Ultrasound

Stethoscopy

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***Cover illustrations*:**
Front cover: The upper left panel shows the *Minivisor*™, the ultrasound stethoscope developed in 1979 at the Thoraxcenter. The upper right panel illustrates the *OptiGo*™, the lower left presents the *SonoHeart*™ and the lower right, the *Terason*™ . In the middle of all is *SonoSite iLook*™, the latest developed ultrasound stethoscope. In the background, a mitral regurgitation obtained with *OptiGo*™ is visualised.
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ULTRASOUND STETHOSCOPY

ULTRAGELUID STETHOSCOPE

PROEFSCHRIFT

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aan de Erasmus Universiteit Rotterdam
op gezag van de Rector Magnificus

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en volgens besluit van het College voor Promoties

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Promotor	*:Prof.dr. J.R.T.C. Roelandt*
Overige leden	*:Prof.dr.ir. N. Bom* *: Prof.dr. A. Hofman* *: Prof.dr. C.A. Visser*
Copromotor	*:Dr. D. Poldermans*

Financial support by the Netherlands Heart Foundation (NHF) for the publication of this thesis is gratefully acknowledged.

Dedicated to my parents and my sister Dora

For Georgios

CONTENTS

CHAPTER 1

INTRODUCTION AND OVERVIEW OF THE THESIS

INTRODUCTION

Our present knowledge about bedside physical examination is rooted in ancient medicine. Pharaonic and later Greek doctors examined patients by inspection and palpation and applied their ear to the patient's chest, listening to the sounds and movements of the heart. This was known as "direct auscultation". It was not before 1819 when the French physician Théophile René Hyacinthe Laennec introduced the stethoscope for "indirect ausculatation"(1). The word stethoscope was derived from the Greek words *stethos* meaning "chest" and s*kopein* meaning "seeing" and in fact is a misnomer.

Since then, many advances in cardiac diagnosis and more particularly in imaging have occurred. X-rays were discovered by Röntgen at the end of the 19th century. The concept of cardiac imaging as part of the physical bedside examination was introduced in 1904 by W. Rollins who combined a fluorescent screen and a stethoscope, the so-called "Seehear" instrument (2). Probably, the most important advance was the use of reflected ultrasound-echocardiography and was developed by Edler I and Hertz H in the 1950s (3).

In 1978, the first small hand-held ultrasound device was constructed by Ligtvoet et al (4) and introduced as part of the physical examination by Roelandt et al in Rotterdam (5,6). However, the concept was ahead of its time and in combination with poor image quality, practical limitations and reimbursement issues its further development was discontinued.

Today, advances in microcomputer technology have led to the construction of sophisticated small hand-held ultrasound devices with high imaging quality and low cost.

These devices are referred to in the literature with various names: hand-held ultrasound or hand-carried cardiac ultrasound devices, personal ultrasound imagers (PUI), small personal ultrasound devices (SPUD), point-of-care echocardiography, ultrasound cardioscopes or ultrasound stethoscopes and hand-held scanners.

In this thesis we report the many evaluation studies with the hand-held ultrasound device in the assessment of different cardiac pathologies and in different clinical settings. The reason for using the term "ultrasound stethoscopy" is that these devices are augmenting our physical examination by allowing to visualise the heart and hence extend our physical sense of "seeing". Since stethoscopy stands for "seeing the heart" as previously mentioned, the term ultrasound stethoscope seems to be the most appropriate term describing these instruments.

One could argue that the introduction of echocardiography at the bedside could weaken the importance of auscultation and the physical examination in particular. However, it was echocardiography that brought out the limitations of physical examination in many cardiac

conditions and also exposed human auditory limitations (7-10). Although auscultation entered a modern era with the introduction of electronic stethoscopes (11), physicians rely on more sophisticated technology. Inadequate training and time pressure due to increasing work load of patients in combination with the availability of advanced technologies are the reasons of poor auscultatory proficiency seen in recently trained physicians particularly in developed countries (12). Nevertheless, we have to admit that direct observation such as seeing is more accurate for cardiac diagnosis than indirect observation such as hearing. "Seeing" enables the preclinical detection of pathologies and especially pathologies that are beyond physical signs, e.g. small mass lesions.

The first reactions from experienced echocardiographers to the ultrasound stethoscope were related to its capabilities/limitations and the training required for physicians who use it (13). The last 2 years refinements in the technology of the ultrasound stethoscopes and addition of modalities like spectral Doppler and M-Mode have improved the diagnostic potentials of these devices.

No doubt that training is required to use an imaging device. Recently the American Society of Cardiology (14) published guidelines regarding the use of ultrasound stethoscopes recommending Level I of training (15) as an absolute minimal level required. However, recent studies have shown that it is possible to train physicians and students for the detection of significant pathologies in a short period (16,17).

We have to accept that the idea of a "personal" ultrasound stethoscope is appealing and in combination with its low cost it is clear that in future larger number of physicians and not only cardiologists will have access to this technology. The use of these devices by general practitioners can lead to early diagnosis and management of patients and hospitals will benefit from the lower rate of inappropriate referrals. Moreover, introducing the ultrasound stethoscope into the medical school curriculum like the stethoscope will result in physicians capable of using these devices as an extension to physical examination.

Having worked with ultrasound stethoscopy the last 2 years I can say that such devices are friendly to use and make both feel comfortable, physician and patient.

For the first time we have direct imaging of the heart at the bedside examination wherever the physical examination is needed.

Characteristically, performing echo examinations with the ultrasound stethoscope at the outpatient cardiology clinic blinded to the physical examination of colleagues, I could

appreciate the superiority of direct bedside imaging since most of the times the request for an echocardiographic study could have been avoided.

The enthusiasm with which colleagues accepted the ultrasound stethoscope and incorporated it into their physical examination was a proof of recognition of the ability of this technology to increase the diagnostic accuracy at the bedside.

To my biggest surprise, during my presentations about ultrasound stethoscopy at international congresses and following highly scientific sophisticated topics like shear stress and strain rate tissue imaging, it was the ultrasound stethoscopy session that caught the attention of the audience. Being afterwards approached not only by cardiologists but also physicians of other specialities, I realised that we have entered a new era in daily clinical practice.

Ultrasound stethoscopy is a fast developing field in cardiology. Physicians should embrace this innovation and add it to their physical examination. This will result in better patient's care and cost savings since a definitive diagnosis is made in the majority of patients leading to their instant management.

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OUTLINE OF THE THESIS

The first chapter gives an introduction to the thesis. Methodology and an outline of the thesis are thoroughly presented.

This thesis consists of three parts.

Part I:

Part I (chapter 2-3) presents the ultrasound stethoscope as a diagnostic tool.

Chapter 2 introduces ultrasound stethoscopy as a new imaging tool in daily clinical practice. Clinical and scientific background and an overview of the potential applications of ultrasound stethoscopy are brought to attention.

Chapter 3 describes our first experience of the utility of such a prototype device in the diagnosis of cardiac pathomorphology and global and regional left ventricular function in 114 consecutive outpatients. The results of a standard echocardiographic system were used as a reference.

Part II:

Part II (chapter 4-8) discusses the evaluation of an ultrasound stethoscope as a potential screening tool for specific cardiac pathologies.

In chapter 4, 100 patients at risk for abdominal aortic aneurysm were screened for this disorder with an ultrasound stethoscope. The results of a standard echocardiographic system were used as a reference. An abdominal aortic aneurysm was defined as a focal transverse enlargement of the aorta >30mm with the standard echo system. This study is presented also as a short report (pilot study) in the same chapter.

The enhanced diagnostic accuracy by combining new imaging modalities like ultrasound stethoscopy, intravascular ultrasound and spiral computed tomography can be appreciated in chapter 5.

Next, we screened 100 consecutive hypertensive patients, who visited the hypertensive outpatient clinic for left ventricular hypertrophy (chapter 6). Measurements of the thickness of the anterior septum and posterior wall and of the end-diastolic dimension of the left ventricle using the parasternal 2D-long axis view were performed with both imaging devices. Left ventricular hypertrophy was defined as an increase in left ventricular mass ≥ 134 g/m^2 for men and ≥ 110 g/m^2 for women, when indexed for body surface area and ≥ 143 g/m for men and

≥102 g/m for women, when indexed for height. Again, the results of a standard echocardiographic system were used as a reference.

Chapter 7 describes the diagnostic potential of an ultrasound stethoscope in screening for left ventricular dysfunction. In 88 consecutive patients with suspected left ventricular dysfunction, visual estimation of left ventricular ejection fraction made with the ultrasound stethoscope was compared to a quantitative assessment of left ventricular ejection fraction on the standard echo system, using the Simpson's biplane discs method and to BNP measurements. The inferior vena cava collapse was also assessed with both devices as a potential screening parameter for left ventricular dysfunction.

In chapter 8, we proceeded further to evaluate the effect of myocardial contractile reserve, assessed with dobutamine stress echocardiography, on plasma BNP levels in patients with reduced left ventricular systolic function. Sixty-one consecutive patients referred to dobutamine stress echocardiography for the evaluation of known or suspected coronary artery disease were evaluated.

Part III:

This part is evaluating the cost-effectiveness of ultrasound stethoscopy in clinical practice (chapter 9-11).

Chapter 9 presents the utility and cost-effectiveness of ultrasound stethoscopy during cardiac consultation rounds in 107 consecutive patients from non-cardiac departments with suspected cardiac disease. The consultant cardiologist performed after the physical examination an echocardiographic study with the ultrasound stethoscope and noted whether the findings of the ultrasound stethoscope were adequate for final diagnosis. All patients subsequently underwent a study with a standard echocardiographic device. The total cost when full echocardiography was employed was compared to the cost when the ultrasound stethoscope was used.

An example of instant definitive diagnosis during consultation rounds is presented in chapter 10. The diagnosis of an endocarditis of the tricuspid valve in a 20-year-old patient was established with an ultrasound stethoscope. This was verified with a transesophageal study with a standard echocardiographic device.

In chapter 11, our objective was to assess the diagnostic utility and practicality of ultrasound stethoscopy in an outpatient cardiology clinic evaluating 300 new patients. Echocardiographic

examination was performed blinded to the physical examination. The number of patients in which the ultrasound stethoscope was able to confirm or reject the referral diagnosis and the number of unexpected findings were assessed. These data were compared to the diagnosis and request for a standard echocardiographic study by the cardiologist.

Finally, chapter 12 provides conclusions and summarizes all the above studies giving an insight and thoughts to our findings. Limitations and future perspectives of ultrasound stethoscopy are discussed.

CHAPTER 2

ULTRASOUND STETHOSCOPY

JRTC Roelandt, E Vourvouri, D Poldermans.

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ABSTRACT

Small personal ultrasound imagers allow to see the heart and its pathology during the physical examination. Seeing the invisible pathology strengthens its diagnostic accuracy and provides valuable quantitative information for patient management. These devices will be useful in the emergency room and critical care environment where the diagnosis or exclusion of some life threatening conditions will shorten delays in therapy. Better indications and more targeted referral for expensive imaging technologies will lead to significant cost savings. "Focussed" or goal-oriented echocardiographic examinations with these devices allow to answer specific questions, to follow-up common conditions and to test the effect of therapy at the bedside or in office practice.

Echocardiography is currently the most widely used and cost-effective diagnostic imaging tool in cardiology. Since it is often the best or even the only applicable method, it has largely supplanted other imaging modalities in a wide variety of health care environments. Miniaturisation and digital techniques recently resulted in the development of high resolution battery-powered personal ultrasound imaging devices with excellent grey-scale and colour blood flow imaging capabilities. These personal imagers are appropriately named "ultrasound stethoscopes" since they allow to look into the chest (stethos=chest and skopein=see) and see the heart and its pathology during the physical examination. They can be used anytime anywhere just like a conventional stethoscope.[1]

We will discuss the potential of these small ultrasound imaging devices in different clinical scenarios and how they may extend the physical examination and the practice of cardiology.

ULTRASOUND STETHOSCOPES

Two small hand-held ultrasound imagers have recently been introduced (SonoHeart™, SonoSite, Inc. Bothell, WA, USA and OptiGo™, Agilent Technologies, Andover, MA, U.S.A.) (figure 1). They are based on miniaturised digital technology and make use of phased array transducers providing high-resolution two-dimensional dynamic grey-scale tissue imaging combined with colour Doppler flow imaging (directional for the SonoHeart™). The upgraded SonoHeart Plus™ device features second harmonic imaging and has integrated M-mode and pulsed-wave Doppler capabilities as well as an electrocardiographic reference lead.

The devices operate on a rechargeable battery or AC current and have measurement packages including linear measurement callipers. The internal memory of the SonoHeart™ allows storage up to 120 images, which can be downloaded into a PC and there is a video output, which can be connected to a monitor or to a VCR for permanent recording. The OptiGo™ allows images to be documented on a CompactFlash card.

Other companies are also developing miniaturised ultrasound imaging systems. The Terason™ device (Teratech Corp, Burlington, MA, USA) has the micro-miniaturised ultrasound system incorporated in the transducer and connects to a notebook PC (figure 1). The small ultrasound devices should not be confused with the portable desktop systems which are full featured systems.

The examination procedure with these devices is the same as with standard echocardiography and all precordial windows can be used for structure and blood flow imaging. Our experience

with the SonoHeart™ and OptiGo™ device indicates that morphologic data obtained in standard cardiac views and basic linear measurements of structures and cavities adequately compare with those documented with standard equipment.[2]

CLINICAL USES

The ***physical examination*** remains the cornerstone of the initial evaluation of a patient with suspected cardiovascular disease. However, notable shortcomings in examination skills and more particularly in auscultation have been documented even after training with innovative instructional methods.[3-6] In addition, over the years, echo/Doppler studies have brought out the limitations of the physical examination in many cardiac conditions, particularly in the early stages of disease and no quantitative information is obtained.[7] "Visualising the heart" with the ultrasound stethoscope as part of the physical examination provides additional information beyond what we can perceive with palpation and auscultation and allows to rapidly confirm a cardiac abnormality (valve disease, shunt (figure 2), cavity dilatation, hypertrophy, pericardial effusion, wall motion abnormality) and often to make a specific diagnosis in any clinical setting (table 1 and figure 3).

TABLE 1

THE ULTRASOUND STETHOSCOPE

Rapid clinical diagnosis
Source of murmurs
Dilated heart
Pericardial effusion, emergent tamponade
Pulmonary embolus
Valvular disease
Mass lesion
Wall function
Dilatation abdominal aorta/aneurysm

Incidental findings are also regularly recognised.[8,9] The routine physical cardiac examination can be extended by imaging and by obtaining limited quantitative measurements of the inferior vena cava, liver, spleen and abdominal aorta. The loss of inspiration narrowing of the inferior vena cava is a reliable and sensitive marker of elevated central venous pressure and right heart failure (figure 4).[10] The major strength of a limited echo/Doppler examination is its

specificity that allows to exclude a cardiac abnormality with great certainty after limited training. However, it is crucial to have sensitive colour flow imaging capabilities.
Standard echocardiography involves a comprehensive examination with complex equipment by an operator with considerable training and experience. However, the diagnosis and follow-up of many cardiac conditions requires only a fraction of the potential of these expensive facilities and a specific clinical question can often be answered within little time and with little examination protocols.[9,11-13] The ultrasound stethoscope is very suitable for such a ***"focussed"*** or ***"goal-oriented"*** examination. The resolution of a pericardial effusion after a pericardiocentesis (figure 5), cardiac dimensions and left ventricular (LV) function both of which are important parameters in the follow-up of many patients are rapidly assessed at the bedside (agreement for semi-quantitative LV size assessment between standard echocardiography and SonoHeart™ in 111 consecutive patients was 99%; kappa value 0.970 and for ejection fraction 93%; kappa value 0.871).[1] Patients with hypertension and LV hypertrophy have an increased risk of a cardiovascular event and the success or failure of their antihypertensive treatment can be assessed by wall thickness measurements (figure 6).[9,12,14]

"Goal-oriented" echocardiography will undoubtedly become part of the initial physical examination by primary care physicians to identify or exclude a cardiac condition who will use telecommunication technology for consultation in the future.[15]

The ultrasound stethoscope can effectively assist in the initial evaluation and rapid diagnosis of potentially life threatening conditions in the ***intensive care environment*** or in situations where quick-decision making is essential. In many such situations standard echocardiography is not rapidly available. The ultrasound stethoscope carried by the attending cardiologist provides data inaccessible by clinical examination and allows to immediately diagnose or exclude an emergent tamponade, a dilated heart and valvular pathology (e.g. calcific aortic stenosis in low output state) (figures 7 and 8).
Pericardiocentesis can be guided and the effects of acute interventions (e.g. fluid challenge in hemodynamically compromised patients, inotropic drugs) monitored through estimation of cavity dimensions, ejection fraction and wall dynamics (figure 9).
In a recent study by Goodkin et al[16], the potential of a hand-held device to rapidly obtain important clinical information during the physical examination in critically ill patients was demonstrated. However, proper management of these patients often requires hemodynamic data which are obtained with standard equipment. Immediate echocardiographic assessment

in the ***emergency room*** has been reported to considerably shorten the time to diagnosis of penetrating cardiac injury and to improve the chances of survival.[17-20] Right ventricular involvement in acute myocardial infarction and the mechanical complications of a myocardial infarction are readily diagnosed in the ***coronary care unit***. Echocardiography of the right heart is of great value in patients with acute pulmonary embolism.[21] The demonstration of right ventricular dilatation and paradoxical septal motion in patients clinically suspected raises the level of suspicion significantly while their absence does not exclude pulmonary embolism. On the other end, many conditions that clinically mimic pulmonary embolism are rapidly identified.[22] Regional wall function abnormalities are reliably detected (90% agreement in 204 segments of 34 patients), a potential which can be utilised in chest pain clinics for rapid screening the context of acute chest pain and a non-diagnostic electrocardiogram in chest pain clinics.[3]

The ultrasound stethoscope could be used for ***screening*** and identifying unexpected cardiac disorders with a low prevalence in a specific population. However, the sensitivity of these devices for identifying certain conditions is still to be defined and the competence and training level of the examiner is an important aspect to consider. The feasibility of community screening for asymptomatic LV dysfunction has been demonstrated.[23]

The ultrasound stethoscope allows rapid screening for an occult aortic abnominal aneurysm in patient groups "at risk" (patients with coronary artery disease, hypertension, elderly) (figure 10).[24-26] Physical examination is notably insensitive in moderately enlarged aneurysmata and obese patients. Aortic diameter measurements compared well to those obtained with standard equipment (agreement 97% in 100 consecutive patients; kappa value 0.810) and are obtained in a few minutes during a routine physical examination.

Limited echocardiography allows to screen for left ventricular hypertrophy (agreement with standard echocardiography in 100 consecutive patients 92%, kappa value 0.730) and to follow the effect of treatment in office practice.[12]

Mitral valve prolapse is often suspected in otherwise asymptomatic individuals. This disorder can be excluded or confirmed in a limited number of standard views (figure 11).[27]

Potentially dangerous conditions can be identified in preparticipation screening of athletes. Hypertrophic cardiomyopathy, a dilated ascending aorta (Marfan) (figure 12) and valvular abnormalities (bicuspid valve, mitral valve prolapse) are the most common disorders and are reliably detected by experienced examiners.[24-28] However, screening for cardiac disorders in young athletes and asymptomatic individuals involves a high risk of a false positive diagnosis.

DISCUSSION

In 1904, W. Rollins described the "Seehear", a device combining a fluoroscope with a standard stethoscope extending the clinical perception of the auscultation with seeing. Clearly, ultrasound offers obvious advantages over x-rays. We developed and used an ultrasound stethoscope (Minivisor™, Organon Teknica) as early as 1978.[29-32] and in 1988, a hand-held sector scanner (ScanMate™, Damon Corp) was introduced by the Rochester group.[30,31] However limited imaging performance and reimbursement issues did not stir the enthusiasm of cardiologists who were confronted in those days with the rapidly expanding capabilities and applications of the high-end ultrasound systems. Now, technology allows to construct small personal imaging systems with excellent structure and blood flow imaging. Expanding our routine physical examination with a small personal imager will significantly strengthen our diagnostic capabilities (table 2)

TABLE 2

THE ULTRASOUND STETHOSCOPE

Seeing the invisible during the physical examination provides:
Higher diagnostic specificity and sensitivity
Early (preclinical) diagnosis
Functional assessment
Blood flow information
Inferior vena cava collapse
Quantitative information
Abdominal aorta measurement

On the basis of normal structure and functional findings in the absence of blood flow turbulence, all of which can be tested in a limited number of imaging views, a cardiac disorder can be excluded with a high degree of certainty. This high negative predictive value is ideal for rapid screening to avoid referral of normals and for a more cost-effective use of our expensive diagnostic imaging facilities. Personal imagers will therefore have an impact not only on the physical examination but also on the use of echocardiography and other imaging modalities by targeted referral. A major application will become its use in a critical care environment. Direct diagnosis or exclusion of some life threatening conditions will shorten delays in proper management and therapy and lead to important cost-savings. These

devices are extremely suited for a limited "focussed" ultrasound examination to follow the course of a disease or to test the effect of therapy in the outpatient clinic in office practice.

Obviously, a small ultrasound imager must be used as an adjunct of the physical examination and cannot substitute for the high-end ultrasound systems.[15] Therefore, its use involves some compromises which will be learned when applications are expanding. Training of non-echocardiographers may become an important issue and should focus on criteria of normalcy and identifying both major and acute cardiac disorders. In fact, the device should be used in a way comparable to auscultation; whenever there is doubt, further echo/Doppler is examination is indicated. Training programs and continuing medical education including performance testing can be organised with modern electronic means. In the future, advances in communications and software will allow for diagnostic support from experienced laboratories or intensive care units.

It should be remembered that the real value of any imaging technology is intimately dependent on our intellectual contribution: how, when and what clinical scenario it will have its optimal clinical impact.

Acknowledgement

We are grateful to SonoSite Inc. and Agilent Technologies Inc. for providing the small ultraound imagers for clinical evaluation.

Figure 1

Photographs of the (A) Minivisor™ developed in 1978.[32-34] and currently available hand-held ultrasound devices (B) OptiGo™, (C) SonoHeart™ and (D) Terason™.

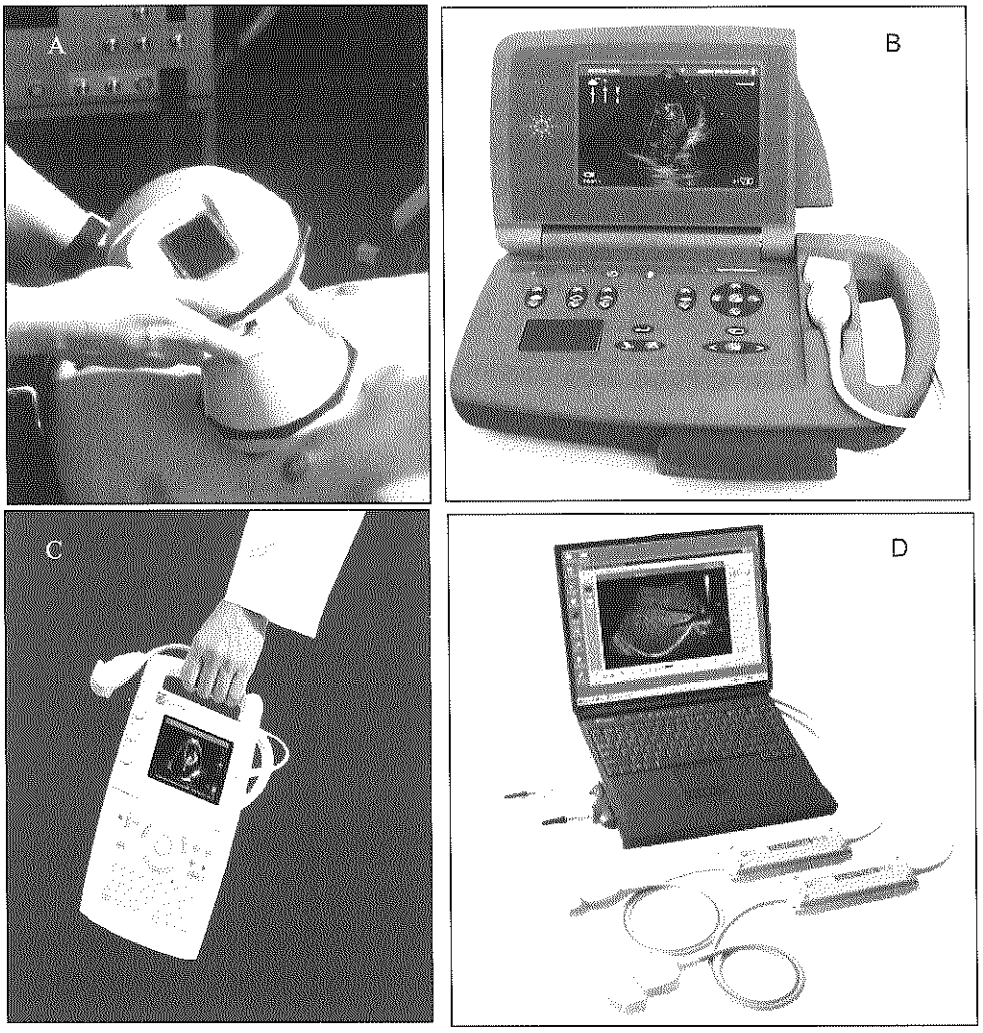


Figure 2

Apical four chamber view of a patient with an atrial septum defect of the secundum type. Both atria are dilated and the left-to-right shunting blood flow through the defect is visualised (OptiGo^{TM}).

