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Research article

Differential Diagnostics of Wide QRS Complex Arrhythmias with Left Bundle Branch Block Morphology Using Slow Conduction Index

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Differential diagnosis of wide QRS complex arrhythmias is one of the most challenging tasks in routine practice arrhythmology. The analysis of the wide QRS complex morphology has been introduced due to the complex problem of detecting atrial waves on ECG. A slow conduction index based on the ratio of the initial and terminal QRS amplitudes is one of the solutions to evaluate conduction velocity based on the surface ECG due to a significant variability of QRS morphology and real complexity of its detailed assessment. However, one of the significant limitations of this algorithm is a need to search for the RS wide complex type and randomly select an ECG lead with this morphology which can finally create a contradictory result.

AIM: To evaluate a possibility of using the slow conduction index for differential diagnosis of wide QRS complex arrhythmias with left bundle branch (LBBB) morphology in any of 12-leads ECG followed by evaluation of the obtained diagnostic accuracy values.

MATERIALS AND METHODS: The study included 280 single premature wide QRS complexes with LBBB morphology recorded during holter ECG monitoring in randomly selected 28 patients. Atrial extrasystoles were recorded in 14 patients and ventricular extrasystoles were captured during sinus rhythm in other 14 patients. A ROC analysis was used for the qualitative and quantitative assessment of a slow conduction index diagnostic values based on sensitivity (Sn), specificity (Sp) and accuracy (Acc).

RESULTS: The highest values of Sn and Sp were obtained for a slow conduction index in the leads aVL, V2, aVF, V5 and III, and the lowest — for the leads I, V3 and V6 based on the calculated area (AUC) under the ROC curves ($p < 0.001$ for all leads).

CONCLUSION: The study presented the fundamental possibility of using a slow conduction index in any of 12-lead ECG for the differential diagnosis of wide QRS complex arrhythmias with LBBB morphology.

Keywords: differential diagnosis; wide QRS complex; left bundle branch block.

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Научная статья

Использование индекса медленного проведения в дифференциальной диагностике аритмий с широкими комплексами QRS и формой блокады левой ножки пучка Гиса

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Актуальность. Дифференциальная диагностика аритмий с широкими комплексами QRS является одной из сложнейших задач в практической аритмологии. В связи со сложностью выявления волн предсердной активности на ЭКГ часто используется подход, основанный на анализе формы комплекса QRS. Учитывая выраженную вариабельность формы QRS и сложность объективной оценки, было предложено оценивать на ЭКГ скорость распространения возбуждения по миокарду желудочков на основе так называемого индекса медленного проведения — соотношения амплитуд начальной и конечной частей комплекса QRS. Однако одним из существенных ограничений данного алгоритма является необходимость не только искать отведения с формой широкого комплекса по типу RS, но и произвольно выбирать такое отведение при наличии нескольких похожих, что может приводить к противоречивым результатам.

Цель исследования — изучение возможности использования индекса медленного проведения для дифференциальной диагностики аритмий с широкими комплексами QRS и формой блокады левой ножки пучка Гиса (ЛНПГ) во всех 12 отведениях ЭКГ с последующей оценкой его диагностической значимости.

Материалы и методы. В исследование было включено 280 одиночных преждевременных широких комплексов QRS с формой блокады ЛНПГ, выявленных при односуточном и многосуточном мониторировании ЭКГ у случайно выбранных 28 пациентов. У 14 больных регистрировались предсердные экстрасистолы и у 14 — желудочковые экстрасистолы во время синусового ритма. Для качественной и количественной оценки диагностической значимости использовался ROC-анализ с определением информативности диагностического теста на основании чувствительности (ЧВ), специфичности (СП) и диагностической точности (ДТ).

Результаты. Наиболее высокие значения ЧВ и СП индекса медленного проведения для широких комплексов QRS были получены в отведениях aVL, V2, aVF, V5 и III, а наиболее низкие — в отведениях I, V3 и V6 согласно анализу рассчитанной площади (AUC) под ROC кривыми ($p < 0{,}001$ для всех отведений).

Заключение. В проведенном исследовании была показана принципиальная возможность использования индекса медленного проведения для дифференциальной диагностики аритмий с широкими комплексами QRS и формой блокады ЛНПГ в любом отведении ЭКГ.

Ключевые слова: дифференциальная диагностика; широкие комплексы QRS; блокада левой ножки пучка Гиса.

