Cryptogenic Acute Ischemic Stroke: Assessment of the Performance of a New Continuous Long-Term Monitoring System in the Detection of Atrial Fibrillation

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Abstract

Background: Long-term monitoring has been advocated to enhance the detection of atrial fibrillation (AF) in patients with stroke.

Objective: To evaluate the performance of a new ambulatory monitoring system with mobile data transmission (PoIP) compared with 24-hour Holter. We also aimed to evaluate the incidence of arrhythmias in patients with and without stroke or transient ischemic attack.

Methods: Consecutive patients with and without stroke or TIA, without AF, were matched by propensity score. Participants underwent 24-hour Holter and 7-day PoIP monitoring.

Results: We selected 52 of 84 patients (26 with stroke or TIA and 26 controls). Connection and recording times were 156.5 ± 22.5 and 148.8 ± 20.8 hours, with a signal loss of 6,8% and 11,4%, respectively. Connection time was longer in ambulatory (164.3 ± 15.8 h) than in hospitalized patients (148.8 ± 25.6 h) (p = 0.02), while recording time did not differ between them (153.7 ± 16.9 and 143.0 ± 23.3 h). AF episodes were detected in 1 patient with stroke by Holter, and in 7 individuals (1 control and 6 strokes) by PoIP. There was no difference in the incidence of arrhythmias between the groups.

Conclusions: Holter and PoIP performed equally well in the first 24 hours. Data transmission loss (4.5%) occurred by a mismatch between signal transmission (2.5G) and signal reception (3G) protocols in cell phone towers (3G). The incidence of arrhythmias was not different between stroke/TIA and control groups. (Arq Bras Cardiol. 2018; 111(2):122-131)

Keywords: Atrial Fibrillation; Stroke; Electrocardiography, Ambulatory; Cell Phone; Ischemic Attack, Transient.

Introduction

Atrial fibrillation (AF) is the main predictive factor of stroke.[1] Many studies have suggested that frequent short runs of atrial tachycardia (AT) or supraventricular extrasystoles (SVES) may yield early left atrial remodeling and predict AF and increased risk for stroke.[2-4] The risk for stroke is independent of clinical presentations of AF and recent studies have shown that in up to 30% of the cases, arrhythmia is diagnosed before, during or following an ischemic event.[5]

The diagnosis of AF requires documentation, and the detection of paroxysmal AF may be challenging.[6] By convention, the diagnosis of AF requires a minimum duration of 30 seconds.[7] The prognostic value of short episodes of AF is still debatable, and some authors have suggested that their occurrence may not be a benign condition.[8] Detection of paroxysmal AF has been performed by different monitoring techniques, and the importance of its early detection is due to the fact that the prompt initiation of anticoagulation significantly reduces the risk of stroke recurrence by up to 40%.[8-10] The American Heart Association and the Stroke Association recommend a long-term electrocardiographic monitoring of 30 days for the diagnosis of AF in post-cryptogenic stroke (class IIa; level of evidence C). Further evidence in support of this recommendation and for the establishment of the role of short AF episodes is still needed.[11,12]

The aim of this study was to evaluate the performance of a new ambulatory electrocardiographic monitoring system using cell phone transmission in the diagnosis of AF during the acute phase of stroke or transient ischemic attack (TIA) and compared it with 24-hour Holter, and to evaluate the incidence and the type of supraventricular arrhythmias in patients with and without stroke/TIA in its acute phase.[13]

Methods

Subjects: patients with recent (less than 15 days of the event) stroke/TIA were enrolled based on clinical and imaging findings. Stroke was classified as cryptogenic based on the Trial of Org 10172 in Acute Stroke Treatment (TOAST).[14] Ambulatory patients without stroke/TIA, but with risk factors for these events (control group) were also included, and both groups had normal sinus rhythm at electrocardiography (ECG) and no history of AF or atrial flutter (AFL).

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Exclusion criteria were previous AF or AFL or admission electrocardiogram showing any of these conditions, hemorrhagic stroke, age younger than 18 years, residence in areas with no mobile phone coverage, need for intensive care due to severity of disease or difficult management of disease, sequela of neurologic injury, and patients with important cognitive impairment that could negatively affect the ability to understand the instructions related to the use of the devices. Patients with suspected stroke/TIA were seen at two medium-sized public hospitals in the city of Curvelo, Minas Gerais, Brazil, between August 2016 and April 2017. Control patients were enrolled during outpatient visits. Patients' follow-up and therapeutic approach were left to the assistant physicians' discretion. Patients or legal caregivers were invited to participate in the study, which was approved by the research ethics committee of University Hospital of São José/FELUMA, and all participants signed an informed form.

Measurement tools: the diagnosis of stroke/TIA was confirmed by computed tomography (CT) and/or magnetic resonance imaging (MRI), and classified for etiologies using the TOAST[14] criteria. CT and MRI tests were performed by radiologists experienced in the Siemens Somatom Spirit or Toshiba Asteion4 CT scanners and the GE Optima MR360 1.5T.

