Diagnosing arrhythmias in general practice: the BEAT study
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Chapter 1

General introduction
INTRODUCTION

Palpitations and light-headedness are common symptoms for patients to visit their general practitioner (GP). In the majority of patients no underlying cardiac disease is present. However, these symptoms might be indicative of (serious) cardiac arrhythmias, such as supra-ventricular re-entry tachycardia and atrial fibrillation. Those patients who do not have a (serious) cardiac disease may benefit by effectively ruling out a cardiac origin of their symptoms. A careful diagnostic approach therefore includes identification as well as rejection of possible cardiac causes of the symptoms.

Since episodes of palpitations and light-headedness are often of short duration or can occur in paroxysms, it is often difficult to establish a diagnosis during consultation as the symptoms rarely coincide with a visit to the GP. Also a simple 12 lead ECG seldom provides an answer when not recorded during the presence of symptoms. At present, in more than 30% of episodes of palpitations and light-headedness no diagnosis can be established after initial diagnostic workup.

A paradox exists for any GP when patients consult with palpitations or light-headedness. If the GP conducts a limited diagnostic work up a potentially life-threatening, yet treatable, cardiac disease might be overlooked. On the other hand, in some patients the GP may conduct too many diagnostic interventions in the absence of a cardiac disease. For instance, in patients suffering from anxiety or stress the GP might create an even more stressful situation, thereby increasing symptoms and anxiety.3-5

Previous research has shown that adequate diagnostic instruments for triage of patients presenting with palpitations and light-headedness are lacking in general practice.1,6 Therefore, in this thesis, the focus will be on the additional value of continuous event recorders in the diagnostic work-up in general practice in patients presenting with symptoms in which a cardiac origin can be suspected.

EPIDEMIOLOGY

The prevalence of palpitations is dependent on definitions and diagnostic methods used and vary substantially in different populations. In studies in primary care in the Netherlands approximately 8/1000 patients per year present a new onset of irregular, pounding and/or racing heartbeat, with women presenting twice as often as men.1 Some of the underlying arrhythmias that cause palpitations are significantly correlated with advancing age.7-11 For instance, the incidence of atrial fibrillation approximately doubles with each decade of adult life and ranges from 2-3 new cases per 1000 people per year between the age of 55 and 64, to 35 new cases per 1000 people per year between the age
of 85 and 94. In a population based study, the incidence of Paroxysmal Supraventricular Tachycardia (PSVT) was approximately 1-3 cases per 1000 persons. AV-nodal re-entry tachycardia (AVNRT) is more common in patients who are of middle age or older, while adolescents are more likely to have SVT mediated by an accessory pathway. The risk of developing PSVT was twice as high in women to men.

**ETIOLOGICAL CLASSIFICATION**

The aetiology of palpitations is divers. Palpitations may be caused by both cardiac and non-cardiac sources. Within these two sources, the following underlying causes can be distinguished.

1. **Cardiac causes of palpitations**

The clinical significance of the cardiac cause of palpitation depends upon the nature of the arrhythmia, the presence of cardiovascular co-morbidity and the possible consequences of the arrhythmia in daily life. Palpitations can result from isolated ectopic beats, any bradycardia (frequency <60 beats/min), any tachycardia (frequency >100 beats/min) and from increased cardiac volume.

**Supraventricular tachycardias (SVT)** are the most frequently encountered arrhythmias in the GP setting. The most common form is a sinus tachycardia. Atrial fibrillation and or re-entry tachycardias are other possible diagnoses.

Sinus tachycardia usually is a physiological response to elevated metabolism during exercise, pain, fever, panic or anxiety or a reaction to extracardiac pathology like anaemia or hyperthyroidism. It is never a cardiac disease on its own and is therefore considered a less relevant arrhythmia. Sinus tachycardia may in rare instances indicate cardiac pathology such as heart failure, when the damaged heart tries to fulfil demands by increasing its rhythm.

