Rune Wiseth

AORTIC VALVE REPLACEMENT

Doppler Echocardiographic Studies

University of Trondheim
Department of Medicine
Section of Cardiology
Trondheim - Norway

TAPIR

Rune Wiseth

AORTIC VALVE REPLACEMENT

Rune Wiseth

AORTIC VALVE REPLACEMENT

Doppler Echocardiographic Studies

TAPIR
1993

Publication from the University of Trondheim
Department of Medicine
Section of Cardiology
University Hospital
N-7006 Trondheim, Norway

ISBN 82-519-1472-8

TABLE OF CONTENTS

ACKNOWLEDGEMENTS

The present work was carried out at the Section of Cardiology, Department of Medicine, University Hospital of Trondheim during the years 1988 - 1992.

Sincere thanks are directed to my mentors Professor Liv Hatle and Dr. Terje Skjærpe for their continuous support and encouragement. Their profound experience in clinical cardiology combined with a thourough insight into hemodynamics and into the field of Doppler echocardiography made a fundamental basis for the present work.

Professor Rolf Rokseth was the chief of the Section of Cardiology during my period as a research fellow. His never failing interest in this work, his kind criticism and advices in preparing manuscripts are highly appreciated.

During my research fellowship I had the opportunity to work close with Ole Rossvoll and Stein Samstad, parts of this work would not have been possible without their contribution.

I will also thank Jørn Bathen and Lars Hegrenæs for their willingness to help with practical solutions in order to make this project feasible.

I am grateful for all help and assistance given by the nurses at the Cardiological Laboratory, and special thanks are directed to Reidun Skjeldam, Torild Nergård and Marit Olstad Røe.

This work had not been possible without a close collaboration with the Section of Thoracic and Cardiovascular Surgery at the University Hospital of Trondheim under the leadership of Professor Olaf W. Levang. His profound experience in valve surgery has been of great value during the planning and accomplishment of this work, and I appreciate stimulating discussions with him and other members of his staff.

My decision to specialize in cardiology was taken when I was working at Innherred Hospital during the years 1981-86. Sincere thanks are directed to my former chief and very good friend Per Otto Foss for extremely stimulating years at his department.

I am grateful to the Norwegian Council on Cardiovascular Diseases that supported the present work by granting me a research fellowship from February 15th 1988 to March 31th 1991. Financial support was also received from the Blix Family Fund for Medical Research and from the Cardiac Research Fund of the Regional Hospital of Trondheim.

Finally, I direct my sincere thanks to my wife Kirsten and our children Hanne and Marie for their patience and tolerance during these and all other years.

LIST OF PAPERS

I Wiseth R, Hegrenaes L, Rossvoll O, Skjaerpe T, Hatle L. Validity of an early postoperative baseline Doppler recording after aortic valve replacement.
Am J Cardiol 1991;67:869-872.

II Wiseth R, Levang OW, Sande E, Tangen G, Skjaerpe T, Hatle L.
Hemodynamic evaluation by Doppler echocardiography of small ($\leq$21mm) prostheses and bioprostheses in the aortic valve position.
Am J Cardiol 1992;70:240-246.

III Wiseth R, Levang OW, Tangen G, Rein KA, Skjaerpe T, Hatle L.
Exercise hemodynamics in small ($\leq$21 mm) aortic valve prostheses assessed by Doppler echocardiography.
Am Heart J 1993;125:138-146.

IV Wiseth R, Rossvoll O, Levang OW, Skjaerpe T, Hatle L.
Two-dimensional echocardiography for prediction of aortic valve prosthesis size. A comparative study of the Medtronic-Hall and the Carpentier-Edwards supra-annular valves.
Scand J Thor Cardiovasc Surg 1993;26:000. (To be published June 1993)

V Wiseth R, Skjaerpe T, Hatle L. Rapid systolic intraventricular velocities after valve replacement for aortic stenosis.
Am J Cardiol 1993;71:944-948.

VI Wiseth R, Samstad S, Rossvoll O, Torp HG, Skjaerpe T, Hatle L.
Cross-sectional left ventricular outflow tract velocities before and after aortic valve replacement: A comparative study with two-dimensional Doppler ultrasound.
J Am Soc Echo 1993;6:279-285.

The papers will later be referred to by their Roman numerals.

INTRODUCTION

When valve replacement was introduced in the treatment of patients with severe aortic valve disease more than 30 years ago (1), a new era started in the management of these patients. The natural history of symptomatic aortic valve disease is well documented and associated with a poor prognosis (2-4). Numerous reports during the last decades have demonstrated excellent clinical results with symptomatic relief, improved functional capacity and a better life expectancy following valve replacement for symptomatic aortic valve disease (5-9). However, the fact can not be neglected that even normally functioning prostheses are inferior to a normal native valve for several reasons. In spite of continuous efforts to improve prosthetic valves, no prosthesis yet developed approximates well the performance of a normal native valve which will serve the most people lifelong with excellent hemodynamics, no significant degeneration and no thromboembolic problem. The patient who has undergone valve replacement is faced with a new set of potential long-term problems including embolization, endocarditis, perivalvular leaks and prosthesis dysfunction. The need for permanent anticoagulation therapy in mechanical prostheses and a limited durability of bioprostheses are important factors making prostheses inferior to a normal native valve.

All prostheses currently in use are mildly stenotic. In the majority of patients this obstruction is neglible and without hemodynamic significance. However, a signficant prosthesis gradient may result after aortic valve replacement. This may be caused by a prosthesis dysfunction or it may result from a discrepancy between the size of the prosthesis and the patients body surface area, a "patient-prosthesis mismatch" (10). The

risk of unfavourable hemodynamics is inversely related to prosthesis size, and hemodynamic evaluation of small aortic valve prostheses are therefore of special interest. The risk of valve related morbidity, unfavourable hemodynamics and prosthesis malfunction necessitate a diagnostic tool to assess prosthesis function routinely in the follow-up of patients as well as in evaluating patients with suspected prosthesis dysfunction.

Assessment of prosthesis function

Clinical examination. A clinical examination including the patient history is an inevitable first step in the evaluation of patients with prosthetic valves. This may reveal the presence of heart failure, and during auscultation the presence of a regurgitant murmur and the presence or absence of distinct opening and closing clicks of mechanical valves are important signs to note. However, although indicative, the clinical examination alone will not be sufficient in assessing prosthesis function, and supplementary dignostic tools are needed.

Heart catheterization. Until recently the gold standard in hemodynamic assessment of prosthetic valves has been heart catheterization. There are numerous studies reporting invasively obtained gradients and valve areas for different types of aortic valve prostheses (5,11-19). Also, exercise hemodynamics have been assessed during invasive procedures (15,19-23). Heart catheterization, however, is not without risk, it is cumbersome to the patient and it is not suitable as a routine method in the follow-up of patients. Furthermore, exercise hemodynamics are difficult to assess during catheterization.

Cinefluoroscopy. Even in the era of echocardiography cinefluoroscopy may yield important additional information in cases with suspected prosthesis dysfunction. Valve dehiscence may be clearly visualized as an exaggerated motion of the housing ring. A limited excursion of disc or leaflets in mechanical valves due to thrombus formation or pannus ingrowth may be detected by cinefluoroscopy.

Doppler echocardiography. During the last years Doppler echocardiography is established as a valuable tool and the routine method in evaluating patients with prosthetic valves. This technique allows for a noninvasive assessment of cardiac performance including prosthesis function. Repeat studies may well be performed without any risk and with minimal discomfort to the patient.

M-mode and two-dimensional (2D) echo. With M-mode and 2D echo chamber sizes, myocardial thickness and contractility are well assessed. These are important parameters in the follow-up after aortic valve replacement. In assessing prosthesis function, however, M-mode and 2D echo are of less value. With M-mode an impediment of the free movement of the valve structure (poppet, disc, leaflet) in a mechanical valve may be demonstrated, but the findings may be difficult to interpretate (24), and cinefluoroscopy may be more helpful than echocardiography in such cases. Two-dimensional echo may demonstrate thickening and calcification of bioprostheses undergoing tissue degeneration, and in case of valve dehiscence a "rocking" movement of the prosthesis may be detected. An important limitation for the 2D echo technique is the strong echoes made by the prosthesis itself, thus making both sensitivity and specificity of this technique rather low.

Doppler. With the Doppler technique a thorough assessment of prosthesis function is possible. By means of the Bernoulli equation gradients are calculated from the Doppler-obtained velocities across prostheses (25), and prosthetic valve areas may be calculated by the continuity equation in the same way as in native aortic stenosis (26).

With Doppler echocardiography prosthetic and periprosthetic leaks may be detected, localized and quantified (27-29), although in cases with minor leaks the differentiation between a prosthetic and a periprosthetic leak may be difficult (27).

The Doppler echocardiographic technique has made it possible to study larger groups of patients thus obviating the risk of a bias being introduced when a selected group is studied in order to assess hemodynamics of a certain valve or when different valve types are to be compared.

A complete hemodynamic evaluation of prosthesis function should include exercise studies as gradients that are low or moderate at rest could possibly significantly increase during exercise (15,30-31). So far there has been a paucity of noninvasive exercise data on prosthetic valves, but there are reports indicating that exercise studies are suitable and may yield valuable information in assessing prosthesis function (30-32).

Furthermore, Doppler echocardiography makes it possible to serially study patients both in a long-term follow-up as well as in the often hemodynamically unstable period early postoperatively. In general, a thorough hemodynamic evaluation is possible with this technique that could have the potential of supporting us with a considerable amount of clinically relevant information in patients with prosthetic valves, information that has not been readily attainable with invasive methods. Based on these anticipations the present work was planned.

THE AIMS OF THE STUDY

The aims of the study were:

1) To assess the validity of an early postoperative baseline Doppler recording of prosthesis gradient as a reference for later follow-up in patients undergoing aortic valve replacement.

2) To assess resting and exercise hemodynamics in an unselected group of patients with a small ($\leq$21 mm) aortic valve prosthesis.

3) To assess the potential role of preoperative echocardiography in predicting aortic valve prosthesis size.

4) To study early postoperative hemodynamics following valve replacement for severe aortic stenosis with special reference to the occurrence of systolic gradients in the left ventricle.

5) To assess whether aortic valve replacement results in changes in the left ventricular outflow tract velocity distribution that could influence the validity of Doppler-obtained stroke volume estimates.

METHODS

Patients.

Cardiac surgery was started at the University Hospital of Trondheim in 1983. All patients studied in the present work were operated at this hospital in the period from 1983-1990. In 1983 Doppler echocardiography was already well established in the clinical routines at the Section of Cardiology, and from the start of cardiac surgery a follow-up program was established for patients undergoing valve replacement. This program included a baseline Doppler echocardiographic examination before discharge from hospital and repeat examinations at 3 and 12 months postoperatively. It was my privilege when I started as a research fellow to analyse data from the control program, and this analysis forms the basis for Paper I.

The University Hospital of Trondheim provides cardiac surgery in an area of 640 000 inhabitants (Health Region IV). In the recruitment period to this study all patients receiving a heart valve prosthesis in this area were operated at the University Hospital of Trondheim with a very few exceptions. Therefore the group with a small ($\leq$21mm) aortic valve prosthesis studied in Papers II & III represents an unselected material of patients receiving a small prosthesis during a 7-year period from a representative and stable background population.

The control program outlined above with a postoperative Doppler echocardiographic examination three months postoperatively was continued during my period as a research fellow. This made a clinical research "model" that formed the basis for further prospective studies, and this "model" was used in Papers IV & VI.

Instruments.

In the Papers I-V conventional Doppler echocardiographic equipment that is further described in the separate papers was used.

The exercise study in Paper III was performed with an Irex Meridian ultrasound system. This was a technically difficult study as prosthesis gradients were recorded during ongoing exercise in the sitting position. It was aimed at an exercise test relevant for and at least as demanding as the patients ordinary physical activities during daily life. Important for this particular study was that the Irex machine allows for continuous strip-chart recording that made it possible to "pick up" cycles with technically adequate recordings of transvalvular gradients. To obtain adequate recordings of velocities across prostheses in the sitting position, the use of a small stand-alone Doppler transducer only 1.5 cm in diameter was essential. In a pilot project prior to this study we experienced a considerably lower success rate when a larger stand alone probe or when a combined Doppler and imaging probe was used. Among the 30 patients included in the study adequate recordings were obtained in 25, and with the design of the study this success rate was judged as acceptable.

In Paper VI instantaneous cross-sectional velocity profiles in the left ventricular outflow tract (LVOT) were constructed by extracting velocity information from color flow maps as digital data. This computer-based technique was developed at the University Hospital of Trondheim in close collaboration between the Section of Cardiology and the Department of Biomedical Engineering. It was first described in 1989 by Samstad et. al (33). The technique has been used to study velocity profiles across the mitral valve in normal subjects and in various groups of patients (33-34). It has also been used to study LVOT

velocity profiles in the aortic annulus in normal subjects (35). When velocity data are extracted from a color flow map to construct instantaneous velocity profiles, the sweep time of the transducer must be corrected for when pulsatile flow is studied, otherwise a flat velocity profile will artificially appear skewed due to the lag in data collection (33). With the technique used in Paper VI a linear interpolation algorithm is used to correct for this time distortion (33), and the validity of the method is demonstrated with in vitro studies (36).

Calculation of hemodynamic parameters.

The present work is entirely noninvasive and hemodynamic parameters are deduced from Doppler and echocardiographic measurements according to standard formulas listed below.

Gradients. Velocities across the prostheses were recorded with continuous wave Doppler, and from the highest velocities obtained, prosthesis gradients were calculated according to the Bernoulli equation with correction for prevalvular velocities (25);

1) Gradient $= 4(V_{valv}^2 - V_{lvot}^2)$

where V_{valv}=velocity across prosthesis and V_{lvot}=left ventricular outflow tract velocity. In the exercise study (Paper III), however, it was not possible to correct for V_{lvot} in the Bernoulli equation, inasmuch as adequate recordings of V_{lvot} during exercise only occasionally were obtained. Therefore, the prosthesis gradients at exercise as well as the actual exercise-induced increase in gradients may to some extent be overestimated in this study. These methodological aspects are specifically discussed in Paper III.

Cardiac output (CO) was calculated according to the formula

2) $\mathbf{CO = VTI_{lvot} \times A_{lvot} \times HR}$,

where VTI_{lvot} = velocity time integral in the left ventricular outflow tract recorded by pulsed Doppler, A_{lvot} is the left ventricular outflow tract area and HR is the heart rate.

Prosthesis valve area (PVA) was calculated using both the standard continuity equation (26);

3) $\mathbf{PVA_{stand} = A_{lvot} \times VTI_{lvot}/VTI_{valv}}$

and the simplified continuity equation (26,37);

4) $\mathbf{PVA_{simpl} = A_{lvot} \times V_{lvot}/V_{valv}}$

where A_{lvot} is the left ventricular outflow tract area, VTI_{lvot} and VTI_{valv} are the velocity time integrals in the left ventricular outflow tract and across the prosthesis respectively, and V_{lvot} and V_{valv} are the maximum velocities in the same positions.

Dimensionless obstruction index. By eliminating A_{lvot} from the continuity equation, the systolic performance of aortic valve prostheses is assessed by just relating the subvalvular to the valvular velocity time integrals and subvalvular to valvular velocities (38). This dimensionless obstruction index (DOI) was calculated according to the equations;

5) $\mathbf{DOI_1 = VTI_{lvot}/VTI_{valv}}$ and

6) $\mathbf{DOI_2 = V_{lvot}/V_{valv}}$

with abbreviations as in equations 3 and 4.

SUMMARY OF RESULTS

Paper I.

The validity of an early postoperative baseline Doppler recording of prosthesis gradient as a reference for later comparison was assessed in 131 patients undergoing aortic valve replacement (53 bioprostheses, 78 mechanical). Although the hemodynamic state was markedly different with increased heart rate and decreased left ventricular ejection time index, gradients recorded at baseline were representative for findings at 3-5 months later. A minor decrease in gradients was found with time, the change was statistically significant for bioprostheses and valves $\leq$ 23 mm, whereras no significant changes were found for mechanical valves or valves of a larger size. In the great majority of patients (82%) the change in mean gradient from baseline was within $\pm$5 mm Hg. When the mean gradient changed by more than $\pm$5 mm Hg, the direction of the change was usually from higher toward lower values. Only 7 patients (5% of total) showed an increase in mean gradient $>$ 5 mm Hg from baseline to the second examination.

Papers II & III.

Hemodynamics at rest and during exercise were studied in an unselected group of patients receiving a small ($\leq$21 mm) aortic valve prosthesis during a 7-year period. Acceptable hemodynamics were found at rest, only 2 out of 46 patients had a mean gradient $>$ 25 mm Hg. The Carpentier-Edwards supraannular (CES) 21 mm, the Medtronic-Hall (MH) 20 and 21 mm valves were compared with no statistically significant differences in gradients, neither did the ratios of subvalvular to valvular velocities or velocity time integrals ("dimensionless obstruction index") differ. The prosthesis area was slightly larger for the MH 21 mm compared to the CES 21 mm valves, this difference, however,

could be caused by a smaller stroke volume in the CES group as valve opening is progressive with flow for this prosthesis. Prosthesis valve areas obtained with the simplified (velocities) and the standard (velocity time integrals) continuity equation were highly correlated both for mechanical and biological prostheses. An inverse relationship was demonstrated between left ventricular outflow tract diameters and maximal subvalvular flow velocity. This emphasizes the necessity of making correction for subvalvular velocities (equation 1, page 15) when applying the Bernoulli equation in patients with small aortic valve prostheses, otherwise gradients will be overestimated to a varying degree.

In 25 patients with a $\leq$21 mm aortic valve prosthesis exercise hemodynamics were assessed by a symptom-limited bicycle test in the upright position. Exercise induced a moderate increase in gradients; from 30$\pm$8/16$\pm$4 mm Hg (peak/mean) at rest to 46$\pm$12/24$\pm$7 mm Hg during exercise. A linear relationship was demonstrated between gradients at rest and during exercise.

In a subgroup (56%) additional findings were abnormal intraventricular flow that occurred in two distinct patterns; late systolic midventricular velocities directed toward the LVOT and flow directed toward the apex in the isovolumic period. The frequency of these flow phenomena increased with exercise. Such flow patterns, that are typically found in patients with hypertrophic cardiomyopathy, could be markers of impaired diastolic filling and of abnormal and asynchronous relaxation. Therefore, combined with the rather moderate increase in gradients with exercise, the frequent occurrence of these intraventricular velocity patterns made us suggest that factors other than prosthesis gradients should be addressed in a total hemodynamic assessment of patients with small aortic valve prostheses.

Paper IV.

The value of 2D echo in predicting prosthesis size was assessed and compared for the Medtronic-Hall (MH) and the Carpentier-Edwards supraannular (CES) aortic valves. The annulus diameter correlated significantly with the prosthesis size for both valve types (MH, r=0.88, CES, r=0.73). Average prosthesis size was similar to the average preoperative annulus diameter for the MH valves while the size of the CES valves implanted on an average exceeded annulus diameter by 1.5 mm. The study demonstrated that with a certain annulus diameter prosthesis size may vary according to prosthesis type, and with a narrow annulus the need for a root enlarging procedure may depend on what prosthesis type is to be used. Postoperative hemodynamics were assessed in the majority of patients with special reference to the small valves. Prosthetic valve area was significantly smaller in the CES 21 mm compared to the MH 21 mm valves. However, when the prosthetic valve area was divided by the preoperative annulus area, the valves did not longer significantly differ. With this approach an index expressing the ability of a certain prosthesis to make the most of the root space available is obtained, and the concept of taking into consideration the preoperative annulus dimension is proposed as a mean toward a better overall judgement of the hemodynamic properties of a certain valve.

Paper V.

The frequency and severity of intraventricular gradients during the first week following valve replacement for severe aortic stenosis was assessed by Doppler echocardiography. Intraventricular gradients (defined as the presence of systolic intaventricular velocities $\geq$ 2 m/s at least once during the first week) were found in 13 out of 25 patients (52%) and were most frequent at postoperative day 3. These gradients were mostly mild and

transient. However, in 4 patients severe gradients > 64 mm Hg (>4 m/s) were found. Patients with intraventricular gradients postoperatively had significantly smaller end-diastolic and end-systolic diameters at a preoperative M-mode recording, and the fractional shortening was significantly higher. It is concluded that the risk of developing intraventricular gradients following valve replacement for aortic stenosis may be predicted by a preoperative M-mode study, and patients with a small left ventricular cavity dimension and maintained contractility should be carefully monitored in the early postoperative period. The study demonstrates that Doppler echocardiography may serve as a valuable supplement in the early postoperative monitoring following valve replacement for severe aortic stenosis.

Paper VI.

Flow velocity distribution in the LVOT was studied in 10 patients undergoing valve replacement for aortic stenosis. By means of a computer-based technique cross-sectional velocity profiles were constructed by extracting velocity information as digital data from color flow maps. LVOT velocity profiles were variably skewed both before and 3 months after surgery, and no systematic or uniform changes could be detected after valve replacement. The highest velocities were typically localized in the region from the center of the outflow tract diameter toward the septum both before and after surgery. At the time of peak flow the maximum velocity overestimated the cross sectional mean velocity to the same extent at both recordings, and the ratio of the maximum to the mean velocity time integral was similar before and after surgery. Therefore, according to this study valve replacement in patients with aortic stenosis do not result in a change in LVOT velocity distribution that will influence stroke volume estimate with the Doppler technique. There

are, however, several important limitations of the study, and in order to more thoroughly delineate LVOT velocity profiles in relation to aortic valve replacement the need for further studies is underlined (several imaging planes, various subgroups of patients, different hemodynamic states).

GENERAL DISCUSSION

Doppler echocardiography has the potential of thoroughly assessing hemodynamics in patients with prosthetic aortic valves. Besides evaluation of prosthesis function additional important hemodynamic information may be obtained and the technique is eminently suited as a clinical routine method. Unselected groups may be studied, and repeated recordings are easily undertaken in order to assess reproducibility and to follow patients over time. In the present work exercise hemodynamics in patients with prosthetic aortic valves were studied, 2D echo was found reliable in predicting prosthesis size and hemodynamic information with the potential of influencing clinical decision making was obtained in the early postoperative period following valve replacement for aortic stenosis. Although Doppler echocardiography for several years has been established as a valuable tool in evaluating patients with prosthetic valves, the present work has underlined its utility and has even demonstrated a possible extension of its use in obtaining information of practical clinical relevance in the handling of these patients.

Doppler gradients across aortic valve prostheses.

Although the accuracy of the Bernoulli equation in assessing gradients across native aortic valve stenosis is well documented (39-40), data reported for aortic valve prostheses are somewhat conflicting (27,41-44). As design and flow characteristics may vary considerably with different prosthesis types, the Doppler technique cannot be assumed to remain equally accurate for calculating prosthesis gradients. Burstow et. al (41) demonstrated excellent correlations between Doppler and catheter peak and mean gradients

studied simultaneously in patients with both mechanical and biological aortic valve prostheses. Nonsimultaneous studies have also demonstrated fairly good correlations between Doppler and catheter gradients (27,42), while others found considerably higher Doppler than catheter gradients in patients with ball valves (43), and with bileaflet valves (44). As for native aortic stenosis an underestimation of prosthesis gradient will result if the highest velocities across the prosthesis are not recorded or the angle of incidence between the Doppler beam and the direction of blood flow is greater than about 20^{o} (45). On the contrary, several factors could cause Doppler gradients across aortic valve prostheses to exceed catheter gradients (46-47), and such factors are briefly discussed below.

1) Prevalvular velocities. In deriving transprosthetic Doppler gradients by means of the Bernoulli equation, LVOT velocities should be corrected for, otherwise an overestimation will result (25). However, in most studies reporting Doppler gradients in aortic valve prostheses, LVOT velocities are neglected. There are only a few reports where the LVOT velocities are corrected for as shown in equation 1 on page 15 (28,44,48). In most patients LVOT velocities are low and peak and mean gradients will differ by 3-4 and 1-2 mm Hg, respectively, whether LVOT velocities are corrected for or not. In Papers II & III, however, it is demonstrated that a considerable overestimation of gradients may occasionally result if LVOT velocities are not considered. An inverse relationship was demonstrated between the LVOT diameter and the LVOT velocity. Accordingly, the use of equation 1 will be more important in patients with a small prosthesis and a narrow outflow tract. Furthermore, the significance of the LVOT velocities in the Bernoulli equation should be considered when interpretating exercise gradients obtained with

continuous-wave Doppler. The LVOT velocities increase during exercise, and both the actual gradient and the gradient increase during exercise will to some extent be overestimated when assessed by continuous-wave Doppler. This is illustrated in Paper III. These important methodological considerations are not addressed in previous reports on exercise Doppler in evaluating aortic valve prosthesis function (30-31).

Based on our data it is claimed that LVOT velocities should routinely be recorded and corrected for when using the Bernoulli equation in aortic valve prostheses.

2) Pressure recovery. Conservation of energy dictates that the local fluid pressure will decrease as the local flow velocity increases. The velocity of the jet will be at a maximum and the local pressure at a minimum at the level of the prosthesis where the cross-sectional area is at a minimum (46-47,49-50). Farther away from the valve flow expands to fill the aorta, the velocities will again decrease and the aortic pressure increases (pressure recovery). While Doppler measurements accurately reflect the highest gradient along the interrogation line, catheterization measures the recovered pressure distal to the valve. The catheter gradient equals the ventricular minus the aortic pressure and practically the aortic pressure is usually measured at a distance of $\geq$ 2 cm from the valve plane. According to in vitro studies (46) there is some degree of pressure recovery at that site, thus explaining the discrepancy between Doppler and catheter gradients reported by some investigators (43-44).

