

# Initial Clinical Experience with a Hand-held Device (Thrombocheck<sup>®</sup>) for the Detection of Bileaflet Prosthetic Valve Malfunction

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**Background and aim of the study:** Early recognition of subclinical prosthetic valve malfunction may promote early treatment and avoidance of serious complications. Echocardiography cannot be applied on a daily basis; thus, a hand-held device (Thrombocheck<sup>®</sup>) which is capable of detecting subtle changes in the acoustic sounds of prosthetic valve has been developed for the routine home monitoring of heart valve function. Herein is reported the authors' initial clinical experience with this device.

**Methods:** Seventy-one consecutive patients with one or more bileaflet prosthetic mechanical valves at any position were assessed both by transthoracic echocardiography (TTE) and by Thrombocheck. These patients attended the authors' clinic for either routine echocardiography (n = 62) or for the detection of prosthetic valve malfunction (n = 9). Cine-fluoroscopy and transesophageal echocardiography were used selectively to confirm prosthetic valve malfunction. The Thrombocheck was held for 1 min

in the subxiphoid position perpendicular to the patient, and indicated either normal function (OK), abnormal function (Warning) or 'no signal'.

**Results:** The study patients had in total 82 bileaflet valves (47 mitral, 31 aortic, four tricuspid). Eight patients (11.3%) had a 'no signal' indication. Of the remaining 63 patients, 10 (15.9%) had a 'warning' alarm (eight patients had current abnormal leaflet motion, one patient had a recent history of abnormal leaflet motion, and one had no evidence of prosthetic valve malfunction). The sensitivity and specificity for detecting abnormal prosthetic valve malfunction were 90% and 98%, respectively.

**Conclusion:** The Thrombocheck had an excellent sensitivity and specificity for the detection of prosthetic valve malfunction in a cohort of patients with bileaflet mechanical prosthetic heart valves.

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Mechanical prosthetic heart valves carry an annual complication rate of 2-3%, including malfunction due to thrombosis and tissue ingrowth (1). These complications are associated with high morbidity and mortality rates. The early recognition of subclinical prosthetic valve malfunction may allow early treatment and avoidance of serious complications (hemodynamic instability or thromboembolism). Echocardiography, which is applied for the routine follow up of patients with prosthetic valves, cannot be utilized on a daily basis and also requires skilled echocardiographers to perform the investigations. Several reports have shown a typical pattern of closing of the prosthetic valves on real-time sound spectroanalysis under

normal conditions and with dysfunction of the prosthetic valves (2-5). Fritzsche et al. (6) showed that the acoustic sounds of the prosthetic valve remain constant under similar conditions, and that patients' valve signals did not change significantly over a six-month period. The results of animal studies have shown that frequent control of the heart valve sounds can detect very subtle changes in the integrity of the heart valve sounds before they lead to hemodynamic or thromboembolic consequences that are readily detectable by echocardiography (7).

Thus, a hand-held device – the Thrombocheck<sup>®</sup> – has been developed for routine home monitoring of heart valve function. The dimensions of the Thrombocheck are approximately 18×7×2 cm. The individual signature of the heart valve sound (a clicking noise) is computed from its acoustic information using Fourier transformation. The Thrombocheck consists of a microphone and a digital signal processor, and functions by detecting valve acoustic sounds ranging from

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4 to 22 kHz; it is also able to detect subtle changes in the acoustic sounds (clicking noise).

Herein are reported the results of a routine application of this new hand-held device in clinical practice.

## Clinical material and methods

### Patients

Between April 2004 and January 2005, 71 inpatients or outpatients (25 males, 46 females; mean age  $58.5 \pm 13.3$  years; range: 25 to 82 years) received a total of 82 bileaflet valves (47 mitral, 31 aortic, four tricuspid) (Table I). The annular diameters of the mitral, aortic and tricuspid valves ranged from 25 to 31 mm (median 27 mm), 19 to 25 mm (median 21 mm), and 27 to 33 mm, respectively. The valve models included were St. Jude Medical (St. Paul, Minnesota, USA), CarboMedics (Sulzer Carbomedics, Austin, TX, USA) and Sorin Bicarbon (Sorin Biomedica, Saluggia, Italy).

Patients were assessed both by echocardiography and by the hand-held device (Thrombocheck) on the same day. Each patient was tested once with the Thrombocheck, except for those who suffered from prosthetic valve malfunction, who were usually tested again following medical intervention. The study patients were referred to echocardiography for either routine examination or for suspected prosthetic valve malfunction. The patients examined in each of these indications were consecutive.

### Investigations

Transthoracic echocardiography (TTE) was performed using a Sonos 5500 instrument (Philips, Andover, MA, USA) with second harmonic capabilities. All of the prosthetic valves were carefully assessed both for hemodynamics and for leaflet motion in multiple views, as reported previously (8). Transesophageal echocardiography (TEE) was performed as needed using the same echocardiographic machine and a multiplane 3.7/5 MHz probe.

