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ORIGINAL ARTICLE

Extrasystoles or short bradycardias of the newborn seldom require subsequent 24-hour electrocardiographic monitoring

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Abstract

Aim: To retrospectively assess the indications for and findings on 24-hour electrocardiographic (Holter) monitoring in newborns, focussing on bradycardias and extrasystoles.

Methods: Data included 337 term-born infants. Holter indications were categorised into bradycardias below 80 beats per minute, extrasystoles, any tachycardia and other. Heart rate below 60 beats per minute, pathological atrioventricular conduction, supraventricular or ventricular tachycardia, or either atrial premature contractions over 10% or ventricular premature contractions over 5% of total beats were defined as significant arrhythmia on Holter.

Results: The median age was 6 days (range: 2–62 days). Bradycardia (42%) or extrasystoles (32%) were the most common Holter indications. Fifty-three infants (16%) had significant arrhythmia on Holter. Heart disease or 12-lead electrocardiogram expressing extrasystoles or conduction abnormalities were associated with significant arrhythmias ($p = 0.046$ and $p < 0.001$, respectively). Twenty-seven of 109 infants (25%) with extrasystoles as a Holter indication had abnormal Holter results, but only seven (6.4%) had significant arrhythmia on Holter if the 12-lead electrocardiogram was normal. No pathology was found behind bradycardias below 80 beats per minute in the absence of heart disease.

Conclusion: Among term newborns with extrasystoles or bradycardias, Holter monitoring could be targeted to infants with heart disease or abnormal electrocardiograms.

KEYWORDS
arrhythmia, bradycardia, extrasystoles, Holter, neonatal

Abbreviations: APC, atrial premature contraction; AV, atrioventricular; bpm, beats per minute; CHD, congenital heart disease; ECG, electrocardiogram; HR, heart rate; LV, left ventricular; NICU, neonatal intensive care unit; SD, standard deviation; SVT, supraventricular tachycardia; VPC, ventricular premature contraction; VT, ventricular tachycardia.

1 | INTRODUCTION

Cardiac arrhythmias are common in the neonatal period and are generally benign.[1–3] Supraventricular tachycardia (SVT), ventricular tachycardia (VT), ventricular fibrillation and atrioventricular (AV) conduction abnormalities are clinically significant neonatal arrhythmias that need to be diagnosed early for optimal management.[1–4] These non-benign arrhythmias are more common in patients with congenital heart disease (CHD)—especially after surgical repair—than in patients with a healthy heart.[1,5,6]

The diagnosis of clinically significant arrhythmias requires electrocardiographic documentation. The transitory nature of arrhythmias makes 24-hour ambulatory electrocardiographic (Holter) monitoring, a more sensitive test for arrhythmia detection than the standard 12-lead electrocardiogram (ECG).[4,7] In addition to clinically suspected tachyarrhythmias, common indications for neonatal Holter monitoring in our hospital have been recurrent bradycardias and multiple extrasystoles. In our experience, a large proportion of these infants did not have clinically significant findings on Holter monitoring, suggesting a need to re-evaluate the Holter indications.

The purpose of this single-centre study was to retrospectively assess Holter recording findings in infants up to 2 months of age. Our aim was to evaluate the need for 24-hour Holter monitoring in newborns with bradycardias or extrasystoles. The hypothesis was that most neonatal bradycardias and extrasystoles are benign and transient, and 12-lead ECG can be used for screening significant arrhythmias in these patients.

Key Notes

- Cardiac arrhythmias are common in newborns, and the key is determining which infants require further electrocardiographic monitoring.
- The risk for clinically relevant tachyarrhythmia or bradycardia is low during early infancy if the standard 12-lead electrocardiogram is normal.
- Extrasystoles or short bradycardias of the newborn seldom require subsequent 24-hour electrocardiographic (Holter) monitoring: Holter monitoring could be targeted to infants with heart disease or abnormal electrocardiograms.