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BACKGROUND

The differential diagnosis of wide QRS complex arrhythmias is one of the most difficult scientific and practical tasks in electrocardiology and noninvasive arrhythmology. For more than 60 years, this problem remains unresolved to the end; however, it is still very relevant: cardiologists and specialists in functional diagnostics constantly face the need to differentiate wide QRS tachyarrhythmias in their daily practical work because competent analysis in most cases determines successful therapeutic techniques [1, 2].

The main principle of the differential diagnosis of wide QRS arrhythmias is the analysis of electrocardiograms (ECGs) and the identification of atrial activities and their detailed assessment in relationship with the QRS complex. However, in most cases, it is impossible to clearly visualize the P waves on surface ECG because of their small amplitudes and frequent locations in the ST-T interval when premature ventricular complexes appear. In some cases, when atrial flutter or fibrillation occurs, it is impossible to reliably determine which waves of the atrial electrical activity are conducted to the ventricles.

In all these cases, a different principle based on the analysis of the form of wide QRS complexes should be used. Many scientific groups have developed and proposed various morphological criteria and algorithms for the differential diagnosis of wide QRS arrhythmias [3]. Most of them are based on the assessment of amplitudes and time parameters of wide QRS complexes in leads V1 and V6 [4–7]. Moreover, other authors have shown low diagnostic accuracy (Acc) [8]. This is caused by the high subjectivity of the assessment of the shape of the wide QRS by researchers and the heterogeneity of patient groups, some of whom could have structural changes in the heart. Scar or intense myocardial fibrosis leads to a significant change in the course of excitation along the ventricular myocardium and, accordingly, to a sharp decrease in the diagnostic capabilities of these algorithms [9]. In addition, a significant difference in individual anatomical ratios of the torso and the position of the heart in the chest is an important factor, which also has significant effects on the QRS complex morphology.

One of the approaches to solve these problems is an ECG assessment of the propagation rate of excitations through the ventricular myocardium based on the ratio of the amplitudes of the initial and final parts of the QRS complex. Thus, in 2006, Vereckei et al. proposed the so-called slow conduction index for the differential diagnosis of wide QRS arrhythmias [10]. The slow conduction index is the ratio of the absolute values of the total amplitude of the QRS complex for the first and last 40 ms, which is calculated for a single ECG lead. If the obtained value is < 1, the wide QRS complex has a ventricular origin, and if it is > 1, it is supraventricular (Figure 1). The evaluation results of the diagnostic significance of the proposed criterion showed quite good results: sensitivity (Sn) of 88.2% and specificity (Sp) of 81.9% [10].

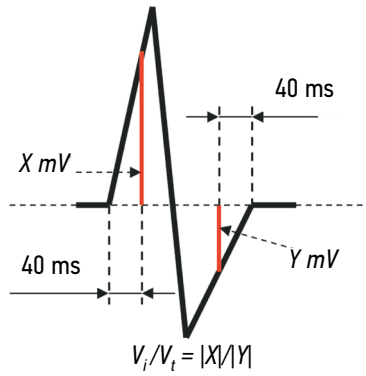

Fig. 1. A method of determining the amplitudes during the initial ($V_i = X\ mV$) and terminal ($V_t = Y\ mV$) 40 ms of QRS complex and slow conduction index calculation ($V_i / V_t = X / Y$).

Furthermore, the special feature of this index is the need to choose an ECG lead with the RS-type wide complex according to the original concept of the proposed criterion. However, this is one of the significant limitations of this algorithm: the need not only to specifically look for leads with the RS-type wide complex but also to arbitrarily choose one of such leads from among several similar ones, which can give contradictory results. In addition, the absence of the RS-type complex shape leads to the failure to use the slow conduction index in practice.

In this regard, this study aimed to analyze the possibility of using this criterion in all 12 ECG leads for the differential diagnosis of wide QRS complex arrhythmias with left bundle branch block (LBBB) morphology, followed by the assessment of the obtained values for its diagnostic significance.

