Mean heart rate [bpm]*	80 (7093)	79 (6688)	78 (68-95)	83 (73-95)	0.10[KW]
Sinus rhythm (no., %)	192 (97%)	56 (95%)	64 (97%)	72 (100%)	0.21
Tachycardia > 100 bpm (no., %)	28 (14%)	5 (8%)	13 (20%)	10 (14%)	0.22
Right axis deviation (no., %)	14 (7%)	3 (5%)	3 (5%)	8 (11%)	0.32
Right bundle branch block (no., %)	10 (5%)	4 (7%)	2 (3%)	4 (6%)	0.64
qR complexes in V1 (no., %)	17 (9%)	5 (8%)	2 (3%)	10 (14%)	0.14
S1Q3T3 pattern (no., %)	53 (27%)	12 (20%)	13 (20%)	28 (39%)	0.02
S1S2S3 pattern (no., %)	16 (8%)	5 (8%)	5 (8%)	6 (8%)	0.98
Notched S wave in V1–V2 (no., %)	28 (14%)	10 (17%)	7 (11%)	11 (15%)	0.64
P pulmonale (no., %)	6 (3%)	1 (2%)	4 (6%)	1 (1%)	0.21
Limb leads voltage < 5 mm (no., %)	11 (6%)	0 (0%)	3 (5%)	8 (11%)	0.02
Inverted T waves in V1–V4 (no., %)	68 (35%)	12 (20%)	18 (27%)	38 (53%)	0.0002
ST-segment depression in V4–V6 (no., %)	19 (10%)	3 (5%)	4 (6%)	12 (17%)	0.04
ST-segment elevation in aVR and/or V1 (no., %)	47 (24%)	9 (15%)	18 (27%)	20 (28%)	0.33
SVA in ECG (no., %)	10 (5%)	1 (2%)	1 (2%)	8 (11%)	0.01
Normal ECG (no., %)	24 (12%)	14 (24%)	9 (14%)	1 (1%)	0.0005

*value expressed as median with interquartile range. Test of significance, p-value: chi-square or Fisher's exact test, KW — Kruskal-Wallis one-way Analysis of Variance. SVA in ECG — supra ventricular arrhythmias in standard electrocardiography (including supraventricular ectopic beats, supraventricular tachycardia and/or atrial fibrillation/flutter)

To maintain clarity of the results, the analysed variables were divided into three parts, representing consecutive diagnostic steps.

Results

The present study population consisted of 204 participants, who were assigned to risk categories according to the recent ESC guidelines. Seven patients were excluded due to missing data. Finally, 197 patients remained in the analysis and were divided into 3 groups according to ESC risk categories: the first group — low-risk APE (59 patients, 30%), the second — intermediate-low-risk (66 patients, 34%) and the third — intermediate-high-risk (72 patients, 36%).

From the first part of analysed variables, only systolic blood pressure significantly differed between the studied groups (p = 0.03) (Table 1). The results of this analysis are also shown graphically as box plots (Figure 1).

From the second part of analysed variables significant differences were found between the risk groups for the following parameters: S1Q3T3 patterns (p = 0.02), limb leads voltage < 5 mm (p = 0.02), inverted T waves in V1–V4 (p = 0.0002), ST-segment depression in V1–V4 leads (p = 0.04), SVA in ECG (p = 0.01), as well as for ECG without any abnormalities (p = 0.0005). The results are presented in Table 2, and graphically for parameters for which the differences were statistically significant in Figure 2.

From the third part of assessed variables, significant differences were noted for VEB and SVEB occurrence between risk groups (p = 0.03 and p = 0.02, respectively). Nevertheless, no significant differences were observed for ns-VT and nsSVT/PAF/PAFI occurrence. Results are presented in Table 3. For the HRV analysis, statistical differences between the three studied groups were noted for all parameters, except for RMS-SD. These differences are graphically presented using box plots (Figure 2). The correlation coefficients between echocardiographic parameters, NTproBNP levels, and results of 24-hour Holter monitoring including HRV indices (Table 4) are also presented.

Discussion

This study aimed to evaluate the usefulness of different electrocardiographic tools in additionally assessing the severity and prognosis of patients with early-stage APE. Significant associations were revealed between various examined ECG signs and indices and APE severity. The present study provides promising results with potential clinical value in assessing the prognosis of APE, especially before cardiac biomarkers and echocardiography become

Table 3. Patient characteristics by acute pulmonary embolism (APE) severity category on admission: 24-hour Holter monitoring standard assessment and timedomain heart rate variability analysis data.