3) Localized gradients. During the recent years both clinical and experimental data have emerged indicating that the relation between Doppler and catheter gradients behaves differently according to prosthesis type. Rothbart et. al. and Ihlen et. al. demonstrated

considerably higher Doppler than catheter gradients in the Starr-Edwards ball valves (43) and the Carbomedics bileaflet valves (44). The findings in these clinical studies are in accordance with in vitro studies where the effect of prosthesis design on the Doppler-catheter gradient relation is described (46,51). In these experimental studies high and localized gradients were demonstrated in the central orifice of bileaflet valves (St. Jude) while lower gradients were found at the same level in the larger side holes. Interestingly, the high central orifice gradients showed an excellent agreement with the Doppler obtained gradients thus reflecting the fact that continuous-wave Doppler measures the highest velocities along the Doppler beam. In comparison of Doppler and catheter gradients the actual agreement was acceptable in bioprostheses (the valve studied was Hancock) and in disc valves (Medtronic-Hall) while Doppler gradients significantly exceeded catheter gradient in ball valves (Starr-Edwards) and in bileaflet valves (St. Jude) (51).

Baseline recording.

There are several reports with reference values for Doppler-derived gradients across normally functioning aortic valve prostheses (48,52-54). There is, however, a considerable overlap among different types and sizes of prostheses, and reported reference values show wide ranges (52,55-57). Besides the characteristics of the prosthesis, gradients depend on several patient related factors including left ventricular function, heart rate, cardiac output and flow period (systolic ejection period) (55,58). Furthermore, the orientation of the prosthesis in the aortic annulus may influence prosthesis gradients (59-60). Therefore, a variety of factors related both to the prosthesis and to the patient contribute to the wide ranges for reference values. Based on these considerations a baseline recording of prosthesis gradient as a reference for later comparison, the patient

thus serving as his or her own control, could possibly be of more value in the follow-up than comparison of gradients with reported reference values. The recent experience from experimental studies that prosthesis design may considerably influence Doppler gradients (46,51) further supports the assumption that a baseline recording - thus making a "fingerprint" of the specific prosthesis - might be of great value in the follow-up. In Paper I the validity of an early postoperative Doppler gradient as a reference for later was demonstrated. In spite of a markedly different hemodynamic state at baseline, gradients recorded before discharge from hospital were representative for later findings. A practical recommendation based on the results in Paper I is that patients undergoing aortic valve replacement should routinely be examined by Doppler ultrasound before hospital discharge. Usually a minor decrease in gradient will occur from early postoperatively to some months later. In the presence of a marked gradient increase, an explanation should be searched for. This could be an increased stroke volume due to a slower heart rate, the presence of a significant leak or an abnormal obstruction.

Small aortic valve prostheses.

The hemodynamic properties of small aortic valve prostheses are questioned and the management of the narrow aortic root remains controversial (61-65). The alternative to a small prosthesis is a root enlargement that may allow insertion of a larger valve (62,66-67), but this will prolong the surgical procedure and may increase the operative risk (64). Besides considerable interest in literature, this topic has been subject of great local interest, and the cardiac surgeons at our institution strongly argued that a thourough hemodynamic assessment of an unselected group of patients with a small aortic valve prosthesis would be of significant interest.

TABLE I. Comparison of prosthesis gradients for different sizes of the Carpentier-Edwards supraannular (CES) and the Medtronic-Hall (MH) valves

	Valve size			
CES	21 mm (n=8)	23 mm (n =15)	25 mm (n =31)	ANOVA p value
Peak gr. (mm Hg)	25± 8 (14-40)	21± 7 (12-38)	19± 6 (9-33)	NS
Mean gr. (mm Hg)	14± 5 (7-23)	12± 4 (12-22)	10± 4 (4-18)	0.042
MH	21 mm (n =19)	23 mm (n =30)	25 mm (n =22)	
Peak gr. (mm Hg)	25±10 (14-60)	24± 7 (11-45)	22± 7 (9-40)	NS
Mean gr. (mm Hg)	13± 5 (7-31)	12± 4 (6-23)	11± 4 (5-19)	NS

In comparison of gradients across the CES and MH 21 mm, 23 mm, and 25 mm valves by one-way analysis of variance (ANOVA) a p value < 0.05 was found only in the analysis of mean gradients across the CES valves. However, after adjustment (Bonferroni) due to the low number of CES 21 mm valves, this difference was not statistically significant.
Ranges are given in parentheses.

Although rather inhomogeneous, the 7-years material analysed in Paper II is thought to be representative for the hemodynamic results generally obtained with a small (mainly 21 mm) aortic valve prosthesis.

Hemodynamics at rest were acceptable, and only two patients had a mean gradient > 25 mm Hg. No data from larger prostheses were included in Paper II. However, in an unpublished study we have compared gradients for the Medtronic-Hall (MH) 21, 23 and 25 mm valves and for the Carpentier-Edwards supraannular (CES) 21, 23 and 25 mm valves (Table I, page 28). A considerable overlap between gradients across valves of different sizes is demonstrated with no significant differences in gradients between 21 and 23 mm valves for neither of the two valve types. These data are in accordance with results from others (44,68), and indicate that acceptable resting hemodynamics usually are obtained with a 21 mm prosthesis.

The comparison of hemodynamic data between different prosthesis types performed in Paper II must be considered in view of the rather low number of patients in some groups. However, Figure 2 in Paper II demonstrates that gradients across the prostheses types studied are in the same ranges, and the clinical relevance of demonstrating any statistical significant differences by analysing a large number of patients could be questioned.

The MH 20 and 21 mm valves are identical except for a thinner sewing ring in the former. It is noteworthy that no pathological leaks were detected in the MH 20 mm group indicating that the thinner sewing ring does not dispose for perivalvular leaks.

Theoretically hemodynamic properties should be equal for the MH 20 and 21 mm valves as the inner orifice areas are identical. Nevertheless, the calculated valve areas tended to be lower for the MH 20 compared to the MH 21 mm valves although these differences did not reach statistical significance. The number of MH 20 mm valves, however, was low.

It should be noted that subvalvular diameter measurements indicated that the MH 20 mm valves are inserted in roots, that relative to the prosthesis size, are narrower than the roots where a 21 mm valve is inserted. This calls attention to the possibility that factors other than prosthesis design and size could influence prosthesis hemodynamics. It could be that a narrow left ventricular outflow tract precludes an effective utilization of the prosthesis area, furthermore, an oblique positioning of a disc valve in the aortic annulus could result in a less than optimal orientation of the major orifice, thus influencing the hemodynamic properties of the prosthesis (59-60).

Rothbart et. al. proposed the "dimensionless obstruction index" (equations 5&6 page 17) as a parameter in assessing aortic valve prosthesis function (69). This index was analysed and reported in Paper II. In an earlier study we demonstrated that the major source of error in determining prosthetic aortic valve area is the subvalvular diameter measurements (70). When using the dimensionless obstruction indices the inaccuracies introduced by diameter measurements are omitted and a more reliable parameter for prosthesis function could be obtained. However, even the dimensionless obstruction indices show wide ranges in some valve types as demonstrated in Paper II, Table I. This could be attributed to measuring inaccuracies. However, these parameters were highly reproducible and the ranges demonstrated for some of the valve types in our study are very similar to data reported by others (71). These wide ranges could therefore reflect real differences in hemodynamics occurring when identical valves are inserted into different patients.

In vitro data support use of the ratio of subvalvular to valvular velocities as a flow independent index of aortic valve prosthesis function (51), and this parameter has proven valuable in differentiating normal from stenotic prostheses (69,71).

So far the dimensionless obstruction index has infrequently been reported in studies

assessing prosthesis hemodynamics, and its role in the follow-up of patients with prosthetic aortic valves remains unanswered. Interestingly, in a recent study this index seemed to be of value in predicting patients with the highest prosthesis gradients during exercise as a ratio of subvalvular to valvular maximal velocity $\leq$ 0.25 was associated with a high frequency of mean gradient > 50 mm Hg during exercise (31). In our material there were no patients where this ratio was that low, the minimum value recorded was 0.27 (Table I, Paper II).

During assessment of resting hemodynamics systolic intraventricular velocities ($\geq$1.5 m/s) with the highest velocities occurring at the end of systole were demonstrated in 6 patients. Based on these findings a characterization of intraventricular flow was included in the exercise protocol (Paper III). Two distinct intraventricular flow patterns were detected; the systolic intraventricular flow described above and intraventricular flow directed toward the apex in the isovolumic relaxation period. These velocity patterns, which increased in frequency during or immediately after exercise, are both described in patients with hypertrophic cardiomyopathy (72-73). The increased systolic intraventricular velocities could be caused by smaller left ventricular cavity size and a contributing factor could be an impaired left ventricular filling caused by an abnormal diastolic function (74-77). The abnormal isovolumic flow toward the apex is thought to be caused by abnormal and asynchronous relaxation leading to increased intraventricular pressure differences resulting in abnormal blood flow movements (72-73). No relationships between the presence of these abnormal flow patterns and exercise capacity could be demonstrated, but the group studied was heterogenous and several factors, including noncardiac ones, probably influenced exercise capacity. Nevertheless, the demonstration of abnormal intraventricular velocity patterns like in hypertrophic cardiomyopathy frequently occurring in these patients

indicates that factors other than the moderate increase in prosthesis gradients could be of significance for the exercise capacity in patients with small aortic valve prostheses. The reasons for the limitation of exercise capacity in hypertrophic cardiomyopathy remain unclear and are probably multifactorial (78-79). Diastolic dysfunction, however, is thought to be an important factor (78). Furthermore, it is demonstrated that even in cases with mild hypertrophy severe impairment of diastolic function may be present (80-81), and even after the hypertrophy has fully regressed after aortic valve replacement diastolic abnormalities are demonstrated to persist (82-83). Based on our findings future exercise studies in patients with aortic valve prostheses should be designed to include other parameters than prostheses gradients as such factors may be important in assessing the overall hemodynamic function in these patients.

Prediction of prosthesis size.

Although acceptable hemodynamics are obtained in the majority of patients undergoing valve replacement, significant residual left ventricular outflow tract obstruction may occur. A predisposing factor for the risk of unacceptable hemodynamics is the relation of prosthesis size to the patients body surface area (10). Therefore, the ability to preoperatively predict prosthesis size is of value to the surgeon in planning the procedure. In Paper IV it was demonstrated that a reliable prediction is possible with 2D echo. The preoperative 2D echo estimate of the aortic root diameter related differently to prosthesis size in Medtronic-Hall and Carpentier-Edwards supraannular valves. Although these differences could well be explained by different design and implantation techniques, there are no previous reports where such differences are quantitated. A preoperative prediction of prosthesis size is of special value in patients with a narrow aortic annulus inasmuch as

the risk of a "patient-prosthesis mismatch" is at maximum in such patients. It is concluded from Paper IV that a 2D echo estimate of aortic root dimension should be included as a routine in the preoperative assessment of patients undergoing aortic valve replacement. This is of particular relevance as due to the Doppler technique an increasing number of patients are referred to aortic valve replacement without a preceding ventriculography, and the only preoperative information about the left ventricular outflow tract relations will be the echocardiographic study. The prosthesis valve area was related to the preoperative annulus dimension in order to obtain an index expressing how effectively a certain prosthesis may utilize the available annulus area. It is proposed to include this index in prospective, randomized studies comparing hemodynamic properties of different prosthesis types.

Intraventricular gradients.

The early postoperative period following valve replacement for aortic stenosis is often hemodynamically unstable with arrhythmias, an imbalanced volume status and varying amounts of pericardial effusion. Although Doppler echocardiography is somewhat hampered by a limited access, it was demonstrated in Paper V that important hemodynamic information may be obtained even in this period. Only one patient had to be excluded from this study because of techniqually inadequate recordings.

Following the relief of a fixed, severe aortic stenosis there are marked changes in hemodynamics, and severe intraventricular gradients may occur with the risk of a less favourable clinical outcome (73,84-85). These gradients will aggravate with hypovolemia, enhanced sympathetic activity and the use of inotropics (73,75-76). Accordingly, the ability to diagnose and assess severity of such gradients may have important therapeutic

implications.

An interesting observation in Paper V was the increased heart rate in patients with intraventricular gradients in the early postoperative period. A causal relationship between the increased heart rate and the occurrence of intraventricular gradients could not be established with the design of the study. The tachycardia might be considered as a compensatory mechanism for a reduced cardiac output due to reduced left ventricular filling caused both by an impaired diastolic function of the hypertrophic left ventricle and an imbalanced volume status with hypovolemia. Therefore, the increased heart rate and the presence of intraventricular gradients could be markers of the same pathophysiological relationships, both indicating a less than optimal hemodynamic status. The frequency of intraventricular gradients was associated with smaller left ventricular cavity dimensions, and with tachycardia diastolic filling and ventricular volumes would be even more reduced, thus resulting in a vicious cycle.

The study demonstrates that Doppler echocardiography is a valuable supplement in the early postoperative monitoring following valve replacement for severe aortic stenosis as clinically important hemodynamic information may be easily obtained.

LVOT velocity profiles.

Cardiac output is an important hemodynamic parameter clinically utilized in assessing systolic function of the heart and in calculating valve or prosthesis area, regurgitation fractions and intracardiac shunts. With Doppler echocardiography cardiac output can be determined noninvasively, and the method correlates well with invasive methods (86-89). There are, however, some fundamental assumptions made when using the Doppler principle in determining cardiac output; 1) the assumption of a fixed and circular orifice,

2) the assumption of a flat velocity profile and 3) the assumption of a negligible angle of incidence between the Doppler beam and the direction of blood flow. In Paper VI the second of these assumptions was studied in order to assess whether valve replacement caused changes in LVOT velocity distribution that could influence stroke volume estimate with the Doppler technique. A nonuniform, skewed velocity profile was found both in aortic stenosis and following valve replacement with the highest velocities typically located from the center of the outflow tract toward the septum. These findings are in accordance with results from studies in normal subjects (35,90). No qualitative or quantitative changes in LVOT velocity distribution could be detected when the preoperative recordings were compared with recordings 3 months after valve replacement. There has been no earlier report comparing LVOT velocity profiles before and after aortic valve replacement, and according to the results in Paper VI limitations and sources of error inherent in the Doppler technique in volume flow estimates are similar before and after aortic valve replacement.

With a nonuniform velocity distribution in the outflow tract, recording of the maximum velocities will result in an overestimation of stroke volume. This overestimation was calculated to about 15% in normal subjects (35). According to the results obtained in Paper VI, this overestimation could be even larger in patients with aortic stenosis or an aortic valve prosthesis. However, when the sample volume is positioned in the left ventricular outflow tract it will not necessarily record the highest velocities. Furthermore, the velocities recorded may to some extent be an underestimation of true velocities due to the angle between the ultrasound beam and the flow direction. This could therefore explain the good correlations obtained between Doppler echocardiography and invasive methods in assessing valve area in native aortic stenosis (26,91-92) as well as acceptable

correlations obtained between invasive and noninvasive methods in cardiac output and valve area calculations in patients with prosthetic aortic valves (69,71,89).

There are some obvious limitations to the study presented in Paper VI. Velocity distribution was studied in just one plane and different results could have been obtained if velocity profiles had been constructed from several imaging planes. Furthermore, velocity distributions in the outflow tract could possibly differ both with hemodynamic state as well as with type of valve lesion. Therefore, several questions remain unanswered and could be subjects to further investigation.

CONCLUSIONS

The present work demonstrates that a variety of clinically relevant information with the potential of influencing decision making in patients with prosthetic aortic valves may be obtained with Doppler echocardiography. The technique is well suited as the routine method in the follow-up of these patients.

With a baseline recording of prosthesis gradient the patient may serve as his or her own control at later follow-ups. A baseline recording should routinely be performed before hospital discharge as the gradient recorded at that time is valid as a reference for later comparison in spite of a considerably different hemodynamic state.

Resting and exercise hemodynamics in an unselected group of patients receiving a small ($\leq$ 21 mm) aortic valve prosthesis during a 7-year period were acceptable. Prosthesis gradients were generally low at rest with only moderate increase during exercise. In patients with small aortic valve prostheses abnormal intraventricular flow patterns typically occurring in patients with hypertrophic cardiomyopathy were detected at rest and increased in frequency during and immediate after exercise. The frequent occurrence of these velocity patterns indicates that factors other than the moderate increase in prosthesis gradients may be of significance for exercise capacity in these patients.

Two-dimensional echocardiography was proven reliable in predicting aortic valve prosthesis size. In the Medtronic-Hall valves average annulus dimension and average prosthesis size were similar, whereas prosthesis size was at an average 1.5 mm larger than annulus diameter for the Carpentier-Edwards supraannular valves. A reliable prediction

of prosthesis size is of particular relevance in patients with a narrow aortic root, and with a preoperative, two-dimensional echo estimate of annulus diameter "patient-prosthesis mismatches" may be avoided.

Frequency and severity of systolic intraventricular gradients during the first week following surgery for severe aortic stenosis were easily assessed by Doppler echocardiography. It was demonstrated that patients with a small left ventricular cavity dimension and maintained contractility were at a particular risk of developing intraventricular gradients, and Doppler echocardiography may provide hemodynamic information of value in clinical decision making in the early postoperative period.

Stroke volume estimate with the Doppler echocardiographic technique assumes a flat velocity profile across the flow area. By means of a computer-based technique, cross-sectional velocity profiles in the LVOT were constructed before and 3 months after aortic valve replacement and compared. No quantitative nor qualitative changes in LVOT velocity distribution could be demonstrated after valve replacement. Accordingly, the limitations and sources of error inherent in the Doppler technique in assessing stroke volume are probably similar before and after aortic valve replacement.

REFERENCES

1 Harken DE, Soroff HS, Taylor WJ, Lefemine AA, Gupta SK, Lunzer S. Partial and complete prostheses in aortic insufficiency. *J Thorac Cardiovasc Surg 1960;40:744-62.*

2 Rapaport E. Natural history of aortic and mitral valve disease. *Am J Cardiol 1975;35:221-7.*

3 Turina J, Hess O, Sepulcri F, Krayenbuehl HP. Spontaneous course of aortic valve disease. *Eur Heart J 1987;8:471-83.*

4 Horstkotte D, Loogen F. The natural history of aortic valve stenosis. *Eur Heart J 1988;9(Suppl E):57-64.*

5 Bjørk VO, Henze A, Holmgren A. Central hemodynamics at rest and during exercise before and after aortic valve replacement with the Bjørk-Shiley tilting disc valve in patients with isolated aortic stenosis. *Scand J Thor Cardiovasc Surg 1973;7:111-30.*

6 Copeland JG, Griepp RB, Stinson EB, Shumway NE. Long-term follow-up after isolated aortic valve replacement. *J Thorac Cardiovasc Surg 1977;74:875-89.*

7 Lytle BW, Cosgrove DM, Taylor PC, Goormastic M, Stewart RW, Golding LAR, Gill CC, Loop FD. Primary isolated aortic valve replacement. Early and late results. *J Thorac Cardiovasc Surg 1989;97:675-94.*

8 Baudet EM, Oca CC, Roques XF, Laborde MN, Hafez AS, Collot MA, Ghidoni IM. A 5 1/2 year experience with the St. Jude Medical cardiac valve prosthesis. Early and late results of 737 valve replacements in 671 patients. *J Thorac Cardiovasc Surg 1985;90:137-44.*

9 Bonow RO, Picone AL, McIntosh CL, Jones M, Rosing DR, Maron BJ, Lakatos E, Clark RE, Epstein SE. Survival and functional results after valve replacement for aortic regurgitation from 1976 to 1983: Impact of preoperative left ventricular function. *Circulation 1985;72:1244-56.*

10 Rahimtoola SH. The problem of valve prosthesis-patient mismatch. *Circulation 1978;58:20-4.*

11 Nitter-Hauge S, Enge I, Semb BKH, Hall KV. Primary clinical experience with the Hall-Kaster valve in the aortic position. Results at 3 months including hemodynamic studies. *Circulation 1979;60(Suppl I):I-55-I-62.*

12 Rothkopf M, Davidson T, Lipscomb K, Narahara K, Hillis LD, Willerson JT, Estrera A, Platt M, Mills L. Hemodynamic evaluation of the Carpentier-Edwards bioprosthesis in the aortic position. *Am J Cardiol 1979;44:209-14.*

13 Levang OW, Nitter-Hauge S, Levorstad K, Frøysaker T. Aortic valve replacement. A randomized study comparing the Bjørk-Shiley and Lillehei-Kaster disc valves. Late hemodynamics related to clinical results. *Scand J Thor Cardiovasc Surg 1979;13:199-213.*

14 Borkon AM, McIntosh CL, Jones M, Lipson LC, Kent KM, Morrow AG. Hemodynamic function of the Hancock standard orifice aortic valve bioprostheses. *J Thorac Cardiovasc Surg 1981;82:601-7.*

15 Horstkotte D, Haerten K, Kørfer R, Spiller P, Budde Th, Bircks W, Loogen F. Hemodynamic findings at rest and during exercise after implantation of different aortic valve prostheses. *Z Kardiol 1983;72:429-37.*

16 Cosgrove DM, Lytle BW, Gill CC, Golding LAR, Stewart RW, Loop FD, Williams GW. In vivo hemodynamic comparison of porcine and pericardial valves. *J Thorac Cardiovasc Surg 1985;89:358-68.*

17 Foster AH, Tracy CM, Greenberg GJ, McIntosh CL, Clark RE. Valve replacement in narrow aortic roots: Serial hemodynamics and long-term clinical outcome. *Ann Thorac Surg 1986;42:506-16.*

18 Khuri SF, Folland ED, Sethi GK, Souchek J, Oprian C, Wong M, Burchfiel C, Henderson WG, Hammermeister KE. Six month postoperative hemodynamics of the Hancock heterograft and the Bjørk-Shiley prosthesis: Results of a Veterans Administration cooperative prospective randomized trial. *J Am Coll Cardiol 1988;12:8-18.*

19 Aris A, Padro JM, Camara ML, Crexells C, Auge JM, Caralps JM. Clinical and hemodynamic results of cardiac valve replacement with the monostrut Bjørk-Shiley prosthesis. *J Thorac Cardiovasc Surg 1988;95:423-31.*

20 Nitter-Hauge S, Semb B, Abdelnoor M, Hall KV. A five year experience with the Medtronic-Hall disc valve prosthesis. *Circulation 1983;68(suppl II):II-169-II-174.*

21 Nicoloff DM, Emery RW, Arom KV, Northrup WF, Jorgensen CR, Wang Y, Lindsay WG. Clinical and hemodynamic results with the St. Jude Medical cardiac valve prosthesis. A three-year experience. *J Thorac Cardiovasc Surg 1981;82:674-8*

22 Wortham DC, Tri TB, Bowen TE. Hemodynamic evaluation of of the St. Jude Medical valve prosthesis in the small aortic annulus. *J Thorac Cardiovasc Surg 1981;81:615-20.*

23 Carrier M, Martineau JP, Bonan R, Pelletier LC. Clinical and hemodynamic assessment of the Omniscience prosthetic heart valve. *J Thorac Cardiovasc Surg 1987;93:300-7.*

24 Kotler MN, Mintz GS, Panidis I, Morganroth J, Segal BL, Ross J. Noninvasive evaluation of normal and abnormal prosthetic valve function. *J Am Coll Cardiol 1983;2:151-73.*

25 Hatle L, Angelsen B. Pressure velocity relationships. In: *Doppler ultrasound in cardiology. Physical principles and clinical applications. 2nd ed. Philadelphia: Lea and Febiger, 1985:22-6.*

26 Skjaerpe T, Hegrenaes L, Hatle L. Noninvasive estimation of valve area in patients with aortic stenosis by Doppler ultrasound and two-dimensional echocardiography. *Circulation 1985;72:810-18.*

27 Kapur KK, Fan P, Nanda NC, Yoganathan AP, Goyal RG. Doppler color flow mapping in the evaluation of prosthetic mitral and aortic valve function. *J Am Coll Cardiol 1989;13:1561-71.*

28 Alam M, Rosman HS, Lakier JB, Kemp S, Khaja F, Hautamaki K, Magilligan DJ, Stein PD. Doppler and echocardiographic features of normal and dysfunctioning bioprosthetic valves. *J Am Coll Cardiol 1987;10:851-8.*

29 Dittrich H, Nicod P, Hoit B, Dalton N, Sahn D. Evaluation of Bjørk-Shiley prosthetic valves by real-time two-dimensional Doppler echocardiographic flow mapping. *Am Heart J 1988;115:133-8.*

30 Tatineni S, Barner HB, Pearson AC, Halbe D, Woodruff R, Labovitz, AJ. Rest and exercise evaluation of St. Jude Medical and Medtronic-Hall prostheses. Influence of primary lesion, valvular type, valvular size and left ventricular function. *Circulation 1989;80(suppl I):I-16-I-23.*

31 Brink RBA, Verheul HA, Visser CA, Koelemay MJW, Dunning AJ. Value of exercise Doppler echocardiography in patients with prosthetic and bioprosthetic cardiac valves. *Am J Cardiol 1992;69:367-72.*

32 Reisner SA, Lichtenberg GS, Shapiro JR, Schwarz KQ, Meltzer RS. Exercise Doppler echocardiography in patients with mitral prosthetic valves. *Am Heart J 1989;118:755-9.*

33 Samstad SO, Torp HG, Linker DT, Rossvoll O, Skjaerpe T, Johansen E, Kristoffersen K, Angelsen BAJ, Hatle L. Cross sectional early mitral flow velocity profiles from colour Doppler. *Br Heart J 1989;62:177-84.*