MATERIALS AND METHODS

Data registration

The study included 280 single premature wide QRS complexes with LBBB morphology identified during 1-day and multiday ECG monitoring in 28 randomly selected patients undergoing hospital treatment at the FSBI Almazov National Medical Research Centre of the Ministry of Healthcare of the Russian Federation from 2010 to 2019. ECG registration was conducted using standard isoline filters, with 35 and 50 Hz, and recording with a sampling frequency of 257 Hz (INCART CJSC, Russia). In all patients, signs of additional conduction pathways or initial bundle branch block were excluded. The diagnosis of ventricular or supraventricular arrhythmias was verified by experts (cardiologists and functional diagnostics specialists) by comparing ECG data with the results of the endocardial electrophysiological examination and by analyzing the ratio of the atrial and ventricular rates under clear visualization of the P waves before the occurrence of premature wide QRS complexes on the surface and transesophageal ECG. Atrial premature

beats were recorded in 14 patients and ventricular premature beats during the sinoatrial rate in 14 patients. ECG samples of patients with ventricular and supraventricular arrhythmias with the shape of the complex forming an LBBB are shown in Figures 2 and 3, respectively.

Data processing

For all wide QRS complexes (*N* = 280) in each of the 12 leads, the QRS complex borders were determined automatically using the KTResult 3 software (INCART CJSC, Russia). The correctness of their automatic determination was

