ORIGINAL ARTICLE

Diagnostic yield is dependent on monitoring duration. Insights from a full-disclosure mobile cardiac telemetry system

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ABSTRACT

Background: Despite the advancement of electrocardiogram (ECG) monitoring methods, the most important factor influencing diagnostic yield (DY) may still be monitoring duration. Ambulatory ECG monitoring, typically with 24–48 hours duration, is widely used but may result in underdiagnosis of rare arrhythmias.

Aims: This study aimed to examine the relationship between the DY and monitoring duration in a large patient cohort and investigate sex and age differences in the presentation of arrhythmias.

Methods: The study population consisted of 25 151 patients (57.8% women; median [interquartile range, IQR], 71 [64–78] years), who were examined with mobile cardiac telemetry during 2017 in the United States, using the PocketECG™ that continuously transmits a signal on a beat-to-beat basis. We investigated the occurrence of atrial fibrillation at a burden of both ≤1% (atrial fibrillation [AF], ≤1%) and ≤10% (AF ≤10%), premature ventricular contractions (PVC; >10 000 per 24 hours), non-sustained ventricular tachycardias (nsVT), sustained ventricular tachycardias (VT ≥30 seconds), atrioventricular blocks (AVB), pauses of >3 seconds duration, and bradycardia (heart rate <40 beats per minute for ≥60 seconds).

Results: The median (IQR) recording duration was 15.4, 8.2–28.2) days. The DY increased gradually with monitoring duration for all types of investigated arrhythmias. Compared to DY after up to 30 days of monitoring, a standard 24 hours monitoring resulted in DY for males/females of 20%/18% for AF ≤1%, 29%/28% for AF ≤10%, 45%/40% for PVCs, 17%/11% for nsVT, 17%/11% for VT ≥30 seconds, 49%/42 for AVB, 27%/20% for pauses, 36%/29% for bradycardia.

Conclusion: A substantial number of patients suffering from arrhythmias may remain undiagnosed due to insufficient ECG monitoring time.

Key words: ECG monitoring, diagnostic yield, mobile cardiac telemetry monitoring, arrhythmias.

INTRODUCTION

Despite significant advances in electrocardiogram (ECG) monitoring methods, one of the most important factors influencing arrhythmia diagnostic yield is still the duration of the monitoring, which varies widely from as short as 10 seconds (wearable consumer devices) to several months or years (implanted devices). Analysis of ECG data may be immediate or postponed. Uncertainty remains regarding necessary monitoring durations in specific clinical situations, such as for detection of infrequently occurring atrial fibrillation, cardiogenic syncope, or suspicion of ventricular arrhythmias, although it has been suggested that longer monitoring durations are necessary [1, 2]. Short recording durations imply a risk of missing infrequent arrhythmic episodes [3]. Mobile Cardiac Telemetry (MCT) addresses these drawbacks,

WHAT'S NEW?

The manuscript draws on a very large database of up to 30-day-long full disclosure electrocardiogram (ECG) recordings with beat-to-beat analysis to show how the diagnostic yield for several clinically important arrhythmias depends on monitoring duration. The detailed analysis of the ECG allows us to present data on diagnostic yield for arrhythmias which have been understudied.

by providing monitoring for an extended period (several weeks) with online access to the diagnostic findings, as well as providing a detailed ECG analysis that enables the assessment of other clinically relevant measures of heart rate and rhythm [4].

The primary aim of the present study was to use MCT recordings of up to 30 days to determine the impact of the recording duration on the diagnostic yield for several clinically important arrhythmias: atrial fibrillation (AF) with burdens below ≤1% and ≤10%, frequent premature ventricular contractions (PVCs), non-sustained (nsVT) and sustained ventricular tachycardias (VT ≥30 seconds), 2nd and 3rd-degree atrioventricular blocks (AVB), pauses, and bradycardia [5]. The secondary objective was to investigate sex-specific and age-related differences in the presentation of all arrhythmias.

