Indications for and the diagnostic yield of 24-hour Holter monitoring: a prospective study at the Korle Bu Teaching Hospital

Alfred Doku<sup>1</sup>, Tom A Ndanu<sup>2</sup>, Bernard Y-A Asare<sup>3</sup>, Charles Antwi-Boasiako<sup>4</sup> and John Kpodonu<sup>1</sup>

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<sup>1</sup>Department of Medicine and Therapeutics, School Of Medicine and Dentistry, College of Health Sciences, University of Ghana, Accra

<sup>2</sup>Department of Community and Preventive Dentistry, School of Medicine and Dentistry, College of Health Sciences, University of Ghana, Accra

<sup>3</sup>Research Web Africa, P. O. Box 2591, Sunyani Brong Ahafo Region, Ghana

<sup>4</sup>Department of Physiology, School of Biomedical and Allied Health Sciences, College of Health Sciences, University of Ghana, Accra

**Corresponding author:** Bernard Yeboah-Asiamah Asare **Conflict of interest:** None declared

E-mail: asiamahyeboah2006@yahoo.com

### **SUMMARY**

**Background:** Holter monitoring (HM) is an important tool used to evaluate symptoms suspected to be caused by arrhythmias. This study was aimed at determining the diagnostic yield of Holter monitoring among symptomatic and asymptomatic patients undergoing HM at the Korle-Bu Teaching Hospital.

**Methods:** This was a prospective study among 400 consecutive symptomatic and asymptomatic patients undergoing HM from August 2006 to December, 2009 at the Korle-Bu Teaching Hospital. Data from the Holter study were analyzed, and symptoms linked to arrhythmias were evaluated to determine the diagnostic yield of HM in symptomatic and asymptomatic patients.

**Results:** The mean age of the patients was  $51.81 \pm 16$  years. The most common indications (symptoms) for HM were palpitation (62.9%) and dizziness (34.0%); about half (53.3%) of the symptomatic patients had only one indication. Among the symptomatic group, 28 in 115 symptoms were linked to arrhythmias giving a diagnostic yield of 24.3% whereas in the asymptomatic group 1 in 33 of symptom was linked to arrhythmia giving a diagnostic yield of 3.0%. The study found an overall diagnostic yield of 19.6%.

**Conclusion:** HM as a regular health check for the general population (asymptomatic cohorts) is not cost effective and does not provide significant data to influence care except when the subject is found to have symptoms.

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Keywords: arrhythmias, indications, Holter monitoring, diagnostic yield, Ghana

### INTRODUCTION

Palpitations<sup>1,2,3</sup>, syncope<sup>4,5</sup>, near syncope, fainting, near fainting, dizziness, easy fatigability, chest pains<sup>6</sup> and dyspnoea<sup>7</sup> are common signs and symptoms presented at the outpatient department which are suspected to be associated with arrhythmias. Palpitations have been found to be caused by several arrhythmias including sinus tachycardia, atrial fibrillation, premature ventricular contractions, or ventricular tachycardia.<sup>8</sup>

Syncope episodes have on the other hand been indicated to be caused by sinus bradycardia, second or thirddegree atrioventricular (AV) block, pace maker malfunction, supraventricular tachycardia and ventricular tachycardia.<sup>1-5,9</sup> Chest pain due to angina pectoris may also be a presentation of a tachyarrhythmia.<sup>10</sup> However, finding the causes for these symptoms pose great challenges in clinical practice in that they are so subjective and may connote other problems or diseases other than arrhythmias.<sup>11,12</sup>

The evaluation of all patients with symptoms suspected to be caused by arrhythmias is critical in linking these symptoms to the underlying arrhythmias, and frequently used evaluation tools include Holter, 24-72 hour ambulatory electrocardiogram (ECG), monitoring (HM).<sup>9,13,14</sup> HM is an important clinical tool for diagnosing of arrhythmias, as it has ability to temporally link symptoms to arrhythmias. <sup>9,15-17</sup> Several authors have found overall diagnostic yield range of 8.6% to 22% in patients presenting with syncope.<sup>15,17-18</sup> Others have reported of diagnostic yields of 35% to 54% in patients with palpitation.<sup>19-21</sup> However, the level of diagnostic yield of HM reported depends on the patient population studied. Data on HM is limited in sub-Saharan Africa and there is paucity of data on the diagnostic yield of HM in Ghana. We present the findings of a group of symptomatic and asymptomatic patients referred for a 24-hour HM to determining the diagnostic yield of HM at the Korle Bu Teaching Hospital, Accra.

