ORIGINAL ARTICLE

The Diagnosis of Coronary Heart Disease in a Low-Prevalence Setting

Follow-up Data From Patients Whose CHD Was Misdiagnosed by Their Family Doctors

Stefan Bösner, Jörg Haasenritter, Heidi Keller, Maren Abu Hani, Andreas C. Sönnichsen, Erika Baum, Norbert Donner-Banzhoff

SUMMARY

Background: The diagnosis of coronary heart disease (CHD) is a challenge for primary care physicians (PCPs). We studied the further course of 57 patients who presented to their PCPs with chest pain and were initially misdiagnosed as not having CHD as the cause of chest pain.

Methods: The 57 misdiagnosed patients were among 1249 consecutive patients aged 35 and above who presented with chest pain to 74 different PCPs (35% of the 209 PCPs initially invited to participate in the study). For each patient, the PCPs recorded the initial history and physical findings and the course over the ensuing six months. An independent interdisciplinary reference panel reviewed all of the data and retrospectively determined each patient's most likely cause of chest pain at the time of inclusion in the study.

Results: For 405 patients (32.4%), the PCPs rated the probability that CHD was the cause of chest pain at 0 to 5%. The reference panel retrospectively diagnosed CHD as the cause of chest pain in 180 patients. The PCPs correctly diagnosed CHD as the cause of chest pain in 123 (68.3%) of these patients and failed to diagnose CHD as the cause of chest pain in 57 of them (31.7%). 26 (45.6%) of the 57 misdiagnosed patients had a history of CHD. Even when the diagnosis of CHD as the cause of chest pain was missed, the PCPs often ordered an ECG (42 of 57 patients, or 73.7%) or referred the patient to a cardiologist or internist (20 of 57 patients, or 35.1%).

Conclusion: Primary care physicians diagnose CHD with moderate sensitivity. Even when they initially fail to make the diagnosis, they often order further tests and consultations that ultimately lead to a correct diagnosis of CHD.

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With a prevalence of up to 4%, chest pain is one of the regular reasons why patients visit their primary care physician (PCP) (1). While a broad spectrum of possible causative diseases must be considered in the differential diagnosis, the focus of attention is coronary heart disease (CHD) or acute coronary syndrome (ACS), which may have a potentially fatal course (2, 3). When a patient presents with chest pain as the main symptom, the PCP must decide whether serious disease is present that requires immediate action, or whether a “watch and wait” strategy is more appropriate. In addition to the history and physical exam findings, the PCP's decision will also be influenced by epidemiological elements such as the prevalence of CHD. In the primary care setting, 8% to 15% of cases of chest pain are caused by CHD (4–7).

There exist a limited number of studies on the diagnostic accuracy of the PCP's initial suspected diagnosis in patients with chest pain, especially in relation to the reference diagnosis CHD (1, 8–11). However, in these studies there is no information about the further course in the subpopulation of chest pain patients with CHD in whom the appropriate diagnosis was not made at first.

In the present study in patients with chest pain, the authors investigated not only the PCP's initial diagnostic assessment as to whether CHD was present, but also follow-up data about the further course of patients who initially received a false-negative diagnosis in regard to CHD. The authors also modeled the influence of the PCP's CHD assessment (diagnostic certainty) on resulting diagnostic measures such as sensitivity and specificity and, linked to that, potential patient flows for the health care system (false-positive CHD diagnoses).

Method

The present study is a secondary analysis of a cross-sectional diagnostic study. The main objective of the study was to assess the diagnostic value of history and clinical findings in relation to the diagnosis of CHD at the primary care level (12) (for other study results not cited in the text see e1–e3).

