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Evaluation of autonomic nervous system function with heart rate variability analysis in preterm infants — a literature review

Ocena aktywności autonomicznego układu nerwowego na podstawie parametrów zmienności zatokowego rytmu serca u dzieci urodzonych przedwcześnie — przegląd piśmiennictwa

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Abstract

Introduction. Preterm birth, despite the constant development of medicine and improved perinatal care, remains one of the greatest challenges in obstetrics. A prematurely born child presents a number of disorders, including abnormalities of the autonomic nervous system (ANS), which affect, among others, the functioning of the heart muscle. One method used to assess the influence of ANS activity on heart rate is the analysis of heart rate variability (HRV), which gives an indirect picture of its influence on the ability to adapt the systolic function of the ANS to external stimuli.

The aim of this study was to evaluate the activity of the autonomic nervous system on the basis of values of HRV parameters in children born prematurely on the basis of a literature review.

Material and methods. The literature review was carried out in accordance with PRISMA statement. Medical databases were reviewed including MEDLINE/PubMed, ProQest, PEDro, Cochrane, and Embase using the key phrases: 'heart rate variability' in combination with 'preterm infants'.

Results. Between 1997 and 2018, 26 publications meeting the inclusion criteria were identified, of which 15 were selected for detailed analysis. Selected time and frequency domain HRV parameters were analysed in the review.

Conclusions. Preterm infants are susceptible to heart rhythm control disorders by the autonomic nervous system expressed by rapid and temporary changes in heart rate. They have higher heart rate and selected HRV parameters, suggesting a dominance of sympathetic activity in heart rate control. In addition, existing studies are not sufficiently systematic to be able to be compared to each other. Therefore, this subject requires further research.

Key words: heart rate variability, autonomic nervous system, prematurity

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Introduction

Every year, around 15 million preterm infants are born worldwide, which means that one child in 10 is born early, and this percentage is growing [1]. Preterm infants show many developmental disorders caused by immaturity of the developing central nervous system (CNS), which are the cause of long hospital stays and often require the implemention of numerous medical procedures, including surgical, pharmacological and rehabilitation procedures [2]. The commonest health problems of preterm infants are: weight and growth deficiency, respiratory distress syndrome, vision and hearing disorders, prolonged hepatitis, feeding problems, risk of infection and early CNS damage caused by hypoxia and cerebral haemorrhage, which in consequence leads to numerous neurological and developmental disorders [2–4].

CNS damage is often accompanied by disorders of the autonomic nervous system (ANS). Abnormal activity of the ANS is associated with cardiovascular system malfunctioning [5]. Damage to sympathetic and parasympathetic fibres leads to pathological changes in the excitation of the sinus node, and thus to uncontrolled changes in heart rate [6]. There are a number of methods that allow for indirect and non-invasive determination of ANS activity, one of which is an evaluation of heart rate variability (HRV) [5].

HRV is defined as periodic changes in the duration of consecutive RR intervals between individual QRS complexes of sinus rhythm [5–7]. The interpretation of the results of parameters obtained in the fields of time, frequency and nonlinear methods allows for a determination of the extent of participation of sympathetic or parasympathetic systems, as well as of the two simultaneously in the regulation of heart rate [5, 8].

Since the publication of the Task Force guidelines in 1996 on the methodological aspects of HRV analysis [7], such a method has become a popular clinical and research tool [8]. HRV analysis from electrocardiographic examination has been particularly useful in cardiology, becoming an important tool for estimating the potential risk of heart disease and diagnosing cardiac rhythm modulation disturbances by ANS [5, 8].

Due to the delay in ANS maturity in newborns, the abovementioned feedback control mechanisms involved in the regulation of heart rate are not fully developed [9]. Therefore, a preterm infant may not adapt sufficiently to environmental, nutritional or iatrogenic external conditions due to ANS immaturity [10].

The aim of this study was to evaluate, on the basis of a review of the world literature, the activity of the ANS, expressed by the values of analysed parameters of HRV in premature children.

Material and methods

Our literature review was constructed on the basis of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement, which contains a set of elements necessary for the proper reporting of systematic literature reviews and/or meta-analyses. The document consists of a 27-part checklist and a four-phase flow chart illustrating the successive phases of the systematic literature review. It contained information on the number of publications found on the basis of the search criteria, the number of studies included and excluded, and the reason for the exclusion. The PRISMA report is not an instrument for assessing the quality of systematic reviews, but it can be useful for critical evaluation and for helping authors to improve the reporting of systematic reviews and meta-analyses. It can be used as a basis for reporting on systematic reviews and other types of research, in particular the evaluation of interventions [11].

In order to find appropriate publications, medical databases were reviewed including MEDLINE/PubMed, ProQest, PEDro, Cochrane and Embase using the key phrase 'heart rate variability' in combination with 'preterm infants'.