34 Samstad SO, Rossvoll O, Torp HG, Sjaerpe T, Hatle L. *Circulation 1992;86:748-55.*

35 Rossvoll O, Samstad S, Torp HG, Linker DT, Skjaerpe T, Angelsen BAJ, Hatle L. The velocity distribution in the aortic annulus in mormal subjects: A quantitative analysis of two-dimensional Doppler flow maps. *J Am Soc Echo 1991;4:367-78.*

36 Samstad SO, Torp HG, Matre K, Rossvoll O, Segadal L, Piene H. Instantaneous cross-sectional flow velocity profiles: A comparative study of two ultrasound Doppler methods applied to an in vitro pulsatile flow model. *J Am Soc Echocardiogr 1990;3:451-64.*

37 Zoghbi WA, Farmer KL, Soto JG, Nelson JG, Quinones MA. Accurate noninvasive quantification of stenotic aortic valve area by Doppler echocardiography. *Circulation 1986;73:452-9.*

38 Rothbart RM, Castriz JL, Hardings LV, Russo CD, Teague SM. Determination of aortic valve area by two-dimensional and Doppler echocardiography in patients with normal and stenotic bioprosthetic valves. *J Am Coll Cardiol 1990;15:817-24.*

39 Hegrenaes L, Hatle L. Aortic stenosis in adults: noninvasive estimation of pressure differences by continuous wave Doppler echocardiography. *Br Heart J 1985;54:396-404.*

40 Currie PJ, Seward JB, Reeder GS, Vlietstra RE, Bresnahan DR, Bresnahan JF, Smith HC, Hagler DJ, Tajik AJ. Continuous-wave Doppler echocardiographic assessment of severity of calcific aortic stenosis: a simultaneous Doppler-catheter correlative study in 100 adult patients. *Circulation 1985;71:1162-9.*

41 Burstow DJ, Nishimura RA, Bailey KR, Reeder GS, Holmes Jr. DR, Seward JB, Tajik AJ. Continuous wave Doppler echocardiographic measurement of prosthetic valve gradients. A simultaneous Doppler-Catheter correlative study. *Circulation 1989;80:504-14.*

42 Sagar KB, Wann S, Paulsen WHJ, Romhilt DW. Doppler echocardiographic evaluation of Hancock and Bjørk-Shiley prosthetic valves. *J Am Coll Cardiol 1986;7:681-7.*

43 Rothbart RM, Smucker ML, Gibson RS. Overestimation by Doppler echocardiography of pressure gradients across Starr-Edwards prosthetic valves in the aortic position. *Am J Cardiol 1988;61:475-6.*

44 Ihlen H, Mølstad P, Simonsen S, Vatne K, Øvrum E, Geiran O, Laake P, Frøysaker T. Hemodynamic evaluation of the Carbomedics prosthetic heart valve in the aortic position: Comparison of noninvasive and invasive techniques. *Am Heart J 1992;123:151-9.*

45 Hatle L, Angelsen B. Maximal velocity. In: *Doppler ultrasound in cardiology. Physical principles and clinical applications. 2nd ed. Philadelphia: Lea and Febiger, 1985:108-10.*

46 Baumgartner H, Khan S, DeRobertis M, Czer L, Maurer G. Discrepancies between Doppler and catheter gradients in aortic prosthetic valves in vitro. A manifestation of localized gradients and pressure recovery. *Circulation 1990;82:1467-75.*

47 Stewart SFC, Nast EP, Arabia FA, Talbot TL, Proschan M, Clark RE. Errors in pressure gradient measurement by continuous wave Doppler ultrasound: Type, size and age effects in bioprosthetic aortic valves. *J Am Coll Cardiol 1991;18:769-79.*

48 Williams GA, Labovitz AJ. Doppler hemodynamic evaluation of prosthetic (Starr-Edwards and Bjørk-Shiley) and bioprosthetic (Hancock and Carpentier-Edwards) cardiac valves. *Am J Cardiol 1985;56:325-32.*

49 Levine RA, Jimoh A, Cape EG, McMillan S, Yoganathan AP, Weyman AE. Pressure recovery distal to a stenosis: potential cause of gradient "overestimation" by Doppler echocardiography. *J Am Coll Cardiol 1989;13:706-15.*

50 Holen J, Waag RC, Gramiak R. Doppler ultrasound in aortic stenosis: In vitro studies of pressure gradient determination. *Ultrasound Med Biol 1987;13:321-8.*

51 Baumgartner H, Khan S, DeRobertis M, Czer L, Maurer G. Effect of prosthetic aortic valve design on the Doppler-catheter gradient correlation: An in vitro study of normal St. Jude, Medtronic-Hall, Starr-Edwards and Hancock valves. *J Am Coll Cardiol 1992;19:324-32.*

52 Panidis IP, Ross J, Mintz GS. Normal and abnormal prosthetic valve function as assessed by Doppler echocardiography. *J Am Coll Cardiol 1986;8:317-26.*

53 Gibbs JL, Wharton GA, Williams GJ. Doppler ultrasound of normally functioning mechanical mitral and aortic valve prostheses. *Int J Cardiol 1988;18:391-8.*

54 Reisner SA, Meltzer RS. Normal values of prosthetic valve Doppler echocardiogrphic parameters: A review. *J Am Soc Echo 1988;1:201-10.*

55 Cooper DM, Stewart WJ, Schiavone WA, Lombardo HP, Lytle BW, Loop FD, Salcedo EE. Evaluation of normal prosthetic valve function by Doppler echocardiography. *Am Heart J 1987;114:576-82.*

56 Ramirez ML, Wong M, Sadler N, Shah PM. Doppler evaluation of bioprosthetic and mechanical aortic valves: data from four models in 107 stable, ambulatory patients. *Am Heart J 1988;115:418-25.*

57 Hatle L, Angelsen B. Aortic valve prostheses. In: *Doppler ultrasound in Cardiology. Physical principles and clinical applications. 2nd ed. Philadelphia: Lea & Febiger, 1985:196-204.*

58 Ren JF, Chandrasekaran K, Mintz GS, Ross J, Pennock RS, Frankl WS. Effect of depressed left ventricular function on hemodynamics of normal St. Jude Medical prosthesis in the aortic position. *Am J Cardiol 1990;65:1004-9.*

59 Olin CL, Bomfim V, Halvazulis V, Holmgren AG, Lamke BJ. Optimal insertion technique for the Bjørk-Shiley valve in the narrow aortic aostium. *Ann Thorac Surg 1983;36:567-76.*

60 Panidis I, Wurzel D, Gonzales R. Effect of prosthetic mechanical aortic valve orientation on Doppler derived gradients in vitro (abstr.). *Eur Heart J 1992;13(suppl.II-IV):236.*

61 Bjørk VO, Henze A, Holmgren A, Szamosi A. Evaluation of the 21 mm Bjørk-Shiley tilting disc valve in patients with narrow aortic roots. *Scand J Thor Cardiovasc Surgery 1973;7:203-13.*

62 Konno S, Imai Y, Iida Y, Nakajima M, Tatsuno K. A new method for prosthetic valve replacement in congenital aortic stenosis associated with hypoplasisa of the aortic valve ring. *J Thorac Cardiovasc Surg 1975;70:909-17.*

63 Pugliese P, Bernabei M, Santi C, Pasque A, Eufrate S. Posterior enlargement of the small annulus during aortic valve replacement versus implantation of a small prosthesis. *Ann Thorac Surg 1984;38:31-6.*

64 Abdelnoor M, Hall KV, Nitter-Hauge S, Lindberg H, Øvrum E. Prognostic factors in aortic valve replacement associated with narrow aortic roots. *Scand J Thor Cardiovasc Surg 1986;20:227-32.*

65 Dalichau H, Hannekum A, Niehues B, Irion A, Herse B. Hemodynamic and angiographic late results following enlargement of narrow aortic root using autologous pericardium in prosthetic aortic valve replacement. *Thorac Cardiovasc Surgeon 1985;33:288-95.*

66 Manouguian S, Seybold-Epting W. Patch enlargement of the aortic valve ring by extending the aortic incision into the anterior mitral leaflet: new operative technique. *J Thorac Cardiovasc Surg 1979;78:402-12.*

67 Misbach GA, Turley K, Ullyot DJ, Ebert PA. Left ventricular outflow enlargement by the Konno procedure. *J Thorac Cardiovasc Surgery 1982;84:696-703.*

68 Teoh KH, Fulop JC, Weisel RD, Ivanov J, Tong CP, Slattery SA, Rakowski H. Aortic valve replacement with a small prosthesis. *Circulation 1987;76(suppl III):III-123-III-131.*

69 Rothbart RM, Castriz JL, Hardings LV, Russo CD, Teague SM. Determination of aortic valve area by two-dimensional and Doppler echocardiography in patients with normal and stenotic bioprosthetic valves. *J Am Coll Cardiol 1990;15:817-24.*

70 Rossvoll O, Skjaerpe T, Samstad S, Wiseth R. Reproducibility of Doppler echocardiographic estimates of stroke volume and valve inner area in patients with aortic valve prostheses. *Eur Heart J 1988;9(suppl.III-IV):23.*

71 Chafizadeh ER, Zoghbi WA. Doppler echocardiographic assessment of the St. Jude Medical prosthetic valve in the aortic position using the continuity equation. *Circulation 1991;83:213-23.*

72 Sasson Z, Hatle L, Appleton CP, Jewett M, Alderman EL, Popp RL. Intraventricular flow during isovolumic relaxation: Description and characterization by Doppler echocardiography. *J Am Coll Cardiol 1987;10:539-46.*

73 Seiler C, Jenni R, Krayenbuehl HP. Intraventricular blood flow during isovolumetric relexation and diastole in hypertrophic cardiomyopathy. *J Am Soc Echo 1991;4:247-57.*

74 Laurent M, Leborgne O, Clement C, Foulgoc JL, Le Helloco A, Almange C, Leborgne P. Systolic intra-cavitary gradients following aortic valve replacement: an echo-Doppler study. *Eur Heart J 1991;12:1098-1106.*

75 Thompson R, Ahmed M, Pridie R, Yacoub M. Hypertrophic cardiomyopathy after aortic valve replacement. *Am J Cardiol 1980;45:33-41.*

76 Wynne J, Braunwald E. The cardiomyopathies and myocartidides. In:*Braunwald E, ed. Heart disease. A textbook of cardiovascular medicine, 3rd edn Saunders, 1988:1421-28.*

77 Harpole DH, Jones RH. Serial assessment of ventricular performance after valve replacement for aortic stenosis. *J Thorac Cardiovasc Surg 1990;99:645-50.*

78 Chikamori T, Counihan PJ, Doi YL, Takata J, Stewart JT, Frenneaux MP, McKenna WJ. Mechanisms of exercise limitation in hypertrophic cardiomyopathy. *J Am Coll Cardiol 1992;19:507-12.*

79 Bonow RO. Determinants of exercise capacity in hypertrophic cardiomyopathy (editorial) *J Am Coll Cardiol 1992;19:513-5.*

80 Spirito P, Maron BJ, Chiarella F, Belotti P, Tramarin R, Pozzoli M, Vecchio C. Diastolic abnormalities in patients with hypertrophic cardiomyopathy: relation to magnitude of left ventricular hypertrophy. *Circulation 1985;72:310-6.*

81 Spirito P, Maron BJ, Bonow RO, Epstein SE. Severe functional limitation in patients with hypertrophic cardiomyopathy and only mild localized left ventricular hypertrophy. *J Am Coll Cardiol 1986;8:537-44.*

82 Monrad ES, Hess OM, Murakami T, Nonogi H, Corin WJ, Krayenbuehl HP. Abnormal exercise hemodynamics in patients with normal systolic function late after aortic valve replacement. *Circulation 1988;77:613-24.*

83 Hess OM, Ritter M, Schneider J, Grimm J, Turina M, Krayenbuehl HP. Diastolic stiffness and myocardial structure in aortic valve disease before and after valve replacement. *Circulation 1984;69:855-65.*

84 Parker DP, Kaplan MA, Connolly JE. Coexistent aortic valvular and functional hypertrophic subaortic stenosis. Clinical, physiologic and angiographic aspects. *Am J Cardiol 1969;24:307-17.*

85 Block PC, Powell WJ, Dinsmore RE, Goldblatt A. Coexistent fixed congenital and idiopathic hypertrophic subaortic stenosis. *Am J Cardiol 1973;31:523-6.*

86 Magnin PA, Stewart JA, Myers S, von Ramm O, Kisslo JA. Combined Doppler and phased-array ecocardiographic estimation of cardiac output. *Circulation 1981;63:388-92.*

87 Sanders SP, Yeager S, Williams RG. Measurement of systemic and pulmonary blood flow and Qp/Qs ratio using Doppler and two-dimensional echocardiography. *Am J Cardiol 1983;51:952-6.*

88 Ihlen H, Amlie JP, Dale J, Forfang K, Nitter-Hauge S, Otterstad JE, Simonsen S, Myhre E. Determination of cardiac output by Doppler echocardiography. *Br Heart J 1984;51:54-60.*

89 Ihlen H, Mølstad P. Cardiac output measured by Doppler echocardiography in patients with aortic prosthetic valves. *Eur Heart J 1990;11:399-402.*

90 Mathison M, Furuse A, Asano K. Doppler analysis of flow velocity profile at the aortic root. *J Am Coll Cardiol 1988;12:947-54.*

91 Otto CM, Pearlman AS, Comess KA, Reamer RP, Janko CL, Huntsman LL. Determination of the stenotic aortic valve area in adults using Doppler echocardiography. *J Am Coll Cardiol 1986;7:509-17.*

92 Oh JK, Taliercio CP, Holmes DR, Reeder GS, Bailey KR, Seward JB, Tajik AJ. Prediction of the severity of aortic stenosis by Doppler aortic valve area determination: Prospective Doppler-Catheterization correlation in 100 patients. *J Am Coll Cardiol 1988;11:1227-34.*

Paper I

Validity of an Early Postoperative Baseline Doppler Recording After Aortic Valve Replacement

Rune Wiseth, MD, Lars Hegrenaes, MD, Ole Rossvoll, MD, Terje Skjaerpe, MD, and Liv Hatle, MD

In 131 patients undergoing aortic valve replacement (53 bioprostheses, 78 mechanical), the pressure decrease across the prosthesis was recorded with Doppler ultrasound at a baseline study early postoperatively (mean 11 ± 5 days) and compared with a repeat measurement 3 to 5 months later. At baseline the hemodynamic state was markedly different, with increased heart rate (89 ± 14 vs 74 ± 13 beats/min, p <0.001) and decreased left ventricular ejection time index (367 ± 21 vs 390 ± 22, p <0.001). A minor and clinically insignificant decrease in pressure decrease with time was found. The 95% confidence interval for the difference was 0.2 to 3.0 and 0.2 to 1.7 mm Hg for the peak and the mean pressure decrease, respectively. The change in pressure decrease was statistically significant for bioprostheses (mean 16 ± 5 vs 14 ± 4 mm Hg, p <0.01) and smaller (≤23 mm) valves (mean 17 ± 4 vs 15 ± 4 mm Hg, p <0.01), whereas no significant changes were found for mechanical valves or valves of a larger size. The change in mean pressure decrease from baseline to the second examination was within ±5 mm Hg for 82% of patients. It is concluded that despite a different hemodynamic state in the early postoperative period, the pressure decrease across aortic valve prostheses obtained at this time can be used as a reference for later comparison.

(Am J Cardiol 1991;67:869–872)

From the Section of Cardiology, Department of Medicine, Regional Hospital, University of Trondheim, Norway. This study was supported in part by grants from the Norwegian Council on Cardiovascular Diseases, Oslo, Norway. Manuscript received July 3, 1990; revised manuscript received November 30, 1990, and accepted December 1.

Address for reprints: Rune Wiseth, MD, Section of Cardiology, Department of Medicine, Regional Hospital, University of Trondheim, N-7006 Norway.

Doppler ultrasound has been established as a valuable tool in the evaluation of aortic valve prostheses.[1-3] The noninvasively obtained pressure decrease has been shown to correlate well with invasive recordings,[1,2,4] and several reports give reference values for velocities and pressure decreases across different types of prosthetic aortic valves.[5-7] There is considerable overlap among different types and sizes of prostheses.[8-10] The pressure decrease across normally functioning prostheses will, in addition to the characteristics of the prosthesis, be influenced by several patient-related factors (heart rate, stroke volume, myocardial function). Therefore, a baseline recording for comparison could be useful in the assessment of prosthetic valve function at follow-up. This could be performed early postoperatively, but the result at this time might be influenced by an altered hemodynamic state (heart rate, loading conditions, pericardial effusion) as well as a more limited access in some patients. The aim of our study was to assess the validity of the pressure decrease obtained across aortic valve prostheses in the early postoperative period as a reference for later comparison.

METHODS

Patients: Patients undergoing aortic valve replacement from 1983 to 1989 were consecutively included in the study when a Doppler ultrasound study with technically adequate recordings could be performed before hospital discharge and a second study 3 to 5 months postoperatively. Patients with more than minor aortic regurgitation at the baseline study were not included and patients who later developed signs of prosthesis malfunction were excluded. Mean time from surgery to the first examination was 11 ± 5 days. A total of 131 patients were included, 53 with a *bioprosthesis* (24 Carpentier Edwards, 28 Carpentier Edwards supraanular, 1 Xenotech), and 78 with a *mechanical valve* (60 Medtronic-Hall, 13 Duromedics, 5 Sorin). A subgroup of 71 patients underwent a third examination 12 to 18 months postoperatively. The Doppler recordings were performed with an Irex III B, Irex Meridian or VingMed CFM 700 with a 2.0- or 2.5-MHz transduc-

TABLE I Pressure Decrease (mm Hg), Heart Rate and Left Ventricular Ejection Time Index at Baseline and at Three to Five Months Postoperatively (n = 131)

	Baseline	3 to 5 Months	95% CI
Peak	27 ± 9 (10–64)	26 ± 8 (12–58)	0.2–3.0
Mean	15 ± 5 (5–34)	14 ± 4 (6–26)	0.2–1.7
HR (beats/min)	89 ± 14 (54–120)	74 ± 13 (45–111)	12–17
LVETI	367 ± 21 (312–429)	390 ± 22 (342–456)	−19 – −27

Ranges are given in parentheses
HR = heart rate; LVETI = left ventricular ejection time index; Mean = mean pressure drop; Peak = peak pressure drop; 95% CI = 95% confidence interval for the difference.

TABLE II Change in Pressure Decrease (mm Hg) from Baseline to Recording at Three to Five Months According to Prosthesis Type and Size

Type and Size	Baseline	3 to 5 Months	95% CI
Bioprostheses (n = 53)			
Peak	28 ± 10 (11–64)	24 ± 7 (13–41)	0.7–5.7
Mean	16 ± 5 (6–34)	14 ± 4 (7–23)	0.6–3.4
Mechanical (n = 78)			
Peak	27 ± 9 (10–48)	27 ± 9 (12–58)	−1.1–2.1
Mean	14 ± 5 (5–30)	14 ± 5 (6–26)	−0.7–1.1
Size 20 to 23 mm (n = 53)			
Peak	31 ± 8 (16–47)	29 ± 8 (18–58)	0.6–4.9
Mean	17 ± 4 (5–30)	15 ± 4 (6–26)	0.4–2.7
Size 25 to 31 mm (n = 78)			
Peak	24 ± 9 (10–64)	24 ± 8 (12–47)	−1.2–2.7
Mean	14 ± 5 (5–34)	13 ± 4 (6–23)	−0.5–1.6

Abbreviations as in Table I.

er. The transprosthetic velocities were recorded by continuous-wave Doppler. A computerized digitizer was used for envelope tracing of the velocity curves and calculation of peak and mean pressure decreases. In patients with sinus rhythm, ≥3 consecutive beats were averaged; in patients with atrial fibrillation, ≥5 consecutive beats were averaged. Left ventricular outflow tract velocities were recorded using pulsed-wave Doppler, with the sample volume positioned just below the prosthesis. The net gradient (corrected for subvalvular velocities) was obtained by subtracting the left ventricular outflow tract velocities (Vlvot) in the Bernoulli equation: net gradient = $4(Vmax^2 - Vlvot^2)$.[5,11] In the first part of the study period, the subvalvular recordings were not routinely documented by strip-chart recording in cases where the subvalvular velocity did not exceed 1 m/s. Recordings for calculating the net transprosthetic pressure decrease at both examinations were available in 41 patients. Left ventricular ejection time was measured from the start of the opening to the start of the closing signal of the prosthesis. Paper speed was 50 to 75 mm/s. Left ventricular ejection time index was calculated according to the formula of Weissler.[12]

Reproducibility: In a recent study from our laboratory, interobserver variability in recordings of peak velocities across aortic valve prostheses was assessed (Rossvoll, unpublished data). With independent analysis of the same recordings, the coefficient of variation was 4%; with both recording and analysis done independently, the coefficient of variation was 7%.

Statistical analysis: All values are expressed as mean ± standard deviation. Paired data were compared using a 2-tailed paired *t* test. The 95% confidence interval for a difference is presented, and when this did not include 0, statistical significance was considered. Linear regression analysis was used comparing the change in uncorrected (total) with the change in corrected (net) gradients between the 2 examinations.

RESULTS

Table I summarizes the data at baseline compared with the findings 3 to 5 months later. A minor but statistically significant decrease in both the peak and the mean pressure decrease was found. There was a marked decrease in heart rate and an increase in left ventricular ejection time index between the examinations. In patients with bioprostheses, a statistically significant decrease in pressure decrease was found, in contrast to the group with mechanical valves (Table II). Table II also lists the pressure decrease related to prosthesis size. In small valves (≤23 mm) there was a statistically significant decrease in pressure decrease not found in larger prostheses.

Figure 1 shows the individual variation in pressure decrease. The change in mean pressure decrease from baseline to the examination 3 to 5 months later was within ±5 mm. Hg in 107 patients (82%). In only 4 patients (3%) did the change in mean pressure decrease exceed ±10 mm Hg. Among the 24 patients with a change in mean pressure decrease >±5 mm Hg, the direction of the change in 17 was toward a lower pressure decrease. Only 7 patients (5%) showed an increase of >5 mm Hg in mean pressure decrease. The changes in peak pressure decrease were highly correlated to the changes in mean pressure decrease (r = 0.96). In absolute values, however, the changes in peak pressure decrease were greater (Figure 1).

Between 3 to 5 and 12 to 18 months, there was a further decrease in heart rate and an increase in left ventricular ejection time index (Table III). Pressure decrease also tended toward a further decrease; however, the change was not statistically significant for the mean

pressure decrease. Figure 2 shows a close correlation between the changes in total gradients and the changes in gradients corrected for subvalvular velocities between the 2 examinations.

Pathologic obstructions: In 2 patients with thrombotic obstruction of a mechanical valve confirmed by surgery or autopsy, the mean gradient exceeded the mean value for normally functioning valves by >6 standard deviations and the increase from baseline for each was 31 and 56 mm Hg. In 2 patients who underwent reoperation for a stenotic bioprosthesis, a mean gradient of 68 and 78 mm Hg was recorded for each.

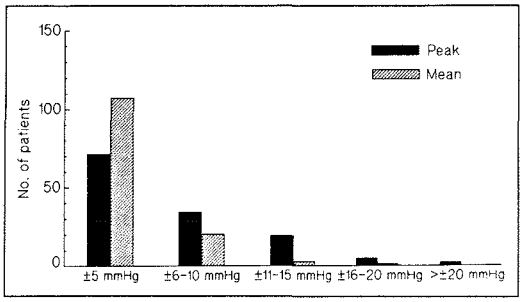


FIGURE 1. Individual variation in the peak and the mean pressure decrease from baseline to the second recording.

DISCUSSION

Hemodynamic state: The markedly different hemodynamic state at baseline is demonstrated by the increased heart rate and the decreased left ventricular ejection time index. A shortening of the left ventricular ejection time early after aortic valve replacement is mainly thought to be caused by a more rapid rate of shortening of the ventricular muscle as the afterload is substantially reduced, especially in the case of aortic stenosis.[13-15]

Theoretically, the altered hemodynamic state early postoperatively could by different mechanisms influence the pressure decrease across aortic valve prostheses in either direction. With increase in heart rate, diastolic filling and stroke volume will decrease, resulting in a reduced pressure decrease. However, for the *same* stroke volume, a decreased ejection time would result in an increased mean pressure decrease. These considerations are in accordance with the results of Thormann et al,[16] where patients with aortic valve prostheses were examined at different hemodynamic states induced experimentally. During pacing at increasing heart rates, the gradient across the prostheses decreased. During isoproterenol infusion, stroke volume increased and systolic ejection period per beat decreased, with a considerable increase in gradient.