Abteilung für Allgemeinmedizin, Präventive und Rehabilitative Medizin, Universität Marburg: Dr. med. Bösner, Haasenritter, Dr. phil. Keller, Abu Hani, Prof. Dr. med. Baum, Prof. Dr. med. Donner-Banzhoff

Abteilung für Allgemeinmedizin, Paracelsus Universität, Salzburg: Prof. Dr. med. Sönnichsen

FIGURE 1

Participating PCPs and patients

Two hundred nine PCPs in Hesse were approached by mail, and of these 74 (35.4%) agreed to take part in the study. Every patient over the age of 35 years with pain in the ventral thoracic region between the clavicle, lowermost costal arch, and posterior axillary line was consecutively recruited for the study. Patients with acute and chronic chest pain and also those with known existing CHD were included. Patients whose most recent chest pain episode was over a month previously, or had already been diagnosed, or who were re-presenting with chest pain were excluded.

Data collection

The PCPs taking part in the study recorded the details of a standardized history and examination on a documentation sheet. They recorded their suspected diagnosis and decisions about any further steps (scheduled further investigations, referral, admission). The PCP's estimate of the probability of CHD on the basis of the history and examination was recorded on a visual analog scale (0% to 100%).

The study assistants carried out telephone interviews with all patients 6 weeks and 6 months after the index consultation, in which they collected data about the further course of the chest pain and any further treatments.

Precautions against selection bias

The study PCPs were recruited via an existing network of research practices held by the authors' department and were trained at a dedicated training session. As part of the quality control measures, the authors checked the routine data of PCPs to determine whether all patients with chest pain had been included in the study.

Reference standard

Because the probability of CHD is small in the great majority of chest pain patients in a primary care practice, an invasive reference standard such as coronary angiography could not be justified on ethical grounds. For this reason, after a 6-month period of follow-up observation, a reference committee consisting of a PCP, a cardiologist, and a staff member from the Department of General Practice/Family Medicine of Philipps University of Marburg analyzed all the patient data. Using this delayed-type reference standard (13) the committee decided whether CHD had been the cause of the chest pain at the time of recruitment. The committee based its decision-making process on the recommendations of the German National Disease Management Guideline for CHD.

Statistical analysis

The analyses relating to diagnostic accuracy and CHD estimation are based on the total group of patients with chest pain. To calculate measures of diagnostic accuracy (estimation of CHD probability) the authors used cross-tabulation. To calculate the sensitivity and specificity of the diagnosis of CHD, the initial binary

TABLE 1

Selected characteristics of the study population (n = 1249)

Patient characteristics	
Age, mean (range)	59 years (35–93 years)
Female patients n (%)	701 (56.1)
Chest pain at the time of recruitment n (%)	660 (52.8)
Patient known to the physician n (%)	1148 (91.9)
Chest pain the reason for the doctor visit n (%)	1092 (87.4)
Acute pain (<48 hours) n (%)	364 (29.1)

coded suspected diagnosis (CHD yes/no) was compared with the reference diagnosis (CHD yes/no). All analyses were carried out using SPSS software (version 17.0) (*eBox*).

Results

PCP and patient characteristics

Most (67%) of the PCPs were men; the mean age was 49 years, and 63.5% of the primary care practices were in an urban environment. The 74 participating doctors saw around 190 000 patients during the overall study period and documented 1355 patients with chest pain. After evaluation of the patient files, seven patients did not fulfill the inclusion criteria and were excluded from the analysis, 99 patients refused to take part and were not included in the study analysis, 60 patients could not be contacted during the follow-up observation period (lost to follow-up), and 11 patients died. However, sufficient clinical data were available for all these patients for a decision to be made as to their reference disease. Three patients dropped out early from the study and were not included in the analysis. For another eight patients the available data were either insufficient, absent, or contradictory, so that no final diagnosis could be made. The reference committee was able to come to a decision about the presence or otherwise of CHD in 1238 patients. Of these, 180 (14.5%) had CHD (*Figure 1*).

Table 1 presents selected characteristics of the overall study population.

Estimation of probability of CHD and diagnostic accuracy

In the large majority of patients the PCPs believed that CHD was unlikely to be the cause of the chest pain. In 820 (66.2%) of the patients the PCPs thought the probability of CHD was 0% to 20%. *Figure 2* shows the distribution of the initial PCP opinion in more detail, summarized in 10% steps.

