

Three-day monitoring of adhesive single-lead ECG patch for premature ventricular complex: a prospective study for diagnosis validation and evaluation of burden fluctuation

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Hyo-Jeong Ahn¹; Eue-Keun Choi^{2, 3}; So-Ryoung Lee^{2, 3}; Soonil Kwon¹; Hee-Seok Song⁴; Young-Shin Lee⁴; Seil Oh²

¹Department of Internal Medicine, Seoul National University Hospital Department of Internal Medicine, Seoul National University College of Medicine Seoul KR

²Department of Internal Medicine, Seoul National University College of Medicine Seoul KR

³Department of Internal Medicine, Seoul National University Hospital Seoul KR

⁴Seers Technology Co., Ltd. Seongnam-si, Gyeonggi-do KR

Corresponding Author:

Eue-Keun Choi

Department of Internal Medicine, Seoul National University College of Medicine

101 Daehak-ro

Seoul

KR

Abstract

Background: Wearable monitoring devices of an electrocardiogram (ECG) are widely used. However, the date of an adhesive single-lead ECG patch (SEP) in the diagnosis and 24-hour burden assessment of premature ventricular complex (PVC) is limited.

Objective: We validated the diagnostic yield of SEP (mobiCARE™ MC-100, Seers Technology) for PVC detection and evaluated the PVC burden variation monitored by SEP over a 3-day monitoring period.

Methods: This is a prospective study of patients with documented PVC on a 12-lead ECG. Patients underwent simultaneous ECG monitoring by the Holter and SEP on the first day. On the subsequent second and third days, ECG monitoring by SEP was continued and completed 3-day extended monitoring. The diagnostic yield of SEP for PVC detection was evaluated by comparison with the results obtained from the first day of Holter monitoring. PVC burden monitored by SEP for three days was used to assess daily and 6-hour PVC burden variation. The number of patients additionally identified to reach PVC thresholds of 10%, 15%, and 20% on 3-day extended monitoring of SEP and clinical factors associated with the higher burden variation were explored.

Results: Recruited data of 134 monitored patients (mean age, 54.6 years; male, 33.6%) were analyzed. The median daily PVC burden was 2.4 (0.2-10.9) % by the Holter and 3.3 (0.3-11.7) % for the 3-day monitoring of SEP. The daily PVC burden detected on the first day of SEP was in agreement with that of the Holter: the mean difference was -0.07%, with 95% limits of agreement (-1.44%, 1.30%). A higher PVC burden on the first day was correlated with a higher daily ($R^2=0.34$) and 6-hour burden variation ($R^2=0.48$). Three-day monitoring by SEP identified 12/42 (28.6%), 10/56 (17.9%), and 4/60 (6.7%) more patients reaching 10%, 15%, and 20% of daily PVC burden, respectively. Younger age was associated with an additional identification of clinically significant PVC burden during the extended monitoring period ($P=.02$).

Conclusions: A SEP accurately detects PVC with a comparable diagnostic yield to the Holter. Performing a 3-day PVC monitoring with SEP, especially among younger patients, may offer a pragmatic alternative for identifying more individuals exceeding the clinically significant burden threshold.

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Original Manuscript

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Hyo-Jeong Ahn¹, Eue-Keun Choi^{1,2}, Soonil Kwon¹, So-Ryoung Lee^{1,2}, Hee-Seok Song³, Young-Shin Lee³, Seil Oh^{1,2}

¹ Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea

² Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea

³ Seers Technology Co., Ltd., Seongnam-si, Gyeonggi-do, Republic of Korea

Address for correspondence:

Eue-Keun Choi, MD, PhD

Department of Internal Medicine,

Seoul National University College of Medicine and Seoul National University Hospital

101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea

Email: choiek17@snu.ac.kr

Abstract

Background: Wearable monitoring devices of an electrocardiogram (ECG) are widely used. However, the date of an adhesive single-lead ECG patch (SEP) in the diagnosis and 24-hour burden assessment of premature ventricular complex (PVC) is limited. We validated the diagnostic yield of SEP (mobiCARE™ MC-100, Seers Technology) for PVC detection and evaluated the PVC burden variation monitored by SEP over a 3-day monitoring period.

Methods: This is a prospective study of patients with documented PVC on a 12-lead ECG. Patients underwent simultaneous ECG monitoring by the Holter and SEP on the first day. On the subsequent second and third days, ECG monitoring by SEP was continued and completed 3-day extended monitoring. The diagnostic yield of SEP for PVC detection was evaluated by comparison with the results obtained from the first day of Holter monitoring. PVC burden monitored by SEP for three days was used to assess daily and 6-hour PVC burden variation. The number of patients additionally identified to reach PVC thresholds of 10%, 15%, and 20% on 3-day extended monitoring of SEP and clinical factors associated with the higher burden variation were explored.

Results: Recruited data of 134 monitored patients (mean age, 54.6 years; male, 33.6%) were analyzed. The median daily PVC burden was 2.4 (0.2-10.9) % by the Holter and 3.3 (0.3-11.7) % for the 3-day monitoring of SEP. The daily PVC burden detected on the first day of SEP was in agreement with that of the Holter: the mean difference was -0.07%, with 95% limits of agreement (-1.44%, 1.30%). A higher PVC burden on the first day was correlated with a higher daily ($R^2=0.34$) and 6-hour burden variation ($R^2=0.48$). Three-day monitoring by SEP identified 12/42 (28.6%), 10/56 (17.9%), and 4/60 (6.7%) more patients reaching 10%, 15%, and 20% of daily PVC burden, respectively. Younger age was associated with an additional identification of clinically significant PVC burden during the extended monitoring period ($P=.02$).

Conclusion: A SEP accurately detects PVC with a comparable diagnostic yield to the Holter. Performing a 3-day PVC monitoring with SEP, especially among younger patients, may offer a

pragmatic alternative for identifying more individuals exceeding the clinically significant burden threshold.

Keywords: premature ventricular complex, single-lead electrocardiogram, wearable device, extended monitor.



Introduction

Premature ventricular complexes (PVCs) are commonly observed in individuals who underwent long-term ambulatory monitoring.[1] Frequent PVCs can result in reversible cardiomyopathy, although patients with PVCs without underlying structural heart disease are usually expected to have a benign clinical prognosis.[2-4]

Several risk factors are known to contribute to the overall risk of developing PVC-induced cardiomyopathy (PIC), and the burden of PVC is one of the most important predictors of clinical deterioration.[1, 5, 6] Although there is no absolute cutoff of PVC burden to identify patients at risk of developing PIC, 16-26% of PVC burden is reported as a significant threshold to develop PIC.[5, 7, 8] Of note, at least 10% of the PVC burden is considered sufficient for developing PIC to warrant a regular assessment of structural and functional cardiac change.[9]

To determine the appropriate treatment strategy for PVC, the burden is one of the essential pieces of information that should be accurately assessed, together with the accompanying symptoms and the presence or absence of structural heart disease. However, defining an exact PVC burden remains a challenge because of its substantial hourly or daily variation, and recent evidence recommends patients undergo ambulatory ECG monitoring throughout the day to observe its maximum burden. [1] The gold standard in evaluating PVC burden has been regarded as 24-hour Holter monitoring, but it is uncomfortable to wear, and the duration is insufficient to appreciate the substantial burden variation demonstrated among individuals.[10, 11]

With the advent of widespread use in wearable electrocardiogram (ECG) patch monitoring, studies suggested that extended monitoring is required to estimate more accurate daily PVC burden [10, 12]. Recently, an adhesive single-lead ECG patch (SEP) enables more convenient extended monitoring to capture fluctuations in PVC burden, but the diagnostic yield of SEP has not been thoroughly validated. Moreover, the optimal duration for ambulatory ECG monitoring for PVC evaluation has not been determined, and the clinical significance of a 3-day monitoring – a shorter period than

studied before [13] – has yet to be explored.