Atrial fibrillation (AF) is considered a relevant arrhythmia because of the sometimes concomitant output failure, the consequences for daily living and the elevated risk for arterial thrombo-embolism. It is an irregular tachy-arrhythmia characterized by uncoordinated atrial activation. It often is secondary to damage to the heart (atherosclerosis or valve-abnormalities), but can also appear as lone atrial fibrillation. Differentiation can be made between paroxysmal, persistent and permanent atrial fibrillation. Although this differentiation has consequences with regards to rate- or rhythm control management, it has no consequences with regards to anticoagulation therapy. AF is associated with an approximately 5-times increased risk of stroke. Regardless of differentiation in paroxysmal, persistent and permanent atrial fibrillation, anticoagulation therapy is warranted depending on concomitant risk factors, expressed in the acronym CHA2DS2-VASC.
Supraventricular re-entry tachycardias are atrial flutter, atrial tachycardia and, in the AV junction, AV-nodal re-entry tachycardia (AVNRT). The latter is characterized by paroxysms of fast regular heartbeats with an acute beginning and ending. Another re-entrant SVT, Wolff-Parkinson-White (WPW) syndrome, is based on an atrio-ventricular re-entry circuit. The relevance of these re-entry tachycardias is that the symptoms often are disabling. Atrial flutter is a regular atrial re-entry tachycardia, usually with a ventricular rate of about 150 beats per minute. Premature ventricular beats (PVC) and premature atrial beats (PAC) may cause concern. Further evaluation and therapy is seldom required after reassuring the patient. Ventricular tachycardia is usually seen in the context of structural or ischemic heart disease, and may be triggered by adrenergic stimuli. Occasionally, however, ventricular tachycardia may originate from the (right) ventricular outflow tract in a structurally normal heart, and is usually attenuated by adrenergic stimuli. Bradycardia is seldom symptomatic and is only seen accidental when for other reasons an ECG is taken or patients complain of dizziness and/or light-headedness. In symptomatic bradycardia, reversible causes like hypothyroidism or side effects of the use of negative chronotropic medication should be excluded first. Otherwise the patient should be referred to specialist care for further evaluation and potential pacemaker therapy.

2. Extra-cardiac causes

Palpitations originating from an extracardiac cause can present as a sinus tachycardia or a bradycardia.

2.a. Psychiatric causes

Palpitations occur in stressful situations and anxiety and can be a symptom of several psychiatric disorders including panic attacks, generalised anxiety disorder and depression. It is a key-symptom of a panic attack according to the DSM-IV. When palpitations are associated with anxiety or panic it is frequently difficult for the patient and hence for the physician to discern whether the feeling of anxiety or panic preceded or resulted from the palpitations.

Some patients have a tendency to somatise their symptoms. Reassurance is important for these patients. As a result these patients might be at risk for extensive diagnostic testing and referral. This testing may intensify anxiety, thereby increasing symptom severity, inducing a futile circle. Heart rhythm disturbances itself also may induce anxiety and/or panic. Patients might erroneously be diagnosed and treated as primarily suffering from anxiety disorder, while in fact heart rhythm disturbances are causal to their symptoms.
2.b. Drug-induced causes and habits
As palpitations may be drug-induced, history-taking should include a careful review of the patient’s drug use. Obvious examples are bradycardia caused by blocking eye drops, or tachycardia caused by broncho-dilating mimetics. Pro-arrhythmia may be seen with the use of anti-arrhythmic drugs. However, pro-arrhythmia can be seen with other drugs as well. For instance, diuretics may cause arrhythmias as a result of hypokalaemia-induced QT prolongation.
Stimulants such as caffeine and nicotine, or the use of illicit drugs (cocaine, amphetamines, cannabis etc.) can lead to sympathetic (hyper) activation and sinus tachycardia.35

2.c. Metabolic causes
A sensation of palpitation may stem from sinus tachycardia and/or increased cardiac contractility, both of which may have various causes: fever, orthostatic hypotension, hypovolaemia, hypoglycaemia, pheochromocytoma, thyroid pathology or anaemia among others. In case of uncertainty these diseases usually can be diagnosed or excluded by available diagnostic tools.31,36-38

DIAGNOSING PALPITATIONS
Electrocardiographic documentation of cardiac rhythm during symptoms provides an accurate diagnosis, but because in many patients symptoms are infrequent and episodic, GPs usually do not have the chance to make an ECG registration during an episode of palpitations. In case no symptomatic ECG is available GPs usually do not have further diagnostic tools to distinguish clinically significant paroxysmal arrhythmias from benign palpitations.5,38 Predictors from history taking and symptoms are not sensitive and specific enough to include or exclude clinically relevant cardiac diseases.29,31

OTHER DIAGNOSTIC METHODS
When patient’s history and physical examination in combination with a standard 12 leads ECG recording cannot determine the cause of the symptoms, referral to a cardiologist might be considered. The cardiologist could employ a Holter device to aid in diagnosing these patients. The 12-lead Holter monitor is a continuous electrocardiographic device that monitors patients for 24 to 48 hours. The device’s results are afterwards evaluated by a cardiologist. As a Holter registers the heart rhythm continuously, sensitivity for recording rhythm disturbances is high but specificity remains low as the device is only
applied for a short period of time and palpitation episodes are often infrequent and the mere frequency of symptoms (palpitations) is in no way correlated to the severity of the underlying cause.