Demographic and clinical data: data of age, sex, skin color, place of residence, anamnesis, previous diseases, family history, weight, height, traditional cardiovascular risk factors, and $CHADS_2$ and CHA_2DS_2-VASc scores were collected, and cardiologic and neurologic tests were also performed.

Complementary tests: 12-lead ECG, transthoracic echocardiography, Doppler examination of carotid and vertebral arteries, chest X-ray (posterior-anterior and lateral views), laboratory tests including complete blood test, urea, creatinine, glucose, transaminases, GGT, potassium, sodium, TSH, free T4, cholesterol (total and fractions), triglycerides, prothrombin time (PT) and partial thromboplastin time (PTT).

Heart rhythm monitoring: during the first week after clinical diagnosis and notification of cryptogenic ischemic stroke or TIA, heart rhythm was monitored by three-channel Holter 24h recorders (DMS 300-8 and DMS 300-9) and analyzed simultaneously with the DMS CardioScan II software (DM Software Inc. Stateline, NV, USA) and electrocardiography (Policardiógrafo IP®, PoIP) (eMaster, Belo Horizonte, MG, Brazil).

PoIP monitoring: PoIP monitors independently collect and transmit electrocardiographic data at real time using the General Packet Radio Services/ *Enhanced Date Rates* for GSM Evolution (GPRS/ EDGE); data are then stored in the cloud. We used the Brazilian cell phone provider *Vivo* for transmission of the data to the PoIP web portal, and the Mozilla Firefox was used as the web browser for analysis of the data. PoIP offers a "Portal de Exames", an app that enables monitoring of different PoIP devices as well as the access to laboratory tests by individual access credentials (Figure 1). Six electrodes were arranged so that frontal plane leads could be monitored beyond V_1-V_2. Patients and family members were instructed and trained for the monitoring technique, quality of transmission signal, battery charge and charging of the lithium-based batteries. The monitoring was closely controlled via internet by the responsible staff members for the correct use of the device, and quality of the electrode contacts; if necessary, family or caregivers were informed about inadequate system operation or the quality of data transmission.

Procedures: Each participant received an electrode pack and a leaflet with a thorax illustration indicating electrodes' colors and correct positioning for replacement. All electrocardiographic recordings were analyzed by the same investigator (RSF), a cardiologist experienced in ambulatory electrocardiography, and all electrocardiographic tracings considered indicative of AF or tachycardia were reviewed by a second investigator (EBS), a cardiac electrophysiologist.

For analysis of PoIP findings, the results were accessed via internet and examined for AF/AFL every 12 hours or every time the monitor button was pressed by the patient/caregiver. Every 24-hour period, all data transmitted by PoIP were exported and reviewed offline, and quantitative analysis of arrhythmias registered. In this analysis, we considered – number of (single or in pairs) SVES, number of nonsustained atrial tachycardia (AT) episodes greater than three consecutive premature atrial complexes and shorter than 30 seconds, sustained AT longer than 30 seconds and number of AF episodes longer or shorter than 30 seconds.

Statistical analysis: categorical variables were expressed as counts and percentages and numerical variables as mean ± standard deviation (SD). Data normality assumptions were verified with the Shapiro-Wilk test. Associations between categorical variables were assessed by Fisher's exact test or the chi-square test of independence. Comparisons of two groups between independent samples were made by the Wilcoxon test, the Mann-Whitney test or the Student's t-test, as appropriate. Analyses were performed using the free R software version 3.3.2 at 5% level of significance. Initial cohort was composed of 58 patients with stroke/acute TIA and 26 controls. For selection of patients with similar characteristics for the groups of interest, we used the propensity score matching (PSM) method. A logistic regression was constructed to estimate the probability of belonging to the stroke/TIA group, considering the following predicting variables – sex, age and $CHADS_2$ corrected by subtracting two points in patients with stroke/TIA. PSM enabled the selection of 26 patients with stroke/TIA matched with controls by the probabilities obtained from the logistic model, so that the analysis of the cohort yielded 52 patients (26 with stroke/TIA and 26 controls) (Figure 2). Sample power to verify the difference between the recording period on the first day of Holter and PoIP use (23.7 ± 1 and 20 ± 3.2h, respectively) was greater than 80%.

Results

Our sample was composed of 52 patients, equally allocated into stroke/TIA and control groups (Figure 2). More than half of patients (51.9%) were men, mean age was 70.7 ± 10.5 years, with 73.1% of patients aged 65 years or older. Mean BMI was 25.5 ± 5.6 kg/m^2, 21.2% were smokers and 19.2% alcohol consumers. Mean corrected CHADS2 and CHA2DS2-VASc scores were 1.8 ± 0.8 and 3.3 ± 1.2, respectively.