2 | PATIENTS AND METHODS

A retrospective chart review was performed among 0- to 2-month-old infants referred for Holter monitoring at Tampere University Hospital from 2011 to 2017. This tertiary hospital has approximately 4500 live births and 1000 neonatal unit admissions per year. The exclusion criteria were poor recording quality, recording not available in PDF, recording duration under 18 h or gestational age under 37 0/7 weeks at birth. Only the first recording of each infant was included (Figure 1).

The clinical practice was to perform 24-hour Holter monitoring on newborns between the age of 5 and 7 days if a tendency for multiple extrasystoles or prolonged periods of a heart rate below 80 beats per minute (bpm) seemed to not be transient. In addition, Holter monitoring was performed on infants with clinically suspected tachyarrhythmias or predisposing factors for arrhythmia. The majority of the neonatal Holter referrals came from neonatologists in close collaboration with paediatric cardiologists. Standard 12-lead ECG was taken from all patients as part of the Holter indication evaluation process. Echocardiography (echo) was performed on infants with suspected heart disease, non-benign arrhythmia (SVT, VT and AV conduction abnormalities) or multiple extrasystoles (approximately 2% or more) on Holter. In the present study, the term SVT was used for all atrial and supraventricular

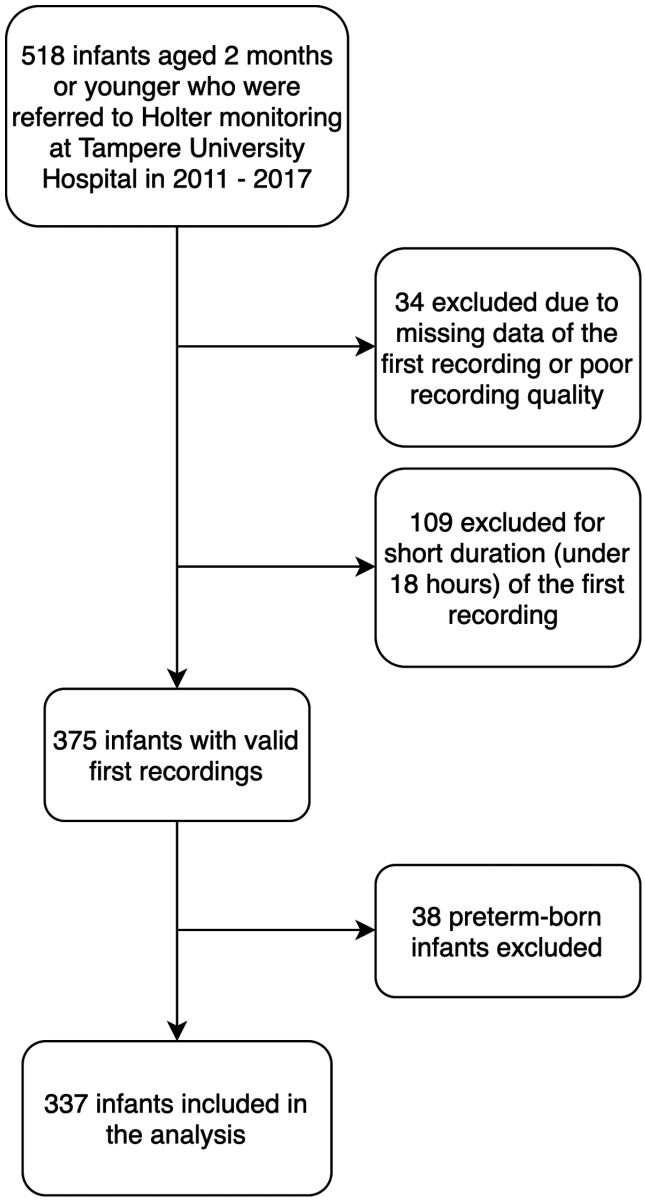

FIGURE 1 Flowchart of patient selection

tachycardias, including AV re-entrant tachycardias, atrial flutter and fibrillation.