METHODS

The study consists of 25 151 up to 30 days long ECG recordings performed with the PocketECG™ device (MediLynx Cardiac Monitoring, Plano, TX, USA) in clinical practice in the United States in 2017. All patients included in the study were 18–100 years old, and analyses were performed according to pre-specified age strata with the cut-off point at the standard age of retirement in the United States set at 65 years. Besides age, sex, and indication for monitoring, no details concerning clinical characteristics and the patient's medical history were available due to the nature of the database. The most frequent ICD-10 codes given as indication for monitoring were R00.2 Palpitations (n = 12 673), I49.8 Other cardiac arrhythmias (n = 4 701), R55 Syncope and Collapse (n = 4 428), I48.0 Paroxysmal atrial fibrillation (n = 3 479), R42 Dizziness and Giddiness (n = 3 237), I48.91 Unspecified atrial fibrillation (n = 2372), R00.1 Bradycardia (n = 1872), R06.00 Dyspnea (n = 1 716), R00.00 Tachycardia (n = 1261), G45.9 Transient ischemic attack (n = 1247), I47.1 Supraventricular tachycardia (n = 930), I48.92 Unspecified atrial flutter (n = 748), I45.89 Other conduction disorders (n = 669), I48.1 Persistent atrial fibrillation (n = 662), I45.9 Conduction disorder (n = 481). All patient information was de-identified, the research reported in this paper adhered to ISO/IEC 27001:2013 "Information technology — Security techniques — Information security management systems — Requirements" and the Ethics Review Board of Sweden has waived the need for ethics approval for studies using this data (decision no. 2019-03227).

PocketECG™ is a Food and Drug Administration (FDA) approved mobile ECG recorder that continuously transmits a full ECG signal, with real-time algorithmic detection of arrhythmias and validation by trained ECG technicians [6, 7]. Data were analyzed in a beat-by-beat manner, which enabled precise assessment of the number of arrhythmic episodes together with the exact time of occurrence and duration of each episode. Pocket ECG is most often prescribed for 30 days. The real-time analyses of the ECG signal are available to the referring physician throughout the ECG monitoring, and this allows for the clinicians to shorten or extend the monitoring duration based on the ongoing results. Therefore, the included recording durations vary within the investigated sample.

Endpoint ascertainment

The diagnostic yield that was measured at different monitoring durations included arrhythmias. All arrhythmias were algorithmically detected and manually verified. AF was defined as ≥30 seconds of irregular ventricular activity without P waves. We examined all patients with paroxysmal and persistent AF and selected for analysis only patients with a low AF burden. For these analyses, patients with a total AF burden ≤1% and ≤ 10% were included, to identify a subset with infrequent arrhythmia for whom necessary monitoring duration is not known. PVCs were defined as wide-QRS premature beats (duration greater than 120 ms) that were not preceded by a P wave and were followed by a complete pause before the next regular heartbeat [8]. Frequent PVCs were defined as ≥10 000 PVCs/24 hours [9]. Sustained ventricular tachycardia was defined as a ventricular tachycardia >100 bpm lasting at least 30 seconds [10]. Non-sustained (nsVT) was defined as 4 or more consecutive beats arising below the atrioventricular node with an RR interval of <600 ms (>100 bpm) and lasting <30 seconds [11]. PocketECG system distinguishes triplets from VT, and this distinction was maintained in analyses. Second-degree AVB was defined as delay or disturbance in the transmission of an impulse and sub-classified into Mobitz type 1 when there was a progressive prolongation of the PR interval culminating in a non-conducted P wave, and Mobitz type 2 when there were intermittent non-conducted P waves without a pattern [12]. Third-degree AVB was defined as an absence of all AV nodal conduction [12]. A pause was defined as an RR-interval longer than 3 seconds, and bradycardia was defined as a ventricular rate <40 bpm lasting for at least 60 seconds [13].

Statistical analysis

All analyses were performed in the Python3 language with Anaconda environment for Windows, version 3.8, and using the Pandas, NumPy, and SciPy packages. Kaplan-Meier estimates with 95% confidence intervals (CI) were calculated using the Lifelines Python package [14].