In this study, we investigated (1) the diagnostic yield of SEP for PVC detection through a direct comparison with the 24-hour Holter monitoring and (2) the variation of PVC burden monitored from a 3-day extended monitoring of the SEP and associated clinical factors. Ultimately, we aimed to explore the potential clinical utility of the SEP as a more convenient diagnostic tool of PVC, with the goal of identifying more patients who have clinically significant PVC burden.

Methods

Ethics approval and consent to participate

The institutional review board at Seoul National University Hospital (E-2001-111-1096) authorized this study. All participants provided written informed consent. This study is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline (**Multimedia Appendix 1**)

Study design and patient selection

This is a single-center and prospective cohort study of patients with PVC performed between May 2021 and June 2022. Patients (≥ 19 years old) with documented PVC on a 12-lead ECG and scheduled to evaluate the burden of PVC (the percentage of the number of PVCs over the total QRS complexes) by 24-hour Holter monitoring were included. Since the SEP utilizes a smartphone application to transmit ECG data, those unable to operate and manipulate the application were excluded. The three electrophysiologists (EKC, SRL, and SO) screened and recruited eligible patients at the outpatient clinic. Baseline clinical features, including demographic data, symptoms regarding PVC, comorbidities, lifestyle behaviors, medication history, and echocardiographic parameters were investigated.

Validation of PVC diagnosis by SEP through the comparison with the Holter

The 24-hour Holter (SEER Light, GE Healthcare, Chicago, IL, USA) and the SEP (mobiCARE MC-100, Seers technology, Seongnam-si, Gyeonggi-do, Republic of Korea) recorded three channels (leads I, V1, and V6) and a single channel (lead II), respectively. The process of validating the ECG algorithm for PVC detection in SEP and its performance is detailed in the **Multimedia Appendix 2**. Patients underwent simultaneous ECG monitoring by the Holter and the SEP for the first day of monitoring. After 24 hours of monitoring, the Holter device was detached, and ECG monitoring was continued for the following 48 hours using the SEP; the assessment of PVC burden using Holter monitoring is a part of guideline-adherent practice [14] with patients covering the associated costs

through local health insurance coverage. The detailed specification of the SEP and the attachment method of both devices are described in our prior report. [15] Information on total wear time, the proportion of signal noise, total QRS complexes, and the burden of PVC were collected. An example strip of PVC detection by the SEP is shown in **Multimedia Appendix 3**. To evaluate the diagnostic yield of PVC of the SEP, the burdens of PVC assessed by the Holter and SEP on the first day were compared to each other.

Variability of PVC burden and clinical factors associated with greater variability

The fluctuation of PVC burden was assessed by the change of the daily and six-hour PVC burden monitored over a 3-day period using SEP. The purpose of evaluating daily and six-hour PVC burden variations was to verify its fluctuation characteristics. This analysis enables us to address the challenge of identifying the accurate overall PVC burden and, consequently, determining an appropriate treatment strategy. We defined daily PVC burden variation as the difference between the maximum and the minimum daily PVC burden measured by the SEP. The 6-hour PVC burden was calculated as the burden of PVC in 0-6 am, 6-12 am, 12-6 pm, and 6 pm-0 am. Similarly, the 6-hour PVC burden variation was defined as the difference between the maximum and minimum six-hour PVC burden. We estimated the proportion of patients who are additionally identified to reach a clinically significant daily PVC burden (10%, 15%, or 20%)[12] on the 3-day monitoring. Also, clinical factors associated with the greater variation in PVC burden and thus additionally found to cross the clinically meaningful threshold of PVC burden on the extended monitoring were investigated.

Self-reported questionnaire about the experience of three-day extended ECG monitoring

The participants' clinical experience of 3-day extended ECG monitoring for PVC detection by SEP was evaluated by a self-reported questionnaire. The survey was conducted on a voluntary basis for all the participants without offering any form of compensation on the day the SEP device was returned. Questions ask about the overall convenience of the Holter and SEP, any instances of

unexpected reattachment, and accessibility and intuition of mobile applications for SEP. Participants respond to the questions using a scale ranging from 1 to 5; 1=no, 2= minimally, 3=sometimes, 4=likely, or 5=very likely.

Statistical analysis

Continuous variables are reported as means $\pm$ standard deviations or median (interquartile range, IQR) and compared by Student's t test or Mann-Whitney test. Categorical variables are presented as numbers (%) and Pearson's chi-square test or Fisher's exact test were applied as required. The diagnostic yield of PVC by the SEP was compared to the Holter by Bland-Altman plots with limits of agreement and scatter plots. The degree of agreement for the burden of PVC monitored by each device was analyzed. The associations between individuals' baseline characteristics and the additional identification of significant PVC thresholds (10%, 15%, or 20%) on the extended monitoring were evaluated by multivariable logistic regression analysis. All analyses were performed using Stata (version 17, StataCorp LLC, College Station, TX, USA).

Results

Baseline characteristics

Of the total 156 enrolled patients with documented PVC on a 12-lead ECG, data of 13 patients could not be retrieved due to errors in individuals' smartphones, unfamiliar application use, or missing telemetry data transmission of the SEP. Nine patients withdrew from the examination due to discomfort and skin irritability: 5 patients for frequent alarm and the requirement of keeping their smartphone in close proximity, 2 for skin irritability, and 2 for inexperienced operation of the application. Finally, data from 134 patients with enough wear time of the patch (≥ 4200 min) and whose data was transmitted completely were included in the analysis.

The baseline characteristics of the included patients are described in **Table 1**. The mean age was 54.6 ± 13.3 years, and 45 (33.6%) were male. The majority of the patients complained of symptoms such as palpitation ($n=96$, 71.6%) or dizziness ($n=15$, 11.2%). Hypertension ($n=46$, 34.3%) and diabetes mellitus ($n=21$, 15.7%) were the common comorbidities. Congestive heart failure (CHF) and cardiomyopathy were reported in 8 (6.0%) and 4 (3.0%) of the patients, respectively. Patients frequently took beta-blocker ($n=97$, 72.4%) or calcium channel blockers ($n=10$, 7.5%) to relieve symptoms and PVC burden.

Table 1. Baseline characteristics of patients with premature ventricular complex.

Abbreviations: TIA, transient ischemic attack; TE, thromboembolism; AAD, antiarrhythmic drug; RAAS, renin-angiotensin-aldosterone system.