Indications for Holter monitoring were gathered from referral texts and categorised into four groups according to the primary indication: bradycardia (heart rate <80 bpm), extrasystoles, tachycardia (inappropriate for clinical condition) and other (e.g., conduction abnormalities on ECG). Birth data, medications and diagnoses were obtained from patient records. CHDs requiring operative treatment, medication or close cardiac follow-up as well as structurally normal hearts with left ventricular (LV) dysfunction were coded as significant heart disease. To compare ECG and Holter results, standard 12-lead ECGs taken nearest to the Holter monitoring were retrospectively interpreted by a paediatric cardiologist (KY). ECG was coded as abnormal if extrasystoles, non-sinus rhythm, long QT interval or AV conduction abnormalities were present. Reference ranges used for normal ECGs were taken from Davignon et al.[8] for newborns ages 1–7 days and Rijnbeek et al.[9] for the rest.

A SEER Light or SEER Light Extend Holter recorder (GE Medical Systems Information Technologies) with two-channel or three-channel (2016 and onwards) recording was used. The intended recording time was 18–24 h. Holter data analysis was performed with the MARS V8 software (GE Medical Systems Information Technologies). The software automatically analysed the heart rate, maximum R-R interval, number of QRS complexes and number and runs of atrial premature contractions (APCs) and ventricular premature contractions (VPCs). The software calculated heart rate in bpm from 10 R-R intervals. A diary of the symptoms and activities was kept during the recording. After automated analysis, Holter data were checked for any misinterpretation of the software and edited manually by trained nurses. Wide-complex extrasystoles were manually categorised into VPCs or aberrant APCs if the automated analysis reported these in large numbers. The results were verified and interpreted by physicians specialised in clinical physiology. For this study, minimum and maximum heart rate was manually corrected for measurements of true sinus rhythm if they occurred during non-sinus rhythm.

2.1 | Statistical analyses

The main outcome variable was abnormal Holter defined as clinically significant arrhythmia on Holter: minimum heart rate under 60 bpm, Mobitz Type 2 or 3rd-degree AV block, sinus pause over 2 s, delta wave, SVT or VT (three or more consecutive ectopic beats), or either APCs over 10% or VPCs over 5% of total beats on the recording.

Means and standard deviations (SDs) were calculated for normally distributed variables, and medians and ranges were calculated for variables with a skewed distribution. Frequencies and percentages were used for categorical variables. For two-group comparisons, the independent samples *t*-test (two-sided) for normally distributed continuous variables and the Mann–Whitney *U*-test for nonparametric variables were used. Fisher's exact test was used for categorical variables. The statistical significance level was defined as $p < 0.05$. Statistical analyses were performed using IBM SPSS Statistics for Macintosh (version 26.0; IBM). The research project was approved by the Regional Ethics Committee of Tampere University Hospital.

TABLE 1 Demographic data of included infants ($N = 337$)

Demographic	
Number of boys, *n* (%)	200 (59)
Gestational age at birth (week), median (range)	40.1 (37.0–42.3)
Birth weight (g), mean (SD)	3590 (510)
Apgar score at 5 min, median (range)	9 (1–10)
Cord pH, mean (SD)	7.24 (0.09)
Caesarean section, *n* (%)	51 (15)
Any resuscitation at birth, *n* (%)	44 (13)
Significant congenital heart disease, *n* (%)	13 (3.9)
Referred to Holter monitoring from	
NICU or neonatal ward, *n* (%)	251 (74)
Maternity ward, *n* (%)	39 (12)
Paediatric ward, *n* (%)	27 (8.0)
Paediatric Cardiology Clinic, *n* (%)	20 (5.9)

Abbreviations: NICU, neonatal intensive care unit; SD, standard deviation.