Characteristic	All APE patients (n = 197)	Low-risk APE (n = 59)	Intermediate low--risk APE (n = 66)	Intermediate high risk APE (n = 72)	p-value
Standard 24-Holter monitoring assessment					
Sinus rhythm (no., %)	190 (96%)	55 (93%)	65 (98%)	70 (97%)	0.32 [F]
VEB [n/24h]*	10 (1–145)	4 (1–24)	15 (2–104)	14 (2–285)	0.03
Pairwise comparisons		A	A; B	B	
ns-VT (no., %)	13 (7%)	3 (5%)	3 (5%)	7 (10%)	0.42 [F]
SVEB [n/24h]*	28 (5–173)	17 (257)	32 (7–239)	38 (8–199)	0.02
Pairwise comparisons		A	B	B	
nsSVT/PAF/PAFl (no., %)	84 (43%)	20 (34%)	31 (47%)	33 (46%)	0.31 [F]
Time-domain heart rate variability evaluation					
Mean heart rate [bpm]*	75 (69–87)	74 (67–82)	74 (66–85)	79 (71–89)	0.04
Pairwise comparisons		A	A	B	
SDNN [ms] *	97 (73–130)	114 (93–146)	90 (72–133)	81 (64–115)	0.001
Pairwise comparisons		B	A	A	
SDANN [ms] *	87 (64–114)	100 (81–125)	81 (64–119)	76 (58–106)	0.01
Pairwise comparisons		B	A, B	A	
RMS-SD [ms] *	26 (21–36)	26 (22–38)	29 (21–36)	25 (19–32)	0.15
Triangular Index*	13 (10–19)	16 (12–20)	12 (11–19)	12 (9–16)	0.02
Pairwise comparisons		B	A, B	A	

*value expressed as median with interquartile range. Test of significance, p-value: Kruskal–Wallis one-way Analysis of Variance, F — chi-square or Fisher's exact test. *pairwise comparisons* (Test POST-HOC Conover-Iman): similar letters = insignificant difference, different letters = significant difference, ns-SVT/PAF — patients presenting non-sustained episodes of supraventricular tachycardia and/or paroxysmal atrial fibrillation/flutter in 24-h Holter monitoring; ns-VT — patients presenting episodes of non-sustained ventricular tachycardia in 24-hour Holter monitoring; RMS-SD — root mean square standard deviation; SDANN — standard deviation of five-minute mean N-N interval; SDNN — standard deviation of intervals of all normal beats; SVEB — number of supraventricular premature beats in 24-h Holter monitoring; Triangular Index — integral of the density of the NN interval histogram divided by its height; VEB — number of ventricular premature beats in 24-hour Holter monitoring

available. The ECG is a prompt, easy to obtain and low-cost examination. Likewise, taking the present findings into account, Holter monitoring also remains a cost-effective examination with a valuable impact on establishing prognosis in patients with APE. The large cohort of included patients is also worth underlining, although the vast majority of patients were enrolled in the study before the currently used therapeutic strategy, which includes, among others, interventional treatment in the pulmonary circulation, and potential pre-emptive administration of thrombolytic treatment in patients at high risk of cardiogenic shock.

Several ECG phenomena are connected with APE [7]. In the study conducted on over 350 individuals, Kukla et al. observed significantly more frequent occurrence of atrial fibrillation, right axis deviation, S1Q3T3, RBBB, ST segment depression in leads V4–V6, ST segment depression in lead I, negative T waves in leads V1–V3, negative T waves in leads V4–V6 and negative T waves in leads III in patients with intermediate and high-risk APE, in comparison to individuals with low-risk APE. What is more, some of the above-mentioned ECG signs remained independent predictors of death and complications during hospitalization [8]. In the present study population, similar abnormalities in ECG were seen, however, no deaths were observed during hospitalization.

In the systematic review of 39 studies, including 9198 patients, ECG features that were found to be good predictors for in-hospital mortality in patients with APE included S1Q3T3, complete RBBB, T-wave inversion, right axis deviation, and AF [9]. It is also considered to be useful in assessing prognosis in APE, including the risk of cariogenic shock. Another study, conducted on 500 individuals with APE, including 92 patients with cardiogenic shock, revealed that low QRS voltage, RBBB, and ST-segment elevation in lead V1 were statistically significant predictors of cardiogenic shock, even in the multivariate analysis [10]. ECG is also reported to be of special potential prognostic value in elderly APE patients [11].