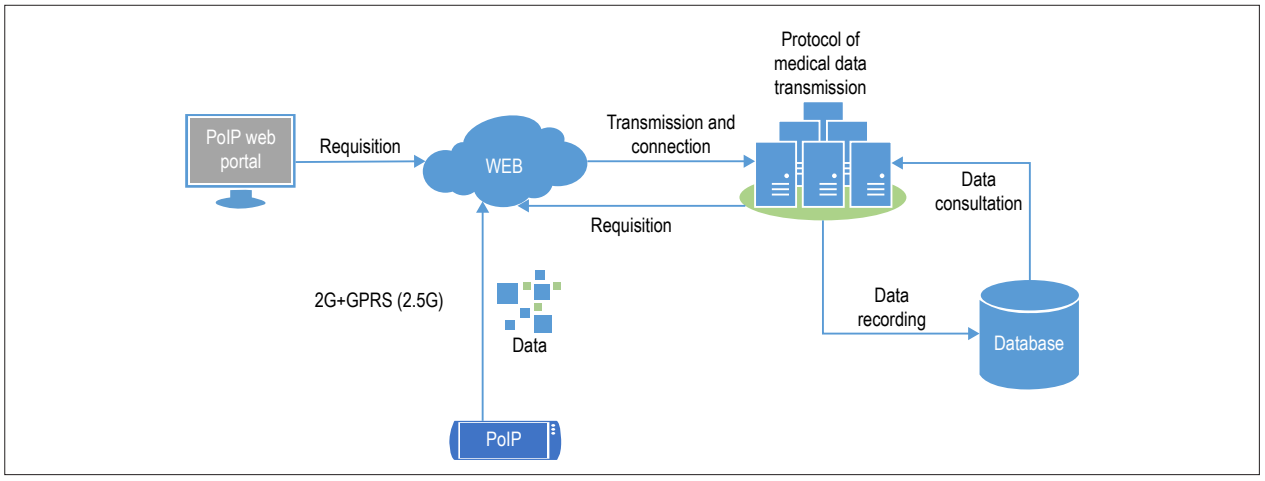

Figure 1 – *Conceptual diagram of PoIP – as can be seen in the diagram, PoIP uses the concept of real-time transmission of the data by the EDGE technology. Wireless data transmission is performed by standard protocol to internet access in mobile devices by GPRS-EDGE – Generic Packet Radio Service, commonly known as 2.5G*