Out of the 180 cases in which the reference committee determined the presence of CHD, the PCP opinions (after the initial history and examination) were shown to be true positive in 123 cases (68.3%) and false negative in 57 (31.7%).

False-negative CHD diagnoses: patient follow-up data

In the 57 patients in whom the PCPs initially wrongly suspected another disease than CHD as the cause of the chest pain, in half the cases ($n = 29$) the chest pain was taken to be musculoskeletal (chest wall syndrome), and in another 11 cases other cardiovascular diseases (e.g., peri- or myocarditis, cardiac arrhythmias, or cardiac insufficiency) were assumed to be the cause. *Table 2* lists the various suspected diagnoses.

Among these 57 patients, despite thinking that another diagnosis than CHD was more likely, the PCPs had 42 patients (73.7%) undergo an ECG and referred six of them (10.5%) to a cardiologist after the index consultation. During the follow-up observation period of 6 months, another seven patients were referred to a

Estimated probability (%) of CHD on the basis of history and physical examination ($n = 1238$)

cardiologist and six to a general internal medicine specialist.

The reference committee classified 46 of the 57 false-negative cases as stable CHD, seven as unstable angina pectoris, and four as myocardial infarction. Two out of the total of 11 fatalities in the overall study population ($n = 1249$) occurred in this group ($n = 57$). One of these patients was determined by the reference committee to have had unstable angina at the time of the index consultation with the PCP and the other stable CHD. The patient with unstable angina suffered a cardiovascular arrest 12 weeks after the index consultation, during a hospital stay for continuing treatment of diabetic foot syndrome (the physician's report stated suspected myocardial infarction or pulmonary embolism); attempts at resuscitation failed. The second patient, who had stable CHD, reported improvement of his symptoms in terms of the frequency of pain at the telephone interview at 6 weeks; the clinical data strongly suggested angina pectoris. Later during the follow-up period his PCP referred him for further cardiological diagnostic procedures because his symptoms were becoming worse. Although the PCP made strenuous attempts to convince him that inpatient treatment was necessary, the patient refused any kind of further procedures and died at the end of 6 months from acute heart failure. In both patients the existence of CHD was already known and the PCP had started appropriate treatment to improve the prognosis (acetylsalicylic acid, beta-blockers, statins) before the index consultation took place.

TABLE 2

PCP's suspected diagnosis in patients with initially unrecognized CHD (n = 57)

PCP's suspected diagnosis* ¹	
Chest wall syndrome* ² n (%)	29 (50.8)
Other cardiovascular disease n (%)	11 (19.3)
Psychogenic disease n (%)	3 (5.3)
Reflux disease n (%)	3 (5.3)
Other orthopedic disease n (%)	2 (3.5)
Other disease n (%)	2 (3.5)
No detailed information n (%)	7 (12.3)

*¹In 26 (45.6%) of the patients CHD had already been diagnosed previously and in 9 (15.8%) the clinical suspicion of CHD had been recorded.

*²Musculoskeletal causes

Diagnostic accuracy and patient flows

Given the unrecognized cases of CHD, it needs to be asked whether PCPs should lower their diagnostic threshold, i.e., whether they should also treat patients with less severe symptoms as CHD cases, e.g., refer them to a cardiologist. *Figure 3* shows the effects of changing the diagnostic threshold in this way.

Most of the CHD patients (according to reference criteria, 119 out of 180) are in the area of higher estimated probability (>50%). If PCPs were to lower their “diagnostic threshold” in order to miss even fewer cases of CHD, this would lead to only a moderate increase in sensitivity but a marked drop in specificity, with a sharp rise in the number of false-positive findings. Because PCPs work in a low-prevalence setting, there would be only a slight rise in negative predictive value.