## **METHODS**

#### Study design and setting

The study was a hospital based prospective study aimed at determining the diagnostic yield of HM carried out at the Korle Bu Teaching Hospital, Accra Ghana. KBTH is a tertiary and the national referral hospital in Ghana with a bed capacity of 2000, daily visits of 1,500 and admissions of 500 patients. The hospital's Cardiothoracic Centre offers services including HM (24-72 hour ECG) and ambulatory blood pressure.

#### Study population, sample and data

Data for the study were collected from symptomatic and asymptomatic patients aged 18 years and above who underwent HM from August 2006 to March 2009. Symptomatic patients were patients with unexplained symptoms or with complaints of palpitation, dizziness, fainting attacks, near fainting attacks, syncope, chest pains and fits/seizures (symptomatic) referred for HM.

Asymptomatic patients were undergoing the standard routine medical checkup including screening for cardiovascular risk factors, cardiovascular diseases and cancers. However, patients had the option of undergoing a 24-hour ambulatory blood pressure (BP) monitoring to ascertain BP/heart rate trend, or 24-hour Holter monitoring to ascertain Heart rate profile as well as asymptomatic arrhythmia.

During the study period, 400 consecutive patients from the cardiology department, other departments of the KBTH and referred from other hospitals in Ghana underwent a 24-hour Holter study using Microvit MT 101 Holter device from Schiller with MT 200 Evaluation Software as the program for Holter analysis. Patients were excluded from the study if they had a mental illness or could not follow through with the instructions for Holter monitoring; clinical evidence of anaemia; New York Heart Association class IV heart failure; received anti-arrhythmic treatment within the previous four months; and complete atrioventricular (AV) block with normal idioventricular rhythm (ventricular rate <40 beats per minute). HM done on patients were analyzed for various arrhythmias.

Any relevant symptoms occurring during the 24 -hour period recorded by participants are traced and the prevailing ECG tracing noted. In addition, the common activities that precipitated the arrhythmia were traced even if those activities did not lead to symptoms. For each symptom or activity time recorded by participant, the corresponding Holter recording was traced 10 minutes before and after to allow for errors made by participants in writing the exact event time. The arrhythmias were analyzed for both symptomatic and asymptomatic patients. A structured questionnaire was used to collect data on the basic clinical characteristics of patients were obtained, including demographic data, medical history, medication, and echocardiography findings before they were enrolled in the HM.

Findings from the HM were defined as;

- A normal Holter study: patient with normal sinus rhythm (NSR), heart rate (HR) 40-100 beats per minute during sleep and 50-120 beats per minute during waking period, HR variability of < 20 %, bundle branch block (partial or complete; intermittent or permanent), 1<sup>st</sup> degree AV block, missed beats, pause less than 1.5 second and accessory pathway conduction with or without pre-excitation with HR < 100 beats per minute.
- An abnormal Holter study include a finding of any of significant sinus bradycardia (HR < 50bpm during waking period and <40 bpm during sleep), sinus tachycardia(HR>120bpm during waking and > 100 bpm during sleep), atrial tachycardia, multifocal atrial tachycardia, atrial flutter, atrioventricular nodal reentry tachycardia(AVNRT), atrioventricular reentry tachycardia(AVRT), atrial fibrillation, premature atrial complex, premature ventricular complex, accelerated idioventricular rhythm (AIVR), ventricular tachycardia, ventricular fibrillation, torsades de pointes, sinoatrial (SA) block type 2, significant pauses (R-R interval > 1.5 second), 2<sup>nd</sup> degree AV block (Mobitz type 1 and 2) and complete AV block. Sinus arrhythmia: R-R interval or HR variability of 20 % or more without SA block.
- Holter study considered diagnostic when any of the above-mentioned arrhythmia are linked to relevant symptoms.

The diagnostic yields of Holter monitoring in symptomatic and asymptomatic patients as well as the overall diagnostic yield were determined.

