

# Sinoatrial Wenckebach periodicity as an independent marker for the development of high-degree sinoatrial exit block

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## Abstract

**Background:** *The present study of patients with Wenckebach-type second-degree sinoatrial block (W-block) evaluated the probability of the development of a more advanced grade of sinoatrial block. Data on the clinical significance of W-block are limited. It is unknown whether W-block predicts a more advanced grade of sinoatrial block.*

**Methods:** *Standard ECGs of 412 patients with symptoms that might have been related to cardiac arrhythmias were reviewed for the presence of W-block. In the initial ECG W-block occurred in 29. During the follow-up period of  $62 \pm 35$  months the main end-point was the first episode of type II second-degree sinoatrial block. An additional end-point was the occurrence of a sinus pause greater than 3 s or the development of type II second-degree sinoatrial block.*

**Results:** *Of the 29 patients with W-block initially, 6 (20.7%) developed higher grade sinoatrial block, and sinoatrial arrhythmic events occurred in 9 (31%). In the 383 patients without W-block subsequent episodes of higher grade sinoatrial block occurred in 14 (3.7%) and sinoatrial arrhythmic events in 28 (7.3%). A multivariate Cox analysis identified W-block as an independent marker for developing type II second-degree sinoatrial block (HR = 3.72, 95% CI 1.39–9.99) and for the occurrence of sinoatrial arrhythmic events (HR 3.01, 95% CI 1.37–6.58).*

**Conclusions:** *In patients with symptoms that might be caused by cardiac arrhythmias the presence of W-block in a standard ECG indicates a high probability of developing a more advanced grade of sinoatrial block. (Cardiol J 2007; 14: 391–395)*

**Key words:** sinoatrial node, arrhythmia, electrocardiography, prognosis

## Introduction

For many years second-degree sinoatrial Wenckebach block (W-block) was considered an

unusual arrhythmia occasionally detected on a standard electrocardiogram (ECG). With the advent of Holter monitoring W-block has come to be recognised with increasing frequency. The need for understanding the clinical implications and prognostic value of W-block has grown as its recognition has increased. Sinoatrial Wenckebach periodicity occurs in a variety of conditions and may be considered a marker of sinoatrial node dysfunction in patients with a history of syncope, presyncope or dizziness. To date no information has become available with respect to the prognostic significance of W-block. The present study was performed to

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examine the value of W-block as detected on a standard ECG for the prediction of conduction deterioration to a higher grade of sinoatrial block.

### Methods

Standard 12-lead ECGs for 412 patients (mean age  $60 \pm 17$  years, 267 men and 145 women) with symptoms that might be related to cardiac arrhythmias (syncope, presyncope, dizziness or palpitations) were reviewed to identify subjects with W-block. Patients with evidence of prior or coincident higher degree sinoatrial exit block, patients with atrial fibrillation or flutter and second-degree or complete atrioventricular block at the time of the standard ECG recording and patients treated with class I or III antiarrhythmic drugs at presentation were not included in the study group. The criteria for the diagnosis of W-block were the following [1, 2]: 1) a sequence of gradually shorter PP intervals followed by a longer PP interval, which was less than twice the length of the preceding PP interval or 2) the alternation of short and long PP intervals with a long PP interval shorter than two short PP intervals (3:2 sinoatrial Wenckebach periodicity). Type II second-degree sinoatrial block was diagnosed by the periodic absence of one or more consecutive P waves of sinus rhythm (the interval from the last normally-timed P wave to the first post-block P wave was equal to a simple multiple of the normal PP interval). This type of sinoatrial block was also recognised when the duration of the pause was slightly ( $\leq 0.1$  s) less or greater than the exact multiple of the basic PP interval [3]. Sinus pause was defined as the occurrence of a long PP interval ( $> 3$  s) that was not a multiple of the basic sinus cycle length.

In 192 patients there was clinical evidence of organic heart disease at the time of or before the recognition of W-block; 141 patients had a history of previous myocardial infarction or documented coronary heart disease.