The following HRV parameters were analysed: heart rate (HR) and/or mean RR interval (mRR); selected parameters of time analysis: standard deviation of NN intervals (SDNN); determining the total variation of sinus rhythm; square root of the mean square root of the sum of squares of differences between consecutive RR intervals (rMSSD) and the percentage of differences between successive sinus RR intervals that exceed 50 ms (pNN50) as an indicator of short-term variability; triangular interpolation of the histogram of NN intervals (TINN) calculated as the length of the base of the triangle which approximated the distribution of NN intervals on the time axis and of frequency analysis: total power (TP); determining the total effect of harmonic components on sinus rhythm and giving a comprehensive idea of the examined rhythm variation; power of the spectrum in the low frequency range (LF); power of the spectrum in the high frequency range (HF); power of the spectrum in the very low frequency range (VLF); power of the spectrum in the ultra low frequency range (ULF); and the ratio of low to high frequency spectrum power (LF/HF) as an indicator of sympathetic-parasympathetic functional equilibrium. Detailed characteristics of parameters and results are presented in Tables 1 and 2.

Results

Between 1997 and 2018, 26 publications that met our inclusion criteria were identified. Among the identified publications, 15 papers were included in the detailed

Table 1. Electrocardiographic (ECG) test characteristics and edition of data for heart rate variability (HRV) analysis and measured HRV parameters

Author, year of publication, ref.	ECG test characteristics and edition of data for HRV analysis	HRV parameters [unit] [for frequency parameters frequency bands]
Lindh et al., 1997 [22]	Sampling frequency: 1,000 Hz, secondary sampling rate 5 Hz, R-peaks detected by algorithm based on first ECG difference. Inverse of RR interval was used as instant HR	HR [bpm], LF power [log mHz^2], HF power [log mHz^2], LF/HF power
Mazursky et al., 1998 [21]	Chest and abdomen electrodes, 7-min ECG, 1 kHz sampling frequency	HR [bpm], LF [ms^2] (0.02–0.15 Hz), HF [ms^2] (0.15–1.5 Hz), LF/HF
Nakamura et al., 2005 [19]	150-min ECG recording, sampling rate: 1 kHz, secondary RR-sampling at 4 Hz using linear interpolation, Fourier transformer power spectrum calculation	LF [%] (0.04–0.15 Hz), HF [%] (0.15–0.4 Hz), LF/HF
Indic et al., 2008 [12]	90-min ECG, R-peaks detected using derivatives and a threshold algorithm, RR-series corrected for any artifacts and erroneously detected R-peaks, secondary sampling at 3 Hz	LF [ms^2], HF [ms^2], TP [ms^2]
Thiriez et al., 2009 [23]	Biopack system, chest drain, sampling rate: 1,000 Hz coarse-grained spectroscopic analysis (CGSA) of RR interval series to determine HRV power spectrum for each infant before Fourier transform	LF [ms^2] (0–0.2 Hz), HF [ms^2] (0.2–2 Hz), LF/HF, TP [ms^2]
Krueger et al., 2010 [14]	300-second, 3-lead ECG, sampling rate: 500 Hz, Matlab signal filtering, QRS complex detection algorithm	TP [ms^2] (0.04–2.0 Hz), HF [ms^2] (0.30–1.3 Hz), LF/HF
McCain et al., 2010 [18]	RR intervals recorded by ANSAR-1000 system, chest-placed electrodes, Fourier transformer frequency calculation, 10 min before, during and after feeding, 10 min after feeding	HR [bpm], LF [ms^2] (0.04–0.15 Hz), HF [ms^2] (0.15–1.0 Hz), LF/HF
Selig et al., 2011 [20]	An average 26-min ECG recording. Electrocardiographic data (1,000 consecutive RR intervals) detected digitally on the Polar Advanced S810i device. Discrete Fourier transformer used to decompose sequential RR interval series	SDNN [ms], RMSSD [ms], LF [ms^2], VLF [ms^2], HF [ms^2], LF/HF
Smith et al., 2013 [13]	ECG data from Mortar H12 and Holter monitors, 10 min before therapy, during therapy and 10 min after therapy, three bipolar leads, two chest leads, one grounding lead and Mason-Liker limb leads. Sampling frequency: 1,000 Hz, analogue ECG data converted to digital signal, R-peaks identified for HRV analysis	HR [bpm], SDNN [ms], RMSSD [ms], HF [ms^2]
Smith et al., 2013 [24]	8-hour ECG recording from Mortar H12 and Holter monitors, sampling rate: 1,000 Hz; from ECG data, variance in HF and LF regions isolated	HR [bpm], LF/HF
Dimitrijević et al., 2016 [10]	24-hour Holter ECG test analysing only normal NN intervals over at least 18 h using time analysis method. Other ectopic rhythms and artifacts manually identified and then excluded from HRV analysis	HR [bpm], SDNN [ms], RMSSD [ms]
Kommers et al., 2016 [15]	30 min 3-lead ECG, sampling rate: 125 Hz; QRS complex detection algorithm with special attention to R-peaks for RR intervals; 20 Hz secondary sampling using linear interpolation — calculation of frequency parameters using discrete Fourier transform	HR [bpm], SDNN [ms], RMSSD [ms], pNN50 [%], LF [ms^2] (0,04–0,15 Hz), HF [ms^2] (0,4–1,5 Hz), LF/HF
Silva et al., 2018 [16]	15-min ECG recording, back lying test with Polar RS800CX transmitter and watch; analysis with Kubios HRV Premium software	HR [bpm], SDNN [ms], RMSSD [ms], pNN50 [%], LF [ms^2], HF [ms^2], LF/HF, TP [ms^2]
Jost et al., 2018 [25]	Sampling frequency: 500 Hz, two electrodes placed on both sides used for test. At the same time, video recordings made during measurements. Synchronisation of sEMG measurement and video recording performed online in Polybench software	SDNN [ms], RMSSD [ms]
Latremouille et al., 2018 [17]	To analyse the parameters in time and frequency domain, 5-min episode from ECG recording was used. Three ECG leads were located on child's limbs. Sampling frequency: 5–80 Hz	SDNN [ms], RMSSD [ms], pNN50 [%], LF [ms^2], VLF [ms^2], HF [ms^2], LF/HF, TP [ms^2]