Discussion

The initial estimations of CHD by the participating PCPs in patients presenting with chest pain agree with available epidemiological data on the prevalence of CHD in the primary care setting (4–7). Most of the false-negative cases of CHD were initially classified as chest wall syndrome, and in a third of these cases the PCPs initiated further cardiological diagnostic procedures. Altering the subjective diagnostic threshold, while leading to a moderate rise in sensitivity, would also cause a marked drop in specificity and would increase the number of false-positive cases that would be referred for unnecessary further diagnostic workup.

Strengths and weaknesses of the study design

The strengths of this study are its prospective design, the large, representative study population, and the low drop-out rates. Procedures such as the audit of participating practices reduced the possibility of selection bias. Because participation in the study was voluntary,

it cannot be entirely ruled out that participating PCPs were especially highly motivated and this could have distorted results. Perhaps the participating physicians had particularly strong faith in their diagnostic abilities. However, one cannot automatically assume on the basis of this that their diagnostic abilities differed systematically from the mean of all PCPs.

An interdisciplinary reference committee represented the best reference standard possible for this kind of study. However, since we exerted no influence on the further investigations initiated by the PCPs, the reference committee had only limited clinical data for some of the patients.

Estimation of CHD probability and diagnostic accuracy

In the great majority of patients with chest pain the PCPs were of the opinion that CHD was unlikely. This initial assessment agrees with the findings of various epidemiological studies in the field of primary care, which describe a CHD prevalence of 8% to 15% (4–7). Set against this is a CHD prevalence of over 50% in patients who present to a hospital emergency department with chest pain (2, 15).

The first opinion of the PCPs regarding the presence of CHD showed at best moderate diagnostic accuracy, with a sensitivity of 68% (9). Other studies in the primary care setting have given comparable or rather better results, with sensitivities of 72% (8) and 82% respectively (1). Studies of patients with chest pain at a hospital emergency admission or a cardiological outpatient department showed sensitivities of 78% (16) and 83% (17) respectively in terms of physicians' first opinions about whether the patients had CHD.

False-negative CHD diagnoses

How far it makes sense to increase the sensitivity of a diagnostic procedure depends among other things on what consequences an initial wrong diagnosis by the PCP has for the cohort of the false-negative patients. This is why the authors of this evaluation study looked more closely at the false-negative cases.

Out of the 57 patients in whom the PCPs missed the presence of CHD, 29 had a chest wall syndrome diagnosed. This agrees with the observations of Verdon et al. who, in a study on chest wall syndrome in 672 consecutive general practice patients with chest pain, described the pain as localized to the left side in the majority of patients (18). The fact that the PCPs had the patients undergo ECG in 72% of these cases, and 20 of the 57 patients (37%) were referred either immediately or later on to a cardiologist or internal medicine specialist, shows that the PCPs were still keeping the possibility of CHD in mind. This underlines the importance of primary care practice with its low-threshold contact opportunities between physician and patient, in the course of which an initial decision can be revised at any time (“watch and wait” strategy). Because of the particular way in which the PCP works (firsthand knowledge of the patient's medical history, repeated

FIGURE 3

Effects of changing PCPs' subjective diagnostic threshold on the resulting diagnostic parameters and false-positive cases (n = 1238). The figure shows the connection between PCP assessment regarding CHD and the resulting measures of diagnostic accuracy (sensitivity, specificity, positive and negative predictive value) and numbers of patients suspected of having CHD who would be referred for further diagnostic investigations (false-positive cases). Dashed lines symbolize various diagnostic threshold values. For example, if the PCP were to refer every patient with a greater than 5% estimated probability of having CHD for further diagnostic investigations, this would lead to a patient flow of 833 (67.3%) of the patients who visit the PCP for chest pain. Out of these 833 patients, 667 (false-positive cases) would undergo unnecessary further investigations. If only patients with an estimated probability of CHD greater than 20% were referred, the specificity would rise to 74%, with a patient flow of 418 (33.8%) with 274 false-positive cases.