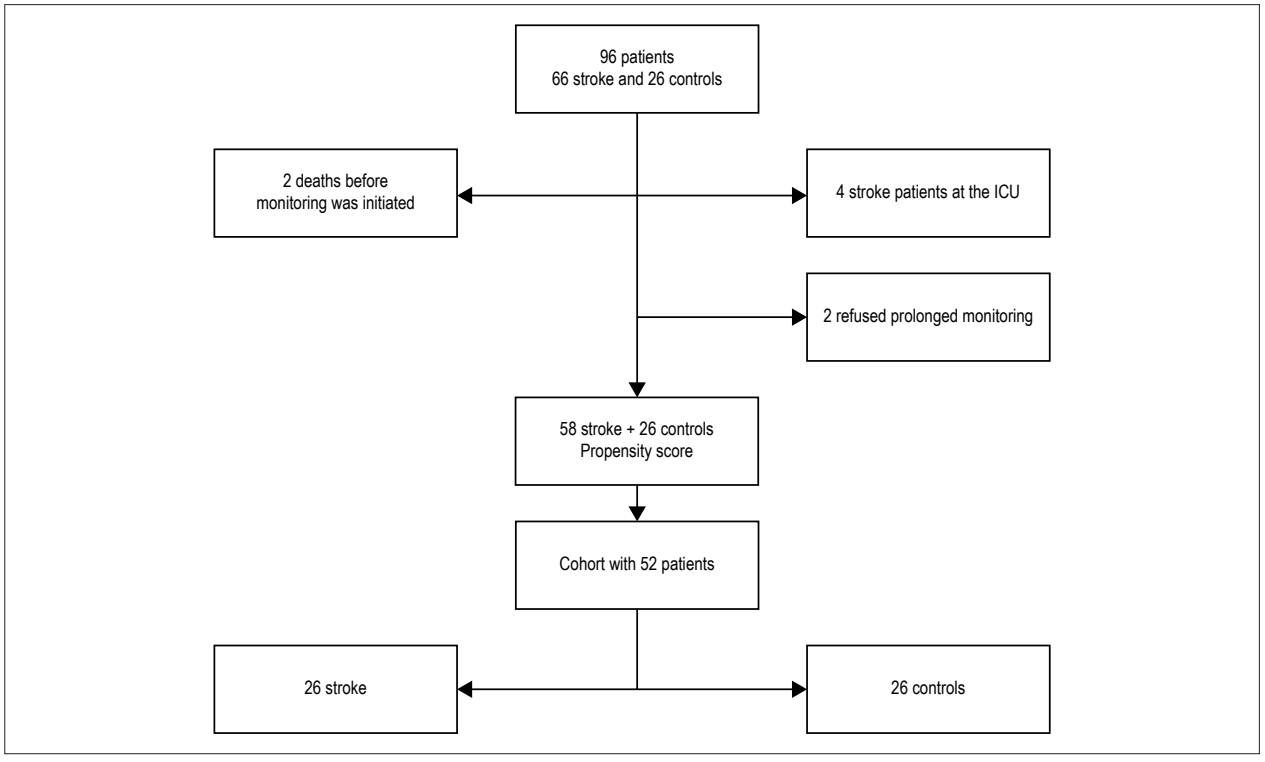

Figure 2 – *Flowchart depicting selection of the study groups*

The most frequent comorbidities were arterial hypertension (84.6%) and diabetes mellitus (51.9%). Among control patients, a significantly higher (p = 0.03) proportion of smokers was found in stroke patients aged 65 years or older (p = 0.04). No other difference was found between the groups (Table 1).

Complementary tests

Echocardiography: the only statistically significant difference between the groups was a lower (although within normal range) ejection fraction (p = 0.04) values in the stroke/TIA group. *Clinical analysis*: the only statistically significant difference was found in free T4 (p = 0.03), which was higher in stroke/TIA, but also within the normal range. No other difference was found between the groups.

Data transmission analysis

Mean recording period was 23.5 ± 0.6 hours by Holter monitoring and 148.8 ± 20.8 hours by PoIP, with no significant

Table 1 – Patients' characteristics by study groups

Variables	Sample (n = 52)	stroke/TIA (n = 26)	Controls (n = 26)	P-value
Clinical data				
Male sex	27 (51.9%)	14 (53.8%)	13 (50%)	1.000[Q]
Age (years)	70.7 ± 10.5	70.9 ± 11.4	70.6 ± 9.7	0.917[T]
≥ 65 years	38 (73.1%)	20 (76.9%)	18 (69.2%)	0.755[Q]
White race	40 (76.9%)	17 (65.4%)	23 (88.5%)	0.100[F]
BMI (kg/m^2)	25.5 ± 5.6	25.6 ± 4.2	25.4 ± 6.9	0.498[W]
> 30 kg/m^2	11 (21.2%)	3 (11.5%)	8 (30.8%)	0.173[F]
Smoking	11 (21.2%)	9 (34.6%)	2 (7.7%)	0.038[F]
< 65 years	3 (21.4%)	2 (33.3%)	1 (12.5%)	0.539[F]
≥ 65 years	8 (21.1%)	7 (35%)	1 (5.6%)	0.045[F]
Alcohol consumption	10 (19.2%)	7 (26.9%)	3 (11.5%)	0.291[F]
Corrected $CHADS_2$	1.8 ± 0.9	1.8 ± 1	1.9 ± 0.8	0.831[W]
Corrected CHA_2DS_2-VASc	3.3 ± 1.2	3.3 ± 1.3	3.3 ± 1.2	0.598[W]
Comorbidities				
Arterial hypertension	44 (84.6%)	23 (88.5%)	21 (80.8%)	0.703[F]
Diabetes mellitus	27 (51.9%)	13 (50%)	14 (53.8%)	1.000[F]
Previous stroke[2]	6 (11.5%)	6 (23.1%)	-	
Previous TIA[2]	6 (11.5%)	6 (23.1%)	-	
Coronary insufficiency	5 (9.6%)	2 (7.7%)	3 (11.5%)	1.000[F]
Congestive heart failure	5 (9.6%)	3 (11.5%)	2 (7.7%)	1.000[F]
Kidney failure	2 (3.8%)	2 (7.7%)	-	
Echocardiography				
Aorta (mm)	32.6 ± 3.9	33.6 ± 4.3	31.6 ± 3.3	0.079[T]
Left atrium (mm)	36.9 ± 4.5	36.3 ± 4	37.6 ± 4.9	0.296[T]
Ejection fraction (%)	63.6 ± 10.3	61 ± 11.3	66 ± 8.9	0.049[W]
Interventricular septum (mm)	10.3 ± 1.4	10.7 ± 1.4	10 ± 1.3	0.086[W]
RV posterior wall (mm)	9.9 ± 1.3	10.1 ± 1.4	9.8 ± 1.3	0.356[W]
Laboratory data				
Glucose (mg/dl)	113 ± 57.5	125.5 ± 76.6	100.5 ± 23.5	0.098[W]
Glycated hemoglobin (%)	6.1 ± 0.7	6.1 ± 0.8	6.1 ± 0.7	0.848[T]
Creatinine (mg/dl)	1.01 ± 0.38	1.06 ± 0.44	0.96 ± 0.31	0.614[W]
HDL (mg/dl)	53.1 ± 15.7	48.8 ± 11.8	57.1 ± 18.1	0.059[T]
LDL (mg/dl)	87.2 ± 30.8	91.1 ± 33.8	83.3 ± 27.7	0.376[T]
Triglycerides (mg/dl)	142.8 ± 96.3	112.4 ± 42.9	171.9 ± 122.4	0.060[W]
TSH (nU/L)	3 ± 3.21	2.70 ± 2.39	3.22 ± 3.82	0.459[W]
Free T4 (ng/dl)	1.03 ± 0.23	1.10 ± 0.25	0.96 ± 0.20	0.038[T]