## Data analysis

Data from structured questionnaire and Holter interpretation were entered, cleaned and analyzed using Statistical Package for Social Sciences (SPSS) version 16.0.

Descriptive statistics were used to summarize results into tables, frequencies and percentages. Continuous variables were summarized as mean and standard deviation.

#### Ethical approval and consent to participants

The protocol for this study was submitted to the research and ethics committee of the University of Ghana Medical School and ethical clearance granted (MS-Et/M.4-P.8/2008-09). Consent was obtained from all participants before they were enrolled. A 24 hour study hotline was established and participants could call the study physician for any concerns. Participants were reimbursed for calls made to the hotline.

## RESULTS

Four hundred HM was done during the study period. Out of which 387 (96.8%) were included in the analysis. The ages of the patients ranged between 18-88 years, with the mean age of  $51.81 \pm 16$  years. Most of patients were males (55%). The baseline clinical characteristics are shown in Table 1.

Table 1 Baseline characterist	tics
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Characteristics	Frequency, n=387(%)
Sex	
Males	213(55.0)
Females	174(45.0)
Hypertension	265(68.5)
Structural heart diseases	30(10.5)
Drugs	
Beta blockers	54(14.0)
Calcium channel blockers(	97(25.0)
DHP)	
Tricyclic antidepressant (TCA)	1(0.3)
Digoxin	6(1.6)
Diuretics	22(5.7)

#### Indications for HM among symptomatic patients

Table 2 shows the indications (symptoms/complaints) and their frequency for Holter among the symptomatic patients.

The most common indications observed were palpitation (62.9%), dizziness (34.0%) and chest pains (24.8%). About half (53.3%) of the cases had a single complaint, while 43.6% had more than one different complaints/indications for Holter monitoring (Table 2).

## **Results from Holter monitoring**

The study revealed Holter abnormalities in 93.8% of the study participants; 93.1% of symptomatic patients whereas 96.0% of asymptomatic patients had abnormalities. Common abnormalities included premature atrial complexes (71.6%), premature ventricular complexes (54.0%) and significant sinus tachycardia (40.0%) (Table3).

#### Symptoms and their diagnostic yield during HM

**Table 4** shows the symptoms that patients experienced during the Holter monitoring and the corresponding diagnostic yields.

Hundred and fifteen symptomatic patients (40%) and 33 asymptomatic patients (33.6%) had symptoms during the monitoring. Palpitation was observed among 24.6% of symptomatic patients and 17.3% of asymptomatic subjects. Dizziness was experienced by 15.2% of symptomatic subjects and 12.2% of asymptomatic subjects. Chest pains and dyspnoea were fairly common in both groups.

Table 2 Indications	for Holter	monitoring	in sympto-
matic patients			

Indications and frequency	Symptomatic pa- tients, n=289(%)
Symptoms/complaint*	
Palpitation	190(65.7)
Dizziness	104(36.0)
Chest pains	75(26.0)
Intermittent dyspnoea/ easy fatigue	55(19.0)
Syncope	53(18.3)
Near fainting attack	23(8.0)
Fainting attack	5(1.7)
Seizure	5(1.7)
Number of symptoms per patient	
One	163(56.4)
Two	91(31.5)
Three	30(10.4)
Four	12(4.2)
Five	2(0.7)

\*multiple responses allowed

### Table 3 Results from Holter monitoring

Arrhythmias	Symptomatic patients n=289(%)	Asymptomatic patients n=98(%)
Sinus arrhythmias*	49(17.0)	14(14.3)
Significant sinus bradycardia	56(19.4)	16(16.3)
Significant sinus tachycardia	114(39.4)	41(41.8)
PAC	195 (67.7)	82 (83.7)
Atrial flutter	7 (2.4)	0 (0.0)
Atrial fibrillation	11(3.8)	(0.0)
Multifocal atrial tachycardia	1 (0.3)	0 (0.0)
Paroxysmal atrial tachycardia	11 (3.8)	0 (0.0)
Junctional tachycardia	9 (3.1)	1 (1.0)
PVC	161 (55.8)	48 (49.0)
AIVR	10 (3.5)	2 (2.0)
VT (Non-sustained )	15 (5.2)	0 (0.0)
2 <sup>nd</sup> degree SA block	10 (3.5)	1 (1.0)
Sinus pause	43(14.9)	11(11.2)
2 <sup>nd</sup> degree AV block	18(6.2)	6(6.1)
Complete AV block	6(2.1)	0(0.0)

