

# Holter monitoring at Tygerberg Hospital, 1979 - 1983 — an appraisal

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## Summary

Over a period of 4 years Holter monitoring was performed on 607 patients in the Division of Cardiology at Tygerberg Hospital. Indications for monitoring were broadly grouped into four categories: (i) evaluation of symptoms suggestive of disorders of cardiac rhythm (210 patients); (ii) evaluation of arrhythmias associated with a specific underlying cardiac condition (139 patients); (iii) evaluation of a previously documented or suspected arrhythmia (233 patients); and (iv) miscellaneous reasons (25 patients).

Findings are presented and aspects of Holter monitoring are discussed. Finally, some recommendations for improving the clinical value of our Holter analyses are made.

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While physicians have long appreciated the importance of specifically diagnosing arrhythmias, the association between arrhythmias and certain cardiac and neurological symptoms has only recently become well understood. The advent of Holter monitoring some 20 years ago has provided a tremendous technological advance in the recording and analysis of these arrhythmias, but in some situations technological advances have exceeded our knowledge of the data accumulated.

Although Holter monitoring has become established as a useful tool in the investigation of a wide range of cardiac conditions, its usefulness and limitations are often not well appreciated outside the cardiology departments where it is executed. The analysis of records is time-consuming and exacting, and an efficient service demands good communication between the patients, doctors and technical staff. A retrospective study was therefore undertaken to examine the indications for and results and possible shortcomings of the Holter monitoring service in the Division of Cardiology at Tygerberg Hospital during the 4-year period January 1979 - April 1983.

## Patients and methods

Between January 1979 and April 1983 Holter monitoring was performed 696 times on 607 patients in the Division of Cardiology. Patients were referred mainly by doctors within the Division of Cardiology, but referrals were also received

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from a wide range of other departments within the hospital as well as from local private physicians. The patients' ages ranged between 1 day and 84 years (mean 54 years). The only patients excluded were those under study as part of clinical research trials.

## Monitoring

All referred patients were screened by a senior member of the Division before 24-hour monitoring was performed. Modified lead II and III positions were used and completed tapes were analysed on an Oxford Medilog ECG analysis system. Where feasible, patients were instructed to keep a diary during the monitoring period and to indicate symptoms by triggering the 'event button'.

Monitoring and analysis was performed by one person (H.W.W.). Representative real-time ECG strips were taken when changes were noted in the morphological features of the tracing, during arrhythmias or when symptoms were noted. Examples of the normal baseline ECG were also taken. Where relevant, a quantitative estimate of ectopic beats was given. Comments were also frequently included. Interpretation and reporting was carried out by various senior members of the Division, and the results were documented on cards in a 'tickler box'-type file. The criteria for a positive response on Holter monitoring are listed in Table I.

**TABLE I. CRITERIA FOR A POSITIVE RESPONSE ON HOLTER MONITORING**

<b>Disorders of impulse formation and conduction</b>
Marked sinus bradycardia (< 40/min)
Sinus arrest, sinus pause or sinus node exit block
First-degree AV block (P-R interval > 0,22 second in adults)
Second-degree AV block
Mobitz I
Mobitz II
Third-degree AV block (complete)
Intraventricular conduction disorders
Pre-excitation syndromes
Tachycardia-bradycardia syndrome (sick sinus syndrome)
<b>Atrial arrhythmias</b>
Atrial ectopic beats 30/h
Paroxysmal atrial tachycardia
Atrial flutter or atrial fibrillation
<b>Junctional arrhythmias</b>
Junctional ectopic beats 30/h
Junctional rhythms
<b>Ventricular ectopic activity</b>
Ventricular ectopic beats 30/h
Multiform ectopic beats or couplets
Three or more consecutive beats (ventricular tachycardia)
R-on-T phenomenon

AV = atrioventricular.



## Results

The indications for Holter monitoring fell into four broad categories: (i) 210 patients (34,6%) were evaluated for arrhythmias as a cause of a particular symptom; (ii) 139 patients (22,9%) were evaluated for arrhythmias associated with an underlying cardiac condition (excluding ischaemic heart disease); (iii) 233 patients (38,4%) were evaluated for known or suspected arrhythmias to document their presence or quantify their severity; and (iv) a miscellaneous group of 25 patients (4,1%), including those evaluated for ST-segment changes and those in whom the indication was uncertain from the record cards.