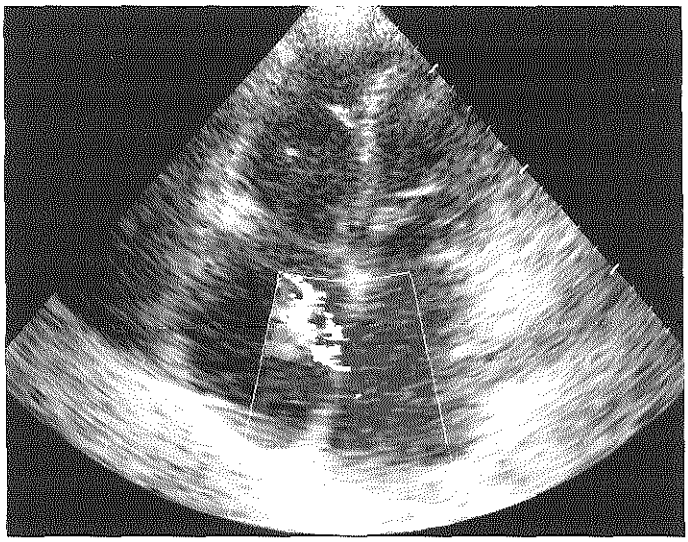


Figure 3

Apical four chamber view of a 25-years-old-female with systemic lupus erythematosus and shortness of breath. The referral diagnosis was: pericarditis? The patient has regurgitant jets of aortic regurgitant (A) and mitral regurgitation (B), but no pericarditis (OptiGo^{TM}).

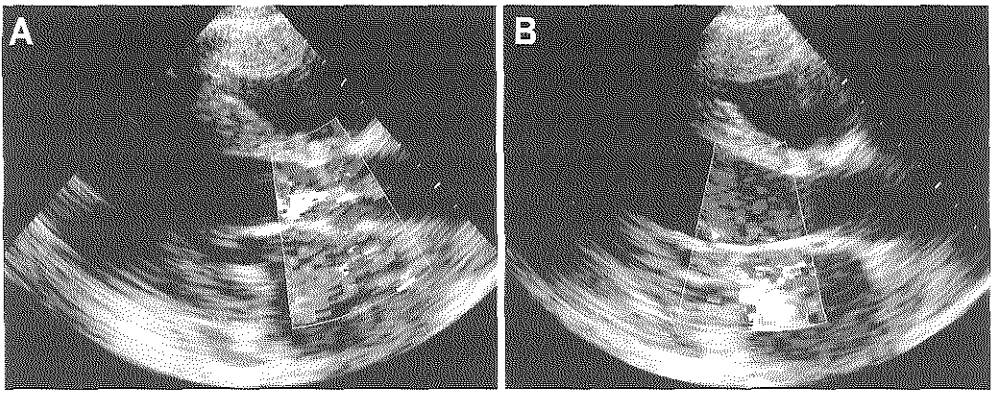


Figure 4

Imaging of the inferior vena cava (IVC) through the liver during expiration (A) and inspiration (B). The caliper function allows measurement of the IVC dimension during expiration (2.6 cm) and during inspiration (1.9 cm). A collapse of less than 50% indicates an elevated right-sided filling pressure[37] (OptiGo™).

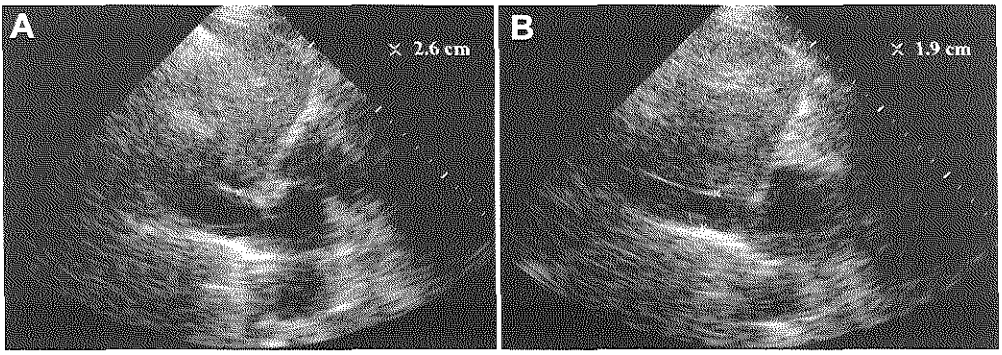


Figure 5

Long-axis views of patients with pericardial effusion (PE). (A) A small PE postoperatively and (B) a large PE of a patient with clinical signs of tamponade (SonoHeart™).

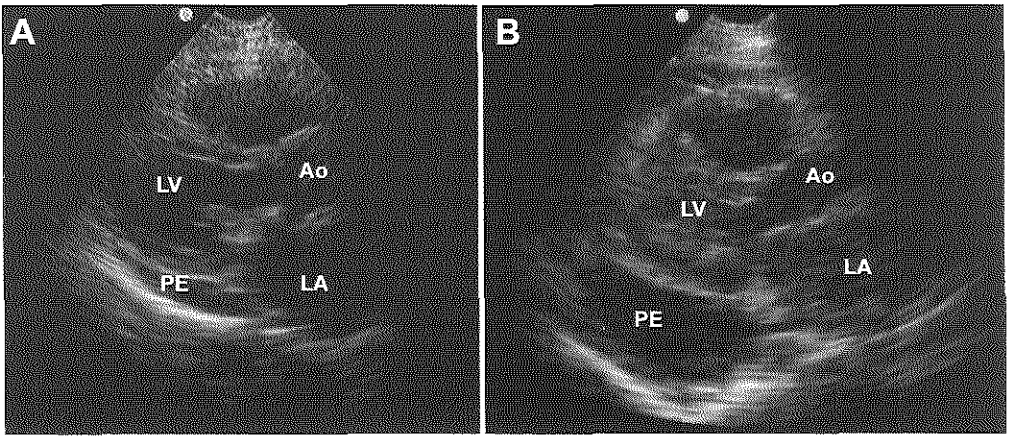


Figure 6

Measurement of septal thickness in a 49-years-old man with hypertension using the integrated calliper function. Thickness is 1.3 cm (normal < 1.2 cm) (SonoHeart™).

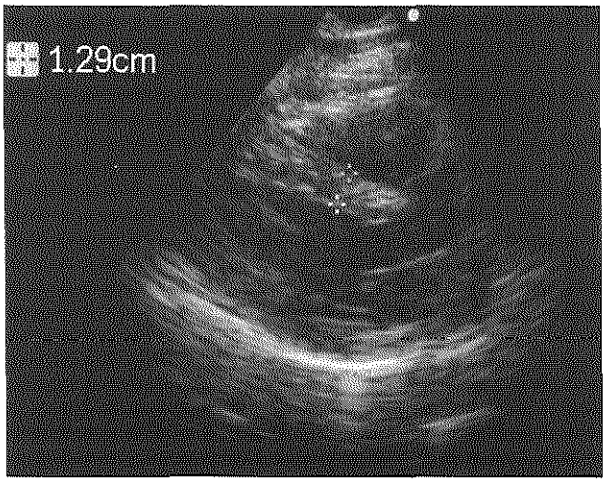


Figure 7

Long-axis view of a 72-years-old man with no history of cardiac disease and progressive dyspnea. His referral diagnosis was: cardiomyopathy?

A calcific aortic valve is seen with turbulent flow in the aorta in systole and a regurgitant jet in the outflow tract in diastole. The left ventricular end-diastolic dimension is 60 mm. The patient has degenerative calcific aortic stenosis and regurgitation (OptiGo™).

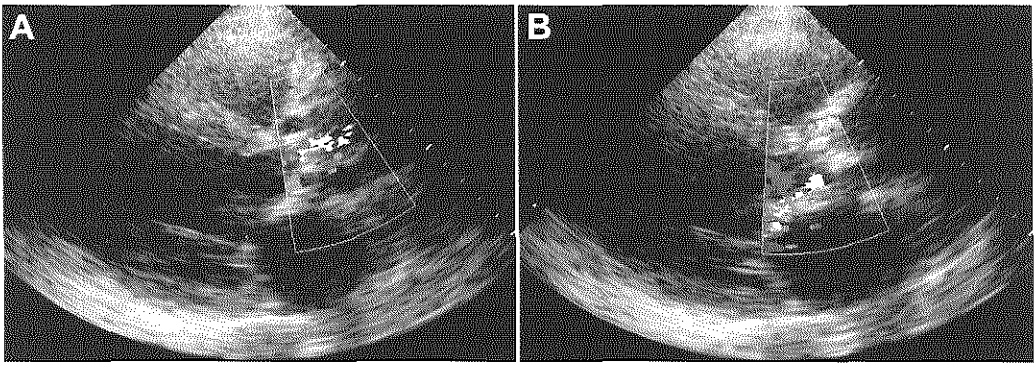


Figure 8

Apical four chamber view of a 45-years-old male with dilated cardiomyopathy. (A) A mitral regurgitant jet is visualised (SonoHeart^{TM}). The imaging quality of the hand-held device can be appreciated against that of a standard echocardiographic system (HP, Sonos 5000^{TM}).

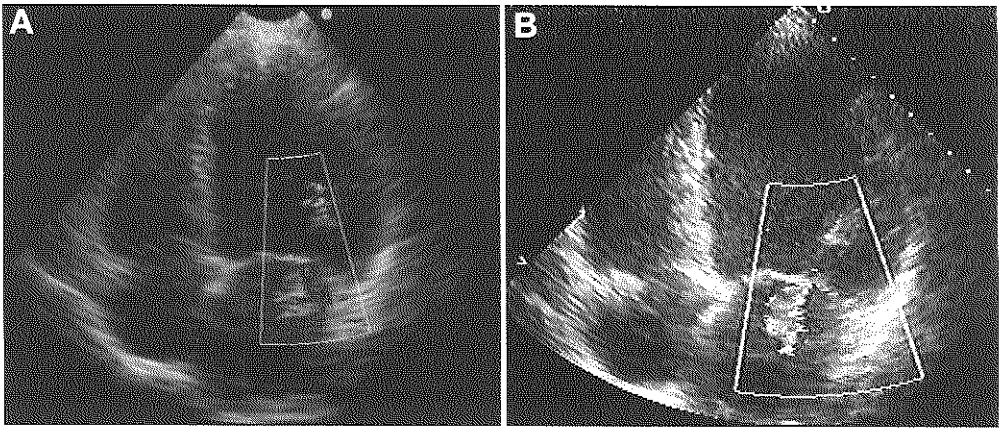


Figure 9

Principle of estimating of left ventricular ejection function in the parasternal long axis view. A calliper function allows to measure the left ventricular dimensions in end-diastole (5.26 cm) and end-systole (2.99 cm) – the fractional shortening is 45% (SonoHeart^{TM}).

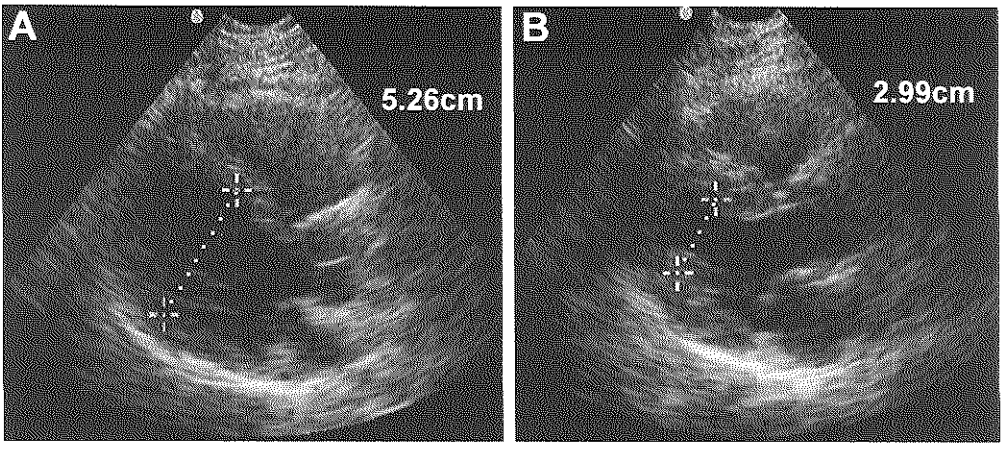


Figure 10.

Imaging of the abdominal aorta. (A) Normal abdominal aorta - dimension 2.1 cm (OptGo ™) and (B) aneurysm of the abdominal aorta (dimension 5.0 cm) (SonoHeart ™).

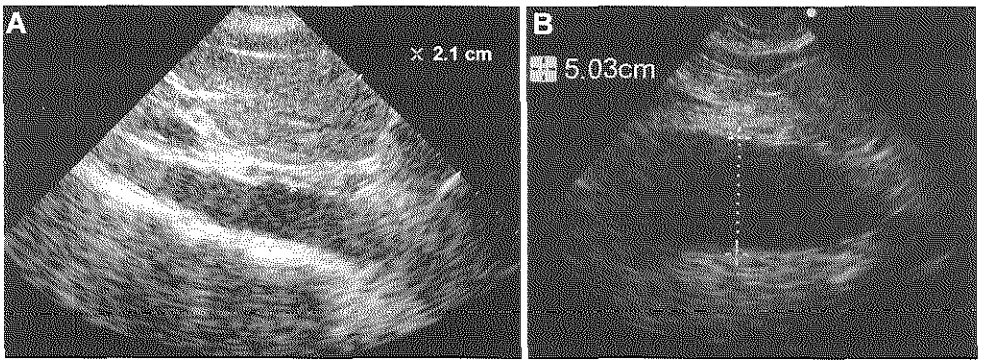


Figure 11

Apical four chamber view of a 65-years-old female with prolapse of the posterior mitral leaflet and eccentric jet towards the interatrial septum. The patient was referred for the evaluation of palpitations and was known to have a systolic murmur (OptiGo™).

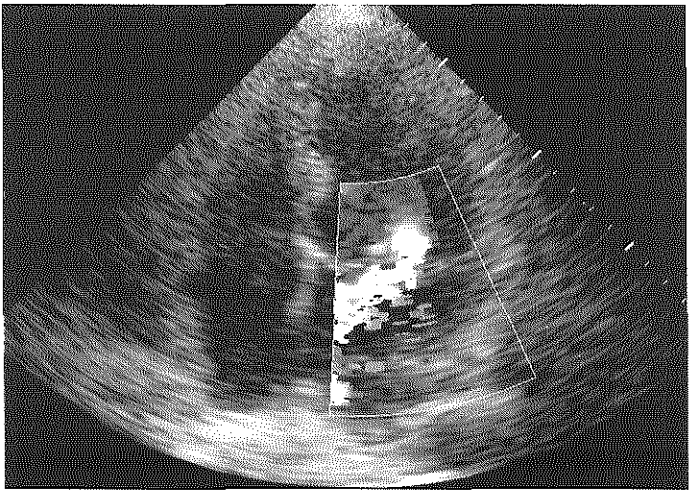
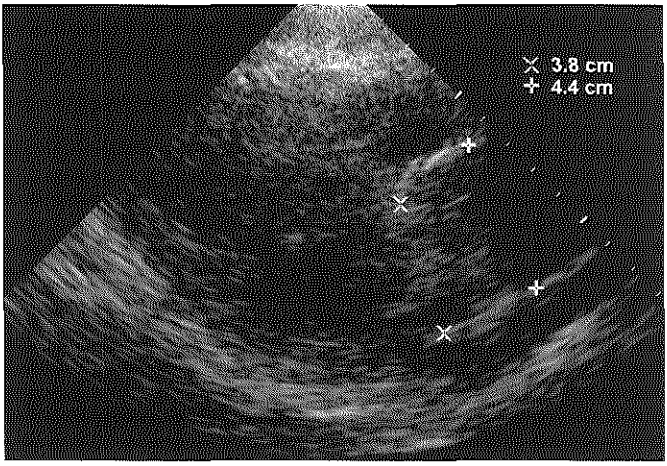


Figure 12

Long-axis view of a 74-years-old male with lung infection. The patient was referred for pre-operative cardiac evaluation. A dilatation of the ascending aorta measuring 4.4 cm is seen (OptiGo ™).



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CHAPTER 3

EXPERIENCE WITH AN ULTRASOUND STETHOSCOPE.

EC Vourvouri, D Poldermans, J de Sutter, FB Sozzi, P Izzo, JRTC Roelandt.
J Am Soc Echocardiogr 2002;15:80-5.

Experience with an Ultrasound Stethoscope

Eleni C. Vourvouri, MD, Don Poldermans, MD, Johan De Sutter, MD, Fabiola B. Sozzi, MD, Paolo Izzo, MD, and Jos R.T.C. Roelandt, MD, *Rotterdam, The Netherlands*

Background: **To test the diagnostic potential of the SonoHeart, a battery-powered hand-held ultrasound imaging device, in an outpatient clinic setting.**
Methods: **A total of 114 patients with a variety of cardiac diseases were examined by 2 independent cardiologists with the hand-held device using the standard echocardiographic system (SE) as a reference. Global right ventricular (RV) and left ventricular (LV) function (scored as normal, mildly to moderately, or severely reduced) and internal cavity dimensions were assessed. Regional wall motion of 6 segments using a 2-point score (1 = normal wall motion, 2 = abnormal wall motion) was evaluated in 34 patients on-line.**
Results: **There was a good agreement between the 2 imaging devices for evaluation of global LV (93%) and RV function (99%), regional wall motion (90%), dimensions of the LV (99%) and the RV (99%), and the left (96%) and right atria (99%). Furthermore, SonoHeart identified hypertrophic cardiomyopathy, pericardial effusion, and abnormalities of valves.**
Conclusion: **The SonoHeart device allows rapid and accurate diagnosis, whenever needed in the outpatient clinic.** (J Am Soc Echocardiogr 2002;15:80-5.)

Cardiac ultrasound has become an important and effective noninvasive diagnostic imaging tool over the years, and better imaging performance has been realized with more expensive and complicated systems. To broaden the availability of ultrasound imaging and to increase its versatility in application, small, easy-to-use, and low-cost echocardiographic devices have recently been developed. These devices act like an ultrasound stethoscope (from the Greek words stethos = chest and skopein = see), being ultraportable and providing information beyond physical examination at the bedside.

The aim of this study was to evaluate the potential and diagnostic accuracy of a prototype hand-held ultrasound system (SonoHeart System, SonoSite, Inc, Bothell, Wash) for the assessment of cardiac pathomorphology and global and regional function in an unselected outpatient population, using the results of high-end 2-dimensional (2D) echocardiographic equipment for performance comparison.

From the Department of Cardiology, Thoraxcenter, Erasmus Medical Center Rotterdam, The Netherlands.

Reprint requests: Prof Dr J.R.T.C. Roelandt, MD, Department of Cardiology, Thoraxcenter, Erasmus Medical Centre, Dr. Molewaterplein 40, 3015 GD Rotterdam, The Netherlands. (E-mail: *roelandt@card.azr.nl*).

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STUDY PATIENTS AND METHODS

The Ultrasound Stethoscope

The SonoHeart (SonoSite Inc) hand-held ultrasound system (Figure 1) is a small hand-held ultrasound device measuring 33.8 × 19.3 × 6.1 cm and weighing 2.4 kg. It is equipped with a small (15 mm) 2 to 4 MHz phased-array broadband transducer and operates on a rechargeable lithium ion battery or alternating current. The 2D control settings comparable with a standard echocardiographic device and a color power Doppler flow mapping are integrated to the unit. Quantitative assessment of the heart is possible with inclusive callipers (Figure 2). SonoHeart has a storage memory of 50 images and can be connected to a video recorder, a printer, or an external monitor.

Study Population

We studied 114 unselected patients (72 men) with a mean age of 52 ± 17 years, referred to our outpatient clinic for left ventricular (LV) function assessment (n = 60), follow-up of known congenital heart disease (n = 13), follow-up of known valvular disease (n = 15), evaluation of LV hypertrophy (LVH) (n = 15), and evaluation of pericardial effusion (n = 11).

Study Design

All patients underwent 2 consecutive echocardiographic examinations by 2 different investigators: one examination by means of a standard echocardiographic system (SE), Hewlett-Packard (Sonos 5500, Andover, Mass) or Vingmed (System V, Horten, Norway), and the other by means of the

Table 1 Accuracy of left atrial size assessment (111 patients)

	Ultrasound stethoscope		
2D standard echo	Normal	Enlarged	Severely enlarged
<4 cm	87	0	0
4-6 cm	1	21	0
>6 cm	0	0	2

Kappa, 0.974
2D, Two-dimensional.

Table 2 Accuracy of left ventricular size assessment (111 patients)

	Ultrasound stethoscope		
2D standard echo	Normal	Enlarged	Severely enlarged
<5.5 cm	91	1	0
5.5-7 cm	0	19	0
>7 cm	0	0	0

Kappa, 0.969
2D, Two-dimensional

SonoHeart device. Each investigator was blinded to the results of the other investigator.The time spent for the bedside examination with SonoHeart was always less than 5 minutes.

The patients were evaluated on-line for the following parameters: presence of pericardial effusion, left atrial (LA) enlargement (internal diameter >40 mm in the parasternal long axis view), LV enlargement (end-diastolic diameter >55 mm in the parasternal long axis view), LVH (defined as a septal thickness >12 mm), right atrial (RA) enlargement (internal transverse diameter >35 mm in the 4-chamber view), and right ventricular (RV) enlargement (end-diastolic transverse diameter >43 mm in the 4-chamber view). Also, gross morphologic assessment of the valves was performed.

In all patients the global RV function and the LV ejection fraction (EF), and in 34 patients, who where referred for stress echocardiography, the regional wall motion were estimated. With both imaging techniques, the scoring was performed on-line during the examination procedure. Global LV function was defined as normal when the estimated EF was greater than 55%, mildly to moderately reduced when the estimated EF was 35% to 55%, and severely reduced when the estimated EF was less than 35%.The scoring of the regional wall motion for testing the efficacy and feasibility of the SonoHeart was simplified, by dividing the LV into 6 segments (anterior, inferior, septal posterior, septal anterior, lateral, and posterior wall) and by using a 2-point score: 1 for normal wall motion, including mild hypokinesia, and 2 for abnormal wall motion, including severe hypokinesia, akinesia, and dyskinesia.

Figure 1 Photograph of SonoHeart device, hand-held ultrasound imager, used in this study.

Statistical Analysis

The agreement for segmental and global wall motion was assessed from 2 × 2 and 3 × 3 tables with weighted kappa statistics. Kappa values 0.4, between 0.4 and 0.75, and 0.75 or greater were considered to represent poor, fair-to-good, and excellent agreement respectively, based on Fleiss's classification.[1]

RESULTS

Visualization

Three patients had poor echo windows with both imaging techniques and were excluded from the study, leaving 111 patients for analysis.

Agreement

The results for detection of LA and LV enlargement with both examination techniques are summarized in Tables 1 and 2.

The agreement for RV and RA size was 99%. A thrombus in the RA was identified with both imaging techniques in 1 patient.

Pericardial effusion was correctly assessed with SonoHeart in 11 patients and LVH (Figure 3) in 7 of

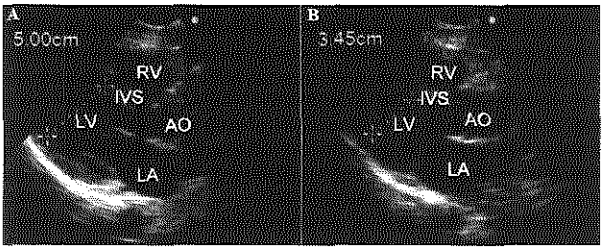

Figure 2 Diastolic (**A**) and systolic (**B**) left ventricular long-axis views of normal subject obtained with SonoHeart device. Measurements of diameter of left ventricle at end-diastole (**A**) and end-systole (**B**) are shown. *LA* = Left atrium; *LV* = left ventricle; *AO* = aorta; *RV* = right ventricle; *IVS* = interventricular septum.

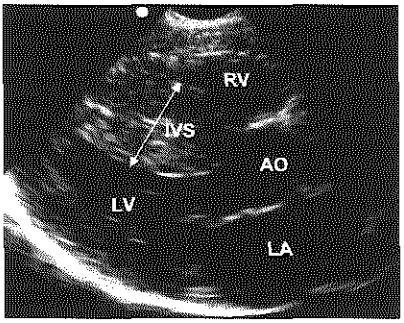

Figure 3 Long-axis view of patient with hypertrophic cardiomyopathy obtained with SonoHeart device (abbreviations as in Figure 2). The *arrow* indicates the increased septal thickness.

8, resulting in an agreement of 100% and 87.5%, respectively. In 1 patient pericardiocentesis was performed under SonoHeart guidance (Figure 4).

In 20 patients, the morphologic abnormalities of the aortic (calcification, Figure 5) and the mitral valve (calcification, prolapse) were identified with the SonoHeart device and confirmed by the SE. Furthermore, the diagnosis of a chordal rupture of the mitral valve was made by SonoHeart and verified by the SE in a patient presenting with acute dyspnea in the outpatient clinic.

Finally, the SonoHeart identified the morphologic characteristics of surgically corrected congenital cardiac abnormalities in 13 follow-up patients, including atrial septum defect (ASD) (Figure 6), ventricular septum defect, tetralogy of Fallot, Ebstein anomaly, transposition of the great arteries, and subvalvular aortic membrane.

Evaluation of Global and Regional Left and Right Ventricular Systolic Function

The agreement between both imaging techniques for all 111 patients was 93% for global and 89% for regional LV systolic function (Tables 3 and 4).

The agreement for global RV systolic function was 99%.

Interobserver Variability

There was a good correlation of the 2 independent observers' evaluations of regional wall motion between the SE (81%) and the SonoHeart device (76%).

DISCUSSION

In the late 1970s, Roelandt et al[2-4] introduced the first portable battery-powered 2D echocardiographic instrument to be used as part of the clinical examination. Today, this vision of the past has become a reality as a result of miniaturization and digital technology.