HR — heart rate; bpm — beats per minute; LF — low frequency; HF — high frequency; TP — total power; SDNN — standard deviation of NN intervals; RMSSD — square root of the mean square root of the sum of squares of differences between consecutive RR intervals; VLF — very low frequency; sEMG — thoracic surface electromyography; pNN50 — percentage of differences between successive sinus RR intervals that exceed 50 ms

Table 2. Basic characteristics of study groups and procedures with results

Author, year of publication	Characteristics of study group	Test procedure	Results
Lindh et al., 1997 [22]	Eight infants born prematurely Gestational age: range: 24–33 weeks Birth weight: no data available	Video analysis and HR measurements began with observations at rest for 5 min, then the sole of the foot was stimulated. After foot flexors responded to stimulation, child left alone for 3 min. During study, infant remained lying on its back with camera pointing at face. Each child examined once	At rest: • HR: 155 ± 0.16 • LF power: 3.4 ± 0.7 • HF power: 2.6 ± 0.8 • LF/HF power: 0.8 ± 0.3 In response to stimulation: • HR: 164 ± 15 • LF: 3.5 ± 0.5 • HF: 2.6 ± 0.7 • LF/HF: 0.8 ± 0.4
Mazursky et al., 1998 [21]	28 infants born prematurely Gestational age: 27,3 (range: 24–30 weeks) Birth weight: 1042,67 g (range: 700–1510 g)	ECG examination during verticalisation test. During each test, lying position of the newborn was adequately protected. Before verticalisation test, 1-min horizontal ECG performed. Then table on which the infant rested was lifted to a 45° angle, and in this position another 1-min ECG performed. Throughout whole study, respiratory rhythm was also observed. Examinations were carried out between 10am and 3pm, while baby was asleep	• HR: postconceptional age range 28–32 weeks: 155 ± ± 62 bpm, postconceptional age range 35–39 weeks: 152 ± 64 bpm • LF: data presented on figures • HF: data presented on figures LF/HF in leaning tilt of 45° LF/HF in lying position (Values in form of diagram)
Nakamura et al., 2005 [19]	11 infants born prematurely Gestational age: 30.63 (range: 26 to 34 weeks) Birth weight: 1,363.72 g (range: 467–2,108 g)	Data collected using ECG-assisted recording of ventricular contractions. Test performed between 6pm and 6am and recording lasted 2.5 h. Children remained in incubators all the time. For children who remained in intensive care unit for several days, HRV analysis data collected every day; for those who remained in unit for several months, every two days	Group A: • LF: 0.51 ± 0.26 • HF: 0.051 ± 0.26 • LF/HF: 10.3 ± 9.4 Group B: • LF: 0.24 ± 0.034 • HF: 0.022 ± 0.36 • LF/HF: 12.2 ± 15.9
Indic et al., 2008 [12]	10 infants born prematurely Gestational age: no data available Birth weight: no data available	For HRV analysis, each child underwent ECG of 1.5 h	Infants 2, 3, 7, 8 and 10: • TP: values given in diagram • LF: 0.29/0.17/0.24/0.15/ /0.20 • HF: 0.14/0.31/0.16/0.20/ /0.13
Thiriez et al., 2009 [23]	19 infants born prematurely Gestational age: 32.05 (range: 25.6–34.6 weeks) Birth weight: 1,520 g (range: 700–2,380 g)	ECG electrodes placed on chest when children lying on their backs. Chest movements and breathing visually controlled to ensure no apnoea. Children examined during nap after breastfeeding. ECG recording collected while baby asleep and was quiet so that ECG recording could last at least two min	1. Children of non-smoking mothers: • LF/HF: 8 (1–11) • TP: 23 (15–64) 2. Children of smoking mothers: • LF/HF: 5 (1–21) • TP: 28 (16–41)
Krueger et al., 2010 [14]	31 infants born prematurely Gestational age: range: 28–34 weeks Birth weight: 1,061.1 g (range: 654–1,470 g)	HRV analysis performed during seven weekly test sessions. For this purpose, ECG lasting 300 s was used, while children in incubators in intensive care unit. Data collected no earlier than 15 min after feeding while child was in active sleep and usually at same time from 10am to 12 noon	Graphical presentation of results