### Evaluation of symptoms

The symptoms evaluated and number of patients showing a positive response on Holter monitoring are listed in Table II. The most common indication was 'syncope' (150 patients). This represented a wide range of symptoms suggestive of transient cerebral ischaemia, such as presyncope, dizziness, vertigo and fainting. Forty-nine (33%) of these patients showed positive Holter responses, and these are listed in Table III. It could not be determined with certainty from the record cards how many of these represented true-positive and how many false-positive responses, but a number of highly significant arrhythmias were detected (among others, 6 patients (4%) had episodes of ventricular tachycardia, 13 (9%) had tachycardia-bradycardia syndrome (sick sinus syndrome (SSS)) and 1 patient had pacemaker failure).

**TABLE II. SYMPTOMS EVALUATED IN 210 SYMPTOMATIC PATIENTS AND NUMBER SHOWING A POSITIVE RESPONSE ON HOLTER MONITORING**

Symptom	Patients		Positive responses	
	No.	%	No.	%
'Syncope'	150	71,4	49	33
Palpitations	47	22,4	15	32
Systemic emboli	13	6,2	4	31
<b>Total</b>	<b>210</b>	<b>100</b>	<b>68</b>	<b>32</b>

The other common symptom assessed was palpitations (47 patients). Fifteen of these patients (32%) showed a positive response. The commonest abnormality detected was ventricular ectopic activity (21%) and 1 of these patients had episodes of ventricular tachycardia (Table III). Thirteen patients with systemic emboli (10 cerebral and 3 peripheral) were evaluated; 2 had episodes of atrial fibrillation.

### Arrhythmias associated with specific cardiac conditions

One hundred and thirty-nine patients with eight specified cardiac conditions (other than ischaemic heart disease) were evaluated for associated arrhythmias. The conditions and number of positive responses are listed in Table IV. The arrhythmias were sought either to prove the diagnosis (e.g. SSS and conducting system disease (CSD)), or as a complication of the underlying disorder. Fifty-two patients with suspected SSS were investigated; 36 (69%) showed arrhythmias highly suggestive of this diagnosis (Table V). Sixteen (35%) of 46 patients with previously documented CSD gave a positive

**TABLE IV. NUMBER OF POSITIVE RESPONSES ON HOLTER MONITORING IN 139 PATIENTS WITH SPECIFIC CARDIAC CONDITIONS**

Cardiac condition	No. of patients	Positive responses	
		No.	%
<b>SSS</b>	<b>52</b>	<b>36</b>	<b>69</b>
<b>CSD</b>	<b>46</b>	<b>16</b>	<b>35</b>
Pacemaker evaluation	12	4	33
Mitral valve prolapse	8	—	—
Post-cardiac surgery	7	1	14
<b>Pre-excitation syndromes</b>	<b>8</b>	<b>3</b>	<b>37</b>
<b>Cardiomyopathy</b>	<b>5</b>	<b>3</b>	<b>60</b>
<b>Hypertrophic type</b>	<b>2</b>	<b>—</b>	<b>—</b>
<b>Atrial myxoma</b>	<b>1</b>	<b>1</b>	<b>100</b>
<b>Total</b>	<b>139</b>	<b>64</b>	<b>46</b>

**TABLE III. POSITIVE RESPONSES ON HOLTER MONITORING IN 68 OF THE 210 SYMPTOMATIC PATIENTS**

	Symptom					
	Syncope (N = 150)		Palpitations (N = 47)		Emboli (N = 13)	
	No. pos.	%	No. pos.	%	No. pos.	%
Arrhythmia						
<b>Bradycardia</b>	<b>6</b>	<b>4</b>	<b>—</b>	<b>—</b>	<b>—</b>	<b>—</b>
Sinus	4					
Sinus arrest	2					
<b>Supraventricular tachycardia</b>	<b>15</b>	<b>10</b>	<b>3</b>	<b>6,4</b>	<b>3</b>	<b>23</b>
Atrial fibrillation	8		—		2	
PAT	7		3		1	
<b>Ventricular ectopic activity</b>	<b>14</b>	<b>9</b>	<b>10</b>	<b>21,3</b>	<b>1</b>	<b>8</b>
VEB*	8		9		1	
Ventricular tachycardia	6		1		0	
<b>Tachycardia-bradycardia syndrome</b>	<b>13</b>	<b>9</b>	<b>2</b>	<b>4,3</b>	<b>—</b>	<b>—</b>
<b>Pacemaker failure</b>	<b>1</b>	<b>1</b>	<b>—</b>	<b>—</b>	<b>—</b>	<b>—</b>
<b>Total</b>	<b>49</b>	<b>33</b>	<b>15</b>	<b>32</b>	<b>4</b>	<b>31</b>