The normality of continuous variables was assessed visually, and normally distributed continuous variables were reported as means (standard deviation [SD]) while skewed variables were reported as medians (interquartile range [IQR]). Dichotomous variables (sex and arrhythmia occurrence) were reported as counts (percentages). Arrhythmia occurrence of each specific arrhythmia event of interest was also handled as time-to-event data, with the time to an event defined as days between the initiation of recording until the first occurrence of each arrhythmia of interest. The cumulative DY, according to monitoring duration, was calculated for each consecutive day of monitoring using Kaplan-Meier curves with recording duration as the time scale in which the arrhythmia of interest was considered the outcome event. Subjects were censored at the time of the end of monitoring, either after 30 days of monitoring or at the time registration ended if this occurred before 30 days of monitoring had ceased [15]. Ninety-five percent CI were calculated using standard errors derived using Greenwood's Exponential formula [16]. Comparisons of diagnostic yield between men and women were performed using the log-rank test [17]. Diagnostic yield was calculated as a percentage of diagnosed patients after each day of monitoring relative to the total number of diagnosed patients after 30 days of monitoring, with reporting of diagnostic yield values after 24 hours, 48 hours, 5 days, 7 days, and 14 days compared to the diagnostic yield after 30 days. Comparisons of the number of patients with investigated arrhythmia was performed using the χ^2 test (Figures 1 and 2). *P*-values <0.05 were considered statistically significant.

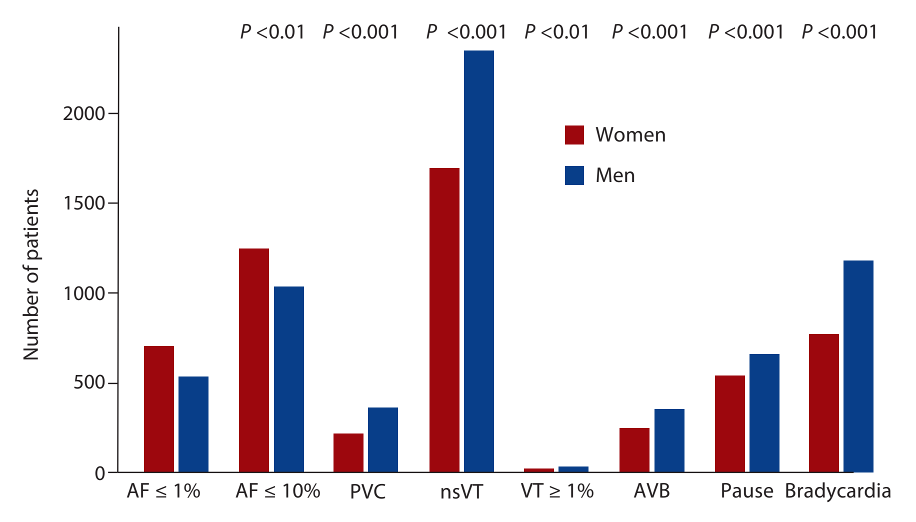

Figure 1. Frequencies of occurrences of different arrhythmias among women and men. Number of patients diagnosed with atrial fibrillation with burden ≤1% and ≤10%, premature ventricular contractions, non-sustained ventricular tachycardias, ventricular tachycardias, atrioventricular blocks, pauses, and bradycardia