Individual variation: For the group as a whole, the differences in pressure decreases from baseline to the recording at 3 to 5 months were small, with narrow confidence intervals, and considered to be without clini-

TABLE III Baseline Data Compared with Repeat Measurements at Three to Five and 12 to 18 Months (n = 71)

	Baseline	95% CI	3 to 5 Months	95% CI	12 to 18 Months
Peak (mm Hg)	27 ± 8	−0.2–3.2	25 ± 8	0.1–2.8	24 ± 7
Mean (mm Hg)	15 ± 5	0–2.0	14 ± 5	−0.1–1.4	13 ± 4
HR (beats/min)	89 ± 14	11–17	75 ± 13	2–7	71 ± 12
LVETI	369 ± 20	−16 – −27	391 ± 22	−10 – −18	404 ± 19

Abbreviations as in Table I

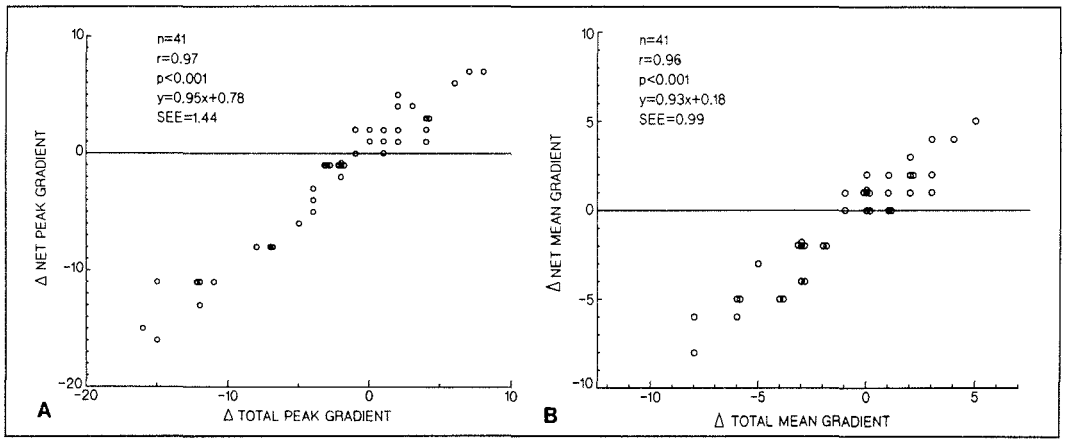


FIGURE 2. Changes in total peak *(A)* and total mean *(B)* pressure decrease versus changes in net (corrected for prevalvular velocities) pressure decrease from baseline to the second examination.

cal significance (Table I). The individual variation in mean pressure decrease was within ±5 mm Hg in 82% of the patients (Figure 1), indicating that the pressure decrease obtained at a hemodynamically more stable state shows no or only minor deviation from baseline in the majority of cases. Among patients where the mean pressure decrease differed by >±5 mm Hg from baseline, the direction of change was mostly toward lower gradients with time. This suggests that in patients with normally functioning aortic valve prostheses, a significant increase in pressure decrease from baseline is rather uncommon. The largest increase in mean pressure decrease was from 10 to 22 mm Hg in a patient with atrial fibrillation and a ventricular rate of 101 beats/min at baseline, and sinus rhythm with a heart rate of 48 beats/min at the second examination. This illustrates that the pressure decrease across normally functioning aortic valve prostheses may occasionally vary considerably when the hemodynamic state is markedly changed. In the presence of a significant increase in pressure decrease, a careful search for valvular and paravalvular leaks as well as an accurate assessment of left ventricular outflow tract velocities is mandatory. If the increased pressure decrease cannot be explained by changes in stroke volume due to a slower heart rate or significant leaks, an abnormal obstruction of the prosthesis should be suspected.

Valve type and size: The pressure decrease obtained at baseline was more representative for later findings in mechanical valves than for bioprostheses and in larger than smaller prostheses (Table II). The difference found according to valve size could be explained by a smaller orifice area causing more change in pressure decrease with changes in flow. The difference noted according to valve type could indicate that in bioprostheses a slight decrease in resistance to flow may occur during the first months after implantation. These findings are in accordance with an in vitro durability study of bioprosthetic valves performed by Schuster and Wagner.[17] They reported a decrease in the transprosthetic peak velocity with time due to an increase in flow area.

Corrected versus uncorrected gradients: As the pressure decrease obtained by continuous-wave Doppler is influenced by prevalvular velocities, the obstruction is most correctly assessed by the net gradient across the prosthesis.[11] However, the very close correlation in differences between the uncorrected and corrected gradients (Figure 2) suggests that in the follow-up of patients, the changes found in gradient will be similar whether the total (uncorrected) or the net (corrected) gradient is used, as long as the changes are due to changes in flow. In the presence of abnormal obstruction, however, this relation is likely to change, and the ratio of the subvalvular to the valvular velocities may prove to be an even more useful parameter in the follow-up of patients with aortic valve prostheses.[3] In clinical practice, therefore, we would recommend that subvalvular velocities always be recorded.

Clinical implications: Although the hemodynamic state is markedly different from early after aortic valve replacement to follow-up, the pressure decrease obtained across aortic valve prostheses at an early postoperative recording is representative as a reference for later comparison. A practical recommendation based on our findings is that patients undergoing aortic valve replacement should routinely be examined by Doppler ultrasound before hospital discharge.

REFERENCES

1. Kapur KK, Fan P, Nanda NC, Yoganathan AP, Goyal RG. Doppler color flow mapping in the evaluation of prosthetic mitral and aortic valve function. *J Am Coll Cardiol* 1989;13:1561-1571.

2. Burstow DJ, Nishimura RA, Bailey KR, Reeder GS, Holmes DR Jr, Seward JB, Tajik AJ. Continuous wave Doppler echocardiographic measurement of prosthetic valve gradients. A simultaneous Doppler-catheter correlative study. *Circulation* 1989;80:504-514.

3. Rothbart RM, Castriz JL, Hardings LV, Russo CD, Teague SM. Determination of aortic valve area by two-dimensional and Doppler echocardiography in patients with normal and stenotic bioprosthetic valves. *J Am Coll Cardiol* 1990;15:817-824.

4. Sagar KB, Wann S, Paulsen WHJ, Romhilt DW. Doppler echocardiographic evaluation of Hancock and Bjørk-Shiley prosthetic valves. *J Am Coll Cardiol* 1986;7:681-687.

5. Williams GA, Labovitz AJ. Doppler hemodynamic evaluation of prosthetic (Starr-Edwards and Bjørk-Shiley) and bioprosthetic (Hancock and Carpentier-Edwards) cardiac valves. *Am J Cardiol* 1985;56:325-332.

6. Panidis IP, Ross J, Mintz GS. Normal and abnormal prosthetic valve function as assessed by Doppler echocardiography. *J Am Coll Cardiol* 1986;8:317-326.

7. Gibbs JL, Wharton GA, Williams GJ. Doppler ultrasound of normally functioning mechanical mitral and aortic valve prostheses. *Int J Cardiol* 1988;18:391-398.

8. Cooper DM, Stewart WJ, Schiavone WA, Lombardo HP, Lytle BW, Loop FD, Salcedo EE. Evaluation of normal prosthetic valve function by Doppler echocardiography. *Am Heart J* 1987;114:576-582.

9. Ramirez ML, Wong M, Sadler N, Shah PM. Doppler evaluation of bioprosthetic and mechanical aortic valves: data from four models in 107 stable, ambulatory patients. *Am Heart J* 1988;115:418-425.

10. Hatle L, Angelsen B. Aortic valve prostheses. In: Doppler Ultrasound in Cardiology. Physical Principles and Clinical Applications. 2nd ed. Philadelphia: Lea and Febiger, 1985:196-204.

11. Hatle L, Angelsen B. Pressure velocity relationships. In: Doppler Ultrasound in Cardiology. Physical Principles and Clinical Applications. 2nd ed. Philadelphia: Lea and Febiger, 1985:22-26.

12. Weissler AM, Harris WS, Schoenfeld CD. Systolic time intervals in heart failure in man. *Circulation* 1968;37:149-159.

13. Benchimol A, Matsuo S. Ejection time before and after aortic valve replacement. *Am J Cardiol* 1971;27:244-249.

14. Parisi AF, Salzman SH, Schechter E. Systolic time intervals in severe aortic valve disease. Changes with surgery and hemodynamic correlations. *Circulation* 1971;44:539-547.

15. Seabra-Gomes R, Sutton R, Parker DJ. Left ventricular function after aortic valve replacement. *Br Heart J* 1976;38:491-496.

16. Thormann J, Gottwik M, Schlepper M, Hehrlein F. Hemodynamic alterations induced by isoproterenol and pacing after aortic valve replacement with the Bjørk-Shiley or St. Jude Medical prosthesis. *Circulation* 1981;63:895-904.

17. Schuster PR, Wagner JW. A preliminary durability study of two types of low-profile pericardial bioprosthetic valves through the use of accelerated fatigue testing and flow characterization. *J Biomed Mater Res* 1989;23:207-222.

Paper II

PARTE II

Hemodynamic Evaluation by Doppler Echocardiography of Small (≤21 mm) Prostheses and Bioprostheses in the Aortic Valve Position

Rune Wiseth, MD, Olaf W. Levang, MD, Endre Sande, MD, Geir Tangen, MD, Terje Skjaerpe, MD, and Liv Hatle, MD

To assess resting hemodynamics of an unselected group of patients with prostheses or bioprostheses sized ≤21 mm implanted into the aortic valve position during a 7-year period, 46 of 50 eligible patients were examined by Doppler echocardiography. The valves were Carpentier-Edwards (CE) supraannular 21 mm (n = 8), Medtronic-Hall (MH) 20 mm (n = 8) and 21 mm (n = 21), and the rest (n = 9) were other valves with only 1 to 3 patients in each group. Gradients, valve areas and dimensionless obstruction indexes (ratio of subvalvular/valvular velocities and velocity time integrals) were compared. By analysis of variance, gradients did not differ significantly between the CE supraannular 21 mm, the MH 20 and 21 mm prostheses (peak/mean 25 ± 8/14 ± 5, 31 ± 13/16 ± 6 and 25 ± 10/13 ± 5 mm Hg; p = not significant). Only 2 patients had a mean gradient >25 mm Hg. The valve area was slightly larger for the MH 21 mm group compared with the CE supraannular 21 mm group (1.34 ± 0.15 vs 1.16 ± 0.14 cm², p <0.05). The dimensionless obstruction indexes did not differ (CE supraannular 21 mm 0.36 ± 0.07/0.40 ± 0.07 (velocities/velocity time integrals), MH 20 mm 0.40 ± 0.12/0.47 ± 0.12, MH 21 mm 0.38 ± 0.05/0.44 ± 0.06; p = not significant). An inverse relation was demonstrated between the left ventricular outflow tract diameter and the subvalvular velocities (r = −0.60, p <0.001), thus emphasizing the necessity of making a correction for prevalvular velocities when applying the Bernoulli equation in calculating gradients across small aortic valve prostheses. It is concluded that acceptable resting hemodynamics are obtained with the CE supraannular 21 mm, the MH 20 and 21 mm prostheses in the narrow aortic root. The moderate obstruction caused by the prostheses is not likely to be a limiting factor for the hemodynamic capacity of these patients.

(Am J Cardiol 1992;70:240–246)

From the Section of Cardiology and the Section of Thoracic and Cardiovascular Surgery, University Hospital, Trondheim, Norway. This study was supported by grants from the Norwegian Council on Cardiovascular Diseases. Manuscript received October 28, 1991; revised manuscript received and accepted March 26, 1992.

Address for reprints: Rune Wiseth, MD, Section of Cardiology, Department of Medicine, Regional Hospital, University of Trondheim, N-7006 Trondheim, Norway.

The hemodynamic properties of small aortic valve prostheses are questioned and the management of the narrow aortic root remains controversial. An alternative to a small prosthesis is root enlargement that may allow insertion of a larger valve,[1-3] but this will prolong the surgical procedure and may increase the operative risk.[4] Patients presenting with a narrow root are often elderly, and a bioprosthesis would be preferable. It has been claimed that small-sized bioprostheses should be avoided because unfavorable gradients may result.[5] The hemodynamic performance of different types of small aortic prostheses and bioprostheses are therefore of clinical interest because the results may influence decision making in patients with a narrow aortic root. With Doppler echocardiography an accurate noninvasive assessment of the prosthesis function is possible. Mean gradients, cardiac output and valve area estimates have been shown to correlate well with invasive measurements,[6-10] and regurgitations can be detected and semiquantified.[7,11,12] Left ventricular outflow tract obstructions may occur, especially in patients with a narrow aortic annulus,[13] and with Doppler ultrasound both the level and the degree of outflow tract obstructions may be established.[14,15] To assess resting hemodynamics in an unselected group of patients with small aortic valve prostheses, all patients receiving a ≤21 mm prosthesis or bioprosthesis at our institution were considered for Doppler echocardiographic study.

METHODS

Patients: In the period from 1983 to 1989 58 prostheses (43 mechanical, 15 biological) with an external diameter ≤21 mm were implanted into the aortic valve position. There were 2 early and 5 late deaths. One patient with a Medtronic-Hall (MH) 21 mm prosthesis was admitted with heart failure 5.5 months after surgery. A thrombotic obstruction was diagnosed by Doppler echocardiography and at reoperation a thrombus was removed. Thus, a total of 50 patients were eligible for the present study. Because of age and geographic considerations 4 patients were not contacted. The remaining 46 (92% of those eligible) all underwent Doppler echocardiographic study.

There were 44 women and 2 men, mean age 66 years (range 23 to 82) and mean body surface area 1.65 ± 0.12 m^2 (range 1.34 to 1.91). The preoperative diagnosis was pure or predominant stenosis in 44 and pure regurgitation in 2 patients. The valves were 8 Carpentier-Edwards (CE) supraannular 21 mm, 8 MH 20 and

TABLE I Peak and Mean Gradients, Valve Areas and Dimensionless Obstruction Indexes for Different Valve Types

Valve Type (mm)	No.	Peak (mm Hg)	Mean (mm Hg)	PVA_1 (cm^2)	PVA_2 (cm^2)	V_{lvot}/V_{valv}	VTI_{lvot}/VTI_{valv}
CE porcine (21)	2	22 ± 4	12 ± 4	1.13 ± 0.27	1.31 ± 0.36	0.41 ± 0.04	0.48 ± 0.06
		18–26	8–15	0.86–1.39	0.95–1.67	0.38–0.44	0.42–0.53
CE pericardial (21)	2	20	12	1.26 ± 0.12	1.30 ± 0.07	0.40 ± 0.04	0.41 ± 0.02
				1.14–1.37	1.23–1.37	0.36–0.43	0.39–0.43
CE supraannular (21)	8	25 ± 8	14 ± 5	1.06 ± 0.16	1.16 ± 0.14*	0.36 ± 0.07	0.40 ± 0.07
		14–40	7–23	0.86–1.31	0.99–1.42	0.27–0.47	0.32–0.52
MH (20)	6	31 ± 13	16 ± 6	1.06 ± 0.22	1.19 ± 0.21	0.42 ± 0.12	0.47 ± 0.12
		11–54	6–25	0.83–1.50	0.95–1.59	0.29–0.66	0.33–0.70
MH (21)	19	25 ± 10	13 ± 5	1.17 ± 0.13	1.34 ± 0.15*	0.38 ± 0.05	0.44 ± 0.06
		14–60	7–31	0.91–1.38	1.03–1.57	0.28–0.46	0.32–0.55
Sorin (21)	3	31 ± 3	17 ± 1	1.07 ± 0.17	1.18 ± 0.16	0.40 ± 0.07	0.44 ± 0.08
		28–35	16–19	0.92–1.30	1.01–1.39	0.29–0.46	0.32–0.51
Duromedics (19)	1	51	27	0.84	1.01	0.33	0.40
Duromedics (21)	1	19	10	1.28	1.40	0.41	0.45

*$p < 0.05$ when comparing Carpentier-Edwards supraannular 21 mm with Medtronic-Hall 21 mm prostheses (standard continuity equation).
Values are mean ± SD.
From the total group of 46 patients, 2 with a Medtronic-Hall 20 and 1 with a Medtronic-Hall 21 mm valve prosthesis were excluded from the analysis because of a history of thromboembolism, and 1 patient with a Medtronic-Hall 21 mm valve was excluded because of a perivalvular leak grade 3. Thus, the number of patients included in this analyses is 42.
CE = Carpentier-Edwards; MH = Medtronic-Hall; PVA_1 = prosthetic valve area (simplified continuity equation); PVA_2 = prosthetic valve area (standard continuity equation); V_{lvot} = velocity in left ventricular outflow tract; V_{valv} = velocity across prosthesis; VTI_{lvot} = velocity time integral in left ventricular outflow tract; VTI_{valv} = velocity time integral across prosthesis.

21 MH 21 mm, and the rest (n = 9) were other valves with only 1 to 3 patients in each group (Table I).

The MH 20 and 21 mm prostheses are identical except for a thinner sewing ring in the 20 mm valve in order to allow insertion in even smaller roots. Mean time from surgery to the Doppler echocardiographic study was 2.2 years. Three patients, all with a CE supraannular 21 mm valve, were examined 1 to 2 weeks postoperatively. In all other patients the time interval from surgery was ≥3 months with a maximum of 38 months in the bioprosthesis group. To reduce the risk of including patients with dysfunctioning prostheses in the comparison between valve types, 3 patients (2 MH 20 and 1 MH 21 mm) with a history of thromboembolic episodes were excluded from the analysis of gradients and valve area.

Doppler echocardiography: An Irex Meridian or Vingmed CFM 700 ultrasound system with a 3.0 MHz transducer for imaging and 2.0 or 2.5 MHz for Doppler recordings was used.

Leaks: Prosthetic leaks were assessed with color flow using the Vingmed CFM 700. Regurgitations were graded on a scale from 0 to 4. Tiny regurgitant jets confined within the left ventricular outflow tract were graded 1+. With a somewhat larger origin and jet area, but with the jet still not extending to the tip of the anterior mitral valve leaflet, the leak was graded 2+, and with extension beyond the leaflet tip without reaching the apex 3+. No one had 4+ regurgitation. To judge the regurgitation as valvular or perivalvular, several imaging planes were used, and it was categorized as perivalvular if the jet was seen to originate outside the valve ring.

Pressure decrease: Velocities across the prostheses were recorded using continuous-wave Doppler from apical, suprasternal and right parasternal positions. From the highest velocities obtained, the pressure decrease was calculated using the Bernoulli equation with correction for prevalvular velocities: Pressure decrease = $4(V_{valv}^2 - V_{lvot}^2)$ where V_{valv} = velocity across prosthesis and V_{lvot} = left ventricular outflow tract velocity.[16]

Intraventricular and left ventricular outflow tract velocities: Pulsed Doppler was used to search for increased velocities within the left ventricle. The sample volume was moved stepwise from the apex up through the left ventricle to the level of the prosthesis. Left ventricular outflow tract velocities were recorded with the sample volume positioned just below the prosthesis.

Cardiac output, prosthesis valve area: From the parasternal long-axis view the inner left ventricular outflow tract diameter was measured just below the prosthesis (Figure 1). Cardiac output (CO) was calculated from the formula $CO = (D/2)^2 \times \pi \times VTI_{lvot} \times HR$, where D = subvalvular diameter, VTI_{lvot} = velocity time integral in the outflow tract and HR = heart rate. With sinus rhythm at least 3, and with atrial fibrillation at least 10 consecutive beats were averaged. The prosthetic valve area (PVA) was calculated using both the standard continuity equation — $PVA = SV/VTI_{valv}$ where SV is stroke volume and VTI_{valv} is velocity time integral across the prosthesis, and the simplified equation — $PVA = A_{lvot} \times V_{lvot}/V_{valv}$ where A_{lvot} and V_{lvot} is the left ventricular outflow tract area and maximal velocity respectively, and V_{valv} is the maximal velocity across the prosthesis.[17,18]

Dimensionless obstruction index: By eliminating the subvalvular area from the continuity equation,[10] the dimensionless obstruction index is obtained. The ratios V_{lvot}/V_{valv} and VTI_{lvot}/VTI_{valv} were calculated and compared for the different valve types.

Statistical analysis: Continuous variables are expressed as mean ± SD. Means of 2 groups were compared using an unpaired *t* test. With multiple comparison, analysis of variance followed by the Student-Newman-Keuls test was used. Statistical analysis of the association between variables was performed using linear regression analysis. A p value <0.05 was considered

significant. Reproducibility is expressed as the 95% limits of agreement between pairs of measurements as described by Bland and Altmann.[19]

RESULTS

Adequate Doppler recordings were obtained in all patients. In 1 patient (MH 21 mm) the sewing ring diameter was used to calculate the outflow tract area as the echocardiographic window did not allow for a subvalvular diameter measurement.

Leaks: One patient with an MH 21 mm prosthesis implanted during ongoing endocarditis had a 3+ perivalvular leak and was excluded from the analysis of pressure decrease and effective orifice area. In 4 patients, all with an MH 21 mm prosthesis, perivalvular leaks grade 1 to 2 were diagnosed. Cardiac output in these 4 was not increased compared with the rest of the MH 21 mm group (4.82 ± 0.44 vs 4.94 ± 0.87 liters/min, p = NS), supporting the judgment of the regurgitations as being mild. Two patients with a bioprosthesis had a grade 1 perivalvular leak.

Pressure decrease: The highest velocities were obtained from the apex in 27 of 34 mechanical valves (78%) and in 10 of 12 bioprostheses (83%). Table I lists the gradients across the different valves, and the variation within each valve type is demonstrated in Figure 2. Only 2 patients had a mean gradient >25 mm Hg. Because of the small number of other valve types, only the CE supraannular 21 mm and the MH 20 and 21 mm prostheses were compared statistically. By analysis of variance no statistically significant differences in gradients were found between these 3 groups.

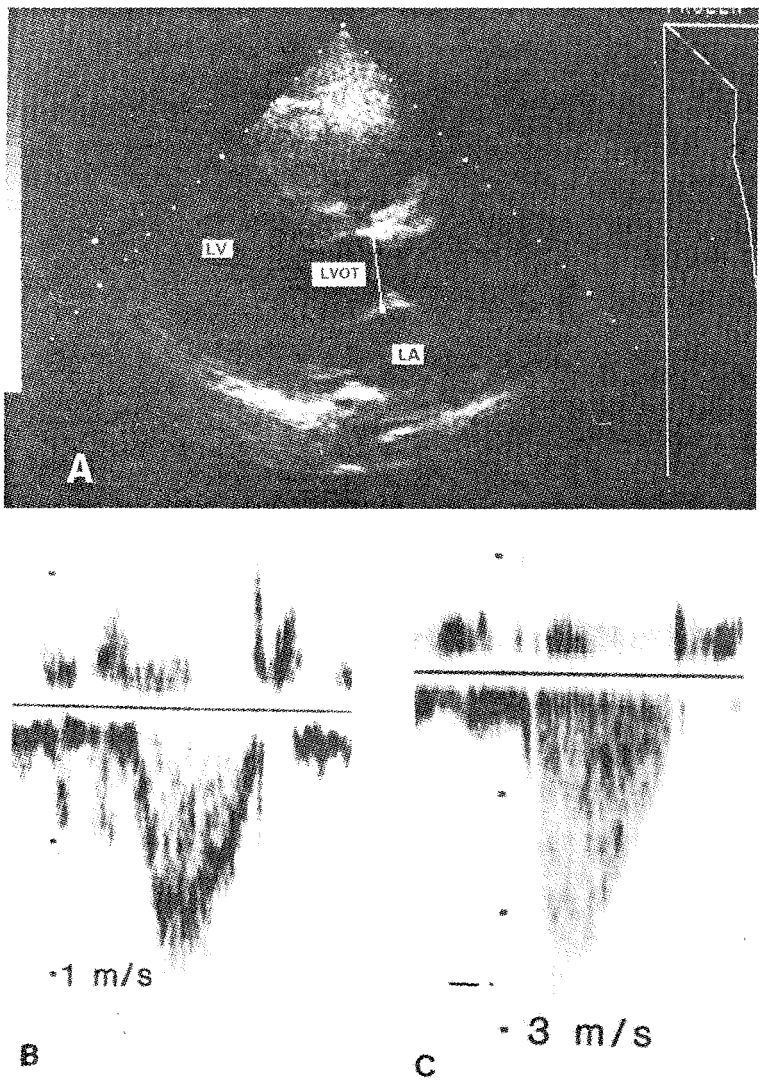


FIGURE 1. Measurement of left ventricular outflow tract (LVOT) diameter *(A)*, pulsed Doppler recording in the left ventricular outflow tract close to the prosthesis *(B)*, and continuous-wave Doppler recording of velocities through the prosthesis *(C)*. LA = left atrium; LV = left ventricle.

TABLE II Comparison of Left Ventricular Outflow Tract Measurements in Carpentier-Edwards Supraannular 21 mm, Medtronic-Hall 20 and 21 mm Valves

Valve Type (mm)	No.	D_{lvot} (cm)	V_{lvot} (m/s)	VTI_{lvot}	CO (liters/min)
CE supraannular (21)	8	1.94 ± 0.1	0.95 ± 0.16	19.2 ± 3.0	4.68 ± 0.90
		1.7–2.0	0.61–1.16	13.8–24.4	3.48–6.52
MH (20)	8	1.80 ± 0.1*	1.23 ± 0.22*	30.3 ± 3.5*	5.19 ± 1.04
		1.7–2.0	0.93–1.61	25.7–34.9	3.84–7.37
MH (21)	20	1.98 ± 0.11	1.02 ± 0.16	24.5 ± 3.7	4.94 ± 0.87
		1.7–2.1	0.63–1.28	16.4–31.3	3.33–6.66

*Medtronic-Hall 20 mm group differs significantly from both the Carpentier-Edwards supraannular and Medtronic-Hall 21 mm groups by the Student-Newman-Keuls procedure.
Values are mean ± SD.
CO = cardiac output; D_{lvot} = diameter of left ventricular outflow tract; other abbreviations as in Table I.