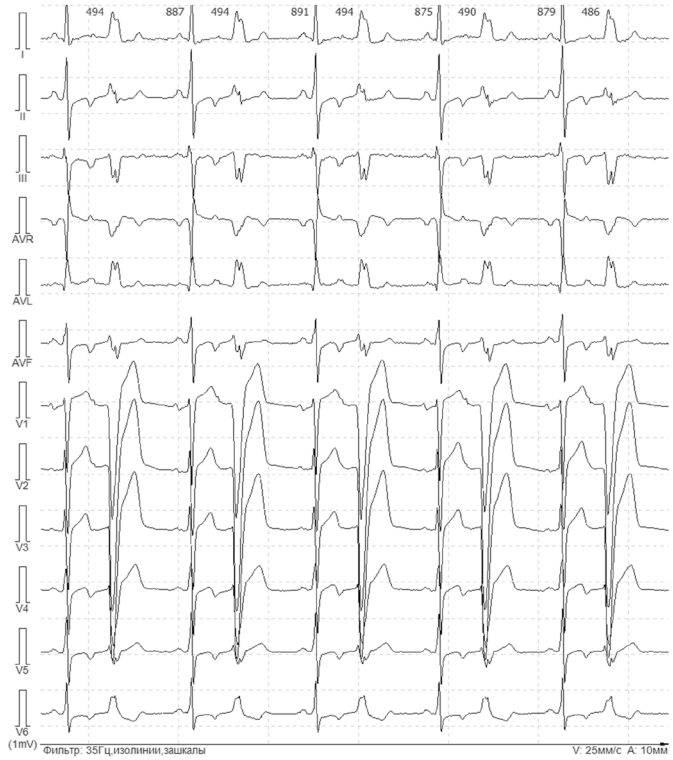

Fig. 2. ECG example of supraventricular extrasystoles with LBBB aberration

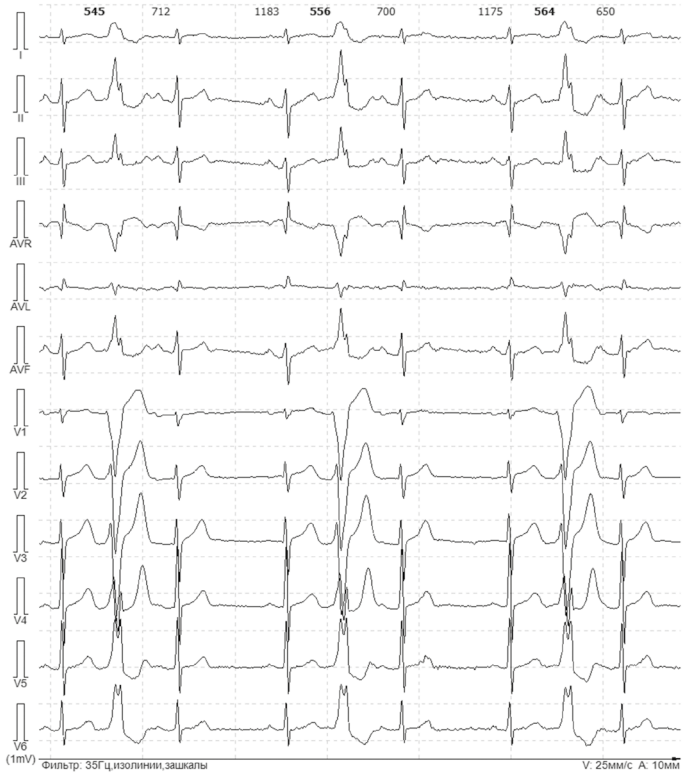

Fig. 3. ECG example of ventricular extrasystoles with LBBB type morphology

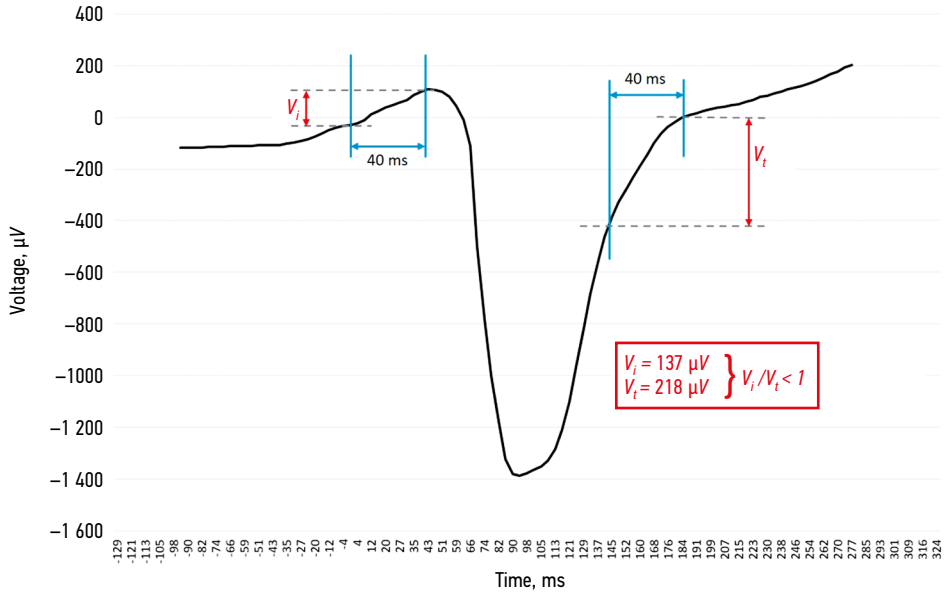

Fig. 4. An example of slow conduction index calculation (V_i/V_t). Voltage (μ*V*) — ECG amplitude (microVolts), time in ms

checked by an expert (a doctor of functional diagnostics), who conducted subsequent corrections if necessary. The obtained amplitude–time parameters for the first and last 40 ms of all QRS complexes were exported from the KTResult 3 software in text format using custom-made software based on the Embarcadero RAD Studio v.10.2 rapid application development environment (Idera Inc., USA) and imported into Microsoft Excel spreadsheets (Microsoft Corporation). Then, the ratio of the absolute values of the total amplitudes of the QRS complexes for the first and last 40 ms in each ECG lead was calculated. Absolute values of amplitude deviations were used for monophase complexes. In the case of a two- or three-phase complex, the sum of the amplitudes of these deviations during the initial or final 40 ms was used. The technique and example of determining the amplitudes and calculation of the slow conduction index are shown in Figure 4.

Statistical analysis

In the first stage, the nature of the data distribution was evaluated using histograms, normal probability plots, Shapiro–Wilk test [11] modified by Royston [12], and the generalized D'Agostino-Pearson test [13]. Initially, p values < 0.05 were assumed to be statistically significant. All data obtained significantly differed from the normal distribution; therefore, nonparametric methods of analysis were used.

In the second stage, a receiver operating characteristic (ROC) analysis was performed [14; 15] to qualitatively and quantitatively assess the diagnostic significance of the slow conduction index and characteristics of premature ventricular contractions (PVC) and supraventricular (premature atrial complexes [PAC]). ROC curves were made separately for each indicator, followed by a detailed analysis of their shape. The areas under the curve (AUCs) were compared based on the values of the standard error calculated using the Hanley and McNeil method [16, 17] and the exact 95% confidence interval (CI) based on the binomial distribution [18]. The informative value of the diagnostic test was based on the calculated values of Sn, Sp, and diagnostic Acc. The Sn, Sp, and Acc were assessed with their 95% CI calculated based on the binomial distribution using the Klopper–Pearson method [19, 20].