Abbreviations: see Table 1

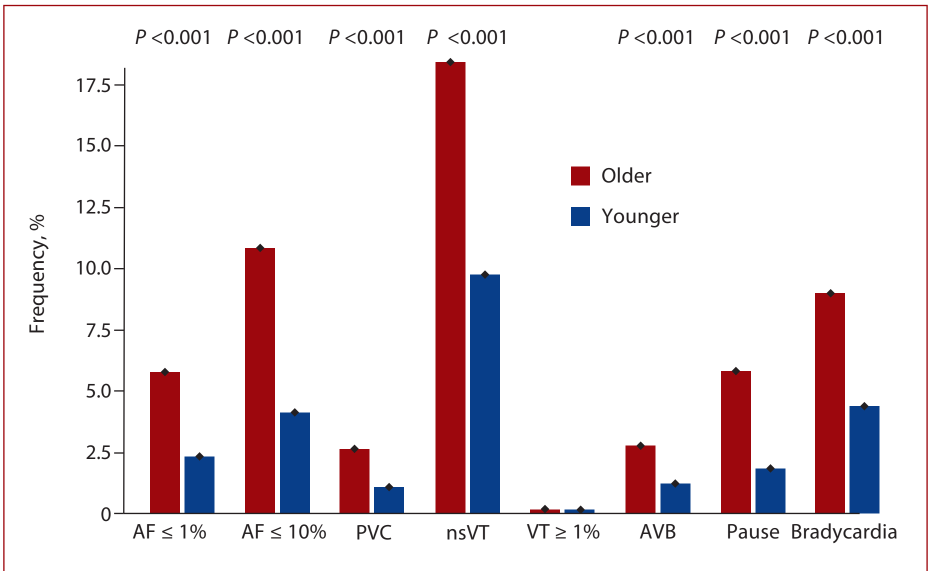

Figure 2. Frequencies of occurrences of different arrhythmias among younger (18–64 years) and older patients (≥65 years). Number of patients diagnosed with atrial fibrillation with burden ≤1% and ≤10%, premature ventricular contractions, non-sustained ventricular tachycardias, ventricular tachycardias, atrioventricular blocks, pauses, and bradycardia

Abbreviations: see Table 1

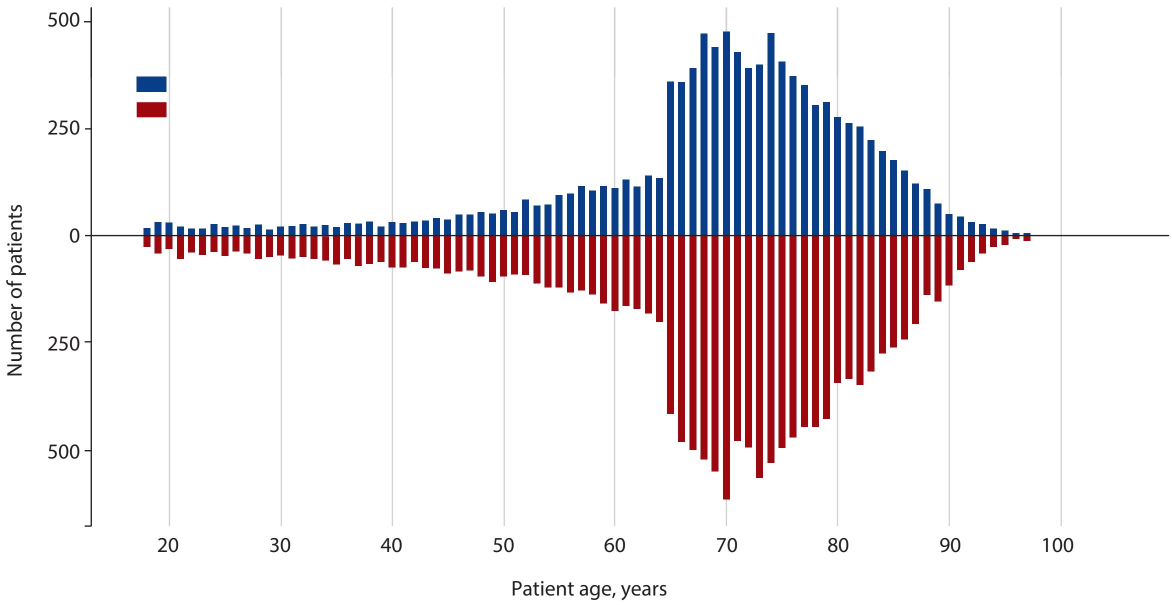

Figure 3. Age distribution among women (red) and men (blue) within the investigated sample

RESULTS

The study population consisted of 14 543 (57.8%) women and 10 608 (42.2%) men. Figure 3 presents the distribution of age in the investigated sample. The median (IQR) age was 71 (64–78) years, and the median recording duration (IQR) was 15.4 (8.2–28.2) days. The mean (SD) active monitoring duration per recording day was 20.27 (3.57) hours.

At least one arrhythmia of interest was found in 10 799 patients (42.9%), of whom 44.2% were women (n = 4 775). All investigated arrhythmias were significantly more frequent in men than in women (all P <0.01, Figure 1) except for AF. The probability of a diagnosis of any arrhythmia of interest was higher for patients ≥65 years compared to younger patients (all P <0.001, Figure 2).

Monitoring duration affects diagnostic yield

Tables 1 and 2 report diagnostic yield after 24 hours, 48 hours, 5 days, 7 days, and 14 days of monitoring by sex. Longer ECG monitoring resulted in higher cumulative diagnostic yield of all arrhythmias, but the strength of the association between diagnostic yield and monitoring time varied. A single day of monitoring diagnosed almost half of the patients with AVB, but fewer than 1 in 5 patients with AF. Two days of monitoring detected approximately half of patients with frequent PVCs, but fewer than a third of AF patients with ≤1% burden.