\*Not abnormal, \*\*p-value from Pearson's or Fisher's exact test, p< 0.05=significant, PAC=premature atrial complexes; PVC=premature ventricular complexes; AIVR= accelerated idioventricular rhythm

The diagnostic yield for palpitation was 29.6% among symptomatic group and 5.9% among the asymptomatic group. Sinus tachycardia, atrial fibrillation (AF), atrial flutter (AFT), Junctional tachycardia/PAT, PVC, and VT were responsible for palpitation. Dizziness, chest pains and dyspnoea in symptomatic group had diagnostic yield of 27.3%, 13.2% and 26 % respectively but zero diagnostic yields in asymptomatic group. Sinus tachycardia and AF/AFT explained dyspnoea while chest pain was associated with sinus tachycardia. Hundred and fifteen (115) of symptomatic patients (40%) had symptoms during the Holter monitoring but only 28 (24%) of these symptomatic patients had their symptoms linked to arrhythmia. Thirty three asymptomatic subjects (34%) had symptoms during the monitor-

ing with only one symptom linked to arrhythmia. The overall diagnostic yields (symptoms-arrhythmia correlation) were 24.0% in symptomatic group and 3.0% in asymptomatic group. An overall diagnostic yield of 19.6% was determined.

Table 4 Symptoms and their diagnostic yield during HM

Symptoms*	Symptomatic patients n (%)	Asymptomatic pa- tients n (%)	Symptoms linke mias	d to arrhyth-	Diagnosti	c yield (%)
			Case n=289(%)	Control n=98(%)	Case (%)	Control (%)
Palpitation	71(24.6)	17(17.3)	21(7.3)	1(1)	29.6	5.9
Dizziness	44(15.2)	12(12.2)	12(4.1)	0(0)	27.3	0
Chest pains	38(13.1)	12(12.2)	5(1.7)	0(0)	13.2	0
Dyspnoea	19(6.6)	9(9.2)	5(1.7)	0(0)	26	0
Near fainting attack	1 (0.3)	0(0)	0(0)	0(0)	0	-
Fainting attack	1 (0.3)	0(0)	0(0)	0(0)	0	-
Seizure	1(0.3)	0(0)	0(0)	0(0)	0	-
Syncope	0 (0)	0(0)	0(0)	0(0)	-	-

\* One subject may have  $l \ge$  symptoms during HM

Table 5 Arrhythmias	causing	(linked to)	symptoms

Palpitation*	Dizziness	Chest pains	Dyspnoea
Sinus tachycardia (8)	S. bradycardia (4)	S. tachycar- dia(5)	S. tachycar- dia(3)
J. tachycardia/PAT (2)	Slow AF/AF (2)		AF/AF (2)
PVC (7)	Morbitz type 2 (3)		
PAC(3)	Complete AVB (2)		
VT (1)	Sinus tachycardia (1)		
Fast AF (2)			
A. flutter (1)			

\* Two cases had two different arrhythmias causing palpitation in them.

Arrhythmia (n), n=number of cases or controls with the arrhythmia causing the symptoms.

## DISCUSSION

In this study palpitation, dizziness, chest pains, syncope, dyspnoea and seizures were found as the symptombased indications for HM among symptomatic patients. Palpitation was the most common symptom-based indications for HM in this current study. These findings are similar to that of Adebayo et al <sup>22</sup> where palpitation, syncope, dyspnoea, dizziness and chest pain were reported as symptom-based indications for HM. The current study found about half (53.3%) of the symptomatic patients had a single complaint. This is consonance with several other studies reporting of a single complaintsusually syncope-as indication for HM.<sup>23-25</sup> Unexplained symptoms such as palpitations, dizziness and syncope are in most guidelines, indications for HM<sup>26</sup>, and this justifies the observations made in our study.