3 | RESULTS

The study population consisted of 337 term-born infants, most of whom were referred for Holter monitoring from the neonatal ward or neonatal intensive care unit (NICU) (Table 1). Echo was performed on 212 infants (63%), and significant heart diseases were found in 18 infants: CHD in 13 and LV dysfunction without CHD in five infants. The median age at the start of Holter monitoring was 6 days (range: 2–62 days). The median recording time was 19 h (range: 18–25 h).

Bradycardia ($n = 143$, 42%) and extrasystoles ($n = 109$, 32%) were the most common indications for Holter monitoring (Table S1). Tachycardia was the indication in 45 infants (13%). Postnatal ($n = 17$, 38%) and foetal ($n = 13$, 29%) SVT was the most frequent Holter indications in the tachycardia group. Other indications ($n = 40$, 12%) included abnormal ECG ($n = 15$) or maternal anti-Sjögren's syndrome (SSA/SSB) autoantibodies ($n = 13$), among others.

Clinically significant arrhythmias (i.e., abnormal Holter results) were found in 53 infants (16%) (Table 2). Abnormal Holter results occurred more often in infants with significant heart disease (6/18, 33%) than in those without (47/319, 15%; $p = 0.046$). Antiarrhythmic treatment (propranolol, flecainide or amiodarone; $n = 13$) during Holter monitoring was not associated with heart rate.

TABLE 2 Holter results by primary indication for Holter monitoring

		Holter Indication				
Parameters	All (*N* = 337)	Bradycardia (*n* = 143)	Extrasystoles (*n* = 109)	Tachycardia (*n* = 45)	Other (*n* = 40)	*p*-Value[a]
Minimum HR <80 bpm[b]	169 (51)	111 (79)	31 (29)	11 (24)	16 (42)	<0.001
Any APC	286 (85)	123 (86)	95 (87)	37 (82)	31 (78)	0.448
Any VPC	183 (54)	73 (51)	59 (54)	31 (69)	20 (50)	0.186
Abnormal Holter	53 (16)	11 (7.7)	27 (25)	6 (13)	9 (23)	0.001
Minimum HR <60 bpm[b]	1 (0.3)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1.0
Delta wave	6 (1.8)	0 (0.0)	1 (0.9)	1 (2.2)	4 (10)	0.001
APCs >10%	5 (1.5)	0 (0.0)	5 (4.6)	0 (0.0)	0 (0.0)	0.026
VPCs >5%	14 (4.2)	1 (0.7)	12 (11)	1 (2.2)	0 (0.0)	<0.001
SVT	20 (5.9)	4 (2.8)	10 (9.2)	5 (11)	1 (2.5)	0.047
VT	13 (3.9)	5 (3.5)	3 (2.8)	2 (4.4)	3 (7.5)	0.549

Note: Data are expressed as *n* (%).

Abbreviations: APC, atrial premature contraction; bpm, beats per minute; HR, heart rate; SVT, supraventricular tachycardia; VPC, ventricular premature contraction; VT, ventricular tachycardia.

[a]Between groups. Fisher's exact test was used.

[b]During sinus rhythm. Five cases missing.

TABLE 3 Holter results by 12-lead ECG results (*N* = 336)

Holter Findings		Pre-Holter 12-lead ECG Findings						
		Abnormal ECG[a] (*n* = 68)	Delta wave (*n* = 4)	APCs (*n* = 28)	VPCs (*n* = 18)	Long PQ interval (*n* = 6)	Long QT interval (*n* = 14)	Normal ECG[a] (*n* = 268)
Abnormal Holter[b]		31 (46)	4 (100)	9 (32)	12 (67)	2 (33)	6 (43)	22 (8.2)
	Delta wave	5 (7.4)	4 (100)	–	–	–	2 (14)	1 (0.4)
	APCs > 10%	5 (7.4)	–	4 (14)	1 (5.6)	–	–	–
	VPCs > 5%	11 (16)	–	1 (3.6)	10 (56)	–	–	3 (1.1)
	SVT	11 (16)	–	5 (18)	2 (11)	2 (33)	3 (21)	9 (3.4)
	VT	5 (7.4)	–	2 (7.1)	1 (5.6)	–	2 (14)	8 (3.0)

Note: Data are expressed as number and percentage, *n* (%), of abnormal Holter findings among ECG findings. Shaded areas illustrate the association between similar ECG and Holter findings.