Numerical variables are expressed as mean ± standard deviation; TIA: transient ischemic attack; [1]Corrected $CHADS_2$ and CHA_2DS_2-VASc scores represent the subtraction of two points from the original scores in the stroke group; [2] previous stroke and TIA were found only in the stroke group (exclusion criteria for controls); [F]exact Fisher's test; [Q]chi-square test of independence; [W] Wilcoxon Mann-Whitney test and [T] Student's t-test for independent samples

difference between the groups, despite higher transmission loss for artifacts among PoIP control subjects. PoIP signal losses were caused by loss of connection (6.8%) and recording signal loss in the server (Table 2).

In the first 24 hours, longer period was required for Holter recording (23.5 ± 0.6 hours) as compared with PoIP (19.2 ± 3.4 hours) ($p < 0.001$).

In the stroke/TIA group, PoIP monitoring was started after 5.4 ± 2.7 days of stroke/TIA during hospitalization, and a shorter connection ($p = 0.02$) and recording period was observed with PoIP (Table 3).

Arrhythmias

AF was detected in one patient by Holter monitoring and in 6 patients by PoIP in the stroke/TIA group, and in only one control by PoIP. Regarding other supraventricular arrhythmias, further cases of nonsustained AT and frequent AT or SVES were identified by Holter monitoring in patients aged 65 years or older in the stroke/TIA group ($p = 0.04$ and 0.04, respectively). In two cases, differential diagnosis of AT and nonsustained AF required revision by the two observers (RFS and EBS). It is worth mentioning, however, that patients who had AF also had AT, and therefore, a misinterpretation of electrocardiographic tracings would not affect the results, due to the occurrence of both conditions in the same patient.

PoIP monitoring revealed that there were no significant differences between the groups regarding tachycardia (Table 4), and all patients with AF also had AT.

Comparisons between Holter and PoIP results showed a higher proportion of AT identified by PoIP in both stroke/TIA ($p = 0.004$) and control ($p = 0.02$) groups. Also, PoIP monitoring revealed a higher proportion of patients with frequent AT or SVES in the stroke/TIA ($p = 0.01$) and control ($p = 0.02$) groups considering total monitoring period, but no difference was found between the groups in the first 24 hours.

Discussion

In the present study that included 52 patients older than 59 years, prolonged rhythm monitoring was performed in 26 patients with acute cerebrovascular events, and initiated only 5 days (mean) after the event. The main findings were high prevalence of arterial hypertension and diabetes mellitus, some connectivity problems and problems related to PoIP signals' recording, and similar profile of cardiac arrhythmias between the study groups.

The most frequent comorbidities were arterial hypertension (84.6%) and diabetes mellitus (51.9%), with similar distribution between the groups studied. This result was expected, since these variables were used in the PSM model, and both comorbidities are also included in the CHADS2 and CHA2DS2-VASc scores. Although these scores provide simple methods for predicting an individual risk of ischemic stroke, the risk estimated by these instruments represent only part of the overall risk (statistical agreement of 0.5). In other words, not all patients with a CHADS2 score equal to 0 or 1 have a low risk, and hence the clinical decision not to anticoagulate patients based only on this score may be erroneous. Despite the higher specificity of a CHA_2DS_2-VASc score ≥ 2, this still underestimates the risk.[15]

For this reason, we analyzed with particular interest the higher prevalence of smoking in stroke/TIA patients ($p = 0.038$), especially among patients older than 65 years ($p = 0.045$). A recent meta-analysis showed that smoking is associated with a modest increase in AF, and that quitting smoking reduces but not eliminates the associated risk of the disease.[16-18] Nevertheless, the addition of smoking to the score does not improve the risk prediction of stroke or TIA.[19]

Monitoring by mobile phone

Although PoIP and Holter monitoring systems had similar performance in the first 24 hours, there were problems with signal connection and transmission during PoIP monitoring. Loss of connection with the cell phone provider accounted for 6.8% of total monitoring time, shorter recording time in the server and lower data losses due to artifacts (Table 2). Loss of connectivity was greater in hospitalized (stroke) patients ($p = 0.024$).