The study found diagnostic yields of 29.6% for palpitation in symptomatic group and 5.9% for palpitation in asymptomatic group. Ringquist et al <sup>21</sup> have reported a diagnostic yield of 54% for palpitation during the HM. This higher diagnostic yield obtained by Ringquist et al  $^{21}$  in symptomatic patients could be due to a smaller sample size (89) in their study compared to 190 (i.e. number cases referred on account of palpitation) in our study. Kinlay et al  $^{20}$  found palpitation occurring in 15 (35%) cases during the HM but none of these arrhythmic symptoms were linked to arrhythmia (i.e. diagnostic yield of zero). Diamond et al  $^{27}$  had palpitation occurring in 64% of cases during the monitoring with diagnostic yield of 44%. Again the sample sizes were smaller in both later studies and hence this difference could have accounted for the disparity between their findings and that of our study.

The diagnostic yield of 27.3% for dizziness in symptomatic subjects and diagnostic yield of 0% in asymptomatic subjects were found. The diagnostic yield in symptomatic subjects is comparable to 13% obtained by Ringquist et al <sup>21</sup> but Clark et al<sup>28</sup> found lower diagnostic yield of 2%. Pianzola et al<sup>29</sup> and Baratta et al <sup>30</sup> have on the other hand reported of no arrhythmia-symptoms link (diagnostic yield=0) for dizziness/ near fainting attack as in the asymptomatic subjects in our study. A diagnostic yield of 13.2% in symptomatic subjects and 0% in asymptomatic subjects was found for chest pain. The diagnostic yield in symptomatic subjects is far higher compared to the 0% diagnostic yield reported by Baratta et al<sup>30</sup> and, Hegazy and Lofty<sup>6</sup> even though the latter researchers studied 1319 children, and hence age and sample size may contribute to the observed difference.

Chest pains as arrhythmic symptom is based on ischemia induced by tachyarrhythmia against a background of CAD<sup>10,31</sup>, and since CAD is negligible in children, one expects this symptom to be less in children as obtained by Hegazy and Lofty.<sup>6</sup> One of the symptomatic patients with chest pains had ST segment depression with sinus tachycardia during the episode of the chest pains which confirms ischemia (angina pectoris) as the cause of the chest pain.

Dyspnoea occurred in 19 cases (6.6%) and nine controls (9.2%) but symptom-arrhythmia correlation occurred in only 5 cases with diagnostic yield of 26%. This yield is higher than the 13% obtained by Zeldis et al. <sup>32</sup> The 5 symptomatic patients had structural heart diseases (dilated cardiomyopathy and left ventricular hypertrophy) which could cause dyspnoea on their own rather than dyspnoea from only the prevailing arrhythmia.

Syncope/fainting attack was observed in one patient among only the symptomatic group but was link to no arrhythmia (the Holter ECG tracing at the time was normal). Generally, syncope or fainting attacks are less likely to occur during the Holter monitoring and they have the lowest diagnostic yield in literature. As Ringquist et al <sup>21</sup> demonstrated, diagnostic yield for syncope was 8% compared to 13% for dizziness and 54% for palpitation. On average, the yield for syncope is 2% <sup>24,25,28</sup>, the highest was 22% <sup>15</sup> and the lowest is 0%.<sup>29,30</sup> Yields for syncope and fainting attacks are much higher in the elderly and in those with structural heart diseases.<sup>14</sup>

In the elderly, there are degenerative changes and are likely to develop symptomatic bradycardia including pauses and higher degree AV block, and also patients with structural heart diseases such as ischemic heart disease, congenital heart disease, valvular heart disease and cardiomyopathies are likely to have tachyarrhythmia and bradyarrythmia hence the high yield for syncope in such patients.

One case had a seizure during the Holter monitoring but there was no link between the seizure and arrhythmia (the Holter ECG tracing was normal at the time of the episode). Seizures may cause syncope and some causes of syncope can also cause seizure, either of which (syncope and seizures) can be caused by arrhythmia. Arrhythmia causing seizures (Stokes-Adam attack) is rare.<sup>33</sup>

Our current study found diagnostic yields (symptomsarrhythmia correlation) were 24.0% in symptomatic group and 3.0% in asymptomatic group and an overall diagnostic yield of 19.6%. This difference in the diagnostic yield in the two groups is supported by the findings of Luxon et al<sup>34</sup> in which haemodynamically significant arrhythmia were found to occur in 32% of cases with transient neurological symptoms compared to only 3% in controls. The larger diagnostic yield in the symptomatic group could be due to underlying higher prevalence of hypertension and structural heart diseases which according to Zimetbaum and Josephson<sup>14</sup> increase diagnostic yield. The higher stimulant use in the asymptomatic group might have influenced the prevalence of arrhythmia <sup>35-39</sup> in this group but not the likelihood of these arrhythmias causing symptoms.