	Total N=134
Age (years)	54.6 ± 13.3
Sex (Male)	45 (33.6%)
Body mass index (kg/m²)	24.3 ± 3.4
Symptom	
Palpitation	96 (71.6%)
Syncope	3 (2.2%)
Dizziness	15 (11.2%)
Comorbidities	
Hypertension	46 (34.3%)
Diabetes mellitus	21 (15.7%)
Congestive heart failure	8 (6.0%)
Cardiomyopathy	4 (3.0%)
Coronary artery disease	0 (0.0%)
Hypo/Hyperthyroidism	5 (3.7%)
Stroke/TIA/TE	3 (2.2%)
Lifestyle behaviors	
Current Smoking	8 (6.0%)
Alcohol intake	16 (11.9%)
Medications	
Beta-blocker	97 (72.4%)
Calcium channel blocker	10 (7.5%)
Amiodarone	3 (2.2%)
Class1c AAD	3 (2.2%)
RAASc blockade	20 (14.9%)
Diuretics	5 (3.7%)
Statin	29 (21.6%)
Antiplatelet	15 (11.2%)
Ejection fraction (%)	58.8 ± 6.0 (%)

Diagnostic performance of PVC detection and burden of SEP compared to the Holter

An example of PVC detection by the adhesive single-lead ECG patch is presented in **Multimedia Appendix 3**. Detailed parameters of monitoring and the overall burden of the PVC were compared between the two monitoring methods (Holter and SEP) and summarized in **Table 2**. The total mean wear time was 1395.1 ± 33.5 min for the Holter and 4318.0 ± 12.4 min for the SEP. The transmitted data were retrieved without significant noise for both devices (0.1% for the Holter vs. 0.9% for the SEP). The median PVC burden of all enrolled patients was 2.4 (0.2-10.9) % for the Holter and 3.3 (0.3-11.7) % for the SEP during 3-day extended monitoring without significant difference ($P=.58$). On the first 24-hour monitoring of the SEP, the burden of PVC among all patients was 7.5 ± 10.0 [median (IQR), 2.8 (0.3-11.0)] % without a significant difference with PVC burden on Holter ($P=.24$). For those with PVC burden $\geq 5\%$, the overall PVC burden was detected as 13.3 (8.0-24.0) % for the Holter and 13.2 (9.7-20.5) % for the SEP during 3-day extended monitoring, respectively ($P=.10$). On the first 24-hour monitoring of the SEP, the burden of PVC among patients with a burden $\geq 5\%$ was 16.5 ± 9.9 [median (IQR), 13.7 (8.1-24.4)] %. The p-value compared to the PVC burden detected on Holter was 0.82 (**Table 2**).

Table 2. Evaluation of premature ventricular complex by Holter and the adhesive single-lead electrocardiogram patch. Abbreviations: ECG, electrocardiogram; PVC, premature ventricular complex; No., number; N/A, not applicable.

	Holter	Single-lead ECG patch	P
Wear time (min)	1395.1±33.5	4318.0±12.4	N/A
Noise (%)	0.1 (0.1-0.1)	0.9 (0.4-2.3)	<.001
Average heart rate	71.1±8.3	72.0±7.8 ^{a)}	0.01
Minimum heart rate	52.1±39.5	49.1±23.6 ^{a)}	0.44
Maximum heart rate	122.4±18.1	131.8±20.8 ^{a)}	<.001
PVC information			
No. of patients with PVC burden ≥5%	56 (41.8)	57 (42.5)	<.001
No. of patients with PVC burden ≥10%	37 (27.6)	38 (28.4)	<.001
No. of patients with PVC burden ≥15%	23 (17.2)	22 (16.4)	<.001
Burden of PVC among all patients (%)	7.4±10.0 2.4 (0.2-10.9)	7.3±9.4 ^{b)} 3.3 (0.3-11.7) ^{b)}	0.58
Burden of PVC among patients with burden ≥5% (%)	16.4±9.9 13.3 (8.0-24.0)	15.8±9.3 ^{c)} 13.2 (9.7-20.5) ^{c)}	0.10

a), b), c) The estimated values are the mean ± standard deviation and median [interquartile range (IQR)] of PVC burden detected during 3-day extended monitoring.

a) On the first 24-hour monitoring of the single-lead ECG patch, the average, minimum, and maximum heart rate was 72.2±8.3, 48.8±6.2, and 123.2±17.7, respectively. The p-values with the comparison of each value of Holter were <0.001, 0.042, and 0.002, respectively.

b) On the first 24-hour monitoring of the single-lead ECG patch, the burden of PVC among all patients was 7.5±10.0 [median (IQR), 2.8 (0.3-11.0)] %. The p-value with the comparison of PVC burden detected on Holter was 0.242.

c) On the first 24-hour monitoring of the single-lead ECG patch, the burden of PVC among patients with burden ≥5% was 16.5±9.9 [median (IQR), 13.7 (8.1-24.4)] %. The p-value with the comparison of PVC burden detected on Holter was 0.817. The overall distribution of PVC burden is presented in **Figure 1A**. Most of the patients (n=97, 72.4%) had a PVC burden of less than 10%. PVC burden was reported as 10-19.9% and ≥20% in 18 (13.4%) and 19 (14.2%) patients, respectively. An individual comparison of the participants' PVC detection performed

by the Holter to the SEP is shown in **Figure 1B**. The PVC burden evaluated by the Holter was repeated with almost the same value as the PVC burden estimated by the SEP on the first day, whereas PVC burden variation was observed across days on the SEP (**Figure 1B**). Validation of the diagnostic yield of the SEP was performed by Bland-Altman analysis and high agreement of the PVC detection between the Holter and the SEP was confirmed with a mean difference -0.07% and 95% LOA -1.44% to 1.30% (**Figure 2A**). PVC burdens detected by the Holter and measured on the first day of the SEP were highly correlated with each other (**Figure 2B**, $R^2=0.995$), indicating accurate detection of PVC by the SEP.

Variability of PVC burden and clinical factors associated with greater variability

PVC burden varied widely from day-to-day and hour-to-hour, as shown in **Figure 1B**. Greater variability of PVC burden was observed when evaluated by six-hour. In the same patient, the maximum daily PVC burden was 1.68 (1.31-3.02) fold higher than the minimum daily burden and the maximum 6-hour burden was 12.08 (4.00-57.50) fold higher than the minimum 6-hour burden; for those with PVC burden $\geq 1\%$, the maximum daily and 6-hour PVC burden was 1.52 (1.28-2.07) fold and 12.17 (5.06-49.46) fold higher than each minimum burden.

Moreover, the variation was dependent on the individuals' burden value; patients with higher PVC burden exhibited greater daily or hourly burden variation. Daily and 6-hour burden variations according to the value of PVC burden are presented in **Figure 3**, showing a moderate to a high degree of correlation ($R^2=0.337$ for daily and 0.483 for 6-hour burden variation). An example of ECG strip of an individual presenting a high variation of daily and 6-hour PVC burden monitored on SEP is shown in **Multimedia Appendix 4**.

The number of patients with PVC burden lower than the clinically significant thresholds was 42 for 10%, 56 for 15%, and 60 for 20%. Three-

day extended monitoring additionally identified those who reached 10%, 15%, and 20% in 12/42 (28.6%), 10/56 (17.9%), and 4/60 (6.7%) patients, respectively (**Figure 4**). Clinical features of those crossing over the PVC burden cutoff of 10%, 15%, or 20% on the 3-day extended monitoring were compared to the others in **Multimedia Appendix 5**. Patients who could be additionally identified to reach clinically significant thresholds on the 3-day extended monitoring were younger ($P=.03$), had more CHF ($P=.01$) or cardiomyopathy ($P=.01$), and were using more amiodarone ($P=.04$). When multivariable logistic regression analysis was performed, young age was independently associated with possible additional detection of PVC burden with clinical significance (**Table 3**); OR 0.95 (0.92-0.99), $P=.02$ for age.