*1 According to the reference committee after 6 months

contact with the patient), special strategies are available that allow him or her to recognize potentially dangerous but preventable medical developments (“safety netting”) and manage them appropriately (19).

Diagnosing CHD—a dilemma for PCPs

PCPs are under pressure not to miss CHD under any circumstances in a patient with chest pain. At the same time, however, they are faced with the dilemma that, for CHD diagnosis, increasing the sensitivity means reducing the specificity. This results in a large number of unnecessary further investigations with their associated costs. If PCPs were to refer every patient with a doubtful diagnosis for further investigation (Figure 3), there would be, for every patient with CHD, about 15 patients in whom unnecessary diagnostic procedures were carried out. On the other hand, undiagnosed CHD can have fatal consequences for the patient concerned; such cases often become the subject of expert medical evidence and lawsuits.

Despite this, the PCP filter function is essential even in patients with chest pain (low-prevalence setting), so that the medical specialists who receive the patient referrals can use their diagnostic tools—appropriate for the high-prevalence setting—in a sensible and hence cost-effective way.

As we have shown with our cross-sectional study of false-negative CHD diagnoses at the time of initial consultation, this filter is of course not perfect. Nevertheless, a longitudinal analysis of our data shows the PCPs continuing to adjust their management of patients with angina who were not initially classified as such. At least one-third of the patients who initially received a false-negative diagnosis were later referred to a cardiology or internal medicine department. Neither of the two deaths in this group was related in time to the index consultation, and both of the patients involved were known to have CHD and had received appropriate treatment from their PCPs to improve their prognosis.

Clinical decision rules

Aside from lowering the diagnostic threshold, which would be inevitably associated with lower specificity and unnecessary further diagnostic investigations, another possibility is optimizing diagnosis through the use of better tests or test strategies. While a new test such as the highly sensitive troponin T assay (20) can be very helpful in indicating the prognosis in stable CHD, its diagnostic utility in CHD in the primary care setting has not yet been studied. ECG and traditional troponin tests have only limited significance for ruling out CHD or acute coronary syndrome (ACS) in the

primary care context, since a normal ECG is not an appropriate basis for ruling out CHD and a negative troponin test has significance only when measured 8 to 12 hours after the onset of chest pain (21, 22).

Since, therefore, the diagnosis will continue to rely on the history and physical exam findings, an alternative approach to a solution may lie in the combined use of data from the history and findings—so-called clinical decision rules (23, 24). An example is the Marburg Heart Score, a validated decision rule that can help PCPs to further optimize their filter function in assessing patients with chest pain (23, 25).

Conflict of interest statement

The authors declare that no conflict of interest exists.

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KEY MESSAGES

- Because of the relatively low prevalence of CHD in primary care practices, diagnosing CHD in a patient with chest pain is a challenge for PCPs.
- In the present study, 31.7% of patients with CHD initially received a false-negative diagnosis from their PCP.
- “Watch and wait” is a fundamental characteristic of the way PCPs work. Even when PCPs believed another diagnosis to be a more likely cause of the chest pain, they nevertheless continued to pursue a differential diagnosis in relation to CHD in some of their patients.
- Lowering the “diagnostic threshold” for CHD in primary care practice must be regarded as problematic; in many patients it would lead to unnecessary further diagnostic investigations.
- Optimization of CHD diagnosis through the use of better tests or clinical decision rules at the primary care level is a possible solution.

Corresponding author

Dr. med Stefan Bösner, MPH
Abteilung für Allgemeinmedizin, Präventive und Rehabilitative Medizin
Universität Marburg
Karl-von-Frisch-Str. 4
35043 Marburg, Germany
boesner@staff.uni-marburg.de

For eReferences please refer to:
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eBOX

● **Method**

This was a cross-sectional diagnostic study. The main study objective was to identify the diagnostic value of history and physical examination in relation to the diagnosis of coronary heart disease (CHD) in the primary care setting (12). The article presents a secondary analysis investigating care issues relating to CHD patients initially given a false-negative diagnosis. For further study analyses, see e1–e3.