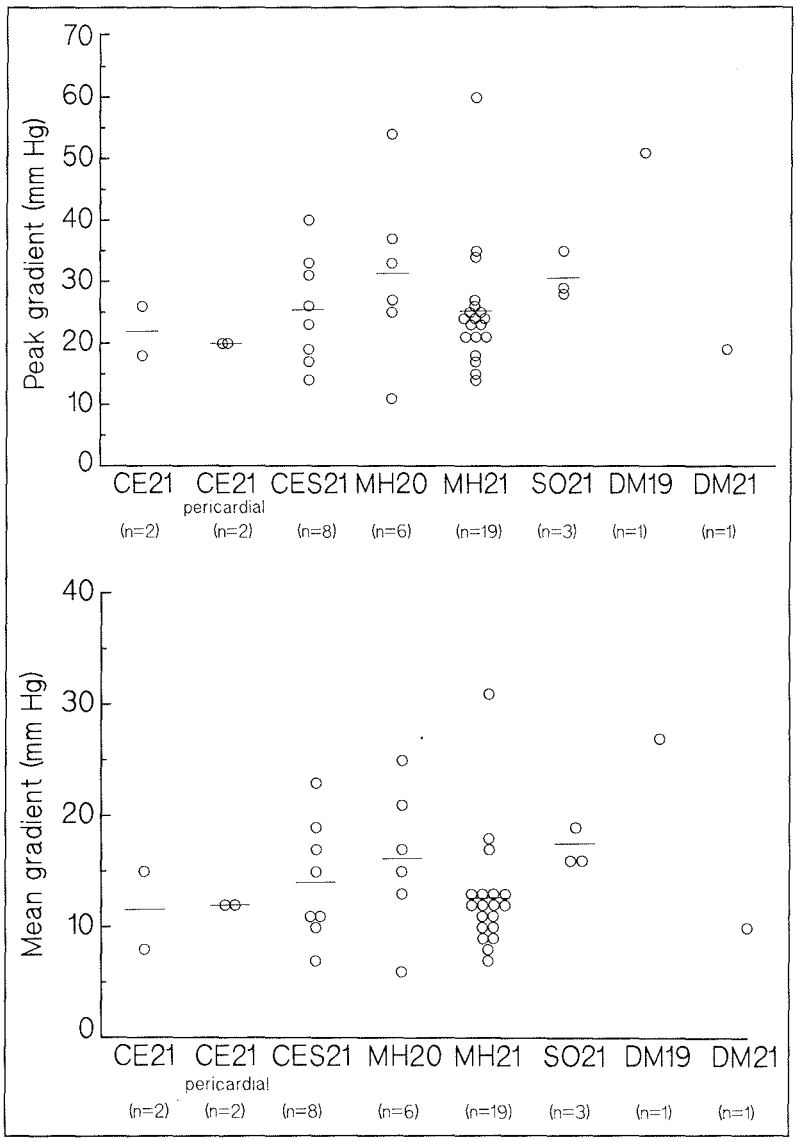


FIGURE 2. Peak *(top)* and mean *(bottom)* gradients for different valve types. CE= Carpentier-Edwards; CES = Carpentier-Edwards supraannular; DM = Duromedics; MH = Medtronic-Hall; SO = Sorin.

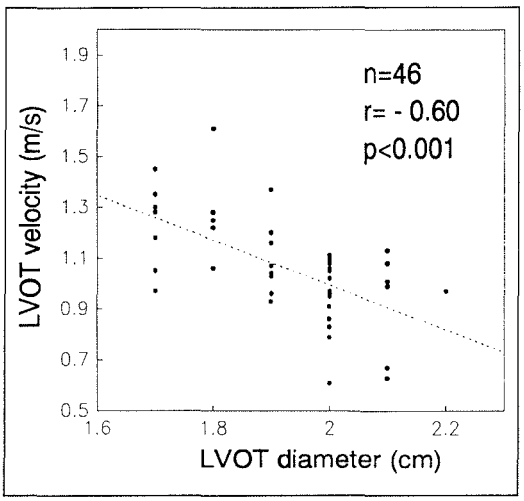


FIGURE 3. A negative correlation was demonstrated between the left ventricular outflow tract (LVOT) diameter and velocities.

Subvalvular diameters and velocities (Table II): The subvalvular diameter was significantly smaller in the MH 20 mm group, with an average difference of 0.18 cm between the MH 20 and 21 mm prostheses. The subvalvular velocities and velocity time integrals were higher in the MH 20 mm group compared with the CE supraannular and the MH 21 mm groups. A negative correlation was found between the subvalvular diameters and outflow tract velocities (Figure 3). The highest subvalvular velocity recorded was 1.61 m/s.

Prosthetic valve area, dimensionless obstruction index (Table I): The valve areas calculated by the simplified and standard continuity equation were highly correlated (Figure 4). With the standard continuity equation, a significantly smaller area was found for the CE supraannular valves than for the MH 21 mm group. When comparing the MH 20 and 21 mm valves, areas tended to be lower for the 20 mm group, although this did not reach statistical significance ($p = 0.06$). The dimensionless obstruction indexes did not differ among the groups (Table I).

Intraventricular velocities: Six patients (13%) had intraventricular velocities >1.5 m/s and a characteristic pattern of the velocity curve with the highest velocities at end systole (Figure 5). These velocities were usually recorded at the midventricular level, and were not considered to represent left ventricular outflow tract obstructions. The highest midventricular velocity measured was 3.8 m/s, corresponding to an intraventricular gradient of 57 mm Hg. The patients with this flow pattern did not differ with respect to age or time interval from surgery. Heart rate tended to be higher (77 ± 12 vs 68 ± 11 beats/min, $p = 0.07$) and left ventricular ejection time shorter (281 ± 39 vs 311 ± 35 m/s, $p = 0.06$) in these patients, indicating a somewhat hyperdynamic circulatory state.

Reproducibility: In a recent study we found the subvalvular diameter measurement to be a major source of variance in calculation of stroke volume and orifice area in patients with aortic valve prostheses (Rossvoll, unpublished data). In the present study the diameter was measured independently by 2 observers in 15 randomly selected patients. The difference in diameter recordings was within 2 mm in 13 of 15 patients (87%), with identical measurements in 6. To assess reproducibility of valve area measurements, 9 patients were reexamined within 1 to 14 months. The upper and lower limits of agreement were $0.34/-0.14$ cm^2 and $0.32/-0.16$ cm^2

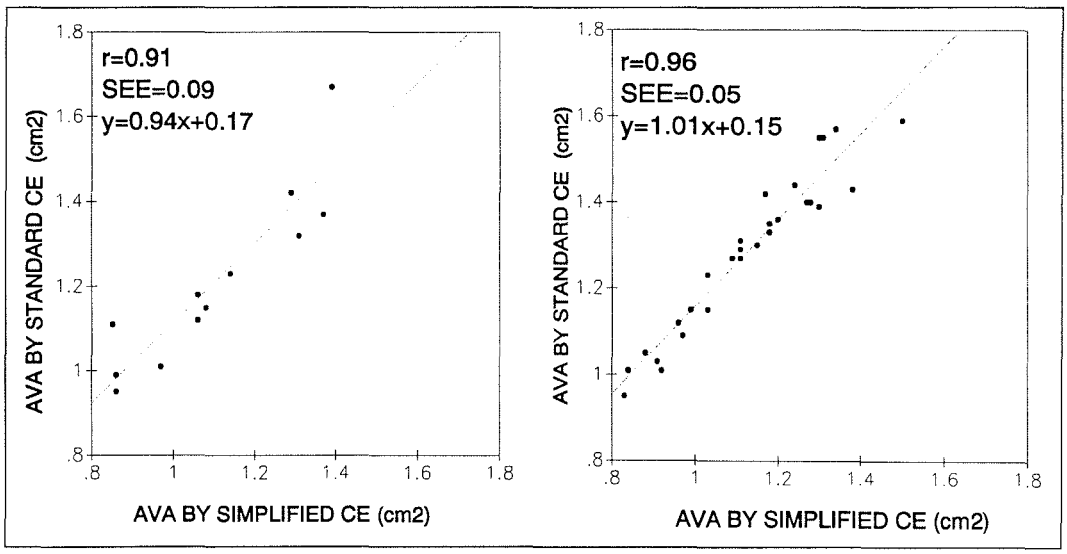


FIGURE 4. The prosthetic aortic valve areas (AVA) obtained with the simplified and the standard continuity equation (CE) were highly correlated for both bioprostheses *(left)* and mechanical valves *(right)*.

with the simplified and standard continuity equation, respectively. The limits of agreement for the dimensionless obstruction index were 0.09/−0.07 (velocities) and 0.08/−0.03 (velocity time integrals).

DISCUSSION

Resting hemodynamics of small (≤21 mm) aortic valve prostheses and bioprostheses are well assessed by Doppler echocardiography. No patient was excluded because of technically inadequate recordings. The predominant characteristics of the patients studied (female sex, small body surface area) are considered representative for an unselected group of patients with a small aortic prosthesis. A similar profile of patients with a narrow aortic annulus is described by others.[20,21]

Perivalvular leaks: Perivalvular leaks were diagnosed in 7 patients (15%). Except for the patient with a 3+ leak after reoperation during endocarditis, the leaks were assessed as minor and without hemodynamic significance. It is noteworthy that no case of pathologic leak was found with the MH 20 mm prosthesis indicating that the thinner sewing ring does not predispose for perivalvular leaks. To our knowledge there is no earlier report presenting noninvasive hemodynamic data of this prosthesis.

Pressure decrease: The pressure decrease recorded across these ≤21 mm valves was acceptable; only 2 patients had a mean gradient >25 mm Hg. Earlier reports on hemodynamic properties of small aortic valve prostheses are mostly based on invasive studies. The average mean gradient of 13 mm Hg across the MH 21 mm prostheses in this study corresponds well with an average mean gradient of 12 mm Hg reported from catheterization of 9 patients with this prosthesis.[22] A mean gradient of 19 mm Hg is reported after catheterization of 16 patients with a 21 mm CE pericardial valve.[23] In our study the CE valves had favorable gradients (Figure 2), indicating that they provide an acceptable alternative in the narrow aortic annulus when a tissue valve is desired. There are few reports on noninvasively obtained gradients across 21 mm prosthetic valves. After a review of published reports, Reisner and Meltzer[24] reported noninvasive data of 25 St. Jude Medical, 5 Bjørk-Shiley and 7 CE pericardial 21 mm valves. The average peak and mean gradients ranged from 27.3 to 30.5 and from 14.4 to 16.0 mm Hg, respectively. The results in our study are in the same ranges.

Prosthetic valve area: An excellent correlation between valve areas obtained with the standard and simplified continuity equation has been described for bioprostheses.[25] According to our study the 2 methods relate similarly in mechanical valves (Figure 4). Earlier reports on prosthetic valve areas are mostly based on invasive measurements using the Gorlin formula,[26] but the adequacy of this formula in predicting prosthetic valve area is questioned.[27] So far there is a paucity of noninvasive data on valve areas in ≤21 mm aortic valve prostheses and bioprostheses. Similar to our results an area of 1.39 ± 0.55 cm^2 is reported for the 21 mm Ionescu-Shiley pericardial valve,[28] and 1.02 ± 0.10 cm^2 for the 21 mm Medtronic-Intact bioprosthesis.[25] In vitro studies have demonstrated a progressive opening of the CE bioprostheses with increasing flow rates.[23] The smaller orifice area calculated for the CE compared to the MH 21 mm valves in this study could therefore be attributed to a lower stroke volume in the former group (57 ± 12 vs 75 ± 12 ml, $p < 0.001$). Although the MH 20 and 21 mm prostheses have identical inner orifice areas, valve area tended to be lower and gradients higher for the 20 mm valves. The discrepancy between the 1 mm difference in external diameter and the difference of 1.8 mm in subvalvular diameter in the 2 groups could indicate that the 20 mm prostheses are inserted in roots that, relative to the prosthesis size, are narrower than the roots where a 21 mm prosthesis is inserted. This could result in a more oblique positioning in the aortic annulus, and the orientation of the major orifice could be less than optimal precluding an effective utilization of the prosthesis area.

Dimensionless obstruction index: This parameter did not significantly differ between the groups (Table I). With this index, the sometimes difficult and time-

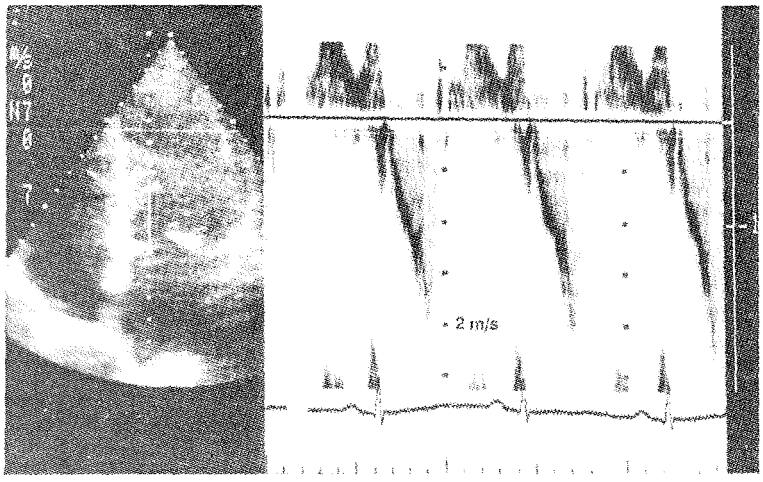


FIGURE 5. Increased midventricular velocity recorded close to the septum. Note the typical shape of the *curve* with the highest velocity occurring at the end of systole.

consuming diameter measurement and the inaccuracies it may introduce are omitted. To our knowledge this index has not been reported earlier for ≤21 mm aortic valve prostheses, but this parameter may prove valuable in the follow-up of patients with aortic valve prostheses and should be further evaluated.

Subvalvular velocities: With decreasing left ventricular outflow tract diameter, increasing subvalvular velocities were found (Figure 3). This finding emphasizes the necessity of making correction for prevalvular velocities when applying the Bernoulli equation in aortic valve prostheses.[16] Otherwise gradients will be overestimated to a varying degree with the largest overestimation occurring in patients with a narrow outflow tract. In our study this is illustrated with the MH 20 mm valve. Without correction the calculated peak and mean gradients across this valve would on average have been 6 (19%) and 4 (25%) mm Hg higher than the values listed in Table I. Occasionally a subvalvular obstruction may occur after valve replacement in a narrow aortic root.[13] The highest outflow tract velocity recorded in this study was 1.61 m/s, indicating no significant subvalvular obstruction in any of these patients.

Clinical implications: Resting hemodynamics in an unselected group of ≤21 mm aortic valve prostheses and bioprostheses implanted during a 7-year period were acceptable. The moderate obstruction caused by the prostheses is not likely to be a limiting factor for the functional capacity in these patients. When assessing function of prosthetic aortic valves noninvasively, subvalvular velocities should routinely be recorded; otherwise the transprosthetic gradient will be overestimated to a varying degree.

REFERENCES

1. Konno S, Imai Y, Lida Y, Nakajima M, Tatsuno K. A new method for prosthetic valve replacement in congenital aortic stenosis associated with hypoplasia of the aortic valve ring. *J Thorac Cardiovasc Surg* 1975;70:909–917.

2. Manouguian S, Seybold-Epting W. Patch enlargement of the aortic valve ring by extending the aortic incision into the anterior mitral leaflet: new operative technique. *J Thorac Cardiovasc Surg* 1979;78:402–412.

3. Misbach GA, Turley K, Ullyot DJ, Ebert PA. Left ventricular outflow enlargement by the Konno procedure. *J Thorac Cardiovasc Surgery* 1982;84:696–703.

4. Abdelnoor M, Hall KV, Nitter-Hauge S, Lindberg H, Øvrum E. Prognostic factors in aortic valve replacement associated with narrow aortic roots. *Scand J Thorac Cardiovasc Surg* 1986;20:227–232.

5. Horstkotte D. Prosthetic valves or tissue valves — a vote for mechanical prostheses. *Z Kardiol* 1985;74(suppl VI):19–37.

6. Sagar KB, Wann S, Paulsen WHJ, Romhilt DW. Doppler echocardiographic evaluation of Hancock and Bjørk-Shiley prosthetic valves. *J Am Coll Cardiol* 1986;7:681–687.

7. Kapur KK, Fan P, Nanda NC, Yoganathan AP, Goyal RG. Doppler color flow mapping in the evaluation of prosthetic mitral and aortic valve function. *J Am Coll Cardiol* 1989;13:1561–1571.

8. Burstow DJ, Nishimura RA, Bailey KR, Reeder GS, Holmes DR Jr, Seward JB, Tajik AJ. Continuous wave Doppler echocardiographic measurement of prosthetic valve gradients. A simultaneous Doppler-Catheter correlative study. *Circulation* 1989;80:504–514.

9. Ihlen H, Mølstad P. Cardiac output measured by Doppler echocardiography in patients with aortic prosthetic valves. *Eur Heart J* 1990;11:399–402.

10. Rothbart RM, Castriz JL, Hardings LV, Russo CD, Teague SM. Determination of aortic valve area by two-dimensional and Doppler echocardiography in patients with normal and stenotic bioprosthetic valves. *J Am Coll Cardiol* 1990;15:817–824.

11. Alam M, Rosman HS, Lakier JB, Kemp S, Khaja F, Hautamaki K, Magilligan DJ, Stein PD. Doppler and echocardiographic features of normal and dysfunctioning bioprosthetic valves. *J Am Coll Cardiol* 1987;10:851–858.

12. Dittrich H, Nicod P, Hoit B, Dalton N, Sahn D. Evaluation of Bjørk-Shiley prosthetic valves by real-time two-dimensional Doppler echocardiographic flow mapping. *Am Heart J* 1988;115:133–138.

13. Bjørk VO, Henze A, Holmgren A, Szamosi A. Evaluation of the 21 mm Bjørk-Shiley tilting disc valve in patients with narrow aortic roots. *Scand J Thorac Cardiovasc Surg* 1973;7:203–213.

14. Hatle L. Noninvasive assessment and differentiation of left ventricular outflow obstruction with Doppler ultrasound. *Circulation* 1981;64:381–387.

15. Sasson Z, Yock PG, Hatle LK, Alderman EL, Popp RL. Doppler echocardiographic determination of the pressure gradient in hypertrophic cardiomyopathy. *J Am Coll Cardiol* 1988;11:752–756.

16. Hatle L, Angelsen B. Pressure velocity relationships. In: Doppler Ultrasound in Cardiology. Physical Principles and Clinical Applications. 2nd ed. Philadelphia: Lea & Febiger, 1985:22–26.

17. Skjaerpe T, Hegrenaes L, Hatle L. Noninvasive estimation of valve area in patients with aortic stenosis by Doppler ultrasound and two-dimensional echocardiography. *Circulation* 1985;72:810–818.

18. Zoghbi WA, Farmer KL, Soto JG, Nelson JG, Quinones MA. Accurate noninvasive quantification of stenotic aortic valve area by Doppler echocardiography. *Circulation* 1986;73:452–459.

19. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;1:307–310.

20. Gill CC, King HC, Lytle BW, Cosgrove DM, Golding LAR, Loop FD. Early clinical evaluation after aortic valve replacement with the St. Jude Medical valve in patients with a small aortic root. *Circulation* 1982;66(suppl I):I-147–I-149.

21. David TE, Uden DE. Aortic valve replacement in adult patients with small aortic annuli. *Ann Thorac Surg* 1983;36:577–583.

22. Nitter-Hauge S, Semb B, Abdelnoor M, Hall KV. A five year experience with the Medtronic-Hall disc valve prosthesis. *Circulation* 1983;68(suppl II):II-169–II-174.

23. Cosgrove DM, Lytle BW, Gill CC, Golding LAR, Stewart RW, Loop FD, Williams GW. In vivo hemodynamic comparison of porcine and pericardial valves. *J Thorac Cardiovasc Surg* 1985;89:358–368.

24. Reisner SA, Meltzer RS. Normal values of prosthetic valve Doppler echocardiographic parameters: a review. *J Am Soc Echo* 1988;1:201–210.

25. Dumesnil JG, Honos GN, Lemieux M, Beauchemin J. Validiation and applications of indexed aortic prosthetic valve areas calculated by Doppler echocardiography. *J Am Coll Cardiol* 1990;16:637–643.

26. Gorlin R, Gorlin SG. Hydraulic formula for calculation of the area of the stenotic mitral valve, other cardiac valves and central circulatory shunts. *Am Heart J* 1951;41:1–18.

27. Cannon SR, Richards KL, Crawford MH, Folland ED, Pierpont G, Sethi GK, Hammermeister KE. Inadequacy of the Gorlin formula for predicting prosthetic valve area. *Am J Cardiol* 1988;62:113–116.

28. Teoh KH, Fulop JC, Weisel RD, Ivanov J, Tong CP, Slattery SA, Rakowski H. Aortic valve replacement with a small prosthesis. *Circulation* 1987;76(suppl III):III-123–III-131.

Paper III

Exercise hemodynamics in small (≤21 mm) aortic valve prostheses assessed by Doppler echocardiography

Exercise Doppler echocardiography was used to assess hemodynamics in 25 patients with a ≤21 mm aortic valve prosthesis (14 with a Medtronic-Hall 21 mm valve, three with a Medtronic-Hall 20 mm valve, three with a Sorin 21 mm valve, one with a Duromedics 21 mm valve, and four with a Carpentier-Edwards 21 mm valve). A symptom-limited upright bicycle exercise test was performed, and Doppler gradients were recorded during exercise. Gradients increased with exercise from 30 ± 8/16 ± 4 mm Hg (peak/mean) at rest to 46 ± 12/24 ± 7 mm Hg during exercise; both $p < 0.001$. Mean exercise gradient exceeded 30 mm Hg in five patients, and the highest mean gradient recorded was 37 mm Hg. Within the group of mechanical valves, gradients at exercise were similar for different types of valves. A linear relationship was found between gradients at rest and during exercise (peak $r = 0.75$, mean $r = 0.77$; both $p < 0.001$). Additional findings were midventricular velocities exceeding 1.5 m/sec in late systole in 10 patients (40%) and intraventricular flow (≥0.2 m/sec) toward the apex during isovolumic relaxation in 11 patients (44%). The patients with these velocity patterns had significantly smaller left ventricular cavities (end-diastolic diameter 39.8 ± 4.8 vs 46.5 ± 4.2 mm, $p < 0.01$; end-systolic diameter 24.2 ± 3.0 vs 28.5 ± 4.5 mm, $p = 0.013$). We conclude that the limitation of exercise capacity in these patients with small aortic prosthetic valves is likely the result of other or additional factors besides the moderate increase in gradients with exercise. (Am Heart J 1993;125:138.)

Rune Wiseth, MD,[a] Olaf W. Levang, MD,[b] Geir Tangen, MD,[b] Kjell A. Rein, MD,[b] Terje Skjaerpe, MD,[a] and Liv Hatle, MD[a] *Trondheim, Norway*

The hemodynamic properties of small aortic valve prostheses are questioned, and the management of the narrow aortic anulus remains controversial.[1-3] The alternative to a small prosthesis with the risk of an unacceptable residual outflow obstruction is a root enlargement that may allow insertion of a larger valve.[1, 4, 5] However, this will prolong the surgical procedure and may increase the operative risk.[3] Therefore studies assessing the hemodynamic function of small aortic valve prostheses are of clinical interest, inasmuch as the results may influence decision making in patients with a small aortic root. A complete hemodynamic evaluation of prosthetic valves should include assessment of exercise hemodynamics. Tatineni et al.[6] described prosthesis size to be an independent predictor of exercise tolerance after aortic valve replacement. A negative influence of a small prosthesis on exercise capacity has been suggested to be the result of high gradients during exercise that are not always seen at rest.[7] Until recently the only quantitative method for evaluating prosthetic function was cardiac catheterization, and hemodynamic data of small aortic valve prostheses are mostly based on invasive studies with only a few reports including exercise data.[8-10] With Doppler echocardiography both resting and exercise hemodynamics of prosthetic valves may be evaluated.[6, 11, 12] So far there is a paucity of noninvasive data on small aortic valve prostheses,[13] and exercise data are reported for only a very few cases.[6]

The purpose of this study was to assess exercise hemodynamics with Doppler echocardiography in an unselected group of patients with a small (≤21 mm) aortic valve prosthesis implanted during a 7-year period. It was aimed at an exercise test relevant to and at least as demanding as the patients' maximal physical activity during ordinary daily life.

From the Sections of Cardiology[a] and Thoracic and Cardiovascular Surgery,[b] University Hospital.

Supported by grants from the Norwegian Council on Cardiovascular Diseases.

Received for publication Feb. 24, 1992; accepted July 24, 1992.

Reprint requests: Rune Wiseth, MD, Section of Cardiology, Department of Medicine, Regional Hospital, University of Trondheim, N-7006 Trondheim, Norway.

4/1/42165

0002-8703/93/$1.00 + .10.

METHODS

Patients. In the period from 1983 to 1989, a total of 58 aortic valve prostheses (43 mechanical and 15 biological) with an external diameter ≤21 mm were implanted. There were two early and five late deaths. One patient with a Medtronic-Hall 21 mm prosthesis (Medtronic Inc., Minneapolis, Minn.) was admitted with heart failure 5½ months after surgery. The diagnosis of impeded disc movement caused by thrombotic obstruction was made by Doppler echocardiography and at a successful reoperation a thrombus was removed. Three patients who had surgery during the latter part of the study period did not exercise because of a postoperative interval of only 1 to 2 weeks. Thus a total of 47 patients were eligible for the study. Because of age and geographic considerations, four patients were not contacted (mean age 78 ± 4 years). Among the remaining 43 patients, 10 were excluded because of inability to exercise or contraindications (general physical incapacity in four, hip lesion in one, sequelae of apoplexia in two, claudication in two, and recent cerebral ischemic attack in one); mean age was 70 ± 6 years. Three patients were excluded for other reasons (atrial fibrillation in one, paravalvular leak in one, and administrative in one). The remaining 30 patients underwent exercise testing after informed consent was obtained. Technically adequate recordings during exercise were obtained in 25 (83%), and these constitute the study group. The valves inserted in the patients undergoing a successful exercise study included Medtronic-Hall 21 mm (n = 14), Medtronic-Hall 20 mm (n = 3), Sorin 21 mm (n = 3), Duromedics 21 mm (n = 1), and Carpentier-Edwards 21 mm (n = 4) (Baxter Healthcare Corp., Edwards Division, Santa Ana, Calif.).