The SonoHeart device is easy to use, is ultraportable with excellent imaging quality, and gives in addition quantitative information about dimensions within the heart. Our study demonstrates the utility of such a device for assessing pathomorphology and function of the heart, and the results are comparable with those obtained by SE. We included in our study a group of patients with corrected congenital heart disease to test the clinical potential of the SonoHeart device in identifying the complex disease seen in these patients. It has proven to be as reliable as the SE for the rapid

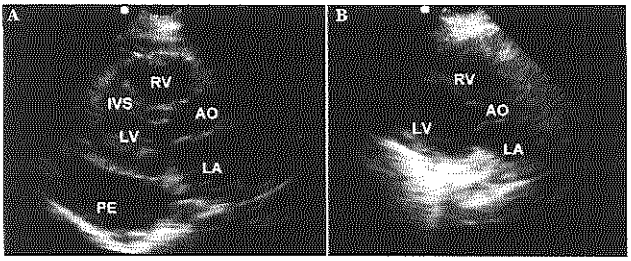

Figure 4 Parasternal long-axis view of patient with pericardial effusion before (**A**) and after pericardiocentesis obtained with SonoHeart device (**B**) (abbreviations as in Figure 2; *PE* = pericardial effusion).

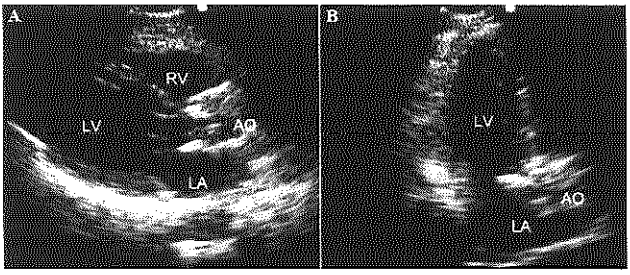

Figure 5 Parasternal (**A**) and apical (**B**) long-axis views of patient with calcified aortic valve stenosis with SonoHeart device (abbreviations as in Figure 2).

detection or exclusion of a morphologic abnormality. This does not indicate though that it can be substituted for the SE because most cardiac congenital diseases require extensive 2D and Doppler analyses.

We proved that SonoHeart can become an extension of physical examination enhancing our clinical senses and increasing the accuracy and sensitivity of diagnosis. The ultraportability and ease of use suggest that similar data and results can be obtained in other clinical scenarios, which are indicated in Table 5. It can be used as a screening tool for cardiac abnormalities such as hypertrophic cardiomyopathy, LVH, ASD, abdominal aorta aneurysm,[5] mitral valve prolapse (MVP), or enlargement of the heart. Prior studies that used limited imaging protocols for most of these diseases (hypertrophic cardiomyopathy,[6] LVH,[7-9] MVP[10]) have provided evidence that a limited imaging study is feasible.

The SonoHeart device can be used as a rapid diagnostic tool in emergency scenarios where rapid decisions are essential. Thus, giving immediate answers about EF and regional wall motion abnormalities, presence of pericardial fluid or tamponade, or the cause of a new murmur in unstable patients, SonoHeart can play a decision-making role.

Taking into account that most of the patients are referred for echocardiography to answer a single clinical question (like follow-up of EF or pericardial effusion after pericardiocentesis or search for the source of embolism), a new strategy of limiting echo services starts to emerge in daily clinical practice.[11] Thus, a focused imaging protocol could be used to screen for the referral disorder and to proceed to a full study only in the discovery of any abnormality. Such a limited echo strategy could be most effectively applied with the use of a hand-held ultrasound device such as SonoHeart. Recently, Bruce et al[5] demonstrated the efficacy and high accuracy of that device in screening patients at risk for abdominal aortic aneurysms.

The implementation of a limited echo or screening policy will lead to cost savings in terms of bene-

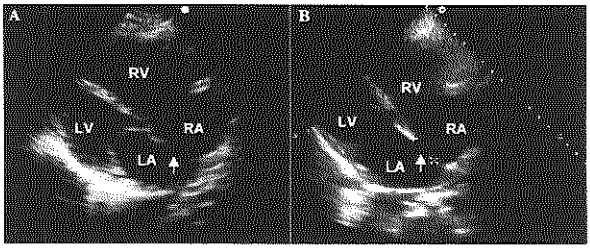

Figure 6 A, Foreshortened apical 4-chamber view of patient with atrial septum defect of secundum type (*arrow*) obtained with SonoHeart device (abbreviations as in Figure 2; *RA* = right atrium). B, Same view obtained with SE system (Hewlett-Packard).

Table 3 Agreement between left ventricular ejection fraction estimated by the SonoHeart device and a standard echocardiographic system

	SonoHeart estimation of EF		
	>55%	35%-55%	<35%
Standard echo estimation of EF			
>55%	61	1	0
35%-55%	5	31	0
<35%	0	2	11

Agreement, 93%.
Kappa, 0.871.
EF, Ejection fraction.
Number of patients: 111. The numbers inside the table express the number of patients.

Table 4 Agreement of regional wall motion analysis between the SonoHeart and a standard echocardiographic system

	SonoHeart	
	Normal	Abnormal
Standard echo		
Normal	92	5
Abnormal	15	92

Agreement, 90%.
Kappa, 0.80.
Number of patients: 34.
Number of segments: 204. The numbers inside the table express the number of segments.

fit to all subjects, reducing the time spent imaging healthy patients.

Limitations

For the evaluation of regional wall motion, the LV was divided into 6 segments and not into 16 segments, which is proposed by the American Society of Echocardiography. Because this was an on-line assessment and we had no recording facilities, we limited the analysis in 6 myocardial segments. The same segments were independently scored later from the SE and compared with the data of the hand-held device. The hand-held device cannot substitute for the SE, but our purpose was to demonstrate the feasibility and efficacy of the SonoHeart device as a screening device in recognizing and distinguishing normal from abnormal wall motion. Within this concept, the study proved that such small devices potentially could be used in acute coronary syndromes to exclude/identify regional wall motion abnormalities. Furthermore, because of the small number of patients who were included, this study should be considered as a pilot study for later wall motion studies.

Another limitation is related to the fact that we focused on 2D evaluation of anatomy and function of the heart, without including the color flow modality. Refinements in the technology of color power Doppler flow mapping in the device since beginning this study have made this now reliable, however.

In Europe, most of the studies are being performed by cardiologists. The SonoHeart instrument should not be used by sonographers but by a trained cardiologist. This study was performed by a junior

Table 5 Clinical utility of the hand-held ultrasound device

Emergency department, CCU, and ICU
Hospital ward rounds
Outpatient clinic
Surgical theater
Cardiac catheter laboratory
Private office practice

staff member who had experience in echocardiography. Training and licensing for noncardiologists to use these devices will become an important issue in the future.

Conclusion

The hand-held ultrasound device, performing as a "real" stethoscope, makes ultrasound imaging an excellent tool immediately available for the diagnosis and assessment of cardiac patients whenever cardiac physical examination is indicated, improving the health care service.

We are grateful to Wim B. Vletter and Jackie McGhie for their expert technical assistance and to Eric Boersma, PhD, for statistical advice.

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CHAPTER 4

ABDOMINAL AORTIC ANEURYSM SCREENING USING A HAND-HELD ULTRASOUND DEVICE

EC Vourvouri, D Poldermans, AFL Schinkel, FB Sozzi, JJ Bax, JRTC Roelandt.
The Thoraxcenter Journal 2002;14:40-42.

ABSTRACT

Aim: To assess the diagnostic potential of a hand-held battery powered ultrasound imaging device (SonoHeart™) in screening of patients for abdominal aortic aneurysm (AAA) using a standard echocardiographic system (SE) as a reference.

Methods and results: 100 hypertensive patients were enrolled. Two independent investigators performed focussed echocardiography of the abdominal aorta with both devices. An AAA was defined as a focal transverse enlargement of the aorta >30mm with the SE.

Results: We studied 65 men and 35 women (aged 60±11 years; mean duration of hypertension: 13±11 years; mean blood pressure: systolic 150±20 mmHg and diastolic 89±11 mmHg). The abdominal aorta was visualised in all patients and the time required for screening was <5 minutes with both imaging devices. SE showed an AAA in 9 (9%) patients. The agreement between both imaging methods was 98%, kappa 0,88. Using SE as the gold standard, the sensitivity and specificity of the hand-held device for screening of the presence of an AAA were 88% and 98% respectively.

Conclusions: Such small hand-held ultrasound devices can achieve efficient and low cost screening of AAA in a high-risk population, minimising the mortality rate from ruptured AAA. Furthermore, they can permit regular follow-up of known small AAAs.

Key Words: Abdominal Aortic Aneurysm, Cardiac Ultrasound, Ultrasound Stethoscope, SonoHeart™

INTRODUCTION

Rupture of an abdominal aortic aneurysm is a devastating event with a perioperative mortality rate of 50% that is if patients reach the hospital in time [1-3]. In contrast, patients undergoing elective aortic surgery experience a perioperative mortality of only 2-3% [4-6]. It is therefore recommended that patients at risk are screened by ultrasound and undergo prophylactic surgery if the diameter exceeds 60 mm [7]. The proposed screening method is ultrasound. Compared to physical examination it is more accurate and in contrast to computerised tomography it is much less expensive, widely available and has comparable diagnostic accuracy [8,9].

The aim of the present study was to evaluate the potential and diagnostic accuracy of a recently developed portable hand-held ultrasound system for screening of AAAs in patients at risk using a standard two-dimensional echographic examination as a reference.

STUDY PATIENTS AND METHODS.

Study population.

One hundred consecutive hypertensive patients visiting the outpatient clinic (65 men, mean age 60 ± 11 years) were enrolled in the study. The investigators performed no physical examination. Patient characteristics are presented in Table 1.

Echographic examination.

The SonoHeart™ (SonoSite Inc, Bothell, Washington, USA) ultrasound system (Fig. 1) is a small portable hand-held ultrasound device (weight 2,4 kg). It is equipped with a 2-4 MHz phased array broadband transducer and operates on a rechargeable lithium ion battery or alternating current. The two-dimensional control settings are comparable to a standard echocardiographic device and a colour power Doppler flow mapping is integrated to the unit. Quantitative assessment of the heart is possible with inclusive linear measurement callipers.

Study design.

All patients underwent two consecutive echocardiographic examinations by two different investigators: one examination by means of a standard echocardiographic system, Hewlett Packard (Sonos 5500;Andover, Mass) or Vingmed (System V; Horten, Norway), and the

other by means of the SonoHeart™ device. Each investigator was blinded to the results of the other investigator. Information about a known or suspected AAA was withheld from the investigators at the time of the examination with both imaging methods. If an AAA (diameter >30 mm) was detected the referring physician was notified.

The scanning of the abdominal aorta was performed from the subcostal position in the midline, approximately 2 cm below the xyphoid with the transducer angled toward the patient's left side. The abdominal aorta was identified as a pulsatile vascular structure. In case of doubt, colour Doppler was used to demonstrate blood flow away from the heart. Measurements were done in the 2D transverse (anteroposterior) plane with both imaging devices. The maximum diameter of the aorta was measured by positioning the callipers from leading edge to leading edge. The inter- and intraobserver variability were 96% and 98% respectively.

Statistical analysis.

Descriptive statistics were reported as mean ±SD or by frequency percentages. The differences between the measurements of the two devices are presented with the Bland-Altman plot graphic [10]. The agreement for the measurements between the two examination techniques was assessed from 2x2 tables using weighted kappa statistics. Kappa values 0,4, between 0,4 and 0,75, and >0.75 were considered to represent poor, fair to good and excellent agreement respectively, based on Fleiss's classification [11].

Table 1 Patients characteristics

Age (years)	60±11
Male, n (%)	65 (65%)
Years of HT	13±11
Heart rate (bpm)	71±11
SBP (mmHg)	150±20
DBP (mmHg)	89±11
BMI (kg/m^2)	27±4

HT=hypertension; SBP=systolic blood pressure;
DBP=diastolic blood pressure;
bpm=beats per minutes; BMI=Body Mass Index.

RESULTS

Echographic examination and agreement.

Visualisation of the abdominal aorta was feasible in all patients with both devices. The average diameter of the abdominal aorta was 23,5±7,7 mm (14,4 range to 67mm) for the SE and 23,1±7,3 mm (13 range to 62,1 mm) for the hand-held device. The SE identified an AAA in 9 (9%) patients. One of these AAAs is shown in Figure 2. The agreement between the two methods in detecting an AAA was 98%, kappa 0,88 (Fig. 3 A).

There was disagreement in two patients. One patient had an aortic dimension of 32,4 mm (AAA) by SE and 27,8 mm (normal) by the hand-held device. Conversely, in one patient the diameter of the abdominal aorta was 31,1 mm (AAA) with the hand-held device versus 27,6 mm (normal) by SE. The Bland-Altman plot confirms the high correlation between the two devices in identifying an AAA (Fig. 3 B). In four out of the nine patients with an AAA CT scan confirmed the diagnoses. In the remaining five patients no further examination was performed due to the small size of the AAA (mean transverse diameter: 35 mm). The time spent to visualise the abdominal aorta was always less than 5 minutes with both examination techniques. Using SE as the gold standard for the detection, the sensitivity and specificity of the hand-held device for screening of the presence of an AAA were 88% and 98% respectively.

Figure 1.

Photograph of the SonoHeart™ device, a hand-held ultrasound imager, used in this study.

Figure 2.

A focal transverse enlargement of an abdominal aorta at a short-axis image detected by the hand-held ultrasound device. The maximum diameter measured was 62 mm versus 67mm measured by the standard echocardiographic system.

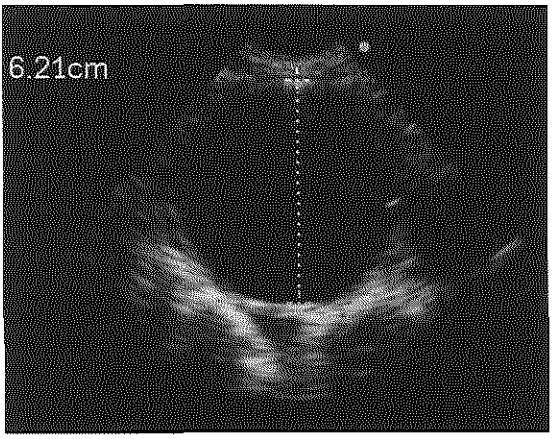
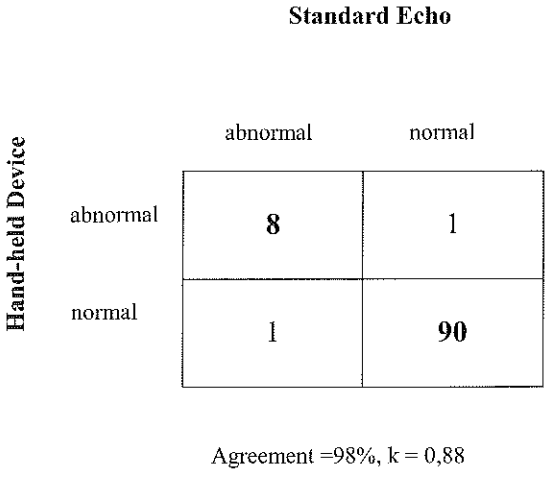


Figure 3.

A. Agreement of dimensions of the abdominal aorta measured by the hand-held device and the standard echocardiographic system. Number of patients:100. The numbers inside the table express the absolute number of patients. Abnormal = patient with an aneurysm of the abdominal aorta.

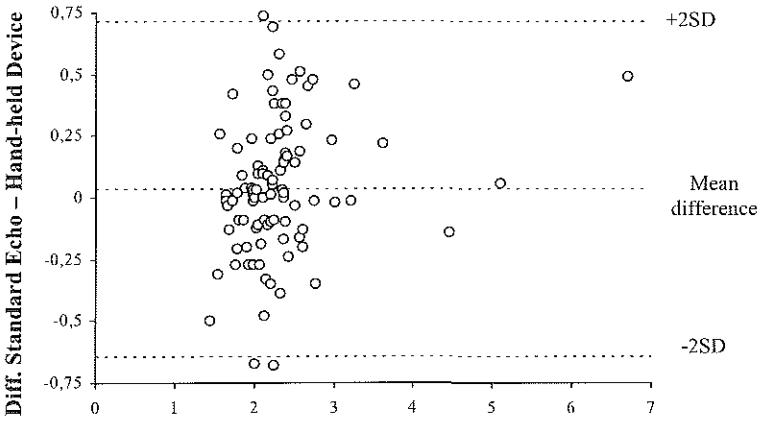
B. Bland-Altman plot, demonstrating the magnitude of the difference between the measurements of the abdominal aorta with the two techniques (differences plotted against their mean average). 2 SD = 2 standard deviations of the mean difference in the measurements of the two devices.

A



Agreement =98%, k = 0,88

B



DISCUSSION

This study demonstrates both the feasibility and diagnostic accuracy of a hand-held ultrasound device in screening for AAA in the outpatient clinic. The agreement between the hand-held device and the standard echo device was excellent. In only 2 out of the 100 patients there was a disagreement in the diagnosis of an AAA.

Early AAA detection can prevent the occurrence of ruptured AAA. The cost-effectiveness of random population screening for AAA has been questioned in the past [12]. However, several studies have shown that screening saves lives [1-6]. The perioperative mortality associated with emergency aneurysm surgery can be as high as 50%, compared to 2-3% for an elective procedure. Mass screening is probably not cost-effective, but selective screening of high-risk patients (male gender, smoking, elderly age (>65 years), hypertension, coronary artery disease and family history) is recommended [13].

Physical examination is unreliable in patients with a small AAA (30-39 mm) since the sensitivity in these patients is only 29%. Albeit the sensitivity of physical examination increases with an increase of the diameter of the AAA it is only 76% in patients with a diameter of more than 50 mm [8]. Computed tomography and magnetic resonance imaging are highly accurate in detecting aneurysms and quantifying their severity. However, they are inappropriate for screening programmes since they are expensive, time consuming and not widely available [14]. Ultrasound on the other hand, because of its low cost and availability has been proven to be safe and efficient for surveillance of small AAAs [7] and seems to be the most appropriate screening tool [15]. A small hand-held device could increase the utility of ultrasound in this field since it is easy to use and ultra-portable. Moreover, such a device could become a practical tool to screen patients at risk in the general practice. This may form the basis for a study to evaluate the cost-effectiveness of selective screening and elective surgery in a population at risk.

The 9% prevalence of AAA in our study group was relatively high. Scott et al [16], defining an AAA by a diameter of >30 mm, evaluated a group of elderly men and women aged 65-80 years and found an overall prevalence of 4,0% in women and 7,6% in men. The high prevalence in elderly men was confirmed by the study of Twomey et al [17]. They screened elderly hypertensive men attending hospital or general practitioner clinics and recorded a prevalence of 11,3% and 6,6% respectively. In a recent study published by Bruce et al [18] who screened hypertensive patients for AAA with a similar with our study device, a prevalence of 8% was found.

Limitations

Using the subcostal position we evaluated only an average length of 14 cm of the proximal abdominal aorta. However, the majority of AAAs are located infra-renally and may also extend into the iliac arteries [19]. Our aim was to test the accuracy and utility of a newly developed hand-held ultrasound device in detecting AAA compared with complicated, state-of the-art, echocardiographic equipment. Within this concept the study proved that such small devices are as accurate in identifying an AAA as standard echocardiographic systems.

Conclusion

The implementation of a selective screening policy can prevent rupture of AAA and thus reduce the mortality rate. Ultrasound seems to be the most appropriate imaging method considering the accuracy, availability and cost. The hand-held ultrasound device, being ultra-portable and inexpensive could become part of the clinical examination in high-risk patient groups performing like an excellent screening tool.

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ABDOMINAL AORTIC ANEURYSM SCREENING USING A HAND-HELD ULTRASOUND DEVICE A PILOT STUDY

EC Vourvouri, D Poldermans, AFL Schinkel, FB Sozzi, JJ Bax, H van Urk et al.
Eur J Vasc Endovasc Surg 2001;22:352-54.

ABSTRACT

This study shows the usefulness of a small, portable hand-held ultrasound device for the screening for abdominal aortic aneurysms.

Key Words: Abdominal Aortic Aneurysm, Hand-held Ultrasound Device

INTRODUCTION

The perioperative mortality associated with emergency abdominal aortic aneurysm surgery can be as high as 50% [1] whereas it is 5-10% for an elective procedure [2]. It is therefore recommended that patients undergo prophylactic surgery if the diameter exceeds 55 mm [3].
The aim of the present study was to evaluate the potential and diagnostic accuracy of a recently developed portable hand-held ultrasound system for screening for AAAs in patients at risk. A standard two-dimensional echographic system was used as a reference (SE).

REPORT

One hundred consecutive hypertensive patients visiting the outpatient clinic were enrolled in the study (Table 1). An AAA was defined as a focal transverse enlargement of the aorta >30 mm with the SE.
All patients underwent two consecutive echographic examinations by two different investigators blinded to each others results. One by SonoHeartTM (SonoSite Inc, Bothell, Washington, USA) (Fig. 1) and one by a standard echocardiographic system [Hewlett Packard (Sonos 5500) or Vingmed (System V)].
Measurements of the abdominal aorta were performed from the subcostal position in the 2D transverse plane with both imaging devices.
The inter –and intraobserver variability were 96% and 98% respectively showing a very good reproducibility.

Descriptive statistics were reported as mean ±SD or by frequency percentages. The agreements between the measurements of the two devices are determined by Bland-Altman analysis and 2x2 tables using weighted kappa statistics.

Visualisation of the abdominal aorta was feasible in all patients with both devices. The SE identified an AAA in 9 (9%) patients. The agreement between the two methods in detecting an AAA was 98%, kappa 0.88 (Fig. 2A). The Bland-Altman plot shows a high correlation between the two devices in identifying an AAA (Fig. 2 B).

Table 1 Patients characteristics

Age (years)	60±11
Male, n (%)	65 (65%)
Years of HT	13±11
Heart rate (bpm)	71±11
SBP (mmHg)	150±20
DBP (mmHg)	89±11
BMI (kg/m^2)	27±4

HT=hypertension; SBP=systolic blood pressure;
DBP=diastolic blood pressure;
bpm=beats per minutes; BMI=Body Mass Index.

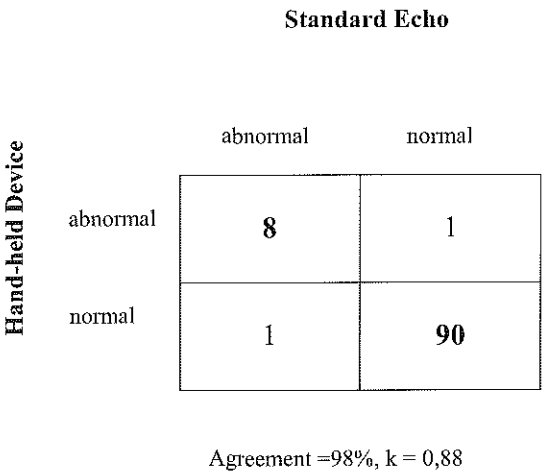
Figure 1.

Photograph of the SonoHeart^{TM} device, a hand-held ultrasound imager, used in this study. It is battery powered and has two-dimensional control settings comparable to a standard echocardiographic device. A calliper is integrated in the unit for dimension measurements.

Figure 2.

A. Agreement of dimensions of the abdominal aorta measured by the hand-held device and the standard echocardiographic system. Number of patients:100. The numbers inside the table express the absolute number of patients. Abnormal = patient with an aneurysm of the abdominal aorta. B. Bland-Altman plot, demonstrating the magnitude of the difference between the measurements of the abdominal aorta with the two techniques (differences plotted against their mean average). 2 SD = 2 standard deviations of the mean difference in the measurements of the two devices. Using SE as the gold standard the sensitivity and specificity of the hand-held device for screening of the presence of an AAA were calculated as well as the positive predictive value (PPV), negative predictive value (NPV), accuracy and likelihood ratio of a positive or a negative test.

A



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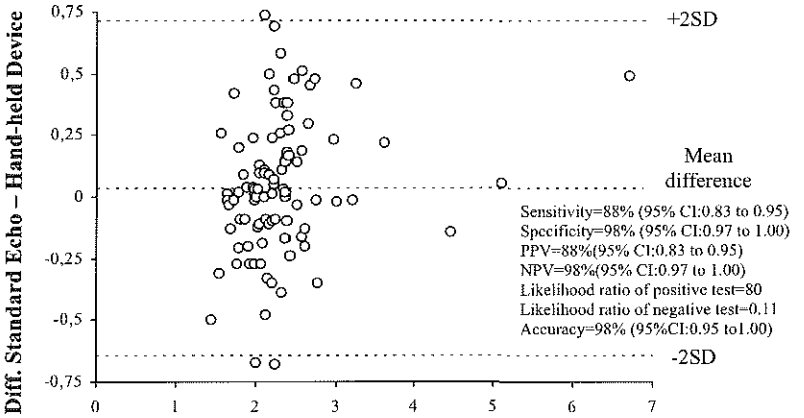

DISCUSSION

This study demonstrates both the feasibility and diagnostic accuracy of a hand-held ultrasound device in screening for AAA in the outpatient clinic. The prevalence of AAA in our study group was in concordance to the results of Bruce et al [4] who screened hypertensive patients with a similar with our study device.

Physical examination is unreliable in detecting AAA since the sensitivity for small AAA (30-39 mm) is 29% and increases to only 76% for aneurysms of more than 50 mm [5]. Computed tomography and magnetic resonance imaging play a significant role whenever details of the aneurysm are required for further management decision.

Ultrasound is recommended for the surveillance of small AAAs [3] and seems to be the most appropriate screening tool. A small hand-held device could increase the utility of ultrasound in terms of the implementation of screening programmes. It is easy to use and gives an instant yes or no regarding the presence of an aneurysm of the abdominal aorta at the bedside. Its cost is about the 1/10th of the price of a high-end SE.

Study limitation: This study was performed by a cardiologist with experience in echocardiography. Training and licensing for using these devices for non-cardiologists will become an important issue in the future.

Conclusion

Small hand-held ultrasound devices could become part of the clinical examination in patients at risk for abdominal aortic aneurysm performing like an excellent screening tool.

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CHAPTER 5

ANEURYSM OF THE ABDOMINAL AORTA

G Sianos, E Vourvouri, K Nieman, JMR Ligthart, A Thury, PJ de Feyter et al.
Circulation 2001;104: e10-e11.