● **Participating primary care physicians and patients**

For this study, 209 primary care physicians (PCPs) in Hesse were approached by mail; 74 (35.4%) of them agreed to take part. Participating practices consecutively recruited all patients with chest pain (whether as the reason for the doctor visit or reported in response to questioning from the physician). The recruiting period for each practice was 12 weeks, with four different starting times between October 2005 and July 2006. The PCPs received 30 euros per recruited patient as compensation.

Every patient over age 35 who had pain in the ventral thoracic region between the clavicle, lowermost costal arch, and posterior axillary line was recruited for the study. Patients with acute and chronic chest pain and also those with known existing CHD were included. Patients whose most recent chest pain episode was over a month previously, or had already been diagnosed, or who were re-presenting with chest pain were excluded. In emergency situations in which there was no time to obtain informed consent from the patient, the PCP recorded the information relevant to the study and obtained the necessary informed consent at a later date. The study design was approved by the ethics committee of the Faculty of Medicine at the University of Marburg and conforms with the guidelines of the Helsinki Declaration.

● **Data collection**

The PCPs taking part in the study recorded the details of a standardized history and examination on a documentation sheet. The index tests evaluated in this included the PCP's first impression of the patient, the duration, course over time, character, and location of the pain, any accompanying autonomic symptoms, risk factors and previous medical history, and relevant physical findings. The PCPs also recorded their suspected diagnosis and decisions about any further steps (scheduled further investigations, referral, admission). The probability of the presence of CHD as estimated by the PCP was given on a visual analog scale (0% to 100%).

The authors carried out telephone interviews with all patients 6 weeks and 6 months after the index consultation. In these interviews they collected data about the further course of the pain and any treatment (specialist physicians, hospital treatment, changes of medication). Medical specialist reports and hospital discharge letters were requested via the PCP's office.

● **Precautions against selection bias**

The study PCPs were recruited via an existing network of research practices held by the authors' department and were trained at a dedicated training session. This session emphasized the importance of consecutive recruitment of patients, irrespective of the PCPs' estimate of the probability of CHD. As part of the quality control measures, the authors checked whether the data collected by the PCPs as part of their routine clinical practice included all patients with chest pain.

● **Reference standard**

Since in the great majority of chest pain patients in a primary care practice the likelihood of CHD is small, an invasive reference standard such as coronary angiography could not be justified on ethical grounds. For this reason, after a 6-month period of follow-up observation, a reference committee consisting of a PCP, a cardiologist, and a staff member from the Department of General Medicine of Philipps University of Marburg analyzed all the patient data. Using this delayed-type reference standard (13) the committee decided whether CHD had been the cause of the chest pain at the time of recruitment. This design is based on the assumption that a serious disease such as CHD will be revealed as the cause of symptoms within the time given (6 months). The committee drew on the recommendations of the National Disease Management Guideline for CHD for its decision-making process (14).

The history forms part of the definition of acute or chronic CHD. Having access to the original documentation form on which the data relating to the patient's history were recorded could therefore influence the judgment of the reference committee. To minimize this "incorporation bias," in the first round the reference committee analyzed only the data from the follow-up observation period, without the information from the index questionnaire (blinded reference standard). In the second round the patient files, in a different order, were made available together with the index test for the experts' reference opinion (unblinded reference standard).

● **Statistical analysis**

The analyses relating to diagnostic accuracy and CHD estimation are based on the overall group of patients with chest pain. To calculate which parameters were of diagnostic value (estimation of CHD probability), the authors used cross-tabulation. To calculate the sensitivity and specificity of a CHD diagnosis, the initial binary coded suspected diagnosis (CHD yes/no) was compared to the reference diagnosis (CHD yes/no). All analyses were carried out on the unblinded dataset with SPSS software (version 17.0).