Table 3. Clinical factors associated with additional detection of premature ventricular complex burden of threshold 10%, 15%, and 20%.
Abbreviations: OR, odds ratio; CI, confidence interval; PVC, premature ventricular complex.

Variable	Univariable analysis		Multivariable analysis	
	OR (95% CI)	<i>P</i>	β (95% CI)	<i>P</i>
Age	0.961 (0.928-0.996)	0.03	0.954 (0.918-0.993)	0.02
Congestive heart failure	6.875 (1.562-30.256)	0.01	–	–
Cardiomyopathy	19.94 (1.960-202.893)	0.01	–	–
Amiodarone	12.556 (1.082-145.709)	0.04	–	–
Burden of PVC	1.024 (0.982-1.069)	0.27	–	–

Patients' experience on three-day extended ECG monitoring

The survey on the experience of Holter and SEP was returned from 124 patients among the included participants (response rate, 124/134=92.5%), and the result is described in **Multimedia Appendix 6**. Overall, patients complained of less discomfort and less skin-irritability for the SEP compared to the Holter ($P<.001$ and $P=.02$), but they experienced more willingness to stop monitoring for the SEP due to the longer duration of the examination. Indeed, patients experienced more reattachment experience for the SEP (12.5% for the Holter and 55.9% for the SEP, $P=.02$). Taken together, patients were more favorable to using the SEP than the Holter; 75.7% of patients responded to choosing a patch monitor for their next examination.

Discussion

Principal results

Our principal findings are as follows: (1) the SEP can diagnose PVC with comparable accuracy to the 24-hour Holter, (2) a wide variation of PVC burden, which was proportional to the overall PVC frequency, was also confirmed on the records of the SEP, (3) three-day extended monitoring could identify those who reach clinically significant cutoff of PVC burden, and (4) young age is associated with an additional detection of clinically significant burdens of PVC on extended monitoring.

Comparison to prior work

Ambulatory ECG monitoring is a principal diagnostic tool to evaluate PVC burden and recently developed wearable ECG monitoring devices enable extended monitoring for more than 24 hours.[1, 16, 17] Especially, the SEP is considered as a sufficient and practical method to evaluate an accurate PVC burden and comprehend its wide daily variation.[11, 18] Older studies demonstrated variation of PVC burden up to 23% change across days [19, 20], and more recent studies observed a 2.5-fold median difference between the maximum and minimum 24-hour PVC burden in the same patient over a 14-day monitoring period. [10] About the optimal duration of PVC monitoring, the median time to detect one's maximum PVC burden was reported as 6 (2–11) days [12], and the ideal duration for accurate PVC burden assessment was suggested as 7 days. [13] Although the monitoring period of our study (3 days) is shorter than the time of prior reports, we still observed a considerable intra-individual median daily PVC burden difference of 1.7-fold. Given that the optimal period for monitoring PVCs has not been established and a long recording length could be burdensome by both patients and clinicians, we suggest a compromise of a monitoring

length (3-day) providing an acceptable level of daily PVC burden, which may improve patients' compliance and adherence. Indeed, despite the general comfort of the SEP, our survey revealed that patients felt more likely to discontinue monitoring as monitoring time became longer. Furthermore, an extended monitoring duration could potentially exacerbate patient discomfort and fatigue related to the requirement of carrying their mobile phones for data transmission. This may also intensify discomfort concerning alarm systems and skin irritability. In our study, nine patients withdrew from the examination due to these practical challenges; optimizing the monitoring duration could potentially decrease the dropout rate associated with these issues.

Moreover, a wide variation of daily PVC burden detected on 3-day monitoring enabled us to additionally identify 6.7-28.6% of patients who reach clinically significant thresholds (10%, 15%, or 20%). Compared to the prior study that presented the doubled identification of those who cross the daily PVC burden of 10% from 14-day monitoring [12], the low proportion is due to a shorter duration of monitoring. However, the finding is consistent with the fact that the extended monitoring brings incremental gain in identifying patients reaching the significant cutoffs of daily PVC burden. We observed that the SEP could diagnose PVC with almost the same accuracy as the Holter and 3-day monitoring still could detect patients who might benefit from an advanced treatment modality, such as radiofrequency catheter ablation.

Implications for practice

Several risk factors are known to be associated with the presence of PVC and a greater PVC frequency. Increasing age, a taller height, higher blood pressure, and unhealthy lifestyle behaviors such as smoking and lower physical inactivity are consistently shown to be associated with the presence or higher frequency of PVC. [21-23] However, no studies have demonstrated the clinical factor related to the higher variation of

PVC burden, which might be necessary to stratify patients requiring extended monitoring for a more accurate assessment of PVC burden. We presented that the PVC burden evaluated on the first 24-hour monitoring is correlated not only with the day-to-day, but also with the hour-to-hour variation. The higher frequency of PVCs was linked to a wider variation in overall burden. In addition, we suggested that younger age, presence of CHF or cardiomyopathy, and use of amiodarone are clinical factors that may increase the likelihood that PVC burden reaches clinically significant thresholds on the 3-day extended monitoring. Above all, younger age was consistently associated with the meaningful variation of PVC burden on multivariable analysis. Although an explainable mechanism has not been reported, the fact that older age and a lack of diurnal variation of PVC frequency are related to a higher risk of PIC [24, 25] implies that there might be a link between young age and a greater variation of PVC burden. Our finding could discern patients who require extended monitoring for a more precise evaluation of PVC burden, thus improving the determination of treatment strategy. The variable circadian distribution of PVC burden and its associated clinical factor could also provide additional value as it is demonstrated to predict the outcome of radiofrequency catheter ablation by guiding pharmacologic induction of PVCs from a study of patients with PVC referred for catheter ablation. [25]

Strengths and limitations

Our study has several limitations. First, the diagnostic yield of PVC via the SEP and the degree of variation monitored during three days should be examined in a larger population. Second, since most of the included patients had normal ventricular systolic function, the accurate diagnosis of PVC and changes in PVC frequency monitored by the SEP should be further validated in patients with reduced ejection fraction or structural heart diseases. Third, more than two-thirds of the patients had low PVC burden (<10%); thus, extrapolation of our findings in

patients with higher PVC burden ($\geq 10\%$, or 20%) could be limited. Nonetheless, the distribution of PVC burden in our study may represent the characteristics of patients in real-world settings, suggesting that our findings can be readily applied in a clinical context. Lastly, the external replication of our findings by other wearable ECG patches in a multicenter setting would be required for the confirmation of generalizability.

Conclusions

In this single-center prospective registry of patients with PVC, we have validated that the SEP can accurately diagnose PVC with almost the same yield as the 24-hour Holter. A significant fluctuation in daily and 6-hour PVC burden, which was proportional to one's overall PVC frequency, was observed on the 3-day extended monitoring. Three-day extended monitoring of PVC by SEP could identify more patients exceeding the clinically significant burden threshold; thus, it could be a practical method with acceptable patient adherence to enhance the decision on the optimal treatment strategy (i.e., catheter ablation). Several clinical factors, especially younger age, were associated with a higher variation of daily PVC burden, implying the necessity of extended monitoring for accurate assessment.

Acknowledgments

None

Conflicts of interests

HSS and YSL: stockholders of Seers Technology Co, Ltd. EKC: research grants or speaking fees from Abbott, Bayer, BMS/Pfizer, Biosense Webster, Chong Kun Dang, Daewoong Pharmaceutical Co, Daiichi-Sankyo, DeepQure, Dreamtech Co, Ltd, Jeil Pharmaceutical Co Ltd, Medtronic, Samjinpharm, Seers Technology, and Skylabs. Stock options from Seers Technology, and Skylabs

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Data Availability

All data generated or analyzed during this study are included in this published article and its Multimedia Appendix files. The data of this study will be shared on reasonable request to the corresponding author.