Aneurysm of the Abdominal Aorta

Georgios Sianos, MD; Eleni Vourvouri, MD; Koen Nieman, MD;
Jurgen M.R. Ligthart, BSc; Attila Thuri, MD; Pim J. de Feyter, MD;
Patrick W. Serruys, MD; Jos R.T.C. Roelandt, MD

A 76-year-old man was admitted to the intensive care unit with unstable angina pectoris of Braunwald class IIIB. He was known to have hypertension, which was poorly controlled with medication. Physical examination revealed a pulsating mass in the lower abdomen that was suggestive of an aortic aneurysm. An echocardiographic study with a small, hand-held ultrasound device (SonoHeart, SonoSite Inc) showed an abdominal aortic aneurysm containing thrombotic material (Figure 1). His troponin T level was elevated, and he underwent coronary arteriography, which showed a high-grade stenosis at the bifurcation of left anterior descending artery and the first diagonal branch. The lesion was dilated during the same session, with direct stenting of both branches.

After the intracoronary intervention, intravascular ultrasound imaging of the abdominal aneurysm was performed (motorized pullback with speed of 0.5 mm/s) with a 9 MHz, mechanically rotated imaging transducer (Figure 2). The transducer was rotating in a 9 French, close-end, rounded-tip catheter that was 110 cm in length (Ultra ICE, Boston Scientific).

A multislice spiral computed tomography scan (Somatom plus 4 VolumeZoom, Siemens AG) was also performed (Figure 3). By simultaneous acquisition of four 1-mm slices at a pitch of 5 (5 mm Z-translation per 0.5-s gantry rotation), images of the entire area of the abdominal aorta were acquired within 32 seconds. Contrast between the vessel lumen and surrounding tissues was realized by an intravenous injection of 100 mL of Iomeprol (Bracco-Byk Gulden) at an injection rate of 2.5 mL/s. From the data set, a large stack of axial slices was reconstructed and processed with dedicated volume-rendering software (VoxelView, Vital Images) on a separate graphic workstation.

One month later, the patient underwent surgical resection of the aneurysm. He was asymptomatic at the 6-month follow-up.

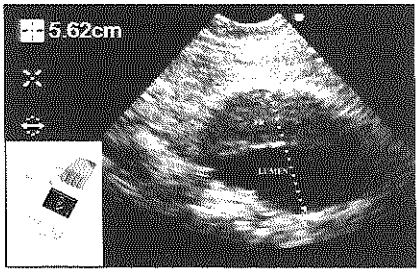

Figure 1. Transverse image of the aneurysm of the abdominal aorta (56 mm in diameter), which contains a large thrombus (TR). The small, hand-held ultrasound device is shown in the insert. Dotted line represents the calipers used for measurement of the diameter of the aneurysm.

From the Department of Cardiology, Thoraxcenter, Erasmus Medical Center Rotterdam, Rotterdam, the Netherlands.

An animated version of this figure can be found at http://www.circulationaha.org

Correspondence to Prof P.W. Serruys, MD, PhD, FESC, FAAC, Department of Interventional Cardiology, Erasmus Medical Center Rotterdam, Thoraxcenter Bd 404, Dr Molewaterplein 40, 3015 GD Rotterdam, the Netherlands. E-mail serruys@card.azr.nl

The editor of Images in Cardiovascular Medicine is Hugh A. McAllister, Jr, MD, Chief, Department of Pathology, St Luke's Episcopal Hospital and Texas Heart Institute, and Clinical Professor of Pathology, University of Texas Medical School and Baylor College of Medicine.

Circulation encourages readers to submit cardiovascular images to the *Circulation* Editorial Office, St Luke's Episcopal Hospital/Texas Heart Institute, 6720 Bertner Ave, MC1-267, Houston, TX 77030.

(*Circulation*. 2001;104:e10-e11.)

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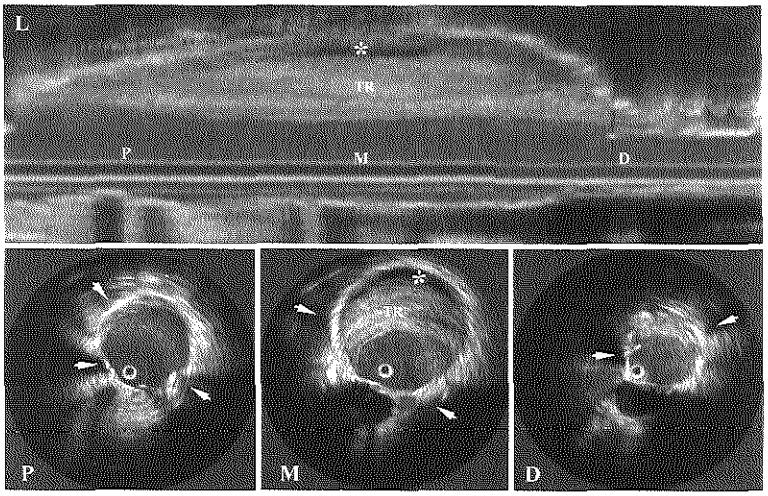


Figure 2. A longitudinal image (L) of the abdominal aortic aneurysm containing thrombus (TR), reconstructed from the sequentially recorded cross-sectional images. The reconstruction was performed on a workstation designed for 3D reconstruction of echocardiographic images (Echoscan, Tomtec). Cross-sectional images corresponding to the proximal (P), middle (M), and distal (D) section of the aneurysm are shown. In the middle section, the gradual decrease in echogenicity toward the outer wall correlates with the organization and age of the thrombotic material. The dark, less echogenic layer (*) adjacent to the outer wall represents chronic organized thrombi whereas the more echogenic layers closer to the lumen indicate more recent thrombosis. The extensive calcifications of the outer wa of the aneurysm are recognized as a highly echogenic rim with acoustic shadowing (arrows). The spontaneous echo-contrast effect within the lumen suggests prothrombotic slow flow and is better recognized from dynamic images, which can be found at http://www.circulationaha.org

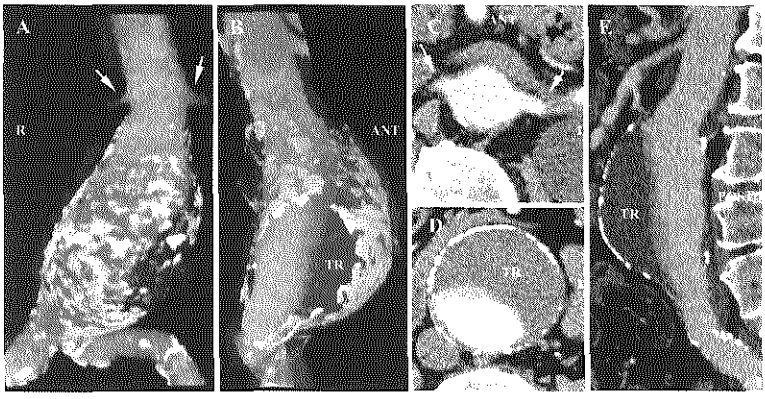


Figure 3. Multislice, computed tomography, 3D volume-rendered images from an anterior (A) and a right lateral (B) perspective in which the large thrombus (TR) is visualized between the contrast-enhanced aortic lumen and the calcifications in the outer wall of the aneurysm. Involvement of the renal arteries (arrows) was excluded (A, C). The thrombus had mainly developed at the anterior side (D), and the diameters measured at the site of maximum dilatation were 64×62 mm. A longitudinal cross-section of the aneurysm, which has been curved along the trajectory of the abdominal aorta and proximal right common iliac artery, is shown in E. ANT indicates anterior POST, posterior; R, right; and L, left.

CHAPTER 6

LEFT VENTRICULAR HYPERTROPHY SCREENING USING A HAND-HELD ULTRASOUND DEVICE.

EC Vourvouri, D Poldermans, AFL Schinkel,
LY Koroleva, FB Sozzi, JJ Bax, JRTC Roelandt.
Eur Heart J 2002, 23:1516-21.

Left ventricular hypertrophy screening using a hand-held ultrasound device

E. C. Vourvouri, D. Poldermans, A. F. L. Schinkel, L. Y. Koroleva, F. B. Sozzi, G. E. Parharidis, J. J. Bax and J. R. T. C. Roelandt

Department of Cardiology, Thoraxcentre, Erasmus Medical Centre Rotterdam, Rotterdam, The Netherlands

Aims To test the diagnostic potential of a hand-held ultrasound device for screening for left ventricular hypertrophy in a hypertensive population using a standard echocardiographic system as a reference.

Methods One hundred consecutive hypertensive patients were enrolled. An experienced investigator performed measurements of the thickness of the anterior septum and posterior wall using the parasternal 2D-long axis view and the end-diastolic dimension of the left ventricle with both imaging devices. Left ventricular hypertrophy was defined as an increase in left ventricular mass $\geq 134\ g \cdot m^{-2}$ for men and $\geq 110\ g \cdot m^{-2}$ for women, when indexed for body surface area and $\geq 143\ g \cdot m^{-1}$ for men and $\geq 102\ g \cdot m^{-1}$ for women, when indexed for height.

Results Sixty-five men and 35 women were studied (age 60 ± 11 years); mean duration of hypertension: 13 ± 11 years; mean blood pressures: systolic 150 ± 20 mmHg and diastolic 89 ± 11 mmHg. The anterior septum and posterior wall were visualized in all patients with both imaging devices. The standard echocardiographic system identified left ventricular hypertrophy by body surface area in 18 (18%) patients and by height in 26 (26%) patients. The agreement between the standard echocardiographic system and the hand-held device for the assessment of left ventricular hypertrophy was 93%, kappa: 0·77 (left ventricular mass/body surface area) and 90%, kappa: 0·76 (left ventricular mass/height).

Conclusions We conclude that hand-held devices can be effectively applied for screening for left ventricular hypertrophy in hypertensive patients.

(Eur Heart J, 2002; 23: 1516–1521, doi:10.1053/euhj.2002.3162)

Key Words: Left ventricular hypertrophy, left ventricular mass, hand-held ultrasound device.

See doi: 10.1053/euhj.2002.3292 for the Editorial comment on this article

Introduction

Left ventricle hypertrophy which expresses end-organ damage from hypertension, is an independent potent marker of cardiovascular risk in arterial hypertension[1–3]. It is considered as an asymptomatic pre-clinical stage of the cardiovascular disease, that may lead to cardiac events[4]. Also, reversal of left ventricular hypertrophy can improve the patient's outcome[5]. Early identification of left ventricular hypertrophy and treatment is therefore the cornerstone of appropriate management. The electrocardiogram (ECG), although commonly available and inexpensive has proven insensitive in detecting the presence of left ventricular hypertrophy[6–8]. Echocardiography is a sensitive means for measurement of left ventricular thickness and has comparable accuracy to the magnetic resonance imaging (MRI) especially in patients with normal left ventricular geometry[9–10]. New and small echocardiographic devices are now becoming available which could be used as screening tools for various pathomorphologies of the heart.

The aim of the present study was to evaluate the potential and diagnostic accuracy of a recently developed portable hand-held ultrasound system for screening for left ventricular hypertrophy in hypertensive patients using a standard two-dimensional echocardiographic system as a reference.

Revision submitted 31 December 2001, and accepted 2 January 2002.

Correspondence: Don Poldermans, MD, PhD, Thoraxcentre, Room Ba 300, Erasmus Medical Centre Rotterdam, Dr. Molewaterplein 40, 3015 GD Rotterdam, The Netherlands.

Table 1 Patients characteristics

Age (years)	60 ± 11
Male, n (%)	65 (65%)
Years of HT	13 ± 11
Heart rate (beats . min $^{-1}$)	71 ± 11
SBP (mmHg)	150 ± 20
DBP (mmHg)	89 ± 11
BMI (kg . m^{-2})	27 ± 4

HT=hypertension; SBP=systolic blood pressure; DBP=diastolic blood pressure; BMI=Body Mass Index.

Study patients and methods

Study population

One hundred consecutive hypertensive patients visiting the outpatient clinic (65 men, mean age 60 ± 11 years) were enrolled in the study. Patient characteristics are presented in Table 1.

Study design

The study protocol consisted of an echocardiographic examination by means of a standard echocardiographic system, Hewlett Packard (Sonos 5500; Andover, Mass, U.S.A.) or Vingmed (System V; Horten, Norway), and an echocardiographic examination by means of a hand-held device. Both studies were performed within 10 days (range 2–7 days) by the same investigator with experience in echocardiography. The order of the second visit was arranged by a study coordinator unaware of the results.

For the evaluation of the intra-observer variability the same observer performed the same test in 30 patients within a week after the last examination, provided they had unchanged characteristics. For the evaluation of inter-observer variability, a second observer, who was blinded to the results of the other investigator, performed the echo study with the hand-held device in 30 patients.

All patients had a baseline electrocardiogram performed. The ECGs were examined for evidence of left ventricular hypertrophy using the Sokolow–Lyon (the sum of the amplitudes of the S wave in V_1 and the R wave in V_5 or V_6, 35 mm) and the sex-specific Cornell criteria (the sum of the amplitudes of the S wave in V_3 and the R wave in aVL, >20 mm in women and >24 mm in men)[11].

All patients were known hypertensives. Blood pressure was measured in the supine position. For the study, we took the average of 12 measurements over 60 min with a 5 min interval using a semi-automatic device (Accutor 2, Datascope, Datascope Corp. CA, U.S.A.).

Echocardiographic methods

Linear measurements of the thickness of the anterior septum and posterior wall and the left ventricular end-diastolic dimension were obtained at the parasternal, two dimensional long axis view with both devices on-line, according to American Society of Echocardiography recommendations[12]. The measurements reported are the mean of five cycles.

Left ventricular mass was calculated from the Devereux-modified American Society of Echocardiography (ASE)-cube equation[10]: 0·80 (1·04 [(IVST+PWT+LVED)^3 − LVED^3]+0·6g. The left ventricular mass index (g . m^{-2}) was calculated by dividing the left ventricular mass by body surface area. Since this index can fail in identifying left ventricular hypertrophy in obese individuals[13] a second index was calculated by dividing the left ventricular mass by height (g . m^{-1}). Body surface area (m^2) was derived from the Du Bois formula[14]: 0·007184 × (weight [kg] $^{0.425}$ × (height [cm])$^{0.725}$. Body mass index (kg . m^2) was derived from the average weight and height.

Left ventricular hypertrophy was defined as an increase in the left ventricular mass index ≥134 g . m^{-2} for men and ≥110 g . m^{-2} for women, when indexed for body surface area[15–17], or ≥143 g . m^{-1} for men and ≥102 g . m^{-1} for women, when indexed for height[13,16].

The inter- and intra-observer variability was 96% and 98%, respectively.

The ultrasound stethoscope

The SonoHeart® (SonoSite Inc., Bothell, Washington, U.S.A.) hand-held ultrasound system (weight 2·4 kg, Fig. 1) was used in this study. It is equipped with a small 2–4 MHz phased array broadband transducer and operates on a rechargeable lithium ion battery or AC power. The two-dimensional control settings are comparable to a standard echocardiographic device and a caliper is integrated in the unit for linear measurements. SonoHeart® has a storage memory of 50 images and can be connected to a video-recorder, a printer or an external monitor. Colour power Doppler flow mapping is also integrated into the system.

Statistics

Descriptive statistics were reported as mean ± SD or by frequency percentages. The difference between the measurements of the left ventricular mass indexed for body surface area and the height of those two devices can be appreciated from Fig. 2 (a) and (b) with the Bland-Altman[18] plot graphic.

The agreement for the measurements between the two examination techniques was assessed from 2 × 2 tables using weighted kappa statistics. Kappa values <0·4, between 0·4 and 0·75, and >0·75 were considered to represent poor, fair to good and excellent agreement, respectively, based on Fleiss's classification[19].

Figure 1 **Photograph of the SonoHeart© device, a hand-held ultrasound imager, used in this study.**

Results

Clinical characteristics

The mean systolic blood pressure was 150 ± 20 mmHg and the diastolic blood pressure 89 ± 11 mmHg. The mean heart rate was 71 ± 11 beats . min^{-1}.

Electrocardiography

Four patients were found to have left ventricular hypertrophy according to the Sokolov–Lyon criteria and 13 according to the Cornell criteria. The sensitivity of the ECG for the detection of left ventricular hypertrophy was, respectively, 5% and 16% and the specificity was, respectively, 96% and 87%.

Measurements and agreement

Visualization was feasible in all patients with both imaging devices. The results of the measurements of the thickness of the anterior septum and the posterior wall and the dimension of the left ventricle with both examination techniques are summarized in Table 2.

The mean left ventricular mass indexed by body surface area was $96{\cdot}2 \pm 36$ g . m^{-2} with the standard echocardiographic system and 103 ± 33 g . m^{-2} with the hand-held device. Using the threshold of ≥ 134 g . m^{-2} for men and ≥ 110 g . m^{-2} for women the standard echocardiographic system identified left ventricular hypertrophy in 18 (18%) patients (nine women and nine men). The agreement between the two methods was 93%, kappa 0·77 (Fig. 3(a)).

The mean left ventricular mass indexed by height was $111{\cdot}5 \pm 43$ g . m^{-1} with the standard echocardiographic system and 120 ± 40 g . m^{-1} with the hand-held device. Using the threshold of ≥ 143 g . m^{-1} for men and ≥ 102 g . m^{-1} for women the standard echocardiographic system identified left ventricular hypertrophy in 26 patients (13 women and 13 men). The agreement between the two methods was 90%, kappa=0·76 (Fig. 3(b)).

Discussion

The presence of left ventricular hypertrophy, calculated as an absolute left ventricular mass has an independent prognostic value on top of age and blood pressure[3,20,21]. Recent studies have reported good reliability for echocardiographic measurements of left ventricular mass[22,23].

Our study showed that this new, hand-held device could be effectively used for screening for left ventricular hypertrophy in office practice. Recently, we demonstrated in a previous study the efficacy and high accuracy of this small imaging device in assessing the pathomorphology and function of the heart enhancing and extending the physical examination to allow goal-oriented examination, such as screening[24].

Although echocardiography can assess left ventricular hypertrophy accurately compared to the 'gold standard' MRI, the World Health Organisation–International Society of Hypertension (WHO–ISH)[25] and the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure[26] do not recommend routine echocardiography in all hypertensive patients. Thus, in patients categorized as high risk patients (having cardiovascular risk factors or an end-organ damage), treatment is already indicated and echocardiography results will not change their management[27]. However, echocardiography is recommended in patients with concomitant heart disease[27,28] and in patients with 'stage one' hypertension (patients with high–normal blood pressure who do not have clinical cardiovascular disease, target organ damage or other risk factors). This is recommended in order to avoid misclassification as 'mild' hypertension in patients that have an end-organ damage as left ventricular hypertrophy[25,26,28,29]. Both, Black and Sheps[30,31] support this view introducing limited echocardiographic protocols.

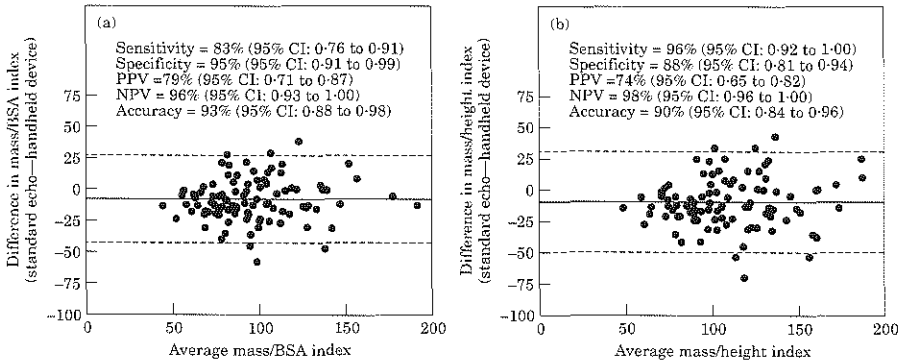


Figure 2 **Bland–Altman plot, demonstrating the magnitude of the difference between the measurements with the two techniques (differences plotted against their mean average) of (a) left ventricular mass indexed for body surface area (BSA) and (b) left ventricular mass indexed for height. SD=2 standard deviations of the mean difference in the measurements of the two devices. Using standard echocardiographic system as the gold standard, the sensitivity and specificity of the hand-held device for screening of the presence of left ventricular hypertrophy were calculated as was the positive predictive value (PPV), negative predictive value (NPV) and accuracy.**

Table 2 Measurements (in cm) of the anterior septum (AS), the posterior wall (PW) and the left ventricular end-diastolic dimension (LVED) with both imaging devices

Type of examination	Mean			SD			Range of measurements		
	AS	PW	LVED	AS	PW	LVED	AS	PW	LVED
Standard echo	1·18	0·92	4·85	0·29	0·20	0·71	0·5 2·2	0·4 1·3	3·4 6·8
Hand-held device	1·21	1·0	4·8	0·26	0·16	0·66	0·7 2·3	0·6 1·4	3·5 6·6
SE-hand-held	−0·03	−0·08	0·05	0·03	0·04	0·05			

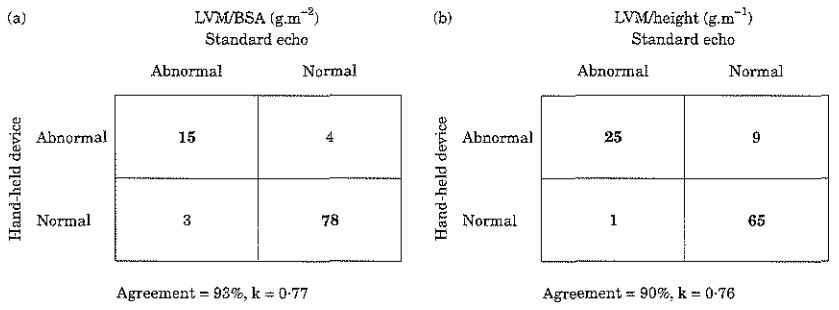
SD=standard deviation; Number of patients:100.

However, the indication of echocardiography in hypertensive patients may be broadened, as this new and inexpensive (~1/10th of the price of a standard echocardiographic system) hand-held ultrasound device becomes widely available. In our view, such small hand-held imaging devices, reducing the cost and being ultra-portable and easy to use, will allow routinely echocardiographic examination in all hypertensive patients. Performing as an extension to physical examination they will provide the clinician with immediate, valuable information about prognosis and risk classification, assisting him in his decision of therapy. Of course, the initiation of aggressive therapy is dependent on not only the presence of left ventricular hypertrophy but also on other parameters such as cardiovascular risk factors and end-organ damage. Furthermore, it is becoming increasingly clear that we should aim for aggressive treatment in most hypertensive patients.

The efficacy of the selected therapy could be followed with the hand-held device by serial estimation of left ventricular mass with every visit at the outpatient clinic. However, the reliability of left ventricular mass measurements depends on many factors, such as the experience of the operator, the age of the patient, the body habitus or the presence of an abnormal left ventricular geometry or emphysema. Furthermore the amount of regression with therapy also plays a significant role in the likelihood of true changes[23].

By analysing the left ventricular geometric pattern, risk stratification can be carried out: patients with normal left ventricular architecture have the best prognosis, those with concentric remodelling or eccentric hypertrophy have intermediate, and those with concentric left ventricular hypertrophy have the worst prognosis[3,25,32]. Furthermore, echocardiography provides us not only with left ventricular mass determination, but with additional valuable information such as left ventricular systolic function or valvular abnormalities.

The method used most frequently for the diagnosis of left ventricular hypertrophy is still standard electrocardiography. Although the ECG has low sensitivity and specificity in recognising left ventricular hypertrophy, it



Number of patients: 100.
The numbers inside the table express the absolute number of patients
Abnormal = left ventricular hypertrophy

Figure 3 **Agreement of the left ventricular mass (LVM) indexed by body surface area (BSA) (a) and by height (b), measured by the hand-held device and the standard echocardiographic system.**

should not be abandoned in patients with known or suspected coronary artery disease as it provides additional information on ischaemia, previous myocardial infarction and rhythm abnormalities.

Left ventricular mass determination, especially with the M-mode based methodology, can be unreliable in an asymmetric heart. In the presence of such an anatomy, the 3D echocardiogram and the ECG-gated magnetic resonance imaging have a higher accuracy and reliability. However, albeit they are superior compared to conventional echocardiographic methods, they have a higher cost and a varied availability[33].

The study was performed by a cardiologist with experience in echocardiography. We believe that physicians can be trained to use this hand-held device and to recognize and distinguish normal from abnormal findings. In case of an abnormal finding or in case of doubt an echocardiographic study with a standard echocardiographic system performed by an experienced investigator should follow. However, training and licensing for use of these devices by non-cardiologists will become an important issue in the future.

Recently, Goodkin *et al.*[34] studied the use of the hand-held device at the point-of-care and compared it to the physical examination. They reported that the use of this device by cardiologists improved the detection of important cardiovascular findings. However, they pointed out that such a hand-held device cannot be a substitute for the final diagnosis, in case of abnormal findings. This is in concordance with the study performed by Spencer *et al.*[35] in critically ill patients. Moreover, Schiller[36] comments that further evaluation of these devices will improve their practical use.

Limitations

In this study, we calculated the left ventricular mass by the Devereux modified (ASE)-cube equation. Due to the absence of the M-mode feature of the hand-held device the measurements were performed with the use of callipers on the two-dimensional parasternal long axis view according to the American Society of Echocardiography recommendations[12]. The same measuring technique was used for both devices for performance comparison.

The hand-held device used in this study had colour power Doppler flow mapping instead of the traditional colour Doppler. Furthermore, it had no Doppler modalities with which to obtain haemodynamic data. By now, spectral Doppler and colour Doppler are integrated in the new generation of personal ultrasound imagers.

Conclusion

The hand-held ultrasound device, being ultra-portable, and inexpensive could become part of the clinical examination in high-risk patient groups, performing like an excellent screening tool.