For better interpretation of this result, we measured the strength of the provider signal using the Network Monitor®

Table 2 – Monitoring period (hours) by study groups

Variables	Sample (n = 52)	Stroke/TIA (n = 26)	Controls (n = 26)	P-value
Holter				
Recording time	23.5 ± 0.6	23.4 ± 0.8	23.5 ± 0.4	0.948
Loss (artifacts)	0.6 ± 1.4	0.6 ± 1.7	0.6 ± 1	0.162
PoIP				
Connection period	156.5 ± 22.5	148.8 ± 25.6	164.3 ± 15.8	0.024
Recording time on the first day	19.2 ± 3.4	19.1 ± 2.5	19.2 ± 4.2	0.514
Recording period	148.8 ± 20.8	143.9 ± 23.3	153.7 ± 16.9	0.080
Loss (artifacts)	50.9 ± 26.2	45.6 ± 26.3	56.1 ± 25.5	0.081

Wilcoxon Mann-Whitney test for independent samples; monitoring period had been planned to be up to 24 hours by Holter andu p to 168 hours (7 days) by PoIP. Comparison of recording periods between Holter and PoIP on the first day: $p < 0.001^W$

Table 3 – Holter monitoring results by study groups

Variables	Stroke/TIA (n = 26)	Controls (n = 26)	p-value[F]
Atrial fibrillation (< 30 seconds)	**1 (3.8%)**	**-**	**-**
Atrial tachycardia (AT)	**16 (61.5%)**	**9 (34.6%)**	**0.095**
< 65 years	1 (16.7%)	2 (25%)	1.000
≥ 65 years	15 (75%)	7 (38.9%)	0.047
Frequent SVES*			
< 65 years	5 (19.2%)	3 (11.5%)	0.703
≥ 65 years	5 (25%)	3 (16.7%)	0.697
Frequent AT or SVES	**17 (65.4%)**	**10 (38.5%)**	**0.095**
< 65 years	1 (16.7%)	2 (25%)	1.000
≥ 65 years	16 (80%)	8 (44.4%)	0.042
Ventricular tachycardia	**6 (23.1%)**	**5 (19.2%)**	**1.000**
< 65 years	-	1 (12.5%)	-
≥ 65 years	6 (30%)	4 (22.2%)	0.719
Frequent SVES	**6 (23.1%)**	**7 (26.9%)**	**1.000**
< 65 years	-	1 (12.5%)	-
≥ 65 years	6 (30%)	6 (33.3%)	1.000

*SVES: supraventricular extrasystoles; [F]Fisher's exact test; *frequent SVES was defined as > de 30 events/hour*

Table 4 – POIP monitoring results by study groups

Variables	Stroke/TIA (n = 26)	Controls (n = 26)	p-value[F]
Atrial fibrillation (< 30 seconds)*	**6 (23.1%)**	**1 (3.8%)**	**0.099**
First 24h	2 (7.7%)	1 (3.8%)	1.000
Atrial tachycardia	**22 (84.6%)**	**18 (69.2%)**	**0.324**
< 65 years	4 (66.7%)	5 (62.5%)	1.000
≥ 65 years	18 (90%)	13 (72.2%)	0.222
First 24h	12 (46.2%)	14 (53.8%)	0.782
Frequent SVES **	**4 (15.4%)**	**6 (23.1%)**	**0.727**
< 65 years	-	1 (12.5%)	-
≥ 65 years	4 (20%)	5 (27.8%)	0.709
First 24h	2 (7.7%)	6 (23.1%)	0.249
Frequent atrial tachycardia or SVES	**22 (84.6%)**	**19 (73.1%)**	**0.499**
< 65 years	4 (66.7%)	5 (62.5%)	1.000
≥ 65 years	18 (90%)	14 (77.8%)	0.395
First 24h	12 (46.2%)	14 (53.8%)	0.782
Ventricular tachycardia	**7 (26.9%)**	**7 (26.9%)**	**1.000**
< 65 years	-	2 (25%)	-
≥ 65 years	7 (35%)	5 (27.8%)	0.734
First 24h	3 (11.5%)	4 (15.4%)	1.000
Frequent ventricular extrasystoles	**8 (30.8%)**	**7 (26.9%)**	**1.000**
< 65 years	1 (16.7%)	1 (12.5%)	1.000
≥ 65 years	7 (35%)	6 (33.3%)	1.000
First 24h	6 (23.1%)	6 (23.1%)	1.000

*SVES: supraventricular extrasystoles; [F]Fisher's exact test; *all cases identified in patients aged ≥65 years; **frequent SVES was defined as > de 30 events/hour*