Sex differences in diagnostic yield

Sex differences in overall diagnostic yield, after the full monitoring duration, are presented in Figure 4. We observed that men, as compared to women, had significantly higher cumulative DY of frequent PVCs (the log-rank test, 4.135; P = 0.042), AVB (the log-rank test, 5.731; P = 0.017), and bradycardia (the log-rank test, 11.920; P = 0.001). For all other arrhythmias, the cumulative diagnostic yield was comparable in men and women.

Age differences in diagnostic yield

The association between age and cumulative diagnostic yield of different arrhythmias is presented in Figure 5. Older subjects (≥65 years) had a significantly higher cumulative diagnostic yield of AVB (the log-rank test, 11.981; P = 0.001), and younger subjects (18–64 years) had a significantly higher cumulative diagnostic yield of sustained ventricular tachycardias (the log-rank test, 9.323; P = 0.002). Otherwise, the cumulative diagnostic yield was comparable in older and younger subjects.

CONCLUSION

The cumulative diagnostic yield increased with ECG monitoring duration regardless of the type of the investigated arrhythmia. The diagnostic yield after 48 hours of monitoring, the typical duration of traditional Holter monitoring, rarely exceeded 50% of the diagnostic yield after 30 days of monitoring, implying that at least half of the patients might remain undiagnosed with a traditional Holter monitoring despite suffering from cardiac arrhythmias that could be diagnosed with longer monitoring durations. Furthermore, even after 14 days of monitoring 10% of patients had not been diagnosed.

We found substantial differences in the frequencies of arrhythmias between women and men. Although more women were examined with ECG monitoring, more men were diagnosed with arrhythmias, which is in accordance with previous research [18]. The finding that the diagnostic yield of AVB, frequent PVCs, and bradycardia was signifi-

Table 1. Diagnostic yield in women calculated after 24 hours, 48 hours, 5, 7, and 14 days

Arrhythmia		AF ≤1%	AF ≤10%	PVCs	nsVT	VT ≥30 s	AVB	Pause	Bradycardia
DY after 24 hours	N	127	354	87	194	2	107	111	224
	DY, %	17.84	28.15	40.09	11.39	11.11	41.63	20.40	28.72
	95% CI	15.17–20.92	25.72–30.76	33.92–46.93	9.97–13.00	2.90–37.58	35.88–47.91	17.25–24.04	25.68–32.03
DY after 48 hours	N	201	505	106	343	2	128	178	322
	DY, %	28.22	40.18	48.85	20.14	11.11	49.81	32.72	41.28
	95% CI	25.00–31.75	37.49–42.99	42.43–55.69	18.31–22.13	2.90–37.58	43.88–56.07	28.95–36.84	37.92–44.82
DY after 5 days	N	343	758	145	686	8	161	317	483
	DY, %	48.10	60.31	66.82	40.28	44.44	62.65	58.27	61.92
	95% CI	44.43–51.91	57.58–63.06	60.53–73.00	38.00–42.65	25.25–69.49	56.76–68.54	54.17–62.44	58.53–65.33
DY after 7 days	N	409	857	159	887	10	181	368	536
	DY, %	57.31	68.25	73.27	52.08	55.56	70.43	67.65	68.72
	95% CI	53.64–61.04	65.63–70.84	67.26–78.97	49.73–54.48	34.88–78.42	64.78–75.89	63.70–71.54	65.45–71.94
DY after 14 days	N	590	1106	186	1308	14	223	472	669
	DY, %	82.75	88.05	85.71	76.81	77.78	86.77	86.76	85.77
	95% CI	79.82–85.48	86.16–89.80	80.71–89.98	74.78–78.78	57.12–93.09	82.32–90.57	83.77–89.45	83.22–88.11
DY after 30 days	N	713	1256	217	1703	18	257	544	780
	DY, %	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
	95% CI	—	—	—	—	—	—	—	—

Abbreviations: ABV, atrioventricular blocks; AF, atrial fibrillation; CI, confidence interval; DY, diagnostic yield; nsVT, non-sustained ventricular tachycardias; PVC, premature ventricular contractions; VT, ventricular tachycardias