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CHAPTER 7

SCREENING FOR LEFT VENTRICULAR DYSFUNCTION USING A HAND-CARRIED CARDIAC ULTRASOUND DEVICE

EC Vourvouri, AFL Schinkel, JRTC Roelandt, F Boomsma, G Sianos, M Bountioukos, et al.
Submitted for publication.

ABSTRACT

Background: A hand-carried cardiac ultrasound (HCU) device is a recently introduced imaging device which may be potential useful in the primary care setting.

Aim: To test the screening potential of a HCU for the detection of LV dysfunction by evaluating LV ejection fraction (LVEF) and inferior vena cava (IVC) collapse. A standard echocardiographic system (SE) and plasma brain natriuretic peptide (BNP) measurements were used as a reference.

Methods: Eighty-eight (88) consecutive patients (56 male, age 59±12 years) with suspected LV dysfunction were enrolled in the study. The HCU-LVEF was visually estimated and the SE-LVEF derived by the Simpson's biplane method. A LVEF ≤35% represented LV dysfunction. An IVC collapse of <50% and BNP levels ≥ 15 pmol/L were considered abnormal. The correlation of the HCU-LVEF, the HCU-IVC and BNP to the SE-LVEF and SE-IVC were analysed independently using twoxtwo tables.

Results: Six patients were excluded because of poor echo images. 17/82 patients had LV dysfunction. Both, the HCU and BNP could identify 16 out of these 17 patients. The agreement for LVEF and IVC collapse between SE and HCU was 98% and 96% respectively. The sensitivity of IVC collapse, HCU-LVEF and BNP in identifying patients with LV dysfunction were respectively 30%, 94% and 94%.

Conclusion: A HCU device can reliably be used as a screening tool for LV dysfunction.

Key words: Left Ventricular Dysfunction, Hand-Carried Ultrasound Device, Ultrasound stethoscope, Brain Natriuretic Peptide, Inferior Vena Cava Collapse,

INTRODUCTION

Congestive heart failure is a disease associated with high morbidity, mortality and cost [1-4]. One of the main precursor forms of heart failure is left ventricular (LV) dysfunction, which at early stages is asymptomatic. Appropriate and early treatment can delay if not prevent the development of chronic heart failure [5-7] which makes screening for this disorder worthwhile [8]. However, clinical diagnosis of LV dysfunction with the existing conventional criteria is often difficult and inaccurate [9-11].

Brain natriuretic peptide (BNP) is a cardiac neurohormone secreted in the ventricles as a response to volume and pressure overload [12,13] and may be elevated in patients with LV dysfunction [14,15]. Studies have suggested measurements of plasma BNP levels as a potential new screening method for the diagnosis of patients with impaired LV dysfunction [14-17].

Echocardiography on the other hand, is known to be the screening method of choice for LV dysfunction assessment [3,18-19] but is considered to be unpractical and costly [15,16,20]. Furthermore, the inspiratory changes in diameter of the IVC collapse as an indicator of right-sided filling pressure can be measured by echocardiography [21-22]. However, the utility of this parameter as a screening parameter for LV dysfunction has not been studied yet.

Hand-carried cardiac ultrasound (HCU) devices aim to bring echocardiography into the community setting allowing screening programmes for various cardiac pathologies [23-25].

The purpose of the current study was to test the diagnostic potential of a HCU device (SonoHeart^{TM}, SonoSite Inc and OptiGo^{TM}, Philips Medical Systems) in screening for LV dysfunction by evaluating LV ejection fraction (LVEF) and the IVC collapse. A standard echocardiographic system (SE) evaluating LV function and IVC collapse and BNP concentration measurements were used as a reference.

The HCU device

Two HCU devices were used: the OptiGo^{TM} (Philips Medical Systems) and the SonoHeart^{TM} Plus (SonoSite Inc) (Figure 1).

Both devices operate on a rechargeable battery or AC current and allow quantitative assessment of the heart with inclusive linear callipers. SonoHeart^{TM} has a storage memory of 50 images which can be downloaded into a PC and has also connection to a VCR, a printer or an external monitor. The OptiGo^{TM} uses a CompactFlash card to archive images which also

can be downloaded into a PC. Colour flow Power Doppler and Colour flow Doppler is integrated to the SonoHeart™ and OptiGo™ respectively. SonoHeart™ Plus has in addition M-Mode and pulsed Doppler.

METHODS

Study patients

The study was approved by the Institutional Medical Ethical Committee and informed consent for the study was obtained from all patients.

Eighty-eight (88) consecutive patients referred from the outpatient cardiology clinic to the echo lab with suspected LV dysfunction were included in the study. All patients were clinically stable and cardiac medication was unchanged during the study period.
Patients characteristics are listed in table 1.

Study protocol

Echocardiographic data

The study protocol consisted of two consecutive echocardiographic examinations: one examination by means of a standard echocardiographic system (Sonos 5500, Andover, Mass) and the other by means of a HCU device (SonoHeart™, SonoSite Inc or OptiGo™, Philips Medical Systems). All images were stored in the memory of the portable devices and as digital loops onto optical discs for the SE. Both studies were performed on the same day by two independent cardiologists blinded to each other's results and to medical history or clinical status of the patient.

LVEF evaluation using SE

Images were acquired with the SE at standard cardiac views. We used LVEF, derived with the previously validated modified Simpson's biplane discs method [26], as our gold standard for classification of LV function. The analysis was performed on a computerised off-line station by an independent third observer blinded to the HCU device and BNP results. The cinematic frames corresponding to end-diastole and end-systole were selected from 2-chamber and 4-chamber views.

LVEF evaluation using a HCU device

Global LV systolic function was estimated visually from the same with the SE cardiac views in all patients. Normal LV systolic function was defined by normal LV end-diastolic (≤ 5.5 cm) and end-systolic (≤3.5 cm) dimensions and no major wall motion abnormalities [27] whereas EF≤35% was considered to represent a severely reduced LV function.

IVC measurements

The expiratory and inspiratory IVC diameter and percent collapse were measured with SE and HCU devices from the subcostal view with the patient in supine position. The diameter was measured within 2 cm of the right atrium origin of IVC. In case of quiet respiration and minimal IVC variation the patient was asked to suddenly inhale ("sniff") and the subsequent IVC was measured (Figure 2). The collapse index (IVC-CI) was calculated by taking the difference of the two dimensions and dividing it by end-expiratory IVC dimensions. An IVC-CI < 50% represented an elevated right atrium (RA) pressure (>10 mmHg) [22].

Measurement of plasma BNP

Before the echocardiographic assessments, blood samples were obtained from the antecubital vein of all patients after they had rested for at least 15 minutes. Blood was collected into chilled tubes containing edetic acid (EDTA) and aprotinin (1.9 mg and 100 klU/ml blood, respectively). Plasma samples were centrifuged promptly (1111g for 10 minutes) and stored at -80°C until final analysis. BNP was measured using a standard commercially available immunoradiometric assay kit (Shionoria BNP kit, Shionogi, Osaka, Japan). Results of BNP concentration were received within 1 month from the echocardiographic examination. A BNP level of ≥ 15 pmol/L was considered to represent severe LV dysfunction and derived from a large study population of more than one thousand patients in our centre.

Invasive hemodynamic data

Right-sided heart catheterisation was performed in a subgroup of 20 patients to compare invasively obtained RA pressure measurements to the RA pressure estimated echocardiographically by the IVC collapse. The hemodynamic data were acquired with fluid-filled Swan-Ganz catheters (Baxter Healthcare Corp., Edwards Critical Care Division, Irvine, California) immediately after the echocardiographic study with the HCU device and before any invasive interventions. Normal RA pressure was considered ≤ 10mmHg. Medication

remained unchanged during the study period. Blood samples for BNP were obtained from all the patients prior to invasive interventions and results were compared to invasive data.

Statistical analysis

Descriptive statistics were reported as mean ± SD for continuous variables and as percentages for categorical variables. The agreement for the two examination techniques in evaluating LVEF and IVC-CI measurements were assessed from 2X2 tables using weighted kappa statistics. The same statistical method was used for the agreement between BNP measurements versus LVEF and between RA pressure measured invasively versus the echocardiographically estimated RA pressure. Kappa values <0.4, between 0.4 and 0.75, and >0.75 were considered to represent poor, fair to good and excellent agreement respectively, based on Fleiss's classification [28]. Differences between proportions were compared using the Chi-square test. The Student's t test was used to compare continuous variables. A value of $p<0.05$ was considered statistically significant.

RESULTS

Patients characteristics

Eighty-eight (88) patients (52 male, age 59±12) referred for echocardiography with suspected LV dysfunction were included in the study. Out of the initial 88 patients, 6 were excluded from the study due to poor visualisation of the LV (2 patients), and IVC (4 patients) leaving 82 patients for analysis. Sixty-four out of 82 patients were classified according to the New York Heart Association functional class I or II, 14 were class III and 4 patients were class IV. The classification was performed by an investigator blinded to the results of the echocardiographic examinations.

Echocardiographic data

Out of the 82 patients to analyse, 17 had an EF ≤35% as assessed by the SE Simpson's biplane discs method. The HCU examination detected 16/17 patients showing a sensitivity of 94% and specificity of 100% in the diagnosis of LV dysfunction (table 2A).

The agreement between the two imaging techniques for the IVC-CI was very good (96%, kappa=0,87) (table 3A). However, there was no correlation between IVC-CI and LVEF assessed by SE (agreement:76%,kappa=0.19) (table 3B).

BNP data

Results of BNP were available for all 82 patients. BNP levels were elevated in 16 out of the 17 patients with LV dysfunction. However, in 8 patients with normal LVEF the BNP levels were also elevated resulting in a sensitivity of BNP in diagnosing patients with LV dysfunction of 94% and a specificity of 88% (table 2B).

Subgroup analysis

20 patients underwent a right-sided heart catheterisation as part of diagnostic procedure. The characteristic data of the patients are listed in table 4. The mean RA pressure measured invasively was 8±9 mmHg. The agreement for the measurement of the RA pressure between the two techniques was 95%, kappa 0.9 (table 5). The correlation between BNP and invasively measured RA pressure was poor (60%, kappa=0.29).

Table 1. Baseline characteristics of the 88 patients with suspected LV dysfunction

	N (%)
Age (years)	52±12
Male, n	57 (59%)
History of MI	34 (39%)
HT, known	15 (17%)
DM, treated	9 (10%)
No history of cardiovascular disease	32 (36%)
Beta-blockers	36 (41%)
Nitrates	15 (17%)
Calcium-antagonists	15 (17%)
Diuretics	12 (14%)
Aspirin/anticoagulants	40 (45%)
Lipid-lowering agents	37 (42%)

CAD=coronary artery disease; MI=myocardial infarction;
HT= hypertension; DM=diabetes mellitus.

Table 2 Agreement between (A) a HCU device and (B) BNP measurements and a standard echo in the assessment of LVEF.

A.

LVEF-(HCU)	LVEF (SE): abnormal	LVEF (SE): normal
abnormal	**16**	0
normal	1	**65**

Agreement =99%, kappa =0.96.
Sensitivity=94% (95%CI:0.77-0.77)
Specificity=100% (95%CI:0.95-0.95)
PPV=100% (95%CI:0.82-0.82)
NPV=98% (95%CI:0.94-0.94)

B.

BNP	LVEF (SE): abnormal	LVEF (SE): normal
abnormal	**16**	8
normal	1	**57**

Agreement =89%, kappa =0.71.
Sensitivity=94% (95%CI:0.73-0.99)
Specificity=87% (95%CI:0.82-0.89)
PPV=67% (95%CI:0.51-0.70)
NPV=98% (95%CI:0.92-1.0)

No of patients: 82.
The numbers inside the tables express the absolute number of patients.
Abnormal LVEF: ≤35%;
Abnormal BNP: ≥15 pmol/L

Table 3. (A) Agreement between a HCU device and a standard echo in the assessment of IVC collapse and (B) correlation between IVC collapse and LVEF

IVC(SE)

IVC-CI (HCU)	abnormal	normal
abnormal	**12**	1
normal	2	**67**

Agreement =96%, kappa =0.87.
Sensitivity=86% (95%CI:0.64-0.92)
Specificity=98% (95%CI:0.94-1.0)
PPV=92% (95%CI:0.68-1.0)
NPV=97% (95%CI:0.93-0.98)

LVEF (SE)

IVC-CI (HCU)	abnormal	normal
abnormal	**5**	8
normal	12	**57**

Agreement =76%, kappa =0.19.
Sensitivity=30% (95%CI:0.12-0.49)
Specificity=88% (95%CI:0.83-0.93)
PPV=38% (95%CI:0.16-0.64)
NPV=83% (95%CI:0.78-0.87)

No of patients: 82.
The numbers inside the tables express the absolute number of patients.
LVEF=left ventricular ejection fraction.
IVC-CI=inferior vena cava collapse index
Abnormal LVEF: ≤35%;
Abnomal IVC-CI: < 50%.

Table 4.

Baseline characteristics of 20 patients that underwent right-sided heart catheterisation

	N
Age (years)	60±5
Male	13
Hypertension	6
DM	3
Known or suspected CAD	19
Dilated cardiomyopathy	1

CAD=coronary artery disease; DM=diabetes mellitus.

Table 5.

Agreement between echocardiographically versus invasively assessed right atrium pressure (RAP)

		(RAP) Invasive measurements	
		abnormal	normal
(RAP) HCU device	abnormal	7	0
	normal	1	12

No of patients: 20.
Agreement =95%, kappa =0.89.
Sensitivity=87% (95%CI:0.57-0.57)
Specificity=100% (95%CI:0.79-0.79)
PPV=100% (95%CI:0.65-0.65)
NPV=92% (95%CI:0.74-0.74)
The numbers inside the tables express the absolute number of patients.
Abnormal RAP: > 10 mmHg.
An IVC collapse <50% with the HCU device was considered to represent abnormal RAP.

Figure 1.
Photograph of the two ultrasound stethoscopes used in this study. (A) The OptiGo™ and (B) the SonoHeart™ plus.

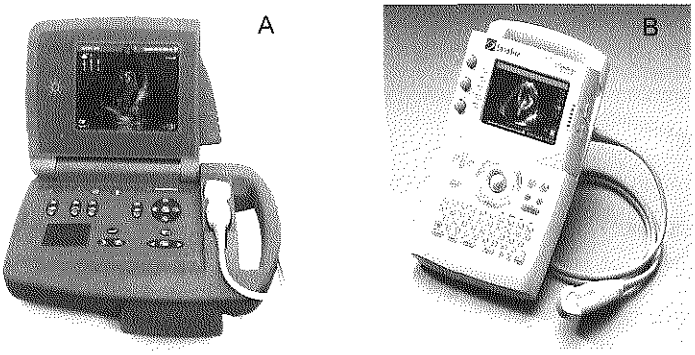
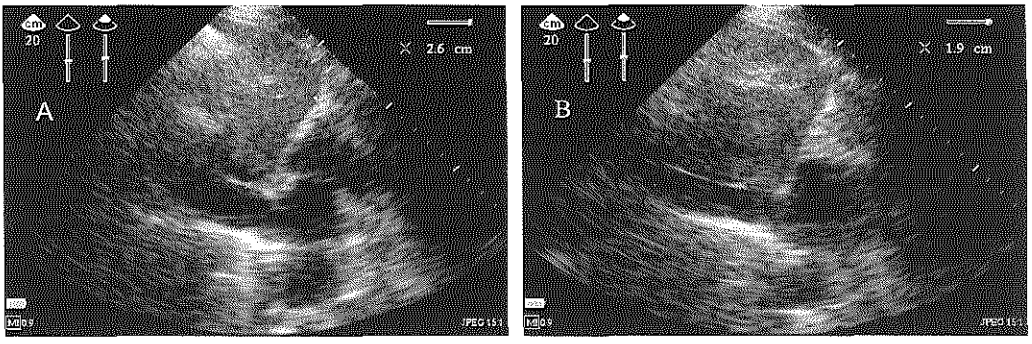


Figure 2.
Imaging of the inferior vena cava during expiration (A) and inspiration (B). A collapse of less than 50% is present, indicating and elevated right-sided filling pressure (OptiGo™).



DISCUSSION

Heart failure and LV systolic dysfunction occur frequently, especially in the elderly population and are related to poor prognosis and considerable health-care cost [3]. Early recognition and initiation of appropriate treatment can improve survival [6]. However, diagnosis of LV dysfunction, especially in asymptomatic patients, may be difficult to assess by physical examination only, even when routine lab values, electrocardiograms and chest X-rays are added [29].

BNP is a 32 amino acid polypeptide containing a 17 amino acid ring structure common to all natriuretic peptides. The source of BNP is the cardiac ventricles and its release is directly proportional to ventricular volume expansion and pressure overload [12,13]. BNP levels are elevated in patients with heart failure and LV dysfunction. Also the effect of treatment in these patients can be monitored with repeated BNP measurements, as suggested by Troughton et al [30]. Furthermore BNP levels seem to be an independent predictor of long-term survival after myocardial infarction [31] and all cause mortality for patients with LV dysfunction [32, 33]. BNP measurements have therefore been proposed as a new simple and inexpensive screening tool for LV dysfunction [14-17, 34,35]. Furthermore the European Society of Cardiology has recently incorporated the BNP measurements into the diagnosis of heart failure [18]. BNP levels are useful in "ruling out" this disorder due to very high negative predictive values, especially in untreated patients. In accordance with previous studies we demonstrated that BNP measurements show high sensitivity in detecting patients with LV dysfunction.

However, we have to take into account that BNP, as an indicator of raised intracardiac pressure, can be elevated in various forms of heart disease besides LV systolic dysfunction including atrial fibrillation, LV diastolic dysfunction, LV hypertrophy and significant valve disease [36-37]. This may explain our results regarding BNP measurements.

Echocardiogaphy as a screening tool for LV dysfunction

According to the guidelines of the European Society of Cardiology, objective evidence of LV dysfunction must be added to clinical symptoms to establish the diagnosis of heart failure. Echocardiography has been proposed to be the screening method of choice to demonstrate cardiac dysfunction [18,19].

However, echocardiography is considered not cost-effective as a screening tool, especially for patients with low probability of cardiac dysfunction, and its availability is often limited in the

different clinical settings. Newly developed HCU devices offer high image quality, ultra-portability and significantly lower capital cost (1/10th of the cost of a SE). The value of such devices for screening for various cardiac pathologies has been shown in previous studies [23-25, 27, 38-39]. The main finding of the current study was that a HCU device, estimating LVEF, is a sensitive tool for screening for LV dysfunction as assessed by SE.

We tested furthermore the hypothesis of diagnosing LV dysfunction by assessing the percentage collapse of IVC. However, this parameter appeared to be of low sensitivity (30%) and positive predictive value (38%) for the detection of LV dysfunction with both devices, SE and HCU echocardiography. To our knowledge, this is the first study that evaluated the parameter of the percentage collapse of IVC as a potential screening parameter for LV dysfunction. In the contrary and as previously shown [22], the correlation of the echocardiogaphically estimated RA pressure, assessed by the IVC collapse, compared to the invasively assessed RA pressure (agreement 95%).

Echocardiography, can provide non-invasively, additional valuable information about other significant abnormalities beyond LV function. Thus, LV hypertrophy, valvular abnormalities or mass lesions can be diagnosed instantly with echocardiography but could be missed by physical examination or a blood test. Furthermore, the addition of the Doppler feature in some of these devices enables the differentiation between systolic and diastolic dysfunction.

Use of ultrasound stethoscopes

The American Society of Cardiology recommends Level I of training as an absolute minimal level required for the use of HCU devices [40]. Studies have shown that minimal echo training may enable physicians to use HCU for interpreting simple abnormalities with high efficacy and accuracy [41-42].

Limitations

The HCU devices used in this study were SonoHeart plus™ and OptiGo™. Although the former has two additional modalities (pulsed Doppler and the M-Mode), we used only the 2D feature for the LVEF and the IVC collapse evaluation to avoid bias between the two devices. There are therefore no data about the diastolic LV function of the heart or flow data.

Furthermore no additional data about other cardiac abnormalities were reported since the purpose of the study was to test the potential of a HCU device as a screening tool for LV dysfunction.

CONCLUSION

Echocardiography is a most practical tool to demonstrate cardiac dysfunction. The HCU devices lead to incorporation of echocardiography into the physical examination and can broaden the availability of echocardiography allowing screening programmes for the identification of patients with LV dysfunction.

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CHAPTER 8

THE INFLUENCE OF LEFT VENTRICULAR MYOCARDIAL CONTRACTILE RESERVE DURING DOBUTAMINE STRESS ECHOCARDIOGRAPHY ON ATRIAL NATIURETIC PEPTIDE AND BRAIN NATRIURETIC PEPTIDE.

AFL Schinkel, EC Vourvouri, J J Bax, F Boomsma, M Bountioukos, V Rizzello et al.
Submitted for publication.

ABSTRACT

Left ventricular (LV) dysfunction is correlated with elevated natriuretic peptides, however the presence of myocardial contractile reserve may inversely influence natriuretic peptide levels in patients with reduced LV function.

Plasma atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) were determined in 66 consecutive patients referred to dobutamine stress echocardiography for the evaluation of myocardial viability. ANP and BNP were measured using immunoradiometric assays. Left ventricular ejection fraction (LVEF) was assessed by echocardiography at rest. Echocardiograms were analyzed using a 16-segment 5-point model. Contractile reserve was defined as an improvement of segmental wall motion score by ≥1 grade following infusion of low-dose dobutamine (10 μg/kg/min) in ≥2 severely dyssynergic segments.

ANP and BNP plasma concentrations were higher in patients with a LVEF≤35% compared to patients with a LVEF>35% (ANP: 11.1 ± 9.7 versus 34.4 ± 37.0, $p<0.0005$, BNP: 62.4 ± 79.0 versus 11.6 ± 14.0 pmol/L, $p<0.0005$, respectively). The presence of contractile reserve influenced the ANP and BNP levels in patients with wall motion abnormalities. Patients with a preserved myocardial contractile reserve had lower ANP and BNP levels than patients without contractile reserve (ANP: 15.7 ± 8.0 versus 44.8 ± 41.9, $p<0.05$, BNP: 17.9 ± 12.0 versus 78.3 ± 89.4 pmol/L, $p<0.05$, respectively). Cardiovascular medical therapy, including beta-blockers and ACE-inhibitors, was comparable between the patient groups.

Plasma natriuretic peptide levels are elevated in patients with LV dysfunction. However, in the presence of preserved myocardial contractile reserve, relatively low ANP and BNP levels are present.

Key words: natriuretic peptides, contractile reserve, left ventricular dysfunction, heart failure

INTRODUCTION

Ischemic left ventricular (LV) dysfunction is the principal cause of congestive heart failure, which is associated with a poor prognosis [1-3]. The management of these patients is challenging, whereas the prevalence of congestive heart failure is increasing over the last decade [2]. Substantial reductions of morbidity and mortality can be achieved with medical therapy, additionally coronary revascularization may improve outcome in patients with severe ischemic LV dysfunction with a preserved myocardial contractile reserve [4-6].

Recently, atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) have been proposed for the detection and management of patients with LV dysfunction [7-11]. ANP is a cardiac hormone that is synthesized and secreted primarily in atrium, whereas BNP is produced in the ventricles in response to changes in wall stretch. Plasma natriuretic peptide concentrations may be elevated in patients with LV dysfunction, and elevated ANP and BNP levels are related to an adverse outcome [7-11]. Previous studies demonstrated that a preserved myocardial contractile reserve is related to a favorable outcome in patients with LV dysfunction. Currently, the relation between the presence of myocardial contractile reserve and plasma natriuretic peptides is not clear. In this study, we investigated the effect of myocardial contractile reserve on plasma ANP and BNP levels in patients referred to dobutamine stress echocardiography with a varying degree of heart failure.

METHODS

Patient population, study protocol

The study population consisted of 66 consecutive patients referred to dobutamine stress echocardiography for the evaluation of known or suspected coronary artery disease. Patients with primary cardiomyopathy, concomitant significant valvular disease, or left ventricular hypertrophy were not included. Plasma ANP and BNP concentrations were determined using immunoradiometric assays. All patients underwent resting echocardiography to assess the LV ejection fraction (LVEF) and to identify dysfunctional myocardial tissue. Left ventricular myocardial contractile reserve was assessed during low-dose dobutamine stress echocardiography. The local medical ethics committee approved the study protocol and all patients gave informed consent.

Cardiac peptide measurements

Before stress echocardiography a blood sample was drawn from a peripheral vein, after the patient had rested for at least 30 minutes in a supine position. The blood sample was drawn into a pre-chilled tube containing edetic acid (EDTA, 1.9 mg/ml) and the protease inhibitor aprotonin (Trasylol, 100 kIU/ml) to prevent breakdown of the cardiac peptides. The sample was placed on ice and promptly centrifuged at 3000 rpm (4°C) for 10 minutes. The plasma was separated and stored at -80°C. Plasma concentrations of ANP and BNP were determined using standard commercially available immunoradiometric assay kits (Shionoria ANP and BNP kits, Shionogi, Osaka, Japan).

Echocardiography

A commercially available imaging system (Hewlett Packard Sonos 5500, Andover, Mass.) and a 1.8 MHz transducer using second harmonic imaging to optimize endocardial border visualization were used. Two-dimensional imaging was performed with the patient in the left lateral position; standard views were recorded on optical disk (cine loops).

After the venous blood samples were drawn, dobutamine stress echocardiography was performed to assess the contractile reserve in dysfunctional myocardium. Following the resting echocardiographic study, dobutamine was administered intravenously, starting at a dose of 5 μg/kg body weight per minute for 5 minutes, followed by a 10 μg/kg/min dose for 5 minutes (low-dose). Incremental doses of 10 μg/kg/min dobutamine were given at 3-minute intervals up to a dose of 40 μg/kg/min, and atropine was added if target heart rate was not achieved.