In this study, only palpitation, dizziness, chest pains and dyspnoea were caused by (linked to) arrhythmias. Palpitation was caused by sinus tachycardia, junctional and paroxysmal atrial tachycardia, ventricular extrasystoles (VES), supraventricular extrasystoles (SVES), non-sustained VT, fast AF and atrial flutter. This finding agrees with those found in literature to cause palpitation<sup>1-3</sup> except that atrial flutter is not a common cause of palpitation. This may be due to the fact that the atrial flutter causing palpitation in this study had variable blocks and hence variable ventricular rates.

Dizziness was found to be linked to sinus bradycardia, slow atrial fibrillation and flutter, and AV block. Since arrhythmias that cause dizziness can cause syncope when severe, then the arrhythmic causes of syncope are similar. The causes for dizziness are similar to what has been mentioned in literature.<sup>4,5</sup>

Tachyarrhythmias are known to cause chest pains in patients with ischaemic heart disease<sup>10,34</sup> and this is supported by the finding in this study of sinus tachycardia causing chest pains. There was ST segment depression during one episode of chest pains which confirms the underlining ischaemia (angina pectoris) as the cause of the chest pains.

Children rarely have ischemic heart diseases/CAD and hence chest pains were not observed by Hegazy and Lofty <sup>6</sup> during Holter monitoring in this age group in spite of the presence tachyarrhythmias. In our study, the participants were adults aged between 18 and 88 years who have high odds of myocardial ischemia and coupled with the fact that there were resting ECG and echocardigraphic findings of ischemia could explain the observed angina pectoris induced by sinus tachycardia.

Dyspnoea was associated with atrial flutter, atrial fibrillation and sinus tachycardia. Tachyarrhythmia can cause heart failure <sup>40</sup> through reduced diastolic filling and hence can reduce cardiac output. The finding of sinus tachycardia, atrial flutter and atrial fibrillation causing dyspnoea (probably through heart failure) is expected even though it is difficult to ascertain whether structural heart diseases in themselves could not have caused the dyspnoea.

## **Study limitations**

The link between symptoms and arrhythmia (diagnostic yield) was obtained based on patients recording of symptoms during the recording.

However, some of the patients might have forgotten to write or note the symptoms in the diary, or the case or control might not have given the right time for the occurrence of the symptoms leading to error in linking the symptoms to arrhythmia and hence error in the calculation of the diagnostic yield. Similarly, when arrhythmia occurred while the subjects were asleep, recording of any symptoms was not feasible.

The period of waking and sleep was ambiguous since a patient might take a nap during the day whilst resting or might be in bed for long period without falling asleep and this had the potential of affecting sinus bradycardia and tachycardia calculated for those periods. The limitation of monitoring period to only 24 hours did not allow for longer arrhythmias and symptoms monitoring and hence that might have reduced the prevalence of certain arrhythmias and the symptoms they might have caused.

This limitation was unavoidable because of logistic constraints since longer duration of HM for the study population will affect the smooth running of HM services at the Centre. The wearing of the Holter device, even though light-weight, might have limited the ability of the wearer to engage in full physical activities which might be a trigger for certain arrhythmias.

# CONCLUSION

This study have demonstrated that routine prescription of HM as a regular health check for the general population is not cost effective and does not provide significant data to influence care in asymptomatic patients . However, HM is an important tool in investigating patients with symptoms suspected to be arrhythmic in origin. The usefulness of this investigation depends on how well patients are selected and educated on HM.

A good clinical history and physical examination, basic investigations, resting ECG and echocardiogram are likely to inform the clinician on the possible cause(s) of patient's complaint and the need for HM, thereby reducing the over prescription of this investigation.

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