Considering that several hypotheses were tested simultaneously using the same set of initial data in this study, the probability of making an incorrect conclusion about at least one of the hypotheses significantly exceeded the initially accepted significance level (p < 0.05). Thus, the Bonferroni adjustment factor was used to adjust the obtained values for multiple testing [21], and p values < 0.001 were considered finally statistically significant. Statistical analysis was performed using Statistica v.12 (Statsoft Inc., USA), IBM SPSS Statistics for Windows version 23 (IBM Corp., Armonk, NY, USA), and MedCalc Statistical Software v.20.115 (MedCalc Software Ltd, Ostend, Belgium).

RESULTS

Clinical characteristics of the patients

The patients were 10 to 76 years old (median, 43 years); among them, 17 (61%) were male. Coronary heart disease (CHD) was diagnosed in 3 patients, hypertension in 6, and chronic heart failure functional class 2 (NYHA) in 2. Echocardiography showed left ventricular hypertrophy in 9 patients (5 with PVC and 4 with PAC) and dilated cardiomyopathy of nonischemic origin in 3 (1 with PVC and 2 with PAC).

Sn and Sp analysis of the slow conduction index in 12 ECG leads

The highest Sn and Sp values of the slow conduction index were obtained in leads aVL, V2, aVF, V5, and III and the lowest in leads I, V3, and V6 according to the analysis of the AUC under the ROC curves. Moreover, a statistically significant difference was noted in all leads (p < 0.001),

even in leads with low AUC values. The calculated CI was quite narrow in all leads. All the obtained values are presented in Table. In the evaluation of the diagnostic value of the QRS shape, AUC did not exceed 0.83 in any of the leads. The shape of the ROC curve together with their 95% CI and cut-off threshold criteria for each ECG lead are shown in Figure 5.

Diagnostic Acc of the slow conduction index in 12 ECG leads

In the evaluation of the diagnostic Acc of the slow conduction index, none of the leads obtained values exceeding 94%. A visual comparison of the diagnostic Acc of the slow conduction index in different ECG leads showed that leads aVL, V2, aVF, V5, and III were the most informative for the differential diagnosis in order of descending of their value (Figure 6). The range of 95% CI for diagnostic Acc values was relatively narrow for the slow conduction index in each ECG lead.

DISCUSSION

Main results

This study explored the possibility of using the slow conduction index for the differential diagnosis of wide QRS