Before surgery all but one patient underwent coronary arteriography. Significant coronary artery disease defined as >75% stenosis of at least one of the major coronary arteries was present in 11 patients preoperatively (44%), nine of whom underwent concomitant coronary artery surgery.

Mean age of the study group was 68 years (range 58 to 80), and mean duration of valve implants was 19 months (range 12 to 31) for the bioprostheses and 35 months (range 3 to 67) for the mechanical valves. All but one patient were women, mean body surface area was 1.65 ± 0.10 m^2, and all patients were in New York Heart Association functional class I or II.

Doppler echocardiography. Before exercise, complete M-mode, two-dimensional, and Doppler echocardiographic studies were done with an Irex Meridian (Irex Technology Group, New Brunswick, N.J.) or VingMed CFM 700 (VingMed Sound A/S, Oslo, Norway) ultrasound system. The thickness of the interventricular septum and posterior wall was measured at the level of the chordae tendineae according to the criteria of the American Society of Echocardiography.[14] In two patients the parasternal echocardiographic window did not allow for adequate M-mode measurements. Velocities across the prostheses were recorded with a continuous-wave Doppler technique from the apical, suprasternal, and right parasternal positions. From the highest velocities obtained, the transprosthetic pressure drop was calculated according to the Bernoulli equation.[15] At rest the gradients were calculated both with and without correction for prevalvular velocities: $\Delta P = 4(V_{valve}^2 - V_{lvot}^2)$ and $\Delta P = 4V_{valve}^2$, where V_{valve} is the velocity across the prosthesis and V_{lvot} is the left ventricular outflow tract velocity. The valve area was calculated by means of the continuity equation.[16]

Mitral flow velocities were recorded by means of a pulsed-wave Doppler technique with the sample volume between the tips of the mitral leaflets. The isovolumic relaxation time was measured as the interval from the closing signal of the prosthesis to the opening signal of the mitral valve. Left ventricular ejection time was measured from the start of the opening to the start of the closing signal of the prosthesis, and the left ventricular ejection time index was calculated according to the formula of Weissler et al.[17]

Exercise protocol. Exercise was bicycling in the upright position. Before the start of exercise velocity recordings across the prosthesis and the mitral valve were repeated after 5 minutes in the upright position with the use of a 2 MHz single Doppler transducer. The peak early (E) and late (A) mitral flow velocities, the E/A ratio, and the isovolumic relaxation time in the supine and upright positions were compared to assess the influence of body position on filling parameters. The gradients across the prostheses in the supine and upright positions were compared. At supine rest the highest velocities across the prostheses were recorded from the apical position in 21 patients; in the remaining four the highest velocities were recorded from the right parasternal position. The same acoustic windows were used at rest and during exercise for comparison of gradients. A symptom-limited exercise test was performed. The starting work load was 25 W with a further increase in work load of 25 W every fourth minute. In a few instances the exercise protocol had to be modified according to the patients' tolerance. Exercise was stopped when symptoms of dyspnea or fatigue occurred, and exercise capacity was expressed as cumulative work in kilojoules.

With continuous strip-chart recording (paper speed 75 mm/sec) at peak exercise, all beats with technically adequate recordings could be analyzed. A computerized digitizer was used for envelope tracing of Doppler velocity curves and calculation of peak and mean gradients. Recordings from at least three beats obtained at peak exercise were averaged and compared with resting baseline data. During exercise it was not possible to correct for left ventricular outflow tract (LVOT) velocities in the Bernoulli equation,[15] inasmuch as adequate recordings of LVOT velocities could be obtained only occasionally. Therefore in a comparison of prosthesis gradients in the resting supine and upright positions and during exercise, gradients not corrected for LVOT velocities were used. Heart rate was calculated from the ECG tracings on the strip chart.

Statistical analysis. Continuous variables are expressed as mean ± SD. Student's unpaired or two-tailed paired t test was used as appropriate. With multiple comparisons, analysis of variance followed by the Student–Newman-Keuls test was used. The association between variables was analyzed by means of linear regression analysis (least

Table I. Gradients and valve areas for different valve types obtained at rest supine

Valve type	*Peak grad[1] (mm Hg)*	*Peak grad[2] (mm Hg)*	*Mean grad[1] (mm Hg)*	*Mean grad[2] (mm Hg)*	*Valve area (cm^2)*
CE 21 mm (n = 4)	27 ± 6	24 ± 5	15 ± 3	14 ± 3	1.12 ± 0.16
MH 20 mm (n = 3)	33 ± 10	26 ± 11	18 ± 5	14 ± 5	1.23 ± 0.25
MH 21 mm (n = 14)	30 ± 8	26 ± 8	15 ± 4	13 ± 4	1.37 ± 0.13
SO 21 mm (n = 3)	36 ± 1	31 ± 3	20 ± 1	17 ± 1	1.18 ± 0.16
DM 21 mm (n = 1)	22	19	11	9	1.4
All (n = 25)	30 ± 8 (15-51)	26 ± 8 (11-46)	16 ± 4 (8-25)	13 ± 4 (6-22)	1.29 ± 0.19 (0.95-1.59)

grad[1], Gradients calculated before correction for LVOT velocities in Bernoulli equation ($\Delta P = 4V_{valve}^2$); *grad[2]*, gradients calculated after correction for LVOT velocities ($\Delta P = 4(V_{valve}^2 - V_{lvot}^2)$); *CE*, Carpentier-Edwards; *DM*, Duromedics; *MH*, Medtronic-Hall; *SO*, Sorin.
Ranges are given in parentheses.

Table II. Changes in resting hemodynamics with change in position from supine to sitting on bicycle

Hemodynamics	*Rest supine*	*Rest sitting*	*p Value*
Heart rate (beats/min)	67 ± 8	75 ± 10	<0.001
Systolic BP (mm Hg)	155 ± 21	148 ± 17	NS
Diastolic BP (mm Hg)	78 ± 9	80 ± 9	NS
Peak grad[1] (mm Hg)	30 ± 8	26 ± 8	<0.001
Mean grad[1] (mm Hg)	16 ± 4	13 ± 4	<0.001
LVET (msec)	313 ± 28	269 ± 31	<0.001
LVETI	421 ± 21	390 ± 20	<0.001
IVRT (msec)	78 ± 13	105 ± 17	<0.001
E (cm/sec) (n = 22)	92 ± 25	65 ± 20	<0.001
A (cm/sec) (n = 22)	94 ± 24	84 ± 19	0.019
E/A (n = 22)	1.00 ± 0.27	0.77 ± 0.16	<0.001

A, Peak late mitral flow velocity; *BP*, blood pressure; *E*, peak early mitral flow velocity; *IVRT*, isovolumetric relaxation time; *LVET*, left ventricular ejection time; *LVETI*, left ventricular ejection time index; *NS*, not significant; other abbreviations as in Table I.

squares). A p value <0.05 was considered statistically significant.

RESULTS

Hemodynamics at rest and effects of posture. Table I shows gradients and valve areas for different valve types obtained at rest in the supine position. The values for different valve types were similar and confined within narrow ranges. For the group as a whole the peak and mean gradients differed by an average of 4 and 3 mm Hg, respectively, whether or not corrections were made for prevalvular velocities in the Bernoulli equation. Table II demonstrates altered resting hemodynamics with a change in body position from supine to sitting. Heart rate and isovolumic relaxation time increased significantly (both $p < 0.001$). Peak and mean gradients, left ventricular ejection time, left ventricular ejection time index, and E/A ratio decreased significantly in the sitting position (all $p < 0.001$).

Exercise. The exercise test was performed without complications, and exercise was stopped because of general fatigue in all instances with every patient judging the work load at least as demanding as his or her maximal physical activity during ordinary daily life. Angina pectoris or arrhythmias were not seen. The heart rate at the end of exercise averaged 80% of the age-predicted maximal heart rate, and exercise capacity defined as cumulative work was 22.1 ± 12.5 kilojoules (range 3 to 45.3) for the total group.

With exercise the prosthetic valve gradient increased in all patients. Heart rate and peak and mean gradients at rest in both the supine and upright positions and at exercise are shown in Table III. The mean gradient at rest did not exceed 25 mm Hg in any patient, and during exercise the mean gradient exceeded 30 mm Hg in five patients (20%). The highest mean gradient recorded during exercise was 37 mm Hg. Inasmuch as these gradients are not corrected for LVOT velocities in the Bernoulli equation, they represent some overestimation. Fig. 1 shows an example from one of the patients where recordings of LVOT velocities were obtained during exercise. Inasmuch as LVOT velocities increase with exercise, continuous-wave registrations without correction for these velocities can also overestimate the true gradient increase. From supine rest to peak exercise the average increase in peak and mean gradients for the

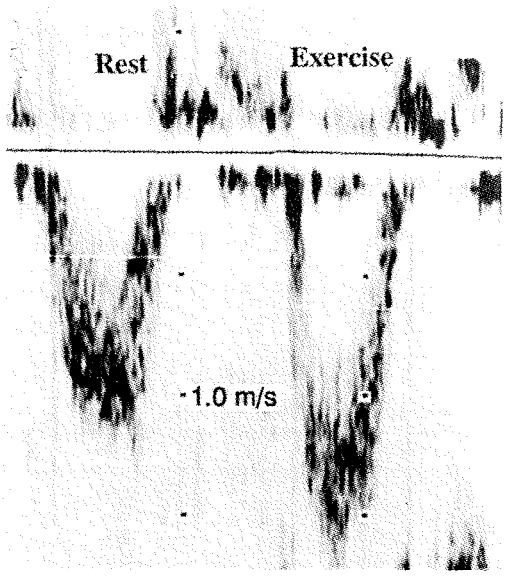


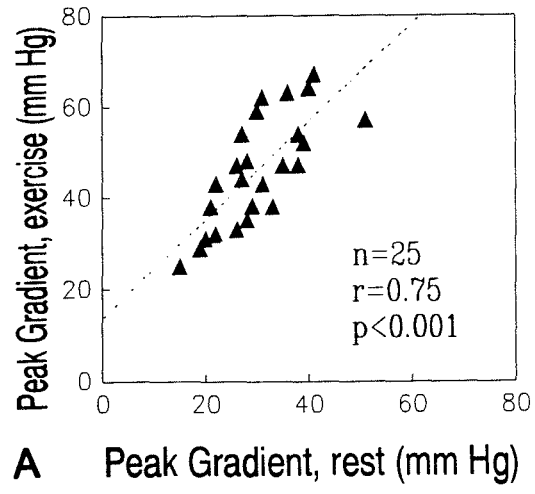
Fig. 1. LVOT velocities increase with exercise, and prosthesis gradients calculated by Bernoulli equation without correction for LVOT velocities will overestimate true gradient increase. In this example LVOT velocity increased from 1.37 to 1.58 m/sec, and gradients calculated from continuous-wave registrations without correction for LVOT velocities overestimated true gradients by 5/3 (peak/mean) mm Hg at rest and by 10/6 mm Hg during exercise.

Table III. Heart rate and gradients at rest supine, rest upright, and during upright exercise

	Rest supine	*Rest upright*	*Exercise upright*
Heart rate	67 ± 8	75 ± 10	122 ± 19*
Peak grad[1] (mm Hg)	30 ± 8	26 ± 8	46 ± 12†
Mean grad[1] (mm Hg)	16 ± 4	13 ± 4	24 ± 7*

Abbreviations as in Table I.
*$p < 0.05$ versus rest supine and rest upright (by one-way analysis of variance followed by Student-Newman-Keuls test).
†$p < 0.05$ versus rest upright.

group as a whole was only moderate: 16 ± 8 and 8 ± 4 mm Hg, respectively. The increase in gradient with exercise tended to be lower for the bioprostheses (peak 10 ± 3/mean 6 ± 2 mm Hg) compared with the mechanical valves (peak 17 ± 8/mean 9 ± 4 mm Hg), although the differences were not statistically significant (peak $p = 0.10$, mean $p = 0.16$). Within the group of mechanical valves the exercise-induced



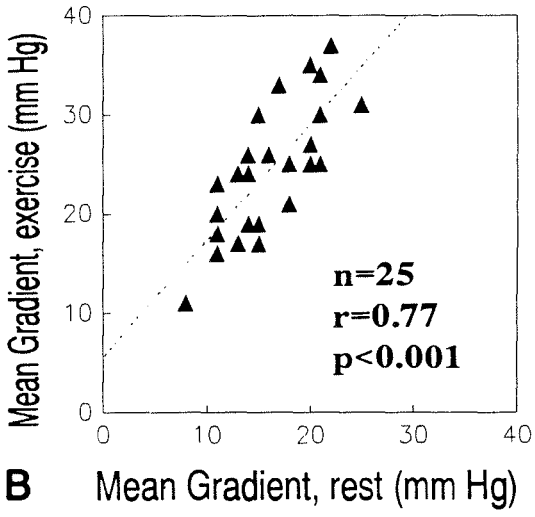


Fig. 2. By linear regression analysis, peak **(A)** and mean **(B)** gradients during exercise were correlated with gradients at rest.

increase in gradients was similar for the different types of valves (Table IV).

A linear regression analysis revealed that both peak and mean gradients at exercise were predicted by the resting gradients (Fig. 2, *A* and *B*). There was no significant correlation between resting gradients and exercise-induced increases in gradients; neither was there any significant correlation between maximal heart rate and gradients at exercise. Duration of valve implants did not correlate with gradients at rest or at exercise.

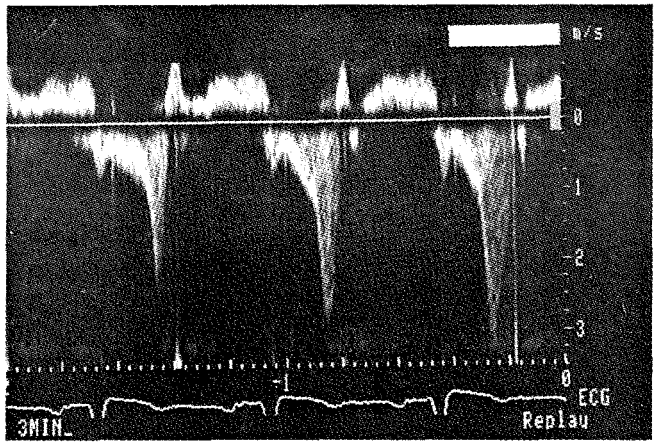


Fig. 3. Increased intraventricular flow velocity (maximum 3 m/sec) in mid and late systole occurring during exercise. Note concave shape of curve with highest velocities occurring at end systole, a typical pattern for dynamic intraventricular obstruction.

Table IV. Gradients at rest supine and during maximal upright exercise for different types of valves

Valve type	*Peak grad[1] rest supine (mm Hg)*	*Peak grad[1] exercise (mm Hg)*	*Mean grad[1] rest supine (mm Hg)*	*Mean grad[1] exercise (mm Hg)*
CE 21 mm (n = 4)	27 ± 6	36 ± 5	15 ± 3	21 ± 3
MH 20 mm (n = 3)	33 ± 10	48 ± 16	18 ± 5	26 ± 9
MH 21 mm (n = 14)	30 ± 8	47 ± 11	15 ± 4	24 ± 6
SO 21 mm (n = 3)	36 ± 1	55 ± 7	20 ± 1	30 ± 4
DM 21 mm (n = 1)	22	43	11	23
All (n = 25)	30 ± 8 (15-51)	46 ± 12 (25-67)	16 ± 4 (8-25)	24 ± 7 (11-37)

Abbreviations as in Table I.

Coronary artery disease. Patients with prior coronary artery bypass grafting were analyzed separately and compared with the rest. Exercise capacity in patients with prior coronary bypass grafting was 23.5 ± 11.6 compared with 21.3 ± 12.9 kilojoules (NS). Peak and mean gradients at rest and during exercise showed similar values for the two groups (resting peak/mean 30 ± 7/16 ± 4 vs 30 ± 9/16 ± 4 mm Hg and exercise peak/mean 46 ± 9/24 ± 4 vs 46 ± 13/25 ± 7 mm Hg, all NS).

Intraventricular flow patterns. Increased midventricular velocities (≥1.5 m/sec) directed toward the LVOT in systole were recorded in five patients at rest and in another five during or immediately after exercise. The shape of this velocity curve was similar to that seen in dynamic left ventricular obstruction with the highest velocities occurring at end systole (Fig. 3). The highest intraventricular velocity recorded was 3.76 m/sec at rest and 4 m/sec immediately after exercise, corresponding to intraventricular pressure gradients of 57 and 64 mm Hg, respectively. Intraventricular velocities (≥0.2 m/sec) directed toward the apex in the isovolumic relaxation period were detected in six patients at rest and in another five immediately after exercise (Fig. 4). In nine patients both flow patterns were demonstrated. Patients with these flow patterns did not differ significantly from the other patients according to age (65 ± 7 vs 66 ± 4 years, NS) or time from operation (2.4 ± 1.4 vs 2.9 ± 2 years, NS). The exercise capacity was similar in the groups with and without these velocity patterns (21.8 ± 12.7 vs 22.5 ± 12 kilojoules, NS), and gradients were not significantly different. In the group with abnormal intraventricular velocities, the peak gradient increased with 50 ± 26% from rest to exercise compared with 62 ± 26% in the rest of the

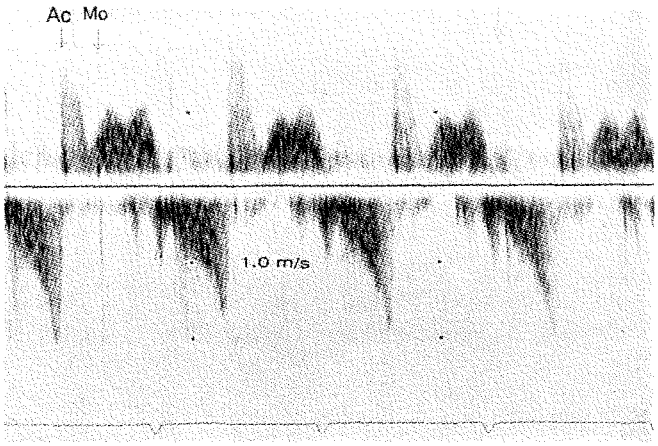


Fig. 4. Intraventricular flow toward apex in isovolumic relaxation period (*Ac*, aortic closure; *Mo*, mitral opening). In this patient there is also a late systolic increase in intraventricular velocities (2 m/sec) directed away from apex.

patients; this difference, however, did not reach statistical significance ($p = 0.264$). In patients with one or both of these flow patterns the left ventricular cavity dimensions were significantly smaller (end-diastolic diameter 39.8 ± 4.8 vs 46.5 ± 4.2 mm, $p < 0.01$; end-systolic diameter 24.2 ± 3.0 vs 28.5 ± 4.5 mm, $p = 0.013$), whereas the septal and posterior wall thicknesses did not differ (septum 12.2 ± 1.5 vs 12.3 ± 2.2 mm, NS; posterior wall 11.4 ± 1.4 vs 10.9 ± 1.2 mm, NS). The left ventricular shortening fractions were similar in the two groups (39 ± 5 vs 40 ± 7, NS).

DISCUSSION

Exercise hemodynamics in patients with small aortic valve prostheses can be assessed by Doppler echocardiography. With technically adequate recordings obtained during exercise in 83%, the success rate was judged acceptable.

Prosthesis gradients. The predominant characteristics of the patients studied (female sex, older age, small body surface area) are considered representative for an unselected group of patients with a small (≤21 mm) aortic valve prosthesis. A similar profile of patients with a small aortic anulus has been described by others,[18, 19] and among such patients the degree of physical activity during daily life may be less demanding. The exercise performed in this study was judged to be more strenuous than the patients' ordinary activities, and the exercise gradients recorded therefore likely represent maximal values for gradients occurring with the daily activities of the patients. Gradients at rest were acceptable with only a moderate increase during exercise. During exercise LVOT velocities may increase, especially in patients with a narrow outflow tract. In an earlier study an inverse relationship was present between the LVOT diameter and the LVOT velocity in patients with aortic valve prostheses (Wiseth R: unpublished data). Therefore the difference between gradients with and without correction for LVOT velocities in the Bernoulli equation may be even greater during exercise, and the recorded increase in gradient during exercise may to some extent overestimate the true increase in gradient (Fig. 1). These considerations lend further support to the judgment of the exercise-induced increase in gradients as being moderate. Peak and mean gradients at exercise correlated with resting values, whereas the increase in gradients was independent of resting values. Exercise gradients did not correlate with heart rate at exercise. This is in contrast to what is demonstrated for mitral valve prostheses, where a linear correlation between heart rate and prosthesis gradient is demonstrated,[12] and it illustrates the different exercise hemodynamics in mitral and aortic valve prostheses. Theoretically an increase in gradient in patients with coronary artery disease could be reduced because of exercise-induced myocardial ischemia resulting in depressed myocardial function. None of our patients had angina during exercise, and inasmuch as gradients and gradient increases in the group with prior coronary artery surgery were similar to the rest, it is unlikely that myocardial ischemia influenced prosthesis gradients.

Body position. Earlier invasive and noninvasive studies of both resting and exercise hemodynamics of aortic valve prostheses have mostly been performed with patients in the supine position.[8, 11, 20] In this study an upright exercise test was chosen, because this is more representative of ordinary physical activities. An upright exercise test followed by an immediate postexercise Doppler recording after the patient has assumed the supine position has been used,[6] but the time delay between exercise and the recordings could influence the results. In our study a 16% decrease in heart rate was noted during the first minute after exercise was stopped; during the second and third minutes after exercise further decreases in heart rate of 7% and 5%, respectively, were noted. This indicates that the relatively largest changes in the hemodynamic state occur in the very early postexercise period, and even a slight delay before Doppler recording could influence the results.

The effects of posture on resting hemodynamics in normal subjects include an increase in heart rate and a decrease in stroke volume with a modest decrease in cardiac output and a decrease in pulmonary artery and left ventricular filling pressures in the upright compared with the supine position.[21-23] With exercise higher heart rates and lower filling pressures are found in the upright compared with the supine position.[21, 22] Higginbotham et al.[23] demonstrated the different mechanisms involved in regulation of cardiac output at submaximal and maximal upright exercise in normal subjects. During low levels of exercise cardiac output increased because of increases in heart rate and stroke volume; at a high level of exercise an additional increase in cardiac output was maintained solely by the increase in heart rate.

In the present study a change in position from supine to sitting significantly influenced resting hemodynamics with decreases in gradients and left ventricular ejection time suggesting a decrease in stroke volume. The diastolic filling parameters were markedly changed demonstrating the influence of body position on left ventricular filling (Table II). Our study was not designed to assess the diastolic function of the left ventricle, and whether the marked changes in filling parameters that occurred with the change in body position can be attributed solely to the reduction in preload or whether these changes could be caused partly by impaired intrinsic left ventricular diastolic properties (abnormal relaxation) remains unanswered. However, by including these parameters it is demonstrated that body position significantly alters hemodynamics including prosthesis gradients, and when exercise Doppler echocardiography is used to assess the hemodynamics of aortic valve prostheses, results may differ according to study protocol.

Intraventricular flow. Results of the Doppler examination revealed two distinct intraventricular flow patterns, one or both occurring in 56% of the patients at rest, during or immediately after exercise. Both the dynamic late systolic intraventricular increase in velocity and the flow toward the apex in the isovolumic relaxation period are described in patients with hypertrophic cardiomyopathy.[24, 25] A late systolic increase in velocity as shown in Fig. 3 suggests good systolic function, and it may also indicate reduced filling.[26, 27] Isovolumic relaxation flow toward the apex is thought to be caused by nonuniform early ventricular relaxation,[24] which is present even in the normal left ventricle, although it is less marked than in hypertrophy.[28] In the present study flow toward the apex during isovolumic relaxation was found in 11 patients (44%), suggesting that asynchronous relaxation was frequently occurring in the group studied. Patients with one or both of these velocity patterns had a smaller left ventricular cavity. We could not demonstrate that this group differed significantly with respect to exercise capacity or prosthesis gradients. It should be noted, however, that exercise capacity in the study group was very heterogeneous and often limited by noncardiac factors. These intraventricular velocity patterns could well be markers of impaired diastolic function, and their frequent occurrence indicates that factors other than prosthesis gradients may be of significance for the hemodynamic capacity in these patients. Monrad et al.[29] demonstrated abnormal exercise hemodynamics with an increase in left ventricular filling pressures several years after aortic valve replacement in patients with normal systolic function, and this finding was not related to the degree of residual left ventricular hypertrophy. They concluded that this abnormality was caused by a primary derangement of diastolic function. Results of a biopsy study in the same group suggested that persistent diastolic dysfunction in patients with prior aortic stenosis may be due to the presence of a relative increase in interstitial fibrosis in the myocardium after muscular hypertrophy has regressed.[30]

Comparison with other studies. There are several invasive studies with exercise data on aortic valve prostheses.[8, 21, 31-34] Exercise data on aortic valve prostheses $\leq$21 mm, however, are reported infrequently, thus making impossible any comparisons with data from the present study. During invasive studies the ability to fully exercise patients may be limited, and this could explain the modest increase in gradient reported in several of these studies.[8, 20, 28] In

a subgroup of 10 younger patients with a Medtronic-Hall prosthesis (size 21 to 27 mm), a mean gradient of 2.9 mm Hg at rest increasing to 6.8 mm Hg during exercise was reported.[8] Horstkotte et al.[33] reported an increase in mean gradient from 18.9 ± 5.2 at rest to 28.5 ± 6.5 mm Hg during exercise in 12 patients with a Bjørk-Shiley 23 mm aortic valve prosthesis.