Abbreviations: APC, atrial premature contraction; ECG, electrocardiogram; SVT, supraventricular tachycardia; VPC, ventricular premature contraction; VT, ventricular tachycardia.

[a]Abnormal ECG definition: ECG expressing non-sinus rhythm, delta wave, either long PQ or QT interval, or extrasystoles. Normal ECG definition: ECG expressing none of the above-mentioned findings.

[b]Abnormal Holter definition: minimum heart rate <60 beats per minute, Mobitz Type 2 or 3rd-degree atrioventricular block, sinus pause over 2 s, delta wave, SVT or VT, or either APCs >10% or VPCs >5%.

3.1 | Bradycardias

A minimum heart rate below 80 bpm was present in 169/332 Holter recordings (51%). One infant had sinus bradycardia below 60 bpm without any related pathology. One infant had predominant junctional rhythm with a mean heart rate of 92 bpm (minimum heart rate of 78 bpm) due to a complex heart defect and absent sinus node. No other bradycardia-related pathology was found in the study population. No infant had a sinus pause lasting over 2 s or Mobitz Type 2 or 3rd-degree AV block. Abnormal Holter results were found in 11/143 infants (7.7%) with bradycardia as the Holter indication (Table 2).

3.2 | Extrasystoles

APCs and VPCs were found on 286 (85%) and 183 (54%) infants' recordings, respectively (Table 2). The numbers of infants having any APCs or VPCs were equal between Holter indications. The median number of beats was seven for APCs (range: 1–30,000)

and four for VPCs (range: 1–56,000). Five infants (1.5%) had APCs >10%, and 14 (4.2%) had VPCs >5%. Of the infants with significant heart disease, 1/18 (5.6%) had APCs >10% and none had VPCs >5%. VPCs >20% were observed in three patients without heart disease.

Of the infants with extrasystoles as the Holter indication, 27/109 (25%) had abnormal Holter results (Table 2), but only seven (6.4%) had significant arrhythmia on Holter if the 12-lead ECG was normal. These arrhythmias were SVT ($n = 4$), VPCs >5% ($n = 2$) and delta wave ($n = 1$).

3.3 | Tachyarrhythmias

Thirty-one infants (9.2%) had SVT ($n = 18$), VT ($n = 11$) or both ($n = 2$) on their Holter recordings (Table 2). The median lengths of SVT and VT were five beats (range: 3–145 beats) and three beats (range: 3–13 beats), respectively. No associations were found between VPCs >5% and VT or between APCs >10% and SVT. Instead, SVT occurred more often on recordings with APCs >5% (4/13, 31%) compared to those with fewer extrasystoles (16/273, 5.9%; $p = 0.008$). Tachyarrhythmias were more commonly observed in patients with significant heart disease (6/18, 33%) than in those without (25/319, 7.8%; $p = 0.003$). In the bradycardia referral group, 8/9 infants (89%) with tachyarrhythmias had either one short VT (3–5 beats) or SVTs shorter than four beats.

3.4 | ECG and its association with Holter results

In total, 336 infants had standard ECGs available for interpretation (Table 3). Sixty-eight ECGs (20%) were classified as abnormal: APCs were found on 28 (8.3%), VPCs on 18 (5.4%) and conduction abnormalities on 22 (6.5%) ECGs. Abnormal Holter results occurred more often among infants with abnormal ECG (31/68, 46%) than among those without extrasystoles or conduction abnormalities on ECG (22/268, 8.2%; $p < 0.001$).