\* > 30/h multiform or couplets.

PAT = paroxysmal atrial tachycardia; VEB = ventricular extra beats.



**TABLE V. ARRHYTHMIAS IN 52 PATIENTS INVESTIGATED FOR SSS**

Arrhythmia	Positive response	
	No.	%
Marked bradycardia (< 40/min)	13	25,0
Sinus arrest ± escape rhythm	8	15,4
Atrial fibrillation + bradycardia	—	—
Sino-atrial block	—	—
Tachycardia-bradycardia syndrome	12	23,0
Other	3	5,8
<b>Total</b>	<b>36</b>	<b>69,2</b>

**TABLE VI. POSITIVE RESPONSES ON HOLTER MONITORING IN 46 PATIENTS WITH PREVIOUSLY DOCUMENTED CSD**

Arrhythmia	Positive response	
	No.	%
Sinus pause, arrest, exit block	4	8,7
First-degree AV block	—	—
Second-degree AV block	8	17,4
Mobitz I	2	4,35
Mobitz II	6	13,05
Third-degree AV block	4	8,7
Intraventricular conduction disorders	—	—
<b>Total</b>	<b>16</b>	<b>34,8</b>

AV = atrioventricular.

**TABLE VII. HOLTER FINDINGS IN 233 PATIENTS EVALUATED FOR KNOWN OR SUSPECTED ARRHYTHMIAS**

Arrhythmia	Positive response	
	No.	%
<b>Supraventricular tachycardia (N = 76)</b>	<b>34</b>	<b>45</b>
PAT	9	11,8
Atrial fibrillation	4	5,3
Atrial flutter	1	1,3
AEB 30/h	9	11,8
<b>Ventricular ectopic activity (N = 167)</b>	<b>105</b>	<b>63</b>
Low grade 2 — 30/h	32	19,2
3 — multiform	9	5,4
4A — couplets	29	17,4
4B — VT	33	19,8
5 — R-on-T	2	1,2

PAT = paroxysmal atrial tachycardia; AEB = atrial extra beats; VT = ventricular tachycardia.

response, indicating a block of a higher degree than present on the resting ECG (Table VI). In 4 of 12 patients evaluated for function of a permanent artificial pacemaker, evidence of malfunction was documented. Of the 8 patients studied who had Wolff-Parkinson-White (WPW) syndrome, it was found to be intermittent in 3. None of these 8 patients was symptomatic and no tachyarrhythmias were documented.

### Evaluation of known or suspected arrhythmias

Two hundred and thirty-three patients were evaluated for known or suspected arrhythmias. The clinical setting was not stated and the correlation with symptoms was not documented in the reports. The arrhythmias assessed were broadly divided into supraventricular tachycardias (76 patients) and ventricular ectopic activity (167 patients) (10 patients had both). The recordings were performed to determine the presence, severity or frequency of an arrhythmia. The results are listed in Table VII. Of note in the patients evaluated for ventricular ectopic activity was the high incidence of so-called 'malignant arrhythmias' (Lown grades 3 - 5) detected — 73 patients (44%).

### Discussion

Implicit in the recognition of abnormality is an understanding of what is normal. While there have been relatively few Holter studies on normal populations<sup>1-4</sup> (the limitations of which have been alluded to by Kennedy<sup>5</sup>), the available data on normal subjects show a high incidence of cardiac arrhythmias. These include arrhythmias widely believed to have a serious prognosis — frequent ventricular ectopic beats, the R-on-T phenomenon, and multifocal beats and ventricular tachycardia.<sup>1,2</sup> The uncertainty related to the prognostic significance of these findings

reinforces the need to interpret Holter recordings in their appropriate clinical context and makes clinical experience in interpretation a valuable and necessary asset.