Author contributions

HJA conceptualized the study design, conducted data curation, performed formal analysis, visualized the data, and had primary responsibility for writing the article. EKC conceptualized and reviewed the study design, performed data collection, reviewed the manuscript, supervised the study, and performed project administration with funding acquisition. SK and SO reviewed the methodology, investigation, and the manuscript. SRL collected data and reviewed the methodology, investigation, and manuscript. HSS and YSL conducted data curation, performed formal analysis, prepared the resources and software, and reviewed the manuscript. EKC is the guarantor of this work and takes responsibility for the integrity and accuracy of the data analysis. All authors read and approved the final manuscript.

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ventricular contraction ablation procedural inducibility and outcomes. Heart Rhythm. 2018 Jan;15(1):99-106. PMID: 28765087. doi: 10.1016/j.hrthm.2017.07.034.

Figure legends

Figure 1. A) Distribution of premature ventricular complex and B) Comparison of the burden of premature ventricular complex evaluated by the Holter and the adhesive single-lead electrocardiogram patch

Abbreviations: PVC, premature ventricular complex; ECG, electrocardiogram.

Figure 2. Agreement for the burden of a premature ventricular complex between Holter monitoring and day 1 of adhesive single-lead electrocardiogram monitoring (MC-100) analyzed by (A) Bland-Altman plot with limits of agreement and (B) scatter plot.

Abbreviations: PVC, premature ventricular complex; LOA, limits of agreement.

Figure 3. Correlation of the burden of a premature ventricular complex with A) daily burden variation and B) six-hour burden variation

Abbreviation: PVC, premature ventricular complex.

Figure 4. Patients additionally identified to reach the daily premature ventricular complex burden of 10%, 15%, and 20% on three-day monitoring of adhesive single-lead electrocardiogram patch

Abbreviations: PVC, premature ventricular complex; ECG, electrocardiogram.



Figure 1. A) Distribution of premature ventricular complex and B) Comparison of the burden of premature ventricular complex evaluated by

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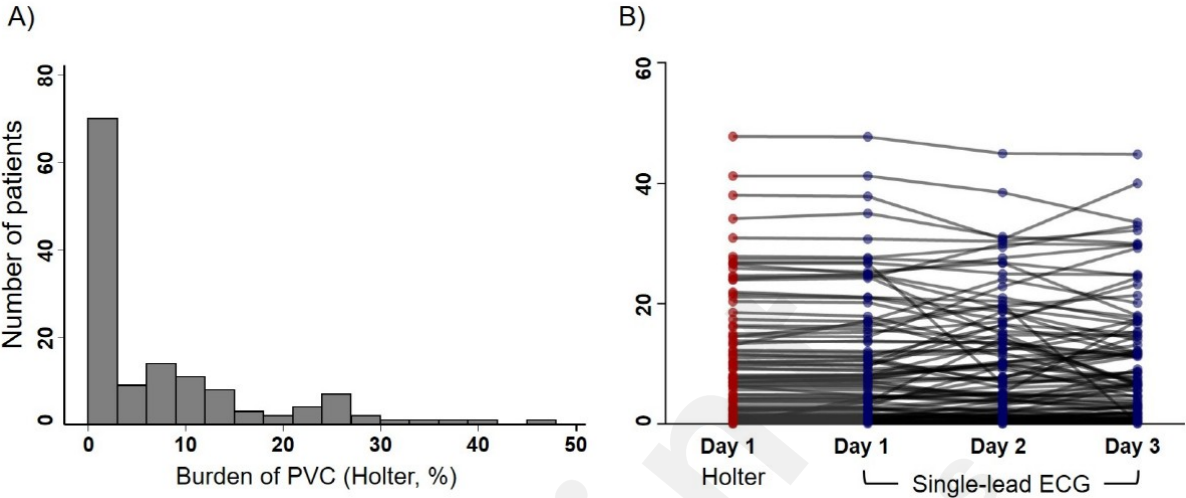


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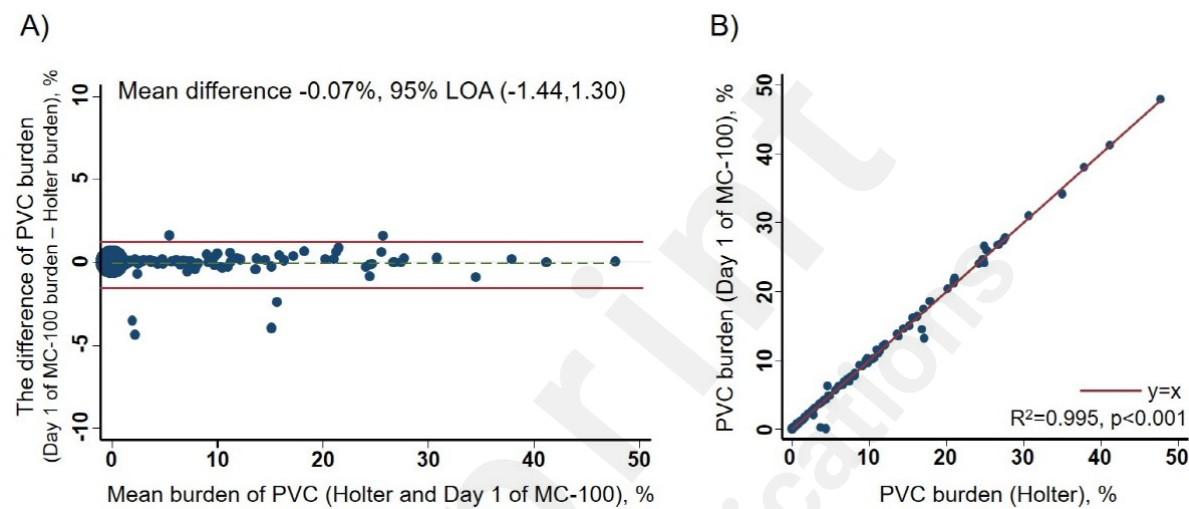