Prosthetic valve malfunction was suspected when

echocardiography showed high gradients across the prosthetic valve, or an increased (>25%) gradient across the prosthetic valve compared to a previous examination, or an inability to demonstrate full range motion of the two discs. In any case of suspicion of valve dysfunction the patient was referred for fluoroscopy and/or TEE.

There were no exclusion criteria for testing the Thrombocheck. In patients with two prosthetic valves with an immobilized leaflet in one of them, the analysis of diagnostic accuracy of the device was applied only to this valve. In the analysis of patients after mitral valve replacement, only those with the double disc mitral valve were included.

### Thrombocheck use

The Thrombocheck was set for double disc sounds, and the same device was used for all patients. The Thrombocheck was held for 1 min in a subxiphoid position perpendicular to the patient, who was lying in a recumbent position. There were three optional textual results on the screen of the device:

OK: this indicated normal function of the prosthetic valve (normal prosthetic valve acoustic signals).

Warning: after three repeat measurements (1 min each) indicated abnormal function of the prosthetic valve (abnormal prosthetic valve acoustic signals).

No signal: the Thrombocheck did not identify valve acoustic signals.

## Results

There were eight patients with a 'No signal' indication (one of them was after isolated tricuspid valve replacement). Of the remaining 63 patients, there was a 'Warning' alarm in 10 (15.9%) with the following clinical and echocardiographic findings: eight patients had evidence of current abnormal leaflet motion (Table II); one patient had no evidence of prosthetic valve malfunction; and one patient was investigated two months after thrombolytic therapy due to valve dysfunction and high gradient across the prosthetic valve. The latter patient was readmitted several months later with obstructive valve thrombosis, and reoperated on; the operative specimen showed combined thrombus and pannus formation. Six patients with abnormal leaflet motion were tested with the device following antithrombotic or thrombolytic treatment (Table II). In four patients with successful thrombolysis, the Thrombocheck showed normal prosthetic valve function ('OK'). In one patient with antithrombotic treatment and chronic abnormal leaflet motions there was a 'No signal' indication. In one patient with recurrent hospital admissions because of abnormal leaflet motions and known high-pressure gradient on the

Table I: Valve position.

Valve position	No. of patients
Isolated AVR	21
Isolated MVR	34
AVR + MVR*	10
MVR + TVR*	5
TVR	1

\*Two patients with single disc mitral valves.

\*Two patients with biological tricuspid valves.

AVR: Aortic valve replacement; MVR: Mitral valve replacement; TVR: Tricuspid valve replacement.

*Table II: Characteristics, therapy and outcome of patients with abnormal leaflet motions.*

Patient no.	Valve position	Valve model	Clinical symptoms	TEE*	Fluoroscopic findings	Thrombocheck findings before treatment	Treatment: Antithrombotic/anticoagulation	Valve function after treatment	Check-up after treatment
1	Aortic	SJM	Dyspnea, chest pain	One leaflet stuck at closed position (gradient 60/36)	One leaflet stuck at closed position	Warning	Heparin and thrombolysis	Normal	OK
2	Mitral	CM	Dyspnea, chest pain	One leaflet stuck at closed position (gradient 18/9)	One leaflet stuck at closed position	Warning	Heparin and thrombolysis	Normal	OK
3	Aortic	SJM	Dizziness	TEE not done (gradient 54/31 by TTE)	Incomplete opening of a leaflet	Warning	Heparin	Abnormal	Warning
4	Aortic	NA	Asymptomatic	Increased gradient across the prosthetic valve (gradient 68/41)	Incomplete opening of both leaflets	Warning	Heparin	Normal	NA
5	Aortic	CM	Asymptomatic	Increased gradient across the prosthetic valve (gradient 63/42)	Incomplete opening of one leaflet	Warning	Heparin	Normal	OK
6	Mitral	CM	Asymptomatic	One leaflet stuck at closed position (gradient 50/40)	One leaflet stuck at closed position	Warning	Heparin and thrombolysis	Normal+	Warning
7	Aortic	CM	Dyspnea, chest pain	One leaflet stuck at closed position, thrombus (gradient 78/48)	One leaflet stuck at closed position	Warning	Heparin and thrombolysis	Normal	OK
8	Mitral	SB	Asymptomatic	One leaflet stuck at closed position, thrombus (gradient 32/15)	NA	Warning	High-dose anticoagulation and aspirin	Abnormal	OK <sup>s</sup>
9	Aortic	CM	Dyspnea	TEE not done (gradient 50/30 by TTE)	Incomplete opening of both leaflets (15-20° missing for each leaflet)	Warning	High-dose anticoagulation and aspirin	Under evaluation	-

\*Gradients across the prosthetic valve expressed as peak/mean mmHg.

+This patient had recurrent prosthetic valve malfunction.

§OK after 7 months; the device could not be calibrated for double disc at later follow up - with repeated valve obstruction.