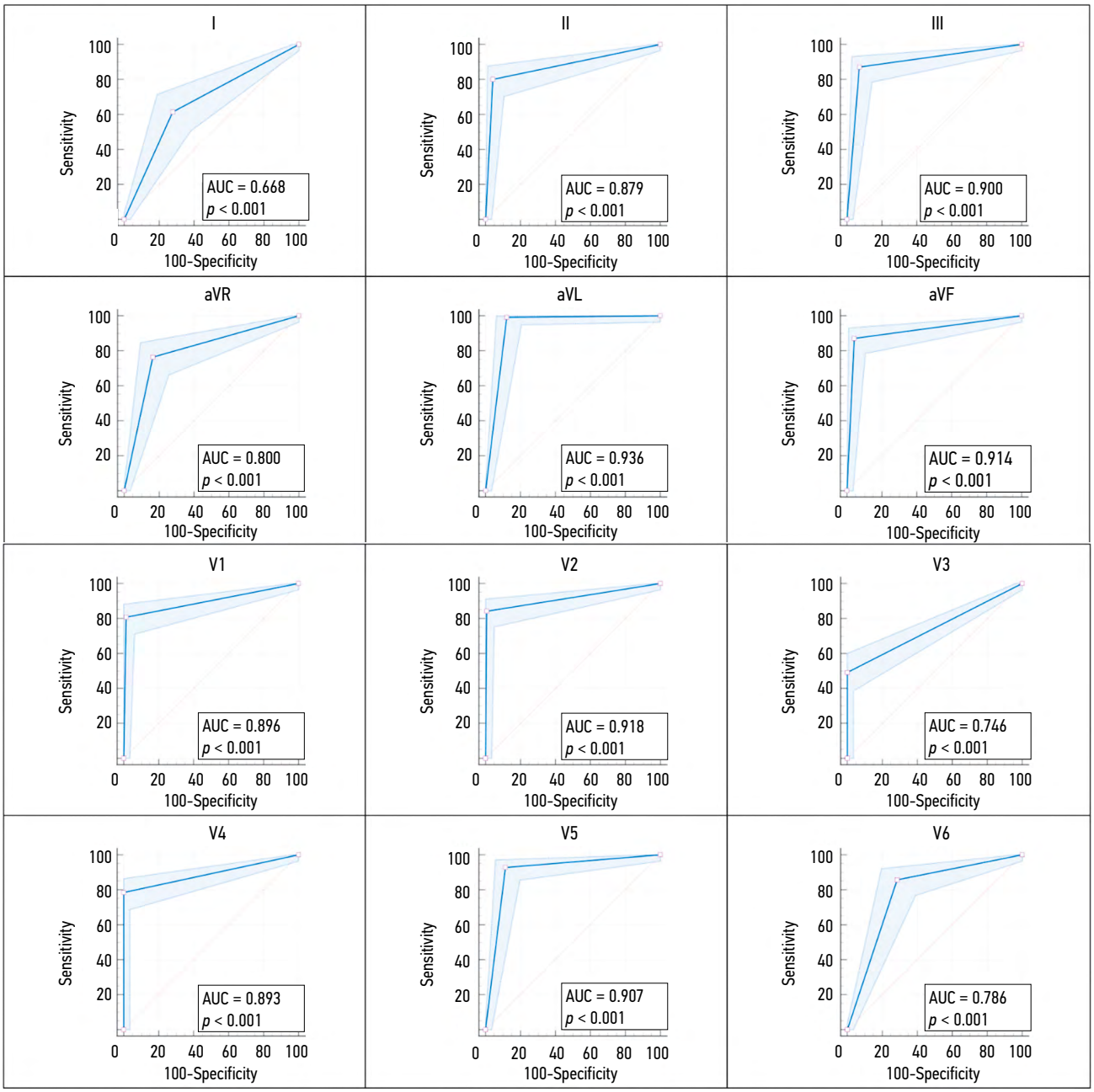

Fig. 5. ROC curves with 95% CI (light blue color) as an illustration of diagnostic value of slow conduction index in 12 lead ECG. Cut-off values are marked as red round marker on each of ROC curves. Area under curve (AUC) with *p*-value are shown at the right bottom corner of each graph

Table. Diagnostic characteristics (Sn, Sp and AUC with 95% CI) of slow conduction index in 12-lead ECG

Lead	Sn (95% CI), %	Sp (95% CI), %	AUC (95% CI)
I	61.4 (53–70)	72.1 (64–79)	0.67 (0.61–0.72)
II	80.0 (72–86)	95.7 (91–98)	0.88 (0.83–0.91)
III	87.1 (80–92)	92.9 (87–97)	0.90 (0.86–0.93)
aVR	76.4 (69–83)	83.6 (76–89)	0.80 (0.75–0.85)
aVL	99.3 (96–100)	87.9 (81–93)	0.94 (0.90–0.96)
aVF	87.1 (80–92)	95.7 (91–98)	0.91 (0.88–0.94)
V1	80.7 (73–87)	98.6 (95–100)	0.90 (0.86–0.93)
V2	84.3 (77–90)	99.3 (96–100)	0.92 (0.88–0.95)
V3	49.3 (41–58)	100 (97–100)	0.75 (0.69–0.80)
V4	78.6 (71–85)	100 (97–100)	0.89 (085–0.93)
V5	92.9 (87–97)	88.6 (82–93)	0.91 (0.87–0.94)
V6	85.7 (79–91)	71.4 (63–79)	0.79 (0.73–0.83)