While there is general agreement that stringent criteria are essential in labelling a response as positive, there is no uniform agreement about these criteria. Various classifications have been used, and the criteria used in this study were derived from several authors.<sup>6-9</sup> In view of the reported frequency of sinus bradycardia in normal people,<sup>1,3</sup> we have accepted sinus rates of less than 40/min ('marked sinus bradycardia') as a positive response. The incidence of reported atrial and junctional ectopic beats was very low in this study; this probably reflects a tendency by the doctor interpreting the recording to disregard them.

### Evaluation of cardiac symptoms

Holter monitoring has proved well suited to the investigation of symptoms attributable to cardiac rhythm disturbances such as transient cerebral ischaemia and palpitations.<sup>7,8,10-14</sup> Thirty-two per cent of the 210 symptomatic patients we evaluated showed a positive response. The incidence (33%) of positive Holter responses in the 150 patients with symptoms suggestive of transient cerebral ischaemia is in keeping with those found in previous studies.<sup>10-13</sup> In the interpretation of the positive responses found in cases of transient cerebral ischaemia it must be established whether the detected arrhythmia could pathophysiologically cause the symptom investigated, and the clinician must interpret the data against the condition of the cerebral vessels and the severity and duration of the arrhythmia. A cause-effect relationship could not be determined in our patients since there were no temporal correlations between symptoms and arrhythmias. Similarly, Holter monitoring has been shown to be accurate in diagnosing the cause of palpitations.<sup>7,8,11</sup> However, most patients do not perceive the majority of abnormal beats that they experience, although paroxysmal tachyarrhythmias of more than momentary duration (8 - 10 beats) tend to be perceived.

### Specific cardiac conditions

The clinical and ECG manifestations of SSS have been well described.<sup>15,16</sup> Holter monitoring has proved useful in the initial diagnosis of this condition and may be of value in documenting the response to specific drug and/or pacemaker therapy.<sup>17,18</sup> Marked bradycardia was the commonest manifestation of SSS (25%), but caution must be exercised in



interpreting the Holter recordings; multiple examinations, assisted by provocative pharmacological and pacing electrophysiological studies, may be required to avoid inappropriate pacemaker therapy.<sup>19-21</sup>

The indication for Holter monitoring in cases of CSD is usually for detection of progression of the block and for follow-up of patients not treated by prophylactic pacemaker insertion. Thirty-five per cent of the 46 patients studied in this series developed higher degrees of CSD than manifested on the resting ECG, 4 having episodes of transient complete atrioventricular block. Besides its value in identifying patients who require pacemakers, Holter monitoring may help to detect pacemaker failure, especially when this is intermittent and routine techniques fail.<sup>17</sup> This was confirmed in our study; 4 of 12 patients in whom routine pacemaker evaluation was negative showed pacemaker failure. One patient with syncope had associated pacemaker failure.

Patients with the WPW syndrome are often said to complain of palpitations unrelated to arrhythmias.<sup>22</sup> Holter monitoring is therefore indicated to document episodes of paroxysmal tachycardia before starting therapy, and routine screening for arrhythmias in patients with pre-excitation is performed by some authors.<sup>17,18,23,24</sup> Holter monitoring is also useful in documenting arrhythmias associated with mitral valve prolapse (Barlow's syndrome),<sup>25,26</sup> cardiomyopathies, notably hypertrophic cardiomyopathy,<sup>27,28</sup> prolonged QT syndrome and others.<sup>17</sup> The low number of patients with asymptomatic WPW syndrome, cardiomyopathies and mitral valve prolapse screened for arrhythmias in this study (21 patients) suggests that patients with these conditions are not routinely referred for screening at Tygerberg Hospital.