CM: CarboMedics; NA: Not available; SB: Sorin Bicarbon; SJM: St. Jude Medical; TEE: Transesophageal echocardiography; TTE: Transthoracic echocardiography.

mitral valve due to prosthesis-patient mismatch, the Thrombocheck showed 'Warning' after treatment, whereas the fluoroscopy showed normal disc movement, and the pressure gradient across the mitral valve returned to baseline.

There was one patient after tricuspid valve replacement with chronic abnormal leaflet motion in whom the Thrombocheck indicated OK.

The testing results of the Thrombocheck and the impact of valve position on its diagnostic accuracy are summarized in Table III. There was only one false-positive test, and one false-negative test. After exclusion of those patients with a 'No signal' indication, the Thrombocheck had a sensitivity and specificity of 90% and 98%, respectively, for the detection of prosthetic valve malfunction. The subgroup analysis according to valve position indicated a sensitivity of 100% and a specificity of 97% for patients with MVR, and 100% specificity and 95% sensitivity for patients with AVR.

## Discussion

In the current study, the hand-held Thrombocheck had an excellent sensitivity and specificity (90% and 98%) for the detection of prosthetic valve malfunction in a cohort of consecutive patients with bileaflet prosthetic heart valves, for both the mitral and aortic positions. A high diagnostic accuracy is an invaluable prerequisite for daily use of the Thrombocheck, as valve malfunction should not be missed and false alarm indications are also undesirable. The high sensitivity of the Thrombocheck provides assurance for both the patient and their physician.

Two of the present patients especially highlighted the accuracy of the Thrombocheck. In one patient (#8, Table II) the Thrombocheck provided various indica-

tions which paralleled with the leaflet motion: it showed 'Warning' early after thrombolysis, and then 'OK' after seven months. A few months later it could not be calibrated for this patient for bileaflet valve, and a repeated obstructive valve thrombosis was diagnosed. The other patient (#9, Table II) had moderately elevated aortic valve gradients (peak 50 mmHg, mean 30 mmHg) in a 19-mm CarboMedics prosthesis, which is not infrequently encountered in small-sized aortic prostheses (9). The Thrombocheck, however, provided a 'Warning' indication. Fluoroscopy showed only 30-degree limitation of the combined travel angle of the valve. These examples illustrate the high sensitivity of the Thrombocheck to detect valve malfunction, even in asymptomatic patients. This early recognition of sub-clinical prosthetic valve malfunction may allow early treatment before the development of serious complications which may lead to hemodynamic instability, thromboembolism and death. It may also detect valve thrombosis at a stage where the thrombus burden will not be associated with a high complication rate when thrombolysis is applied (10).

Follow up of patients with valve malfunction who were treated (by either antithrombotic therapy or intensified anticoagulation) showed resolution of the 'Warning' indication in four patients, further strengthening the reliability of the Thrombocheck. The device may be especially suitable for patients with a prior history of prosthetic valve malfunction and who have a higher likelihood of additional episodes, up to 23% in some series (11).

Ultimately, Thrombocheck is planned for individual application, and one study has reported the use of individual devices in patients in whom there were no difficulties in detecting a valve signal (7). Although in 10% of the present patients the Thrombocheck indicat-

Table III: Effect of valve position on diagnostic accuracy of the Thrombocheck<sup>®\*</sup>

Parameter	All patients	MVR	AVR	TVR
No. of patients	71	47	31	4
No signal indication	8 (10)	6 (13)	5 (16)	1 (25)
Patients excluded from analysis due to abnormality in an additional valve	-	3 <sup>†</sup>	0	0
Patients analyzed for diagnostic accuracy	63	38	26	3
Sensitivity	9/10 (90)	3/3 (100)	6/6 (100)	0/1 (0)
Specificity	52/53 (98)	34/35 (97)	19/20 (95)	2/2 (100)

Values in parentheses are percentages.

\*Statistical analysis was performed after exclusion of patients with a 'No signal' indication.

<sup>†</sup>The associated abnormal valve was aortic in two patients and tricuspid in one patient.

AVR: Aortic valve replacement; MVR: Mitral valve replacement; TVR: Tricuspid valve replacement.

ed 'No signal', this may have been due to use of the same device (i.e. the same acoustic fingerprint) for all patients.

### Study limitations

The number of patients in the current study is limited. In addition, the same hand-held device was applied for all patients. It is expected that if patients were to receive a personal device, which initially would be checked for appropriate valve function, the accuracy of the device would improve further. Moreover, those patients who initially show 'No signal' will not be offered the device. The present study group may not necessarily be representative of patients with prosthetic valves, as it contained a high proportion of cases with valve malfunction. The reason for this over-presentation of abnormally functioning valves was referral bias to the authors' center, where there is a special interest in prosthetic valve malfunction.

*In conclusion*, in this first report of clinical experience with the Thombocheck, the device proved to be simple to use and comfortable for home monitoring. Moreover, it demonstrated an excellent sensitivity and specificity for the detection of prosthetic valve malfunction. It must be borne in mind, however, that the Thombocheck should be used only as an initial screening system; it is not designed to replace echocardiography or fluoroscopy for thorough evaluation of prosthetic valves.

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