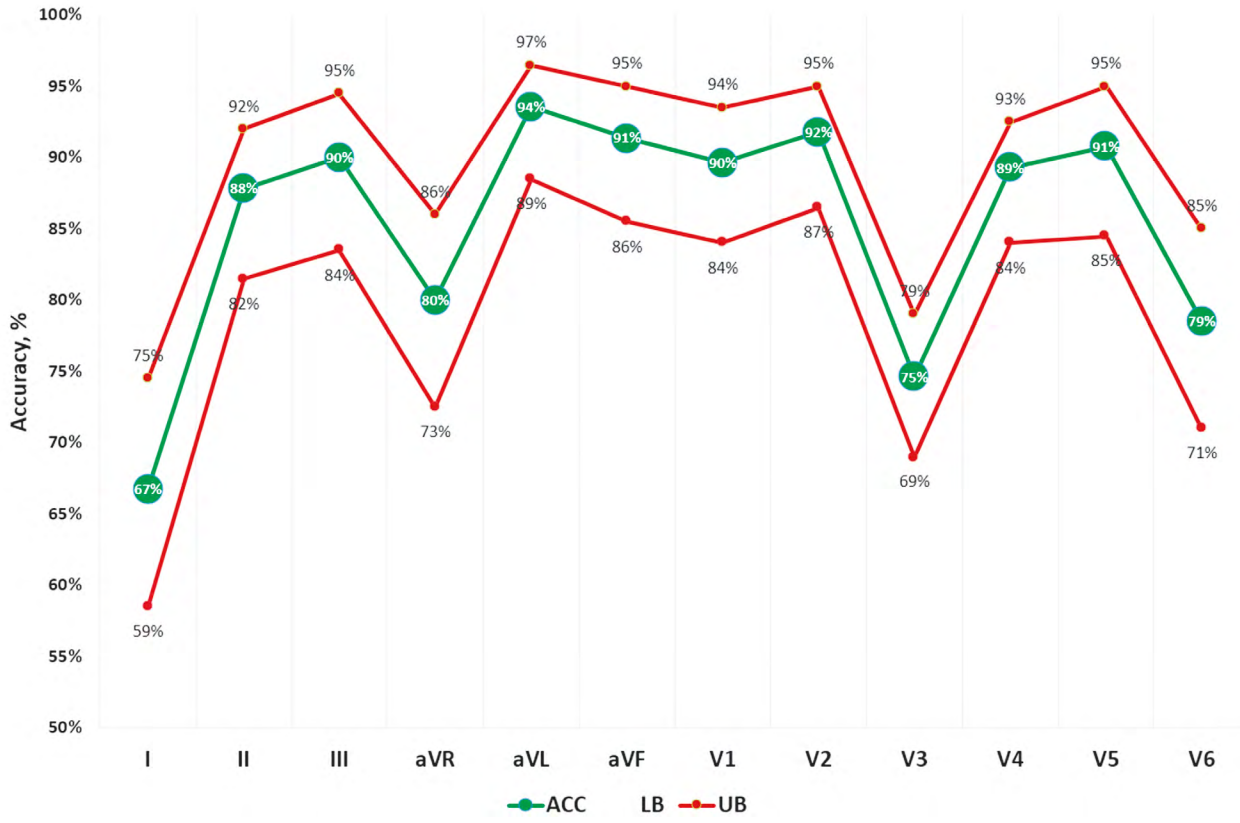

Fig. 6. Line plot of slow conduction index Accuracy (Acc) with 95% CI in all 12 leads. LB-UB – lower bound-upper bound of 95% CI.

arrhythmias with the shape of an LBBB in all 12 ECG leads and assessed the calculated values of diagnostic significance. The obtained results showed the potential for use of this criterion in any of the ECG lead without the need to search for a biphasic wide complex with an RS-type morphology. In addition, the calculated diagnostic Acc showed high Sn and Sp of the slow conduction index in leads II, III, aVL, aVF, V1, V2, V4, and V5 (8 of 12). These results are confirmed by

the fact that the area under the ROC curves was statistically significant ($p < 0.001$) in all leads, even in leads with low AUC values.

In the visual comparison of the diagnostic Acc of the slow conduction index in all leads, a significant advantage was found when this criterion was used in eight of the above leads, whereas when used in only in four leads (I, aVR, V3, and V6), the Acc was lower.

Diagnostic value of the slow conduction index and evaluation of the results relative to previously published data

The analysis of the wide QRS complexes morphology for the differential diagnosis of ventricular and supraventricular arrhythmias appears to be more relevant than the analysis of the ratio of atrial and ventricular rhythms for several reasons. First, in most cases, it is impossible to detect the presence of AV dissociation because of the small amplitude of the atrial P waves on the ECG, which makes this criterion extremely difficult to use in clinical practice. Second, even when atrial activity waves are found, further detailed analysis of the ratios of the atrial and ventricular rhythm is required. Finally, most often, doctors just do not have the time to search for atrial waves on an ECG and conduct further detailed ECG analysis. In addition, the analysis of the amplitude–time characteristics of wide complexes also appears to be a very complicated task because of the abundance of proposed criteria and algorithms, most of which take into account only one or several morphological criteria of wide QRS complexes.