cd. →

Table 2. cd. Basic characteristics of study groups and procedures with results

Author, year of publication	Characteristics of study group	Test procedure	Results
McCain et al., 2010 [18]	3 infants born prematurely Gestational age: 27.3 (range: 24–33 weeks) Birth weight: 873.3 g (range: 580–1,200 g)	Two researchers collected information from each feeding period: the first person fed, the second monitored equipment used for HRV analysis and made behavioural assessment at end of each minute. Study started 10 min before start of feeding, and lasted for entire feeding period and 10 min after it ended. Children remained in bed during this time	Infants 1, 2 and 3: Before feeding: • HR: 139–151/155–156/153–161 • HF: 2.5/2.9/0.9 • LF: 5.2/6.8/2.6 • LF/HF: 2.1/2.3/2.8 During feeding: • HR: 155–180/153–164/161–171 • HF: 1.1/2.0/0.2 • LF: 3.9/7.3/1.3 • LF/HF: 3.6/3.6/6.4 After feeding: • HR: 164–178/135–160/165–170 • HF: 1.4/1.6/0.3 • LF: 4.1/6.3/0.9 • LF/HF: 2.9/3.3/6.9
Selig et al., 2011 [20]	48 infants born prematurely and 78 born on time Gestational age: greater than 37 weeks for term neonates Birth weight: 1,476 g (range: 770–2,380 g)	Research conducted during first few days of life. Firstly, questionnaires filled in, then ECG using Polar device performed, and finally infants physically evaluated	Infants born prematurely: • SDNN: 13.8 ± 6.8 • RMSSD: 5.9 ± 3.7 • LF: 47.9 ± 53.7 • VLF: 47.3 ± 50.7 • HF: 11.4 ± 12.6 • LF/HF: 7.6 ± 6.7 Infants born on time: • SDNN: 22.6 ± 7.9 • RMSSD: 11.1 ± 6.8 • LF: 115.7 ± 87.9 • VLF: 129.8 ± 111.1 • HF: 33 ± 34 • LF/HF: 4.7 ± 2.3
Smith et al., 2013 [13]	17 infants born prematurely. Gestational age: range: 29–32 weeks Birth weight: no data available	For four weeks, each child massaged twice a day for 20 min. Massage consisted of applying soft tissue pressure in following areas while child lying on back: 1) from top of thighs to ankles and feet; 2) chest; 3) arms down to hands; 4) head from crown to neck; and 5) lengthwise from neck to waist. Children were lying down. Every week, in the morning, ECG performed to analyse HRV, starting from baseline at start of examination, then four times after each week	Therapy group: • HF: 158 ± 67 • LF/HF: 6.34 ± 0.04 Control group: • HF: 158 ± 67 • LF/HF: 8.04 ± 0.06
Smith et al., 2013 [24]	10 infants born prematurely Gestational age: 31.4 (± 0.8) — massage therapy group, 30.9 (± 0.7) weeks — control group Birth weight: range: 1,553.2–1,588.7 g	ECG examination started before therapy and sleep control period, while children slept in incubator. Information collected over 8-h period so that two periods of sleep and two therapeutic sessions could be included in study. Professional massage therapists gave infants massage (MT): 20 min of compression with moderate force, followed by stroking of soft tissues and limb movements. In control group, 20 min without manipulation. Sessions lasted from Monday to Saturday for four consecutive weeks:	LF/HF: values given in form of diagram