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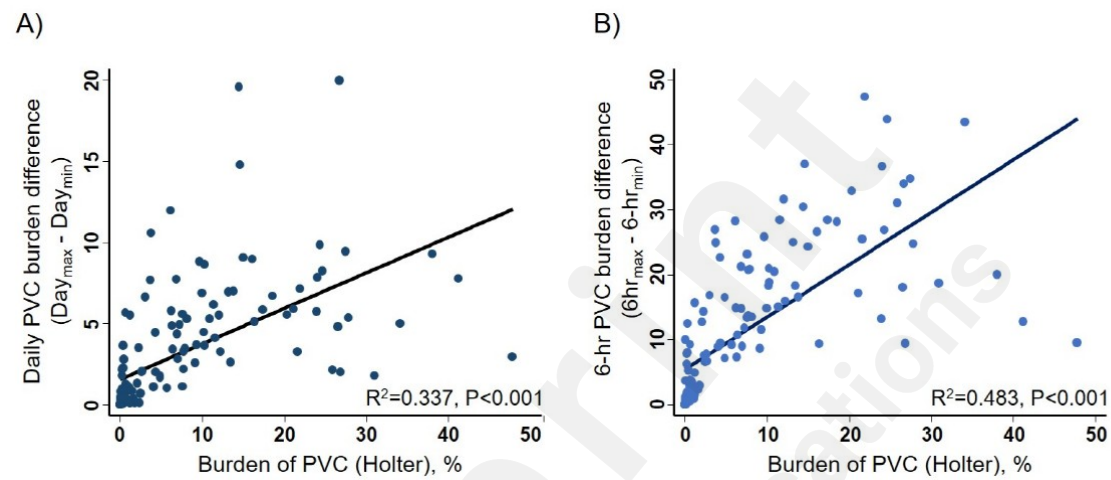
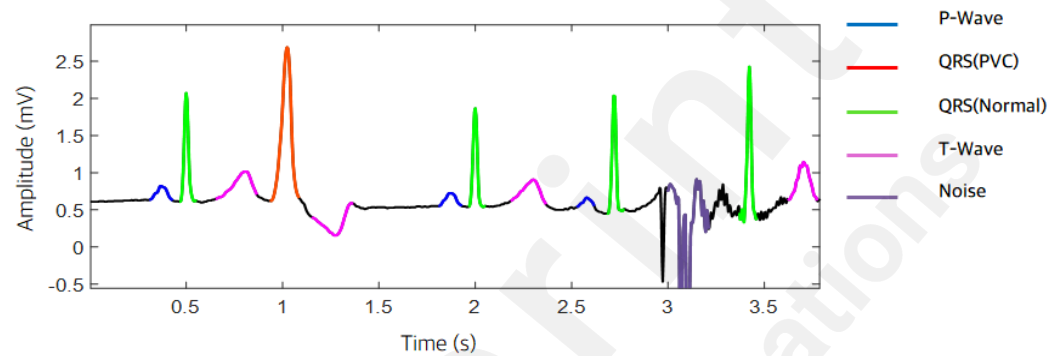
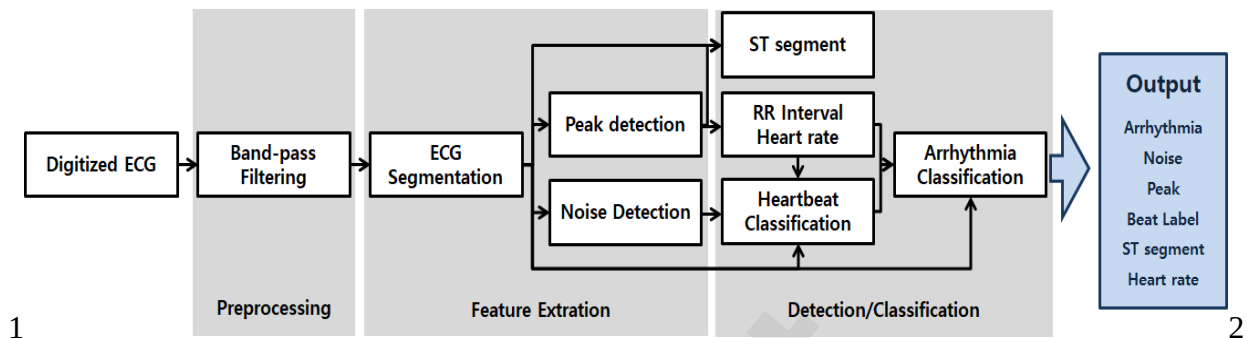


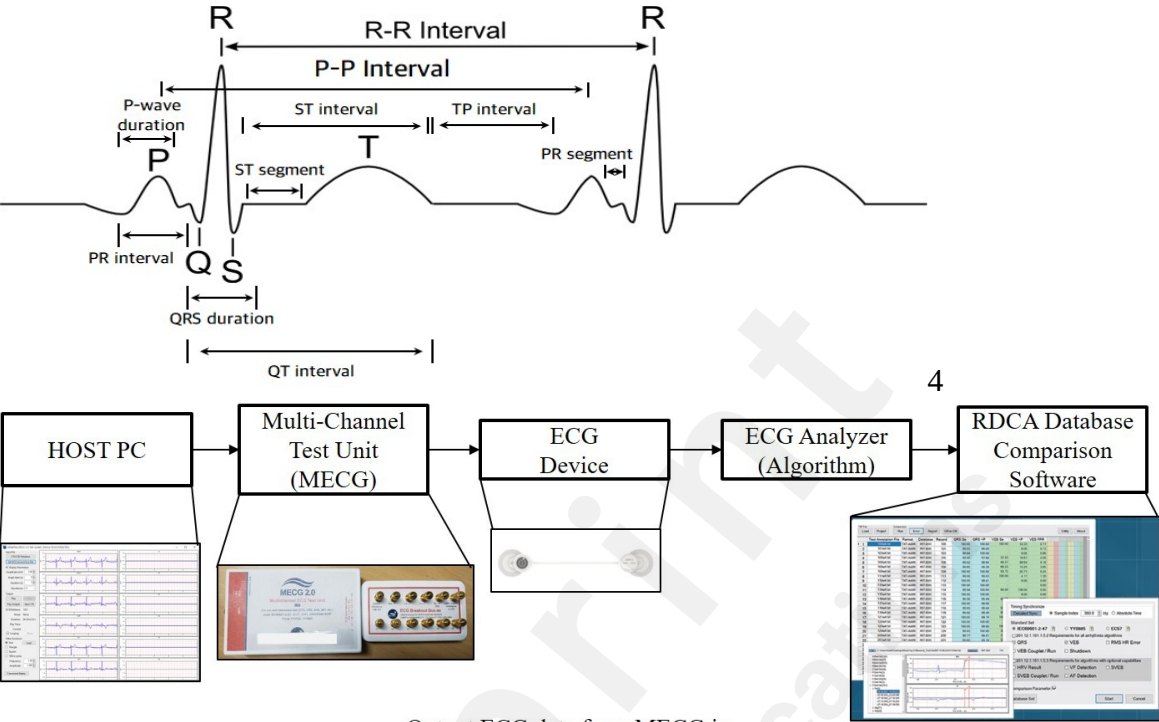
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monitoring of adhesive single-lead electrocardiogram patch