Global LV function, assessment of LVEF

The LVEF was determined off-line by the 2-dimensional biplane disk method using the modified Simpson's rule [13]. The endocardial borders of the 2- and 4-chamber apical views were digitally traced at end-diastole and end-systole. Subsequently, the LV end-diastolic and end-systolic volumes ejection fraction were measured and the LVEF was calculated. A LVEF ≤35% was considered abnormal.

Regional LV function, segmental analysis

Two experienced observers, unaware of the clinical data, scored the digitized echocardiograms offline. In case of disagreement, a majority decision was achieved by a third

observer. The left ventricle was divided into 16 segments according to the American Society of Echocardiography [12]. Regional wall motion and systolic wall thickening were scored using a 5-point grading scale: 1=normal, 2=mildly hypokinetic, 3=severely hypokinetic, 4=akinetic, 5=dyskinetic. Segments with severe hypokinesia, akinesia or dyskinesia were considered abnormal. The wall motion score index (WMSI) was calculated as the sum of the segmental scores divided by the number of analyzed segments. Contractile reserve was defined as an improvement of segmental wall motion score by ≥1 grade following infusion of low-dose dobutamine (10 μg/kg/min) in ≥2 severely dyssynergic segments. Ischemia was defined as new or worsened wall motion abnormalities during high-dose dobutamine stress indicated by a deterioration of segmental wall motion score by ≥1 grade.

Statistical analysis

Values are expressed as mean ± SD, when appropriate, percentages are rounded. Continuous variables were compared using the Student t-test for unpaired samples. Differences between proportions were compared using the Chi-square test. A value of $p<0.05$ was considered statistically significant.

RESULTS

Patient characteristics

The clinical characteristics of the 66 patients are presented in Table 1. A total of 44 patients were in New York Heart Association (NYHA) functional class I/II, 22 in class III/IV.

Global function, LVEF

The LVEF at rest was on average 47±15%, 21 patients had a LVEF≤35%. Dobutamine-stress echocardiography was performed in all patients without side effects. The hemodynamic changes in response to low-dose dobutamine infusion are presented in Table 2.

Wall motion analysis

Segmental wall motion abnormalities were present in 27 patients. Of these patients, 13 patients had a preserved myocardial contractile reserve, the remaining 14 patients had no contractile reserve. The clinical characteristics were comparable in patients with and in

patients without contractile reserve (see Table 3). Patients with a preserved contractile reserve less often had a history of myocardial infarction compared with patients without contractile reserve.

Natriuretic peptide concentrations versus LVEF

The plasma levels of each natriuretic peptide were significantly elevated in patients with an abnormal LV function. Figure 1 demonstrates that the plasma ANP concentrations were significantly higher in the patients with a LVEF≤35% compared to patients with a LVEF>35% (34.4 ± 37.0 versus 11.1 ± 9.7 versus, $p<0.0005$). In line with this, plasma BNP concentrations were higher in patients with a LVEF≤35% than in those with an LVEF>35% (62.4 ± 79.0 versus 11.6 ± 14.0 pmol/L, $p<0.0005$, see Figure 2).

Natriuretic peptide concentrations versus contractile reserve

The presence of contractile reserve influenced the natriuretic peptide concentrations in patients with wall motion abnormalities. The patients with a preserved myocardial contractile reserve had a lower ANP concentration than the patients without contractile reserve (15.7 ± 8.0 versus 44.8 ± 41.9, $p<0.05$, see Figure 3). Also, plasma BNP levels were lower in patients with a preserved myocardial contractile reserve than in patients without contractile reserve (17.9 ± 12.0 versus 78.3 ± 89.4 pmol/L, $p<0.05$, respectively, Figure 4).

Table 1. Baseline characteristics

Men / Women	41 (62) / 25 (38)
Age (years)	63 ± 13
NYHA functional class	1.8 ± 1.0
LVEF (%)	47 ± 15
Ischemia	18 (27)
Diabetes mellitus	2 (3)
Hypercholesterolemia	20 (30)
Smoking	8 (12)
History	
Myocardial infarction	19 (29)
Coronary angioplasty	3 (5)
Coronary bypass surgery	10 (15)
Medical therapy	
Beta-blockers	20 (30)
Calcium channel blockers	10 (15)
Nitrates	8 (12)
ACE-inhibitors	13 (20)
Diuretics	8 (12)
Digoxin	5 (8)
Aspirin	26 (39)
Cholesterol lowering drugs	20 (30)

Data are presented as number (%).

Table 2. Hemodynamic data during dobutamine infusion

	Baseline	*5 μg/kg/min*	*10 μg/kg/min*
Heart rate (bpm)	74 ± 15	81 ± 22*	90 ± 26* †
Systolic BP (mmHg)	131 ± 22	132 ± 25	131 ± 23
Diastolic BP (mmHg)	76 ± 12	75 ± 13	72 ± 11*
Rate pressure product	9595 ± 2446	10554 ± 3039	11693 ± 3862 †

Data presented are mean value ± SD. * $p<0.05$ versus baseline. † $p<0.05$ versus 5 μg/kg/min dobutamine infusion stage. BP = blood pressure.

Table 3. Clinical characteristics in patients with and without contractile reserve.

	CR+	CR-	P-value
Men / Women	10 (77) / 3 (23)	9 (64) / 5 (36)	NS
Age (years)	63 ± 13	66 ± 12	NS
NYHA functional class	2.2 ± 0.8	2.8 ± 0.8	NS
LVEF (%)	39 ± 8	33 ± 14	NS
Ischemia	7 (54)	7 (50)	NS
Diabetes mellitus	0 (0)	1 (7)	NS
Hypercholesterolemia	2 (15)	4 (29)	NS
Smoking	0 (0)	2 (14)	NS
History			
Myocardial infarction	4 (31)	11 (85)	<0.05
Coronary angioplasty	0 (0)	1 (7)	NS
Coronary bypass surgery	2 (15)	6 (43)	NS
Medical therapy			
Beta-blockers	3 (23)	8 (57)	NS
Calcium channel blockers	2 (15)	4 (29)	NS
Nitrates	1 (8)	3 (21)	NS
ACE-inhibitors	2 (15)	7 (50)	NS
Diuretics	2 (15)	5 (36)	NS
Digoxin	1 (8)	4 (29)	NS
Aspirin	4 (31)	10 (71)	NS
Cholesterol lowering drugs	1 (8)	3 (21)	NS

Data are presented as number (%).

Figure 1
Plasma ANP concentrations in patients with a LVEF>35% and in patients with a LVEF≤35%.

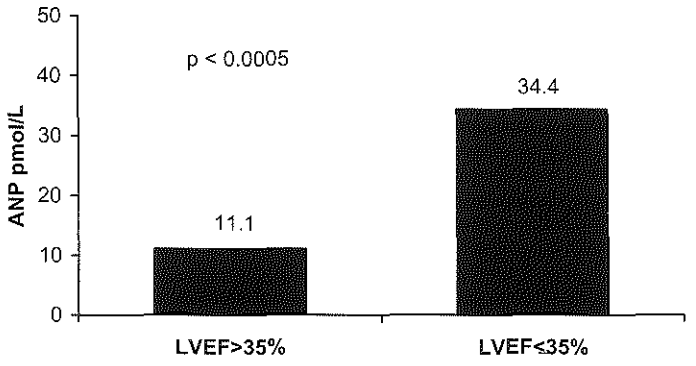


Figure 2
Plasma BNP concentrations in patients with a LVEF>35% and in patients with a LVEF≤35%.

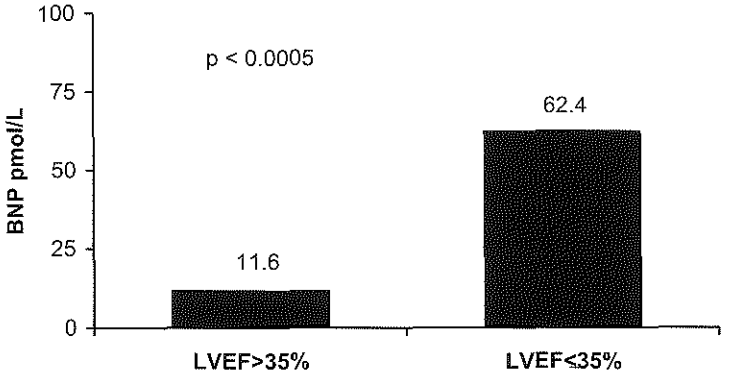


Figure 3
Plasma ANP concentrations in patients with wall motion abnormalities with and without a preserved left ventricular myocardial contractile reserve.

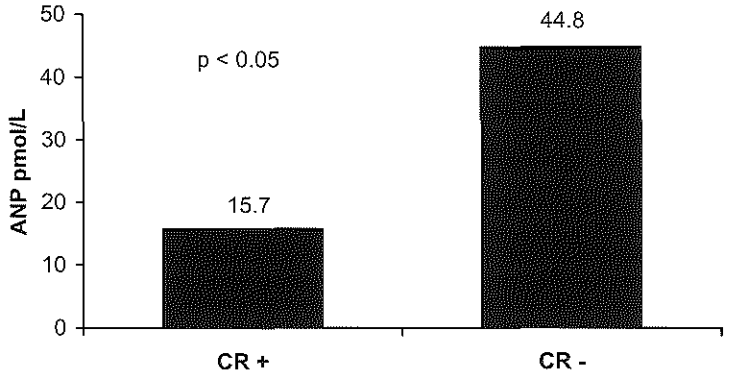
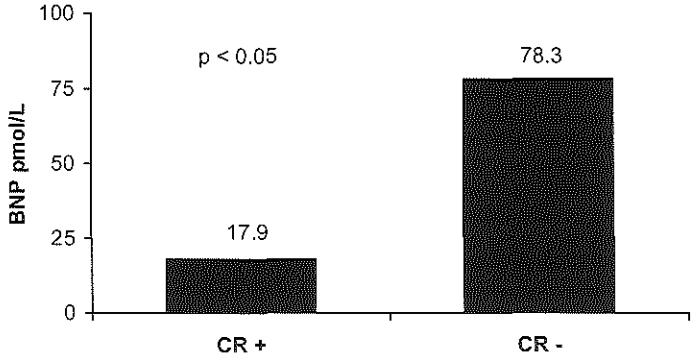


Figure 4
Plasma BNP concentrations in patients with wall motion abnormalities with and without a preserved left ventricular myocardial contractile reserve.



DISCUSSION

Previous studies have demonstrated that plasma natriuretic peptide concentrations are elevated in patients with congestive heart failure [7-11]. Although the number of patient with congestive heart failure due to ischemic heart disease is increasing rapidly [2], there are no data available on the relation between myocardial contractile reserve and plasma natriuretic peptide concentrations. In this study, ANP and BNP levels were determined in a patient cohort with known or suspected coronary artery disease and a varying degree of heart failure. The main finding from the present study is that the presence of myocardial contractile reserve during low-dose dobutamine stress echocardiography influences plasma levels of both natriuretic peptides in patients with an impaired LV function. Plasma ANP and BNP levels were markedly elevated in patients without contractile reserve, compared to patients with a preserved contractile reserve. Cardiovascular medical therapy, including beta-blockers and ACE inhibitors, was comparable between the patient groups.

Pathophysiological role of ANP and BNP

The natriuretic peptides have a major role in the protection of the heart from volume overload [14]. The cardiac hormones ANP and BNP are produced in the atria and ventricles, respectively, in response to an increase in wall stretch, or pressure. Elevated plasma ANP and BNP concentrations have a natriuretic and diuretic effect. In addition, high plasma BNP levels cause a fluid-shift from the capillary bed to the interstitium, decreasing preload and blood pressure. Hence, ANP and BNP are functional counterparts of the renin-angiotensin aldosterone system. Therefore there may be a future for these natriuretic peptides in screening and guiding management in patients with LV dysfunction. In the present study, the ANP and BNP plasma concentrations were significantly elevated in the patients with LV dysfunction, whereas the patients with a normal function had normal natriuretic peptide levels. These findings indicate that an increased wall tension or stretch in abnormally contracting myocardial tissue may lead to elevated plasma natriuretic peptide levels, and confirm the "volume overload" hypothesis for the production and secretion of these peptides. This is in line with the study of Sumida et al. [15] showing that the secretion of natriuretic peptides increases in proportion to the severity of LV dysfunction, and is elevated in infarct regions.

Contractile reserve in patients with LV dysfunction

Since the introduction of the concepts of myocardial viability, hibernation, and stunning, it has become clear that ischemic LV dysfunction is not an irreversible process [16,17]. In more than 50% of the patients with ischemic cardiomyopathy and heart failure, a clinically significant amount of viable myocardium is present and coronary revascularization may be considered [18]. The evaluation of myocardial contractile reserve may have important clinical implications in patients with ischemic LV dysfunction. Recently, Chaudry et al. [19] evaluated contractile reserve during low-dose dobutamine stress echocardiography in 80 patients with ischemic LV dysfunction. Contractile reserve was a significant predictor of survival in these patients. Moreover, the presence of contractile reserve is related to the extent of interstitial fibrosis and predicts the recovery of systolic function after coronary revascularization [20]. Several studies have reported that plasma natriuretic peptides are predictive of long-term survival after myocardial infarction, although the mechanism for this is not clear [21,22]. In the current study myocardial contractile reserve influenced plasma natriuretic peptide levels. Plasma ANP and BNP levels were high in patients without contractile reserve, and relatively low in patients with a preserved contractile reserve. Hence, natriuretic peptides are correlated with myocardial viability in dysfunctional myocardium. This may partially explain why natriuretic peptides predict survival in patients who had a myocardial infarction. Further research is needed to fully elucidate this issue.

CONCLUSIONS

The presence of myocardial contractile reserve influences the plasma natriuretic peptide concentrations in patients with LV dysfunction. Plasma ANP and BNP levels were markedly elevated in patients with LV dysfunction without contractile reserve, compared with patients with a preserved contractile reserve. These findings may give further insights into the role of these natriuretic peptides in patients with LV dysfunction.

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CHAPTER 9

CLINICAL UTILITY AND COST-EFFECTIVENESS OF A PERSONAL ULTRASOUND IMAGER FOR CARDIAC EVALUATION DURING CONSULTATION ROUNDS IN PATIENTS WITH SUSPECTED CARDIAC DISEASE.

EC Vourvouri, LY Koroleva, FJ Ten Cate, D Poldermans, AFL Schinkel, RT van Domburg, WB Vletter J et al.
Heart 2002, in press

ABSTRACT

Aim: To assess the clinical utility and cost-effectiveness of a personal ultrasound imager (PUI) (SonoHeart^{TM}, SonoSite, Inc) during consultation rounds for cardiac evaluation of patients with suspected cardiac disease.

Methods: One hundred seven (107) unselected patients from non-cardiac departments (55% male) were enrolled in the study. The consultant cardiologist (CC) performed after the physical examination an echocardiographic study with a PUI. Final report was given instantly to the referring physician. All patients subsequently underwent a study with a standard echocardiographic device (SE). The CC noted for each patient whether the findings of the PUI were adequate for final diagnosis. The total cost when full echocardiography was employed was compared to the cost when the PUI was used. The time interval from request to diagnosis was also compared.

Results: In 78.5% of patients no further examination with a SE was regarded as necessary. Twenty-three patients (21.5%) required a further detailed examination with the SE because of the need of hemodynamic information. There was an excellent agreement for the detection of abnormalities between the two devices (96%). The total cost was €132 /per patient when the SE and €75 /per patient when the PUI was employed. According to our study, the use of the PUI could lead to a 33.4% reduction of total cost. The mean time from request to diagnosis at our institution was four days for the SE and instantly for the PUI, which potentially could save additional costs.

Conclusions: Immediate echocardiographic assessment during consultation rounds can lead to significant cost savings and to shortening of the time to diagnosis.

Key Words: Cost-Effectiveness, Personal Ultrasound Imager, Hand-held Ultrasound Device, Clinical Usefulness.

INTRODUCTION

During consultation rounds in non-cardiology departments the consulting cardiologist is confronted with specific clinical questions (i.e. presence of pericardial effusion, left ventricular function, source of embolism or inferior vena cava collapse). It has been proven that echocardiography is superior to physical examination in diagnosis of cardiac disorders, especially in their early stages of disease.[1-3] However, the transportation of SE during ward rounds is unpractical and therefore limited. Recently, small hand-held ultrasound imagers have been developed. Being ultra-portable, of high accuracy and at low cost, they can revolutionise the daily clinical practice.

The aim of the present study was to evaluate the clinical utility and cost-effectiveness of a small personal ultrasound imager (PUI) (SonoHeart^{TM} System, SonoSite, Inc) during consultation rounds for evaluation of unselected patients with suspected cardiac disease. The results of high-end standard echocardiographic equipment (SE) were used for performance comparison and verification.

MATERIALS AND METHODS

Study population.

We studied 107 consecutive unselected patients with suspected cardiac disease (55% men) with a mean age of 53 ± 17 years, for whom a consultation by the cardiologist was requested.

Study design

The main inclusion criterion to this study was the request of a physician from a non-cardiac department for cardiac evaluation of a patient. In addition to the physical examination an echocardiographic study was performed with the PUI by the consulting cardiologist at the patient's bedside. The final cardiac report was given instantly to the referring physician for management decision. The necessity of an echocardiographic study with the SE was noted by the consultant cardiologist after the clinical examination of the patient and the PUI study. As a part of the study, all the patients underwent also an echocardiogram by means of a SE, Hewlett Packard (Sonos 5500;Andover, MA) or Vingmed (System V;Horten, Norway). These results were reported by a second investigator blinded to the results of the PUI examination.

Routine logistic procedures of the echocardiographic examinations of the echolaboratory were not changed in this study. Echocardiographic data were obtained in standard cardiac views and basic linear measurements of structures and cavities.[4,5]

The average cost of the normal procedure when a patient is referred to full echocardiography, was calculated and compared to the cost when the PUI was used.

Furthermore, the time interval between the request for echocardiographic examination and the final cardiac report for both the PUI and the SE were compared.

The study was approved by our Institutional Medical Ethical Committee and written informed consent for the study was obtained from all patients.

The Personal Ultrasound Imager.

The SonoHeart™ (SonoSite Inc., Bothell, Washington, USA) hand-held ultrasound system (figure 1) is a small hand-held ultrasound device equipped with a 2-4 MHz phased array broadband transducer and operating on a rechargeable lithium ion battery or AC power. 2D control settings comparable to a standard echocardiographic device and a colour power Doppler flow mapping are integrated to the unit. Distance measurements are possible with inclusive callipers. SonoHeart™ has a storage memory of 50 images and can be connected to a video-recorder, a printer or an external monitor.

Statistical analysis.

Descriptive statistics were reported as mean ± SD or by frequency percentages. The agreement for detection of abnormalities was assessed from 2X2 tables using weighted kappa statistics. Kappa values 0,4, between 0,4 and 0,75, and >0,75 were considered to represent poor, fair to good and excellent agreement respectively, based on Fleiss's classification[6].

In addition, specificity, sensitivity, positive and negative predictive value of the PUI in detecting abnormalities were calculated.

RESULTS

Cardiac visualisation by PUI.

In all of patients, adequate visualisation in order to answer the request was achieved.

Agreement.

The most common referral questions for which a cardiac evaluation was requested are listed in Table 1. The "gold standard" SE examination detected 71 clinically significant findings (Table 2). The agreement in identifying abnormalities between the PUI and the SE was 96%, k=0.93 and is shown in Table 3.

The PUI provided to the cardiologist sufficient information in 78.5% of the patients seen during consultation rounds. In 23/107 patients (21.5%) a further detailed examination with the SE was considered as necessary despite the echocardiographic examination with the PUI. In 18 out of these 23 patients the Doppler study was required for the severity evaluation of regurgitant or stenotic lesions (16 patients) and the diagnosis of pulmonary hypertension (2 patients). In 2/23 patients a SE examination was requested for the verification of severe wall motion abnormalities and in 1/23 patient for a further investigation of a dilated ascending aorta. In 2/23 patients there was a false positive diagnosis of endocarditis. In both cases there was the clinical suspicion of endocarditis by the referral physician. Due to an echodense appearance of the aortic valve with the PUI the clinical suspicion was enhanced and a further analysis with SE was requested by the cardiologist. The SE did not add any further information and the transoesophageal echocardiographic study that followed finally rejected the diagnosis of endocarditis.

There were two major abnormalities missed with the PUI: a moderate mitral regurgitation in a patient with referral question of LV function and a pulmonary hypertension in a patient with referral question of cor pulmonale. The second was referred to SE examination by the cardiologist.

Calculation of cost-effectiveness of the PUI

The average cost of a SE study was estimated by calculating the cardiologist's consultation fee (€72), and the charging cost of a full echocardiogaphic study (€60). The final cost was €132 per patient.

The echo examination by the PUI is considered as part of the physical examination and is therefore not charged. However we implemented in the final cost the capital investment of such a device which is about €15.000. The five year equipment depreciation of this amount is €3.000 /year which results in €3 /patient on a basis of 1000 patients seen during consultation rounds per year. Thus the cost of a consultation visit with the use of the PUI was calculated to be €75 per patient.

Applying these data to our study results, the total cost for the 107 echocardiographic examinations performed was €14.124 for standard procedure, when the SE was used. However with the PUI it was €9.405 since only 23 patients were considered to need further investigation with a SE. Thus, with the use of PUI a cost reduction of 33.4% could be achieved.

In addition, the mean time interval between an echo request by the consultant cardiologist and the final echo report was reduced substantially. At our institution the average time was four days when SE was requested whereas it was instantly when the PUI was employed. In table 4 we can appreciate the logistic flowcharts of an echo study request for in-patients after a consultation visit by the cardiologist.

Table 1.

Reasons for cardiac consultation request for the 107 patients from non-cardiac departments

Referral question	%
Left ventricular function	67.3
Left ventricular dimensions	22.4
Murmur evaluation	18.0
Pericardial effusion	14.0
Rhythm abnormalities	9.3
Left ventricular hypertrophy	8.4
Suspected endocarditis	4.6
Cardiac source of embolism	2.0
Pulmonary hypertension	1.8

85% of the patients were pre-operative patients. For some patients there were more than one referral questions.

Table 2.

List of abnormal findings detected with the SE in 107 patients referred for cardiac evaluation during consultation rounds

Finding	%
Left ventricular dysfunction	33.8
Left ventricular hypertrophy	28.0
Left ventricular dilatation	11.2
Mitral valve regurgitation	7.0
Dilated ascending aorta	7.0
Pericardial effusion	4.2
Aortic valve regurgitation	4.0
Tricuspid regurgitation	3.0
Mitral valve stenosis	1.4
Aortic valve endocarditis	0.9

Number of total findings: 72. Some patients had more than one finding. The regurgitationjets noted are of moderate or severe degree. Patients with trivial or mild regurgitation jets were characterized as normal.

Table 3.

Agreement of detection of patients with abnormalities between the SonoHeart™ and a standard echocardiographic system

		SonoHeart™	
		normal	abnormal
Standard Echo	Normal	**51**	2
	abnormal	2	**52**

No of patients: 107.
Agreement =96%, kappa = 0,92.
Sensitivity=96% (95%CI: 0.89-0.99)
Specificity=96% (95%CI:0.89-0.99)
PPV=96% (95%CI:0.89-0.99)
NPV=96% (95%CI:0.89-0.99)
The numbers inside the tables express the absolute number of patients.

Table 4.

Logistic flowcharts at the Erasmus MC Rotterdam, The Netherlands, of a routine echo study request for patients from non-cardiac departments, after a consultation visit by the cardiologist.

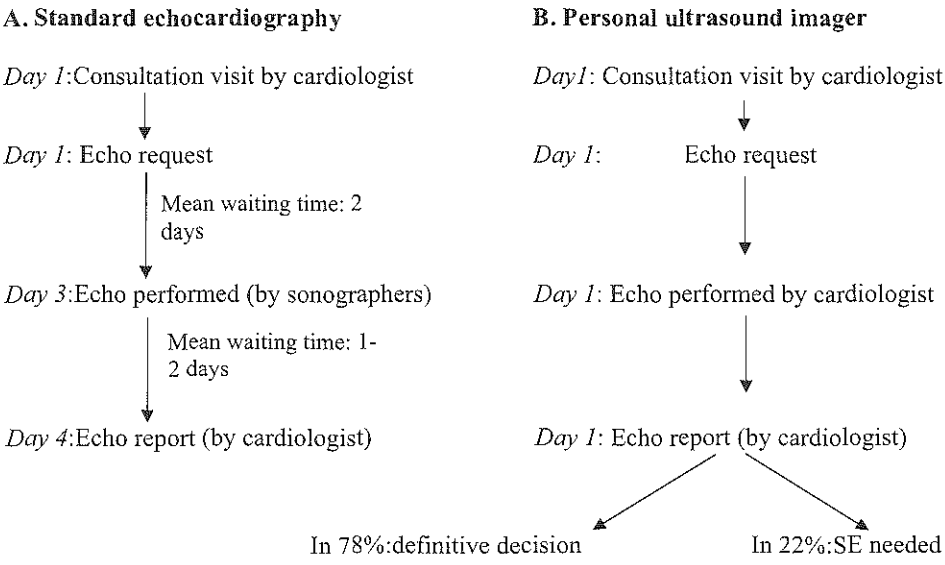

Figure 1.

Photograph of the SonoHeart™ device, the personal ultrasound imager (weight 2.4 kg) used in this study.

DISCUSSION

This study describes the potential utility of a small hand-held ultrasound device during consultation rounds in the evaluation of patients in non-cardiac departments with suspected cardiac disease. In 84 patients (78.5%) the PUI could provide the physician with efficient instant information indicating that a further examination with SE could have been avoided. In patients in whom a complete echo study was considered necessary, it was mostly due to the need of hemodynamic assessment by Doppler. With the addition of this feature in the next generation PUIs the need for SE for patients seen during consultation rounds could be reduced even further.

Prior studies using limited imaging protocols have provided evidence that a limited imaging study is feasible for both the diagnosis and evaluation of most of important cardiac pathologies (hypertrophic cardiomyopathy,[7] left ventricular hypertrophy,[8-11] mitral valve

prolapse,[12] abdominal aortic aneurysm).[13,14] Such limited echo strategy can be effectively implemented with a small hand-held ultrasound device.