In the present study, the potential role of short-term ECG in complementing the diagnosis and prognosis of APE was also examined. An increase was found in the incidence of some ECG signs as the prognosis of APE worsened, such as the occurrence of S1Q3T3 patterns, limbs lead voltage of < 5 mm, inverted T waves in V1–V4, ST-segment depression

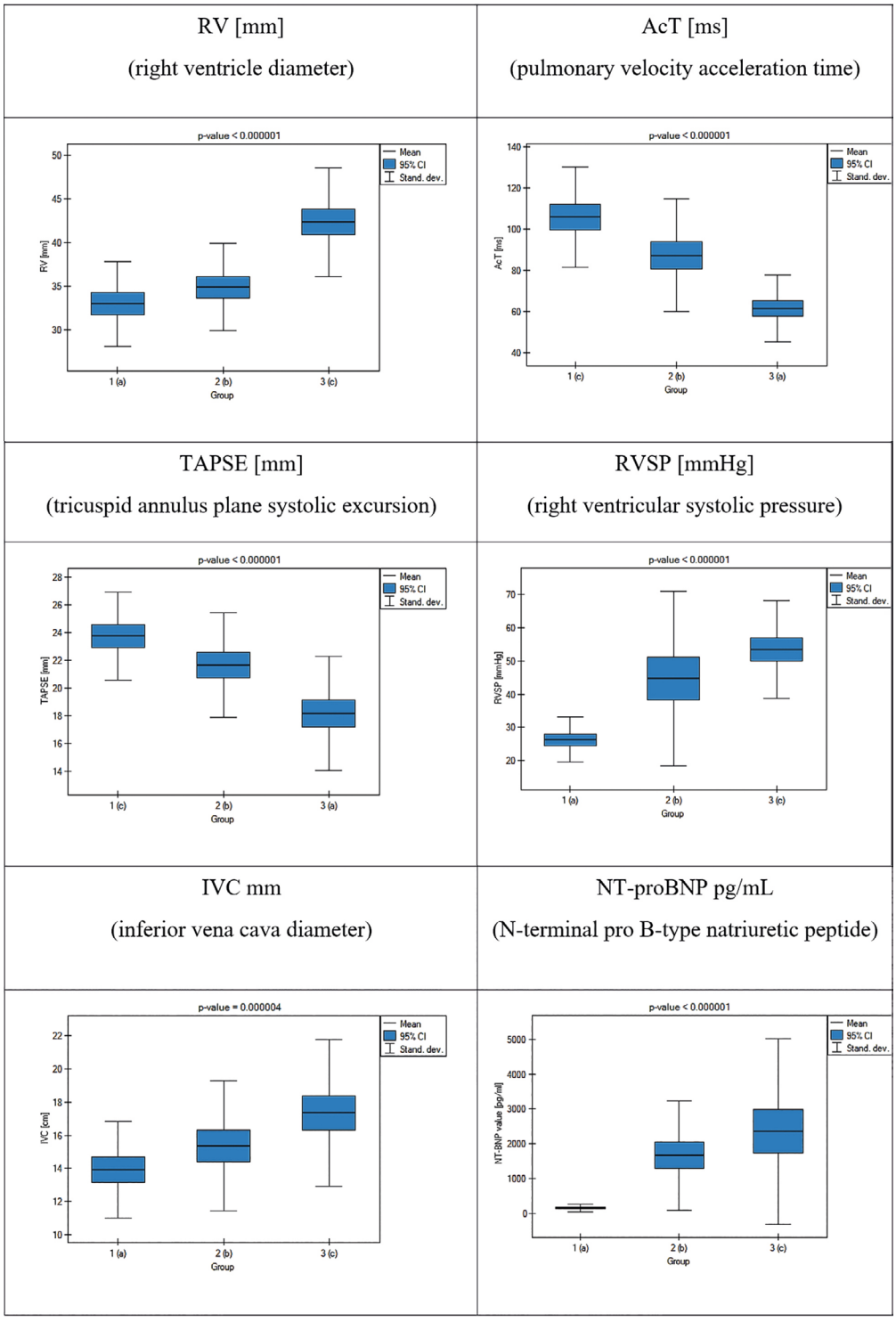

Figure 1: Boxplots of comparisons of selected echocardiographic parameters of right ventricular overload and NT-proBNP concentration for three subgroups of patients with acute pulmonary embolism: with low risk (group 1), intermediate-low risk (group 2), andintermediate-high risk (group 3): above plots p- values for comparisons, abbreviations explained in the Figure.