For some years now, Continuous Event Recorders (CER) have been proven effective in the investigations of palpitations in secondary care settings. Unlike Holter monitors, these devices require manual patient activation to record symptoms and can be used for extensive periods of time (i.e. 2 weeks to several months). Contemporary CERs exist in a variety of models. Storage possibilities vary from registration of only the event itself, registration of only the post event-rhythm, or registration of both pre- and post event rhythm.

The most common type of CER consists of a recorder (with a diameter of approximately 6 cm) attached to the patient’s chest with two patch electrodes. These CERs can store multiple events over a period of time and are small and light, unlike the larger Holter monitor that restricts patients in their daily activities. CERs continually and digitally record a two lead ECG and only save the ECG registration when a patient chooses to activate the recorder following an episode of symptoms. The evolution of this technique made it desirable to evaluate the introduction of the CER in a primary care setting.

**THE BEAT-TRIAL**

Introduction of CER into primary care offers the advantage of a quick entrance to an easy to use diagnostic method for patients who often are confronted with sometimes frightening symptoms. Introducing CER in general practice therefore could be of advantage for two reasons: more adequate and more timely diagnostic management. Open access diagnostics provide a quick and easy way to management of more or less acute symptoms. The strategy might be more adequate because it is aimed at both demonstration as well as rejection of relevant somatic pathology. If the symptoms are not related with a cardiac cause, GPs can reassure patients without further diagnostic evaluation and referral.

However, when introducing a new diagnostic tool in any health care setting, it is essential to study the additional predictive value of the tool. Will the use of a CER generate more diagnosis and/or more diagnostic certainty? What are these diagnoses? And more specific: are more clinically relevant cardiac diseases diagnosed?

Considering the potential benefits, we set up the BEAT trial to determine the clinical usefulness of CER for establishing the diagnosis in new episodes of palpitations and/or lightheadedness in a general practice setting.
The primary aim of the present study will be to evaluate whether GPs are able to establish a diagnosis more often when using a CER as compared to usual care. And, when this is the case, to find out whether a difference can be found concerning the nature of these diagnoses. Secondary aims are to determine which types of diagnoses will be found using the CER, the time needed to diagnose, and the number of days needed until relevant cardiac diagnoses can be established. Patients with palpitations experience a lower quality of life and experience more depression and anxiety than patients without cardiac complaints.40 Besides, a side effect of any diagnostic workup can be a reduction of quality of life (QoL) and/or reduction or increase of anxiety in patients. We studied the QoL of patients during and after the diagnostic phase and compared these with a healthy population.

Although several studies tried to find signs and symptoms that predicted the presence of cardiac disease in unselected patients with palpitations just few were identified and these lacked predictive power.2,31 Therefore we set out to determine which clinical signs and symptoms the GP presently uses to make an assessment. In addition we will examine in patients with palpitations which factors from history and physical examination can assist GPs in identifying patients with a clinically relevant arrhythmia that is not detectable with a standard ECG.

OUTLINE OF THIS THESIS

In chapter 2 we describe the BEAT trial, a prospective randomised controlled trial evaluating the diagnostic yield of the CER in the primary care setting as compared to usual care for patients with palpitations and/or light-headedness presenting for the first time to the general practitioner.

In chapter 3 we explore the time needed to diagnose an episode, and the number of days needed until a relevant cardiac diagnosis can be established.

In chapter 4 we will study the effects on quality of life and possible anxiety reduction or arousal of a CER diagnostic work up and make a comparison with usual care.

In chapter 5 we analyze characteristics of patients, symptoms and signs that GPs use to determine the risk of patients for a serious cardiac disease. As reference standard we use the diagnosis, as established by the cardiologist that interpreted the CER registrations. Besides we tried to find a model to predict the existence of serious cardiac disease.
In **chapter 6**, an overview of devices presently available for diagnosing patients suffering from palpitations is provided. The diagnostic yield of different devices is described and a guide to rational diagnostic testing is presented.

In **chapter 7** we discuss the overall results of the BEAT trial and advantages and disadvantages of using the event recorder in daily general practice. Furthermore we will discuss how to proceed with the CER in the general practice, including issues on feasibility, costs and the benefits of the CER.

**Chapter 8** Summary, Nederlandse samenvatting

![CER](image1.png)

**Fig 1. CER**