Table 2. Diagnostic yield in men calculated after 24 hours, 48 hours, 5, 7, and 14 days

Arrhythmia		AF ≤1%	AF ≤10%	PVCs	nsVT	VT ≥30 s	AVB	Pause	Bradycardia
DY after 24 hours	N	99	301	162	406	6	177	179	426
	DY, %	18.66	28.84	44.51	17.17	17.14	49.44	26.68	35.89
	95% CI	15.54–22.33	26.16–31.73	39.57–49.77	15.71–18.75	8.09–34.23	44.40–54.73	23.50–30.19	33.23–38.69
DY after 48 hours	N	150	423	198	638	13	213	247	571
	DY, %	28.29	40.55	54.40	26.98	37.14	59.50	36.81	48.10
	95% CI	24.59–32.42	37.60–43.64	49.37–59.58	25.24–28.81	23.53–55.23	54.46–64.60	33.29–40.58	45.30–50.99
DY after 5 days	N	266	639	265	1125	19	265	384	797
	DY, %	50.10	61.22	72.80	47.57	54.29	74.02	57.23	67.14
	95% CI	45.84–54.52	58.23–64.22	68.16–77.27	45.58–49.60	38.95–71.10	69.39- 78.45	53.52–60.99	64.46–69.80
DY after 7 days	N	319	735	290	1366	23	285	446	892
	DY, %	60.12	70.37	79.67	57.76	65.71	79.61	66.47	75.15
	95% CI	55.89–64.38	67.55–73.15	75.39–83.63	55.78–59.76	50.21–80.66	75.29–83.61	62.89–70.02	72.66–77.57
DY after 14 days	N	429	902	339	1932	25	319	574	1073
	DY, %	80.94	86.42	93.13	81.69	71.43	89.11	85.54	90.40
	95% CI	77.42–84.23	84.23–88.44	90.23–95.43	80.11–83.22	56.16–85.09	85.62–92.07	82.77–88.08	88.54–91.99
DY after 30 days	N	530	1044	364	2365	35	358	671	1187
	DY, %	100	100	100	100	100	100	100	100
	95% CI	—	—	—	—	—	—	—	—

Abbreviations: see Table 1

cantly higher in men than in women is less documented. In light of this, we hypothesize that men are not only generally more likely than women to suffer from these distinct arrhythmias but also that in men some arrhythmic episodes are more frequent and thus diagnosed earlier.

Moreover, we found that, except AVB and sustained ventricular tachycardias, younger patients experienced arrhythmias at least as often as older patients. Further research is needed to identify reasons for sex and age differences in arrhythmia detection.

In conclusion, an extension of cardiac monitoring to 30 days leads to a substantial increase in diagnostic yield for all studied arrhythmias. In patients for whom the diagnosis of arrhythmia is likely to change clinical management, even a recording duration of 14 days is inadequate since one in every ten patients would not be diagnosed. Extended monitoring with modern ECG devices enables improved accuracy of cardiac arrhythmias detection, leading to substantial benefits both for patients and for the healthcare service.

Strengths and limitations of the study

The main strength of the presented study is the very large number of subjects included in the analysis. This enabled a reliable calculation of the diagnostic yield of both infrequent and serious arrhythmias. Furthermore, to estimate the diagnostic yield of the traditional Holter monitoring, we did not use a separate dataset collected with a Holter device. Instead, we selected shorter recordings from the