Table 5 – Comparisons between Holter and POIP monitoring results

Variable	Holter	POIP	p-value[F]
Atrial fibrillation (< 30 seconds)	**1 (1.9%)**	**7 (13.5%)**	**0.060**
AVC/AIT	1 (3.8%)	6 (23.1%)	0.099
Controls	-	1 (3.8%)	-
First 24h	1 (1.9%)	3 (5.7%)	0.618
Atrial tachycardia	**25 (48.1%)**	**40 (76.9%)**	**0.004**
AVC/AIT	16 (61.5%)	22 (84.6%)	0.116
Controls	9 (34.6%)	18 (69.2%)	0.025
First 24h	25 (48.1%)	26 (50%)	1.000
Frequent SVES*	**8 (15.4%)**	**10 (19.2%)**	**0.796**
AVC/AIT	5 (19.2%)	4 (15.4%)	1.000
Controls	3 (11.5%)	6 (23.1%)	0.465
First 24h	8 (15.4%)	8 (15.4%)	1.000
Frequent atrial tachycardia or SVES	**27 (51.9%)**	**41 (78.8%)**	**0.007**
Stroke/TIA	17 (65.4%)	22 (84.6%)	0.199
Controls	10 (38.5%)	19 (73.1%)	0.025
First 24h	27 (51.9%)	26 (50%)	1.000
Ventricular tachycardia	**11 (21.2%)**	**14 (26.9%)**	**0.647**
Stroke/TIA	6 (23.1%)	7 (26.9%)	1.000
Controls	5 (19.2%)	7 (26.9%)	0.743
First 24h	11 (21.2%)	7 (13.5%)	0.438
Frequent ventricular extrasystoles	**13 (25%)**	**15 (28.8%)**	**0.825**
Stroke/TIA	6 (23.1%)	8 (30.8%)	0.755
Controls	7 (26.9%)	7 (26.9%)	1.000
First 24h	13 (25%)	12 (23.1%)	1.000

*SVES: supraventricular extrasystoles; [F]Fisher's exact test; *frequent SVES was defined as > de 30 events/hour*

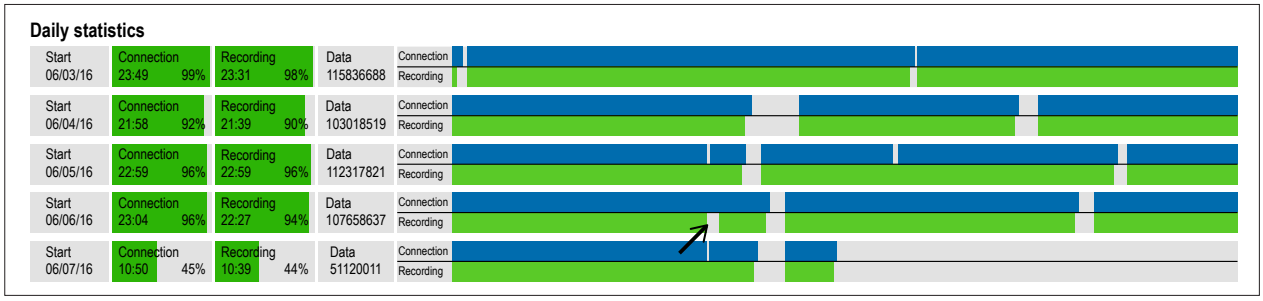

Figure 3 – *PoIP provides daily statistics of connection (blue line) and recoding (green line) data of signal transmission in the server. It is of note that connection and transmission percentages are very similar to each other (day 3/6: 99% and 98%, day 4/6: 92% and 90%, day 5/6: 96% and 96%). Small losses occurred, as on 6/6/2016, when there was a brief period when signal was transmitted but not recorded in the server (arrow)*

software in the ward facilities. We found a high signal variation depending on the site where the measurements were obtained – in the entrance, in the middle and in the ward exit, the signal velocity was 1.6, 12.3 and 0.3 Mbs, respectively, and signal strength was 60, 70 and 20%. Such high signal variation may explain signal losses during the monitoring of patients hospitalized in these areas, which would be lower in the outpatient department.

In addition, transmission losses may occur even in cases of adequate connectivity between PoIP and the mobile phone provider, due to instability of the mobile phone network. During these unstable periods, PoIP remains connected to the provider, and data transmission is restored when connection is recovered (Figure 3). Although such instability periods, are usually short, in our study, they accounted for 11.4% of total monitoring time, *i.e.* approximately 19 hours a week

per patient (Table 2). Also, we found that after the repair of transmission towers and antennas, signal reception was changed from 2.5G (GPRS General Packet Radio Service) to 3G, which negatively affects data transmission. Updating of the technology from 3G to 4G would resolve this issue, as well as reduce the energy expenditure with data package transmission, resulting in optimization of rechargeable battery duration, reduction of charging time and improving monitoring performance.

Greater data loss due to artifacts was seen in control subjects in the PoIP group, which may be justified by the greater freedom of movement of patients in ambulatory treatment.

Arrhythmias detected by PoIP (firs 24 hours) compared with Holter-24

In the first 24 hours, no difference in arrhythmias was observed (AT, SVES, SVES + AT). Despite the longer monitoring period by Holter recordings, all AT runs and the three episodes of AF (2 in the stroke and 1 in the control group).