### Follow-up

During follow-up the clinical status of the patients was evaluated by means of history, physical examination, resting ECG, 24-hour Holter recordings, external ECG event monitoring, ECG monitoring in the hospital setting and an electrophysiological study made of 105 patients to identify an arrhythmic cause of unexplained syncope. The observation period for each patient was the number of months from the date of the initial ECG recording to the date of recognition of type II second-degree

sinoatrial block or to December 31 2004. Twenty-two patients (5%) were lost to follow-up, and observations on these ceased to be taken into consideration from the date of their last hospital visit. Observations on patients who died were considered only until the date of known follow-up status.

For this cohort of patients the main end-point was the first episode of type II second-degree sinoatrial block. An additional end-point of the study was a sinoatrial arrhythmic event, defined as the occurrence of a sinus pause greater than 3 seconds or the development of type II second-degree sinoatrial block.

### Statistical analysis

Continuous data are presented as mean values  $\pm$  SD. The significance of the differences in continuous variables in the two groups compared was assessed by the unpaired Student's test; the significance of the differences in categorical variables was assessed by the  $\chi^2$  test. The cumulative estimation of type II second-degree sinoatrial block development and sinoatrial arrhythmic event occurrence was summarised by Kaplan-Meier actuarial methods [4]. Differences between each pair of survival curves were assessed with the use of the log-rank test. Univariate regression analysis using the Cox proportional hazard model [5] was applied to evaluate variables so as to determine the association with the development of high-degree sinoatrial block or the occurrence of sinoatrial arrhythmic events. Multivariate regression analysis was applied to variables that had a predictive value at the level  $p < 0.10$ . The results of univariate and multivariate Cox analyses are presented as hazard ratios (HR) with their 95% confidence intervals (95% CI). A  $p$  value  $< 0.05$  was considered significant for all analyses.

### Results

Of the 412 patients included in the study 29 (7%) had W-block on their initial standard ECG. In 24 patients the sequences of W-block consisted of two or more consecutively conducted sinus impulses before a long PP interval. In the remaining 5 patients the W-block was type 3:2 and only two consecutive sinus impulses were conducted to the atrium before a blocked sinus impulse. The patients with W-block compared with those without W-block were significantly older ( $65 \pm 13$  years and  $59 \pm 14$  years, respectively;  $p = 0.0448$ ), and had a higher incidence of underlying organic heart disease (69% and 45%, respectively;  $p = 0.0123$ ). There

**Table 1.** Univariate relationship between clinical variables and the development of Type II second-degree sinoatrial block and the occurrence of sinoatrial arrhythmic events.

Variables	Hazard ratios (95% CI)	P value
<b>Type II second-degree sinoatrial block</b>		
Age > 60 years	2.86 (1.09–7.51)	0.03
Sex (male)	0.35 (0.14–0.85)	0.02
Structural heart disease	3.79 (1.38–10.47)	0.001
Syncopal episodes	2.52 (0.97–6.58)	0.06
W-block	6.21 (2.38–16.17)	< 0.0001
<b>Sinoatrial arrhythmic events</b>		
Age > 60 years	3.87 (1.82–8.23)	< 0.001
Sex (female)	0.49 (0.26–0.94)	0.03
Structural heart disease	2.29 (1.17–4.52)	0.02
Syncopal episodes	2.90 (1.40–6.01)	0.004
W-block	4.76 (2.24–10.11)	< 0.001

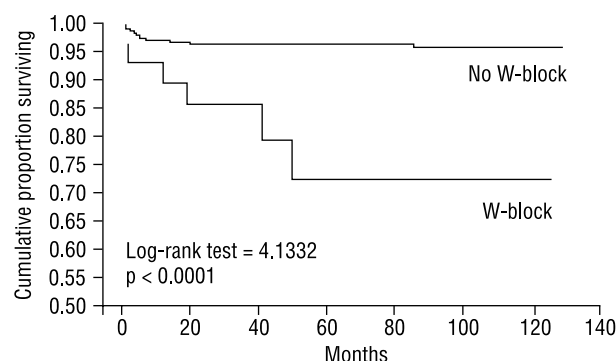
was a non-significant trend towards a greater proportion of women in the group of patients with W-block than in the group of patients without W-block (52% and 34%, respectively;  $p = 0.0532$ ). The proportion of patients with and without W-block who used beta-blockers at presentation was similar in the both groups (35% and 37%, respectively;  $p = 0.8016$ ).