cd. →

Table 2. cd. Basic characteristics of study groups and procedures with results

Author, year of publication	Characteristics of study group	Test procedure	Results
Dimitrijević et al., 2016 [10]	79 infants born prematurely Gestational age: range: 25–36 weeks Birth weight: range: < 1,000–> 2,500 g	Video recording of each participant in trial was made twice: in first month of adjusted age and in third month after due date. During recording, newborn baby remained on colourless base, lying down, wearing only a nappy, with face clearly visible. Recording of data for analysis lasted at least 10 min, when baby showed appropriate behaviour (open eyes, no crying, irregular breathing, movements present) In addition, each child in first month after birth was examined using 24-h ECG to determine HRV parameters At adjusted age of 24 months, each child was subjected to a standard neurological examination	Subgroup N: • HR: 133 ± 9.34 • SDNN: 66.12 ± 11.68 • RMSSD: 22.84 ± 7.84 Subgroup PR: • HR: 140.15 ± 7.93 • SDNN: 58.6 ± 13.39 • RMSSD: 19.35 ± 4.49 Subgroup CS: • HR: 143.1 ± 16.6 • SDNN: 42.1 ± 12.40 • RMSSD: 16 ± 1.94
Kommers et al., 2017 [15]	11 infants born prematurely Gestational age: 28 weeks (range: 26–29) Birth weight: 950 g (range: 836–1,273 g)	Nurses noted start and end times of kangaroo sessions for three months. Data for 60 min before, during, and 60 min after session were collected from children, with at least 10 well-described kangaroo sessions lasting at least 1 h	Before kangarooing: • HR: 159 (146–170) • SDNN: 42 (21–79) • RMSSD: 40 (15–79) • pNN50: 2.3 (0.5–10.3) • LF: 781 (168–4,486) • HF: 513 (64–1,877) • LF/HF: 2.8 (1.6–4.9) During kangarooing: • HR: 156 (145–167) • SDNN: 29 (18–65) • RMSSD: 25 (12–53) • pNN50: 1.3 (0.3–5.3) • LF: 459 (110–2,470) • HF: 165 (37–1,311) • LF/HF: 3.5 (1.8–6.7)
Silva et al., 2019 [16]	46 infants born prematurely Gestational age: mean: 29.7 ± 2.34 weeks Birth weight: 996.4 ± 26 g (scope: 595–1,550 g)	All preterm infants treated with steroids during HRV tests. All patients evaluated for HRV immediately prior to extubation, and received mechanical ventilation during 15-min ECG recording in back position. Preterm infants who required reintubation within 48 h were included in group of failures	Failure: • SDNN: 12.3 ± 5.72 • RMSSD: 8.18 ± 4.36 • pNN50: 0.26 ± 0.37 • HR: 140.5 ± 20.6 • LF: 108.3 ± 98.9 • HF: 41.3 ± 38.6 • LF/HF: 3.59 ± 1.83 • TP: 170.6 ± 147.5 Successful extubation: • SDNN: 12.9 ± 7.23 • RMSSD: 9.45 ± 6.55 • pNN50: 0.81 ± 2.02 • HR: 139.5 ± 16.9 • LF: 114.4 ± 139.2 • HF: 51.9 ± 98.9 • LF/HF: 3.91 ± 2.31 • TP: 186.9 ± 224.5

cd. →

Table 2. cd. Basic characteristics of study groups and procedures with results

Author, year of publication	Characteristics of study group	Test procedure	Results
Jost et al., 2017 [25]	24 infants born prematurely Gestational age: mean: 30.3 ± 2.4 weeks Birth weight: 1,277 ± 341 g	Infants remaining in incubators were treated during first five days of life. sEMG test conducted at 8.30am every day and lasted for 3 h. Three different algorithms for QRS detection were compared	• SDNN: 0.028 (0.011) • RMSSD: –4.379 (0.612)
Latremouille et al., 2018 [17]	15 infants born prematurely Gestational age: average: 27.0 weeks (range: 25.3–28.0 weeks) Birth weight: 855 g (range: 746–1,013 g)	Before extubation, three ECG leads placed on child's limbs; after extubation and 30 min rest its vital signs had stabilised. During this period, patient received appropriate respiratory support depending on which study group assigned to. Then ECG recorded for 30–60 min	CPAP: • SDNN: 12.2 [7.3–23.1] • RMSSD: 7.4 [3.8–18.8] • pNN50: 0.5 [0–0.7] • LF: 33.9 [3.6–123.6] • VLF: 39.8 [22.3–208.4] • HF: 24.5 [2.4–95.8] • LF/HF: 1.7 [0.6–5.6] • TP: 143.8 [29.6–646.6] ns-NIV: • SDNN: 18.4 [14.7–21.2] • RMSSD: 14.5 [8.0–24.8] • pNN50: 0.5 [0.2–2.3] • LF: 49.4 [34.8–143.0] • VLF: 126.8 [63.0–334.5] • HF: 41.4 [8.5–60.0] • LF/HF: 3.2 [0.8–6.9] • TP: 240.1 [128.6–623.0]