value expressed as mean with standard deviation
Test of significance, p-value: one-way ANOVA for independent groups
pairwise comparisons (Test POST-HOC Fisher's LSD): similar letters = insignificant difference, different letters = significant difference

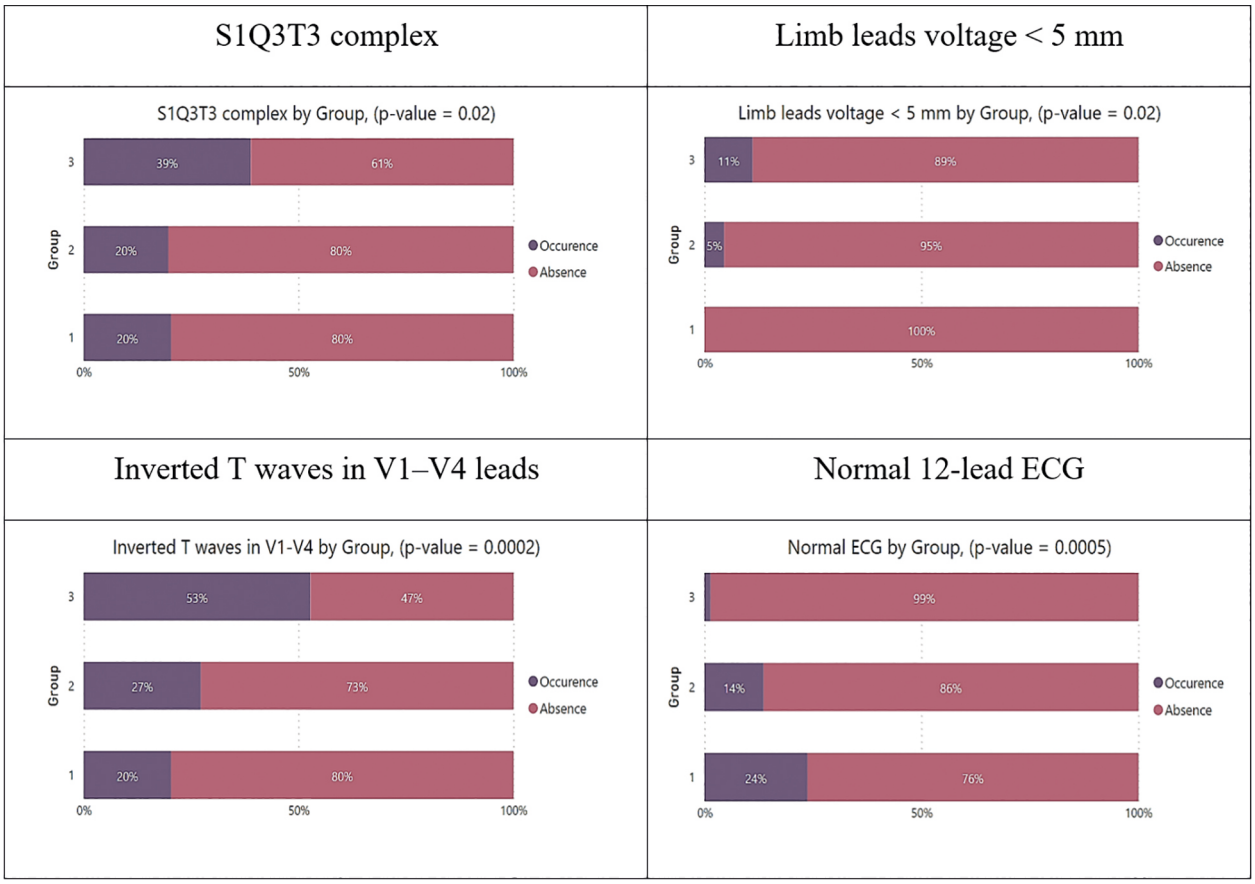

Figure 2: Comparisons of the occurrence of selected electrocardiographic signs for three groups of patients with acute pulmonary embolism: with low risk (group 1), intermediate-low risk (group 2), andintermediate-high risk (group 3): above charts p-values for comparisons.