In a recent study by Tatineni et al.,[6] rest and exercise hemodynamics of St. Jude Medical and Medtronic-Hall prostheses were evaluated by Doppler echocardiography. For Doppler recordings performed with patients in the supine position immediately after upright treadmill exercise, an increase in peak/mean gradients from 21 ± 7/9 ± 4 mm Hg to 35 ± 12/15 ± 6 mm Hg was reported in 20 patients with a Medtronic-Hall aortic valve prosthesis. Mean valve size for this group was 24 ± 3 mm with only two patients having a 21 mm prosthesis (number extracted from figure). They demonstrated a negative correlation between exercise peak gradient and valve size. Among 11 patients with either a Medtronic-Hall 21 mm (n = 2) or a St. Jude Medical 21 mm (n = 9) aortic valve prosthesis, exercise peak gradients ranging from 22 to 52 mm Hg were found (data extracted from figure). This is somewhat lower than our range for exercise peak gradients (25 to 67 mm Hg). These differences could have been the result of differences in patient groups, as well as a difference in exercise protocols.

Conclusions. The resting gradients in this group with ≤21 mm aortic valve prostheses were acceptable with only a moderate increase during exercise. With the mean gradient exceeding 30 mm Hg at maximal exercise in only five patients, this is comparable to a mild aortic stenosis only. Furthermore, these gradients represent some overestimation because of the lack of correction for LVOT velocities in the Bernoulli equation. The moderate obstruction caused by the prostheses is not likely to be a major determinant of exercise capacity in these patients, and other factors should be addressed as well. The results of exercise studies in patients with aortic valve prostheses may depend on which exercise protocol is used, including body position during exercise.

REFERENCES

1. Konno S, Imai Y, Lida Y, Nakajima M, Tatsuno K. A new method for prosthetic valve replacement in congenital aortic stenosis associated with hypoplasia of the aortic valve ring. J Thorac Cardiovasc Surg 1975;70:909-17.
2. Pugliese P, Bernabei M, Santi C, Pasque A, Eufrate S. Posterior enlargement of the small annulus during aortic valve replacement versus implantation of a small prosthesis. Ann Thorac Surg 1984;38:31-6.
3. Abdelnoor M, Hall KV, Nitter-Hauge S, Lindberg H, Øvrum E. Prognostic factors in aortic valve replacement associated with narrow aortic roots. Scand J Thorac Cardiovasc Surg 1986;20:227-32.
4. Manouguian S, Seybold-Epting W. Patch enlargement of the aortic valve ring by extending the aortic incision into the anterior mitral leaflet: new operative technique. J Thorac Cardiovasc Surg 1979;78:402-12.
5. Misbach GA, Turley K, Ullyot DJ, Ebert PA. Left ventricular outflow enlargement by the Konno procedure. J Thorac Cardiovasc Surg 1982;84:696-703.
6. Tatineni S, Barner HB, Pearson AC, Halbe D, Woodruff R, Labovitz AJ. Rest and exercise evaluation of St. Jude Medical and Medtronic-Hall prostheses. Influence of primary lesion, valvular type, valvular size and left ventricular function. Circulation 1989;80(suppl I):I-16-I23.
7. Teoh KH, Fulop JC, Weisel RD, Ivanov J, Tong CP, Slattery SA, Rakowski H. Aortic valve replacement with a small prosthesis. Circulation 1987;76(suppl III):III-123-31.
8. Nitter-Hauge S, Semb B, Abdelnoor M, Hall KV. A five year experience with the Medtronic-Hall disc valve prosthesis. Circulation 1983;68(suppl II):II-169-74.
9. Cosgrove DM, Lytle BW, Gill CC, Golding LAR, Stewart RW, Loop FD, Williams GW. In vivo hemodynamic comparison of porcine and pericardial valves. J Thorac Cardiovasc Surg 1985;89:358-68.
10. Khan SS, Mitchell RS, Derby GC, Oyer PE, Miller DC. Differences in Hancock and Carpentier-Edwards porcine xenograft aortic valve hemodynamics. Effect of valve size. Circulation 1990;82(suppl IV):IV-117-24.
11. Jaffe WM, Coverdale HA, Roche AHG, Whitlock RML, Neutze JM, Barrat-Boyes BG. Rest and exercise hemodynamics of 20 to 23 mm allograft, Medtronic-Intact (porcine), and St. Jude Medical valves in the aortic position. J Thorac Cardiovasc Surg 1990;100:167-74.
12. Reisner SA, Lichtenberg GS, Shapiro JR, Schwarz KQ, Meltzer RS. Exercise Doppler echocardiography in patients with mitral prosthetic valves. AM HEART J 1989;118:755-9.
13. Reisner SA, Meltzer RS. Normal values of prosthetic valve Doppler echocardiographic parameters: a review. J Am Soc Echocardiogr 1988;1:201-10.
14. Sahn DJ, DeMaria A, Kisslo J, Weyman A. The committee on M-mode standardization of the American Society of Echocardiography. Recommendations regarding quantitation in M-mode echocardiography. Results of a survey of echocardiographic measurements. Circulation 1978;58:1072-85.
15. Hatle L, Angelsen B. Pressure velocity relationships. In: Doppler ultrasound in cardiology. Physical principles and clinical applications. 2nd ed. Philadelphia: Lea & Febiger, publishers, 1985:22-6.
16. Skjaerpe T, Hegrenaes L, Hatle L. Noninvasive estimation of valve area in patients with aortic stenosis by Doppler ultrasound and two-dimensional echocardiography. Circulation 1985;72:810-8.
17. Weissler AM, Harris WS, Schoenfeld CD. Systolic time intervals in heart failure in man. Circulation 1968;37:149-59.
18. Gill CC, King HC, Lytle BW, Cosgrove DM, Golding LAR, Loop FD. Early clinical evaluation after aortic valve replacement with the St. Jude Medical valve in patients with a small aortic root. Circulation 1982;66(suppl I):I-147-9.
19. David TE, Uden DE. Aortic valve replacement in adult patients with small aortic annuli. Ann Thorac Surg 1983; 36:577-83.
20. Aris A, Padro JM, Camara ML, Crexells C, Auge JM, Caralps JM. Clinical and hemodynamic results of cardiac valve replacement with the Monostrout Bjørk-Shiley prosthesis. J Thorac Cardiovasc Surg 1988;95:423-31.
21. Thadani U, Parker JO. Hemodynamics at rest and during supine and sitting bicycle exercise in normal subjects. Am J Cardiol 1978;41:52-9.
22. Poliner LR, Dehmer GJ, Lewis SE, Parkey RW, Blomqvist G, Willerson JT. Left ventricular performance in normal subjects: a comparison of the response to exercise in the upright and supine positions. Circulation 1980;62:528-34.

23. Higginbotham MB, Morris KG, Williams RS, McHale PA, Coleman RE, Cobb FR. Regulation of stroke volume during submaximal and maximal upright exercise in man. Circ Res 1986;58:281-91.
24. Sasson Z, Hatle L, Appleton CP, Jewett M, Alderman EL, Popp RL. Intraventricular flow during isovolumic relaxation: description and characterization by Doppler echocardiography. J Am Coll Cardiol 1987;10:539-46.
25. Seiler C, Jenni R, Krayenbuehl HP. Intraventricular blood flow during isovolumetric relaxation and diastole in hypertrophic cardiomyopathy. J Am Soc Echocardiogr 1991;4:247-57.
26. Criley JM, Lewis KB, White RI, Ross RS. Pressure gradients without obstruction. A new concept of "hypertrophic subaortic stenosis." Circulation 1965;32:881-7.
27. Come PC, Bulkley BH, Goodman ZD, Hutchins GM, Pitt B, Fortuin NJ. Hypercontractile cardiac states simulating hypertrophic cardiomyopathy. Circulation 1977;55:901-7.
28. Bonow RO. Regional left ventricular nonuniformity. Effects on left ventricular diastolic function in ischemic heart disease, hypertrophic cardiomyopathy and the normal heart. Circulation 1990;81(suppl III):54-65.
29. Monrad ES, Hess OM, Murakami T, Nonogi H, Corin WJ, Krayenbuehl HP. Abnormal exercise hemodynamics in patients with normal systolic function late after aortic valve replacement. Circulation 1988;77:613-24.
30. Hess OM, Ritter M, Schneider J, Grimm J, Turina M, Krayenbuehl HP. Diastolic stiffness and myocardial structure in aortic valve disease before and after valve replacement. Circulation 1984;69:855-65.
31. Nicoloff DM, Emery RW, Arom KV, Northrup WF, Jorgensen CR, Wang Y, Lindsay WG. Clinical and hemodynamic results with the St. Jude Medical cardiac valve prosthesis. A three-year experience. J Thorac Cardiovasc Surg 1981;82:674-83.
32. Wortham DC, Tri TB, Bowen TE. Hemodynamic evaluation of the St. Jude Medical valve prosthesis in the small aortic annulus. J Thorac Cardiovasc Surg 1981;81:615-20.
33. Horstkotte D, Haerten K, Kørfer R, Spiller P, Budde T, Bircks W, Loogen F. Hemodynamic findings at rest and during exercise after implantation of different aortic valve prostheses. Z Kardiol 1983;72:429-37.
34. Carrier M, Martineau JP, Bonan R, Pelletier LC. Clinical and hemodynamic assessment of the Omniscience prosthetic heart valve. J Thorac Cardiovasc Surg 1987;93:300-7.

Paper IV

Take th9864$$$8 MAC EDIT 19.1.93
MS. No. 8-92

Scand J Thor Cardiovasc Surg 26: 000–000. 1993

TWO-DIMENSIONAL ECHOCARDIOGRAPHY FOR PREDICTION OF AORTIC VALVE PROSTHESIS SIZE

A Comparative Study of Medtronic-Hall and Carpentier-Edwards Supra-annular Valves

Rune Wiseth,[1] Ole Rossvoll,[1] Olaf W. Levang,[2] Terje Skjaerpe[1] and Liv Hatle[1]

From the [1]Section of Cardiology and the [2]Section of Thoracic and Cardiovascular Surgery, University Hospital, Trondheim, Norway

(Submitted May 27, 1992. Accepted for publication September 1, 1992)

Abstract. To assess the value of two-dimensional echocardiography (2D ECHO) for predicting prosthetic aortic valve size, the diameter of the aortic annulus was measured before implantation of a Medtronic-Hall valve in 24 patients and a Carpentier-Edwards supra-annular valve in 34. In the Medtronic-Hall group, the average prosthesis size was similar to the average annulus diameter, i.e. 23.2 ± 2.1 vs 23.0 ± 3.4 mm (NS), 95% confidence interval for the difference −1.0–0.7 mm. In the Carpentier-Edwards group the corresponding figures were 23.5 ± 2.1 and 22.0 ± 2.3 mm ($p < 0.001$), with 95% confidence interval 0.9–2.0 mm. Correlation between annulus diameter indicated by preoperative 2D ECHO and prosthesis size was stronger in the Medtronic-Hall ($r = 0.88$, $p < 0.001$) than in the Carpentier-Edwards group ($r = 0.73$, $p < 0.001$). The authors conclude that prosthetic aortic valve size may be accurately predicted by 2D ECHO, with Medtronic-Hall valve size similar to, and Carpentier-Edwards prostheses on average 1–2 mm larger than the 2D ECHO-estimated annulus diameter.

Key words: Aortic valve prosthesis, prosthesis size, prediction, two-dimensional echocardiography.

Although acceptable hemodynamics are obtained in most patients who undergo aortic valve replacement, residual obstruction of the left ventricular outflow tract may be considerable. A major determinant for risk of unacceptable hemodynamics is the relation of prosthesis size to the patient's body surface area. To avoid "prosthesis-patient mismatch" (13) a root-enlarging operation is occasionally necessary in patients with a narrow aortic valve ring (7, 9, 10). Reliable prediction of prosthesis size is valuable to the surgeon planning the replacement, and both radiologic and echocardiographic methods are used for this purpose (1, 3, 8, 11). Two-dimensional echocardiography has given reliable predictions, while M-mode has been of less value (3, 8). Earlier reports, however, included several valve types, often with only a few patients in each group (3, 8), and there are few published data on the role of echocardiography in predicting size for different types of prostheses.

This prospective study assessed the value of two-dimensional echocardiography for predicting required size of two commonly used prostheses, one mechanical (Medtronic-Hall) and one bioprosthetic (Carpentier-Edwards supra-annular). We hypothesized that, because of differences in design and implantation techniques, the predictive value of the measured annulus diameter for prosthesis size might differ between these valves.

MATERIAL AND METHODS

Patients. Fifty-eight patients (25 men, 33 women) undergoing aortic valve replacement were consecutively included in the study. Their mean age was 67 (range 44–82) years. A Medtronic-Hall (MH) valve (Medtronic Minneapolis, Minn, USA) was implanted in 24 cases and a Carpentier-Edwards supra-annular (CES) valve (Model 2650, Baxter-Edwards, Irvine, Cal, USA) in 34. Some general data are listed in Table I.

Doppler echocardiography. A Doppler echocardiographic study was done 1–3 days before valve implantation, using Irex Meridian or VingMed CFM 700 ultrasound equipment. From the parasternal log-axis view the inner aortic root diameter was measured at the level of the aortic annulus. Gain setting was carefully adjusted and generally set low to prevent augmentation of echoes from calcified valves. In each patient at least four images were frozen in systole and the diameter was measured with

Table I. *Preoperative case characteristics*

CES = Carpentier-Edwards supra-annular, MH = Medtronic-Hall, NS = not significant

	CES valve $n = 34$	MH valve $n = 24$	p
Age (years)	72.1 ± 7.1	60.0 ± 7.1	<0.001
Male/Female	16/18	9/15	NS
Pure stenosis	24/34 (71%)	15/24 (63%)	NS
Mean gradient (mm Hg)	65 ± 19	67 ± 21	NS
Valve area (cm^2)	0.66 ± 0.22	0.75 ± 0.26	NS
Annulus diameter (mm)	22.0 ± 2.3	23.0 ± 3.4	NS

calipers. In two patients with severe calcifications extending into the left ventricular outflow tract we attempted to estimate the annulus diameter that would remain after decalcification, as this was thought to correspond best with prosthesis size.

In 46 patients (23 with MH and 23 with CES valve), Doppler echocardiography was repeated after an average postoperative interval of 3 months. Transprosthetic velocities were recorded, and gradients were calculated according to the Bernoulli equation with correction for prevalvular velocities; Gradient = 4 ($V^2_{valv} - V^2_{lvot}$), where V_{valv} = velocity across prosthesis and V_{lvot} = left ventricular outflow tract velocity (5). For calculation of the prosthetic valve area the continuity equation (16) was used. Finally, the calculated prosthetic valve area was divided by the preoperative aortic annulus area. This gives an index expressing how effectively the prosthesis utilizes the preoperatively available annulus area.

Surgery. Standard techniques were used, with potassium cardioplegia for myocardial protection. The diameter of the aortic annulus was measured with valve sizers and the appropriate valve size was determined. The standard implantation technique for MH valves was annular insertion, but in a few cases with a narrow root a partly supra-annular technique was used, with the sewing ring placed on the top of the noncoronary sinus. Supra-annular implantation was standard for the CES valves. Interrupted sutures were used for both valve types. The surgeon was unaware of the preoperative estimate of annulus diameter, except in one case with severely hypoplastic ring and obvious need for a root-enlarging procedure, in which withholding of this information would have been unethical. This patient was excluded from the analysis.

Statistical analysis. All values are expressed as mean ± SD. For comparisons between preoperative annulus diameter and prosthesis size a two-tailed paired t-test was used, and the 95% confidence interval (95% CI) for the difference was calculated. Comparisons between means of two groups were made with an unpaired t-test. Categorical data were analyzed with chi-square test and association between variables with linear regression analysis; $p < 0.05$ was considered significant. Reproducibility is expressed as the 95% limits of agreement between pairs of measurements as described by Bland & Altman (2).

RESULTS

The patients who received a CES valve were significantly older than those with MH valves. Other preoperative data were similar in the two groups (Table I).

Root diameter vs prosthesis size (Table II). In the CES group, prosthesis size was on average 1.5 mm larger than the echocardiographic estimate of annulus diameter. In the MH group the annulus diameter and prosthesis size were similar. All the MH valve sizes, except for the 20 mm, are in odd numbers of mm, and prediction of prosthesis size was considered correct when the difference from estimated annulus diameter did not exceed 1 mm. Prosthesis size was within ±1 mm of the measured diameter in 21 (62%) of the 34 patients in the CES group and in 17 (71%) of the 24 in the MH group (NS). In cases with discrepancy exceeding 1 mm, the implanted valve was always larger than the measured annulus diameter in the CES group. Three MH patients received a smaller prosthesis than predicted, but all three implanted valves were large (25 mm in 1 case, 27 mm in 2 cases). It is noteworthy that when the prosthesis was ≤23 mm, discrepancy exceeding 1 mm always involved implantation of a larger prosthesis than predicted. This applied to both valve types. The estimated aortic root diameter was strongly correlated to the prosthesis size in the MH group (Fig. 1A). In the CES group the correlation was weaker (Fig. 1B).

Table II. *Comparison between preoperative aortic annulus diameter (measured with 2D echocardiography) and size of implanted prosthesis*

Abbreviations as in Table I

Prosthesis type	Annulus diameter (mm)	Prosthesis size (mm)	95% CI[a)]	*p*
CES ($n = 34$)	22.0 ± 2.3	23.5 ± 2.1	0.9–2.0	<0.001
range	17–27	21–29		
MH ($n = 24$)	23.0 ± 3.4	23.2 ± 2.1	−0.7–1.0	NS
range	18–31	20–27		

a) = 95% confidence interval for difference between prosthesis size and annulus diameter.

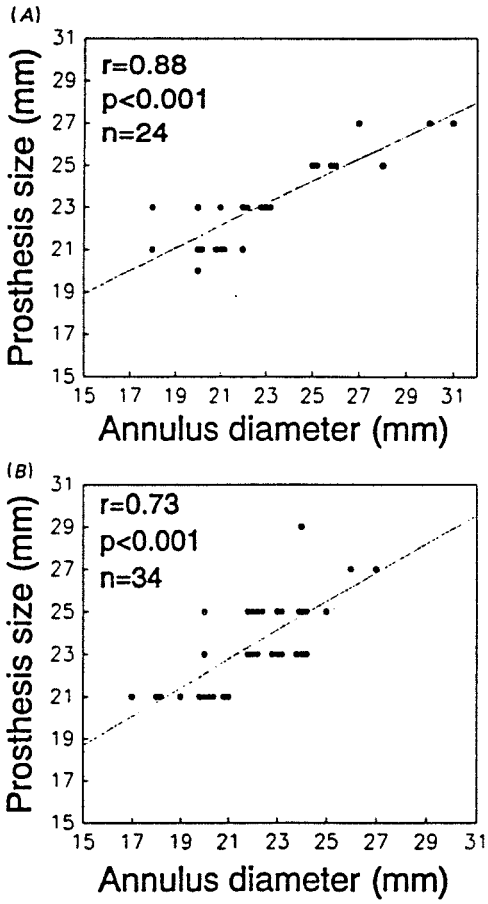


Fig. 1. Linear regression analysis showing strong correlation of preoperatively measured aortic annulus diameter to Medtronic-Hall valve size (*A*) and weaker correlation to Carpentier-Edwards supra-annular valve size (*B*).

Small (≤21 mm) prostheses. These cases were separately analyzed. The preoperative annulus diameter was 19.4 ± 1.3 mm in the CES 21 mm group ($n = 10$) and 20.4 ± 1.2 mm in the MH 21 mm group ($n = 7$) (NS). Prosthesis size significantly exceeded annulus diameter for the CES 21 mm valves (95% CI 0.6–2.6 mm, $p < 0.005$). For the MH 20 and 21 mm valves, prosthesis size and annulus diameter did not significantly differ (95% CI −0.5–1.5 mm).

Postoperative hemodynamics (Table III). Among the 46 patients (79% of the total) who underwent postoperative Doppler echocardiography, the mean prosthesis size was similar in the CES and MH groups. Although gradients did not differ between the groups, analysis of each valve size separately revealed significantly higher mean values in the CES 21 mm ($n = 4$) than in the MH 21 mm ($n = 7$) valves (18.3 ± 3.1 vs 12.4 ± 3.1 mm Hg, $p < 0.05$). For other prosthesis sizes the gradients were similar, with narrow ranges of values (peak 17.8–23.4 mm Hg, mean 9.5–12 mm Hg).

Valve area, relation to preoperative annulus diameter (Table III). When the 21 mm valves were separately analyzed, their estimated area was significantly smaller in the CES than in the MH group (1.05 ± 0.09 vs 1.40 ± 0.20 cm^2, $p = 0.010$). The areas of the other prosthetic sizes did not differ significantly between the two groups. The number of patients in each group was small, however. When the prosthetic valve area was divided by the preoperative annulus area, there was no longer a statistically significant difference between the CES 21 mm and the MH 21 mm valves (0.35 ± 0.07/0.43 ±

Table III. *Hemodynamics at 3-month follow-up*

	CES valve $n = 23$	MH valve $n = 23$	p
Mean prosthesis size (mm)	23.8 ± 1.7	23.3 ± 2.0	NS
Peak gradient (mm Hg)	20.7 ± 7.3	22.7 ± 9.8	NS
Mean gradient (mm Hg)	11.7 ± 4.4	11.8 ± 5.6	NS
Prosthesis valve area (cm^2)	1.59–0.46	1.79 ± 0.51	NS
Prosthesis valve area/left ventricular outflow tract area	0.40 ± 0.08	0.43 ± 0.10	NS

0.05). Nor did this index significantly differ when the total groups were compared (Table III).

Reproducibility. Interobserver variability in preoperative estimates of diameter was assessed from measurements made independently by two observers in 19 randomly selected patients. The two measurements were identical in nine patients and did not differ by more than 2 mm in any case. The 95% limits of agreement between pairs of measurement were −1.1–2.5 mm. The independent measurements made by the two observers were strongly correlated ($r = 0.97$, $p < 0.001$).

DISCUSSION

This study demonstrated reliable prediction of the size of both CES and MH aortic valves, and preoperative measurement of annulus dimension may indicate patients with obvious or likely need for root enlargement. Whereas on average the MH valve size was similar to the estimated annulus diameter, the CES valves were 1.5 mm larger. The CES valve is designed so as to implant the stent in a supra-annular position in order to improve hemodynamics (14). This improvement has been demonstrated in vitro (17), and in vivo testing showed better hemodynamics with the supra-annular than with the Carpentier-Edwards standard porcine valve (4).

Prosthesis gradients result mainly from impedance by the stent and the aortic remnants supporting the cusps (14). With the supra-annular valve, when both stent and aortic remnants are implanted above rather than inside the ring, a larger prosthesis can be used, so that only the cusps are exposed to the column of blood (14). The supra-annular implantation technique can therefore explain why size of CES exceeded the estimated aortic annulus. For the MH valve, the standard annular implantation technique implies that the prosthesis must fit within the aortic ring, which explains the closer agreement between the estimated annulus dimension and prosthesis size.

The differences between the two valve types as regards agreement between annulus diameter and size of prosthesis can therefore be explained by dissimilarities of design and implantation techniques. We have found no earlier report comparing and quantifying the effect of these differences on the relationship between prosthesis size and annulus diameter. This relationship has clinical significance, as with a specified root diameter the implanted valve's size can vary according to prosthesis type, and when the annulus is narrow the need for a root-enlarging procedure may depend on the type of prosthesis to be used. Preoperative echocardiography of patients with aortic valve disease should therefore routinely include estimation of the annulus dimension. This is particularly relevant as, due to use of Doppler technique, increasing numbers of patients are referred for aortic valve replacement without preceding ventriculography. The only preoperative information about relations of the left ventricular outflow tract then is provided by the echocardiographic study.

The supra-annular valve may also be implanted in annular position. Hence there is more flexibility in the choice of prosthesis size, and some size variation may therefore be attributable to the surgeon's personal

technique. These circumstances may explain the weaker correlation between dimensions of the aortic annulus and size of the CES prostheses in this study.

A modified implantation technique with the sewing ring placed on the top of the noncoronary sinus has been described for disc valves (12). This partly supra-annular technique was used in some of our patients who received an MH valve, and could explain why some MH prostheses were larger than the estimated annulus diameter.

Postoperative hemodynamics. Although gradients were higher and valve areas smaller for the CES 21 mm than for the MH 21 mm valves, these differences were minor and their clinical significance could be questioned. In all patients with a 21 mm prosthesis the hemodynamics were acceptable, with highest mean gradient 23 mm Hg in the CES 21 mm group and 19 mm Hg in the MH 21 mm group.

Prosthesis hemodynamics related to annulus dimension. The ratio of effective prosthesis area to preoperative annulus area (Table III) provides an index that expresses the ability of a particular prosthesis to make maximal use of the available root space. This index did not differ significantly between the two prosthesis groups, either for the total groups or for the 21 mm valves. Consideration of the preoperative annular dimension may permit a more complete and better overall judgement of the hemodynamic properties of the valve in question. This judgement may be particularly important in evaluation of small aortic valve prostheses, and prospective studies designed to compare hemodynamics with different valve types should include a preoperative estimate of annulus dimension. Theoretically the outflow tract diameter may influence hemodynamics of identical valves (6, 15), but such influence does not seem to have been evaluated in clinical studies.

Limitations of the study. Allocation of patients to prosthesis type was not randomized, but our standard criteria for selection of prostheses were based mainly on patient age. The predictive value of the two-dimensional estimate of prosthesis size was unlikely to have been influenced by the non-randomized design. In comparing the hemodynamics of two valve types, however, a randomized study is greatly preferable, and consequently our data should be interpreted as indicative rather than conclusive.