HR — heart rate; LF — low frequency; HF — high frequency; ECG — electrocardiography; HRV — heart rate variability; TP — total power; SDNN — standard deviation of NN intervals; RMSSD — square root of the mean square root of the sum of squares of differences between consecutive RR intervals; VLF — very low frequency; pNN50 — percentage of differences between successive sinus RR intervals that exceed 50 ms; sEMG — thoracic surface electromyography; CPAP — continuous positive airway pressure; ns-NIV — non-synchronised noninvasive ventilation

analysis. The full text of five manuscripts was not available, and four papers were rejected: one was commenting on another study, and in one literature review and two papers the analysed parameters did not agree with the assumptions of this review. The analysis included studies in which the results were given for 438 children, both from control and study groups, born between 25 and 36 weeks of gestation. One of the publications did not specify the gestational age [12]. The birth weight oscillated between 467 and 2,380 g. This parameter was not specified in three publications [12–14]. Detailed characteristics of ECG examination, edition of data for HRV analysis, and HRV parameters are set out in Table 1. Characteristics of the study group, procedures and results are set out in Table 2. Frequency analysis was used more frequently in the studies. The most often presented parameter was HF, which was used in 12 studies. In 11 publications results for LF/HF ratio were given, and in 10 publications results for LF parameter were given. Time analysis was performed by seven groups of researchers, using parameters in each of them: SDNN, RMSSD and in three of them pNN50 [15–17].

Discussion

The aim of this paper is to analyse a review of the English-language literature on the issue of cyclical heart rate changes resulting from changes in ANS activity in prematurely born children, and to summarise the results of articles selected for final analysis.

ECG studies were differentiated with regard to the length of recording. In one of the articles, a 24-hour recording was used [10], while in three other publications a 30-minute recording was selected [13, 15, 18]. Eight-hour ECG was used in one article [24], but in others a 150-minute [19], 90-minute [12], 26-minute [20], 15-minute [16], and 7-minute ECG was used [21], and in three studies a 5-minute ECG [14, 17, 22]. In one publication, the length of registration depended on the time required to obtain at least two minutes of electrocardiography (ECG) recording during which the child continued to sleep [23]. Frequency parameters were most often calculated using a discrete Fourier transformer. In selected works, the results for the following parameters of frequency analysis were given:

TP, VLF, LF, HF, LF/HF and time analysis: SDNN, RMSSD, pNN50, of which the most frequently reported were LF and HF. The results are presented mostly in numerical form, although in two studies the results can be read only from diagrams [13, 24].

The main aim of our study was to evaluate the control of the cardiovascular system by the ANS, and the usefulness of HRV analysis in predicting further development of a child born before the due date, as well as to evaluate the use of various forms of therapy in the treatment of neonatal developmental changes resulting from premature childbirth.

The authors of the study from 2016 examined 11 children, on average 18 days after birth, analysing the results before and after the kangaroo session. Case studies showed that preterm infants are susceptible to rapid and temporary HR slowdowns that can lead to misinterpretation of general HRV [15]. We also learned that HRV analysis can be clinically useful in capturing dynamic changes in autonomic regulation in response to kangaroo and other changes in a child's environment [15]. In 2006, an article including 11 infants in their first year of life was published. A higher LF/HF ratio was observed in preterm infants. According to the authors, this suggests lower activity of the parasympathetic nervous system and dominance of the sympathetic part [20]. Dmitrijević et al. [10] decided to investigate the clinical usefulness of indicators of HRV in the time domain evaluated on the basis of a 24-hour ECG recording in improving the predictive value of weak global movement patterns in 79 premature infants. According to their results, the predictive value of the weak repertoire of global movement patterns in premature infants is associated with low values of analysed HRV parameters [10].

Lindh et al. [22], who analysed the results of the group of eight preterm infants, found that HRV spectral analysis as a tool to assess sympathetic and parasympathetic balance is used more frequently in the study of newborns born on time than in the group of preterm infants, and that in preterm infants the ANS is immature and the total power of the spectrum increases with gestational age. The next publication we looked at described the analysis of selected parameters of 28 infants born between 24 and 32 weeks of pregnancy, in which the authors observed how a momentary head-up tilt test affects the variability of heart rate. It turns out that immediately after birth, the change in position slightly affects the analysed values, although it changes with further development, as well as baroreceptor reflex functions [21]. McCain et al. [18] analysed the results of studies of three children with bronchopulmonary dysplasia, conducted successively before, during and after feeding. They observed that in all parts of the study, and in all three children, LF was higher than HF. According to the authors, this trend may be caused by the aforementioned respiratory dysfunction, which in consequence puts additional strain on the cardiovascular system and requires a higher proportion of the sympathetic part of the autonomic system in order to work properly [18].