in V4–V6, as well as the occurrence of supraventricular arrhythmias. What is especially important, in the present study population, standard ECG without any meaningful abnormalities was extremely uncommon in patients with intermediate-high risk APE. Given the inconsistent findings of characteristics for APE symptoms in other short-term ECG reports, 12-lead ECG without any abnormalities potentially appears useful in excluding more severe forms of APE and may play a potential supportive role in selecting patients who may benefit from a home treatment strategy. However, it should be emphasized that there is currently no clinical data on which such an ECG-based strategy could be applied.

As opposed to the role of standard ECG, limited data is presenting 24-hour monitoring and HRV assessment in managing patients with APE. The present results are consistent with the few reports indicating a more frequent occurrence of arrhythmias in patients with more severe APE [12]. Furthermore, Bienias et al. previously reported an association between decreased HRV and severity of pulmonary hypertension of various aetiology, including chronic thromboembolic pulmonary hypertension (CTEPH) [13, 14]. Decreased HRV parameters have also been reported in patients with APE, and some studies present their prognostic role in thromboembolism [14, 15]. The observation of impaired HRV indices was also presented in the authors' previous study on a smaller group of patients with confirmed APE [3]. The main explanation for subsequent observations is a complex deterioration of the cANS function, which occurs in both acute and chronic overload of the RV [16, 17]. In the current study, the authors confirmed their speculations and proved that impaired cANS function, as expressed by Holter-derived HRV parameters, is associated with the severity of APE.

In Holter evaluation were also observed significantly more frequent VEBs in patients with intermediate-risk APE, when compared to subjects with low risk. It is consistent with previous reports that enlighten more frequent occurrences of various arrhythmias in individuals with APE [18]. However, in the present study population, relevant or potentially life-threatening arrhythmia in Holter monitoring occurred only in a few cases, without statistical significance. In other studies, reduced HRV is also described as a prognostic factor of various arrhythmia, including

Table 4. Spearman's/Eta rank correlation coefficient between echocardiographic parameters of right ventricular overload along with N-terminal-pro-B-type-natriuretic-peptide and results of 24-hour Holter monitoring with timedomain heart rate variability parameters for all non-high-risk acute pulmonary embolism (APE) patients (n = 197)

	RV [mm]	AcT [ms]	TAPSE [mm]	RVSP [mmHg]	IVC [cm]	NT-proBNP [pg/ml]
Sinus rhythm [E]	0.13,	0.13,	0.04,	0.11,	0.04,	0.02,
	p = 0.08	p = 0.15	p = 0.53	p = 0.12	p = 0.53	p = 0.77
SVEB [n][S]	-0.002,	-0.17,	-0.04,	0.24,	0.09,	0.24,
	p = 0.97	p = 0.02	p = 0.54	p = 0.001	p = 0.23	p = 0.001
nsSVT/PAF [E]	0.05,	0.16,	0.003,	0.11,	0.18,	0.14,
	p = 0.46	p = 0.03	p = 0.97	p = 0.12	p = 0.01	p = 0.05
VEB [n][S]	0.03,	-0.17,	-0.13,	0.20,	0.08,	0.23,
	p = 0.63	p = 0.01	p = 0.08	p = 0.01	p = 0.27	p = 0.001
ns-VT [n][E]	0.11,	0.06,	0.05,	0.01,	0.03,	0.02,
	p = 0.13	p = 0.41	p = 0.48	p = 0.89	p = 0.65	p = 0.77
mRR [ms][S]	0.03,	0.14,	0.16,	-0.14,	-0.12,	-0.11,
	p = 0.69	p = 0.05	p = 0.03	p = 0.05	p = 0.1	p = 0.13
SDNN [ms][S]	-0.11,	0.23,	0.31,	-0.36,	-0.19,	-0.38,
	p = 0.17	p = 0.001	p = 0.00002	p < 0.000001	p = 0.01	p < 0.000001
SDANN [ms][S]	-0.07,	0.19,	0.29,	-0.32,	-0.17,	-0.37,
	p = 0.3	p = 0.01	p = 0.00004	p = 0.000003	p = 0.02	p < 0.000001
RMS-SD [ms][S]	-0.04,	0.10,	0.12,	-0.1,	-0.004,	-0.13,
	p = 0.56	p = 0.18	p = 0.08	p = 0.15	p = 0.95	p = 0.07
Triangular Index[S]	-0.06,	0.22,	0.23,	-0.32,	-0.18,	-0.37,
	p = 0.37	p = 0.002	p = 0.001	p = 0.00001	p = 0.01	p < 0.000001