Infants with APCs on ECG had APCs >10% or SVT on Holter (9/28, 32%) more frequently than those without (15/308, 4.9%; $p < 0.001$). Infants with VPCs on ECG had VPCs >5% or VT on Holter (10/18, 56%) more often than those without VPCs on ECG (15/318, 4.7%; $p < 0.001$). The presence of VPCs on ECG was not associated with VT only.

4 | DISCUSSION

In the present study, the incidence of clinically significant arrhythmias was low. Extrasystoles or conduction abnormalities on 12-lead ECG and significant heart disease were associated with clinically significant arrhythmias on Holter. Most Holter recordings with an indication of bradycardia or extrasystoles revealed non-significant findings.

The infants with significant CHD or LV dysfunction more often had abnormal Holter results and a higher frequency of tachyarrhythmias, which is in line with previous studies.[1,5,6] Tachyarrhythmias were observed in all Holter indication groups. Nevertheless, most of the tachyarrhythmias in our study population were short, and some of them could be considered incidental findings. Previous studies have reported tachyarrhythmias with a benign course.[10,11]

Extrasystoles are common in newborns,[1–3] but there is no clear threshold for an abnormal amount of them. Although a recent adult study[12] indicated that a high burden of APCs could be a risk factor for SVT, APCs are considered benign in all age groups. We discovered an association between APCs >5% and SVT on Holter, but due to the small number of cases, we could not demonstrate an increased risk for SVT among infants with APCs >10% on Holter. VPCs may be associated with heart disease, and frequent VPCs (>20%) may increase the risk of LV dysfunction even without CHD.[13,14] Due to the low number of cases in the present study, no association could be found between frequent VPCs and significant heart disease.

The proportion of infants with extrasystoles in our study was higher than previously reported[15–17]; however, the median number of extrasystoles was low. It is possible that the sensitivity needed to detect extrasystoles varies between Holter analysing software. In addition, analysing software used in most studies on neonatal Holter reference values is not comparable with the technology available today.

In newborns, a heart rate below 80 bpm has been considered bradycardia.[18] The threshold of 80 bpm has been the cut-off value for further electrocardiographic testing in our clinical practice. In the present study, this threshold for bradycardia would have resulted in abnormal Holter results in up to half of the cases. However, no bradycardia-related pathology was found in the absence of heart disease. Supporting our results, bradycardias have been reported among hospitalised, continuously monitored newborns.[18,19]

Based on our results in a non-selected term-born neonatal population, 12-lead ECG without rhythm or conduction pathology may be sufficient to exclude clinically significant arrhythmia during early infancy. Holter monitoring could be targeted to infants with heart disease, abnormal ECG or a predisposing factor for tachyarrhythmia. The low positive predictive value of abnormal ECG remains problematic resulting in low-yield Holter recordings. In a recent single-centre study on neonatal extrasystoles within a study population of 126 infants without relevant heart diseases, both positive and negative predictive values of ECG for significant arrhythmias on Holter were inadequate.[20] However, compared with the present study, there were many dissimilarities in patient inclusion, the definition of significant neonatal arrhythmia and the timing of the monitoring.

The retrospective study design is a limitation of this study. Holter recordings were performed for various indications, and the retrospective categorisation of indications was somewhat artificial. Nevertheless, we consider our sample size of good-quality Holter recordings adequate compared with the previous studies on neonatal Holter monitoring. Many recordings were invalid for technical reasons, and the large number of excluded cases may have resulted

in selection bias. The study population with diverse postnatal conditions may not represent healthy newborns. For better diagnostic yield, it is advised that Holter recordings be performed during normal daily routines, but the effect of the hospital environment during Holter monitoring is unlikely to be significant in newborns.[17]

In conclusion, most findings on newborns' Holter recordings were benign in this single-centre study. Based on our results, it seems that newborns with normal standard 12-lead ECG and no clinical signs of heart disease do not need Holter monitoring due to bradycardia or extrasystoles. The discovery of extrasystoles or a heart rate below 80 bpm in the majority of the infants studied emphasises the need for new normal limits for Holter parameters derived from recordings of healthy newborns.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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