In 2009, 19 premature infants whose mothers smoked while pregnant were analysed. This publication, similarly to another two in our review, introduced a control group of 21 non-smoking mothers' neonates. The authors' aim was to assess the impact of premature birth in combination with foetal nicotine exposure on autonomic heart rate control. The study showed that neonates of smoking mothers had a lower spectrum power in the low frequency HRV range normalised to total spectral power (LF/TP) than the control group [23]. A year earlier, the presence of cardiopulmonary feedback in 10 premature infants was studied by determining the interaction between HRV and respiration [12]. The results of indices in the frequency domain were given only for five children. These observations indicated mild but present respiratory irregularity of sinus rhythm in premature infants [12]. The next two publications were published in the same year (2013) by the same team of authors [13, 24]. Both studies analysed the influence of massage on selected HRV parameters in a group of premature children [13, 24]. The results indicate an improvement in the parameters of sinus rhythm variability in massaged children, and a lack of improvement in children from the control group who did not undergo therapy. A greater improvement was also observed in boys compared to girls. At the end of the study, the values of HRV parameters of massaged children were comparable to those of children born on time. Based on the results, it was suggested that massage improves ANS function in these infants [13]. The second study compared ANS function and stress responses in preterm infants during sleep and care periods after two weeks of massage therapy twice daily. A total of 21 children from the control and study groups took part in this study. Increasing the value of the LF/HF parameter during care, and lowering this parameter during sleep, in children undergoing therapy suggests an improvement of ANS function, although their values were not statistically significant. In girls, no differences were observed between the study group and the control group [24]. Krueger et al. [14] studied 31 premature babies, additionally randomly dividing them into subgroups A and B. The aim of the study was to provide information on the total frequency range, HF and LF/HF ratio in preterm infants. This observation shows that autonomic work control and HRV mature with age, that HF increases with a simultaneous decrease in LF/HF, and that HF values in girls are higher than in boys, which, according to the authors, may indicate a more mature autonomic system. Silva et al. [16] analysed 46 children, dividing them into two subgroups, the first of which included infants after failure and the second after successful extubation. The aim of the study was to evaluate HRV in intubated preterm infants in an intensive care unit (ICU) immediately before extubation, and to correlate HRV with clinical evaluation results. HRV analysis was an effective indicator in predicting unsuccessful extubation in preterm infants when assessed in the nonlinear domain and in preterm infants weighing less than 1,000 g [16].

In the next publication, 24 children were examined in the first week after birth. The feasibility of thoracic surface electromyography (sEMG) was tested in a group of premature children in order to exclude noise-disturbed data and to obtain time intervals between individual heartbeats for the analysis of HRV [25]. Latremouille et al. [17] identified the differences in HRV parameters between continuous positive airway pressure (CPAP) and non-synchronised noninvasive ventilation (ns-NIV) as the main objective of their study, which involved 15 infants divided randomly into two groups. They found that immediate respiratory support using the two abovementioned methods does not significantly affect HRV [17]. Another group of researchers used their knowledge of linear and nonlinear dynamics in the evaluation of preterm infants and compared the results of these studies to healthy newborns. A statistically significant difference was found between the groups for all variables. The study shows that premature infants have less differentiated HRV than newborns born on time [20].

The publications selected for this review are highly diverse in terms of their methodology, the number of children selected for analysis, the ECG duration, and the analysed parameters. The most frequently chosen duration of ECG recording was 30 minutes. Only once was a 24-hour recording used, despite the fact that this is recommended by Task Force experts as the most reliable for the overall assessment of all factors that may affect the variability of sinus rhythm. Circular rhythms, body temperature, metabolism, sleep cycle and active renin-angiotensin system influence 24-hour HRV records, which are the 'gold standard' of clinical evaluation of cardiac rhythm variability.

Moreover, the length of recording time strongly influences the values in the time domain. Shorter periods may result in lower and underestimated values. The minimum recommended test period for these parameters is: ULF (24 h), VLF (5 min, but recommended to be 24 h), LF (2 min), and HF (1 min), so it is important to consider whether the choice of a shorter recording time will be sufficient for an accurate assessment of the patient's condition. However, we learn from the same work that resting measurements of short duration, measured before, during and after a given therapy, may also help in the evaluation of physiological changes [26].

Certainly, it would be useful to compare different forms of therapy that improve the efficiency of heart rhythm forming mechanisms in the group of preterm infants, to select appropriate parameters that best illustrate abnormalities in the development of the body, and to choose the most effective forms of treatment in this group.

The presented review of the literature marshals the knowledge contained in English language publications, but it is still difficult to compare the results of the research. This is due to the fact that the criteria for inclusion in the study, their construction, methodology and evaluated HRV parameters, are not homogeneous.