S-r_s — Spearman's rank correlation coefficient, E-η — Correlation relation eta. Abbreviation — see Table 1 & Table 3

severe ventricular and supraventricular arrhythmia, mainly AF [19, 20]. However, such an association was not observed in the present study group, which might be attributed to the lack of high-risk patients. Nevertheless, the present findings highlight the possible value of 24-hour Holter monitoring indices in improving the assessment of prognosis in patients with APE without cardiogenic shock. The present results also signal the potential role of cANS deterioration in the clinical course of APE, which is a completely unexplored topic of potentially significant practical importance.

Study limitations

A possible limitation of this study remains the absence of high-risk APE patients. In addition, observation of the study participants was limited to the time of their hospitalization without prolonged follow-up. Despite best efforts, due to the long data collection period and potential various organizational constraints, it is possible that not all consecutive APE patients were included in the study. This may apply especially to patients in more severe conditions, including those with worse mental conditions, who could not consent to participate in the study. The above limitations may be one of the reasons for the lack of deaths due to APE during this study. Also, serum cardiac troponin concentration could not be included in the analysis due to several changes over the years in the laboratory measurement technique at the present study centre, making a comparison unfeasible. Therefore, every patient with at least one elevated cTnT or cTnI level, regardless of whether it was performed in the study or another centre, was treated as having an abnormal cTn level. Moreover, the relationship between electrocardiographic parameters and HRV with the severity of APE reached statistical significance, but the study did not demonstrate a causal relationship.