Ischaemic heart disease is probably the commonest underlying cardiac condition; it was not examined as a separate entity but was a major factor in many of our patients. However, the role of Holter monitoring as regards the many facets of ischaemic heart disease has been well described.<sup>17,29</sup>

## Evaluation of known or suspected arrhythmias

Rational management of arrhythmias demands not only a sound correlation with the clinical condition but also a determination of their frequency and severity. Although an arrhythmia may have already been diagnosed on a standard ECG, Holter monitoring may provide useful adjunctive information about it; also, the frequency of intermittent arrhythmias (for example, paroxysmal atrial tachycardia and atrial fibrillation) may be determined and therapy adjusted appropriately. The decision to treat asymptomatic ventricular premature beats may be difficult, and various studies have been designed to determine the prognostic significance of ventricular ectopic activity, especially after infarction.<sup>6,30-33</sup> The limitation of Holter monitoring in assessing ventricular ectopic activity has been alluded to by Morganroth *et al.*,<sup>34</sup> who demonstrated marked spontaneous variations in arrhythmic activity and suggested that a reduction in ectopic activity frequency of greater than 83% was required if two 24-hour monitoring periods were compared before the effect could be attributed to therapeutic intervention rather than spontaneous variation.<sup>34</sup> Furthermore, there is still little evidence to confirm that suppression of the arrhythmia will prevent sudden death. Nevertheless, anti-arrhythmic therapy is frequently justified by clinical judgement and, as stated by Harrison *et al.*,<sup>18</sup> 'patients with an arrhythmia serious enough to require long-term administration of a potentially toxic and costly drug deserve documentation that the drug is effective'.

## ST-segment changes

'Silent' ischaemic ST-segment changes occurring in patients

with ischaemic heart disease have been described.<sup>35-40</sup> Their reported prevalence has varied widely,<sup>35,38,39</sup> but the prognostic significance has not been established.<sup>41</sup> Holter monitoring is assuming a more important role in the diagnosis of chest pain and may be useful in helping to distinguish between myocardial ischaemia due to a fixed coronary stenosis and that due to coronary artery spasm.<sup>40,42-44</sup>

## Conclusions

Holter monitoring is a valuable clinical tool which allows objective assessment of cardiac rhythm disturbances in a wide range of clinical settings. Over a 4-year period at Tygerberg Hospital it was most extensively used in the investigation of symptoms attributable to disturbances in cardiac rhythm (palpitations and syncope) and in the assessment of known or suspected rhythm disturbances. In other areas, for example in the evaluation of arrhythmias related to mitral valve prolapse, WPW syndrome and hypertrophic cardiomyopathy, it does not appear to have been used to its full benefit. ST-segment evaluation is another area in which Holter monitoring may be more widely used in the future. The main shortcomings in our service, identified by this retrospective study and subsequently improved, are the following:

1. Lack of standardization in data reporting, mainly due to the fact that more than one member of the department is responsible for reporting on Holter recordings.

2. Inadequate documentation of temporal correlation between symptoms and arrhythmias; this makes appraisal of sensitivity and specificity difficult.

3. Insufficient clinical information supplied for many referred patients, especially information regarding current medication.

In an attempt to improve the efficiency and validity of our service we have introduced a new request/report form on which the above points are incorporated and the temporal relationship between arrhythmias and symptoms are documented. It is hoped that this will enhance the sensitivity and specificity of the investigations performed.

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# Chemoprophylaxis with erythromycin stearate or amoxycillin in patients with chronic bronchitis — effects on cellular and humoral immune functions

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## Summary

Twenty-six patients aged between 27 and 71 years with chronic bronchitis were divided into a control group of 6 and two groups of 10 patients each who received either erythromycin stearate or amoxycillin 1500 mg/d for 2 weeks and 1000 mg/d for 12 weeks thereafter. Immunological function tests were

performed before starting chemotherapy and thereafter at 2 weeks and 14 weeks. Clinical evaluations and lung function tests showed no significant changes in any of the groups during the study period. In the control group no changes in cellular and humoral immune functions were noted. In the group receiving amoxycillin decreased responses of lymphocytes to the mitogen phytohaemagglutinin were observed after 14 days. In the erythromycin-treated group, increased polymorphonuclear leucocyte (PMNL) motility and mitogen-induced transformation were observed at 14 days but these increases were not statistically significant. In this group the markedly depressed PMNL migration found in 3 individuals before treatment improved considerably. These results indicate that chemotherapy and chemoprophylaxis with either amoxycillin or erythromycin stearate do not compromise the host immunodefences.

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