**Follow-up**

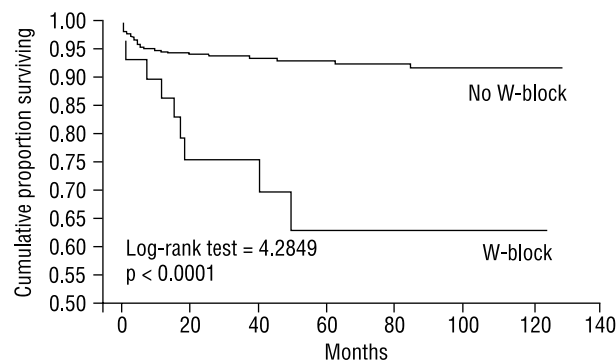
During a period of follow-up ranging from 1 to 127 months (mean  $61 \pm 35$  months; median 57 months) type II second-degree sinoatrial exit block was diagnosed in 20 patients and sinoatrial arrhythmic events were detected in 37. Of the 29 patients who had W-block at the time of entry a higher grade of sinoatrial block developed in 6 (20.7%), and a sinoatrial arrhythmic event occurred in 9 (31%). In the group of 383 patients without W-block, episodes of type II second-degree sinoatrial block were detected in 14 (3.7%), and sinoatrial arrhythmic events were noted in 28 (7.3%). The mean period from the start of the study to the development of type II second-degree sinoatrial block was  $19 \pm 29$  months, median 5 months, and to the occurrence of a sinoatrial arrhythmic event it was  $15 \pm 19$  months, median 6 months.

Table 1 shows the results of the univariate Cox’s analyses for both the end-points of the prospective observation that were assessed. W-block, which had the greatest Wald statistics among the variables evaluated, was the best univariate predictor of type II second-degree sinoatrial block and sinoatrial arrhythmic events. Kaplan-Meier event-free survival curves for patients grouped according to the presence or absence of W-block are shown

in Figures 1 and 2. Actuarial analysis of the two groups compared showed a rapid decline in event-free survival during the first 20 months after W-block



**Figure 1.** Cumulative probability of survival free from type II second-degree sinoatrial block in patients with W-block and in patients without W-block.



**Figure 2.** Cumulative probability of survival free from sinoatrial arrhythmic events in patients with W-block and in patients without W-block.

**Table 2.** Multivariate relationship between clinical variables and the development of Type II second-degree sinoatrial block and the occurrence of sinoatrial arrhythmic events.

Variables	Hazard ratios (95% CI)	P value
<b>Type II second-degree sinoatrial block</b>		
Age > 60 years	1.86 (0.66–3.57)	0.24
Sex (male)	0.31 (0.12–0.77)	0.01
Structural heart disease	3.11 (1.04–9.31)	0.04
Syncopal episodes	2.16 (0.82–5.62)	0.19
W-block	3.72 (1.39–9.99)	< 0.0001
<b>Sinoatrial arrhythmic events</b>		
Age > 60 years	3.22 (1.45–7.15)	0.004
Sex (male)	0.45 (0.24–0.88)	0.018
Structural heart disease	1.49 (0.72–3.14)	0.28
Syncopal episodes	2.71 (1.31–5.64)	0.007
W-block	3.01 (1.37–6.58)	0.006

was detected, followed by a more gradual decline from 20 to 120 months.

The results of the multivariate Cox's analyses are listed in Table 2. Cox's models identified W-block as a significant predictor of type II second-degree sinoatrial block (HR 3.72; 95% CI 1.39–9.99) and sinoatrial arrhythmic events (HR 3.01; 95% CI 1.37–6.58), independent of the age and gender of the patients, the history of syncopal episodes and the presence of underlying structural heart disease.