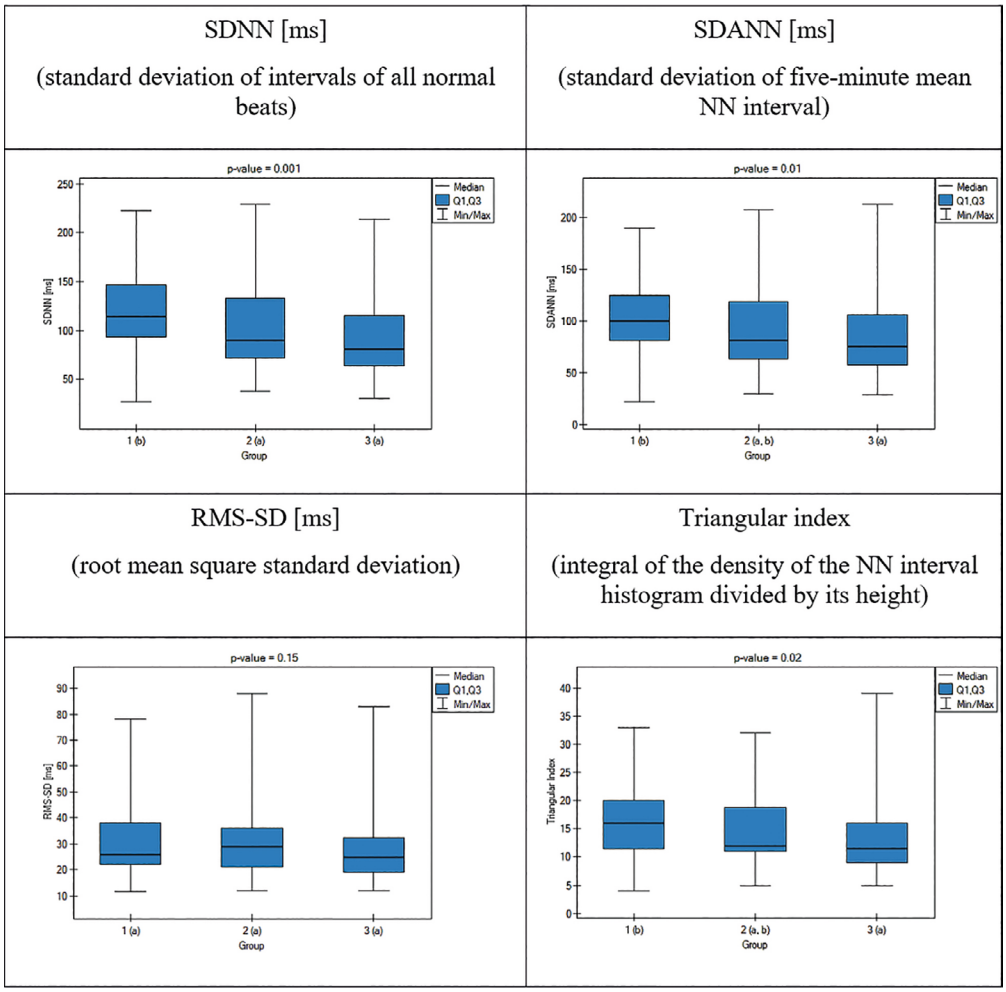

Figure 3: Boxplots of comparisons of results of time-domain heart rate variability parameters for three subgroups of patients with acute pulmonary embolism: with low risk (group 1), intermediate-low risk (group 2), and intermediate-high risk (group 3) — above plots p-values for comparisons, abbreviations explained in the figure.

value expressed as median with interquartile range
Test of significance, p-value: Kruskal-Wallis one-way Analysis of Variance
pairwise comparisons (Test POST-HOC Conover-Iman): similar letters = insignificant difference, different letters = significant difference

Conclusions

The study revealed significantly less frequent occurrence of ECG without any abnormalities in patients with intermediate-risk APE, especially in those from the intermediate-high-risk category. Moreover, 24-hour Holter monitoring with HRV analysis appears to be an additional and potentially important tool for assessing the prognosis in patients with APE, and, in the present study population, cANS function deteriorated with the severity of APE. The present findings indicate the need for further evaluation of short and long-term electrocardiography in patients with APE, to develop standardized procedures and establish their true clinical significance.

Additional information

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Conflict of interests

The authors declare no conflict of interests

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Streszczenie

Wstęp. U pacjentów z ostrą zatorowości płucną (OZP) opisywane są różne nieprawidłowości w zakresie krótko- i długoterminowej rejestracji elektrokardiograficznej (EKG). Jednak ich rola w ocenie ciężkości choroby i szacowaniu rokowania pozostaje niejasna.

Materiały i metody. Do badania włączano kolejnych pacjentów z potwierdzoną OZP niewysokiego ryzyka. Po przyjęciu u pacjentów wykonywano badanie podmiotowe i przedmiotowe, a także 12 odprowadzeniowe EKG, echokardiografię, ocenę stężenia NT-proBNP oraz 24-h monitorowanie metodą Holtera.

Wyniki. Spośród 204 pacjentów do badania ostatecznie włączono 197, w wieku 59 lat (Q1–Q3: 44–73), 54% stanowiły kobiety. Zgodnie z aktualnymi wytycznymi u 59 (30%) pacjentów stwierdzono OZP niskiego ryzyka, u 66 (34%) pośredniego niskiego, u 72 (36%) pośredniego wysokiego ryzyka. Pomiędzy grupami ryzyka stwierdzono istotne statystycznie różnice w częstości występowania: zespołów S1Q3T3 w EKG (p = 0,02), woltażu odprowadzeń kończynowych < 5 mm (p = 0,02), ujemnych załamków T w V1–V4 (p = 0,0002), obniżenia odcinków ST w V1-V4 (p = 0.04), a także w częstości występowania prawidłowego EKG (p = 0,0005). W badanych grupach obserwowano również istotne różnice wartości większości holterowskich parametrów odzwierciedlających funkcję układu autonomicznego serca.

Wnioski. W badaniu potwierdzono potencjalnie istotne znaczenie elektrokardiografii u chorych ze świeżo rozpoznaną OZP. Wyniki wskazują na możliwość wykorzystania rejestracji EKG w pośrednim szacowaniu ciężkości przebiegu OZP, co może zostać wykorzystane podczas oczekiwania na uzyskanie wyników biomarkerów i echokardiografii. Ponadto stwierdzono dysfunkcję układu autonomicznego serca, postępującą wraz z ciężkością OZP. Uzyskane rezultaty wymagają dalszego potwierdzenia oraz oceny przydatności klinicznej.

Słowa kluczowe: ostra zatorowość płucna; elektrokardiografia, monitorowanie metodą Holtera, zmienność rytmu serca, ryzyko wczesnego zgonu

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