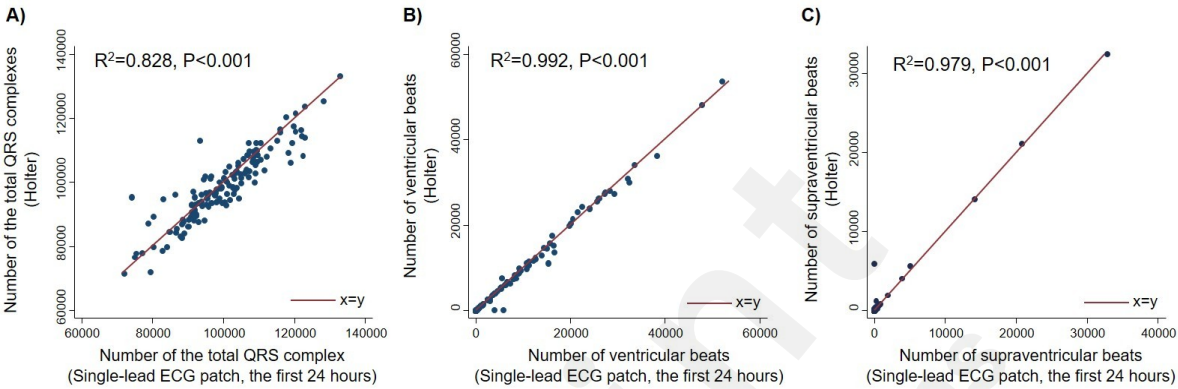
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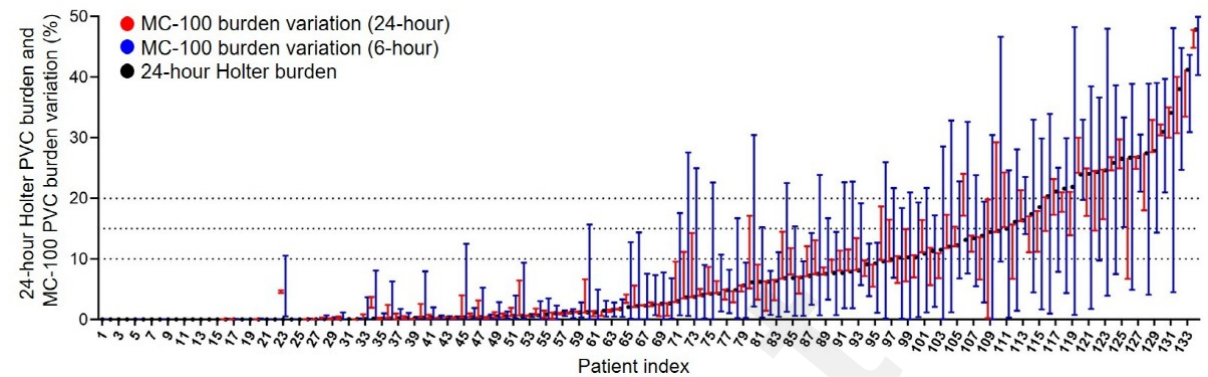
Input the raw test ECG dataset to MECC → Output ECG data from MECC is processed by mobiCARE Cardio. The ECG algorithm of mobiCARE Cardio analyze ECG data and store the result for the RDCA Database comparison software. → The performance of the algorithm is tested by RDCA Database comparison software.

Number	Holter	Single-lead ECG patch (for the first 24 hours)	R ²	P
A) Total QRS complexes	98232 (92794-106375)	99610 (92047-108179)	0.828	<0.001
B) Ventricular beats	2516 (166-10568)	2898 (234-11058)	0.992	<0.001
C) Supraventricular beats	12 (2-42)	13 (4-33)	0.979	<0.001







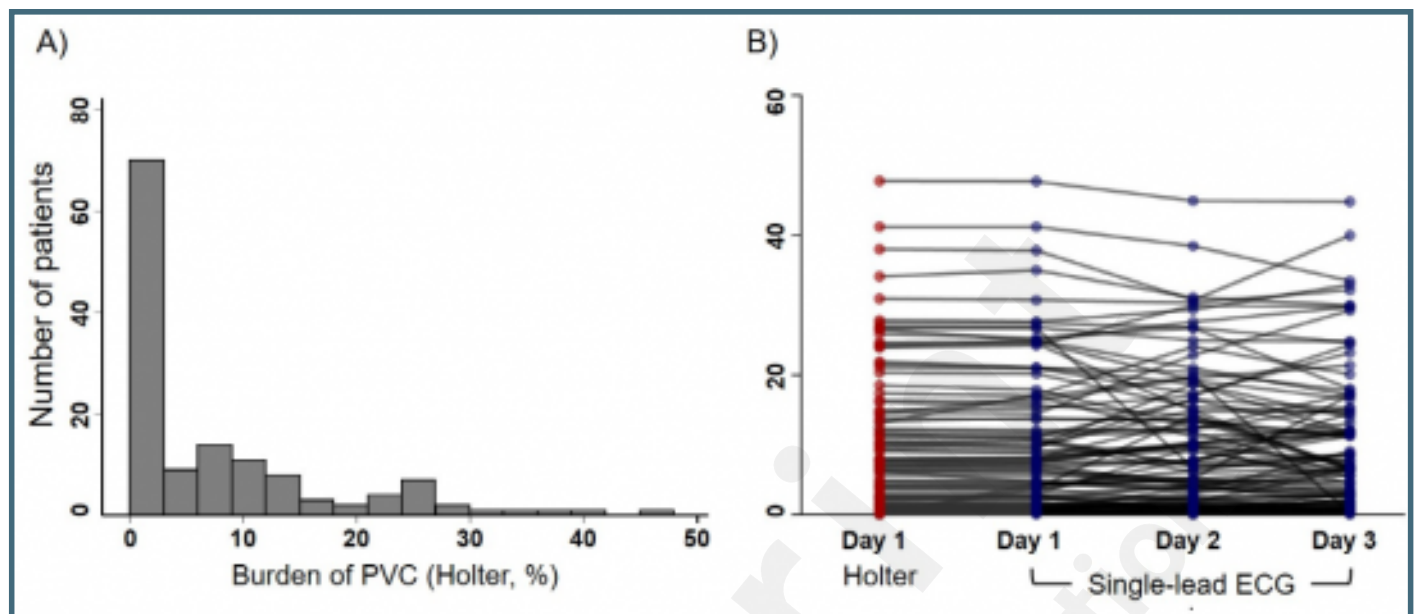


N	1% ≤ Holter burden < N%	Additionally identified to reach PVC burden of N% on the adhesive single-lead ECG patch by	
		Daily burden	6-hour burden
10%	42	12/42 = 28.6%	25/42 = 59.5%
15%	56	10/56 = 17.9%	31/56 = 55.4%
20%	60	4/60 = 6.7%	24/60= 40.0%