Twenty-four hour Holter compared with prolonged monitoring

Comparison between Holter and PoIP monitoring results showed a higher proportion of frequent AT and SVES detected by PoIP monitoring in both stroke/TIA and control groups, which was expected by its longer monitoring period.

Comparison of arrhythmias detected in stroke group and controls

No significant difference was found in the occurrence of AT or nonsustained AF, in the comparison between patients with cryptogenic stroke and a control group matched by sex, age and corrected $CHADS_2$. We report a high prevalence of atrial arrhythmias in 52 patients, including 40 with AT and 7 with AF. In stroke/TIA group, proportion of AF was 23.1% in patients monitored by PoIP, and 3.8% in those monitored by Holter, which is in agreement with the literature (Tables 3, 4 and 5).[20] Some studies have suggested that and additional 24-hour period of monitoring would increase the percentage of new diagnoses of paroxysmal AF in 2-4% stroke patients.[21,22] This confirms the efficacy of prolonged ambulatory ECG in patients at risk of AF and may generate a clinically significant diagnostic yield.[23]

Studies have highlighted the association of frequent SVES and AT with increased risk of stroke.[2,3,4,24-27] Studies involving long-term heart rhythm monitoring in patients with previous stroke/TIA have reported a paroxysmal AF prevalence of 5-20%.[20,28,30-33]

In our study, all AF episodes lasted less than 30 seconds. Although an AF episode ≥ 30 seconds is used as a parameter for the diagnosis of AF,[7] some authors have suggested that short AF episodes have an impact on the risk of stroke/TIA or systemic thromboembolism.[10,33]

One important finding was the lack of difference in the prevalence of atrial arrhythmias between patients with and without stroke or TIA, at similar risk for these conditions. This finding suggests that the atrial arrhythmias detected may be an epiphenomenon. Kottkamp and other authors[15,34] have suggested the presence of a thrombogenic fibrotic atrial cardiomyopathy, with risk for embolic events with no causal connections with atrial arrhythmias. Contractile changes would be responsible for the increased thrombogenic risk during sinus rhythm, in addition to interatrial block and sinus node dysfunction. Even ablation of AF would not be able to impede the progression of fibrotic process.[34] Factors like diabetes, hypertension, age, among others, would be involved in myocardial damage. In our sample, more than 80% of patients had arterial hypertension and more than 50% were diabetic. Non-invasive detection of atrial fibrosis is currently limited to MRI techniques, not available in clinical practice.[34] In this context, AF would be a manifestation of atrial structural changes, and thereby increasing the risk of embolic events.

None of our patients with stroke/TIA had AF before or during stroke. In fact, AF may be detected in only a minority of the cases and may take months, as shown by the TRANDS, ASSERT and IMPACT studies, which included patients with implantable continuous monitoring devices.[35-37]

The paradigm used in most studies is that AF detection would be just a matter of time, but even in a one-year follow up, AF is detected in less than half of patients with cryptogenic stroke. This is a pioneering study in monitoring patients at similar stroke and TIA risk, by including a group with stroke and a control group without the disease. The finding that the incidence of atrial arrhythmias was not different between both groups is consistent with the hypothesis that a factor other than arrhythmia may be involved in the risk for stroke; one possibility is fibrotic atrial cardiomyopathy.

Study limitations

The sample size was insufficient to evaluate individual risk factors. Discrimination between short runs of atrial tachycardia and AF may be difficult, even to an experienced electrophysiologist. P-waves in ambulatory monitoring systems may not be clearly identified as compared with conventional 12-lead ECG. Nevertheless, analysis of isolated episodes and analysis of more than one arrhythmia episode yielded similar results, since all patients that had short AF episodes also had AT.

Mobile phone services currently available still have limited coverage, with absent or deficient signal strength, and unstable transmission velocity, which altogether, negatively affect PoIP data collection. Due to frequent repairs of problems caused by electrical discharges in cell phone towers, access to GPRS may be lost, thereby affecting signal reception, which may be solved by implementation of the 4G technology.

Conclusions

Holter and PoIP showed comparable results in the first 24 hours. The shorter monitoring period was caused by a low signal strength. Data transmission loss in hospitalized patients resulted from a mismatch between the protocol of signal transmission in the cell phone tower (3G) and the signal effectively transmitted (2.5G), which can be mitigated by the adoption of a 4G technology. The incidence of arrythmia was not different between stroke and control groups.

Author contributions

Conception and design of the research, acquisition of data and critical revision of the manuscript for intellectual content: Sampaio RF, Gomes IC, Sternick EB; Analysis and interpretation of the data: Gomes IC; Writing of the manuscript: Sampaio RF, Sternick EB.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Hospital Universitário São José/FELUMA under the protocol number CAAE=35481114.0.0000.5134. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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