The criteria of differential diagnosis of the wide complexes with LBBB morphology in the available literature were previously described mainly for the duration of the QRS complex or for leads V1, V2, and V6 [7, 22, 23], rarely for leads I and AVF [24], and are not described for leads V3 and V4. Criteria such as R duration of > 30 ms, notch of the descending part of the S-wave, distance from the beginning of the QRS complex to the maximum peak of the S-wave ⩾ 70 ms in leads V1 and V2, or presence of any Q-wave in lead V6 had high diagnostic Acc according to many studies [7, 22–24]. Thus, according to Kindall, Brown, and Josephson, it was not possible to differentiate VT and SVT with an Acc of 96%–100% [23], and according to Griffith and de Belder, the Acc was only 74% (86%) for patients with CHD and 60% for those without CHD) [24]. However, no large-scale study has assessed their Acc for arrhythmias with LBBB morphology, and for arrhythmias with any form of QRS complex, the Acc was only 73% for the AVF lead and 60% for the I lead [24].

The development of criteria for the differential diagnosis of arrhythmias with wide QRS complexes is complicated because of various reasons. Initially, the ECG characteristics are largely influenced by many factors: position of the heart in the chest, characteristics of the conductivity of the myocardium and surrounding tissues, electrical potential of skeletal muscles, and characteristics of the transient resistance between the skin surface and registration electrodes, which can change significantly based on their displacement and deterioration of their contact. These factors can significantly influence the QRS complexes morphology; thus, their variability can be very intense even for long-term ECG registration in one patient. In this regard, the correct selection of criteria based on the analysis of the amplitude–time parameters of QRS becomes very important. From among all the currently proposed criteria for the differential diagnosis of arrhythmias with wide QRS complexes, the slow conduction index, from our point of view, is the most suitable for describing the complex process of excitation along the ventricular myocardium. However, this index should be only used in leads with a biphasic or three-phase shape of the wide complex, most often of the RS type, which significantly complicates the diagnosis. Moreover, in the original works of the authors regarding this criterion, this was not clearly explained. Later, the authors suggested using this criterion only for the aVR lead [25]. In practical work, if there is a need to use the slow conduction index for the differential diagnosis of ventricular and supraventricular arrhythmias with wide QRS complexes, any data confirming the potential for use of any ECG leads suitable for analysis from the point of view of a specialist should be available.

In this paper, the diagnostic significance of the slow conduction index does not directly depend on the selection of a lead with a biphasic or three-phase shape of the wide QRS complex. Moreover, in most leads, the use of the slow conduction index showed high Sn, Sp, and Acc. A detailed analysis of the calculated ROC curves showed the presence of a relatively narrow 95% CI, which may indirectly indicate the low variability of the diagnostic value of parameters and their robustness.

Our study showed the potential for use of the slow conduction index in patients with wide complexes and shape of an LBBB, when the differential diagnosis is difficult because of the abundance and difficulty of using other morphological criteria [26]. Of course, the results cannot be a strict pattern identified; thus, additional analysis and verification in a much larger group of patients without structural cardiac disease are needed.

Assessment of the representativeness and study limitations

The study analyzed a relatively small number of arrhythmias with wide QRS complexes; thus, the results may be highly specific for the studied patients. In addition, the use of nonparametric ROC analysis with the calculation of 95% CI significantly increased the robustness of the obtained results. Possible errors in automatic ECG measurement and potential registration errors associated with the registration of artifacts may affect the results, which together with the small sample size can limit the generalizability of this study. Moreover, the consistency and systematicity of the conducted analysis in relation

to the analysis methods used significantly increase the reliability and representativeness of the results.

CONCLUSION

The study showed the potential use of the slow conduction index in the differential diagnosis of arrhythmias with wide QRS complexes in any of ECG leads. In patients with LBBB QRS morphology, the best results of the diagnostic Acc of this index were obtained in leads II, III, aVL, aVF, V1, V2, V4, and V5. Thus, in this study, the use of the slow conduction index in different ECG leads does not depend on the shape of the QRS complex and not only complements but also significantly improves the quality of the differential diagnosis of PVC and PAC with aberrant conduction of LBBB. Given the small sample size, the obtained results require further testing on a larger group of patients with different forms of wide ectopic complexes with LBBB morphology and different localizations of ventricular arrhythmia focus, taking into account the presence of cardiac structural disease.

The study also demonstrated the importance of a comprehensive approach in the analysis of the QRS complex morphology and the need for a consistent detailed analysis of various criteria for the differential diagnosis of arrhythmias with wide QRS complexes.

ADDITIONAL INFORMATION

Competing interests. Conflict of interest. The authors declare no potential conflict of interest.

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