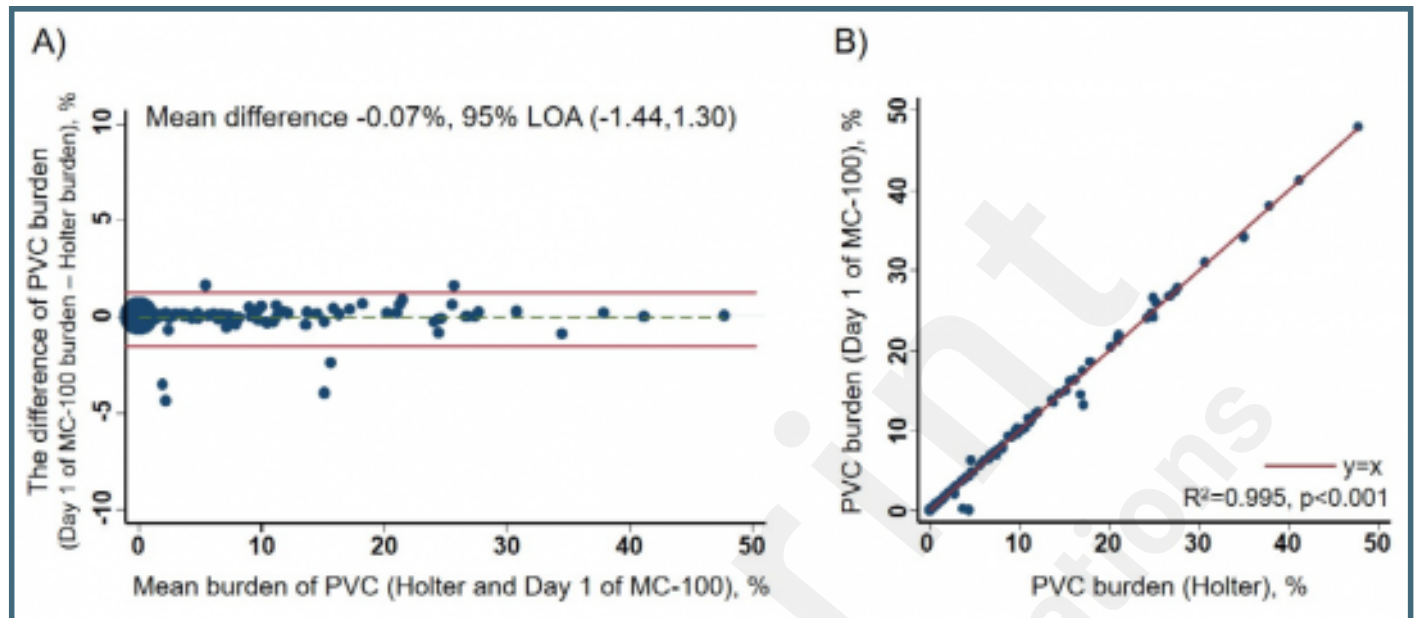
Supplementary Files

Figures

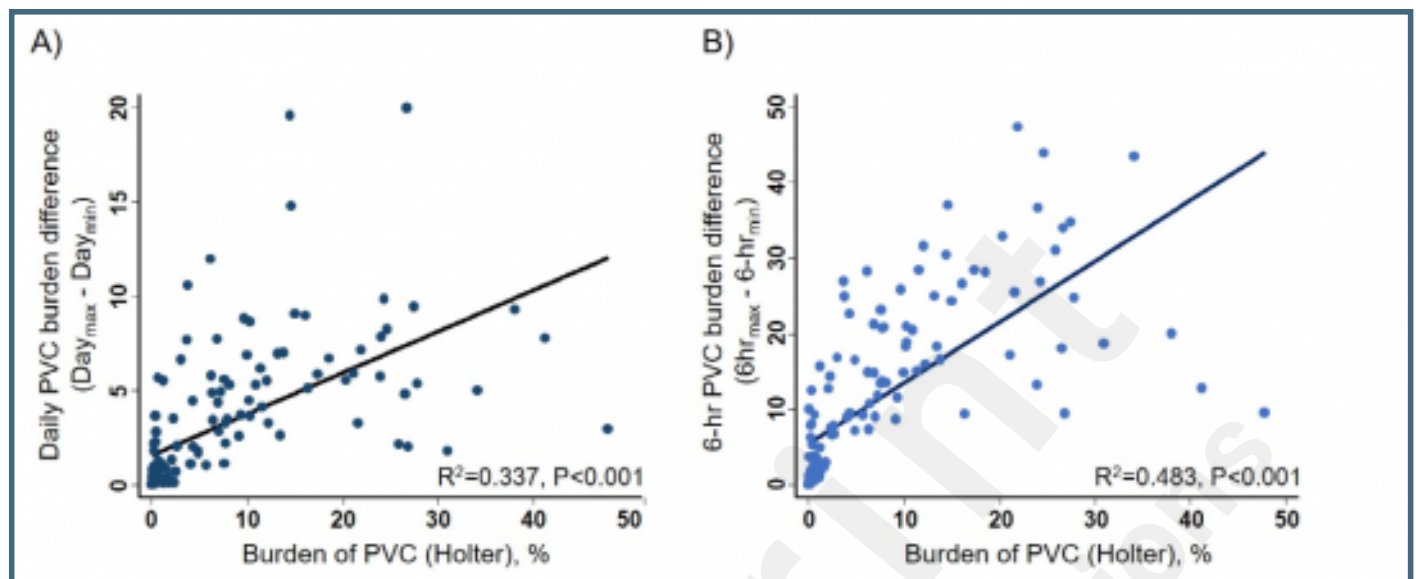
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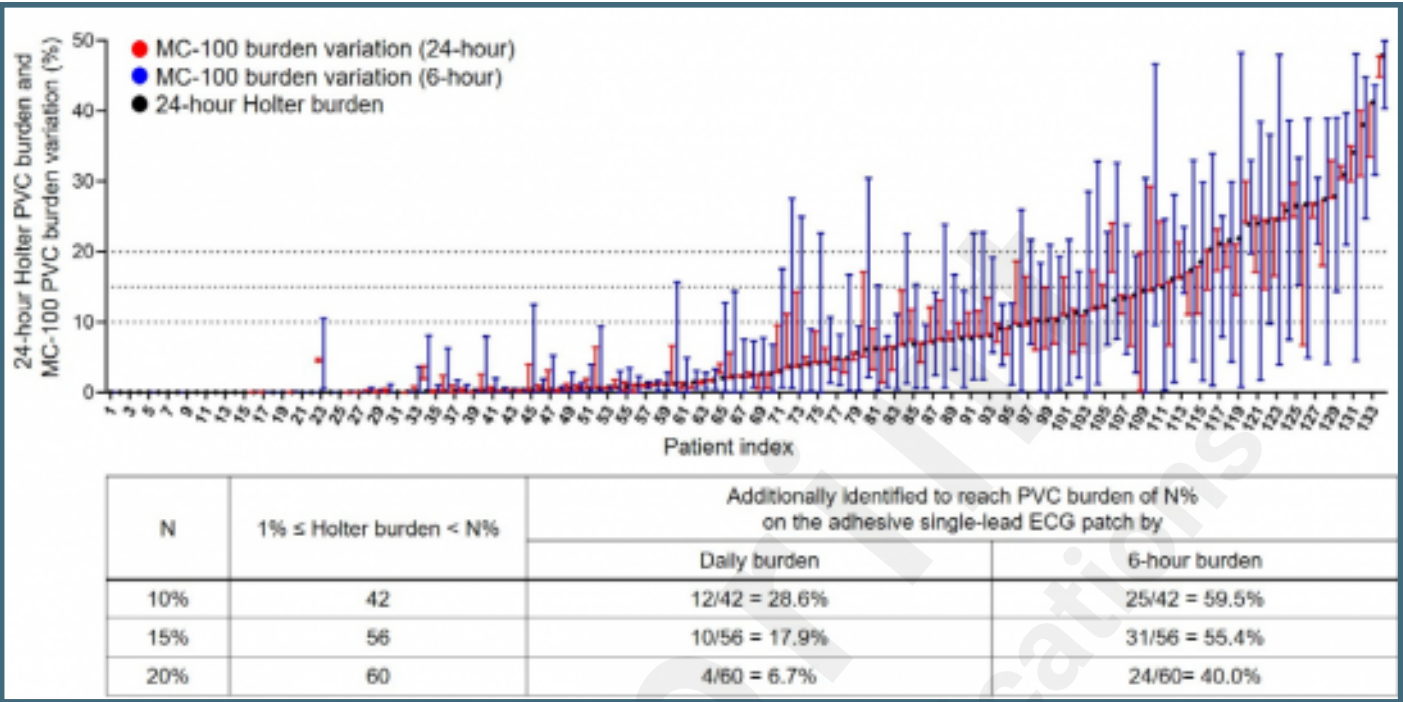
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Correlation of the burden of a premature ventricular complex with A) daily burden variation and B) six-hour burden variation. Abbreviation: PVC, premature ventricular complex.



Patients additionally identified to reach the daily premature ventricular complex burden of 10%, 15%, and 20% on three-day monitoring of adhesive single-lead ECG patch. Abbreviations: PVC, premature ventricular complex; ECG, electrocardiogram.



Multimedia Appendixes

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