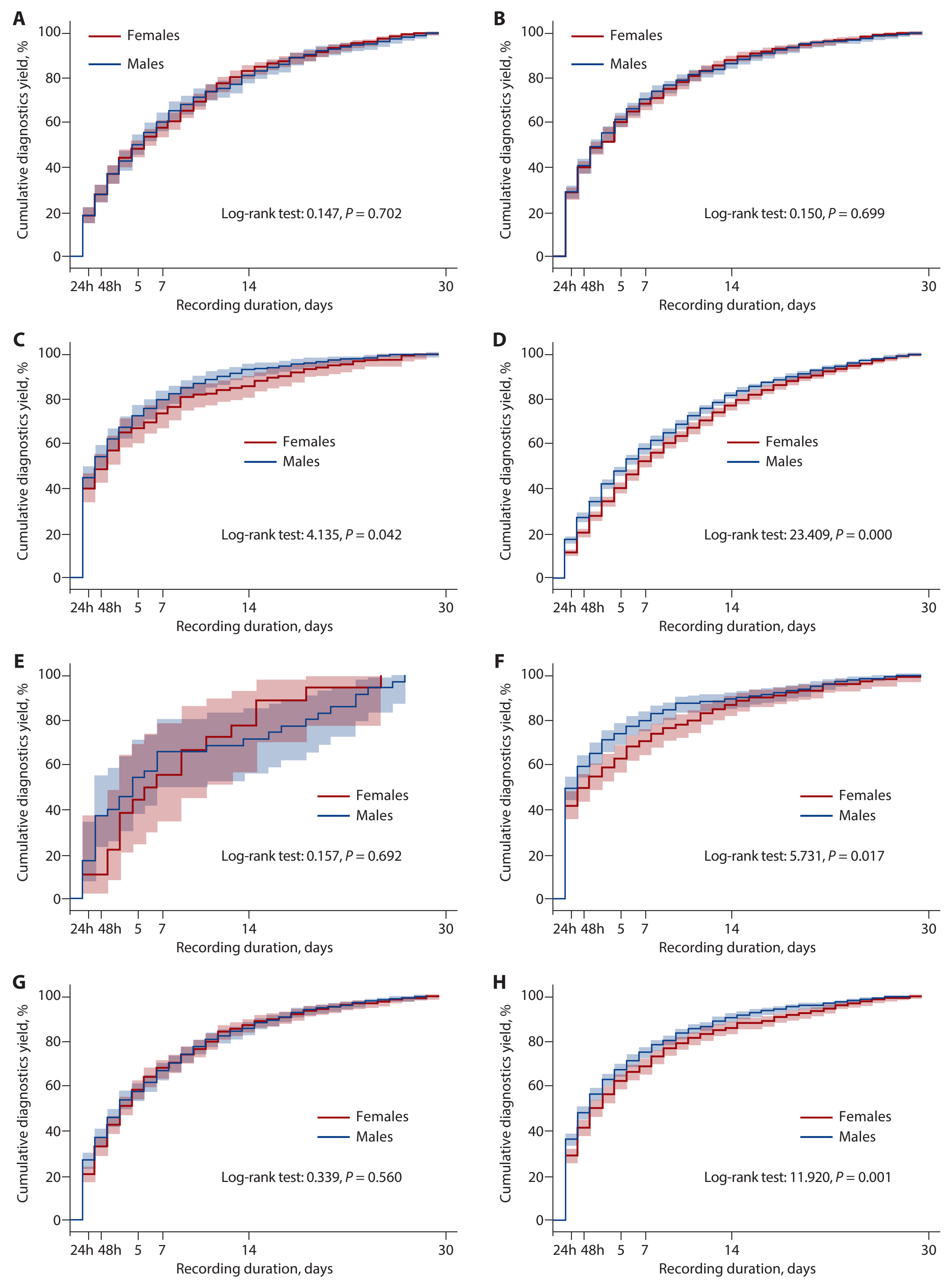

Figure 4. Cumulative DY in women (red) and men (blue) presented for **A.** atrial fibrillation ≤1%, **B.** atrial fibrillation ≤10%, **C.** premature ventricular contractions, **D.** non-sustained ventricular tachycardia, **E.** sustained ventricular tachycardia, **F.** atrioventricular blocks, **G.** pauses, **H.** bradycardia