In most studies, only parameters in the frequency domain were evaluated. According to the recommendations for experiment planning, data analysis and data reporting, it is important to combine HRV frequency analysis with other parameters in the time domain in order to check to what extent they correlate with each other [27]. Moreover, the number of patients in the study groups and the age range of neonates differ significantly. It is also worth noting the number of repetitions, the position in which the neonate is placed, and the interval between repetitions. An important issue related to the movement of the child during the study is that more artifacts in the data set are at risk [27]. Researchers are advised to maintain the structure of three measurements in their experimental projects: measurement at rest, during intervention, and after intervention [27, 28].

The duration of electrocardiographic recording is also important in order to compare the studies. Despite the fact that in 1996 a group of Task Force experts defined standards for the duration of measurements, in selected studies the duration of measurements ranged from a few minutes to 24 hours, which makes it impossible to compare the collected results with others. It should be noted that the devices and programs used for the analysis of the research may also generate differences in the values of a given parameter.

Therefore, it is necessary to specify, in order to increase the repeatability of tests, the following as a minimum: detailed testing methodology, measurement conditions, number of repetitions, ECG recording time, evaluated parameters, selection of devices to be used for measurements, and programs for data analysis.

Conclusions

One of the most important consequences of premature childbirth is the disturbance of ANS development, which in consequence is associated with a malfunction of the heart muscle. Damage to sympathetic and parasympathetic fibres leads to pathological changes in the excitation of the sinoatrial node, and thus to uncontrolled changes in heart rate [6].

Results of the included studies suggested that the ANS is the most important system in the process of controlling heart contractions [5, 29]. The high variability and complexity of heart rhythm is an expression of significant adaptability of the organism and is prognostically beneficial [5, 8]. It is smaller in children, but increases gradually with age.

The electrocardiographic signal is the basis for HRV measurements [30]. The most frequently analysed parameters turned out to be: LF, HF, and LF/HF ratio, while the most frequently chosen duration of ECG examination was a 30-min recording [13, 15, 18].

More and more often in the English literature the topic of the analysis of ANS activity in premature infants using HRV analysis is being discussed. However, studies of this group of patients using HRV analysis are still scarce. Attempts are being made to analyse the influence of therapy related to rehabilitation on the improvement of HRV parameters in premature infants, and so on the improvement of ANS function/activity. However, these studies are not free from limitations. Therefore, further research is needed to determine whether any form of rehabilitation is able to improve the functioning of the ANS in preterm infants.

Conflict(s) of interest

The authors declare no conflict of interest.

Streszczenie

Wstęp. Poród przedwczesny, mimo ciągłego rozwoju medycyny i coraz lepszej opieki okołoporodowej, pozostaje jednym z największych wyzwań w położnictwie. Dziecko urodzone przedwcześnie występuje wiele zaburzeń, między innymi nieprawidłowości funkcjonowania autonomicznego układu nerwowego (AUN), który wpływa między innymi na pracę mięśnia sercowego. Jedną z metod oceny wpływu aktywności AUN na pracę serca jest analiza zmienności rytmu zatokowego (HRV) serca, ukazująca pośredni obraz jego wpływu na zdolność przystosowania funkcji skurczowej mięśnia sercowego względem zewnętrznych bodźców.

Celem pracy jest ocena aktywności AUN na podstawie wartości parametrów HRV serca u dzieci urodzonych przedwcześnie na podstawie przeglądu piśmiennictwa.

Materiał i metody. Przegląd piśmiennictwa przeprowadzono zgodnie z rekomendacjami PRISMA. Dokonano przeglądu medycznych baz danych: MEDLINE/*PubMed*, *ProQest*, PEDro, *Cochrane*, *Embase*, używając kluczowych zwrotów: „zmienność rytmu zatokowego serca" (ang. *heart rate variability*) w połączeniu z „przedwcześnie urodzone dzieci" (ang. *preterm infants*).

Wyniki. Od roku 1997 do 2018 zidentyfikowano 26 publikacji spełniających kryteria włączenia, z których 15 wybrano do szczegółowej analizy. W przeglądzie analizie poddano wybrane parametry analizy czasowej oraz częstotliwościowej HRV.

Wnioski. Dzieci urodzone przedwcześnie są podatne na zaburzenia kontroli rytmu serca przez AUN wyrażone szybkimi i przejściowymi zmianami wartości tętna. Obserwuje się u nich wyższe wartości tętna oraz wybranych parametrów HRV sugerujące dominację aktywności części współczulnej w kontroli rytmu serca. Dodatkowo dotychczasowe badania nie są wystarczająco usystematyzowane, by móc je porównać między sobą. W związku z tym temat ten wymaga podjęcia dalszych badań.

Słowa kluczowe: zmienność zatokowego rytmu serca, autonomiczny układ nerwowy, wcześniactwo

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