### Discussion

The presence of W-block in 7% of patients with symptoms that might be related to cardiac arrhythmias and the high probability of its progression to more advanced grades of sinoatrial block demonstrate that W-block is relatively common and an important medical problem. The present study is, to the best of our knowledge, the first to investigate in a long-term follow-up period the prognostic value of W-block as detected on a standard ECG. The main finding of this study is that in patients presenting with syncope, dizziness or palpitation W-block was an independent predictor of overt sinus node dysfunction. Of all the risk factors analysed in this study W-block appears to be the one which best predicts the development of higher degree sinoatrial exit block. For patients with W-block there was a 5.7-fold increase in the probability of progression to a more advanced grade of sinoatrial block and a 4.2-fold increase in the probability of the occurrence of sinoatrial arrhythmic events. Other independent predictors were the presence of underlying heart disease and female gender for type II second-

-degree sinoatrial block and advanced patient age, female gender and a history of syncopal episodes for sinoatrial arrhythmic events. Thus the presence of W-block may reasonably be considered a hazardous condition, since patients giving evidence of this abnormality are prone to more advanced forms of sinoatrial block. The disclosure of W-block in patients complaining of syncope, presyncope or dizziness should prompt further investigation to try to demonstrate transient high-degree sinoatrial block. This disorder may be identified by repeated Holter recording or constant monitoring of the ECG by means of external or implanted ECG event monitoring.

In this study the diagnosis of W-block was based on a single standard ECG. The question therefore arises as to whether this ECG abnormality was an indication of structural disease of the sinus node or an occasional depression of sinoatrial conduction caused by influence from the autonomic nervous system. The prevailing view about the cause of W-block diagnosed in this study is that an underlying disease process involving the sinus node and atrial myocardium was responsible for the sinoatrial conduction disturbances. The older age of the patients with W-block and the tendency towards the development of more advanced sinoatrial block may support this view. Further recent observations have shown that patients with W-block have significantly higher values of sinoatrial conduction time and sinus nodal recovery time than patients without W-block [6]. Thus W-block, detected on a standard ECG in patients with symptoms that might be related to cardiac arrhythmias, represents a structural disorder of the sinoatrial conduction system rather than functional sinus node dysfunction.

A semantic problem exists over what constitutes the sinus pauses considered as a combined end-point of the study. This additional end-point was included because in the presence of a markedly irregular sinus rhythm or the occurrence of an escape rhythm from the subsidiary foci of type II second-degree as well as third-degree sinoatrial block cannot be diagnosed confidently from a surface ECG. In addition, the prolonged pauses seen following the cessation of supraventricular tachycardia, atrial flutter or atrial fibrillation may be related to high-degree sinoatrial exit block or may be caused by a combination of exit block and depressed automaticity of the sinus node. Direct sinoatrial electrogram recordings in humans have revealed that the pause following the cessation of atrial overdrive is often caused by overdrive-induced sinoatrial block rather than by suppression of sinus node pacemaker activity [7, 8]. Similarly, using this recording technique, Gang et al. [9] have shown that sinoatrial block is an important component of the sinus pause that occurs in patients with the cardioinhibitory form of hypertensive carotid sinus syndrome. Therefore the sinus pauses considered as the combined end-point of this study might have been caused by a transient failure of impulse formation within the sinoatrial node (sinus arrest) or impulse propagation within the sinoatrial node (sinoatrial exit block). It is thus not surprising that the occurrence of sinoatrial arrhythmic events during the follow-up period was strongly associated with the presence of W-block on a standard ECG.

### Limitations

There are several limitations that should be considered when interpreting the results of this study. This investigation was based on a highly selective patient population and included patients with symptoms that might have been caused by cardiac rhythm disturbances, including various manifestations of sinus node dysfunction. It is therefore unclear whether the results of the study can be applied to other populations of patients, particularly to asymptomatic subjects with occasionally recognised W-block.

About one third of our patients were taking beta-adrenergic blocking agents at the time of presentation. In the presence of sinus node dysfunction beta-blockers frequently result in depression of

sinus node automaticity or sinoatrial conduction or both. However, the similarity in the proportion of patients taking beta-blockers in the group of patients with W-block and in the group without W-block suggests that this medication *per se* had no major effect on the results of this study.

Our data were not analysed by blind observers. Although, this could have introduced bias into our analysis, it is likely to be minimal and does not compromise the recognition of Wenckebach periodicals.

### Conclusion

In patients with symptoms that might be related to cardiac arrhythmias the presence of W-block on a standard ECG indicates a high probability of developing a more advanced grade of sinoatrial block.

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