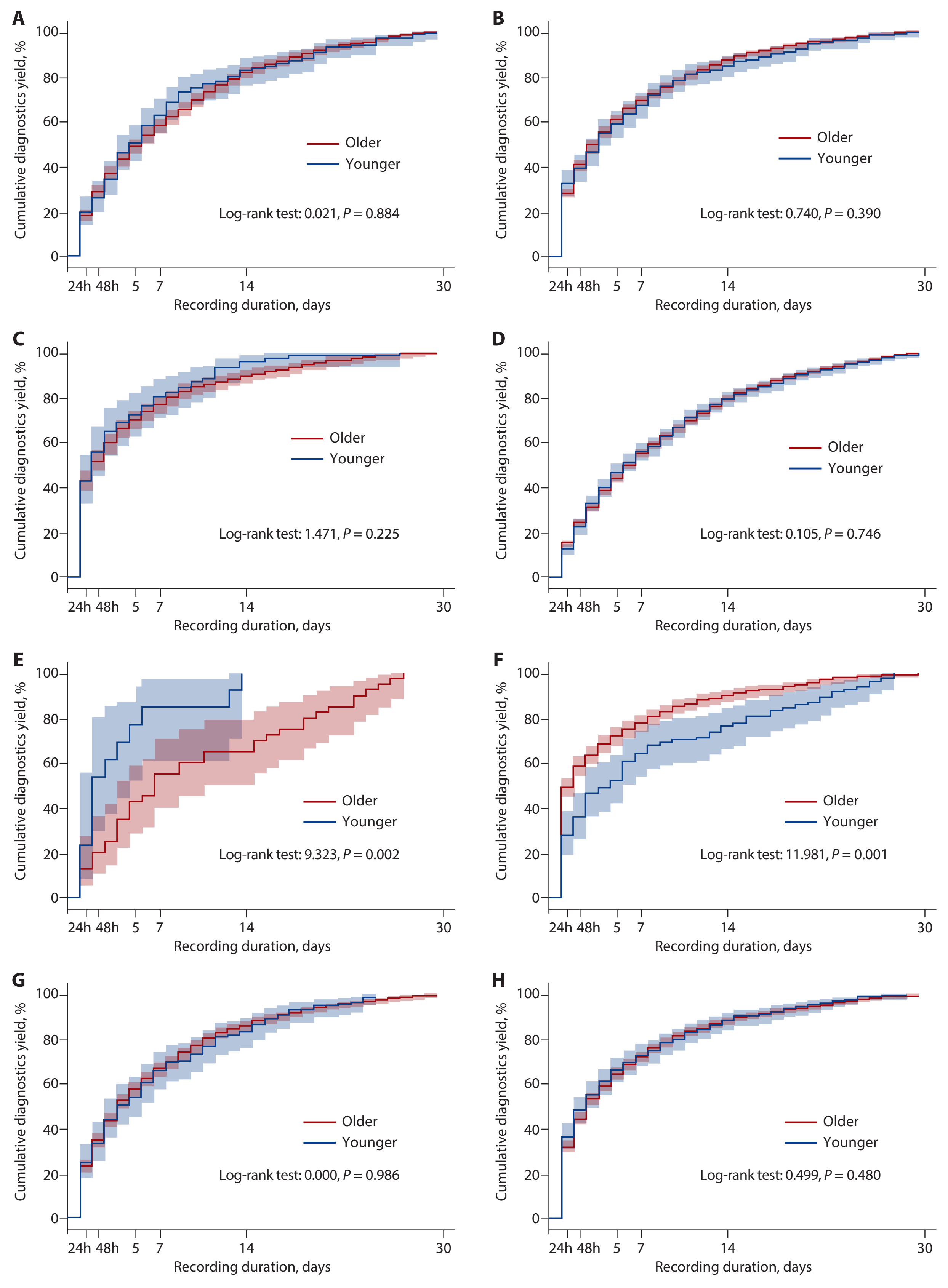

Figure 5. Cumulative diagnostic yield in older patients (red) and younger (blue) presented for **A.** atrial fibrillation ≤1%, **B.** atrial fibrillation ≤10%, **C.** premature ventricular contractions, **D.** non-sustained ventricular tachycardia, **E.** sustained ventricular tachycardia **F.** atrioventricular blocks, **G.** pauses, **H.** bradycardia

long PocketECG™ sessions. As a result, we avoided introducing potential confounding factors such as different data quality, electrodes placement, or arrhythmia detection accuracy. However, some limitations of the presented study also should be noted. The main limitation of the study is the heterogeneity of the investigated sample and the lack of more detailed information regarding the study participants. It is plausible that considering factors such as a patient's medical history, admission criteria, or received treatment may bring insights into the relationship between monitoring duration and the diagnostic yield. It might also shed light on which patient populations could benefit most from extended monitoring.

Article information

Conflict of interest: MJD: Chairman of the Supervisory Board, equity interest in Medicalgorithmics SA. LSBJ: scientific collaboration. LSBJ does not receive any economical/financial reward for her activity. NEN, OW, AMG, MAS: Employee of Medicalgorithmics SA.

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