Today, small hand held ultrasound devices aim the coupling between the physical examination and echocardiography at the point of care. By being ultra-portable and easy to use they are practical for carrying while making consultation rounds. Recently, our group demonstrated in a previous study the efficacy and high accuracy of this small imaging device in assessing pathomorphology and function of the heart enhancing and extending the physical examination allowing goal-oriented examination.[4, 5] In the current study these results were further confirmed.

Cost-effectiveness of PUI during consultation rounds

Like all technological breakthroughs, the PUI has to be evaluated in financial terms as well as by clinical effectiveness in order to gain wide acceptance. The capital investment of such a device is economic (~1/12th of the cost of a SE) and the maintenance costs are low.

In our hospital the total number of the in-patients from non-cardiac departments referred for an echocardiographic examination for the year 2001 was 1125. Thus, for the year 2001, the total cost for the 1125 consultation visits that required an echocardiographic examination with the SE was €148.500. According to our study the cost could be reduced to €98.901 (66.6% of the initial amount) with the use of the PUI.

Eighty-five percent (85%) of the patients in our study were pre-operative patients. In fact, in our hospital the majority of the in-patients referred for cardiac consultation are pre-operative patients. The usual question from anesthesiologists and surgeons is the systolic left ventricular function or evaluation of a murmur that can be reliably be answered by an echocardiographic examination. Thus, the standard approach for these patients is a request for an echocardiographic study further to the physical examination. The instant answer to a request can prevent potential delay in a patient who is planned for surgery and could therefore lead to cost savings. But this is only a hypothesis that has to be investigated.

Recently, Kimura et al [15] reported that the presence of an abnormal initial limited echocardiographic examination at the emergency department had the consequence that the patients had a significant hospital stay length (ie, > 2 days). Furthermore, their study have shown that in the setting of the emergency department, a limited echocardiographic examination has better diagnostic accuracy in identifying cardiac abnormalities than physical examination.

The present study was performed by cardiologists with experience in echocardiography. Immediate decision making diagnosis based on the echocardiographic examination of a PUI during consultation rounds requires level II or III training in echocardiography.[16] Kimura et al [15] have proven the feasibility of training health care providers in obtaining a parasternal long-axis view and the interpretation of significant abnormalities. However, training and licensing for using these devices for non-cardiologists will become an important issue in the future.

Limitations to the study

The impact of the use of the PUI on hospitalisation stay has not been specifically addressed in the current study. This may form the base for future studies.

The personal ultrasound imager that was used for this study had no Doppler modalities to obtain hemodynamic data. By now, spectral Doppler and colour Doppler are integrated in the new generation of personal ultrasound imagers.

Conclusion

During consultation rounds, PUI can help to make an instant diagnosis at the bedside leading to shortening of the time to diagnosis with equal efficacy to a standard echocardiographic device and lower cost.

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CHAPTER 10

DIAGNOSIS OF ENDOCARDITIS OF TRICUSPID VALVE WITH A SMALL PERSONAL ULTRASOUND IMAGER

EC Vourvouri, JW Deckers, FJ Ten Cate, D Poldermans, AFL Schinkel, JRTC Roelandt.

Submitted for publication.

A 20-year-old man with history of drug abuse was admitted to the department of Internal Medicine with general malaise, cough and high fever (38,4°C). The physical examination revealed pulmonary rales compatible with pneumonia. There were no skin lesions, no murmurs and no clinical evidence of right heart failure. The laboratory tests showed elevated levels of CRP (201mg/L), anaemia (haemoglobin 7,0 mmol/L) and leucocytosis (28×10^9/L). An echocardiographic study at the bedside with a personal ultrasound imager (PUI) (OptiGo™, Philips Medical Systems) revealed a large vegetation of the tricuspid valve with a concomitant regurgitation jet (Figure 1 A, B). Venous blood samples for blood culture were obtained.

A transoesophageal study with a standard echocardiographic system (Vingmed System V, Horten, Norway) was performed immediately which verified the diagnosis of infective endocarditis (IE) of the tricuspid valve. (Figure 2). Treatment with high doses of penicilline G plus gentamycine was initiated to the patient the same day. The blood cultures revealed the presence of beta-hemolytic streptococcus, group C. The patient was discharged after 3 weeks in good clinical condition.

Acute IE is a highly destructive and rapidly progressive disease that requires immediate initiation of therapy (1,2). Furthermore murmurs are commonly not audible in patients with tricuspid valve IE and can be missed during physical examination (3,4).

Today, PUIs aim the coupling between clinical examination and echocardiography at the point-of-care. Instant diagnosis can lead to shortening of the time to diagnosis and immediate initiation of treatment.

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Figure 1.

A. Imaging of a vegetation on the tricuspid valve (arrows) in the apical four-chamber view. The small, personal ultrasound imager used is shown in the insert (OptiGo™, Philips Medical Systems).

B. The tricuspid regurgitation of moderate severity is visualised in the same view.

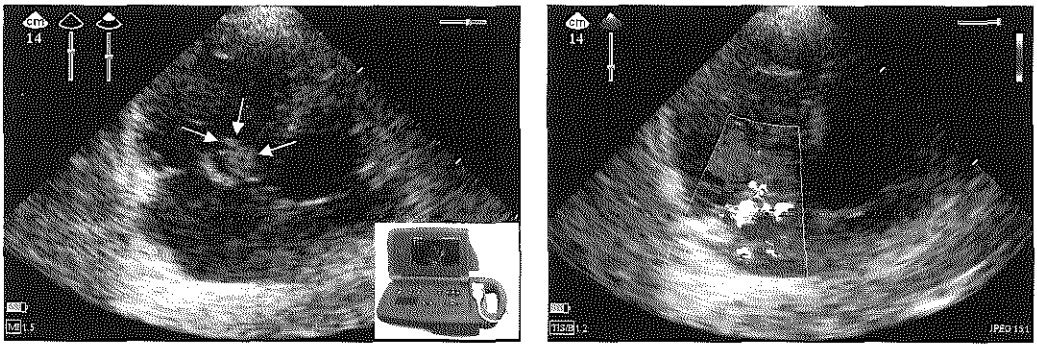
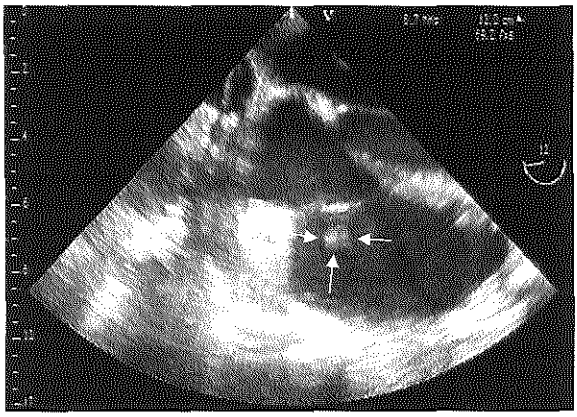


Figure 2.

Four-chamber view of a multiplane transesophageal study (Vingmed System V, Horten, Norway) demonstrating a large mass on the tricuspid valve (arrows).



CHAPTER 11

EVALUATION OF A HAND-CARRIED CARDIAC ULTRASOUND DEVICE IN AN OUTPATIENT CARDIOLOGY CLINIC

EC Vourvouri, D Poldermans, JW Deckers, JRTC Roelandt

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ABSTRACT

Aim: To determine the practicality and diagnostic potential of a hand-carried cardiac ultrasound (HCU) device (OptiGo™, Philips Medical Systems) in a cardiology outpatient clinic. A full-featured standard ultrasound system (SE) was used as a reference.

Methods: 300 consecutive patients referred to the cardiology outpatient clinic for the first time were studied with the HCU device by an experienced investigator prior to their visit to the cardiologist. Thereafter, an echocardiographer blinded to the results of HCU performed a complete study with a SE whenever the cardiologist required it. HCU and SE were independently evaluated for major and minor cardiovascular abnormalities. Major abnormalities were those abnormalities leading to further diagnostic evaluation, change the therapeutic management or alter the prognosis of the patient. The investigator noted whether HCU was able to confirm or reject the referral diagnosis, an unsuspected pathology was detected or further SE investigation was necessary. These data were compared to the request for a SE by the cardiologist and the SE diagnosis.

Results: The cardiologist ordered a SE study in 216 of 300 patients (72%). HCU echocardiography was able to answer the suspected referral diagnosis in 128 of 216 patients (59%). Of the 84/300 patients that were not referred for a SE study, 20% showed a major abnormality with the HCU device. In 63/216 patients a further assessment with SE and in 25/216 patients a transoesophageal study was necessary. The agreement between the two devices for the detection of major abnormalities in the 216 patients was 98%, kappa=0.96. The HCU device missed 26% of minor and 4% of major abnormalities. Overall, 48% of the cardiac abnormalities found by the HCU device in the 300 patients were not suspected on clinical grounds.

Conclusion: Assessment of new patients with a HCU device at the outpatient cardiology clinic often leads to an instant diagnosis and the detection of unexpected cardiovascular abnormalities. These devices significantly augment the yield of the physical examination.

Keywords: ***Hand-carried Ultrasound Device, Ultrasound Stethoscope, Personal Ultrasound Imager, Outpatient Cardiology Clinic***

INTRODUCTION

The physical examination is the cornerstone of the evaluation of patients referred to the outpatient cardiology clinic but often fails to provide a conclusive diagnosis. Palpation and auscultation are not very accurate and since the introduction of echocardiography and Doppler, the limitations of the physical examination in specific cardiac abnormalities and especially in their pre-clinical stage have been demonstrated (1). In addition, the auscultation skills of recently trained physicians have declined due to training shortcomings as a result of the increasing patient volume and time pressure and the increasing reliance on more sophisticated imaging methods (2-5). Consequently, echocardiography is the initial diagnostic imaging test ordered for most of the patients.

In daily practice, most of these outpatient echocardiographic studies are performed several days after the first patient-physician encounter, leading to a delay in final diagnosis and sometimes in the initiation of therapy. Recently, small hand-carried cardiac ultrasound (HCU) devices named also ultrasound stethoscopes have become available and studies have shown their validity in the immediate diagnosis of cardiac pathologies at the point-of-examination (6,7).

The aim of the present study was to determine both, the practicality and diagnostic potential of a HCU device in all patients referred to the outpatient cardiology clinic for the first time ("new" patients). The results of a full-featured standard ultrasound system (SE) were used as a reference.

MATERIALS AND METHODS

Study population and design

During a five-month-period, 300 new patients referred to the outpatient clinic of the Thoraxcenter were examined with an HCU device by a research fellow before their initial visit to the cardiologist. The patients characteristics are listed in table 1. The duration of the echocardiographic examination with the HCU device was maximized to 10 minutes. The investigator had the referral diagnosis and took a brief clinical history of the patient. Qualitative assessment and quantitative results were documented and compared to the suspected diagnosis of the referring physician. He then noted whether or not a SE was needed. Subsequently, the patient was seen by a cardiologist, who was unaware of the HCU evaluation who decided whether an echocardiographic examination was necessary or not.

This examination was performed with a full-featured system SE, (Sonos 5500; Philips Medical Systems) or Vingmed (System Five; Horten, Norway) by an independent operator, who was also blinded to the HCU results. A cardiologist not involved in the study interpreted the SE examinations. The Institutional Medical Ethical Committee approved the study and informed consent was obtained from all patients.

Table 1.

Baseline characteristics of the 300 new patients referred to the outpatient cardiology clinic

Age (years)	53±16
Male, n	57 (19%)
CAD documented/suspected	61 (20%)
HT, known	86 (29%)
DM, treated	11 (4%)
Valve repair, previous	4 (1%)

CAD=coronary artery disease; HT= hypertension; DM=diabetes mellitus.

The HCU device

The OptiGo™ (Philips Medical Systems) (Figure 1) HCU device was used. It is equipped with a small 2.5 MHz phased-array broadband transducer and operates on a rechargeable lithium ion battery or AC power. Two callipers are integrated in the unit for linear measurements of cavity dimensions and wall thickness. Images are documented on CompactFlash card. Color flow Doppler imaging is also integrated in the system.

Echocardiographic diagnosis using the HCU device

Definitions

Cardiovascular abnormalities were classified into major and minor. Of major clinical significance were considered those, which would lead to further diagnostic evaluation, change of the therapeutic management or alter the prognosis (table 2).

The evaluation of valvular or flow abnormalities with the HCU device using the 2D and color Doppler flow mode are presented in table 3 (8,9). These were evaluated with the pulsed and continuous wave Doppler modalities of the SE and their severity was graded using standard methods (8).

Unexpected abnormalities were considered those that were not suspected from the symptoms or were not reported by the referring physician.

Left ventricular systolic function

Normal left ventricular (LV) systolic function was defined by normal LV internal transverse end-diastolic (≤ 5.5cm) and end-systolic (≤3.5 cm) dimensions (in the parasternal long-axis view), absence of wall motion abnormalities and an estimated EF>55%. An estimated EF of 35-55% defined a mildly to moderately reduced LV function and an estimated EF<35% a severely reduced LV function (6).

Right ventricular systolic function

Normal right ventricular systolic function was defined by normal right ventricular dimensions (end-diastolic transverse diameter <45 mm in the 4-chamber view) and an estimated ejection fraction >50%.

Structural abnormalities

LV hypertrophy was defined as an end-diastolic wall thickness of the septum >12mm. A septal thickness of >14mm was considered to represent severe LV hypertrophy.

A dilatation of the aortic root and the ascending aorta was present when the longitudinal diameter was >35 mm for men and >30 mm for women in the parasternal long-axis view.

Statistical Analysis

Descriptive statistics were reported as mean ± SD for continuous variables and as percentages for categorical variables. The agreement between the two examination techniques for the detection of major abnormalities was assessed from 2X2 tables using weighted kappa statistics. Kappa values <0.4, between 0.4 and 0.75, and >0.75 were considered to represent poor, fair to good and excellent agreement respectively, based on Fleiss's classification (10).

Table 2. Major cardiovascular findings

Valvular regurgitation (moderate/severe)
Valvular stenosis
Left ventricular dysfunction
Right ventricular dysfunction
Left ventricular hypertrophy (moderate/severe)
Mitral prolapse
Ventricular septal defect
Atrial septal defect
Pericardial effusion
Mass lesions

RESULTS

General results

Of the 300 new patients the most common referral question/suspected diagnosis sent to the cardiology outpatient clinic are presented in table 4.

The cardiologists requested an echocardiographic examination after their physical examination in 216 of 300 patients (72%). They considered in 84 patients (28%) an echo examination unnecessary.

In 128 of the 216 patients (59%) the HCU findings confirmed or rejected the clinical diagnosis. In these patients the SE examination did not add any significant information to that obtained by the HCU device and the SE examination could therefore have been avoided.

In 88/216 (41%) patients an additional test was considered necessary. In 25/216 (12%) patients a transoesophageal echocardiogram was requested for the evaluation of a cardiac source of embolism. In 63/216 (29%) patients hemodynamic Doppler assessment was needed for the evaluation of the severity of valve stenosis (18 patients); left ventricular outflow tract obstruction (6 patients); regurgitant lesion (36 patients) and congenital pathology (5 patients).

However, in all of these patients the valvular or congenital lesion was detected with the HCU device and a gross estimation of the severity of the regurgitant lesions was possible with the use of the color Doppler flow modality.

Major and minor abnormalities detected with the HCU device and SE

The SE examination detected 158 minor and 143 major (87 patients) cardiovascular abnormalities (some patients had more than one cardiovascular abnormality). The HCU device examination missed 26% of the minor (table 5A) and 4% of the major abnormalities (table 5B). The missed major abnormalities included moderate LV dysfunction, aortic stenosis, moderate aortic regurgitation, moderate mitral regurgitation and a ventricular septum defect. Two of these (1 moderate aortic and and 1 moderate mitral regurgitation) were in the same patient with a poor echo window. Overall, there were 87/216 patients (40%) with major abnormalities. The agreement between the two devices for the detection of major abnormalities was excellent (98%, with a kappa-value of 0.95, see table 6).

Incidental-unexpected major findings

In total, there were 78 unexpected major findings in 64/ 300 patients (21%) and are presented in Figure 2. Importantly, out of these 78 findings 19 were present in 17 of the 84 (20%) patients not referred to SE. In particular these findings were: LVH (7 patients), LV dysfunction (3 patients), valvular stenosis (3 patients), valvular regurgitation (3 patients), dilated ascending aorta (1 patient), MVP (1 patients), PE (1 patient). These data were verified by the SE examination that followed after the specific request of the HCU investigator. Figures 3, 4 and 5 represent examples of major unexpected findings detected with the HCU device and verified with the SE.

Table 3. Evaluation of severity of valvular/flow abnormalities using the HCU device

Valve disorder	Mode of analysis	Definition of severe lesions
Mitral regurgitation	2D	Structural abnormalities (e.g. rheumatic valve; annulus calcification; Mitral valve prolapse; endocarditis) LVEDD≥7cm;LA size≥5.5cm.
	Color Doppler	Color flow regurgitant jet area ≥40% of LA size.
Aortic regurgitation	2D	Structural abnormalities (e.g. degenerative calcified aortic valve, congenitally abnormal valve;dilated aortic root;endocarditis) LVEDD≥7.5cm.
	Color Doppler	Ratio:color flow regurgitant jet width/LVOT diameter≥60%; ratio:color flow regurgitant jet area/LVOT area ≥60%;diastolic flow reversal in ascending aorta.
Tricuspid regurgitation	2D	Underlying cause of TR (rheumatic valve, prolapse, carcinoid disease annular dilatation;Ebstein anomaly;right ventricular infarct); inadequate cusp coaptation; dilatation of annulus(≥4cm).
	Color Doppler	Color-flow jet area≥30% of the RA area.
Pulmonary regurgitation	2D	Regurgitation jet extending more than 2cm, reaching the body of RV cavity. Mild regurgitation was considered physiologic.
Mitral prolapse	2D	Systolic displacement of one or both mitral valve leaflets into the LA, below the plane of the mitral annulus.
Mitral stenosis	2D	Structural abnormalities (e.g. rheumatic disease, degenerative calcification); thickened, calcified valve leaflets and subvalvular apparatus; "hockey-stick" appearance of anterior mitral leaflet in diastole;"fish-mouth" orifice in short-axis; increase of LA size.
Aortic stenosis	2D	Structural abnormalities (e.g. degenerative valvular calcification;bicuspid valve).
	Color Doppler	Turbulent flow above the valve in the aortic root.
Pulmonary stenosis	2D	Lesions (e.g. congentital heart disease, carcinoid disease, vegetation, mass).
	Color Doppler	Turbulent colour flow in the pulmonary outflow tract.
Ventricular septum defect	2D/color Doppler	Visualisation of the defect /Turbulent left-to-right shunt across the ventricular septum.
Atrial septum defect	2D/color Doppler	Visualisation of the defect/Turbulent left-to-right shunt across the atrial septum; dilatation of the RV; abnormal (paradoxical) ventricular septum motion.

LVEDD=left ventricular end-diastolic dimension;LVOT=left ventricular outflow tract;RA=right atrium;RV=right ventricle;LA=left atrium;TR=tricuspid valve regurgitation.

Table 4.

Reasons for referral to the outpatient cardiology clinic

Possible Diagnosis/Question	%
Left ventricular dysfunction	31
Pre-operative cardiac evaluation	15
Rhythm abnormalities	14
Cardiac source of embolism	9.6
Cardiac checking due to family history	7.3
Left ventricular hypertrophy	5.3
Murmur evaluation	4.6
Dyspnea/fatigue/dizziness	4.3
Congenital abnormality	3.6
Miscellaneous	5.5

The pre-operative patient group had either symptoms or a history of cardiac disease.

Table 5.

A. Comparison between the SE system and the HCU device in the detection of minor cardiovascular findings

Finding	SE-finding detected	HCU device-finding missed
Aortic regurgitation	34	7
Mitral regurgitation	73	14
Tricuspid regurgitation	51	20
TOTAL	**158**	**41**

Some patients had more than one cardiovascular abnormality.

B. Comparison between the SE system and the HCU device in the detection of major cardiovascular findings

Finding	SE-finding detected	HCU device finding missed
Aortic stenosis	14	2
Aortic regurgitation	10	1
Mitral stenosis	3	0
Mitral regurgitation	18	1
Tricuspid regurgitation	8	0
Pulmonary stenosis	1	0
LV systolic dysfunction	35	1
RV systolic dysfunction	1	0
LV hypertrophy	38	0
Mitral prolapse	5	0
Ventricular septal defect	4	1
Atrial septal defect	3	0
Pericardial effusion	3	0
TOTAL	**143**	**6**

Some patients had more than one cardiovascular abnormality. The 143 major findings were present in 87 patients; LV=left venticular; RV=right ventricular.

Table 6.

Agreement of detection of patients with major abnormalities between the OptiGo™ and a standard echocardiographic system

		Standard Echo	
		abnormal	normal
OptiGo™	abnormal	**82**	0
	Normal	5	**129**

No of patients: 216.

Agreement =98%, kappa = 0,95.

Sensitivity=94% (95%CI:0.90-0.90))

Specificity=100% (95%CI:0.97-0.97)

PPV=100% (95%CI:0.96-0.96)

NPV=96% (95%CI:0.94-0.94)

The numbers inside the tables express the absolute number of patients.

Figure 1.

Photograph of the OptiGo™ device, the HCU device used in the current study.

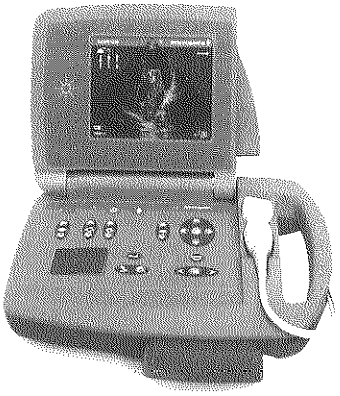


Figure 2.

The total additional-unexpected findings detected in the 300 patients are presented in the pie-type graphic. In total there were 78 such findings. The numbers inside the figure express the absolute number of findings.

LVH=left ventricular hypertrophy; LVD=left ventricular dysfunction; VS=valve stenosis;VR=valve regurgitation.

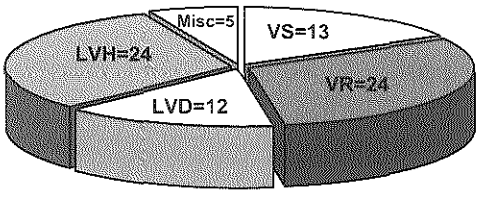


Figure 3.

Parasternal long-axis view of a 54-years-old patient with a calcified aortic valve and turbulent flow above the valve in the aortic root in systole. The patient had no history of cardiac disease and was referred for progressive dyspnea to the outpatient cardiology clinic.

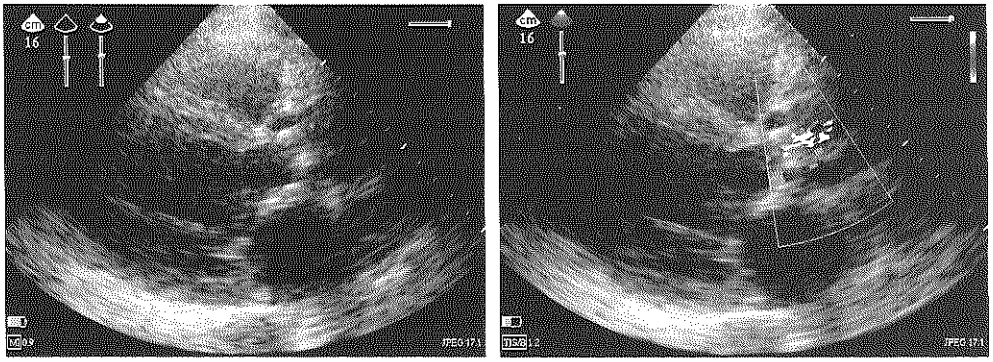


Figure 4.

Parasternal long-axis view of a 46-years-old woman with a history of cancer. She was referred for pre-operative evaluation. The left ventricular end-diastolic dimension is 69 mm. The EF was visually estimated to be <35%. The patient has dilated cardiomyopathy.

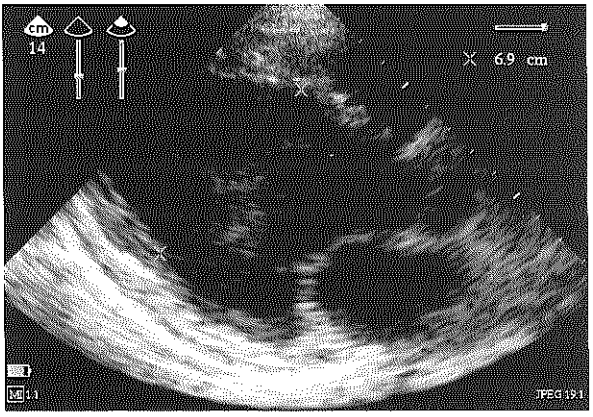
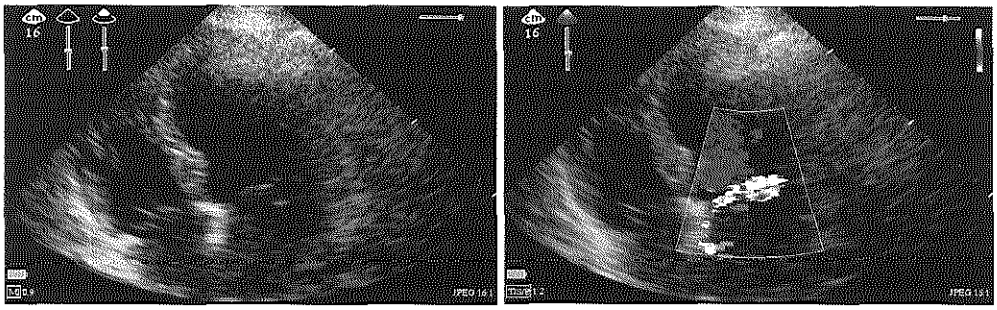


Figure 5.

Apical four-chamber view of a 45-years-old patient with prolapse of the posterior mitral leaflet and eccentric jet towards the interatrial septum. The patient was referred for the evaluation of palpitations and was known to have a systolic murmur.



DISCUSSION

The first HCU device to augment the physical examination was introduced by Roelandt and colleagues in Rotterdam in 1978 (11-13). However, combination of the poor image quality, technical limitations and reimbursement issues discontinued its development. Advances in microprocessor technology have led to new hand-carried echocardiographic systems with excellent image quality and significantly lower cost. Recently, several studies have shown the efficacy and accuracy of these small imaging devices in the diagnosis and evaluation of major pathologies at the point-of-care (6-7,14-16).

The current study shows that in 59% of patients with a request for a full-featured SE examination by the cardiologist, the HCU device provided instant information, which was potentially sufficient to avoid a SE examination. In the other patients, hemodynamic assessment by Doppler was the most common reason for a SE examination. With the addition of this feature in the next generation HCU devices the need for SE for patients seen at an outpatient clinic could be reduced even further, certainly in the hands of a cardiologist experienced in echocardiography examination.

The HCU device missed 41/158 (26%) minor and only 6/143 (4%) of the major abnormalities, providing a positive predictive value in diagnosing the major abnormalities

selected in this study of 100% and a negative predictive value of 97%. In total, twenty-one percent of the patients had unexpected major abnormalities.

Clearly, the patients referred to our outpatient clinic, which is as a tertiary referral centre, have a high prevalence of cardiac disease, which explains the high number of requests for echocardiographic examination. However, since outpatient echocardiographic examinations are often performed days after the patients first visit, the patients are obliged to return to the hospital in order to undergo the examination. Our study shows that the use of a HCU device as part of the clinical examination often leads to a definitive diagnosis avoiding an extra visit to the hospital and rapid initiation of further management or therapy when appropriate.

Furthermore, in 84/300 (28%) patients the cardiologist's clinical judgement by his/her physical examination was thought to be sufficiently accurate and to decide that echocardiographic assessment was unnecessary. However, in 17 out of these 84 patients (20%) major findings with the HCU device were found, showing that the physical examination is more accurate when extended with the HCU device.

Although we did not compare the cardiovascular physical examination to the HCU echocardiographic examination, our results suggest that major abnormalities may be missed with the physical examination alone. This can be explained by the majority of these findings to be beyond physical signs (LVH, LV dysfunction, dilated ascending aorta, PE).

The role of HCU echocardiography is mainly in augmenting our diagnostic accuracy helping us to differentiate normal from abnormal patients and thus leading to target referrals for further diagnostic assessment whenever regarded as necessary.

Recently, Spencer et al (17) compared HCU echocardiography at the point-of-care to the physical examination. They reported that the use of this device by cardiologists reduced the number of missed major cardiovascular findings by the clinical examination. They pointed out that that such a hand-held device cannot substitute for the final diagnosis in case of abnormal findings. Goodkgin et al (18), comparing the results of a HCU device to SE in critically-ill patients, report that although the HCU device provided important anatomic information it missed clinical finding in half of the patient. The main reason was the lack of sensitivity of the color power Doppler feature, the lack of spectral Doppler and image-quality problems. It is obvious that improvements in HCU devices can overcome these technical problems.

The current study with the HCU device was performed by a cardiologist with expertise in both echocardiography and HCU devices. The American Society of Cardiology (19) has recently published guidelines regarding the use of such devices recommending Level I of

training as an absolute minimal level required (20). However, recent studies have suggested that it is possible to train physicians and students for the detection of significant cardiac pathologies in a short period of time (21-23).

The implementation of ultrasound in physical examination by primary care physicians has proven to be feasible and to enhance the accuracy and sensitivity of clinical diagnosis (24, 25). Furthermore, open access echocardiography service used by general practitioners have shown to lead to rapid diagnosis and management of patients without causing an increase of inappropriate referrals to the hospital (26).

HCU devices are about to bring echocardiography into the community setting for the first time. Based on the current results, it seems that the combination of the clinical examination and HCU echocardiography will add important and accurate information for diagnostic and therapeutic purposes in the vast majority of patients at their first visit. In case of doubt or when hemodynamic and quantitative information is needed for further management, an examination with a fully featured SE should follow. As in the past phonocardiography was performed whenever documentation was needed after auscultation, today it is the HCU echocardiography that can play this role.

LIMITATIONS

The HCU device that was used for this study had no spectral Doppler modality to obtain hemodynamic data. The valvular abnormalities were evaluated qualitatively using the 2D and the color flow Doppler feature. However, continuous-wave and pulsed-wave Doppler echo is necessary for an accurate assessment of a valvular regurgitation or stenosis. Furthermore, examination of the transmitral flow gives information about the diastolic function and filling pressures. HCU devices with spectral flow Doppler may further broaden the use of such instruments.

CONCLUSION

A HCU device allows augmented physical examination of patients at their first visit at the outpatient cardiology clinic often leading to a definitive diagnosis and targeted referral for further assessment. Unexpected major findings are regularly detected. This results to improved patient care/throughput and cost savings.

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CHAPTER 12

SUMMARY AND CONCLUSIONS

SUMMARY AND CONCLUSIONS

The studies presented in this thesis demonstrate that the ultrasound stethoscope offer an imaging tool for the assessment of morphology and function of the heart allowing instant diagnosis and management decisions of patients in different clinical scenarios. Furthermore, it is also cost-effective in terms of low capital investment and cost savings.

In our first study (chapter 3) the presence of pericardial effusion, chamber abnormalities and global left ventricular function (LV) were evaluated with a prototype device in an unselected cardiology outpatient cohort. Regional wall motion was assessed in a subgroup of patients. The potential of the ultrasound stethoscope was also evaluated in a small group of patients with known corrected congenital abnormality. A standard echocardiographic system was used as a reference to validate our findings.

We showed that an ultrasound stethoscope is able to provide quantitative and qualitative information of specific cardiac conditions as reliable as the high-end standard echocardiographic system.

Patients with abdominal aortic aneurysm rupture experience high perioperative mortality rate (50%) in contrast to patients undergoing elective aortic surgery (2-3%) (1-4). It is therefore recommended that patients at risk are screened by ultrasound and undergo prophylactic surgery if the diameter exceeds 60 mm (5). Male gender, smoking, elderly age (>65 years), hypertension, coronary artery disease and family history are high-risk parameters. Mass screening is probably not cost-effective but screening of high-risk patients is recommended (6).

In our study (chapter 4) we assessed the screening potential of an ultrasound stethoscope for abdominal aortic aneurysm in high-risk patients. The results of a standard echocardiographic system were used as a reference. This study is presented also as a short report in the same chapter.

Furthermore, a case is reported (chapter 5) about the incidental finding of an abdominal aortic aneurysm containing thrombus, with the ultrasound stethoscope as part of the screening program in our clinic. The patient was admitted to the coronary

care unit with unstable angina and the aneurysm was further verified by intravascular ultrasound imaging and spiral computed tomography.

The study showed that ultrasound stethoscopy allows diagnoses of abdominal aortic aneurysm with high sensitivity and specificity. By being ultra-portable and at low cost ultrasound stethoscopes could become part of the clinical examination in high-risk patient groups and furthermore allow mass screening programmes for this disorder.
In this study, the ultrasound stethoscope identified an abdominal aortic aneurysm in 9% of patients with an excellent agreement with the standard echocardiographic system (98%) that served as the reference of our findings.

LV hypertrophy expresses end-organ damage in hypertensive patients and is associated with cardiovascular events (7-9). Early identification and appropriate treatment can improve outcome (10) and is therefore the optimal management of these patients. Echocardiography, calculating the left ventricular mass, can assess LV hypertrophy accurately (11) but is not recommended routinely in all hypertensive patients by the World Health Organisation-International Society of Hypertension (WHO-ISH) (12).
Ultrasound stethoscopy, as an extension to physical examination, may broaden the use of echocardiography in all hypertensive patients.
Therefore, we screened with an ultrasound stethoscope hypertensive patients for LV hypertrophy calculating the LV mass indexed for height and weight. Again, a standard echocardiographic device was the reference of our findings (chapter 6).

We demonstrated that ultrasound stethoscopy could be used as a screening tool for LV hypertrophy in hypertensive patients, providing valuable information about prognosis and risk classification and thus assisting the physician in his decision of therapy.
In this study, the ultrasound sthethoscope identified LV hypertrophy in 19 (19%) patients (for LV mass indexed for weight) and in 34 (34%) patients (for LV mass indexed for height) with an excellent agreement with the standard echocardiographic system (93% and 90% respectively).

Ischemic LV dysfunction is the main cause of congestive heart failure, which is associated with high morbidity and mortality and high health care costs (13-14).

Appropriate management of these patients can delay if not prevent the development of chronic heart failure (15-16). However, diagnosis of LV dysfunction, especially in asymptomatic patients, may be difficult to establish by the existing conventional criteria (17-19).

Recently, brain natriuretic peptide (BNP) has been proposed as a new screening tool for the early detection of LV dysfunction (20-22). BNP is a cardiac hormone secreted in the ventricles as a response to volume and pressure overload (20) and may be elevated in patients with left ventricular dysfunction.

Echocardiography on the other hand, is known to be the screening method of choice for LV dysfunction assessment (14,23-24) but is considered to be unpractical and costly (25).

We assessed the screening potential of ultrasound stethoscopy for LV dysfunction by estimating visually LV ejection fraction and the inferior vena cava collapse (chapter 7).

A standard echocardiographic system evaluating LV function and IVC collapse and BNP measurements were used as a reference. LV ejection fraction, derived with Simpson's biplane discs method (26) served as our gold standard for classification of LV function.

The ultrasound stethoscopy seem to be a sensitive screening tool for the identification of LV dysfunction while the inferior vena cava collapse is an insensitive parameter in detecting this disorder. Taking into account that echocardiography has the advantage to provide us with additional valuable information like valvular abnormalities we think that ultrasound stethoscopy is the optimal screening tool for LV dysfunction in the future, bringing echocardiography for the first time into the community setting.

Furthermore, we evaluated the relation between the presence of myocardial contractile reserve and plasma BNP in patients with reduced LV function (chapter 8). Contractile reserve was assessed with dobutamine stress echo. Regional wall motion was analyzed visually using the 16-segment model and contractile reserve was assessed as an improved contraction of dysfunctional segments at low-dose dobutamine compared to rest. LV ejection fraction derived by quantitative analysis using the Simpson's biplane method.

We found that plasma BNP is markedly elevated in patients without contractile reserve compared with patients with a preserved contractile reserve. Hence, BNP is correlated with myocardial viability in dysfunctional myocardium.

During consultation rounds the cardiologist is confronted with specific clinical questions like assessment of LV function or presence of pericardial effusion that can accurately be answered by echocardiography. However, the transportation of a standard echocardiographic system is unpractical and therefore limited.
Ultrasound stethoscopes can overcome these problems and integrate to the physical examination. Moreover they can lead to cost savings since the use of ultrasound stethoscopy is considered part of the physical examination and is therefore not charged.
We studied the feasibility and cost-effectiveness of ultrasound stethoscopy when used by cardiologists during consultation rounds in non-cardiac departments of the hospital and in patients with suspected cardiac disease (chapter 9).

We demonstrated that ultrasound stethoscopy leads to definitive diagnosis in the majority of the patients reducing the numbers of referrals to the echo lab. This results in immediate management of patients and cost savings. In 78.5% of the patients the use of ultrasound stethoscopy provided the physician with efficient information indicating that a further examination with a standard echo system could have been avoided. The use of ultrasound stethoscopy led to a 33.4% reduction of total cost.

Furthermore, the diagnosis of a tricuspid valve endocarditis made with an ultrasound stethoscope during consultation rounds is presented (chapter 10). A 20-years-old patient with a history of drug abuse was admitted with general malaise at the internal department. Interestingly there were no clinical signs of endocarditis. A standard echocardiographic examination would probably not have been performed on the same day. The addition of ultrasound stethoscopy into the physical examination resulted to instant management of the patient.

Echocardiography is the initial diagnostic imaging test ordered for most patients who visit the outpatient cardiology clinic for the first time. Physical examination alone often fails to provide conclusive answers (27). However, the outpatient

echocardiographic examinations are often performed days even weeks after the first patient-physician encounter. The implementation of an ultrasound stethoscope in the physical examination could result in immediate diagnosis and management of the patient at their first visit.

As a result, we determined the utility and practicality of ultrasound stethoscopy at the outpatient cardiology clinic in all new patients (chapter 11). We studied the number of patients in which the ultrasound stethoscope was able to confirm or reject the referral diagnosis. These data were compared to the diagnosis and request for a standard echocardiographic study by the cardiologist, who was unaware of the results of the ultrasound stethoscope. Furthermore, the number of patients with unexpected findings was assessed.

Ultrasound stethoscopy allows "ultrasound-extended" physical examination of new patients at the outpatient cardiology clinic, leading to differentiation between normal and abnormal subjects and to target referrals for further diagnostic assessment. Furthermore, incidental, unexpected major finding can be detected.

In our study, in 59% of patients an echo lab referral could have been avoided with the use of the ultrasound stethoscope. Furthermore, in 20% of patients not referred to an echocardiographic examination, major unexpected findings with the ultrasound stethoscope were found, showing that the physical examination is more sensitive when extended with the ultrasound stethoscope.

As we step into the 21st century, ultrasound stethoscopy is a reality. Providing direct imaging of the heart during physical examination, ultrasound stethoscopy has come to enhance our clinical senses and to bring echocardiography at the point-of-care.

Like all scientific innovations the first reaction of experienced echocardiographers to ultrasound stethoscopy was reluctance and related to its limitations and training requirements. Thus, not all the ultrasound stethoscopes have spectral Doppler for hemodynamic data acquisition or second harmonic imaging. Furthermore the capacity of storage of images or the recording facilities may be limited.

Another issue is the training required in order to apply ultrasound stethoscopy. Recently, a first step towards standardization of the use of such devices was done by the American Society of Cardiology (28) publishing guidelines regarding the use of ultrasound stethoscopes and recommending Level I of training, as an absolute minimal level required.

However, recent studies have suggested that minimal echo training may enable physicians to use ultrasound stethoscopy for interpreting simple abnormalities with high efficacy and accuracy (29-31). It seems that for answering simple questions, simple training may be efficient.

We are undoubtedly entering an era of changes in our daily clinical practice of which ultrasound stethoscopy is just the beginning.

Ultrasound stethoscopes in pocket size are already being developed. One can envision that in future the evolution of clinical practice in which the physician plays the major role will be revolutionary: evaluation of myocardial perfusion with ultrasound stethoscopes, three-dimensional imaging capability in ultrasound stethoscopes or wireless transfer of ultrasound bedside data for consultation to remote expert centers will soon become a reality.

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SAMENVATTING

en

CONCLUSIES

De studies die gepresenteerd worden in dit proefschrift geven aan dat de ultrageluidsstethoscoop een instrument is dat vele mogelijkheden biedt bij het beoordelen/vaststellen van de morfologie en het functioneren van het hart. Het geeft een directe diagnose bij de beoordeling en behandeling van patiënten in verschillende klinische situaties. Verder is het kosteneffectief gebleken door de kleine investering en financiële besparingen.

Dit proefschrift bestaat uit 3 delen:

Het eerste gedeelte (hoofdstuk 2-3) presenteert de ultrageluidsstethoscoop als een diagnostisch instrument. Hoofdstuk 2 introduceert de ultrageluidsstethoscoop als een nieuw onderzoeksinstrument in de dagelijks (klinische) praktijk. Verder worden de klinische en wetenschappelijke achtergronden, en een overzicht van het gebruik van een ultrageluidsstethoscoop belicht.
In hoofdstuk 3 beschrijven wij onze eerste ervaringen en de bruikbaarheid/nuttigheid van zo'n instrument voor het diagnosticeren van cardiale pathologie en globale en regionale functie van de linker kamer van het hart, in een niet geselecteerde groep patiënten. Een standaard echocardiografie systeem werd gebruikt als referentie om onze bevindingen te bevestigen.

We hebben bewezen dat een ultrageluid stethoscoop het mogelijk maakt om kwalitatieve en kwantitatieve informatie over belangrijke hartaandoeningen te verkrijgen die net zo betrouwbaar is als informatie verkregen met een standaard echocardiografie systeem.

Het tweede gedeelte van het proefschrift (hoofdstuk 4 –8) bespreekt de evaluatie van een ultrageluidsstethoscoop als een mogelijk onderzoeksinstrument voor enkele specifieke hartaandoeningen.

Patiënten met een geruptureerd aneurysma van de abdominale aorta hebben een hoog sterftepercentage (50%) in tegenstelling tot patiënten die een electieve aorta operatie (2 – 3%) ondergaan. Het is daarom aanbevolen om bij patiënten met een verhoogd risico een ultrageluidsonderzoek te doen, waarbij een profylactische operatie is aangewezen als blijkt dat de doorsnede van het aneurysma >60 mm is. In hoofdstuk 4 stellen we de mogelijkheid van screening met de ultrageluidsstethoscoop vast voor het detecteren van abdominale aorta aneurysmata bij patiënten met een verhoogd risico. Het resultaat van een standaard echocardiografie systeem is gebruikt als referentie. De studie is ook als een korte samenvatting weergegeven in hetzelfde hoofdstuk.

We hebben bewezen dat een ultrageluidsstethoscoop een aneurysma van de aorta abdominalis kan diagnostiseren met een hoge sensitiviteit en specificiteit. De ultrageluidsstethoscoop identificeerde een aneurysma van de abdominale aorta bij 9% van de patiënten, dit kwam zeer goed overeen met de bevindingen van een standaard echocardiografie systeem (98%).
Verder wordt er in hoofdstuk 5 een casus beschreven van een patiënt waarbij bij toeval een trombose in een aneurysma van de abdominale aorta werd ontdekt met de ultrageluidsstethoscoop, tijdens het screeningsprogramma op onze polikliniek.
Vervolgens hebben we 100 opeenvolgende patiënten gescreend op hypertrofie van de spierwand van de linker hart kamer, waarbij de LV massa geïndexeerd werd voor lengte en gewicht (hoofdstuk 6). Echocardiografie is een accuraat diagnostisch instrument voor LV hypertrofie, maar word niet routinematig aanbevolen bij alle patiënten met hypertensie door de Wereld Gezondheids Organisatie-Internationale Society of Hypertension (WHO-ISH).

De ultrageluidsstethoscoop, is een verlengde van het lichamelijk onderzoek, en kan breed gebruikt worden bij alle patiënten met hypertensie. In deze studie, identificeerde de ultrageluidsstethoscoop 19 (19%) patiënten met LV hypertrofie (LV massa geïndexeerd voor het gewicht) en 34 (34%) patiënten met LV hypertrofie (LV massa geïndexeerd voor lengte) met een uitstekende overeenkomst met het standaard echocardiografie systeem (93% en 90% respectievelijk).
Ischemische LV dysfunctie is de hoofdoorzaak van hartfalen, gepaard gaande met een hoge morbiditeit, mortaliteit en een hoge ziektekosten. Een vroege ontdekking van LV dysfunctie kan het ontstaan van hartfalen vertragen of voorkomen, maar de diagnose is moeilijk met de bestaande conventionele criteria. Hoofdstuk 7 beschrijft de diagnostische mogelijkheden van de ultrageluidsstethoscoop bij het screenen op LV dysfunctie, door het visueel beoordelen van de LV ejectie fractie en de collaps van de vena cava inferior. Een standaard echocardiografie systeem en BNP metingen werden gebruikt als referentie voor het vaststellen van de LV functie en de vena cava inferior collaps. De LV ejectie fractie werd bepaald met de Simpson tweevlaks schijf methode en werd gebruikt als referentie methode voor het classificeren van de LV dysfunctie.

We hebben ontdekt dat de ultrageluidsstethoscoop een gevoelig onderzoeksinstrument is voor het identificeren van LV dysfunctie, terwijl de collaps van de vena cava inferior een minder gevoelige maat is voor het opsporen van deze aandoening. Omdat echocardiografie het voordeel heeft additionele waardevolle informatie te verschaffen over bijvoorbeeld klepaandoeningen, denken we dat de ultrageluidsstethoscoop het optimale screeningsinstrument voor LV dysfunctie is.

In hoofdstuk 8 hebben we het effect van myocardiale contractiele reserve, bepaald met dobutamine stress echocardiografie, op het plasma BNP gehalte bij patiënten met beperkte linker ventrikel functie vastgesteld.

In deze studie was het plasma BNP opvallend hoog bij patiënten zonder contractile reserve in vergelijking tot een patiënten met een behouden contractiele reserve. Derhalve is, volgens onze studie, BNP gecorreleerd aan myocard vitaliteit in dysfunctioneel hartspierweefsel.

Het derde gedeelte van dit proefschrift is het evalueren van de kosteneffectiviteit van de ultrageluids stethoscoop in de klinische praktijk (Hoofdstuk 9 – 11).

Tijdens de consultatie rondes van de cardioloog wordt deze geconfronteerd met specifieke klinische vragen, zoals het vaststellen van de LV functie of de aanwezigheid van pericard effusie, die accuraat beantwoord kunnen worden met behulp van echocardiografie. Echter, het transport van een standaard echocardiografie systeem is niet praktisch en daarom beperkt. De ultrageluidsstethoscoop overwint deze problemen en maakt deel uit van het lichamelijk onderzoek. We hebben de uitvoerbaarheid en de kosteneffectiviteit van het onderzoek met de ultrageluidsstethoscoop bepaald, terwijl deze in gebruik was bij de cardioloog gedurende de consultatiebezoeken op de niet-cardiologische afdelingen van het ziekenhuis, bij patiënten waarbij een hartaandoening werd vermoed (hoofdstuk 9).

Bij 78.5% van de patiënten verschafte het gebruik van de ultrageluidsstethoscoop de arts nuttige informatie, zodat onderzoek met een standaard echo systeem zou kunnen worden vermeden. Het gebruik van een ultrageluidsstethoscoop leidde tot een vermindering van de totale kosten van 33.4%.

Een voorbeeld van een directe en definitieve diagnose tijdens de consultatie bezoeken wordt gepresenteerd in hoofdstuk 10. De diagnose van een endocarditis van de tricuspidaalklep bij een 20 jaar oude patiënt werd vastgesteld met de ultrageluidsstethoscoop. Dit werd bevestigd met een transoesofageale studie met een standaard echocardiografie apparaat.

Echocardiografie is vaak het eerste beeldvormende onderzoek dat wordt aangevraagd bij patiënten die de polikliniek cardiologie voor de eerste keer bezoeken. Lichamelijk onderzoek alleen is vaak niet voldoende om conclusies trekken. Echter, de poliklinische echocardiografische onderzoeken worden vaak pas uitgevoerd na enkele dagen en soms zelfs weken na het eerste bezoek van de patiënt. Het integreren van een ultrageluidsstethoscoop in het lichamelijk onderzoek kan resulteren in een directe diagnose tijdens het eerste bezoek van de patiënt. Ons doel in hoofdstuk 11 was het vaststellen van de diagnostische en praktische bruikbaarheid van de ultrageluidsstethoscoop op de polikliniek cardiologie, bij patiënten die

voor de eerste keer waren verwezen naar de polikliniek. Echocardiografie werd uitgevoerd onafhankelijk van het lichamelijk onderzoek. Het aantal patiënten waarbij de ultrageluidsstethoscoop het mogelijk maakte de reden van de verwijzing te bevestigen of af te wijzen, en het aantal onverwachte ontdekkingen werd vastgesteld. Deze gegevens werden vergeleken met de diagnose en de aanvragen voor een standaard echocardiografisch onderzoek door de cardioloog.

We ontdekten dat bij 59% van de patiënten een verwijzingen naar de echo-afdeling voorkomen had kunnen worden met het gebruik van de ultrageluidsstethoscoop. Bovendien werd bij 20% van de patiënten die niet werden verwezen naar de echo-afdeling, een belangrijke, onverwachte ontdekking gedaan met de ultrageluidsstethoscoop. Dit wijst erop dat het lichamelijk onderzoek gevoeliger is wanneer het wordt uitgebreid met de ultrageluidsstethoscoop.

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I dedicate my work to my parents, my sister and to Georgios.

With this thesis I feel that I am closing a big chapter of my life and I am ready for new challenges of life.

CURRICULUM VITAE

AND

LIST OF PUBLICATIONS

CURRICULUM VITAE

Eleni Vourvouri, daughter of Christos and Pelagia was born in Dortmund, Germany, on April 14th, 1968. She has Greek nationality.

Education and Professional Experience

1985	High School Diploma from the German College of Thessaloniki, Greece, with distinction.
1985-92	Faculty of Medicine, Aristotle University of Thessaloniki, Greece. MD Diploma (Ptychio Iatrikes) with magna cum laude.
1992- 94:	Resident in Internal Medicine at the Department of Medicine, Serres General Hospital, Serres, Greece.
1994- 96	Resident in Cardiology at the Department of Cardiology, Serres General Hospital, Serres, Greece.
1996- March 99	Resident in Cardiology at the Department of Cardiology, AHEPA University Hospital, Thessaloniki, Greece.
April 99- July 99	Honorary clinical registrar in Cardiology at the department of Cardiology, University Hospital of Wales, Cardiff, UK.
Oct 1999	Cardiology Diploma, AHEPA University Hospital, Thessaloniki, Greece.
Nov 99- 2002	Research and clinical fellow at the department of Cardiology, Thoraxcenter, Erasmus MC, Rotterdam, The Netherlands.

MEMBERSHIPS

Medical Association of Thessaloniki

North Hellenic Cardiological Society

GMC full registration

Big Register full registration

Member of the Working Group of the European Society of Cardiology in Echocardiography

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tissue Doppler imaging during dobutamine stress echocardiography. *Accepted in ESC 2002.*

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