Conclusions. Relationships between prosthesis size and preoperative diameter of the aortic annulus differ in comparisons between CES and MH valves. CES valves are on average 1–2 mm larger than the annulus diameter, whereas the two measurements are similar with MH valves. The differences can be explained by dissimilarities of design and implantation techniques. Correlation of postoperative hemodynamics to preoperative annulus diameter is proposed, in order to obtain more complete and satisfactory judgement of the hemodynamic properties of different valve types. This approach is particularly relevant for evaluating hemodynamics of small aortic valve prostheses.

ACKNOWLEDGEMENT

This study was supported by grants from the Norwegian Council on Cardiovascular Diseases.

REFERENCES

1. Babb JD, Parr GVS, O'Neill J. Predicting aortic valve prosthesis size. A step toward better matching of patient and prosthesis. J Thorac Cardiovasc Surg 1981; 81: 450–454.
2. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986; *i*: 307–310.
3. Cohen JL, Austin SM, Kim CS, Christakos ME, Hussain SM. Two-dimensional echocardiographic preoperative prediction of prosthetic aortic valve size. Am Heart J 1984; 107: 108–112.
4. Cosgrove DM, Lytle BW, Gill CC, Golding LAR, Stewart RW, Loop FD, Williams GW. In vivo hemodynamic comparison of porcine and pericardial valves. J Thorac Cardiovasc Surg 1985; 89: 358–368.
5. Hatle L, Angelsen B. Pressure velocity relationships. In: Doppler ultrasound in cardiology. Physical principles and clinical applications. 2nd ed. Philadelphia: and Febiger, 1985: 22–26.
6. Khan SS, Mitchell RS, Derby GC, Oyer PE, Miller DC. Differences in Hancock and Carpentier-Edwards Porcine Xenograft aortic valve hemodynamics. Effect of valve size. Circulation 1990; 82 (Suppl IV): 117–124.

7. Konno S, Imai Y, Lida Y, Nakajima M, Tatsuno K. A new method for prosthetic valve replacement in congenital aortic stenosis associated with hypoplasia of the aortic valve ring. J Thorac Cardiovasc Surg 1975; 70: 909–917.
8. Mackay A, Been M, Rodrigues E, Murchison J, De Bono DP. Preoperative prediction of prosthesis size using cross sectional echocardiography in patients requiring aortic valve replacement. Br Heart J 1985; 53: 507–509.
9. Manouguian S, Seybold-Epting W. Patch enlargement of the aortic valve ring by extending the aortic incision into the anterior mitral leaflet: new operative technique. J Thorac Cardiovasc Surg 1979; 78: 402–412.
10. Misbach GA, Turley K, Ullyot DJ, Ebert PA. Left ventricular outflow enlargement by the Konno procedure. J Thorac Cardiovasc Surgery 1982; 84: 696-703.
11. Mukharji J, Sloan TJ, Estrera AS, Lipscomb KM. Measurement of aortic root size by biplane angiography before cardiac valve replacement. Am J Cardiol 1984; 53: 1084–1086.
12. Olin CL, Bomfim V, Halvazulis V, Holmgren AC, Lamke BJ. Optimal insertion technique for the Bjørk-Shiley valve in the narrow aortic ostium. Ann Thorac Surg 1983; 36: 567–576.
13. Rahimtoola SH. The problem of valve prosthesis-patient mismatch. Circulation 1978; 58: 20–24.
14. Relland J, Perier P, Lecointe B. The third generation Carpentier-Edwards bioprosthesis: Early results. J Am Coll Cardiol 1985; 6: 1149–1154.
15. Roberson JA, Crowe CT. Flow measurements. In: Engineering Fluid Mechanics. 3 ed. Boston: Houghton Mifflin, 1985: Chap 13.
16. Skjaerpe T, Hegrenaes L, Hatle L. Noninvasive estimation of valve area in patients with aortic stenosis by Doppler ultrasound and two-dimensional echocardiography. Circulation 1985; 72: 810–818.
17. Yoganathan AP, Woo YR, Sung HW, Williams FP, Franch RH, Jones M. In vitro hemodynamic characteristics of tissue bioprostheses in the aortic position. J Thorac Cardiovasc Surg 1986; 92: 198–209.

Paper V

Rapid Systolic Intraventricular Velocities After Valve Replacement for Aortic Stenosis

Rune Wiseth, MD, Terje Skjaerpe, MD, and Liv Hatle, MD

To assess the frequency and severity of intraventricular gradients after valve replacement for severe valvular aortic stenosis 25 patients (valve area 0.59 ± 0.19 cm²) were studied serially with Doppler echocardiography on postoperative days 1, 2, 3, 5 and 7. Pulsed Doppler was used to search for increased intraventricular velocities. Mid-to-late systolic intraventricular velocities ≥2 m/s were defined as intraventricular gradients. In 13 patients (52%) intraventricular gradients were found at least once during days 1 to 7 (group A) and were most frequent at day 3 (44%). The typical location of these velocities was at the midventricular level close to the septum. In 4 patients intraventricular gradients >64 mm Hg were found. Left ventricular end-diastolic and end-systolic diameters recorded preoperatively were significantly smaller in group A than in the rest (43.6 ± 5.4 vs 50 ± 5.8 mm and 24.6 ± 5.6 vs 33.1 ± 7.3 mm, both p <0.05) and the fractional shortening was significantly higher (44 ± 9 vs 34 ± 9%, p <0.05). It is concluded that intraventricular gradients are frequent during the first week after valve replacement for severe aortic stenosis. These gradients are mostly mild and transient in nature, but significant gradients associated with clinical deterioration may occur. The risk of developing intraventricular gradients postoperatively may be predicted at a preoperative echocardiographic examination, and patients with a small left ventricular cavity size and maintained contractility are at particular risk. With Doppler echocardiography intraventricular gradients may be detected and followed even in the early postoperative period, this noninvasive technique is a valuable supplement in the early postoperative monitoring after valve replacement for severe aortic stenosis.

(Am J Cardiol 1993;71:944–948)

From the Section of Cardiology, University Hospital, Trondheim, Norway. Manuscript received July 15, 1992; revised manuscript received September 18, 1992, and accepted October 29.

Address for reprints: Rune Wiseth, MD, Section of Cardiology, Department of Medicine, Regional Hospital, University of Trondheim, N-7006 Trondheim, Norway.

After valve replacement for severe aortic stenosis there is a marked change in hemodynamics, with the hypertrophic ventricle contracting against a greatly reduced afterload. After relief of a fixed left ventricular outflow tract obstruction, dynamic intraventricular gradients may occur with the risk of a less favorable clinical outcome.[1–4] With Doppler echocardiography, systolic intraventricular gradients can be detected, localized and quantified.[5–7] In a recent study by Laurent et al,[3] intraventricular gradients >25 mm Hg were demonstrated in 5 of 41 patients at a mean interval of 13 days after valve replacement for severe aortic stenosis and in another 4 after provocation with amyl nitrite. The frequency of spontaneously occurring intraventricular gradients in the very early postoperative period after valve replacement for aortic stenosis, however, is not known. The purpose of this prospective study was to assess serially the frequency and severity of systolic intraventricular gradients by Doppler echocardiography during the first week after valve replacement for aortic stenosis. Second, the aim of this study was to describe preoperative parameters associated with the occurrence of intraventricular gradients in the early postoperative period.

METHODS

Patients: The study comprised 25 symptomatic patients (9 men and 16 women, age range 48 to 82 years, mean 69) undergoing valve replacement for pure or predominant aortic stenosis. Mean gradient was 77 ± 20 mm Hg and valve area was 0.59 ± 0.19 cm². A bioprosthesis was implanted in 16 patients and 9 received a mechanical valve.

Preoperative Doppler echocardiography: A complete Doppler echocardiographic study was performed at a mean interval of 3.5 (range 1 to 15) days before surgery. An Irex Meridian or VingMed CFM 700 ultrasound system with a 3.0 MHz imaging and a 2.5 MHz transducer for Doppler recordings was used. M-mode measurements were obtained according to the criteria of the American Society of Echocardiography.[8] The fractional shortening was calculated as the difference between the left ventricular end-diastolic and end-systolic diameters in percentages of the former. The left ventricular mass was calculated according to the formula of Devereux et al.[9] Six patients were excluded from the analysis of M-mode data because measurements were technically inadequate.

Mapping of intraventricular velocities: Pulsed Doppler was used to search for increased velocities within the left ventricle. The sample volume was moved stepwise from the apex through the left ventricle and the outflow tract to the level of the prosthesis. A concave velocity curve typical of dynamic intraventricular ob-

struction with velocities ≥2 m/s was defined as an intraventricular gradient (Figure 1). With velocities exceeding the Nyquist limit, the apparatus was switched to the high-pulse repetition mode or to the continuous-wave mode. Peak velocity was measured and the maximal intraventricular gradient was calculated using the modified Bernoulli equation: gradient = $4V^2$, where V is peak velocity (m/s).

Postoperative Doppler: The study protocol included mapping of systolic intraventricular velocities on postoperative days 1, 2, 3, 5 and 7; thus, a total of 125 (25 × 5) postoperative Doppler recordings were to be performed. Recordings were omitted during assisted ventilation (5 instances) and during intraaortic balloon treatment (2 instances). In 2 patients the recordings on the seventh postoperative day were missed because of administrative reasons. Thus, a total of 116 Doppler recordings were performed from postoperative day 1 to 7 (93% of recordings were planned according to protocol).

Statistical analysis: All values are expressed as mean ± SD. Means of 2 groups were compared using an unpaired Student's *t* test and categorical data were analysed using chi-square statistics. A p value <0.05 was considered significant.

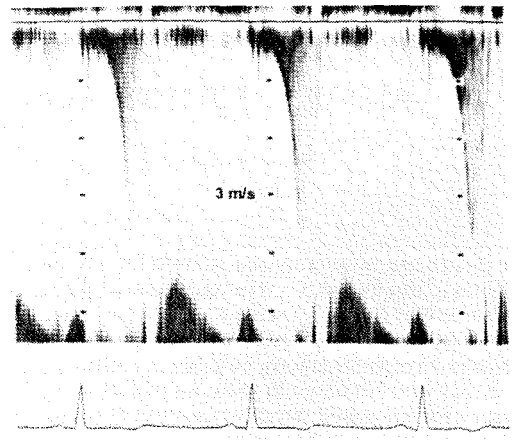


FIGURE 1. Left ventricular velocities (continuous-wave Doppler). Note the typical concave shape of the curve with the highest velocities occurring at the end of systole. The transducer is located at the cardiac apex.

RESULTS

Intraventricular gradients defined as systolic intracavitary velocities ≥2 m/s directed toward the outflow tract were found in 32 of 116 recordings (28%) and were detected at least once during the first postoperative week in 13 patients (52%) (group A). These velocities were typically located close to the septum at the midventricular level (Figure 2). When moving the sample volume further toward the prosthesis, velocities in the outflow tract were always lower (range 0.8 to 1.87 m/s) than the midventricular velocities. The frequency of intraventricular gradients was highest (44%) on the third

TABLE I Number of Examinations on Separate Days and Number and Percentage of Patients with Intraventricular Velocities ≥ 2 m/s on Each Day

	Preop.	Day 1	Day 2	Day 3	Day 5	Day 7
No. of exams	25	22	24	25	23	22
No. with IVV ≥2 m/s (%)	3 (12)	5 (23)	6 (25)	11 (44)	8 (35)	7 (32)

IVV = intraventricular velocities; Preop. = preoperative.

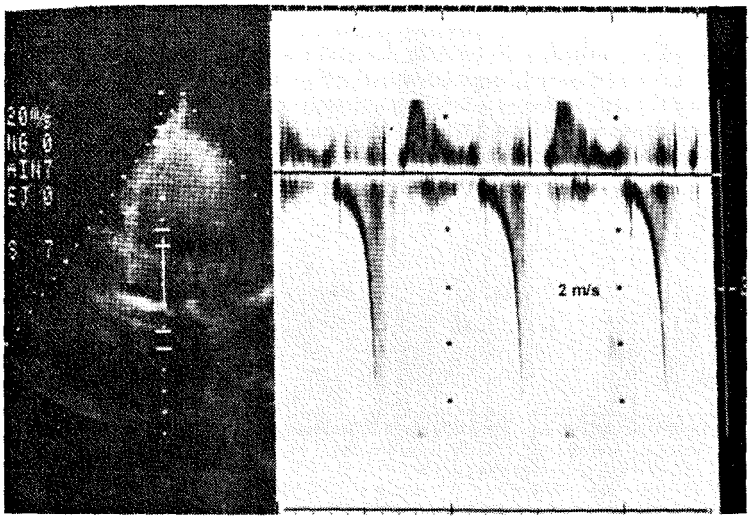


FIGURE 2. The highest velocities recorded were typically located at the midventricular level close to the septum and did not represent left ventricular outflow tract obstructions.

postoperative day (Table I). In 12 patients, intraventricular gradients could not be detected (group B). One group A patient died in pump failure on the seventh postoperative day; this was the only case of early mortality (within 30 days of surgery).

Relation to preoperative and operative data: Groups A and B were similar with respect to age (71 ± 11 vs 68 ± 8 years, p = NS) and severity of valve lesion (mean gradient 80 ± 16 vs 73 ± 22 mm Hg, valve area 0.58 ± 0.17 vs 0.61 ± 0.21 cm^2, both p = NS).

Before surgery intraventricular gradients were found in 3 patients, all these had intraventricular gradients postoperatively. In 1 patient with intraventricular velocities of 3 m/s preoperatively, velocities >4 m/s were present at all postoperative recordings and the maximal velocity recorded was 6.0 m/s (Figure 3).

In Table II preoperative M-mode data are compared for groups A and B. Left ventricular end-diastolic and end-systolic diameters were significantly smaller in group A, and the fractional shortening was higher. Neither thicknesses of septum and posterior wall nor left ventricular mass differed significantly. All patients underwent coronary arteriography preoperatively. Coronary artery disease defined as >75% stenosis in at least 1 of the 3 main coronary arteries was found in 5 of 13 patients in group A and in 6 of 12 in group B (p = NS).

Concomitant coronary artery bypass surgery was performed in 2 patients in group A and 6 in group B. In both groups, 8 patients received a bioprosthesis and 5 patients in group A and 4 in group B received a mechanical valve. Mean prosthesis size was 22.4 ± 1.4 mm in group A and 23 ± 1.6 mm in group B (p = NS).

Heart rate (Figure 4): Preoperatively and on postoperative day 1 heart rates were similar for the 2 groups. From postoperative day 2 heart rates were higher in group A, the difference being statistically significant for postoperative days 2, 3 and 7.

Severity of gradients: Group A could be divided into 2 subgroups according to the severity of intraventricular gradients. In 9 of the 13 patients in group A systolic velocities were only moderately increased ranging from 2 to 2.8 m/s. The remaining 4 patients all had markedly increased velocities ranging from 4.1 to 6 m/s, corresponding to intraventricular gradients of 67 to 144 mm Hg. Clinically, these 4 patients had a protracted

TABLE II Comparison of Preoperative Echocardiographic Measurements in Patients With (group A) and Without (group B) Intraventricular Velocities ≥ 2 m/s in the Early Postoperative Period

	Group A	Group B	p Value
Number	10	9	
Septum (mm)	16 ± 3	15 ± 2	NS
Posterior wall (mm)	14 ± 2	13 ± 2	NS
Septal to posterior wall ratio	1.15 ± 0.11	1.16 ± 0.16	NS
End-diastolic diameter (mm)	44 ± 5	50 ± 6	*
End-systolic diameter (mm)	25 ± 6	33 ± 7	*
Left ventricular mass (g)	257 ± 55	296 ± 67	NS
Left ventricular mass index (g/m^2)	157 ± 40	169 ± 31	NS
Fractional shortening (%)	44 ± 9	34 ± 9	*

*p <0.05.

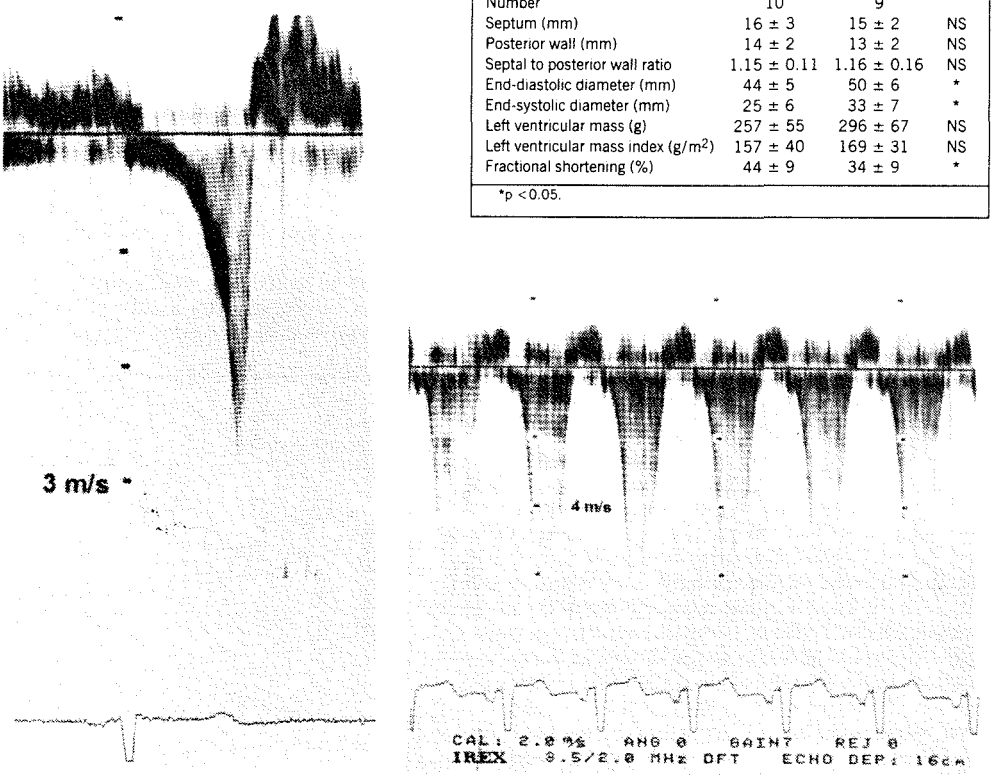


FIGURE 3. Increased intraventricular velocities (3 m/s) recorded before surgery in 1 patient *(left)*. In the same patient a severe intraventricular obstruction (maximal velocity 6 m/s = 144 mm Hg) was present at the seventh postoperative day *(right)*.

postoperative course with dyspnea, fatigue and delayed mobilization. They were all given verapamil and 3 of them were reexamined at 3 months. In 1 the intraventricular gradient disappeared, and the other 2 had only mild gradients (30 to 36 mm Hg) at that time. The fourth patient died 6 weeks after surgery after a cerebral stroke.

Inotropic drugs: Before surgery 5 patients (20%) used digitoxin; none of them had severe intraventricular gradients postoperatively. Two patients with severe intraventricular gradients late in the first postoperative week (day 7) were given digitoxin in the early postoperative course because of atrial fibrillation.

Among the total of 116 postoperative recordings 10 (9%) were performed during ongoing dopamine infusion. In 8 of these recordings intraventricular velocities ≥2 m/s (2 to 3.5) were found. However, in 4 of the 5 patients with intraventricular gradients detected during dopamine infusion, similar or higher gradients were also recorded on other days in the postoperative period without the patient receiving dopamine.

DISCUSSION

This study shows that dynamic systolic intraventricular gradients are frequent in the early postoperative period after valve replacement for severe aortic stenosis, and the risk of developing such gradients is related to left ventricular cavity dimensions and left ventricular contractility as assessed by a preoperative M-mode examination. Intraventricular gradients after aortic valve replacement may have important therapeutic implications,[3,10] and the ability to noninvasively detect, quantitate and follow these gradients represents a valuable supplement to postoperative monitoring.

Pathophysiologic considerations: Theoretically it may be expected that after the relief of a fixed left ventricular outflow tract obstruction, intraventricular gradients similar to that seen in hypertrophic cardiomyopathy could develop when the hypertrophic ventricle contracts against a greatly reduced afterload.[11–13] Additional factors including hypovolemia, enhanced sympathetic activity and the possible influence of inotropic drugs, also may contribute to the development of intraventricular gradients postoperatively.[3,11,12] The dynamic character of these gradients is demonstrated in our study because both their presence and severity changed during the study period. Although the number of patients studied on each day differed slightly, our results indicate that the frequency of intraventricular gradients increased during the first postoperative days (Table I). In patients with severe gradients, these were most often recorded from days 3 to 7. The lower frequency and lesser severity of intraventricular gradients during the very first postoperative days could be due to several factors, including contractility of the myocardium, heart rate and loading conditions.[2,3,12] Rastelli and Kirklin[14] followed intrapericardial pressure during the first postoperative days after aortic valve replacement and found it highest on the third postoperative day. This could be due to some increase in pericardial effusion after removal of drainage catheters. Although there was no case with signs of cardiac tamponade in our study, varying amounts of pericardial effusion were present, and fluctuations in intrapericardial pressure could be important factors in determining the presence and severity of intraventricular gradients.[3]

Outflow tract obstruction versus cavity obliteration: The mechanisms generating dynamic intraventricular gradients remain controversial and may vary.[3,11,15–17] Two different mechanisms for gradient production are proposed in hypertrophic obstructive cardiomyopathy[16,18]: the "true obstruction" associated with systolic anterior movement of the mitral valve and "gradient without obstruction" resulting from cavity obliteration. After aortic valve replacement most intracavitary gradients are found at the midventricular level without the presence of systolic anterior movement.[3] Based on the pulsed Doppler recordings, the typical location of the intraventricular gradients in the present study was at the midventricular level. Although midventricular gradients may not always represent obstruction, their presence is thought to be of hemodynamic significance,[17] and they are ascribed a deleterious role after valve surgery.[3] In our study deterioration of clinical status was present concomitant with high intraventricular gradients, supporting the suggestion that such gradients can be of clinical significance. Most group A patients had only moderate intraventricular gradients ranging from 16 to 31 mm Hg. These gradients are not likely to be of any hemodynamic significance and may occur even in normal ventricles during hypovolemia or increased sympathetic tone, or both.[2,19]

Relation to preoperative echocardiographic data: A decrease in left ventricular cavity dimensions is shown immediately after valve replacement for severe aortic stenosis.[20] Because a midventricular obliteration is proposed as a mechanism of intraventricular gradients following valve replacement for aortic stenosis,[3] this early postoperative reduction in ventricular size may explain the increased risk of developing intraventricular gradients in patients with small left ventricular cavity dimensions as demonstrated in our study. Laurent et al[3]

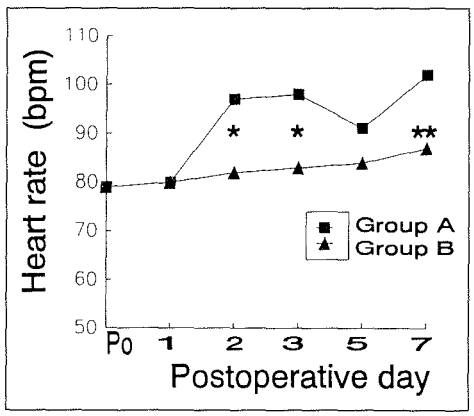


FIGURE 4. Heart rate at the preoperative and at the postoperative (Po) recordings. Postoperatively, heart rate was increased in group A. *p <0.05; **p <0.01.

also demonstrated smaller dimensions of the left ventricle in patients with intraventricular gradients after valve replacement for aortic stenosis. Furthermore, our study indicates that the presence of intraventricular gradients preoperatively is a strong predictor for these to occur postoperatively.

Heart rate, inotropic drugs: Postoperatively heart rate was higher in group A. A causal relation between increased heart rate and intraventricular gradients could not be established with the design of our study. Tachycardia might be considered as a compensatory mechanism for a reduced cardiac output due to reduced ventricular filling caused both by impaired diastolic function of the hypertrophic left ventricle and by an imbalanced volume status with hypovolemia. Therefore, both the increased heart rate and the presence of intraventricular gradients in group A could be markers of the same pathophysiologic relations. However, with tachycardia, diastolic filling and ventricular volumes can be further reduced resulting in a vicious cycle.

This study was not designed to address the influence of inotropic drugs on the occurrence of intraventricular gradients. However, intraventricular gradients were recorded in 8 of 10 recordings obtained during dopamine infusion. These were usually low, and their presence did not seem to depend solely on the inotropic drug because they were also present in the same patients on days without dopamine infusion.

Study limitations: There was no invasive monitoring of the patients during the study period, and the occurrence of intraventricular gradients could not be related to parameters of preload or afterload. Further insight into the mechanisms of these gradients could possibly have been obtained in a study design with concomitant assessment of other hemodynamic parameters.

Clinical implications: During the first week after valve replacement for severe aortic stenosis, dynamic intraventricular gradients are frequent. Although mostly mild and transient in nature, severe gradients with hemodynamic consequences are not rare. Patients with a small left ventricular cavity dimension and maintained contractility are at particular risk. To avoid severe intraventricular gradients, such patients should be carefully monitored to avoid hypovolemia and the use of inotropics should be restricted. With the Doppler technique the presence and severity of intraventricular gradients are easily assessed and the response to therapeutic interventions may be followed. This innocuous technique is therefore a valuable supplement in postoperative monitoring of patients after valve replacement for severe aortic stenosis.

1. Parker DP, Kaplan MA, Connolly JE. Coexistent aortic valvular and functional hypertrophic subaortic stenosis. Clinical, physiologic and angiographic aspects. *Am J Cardiol* 1969;24:307–317.

2. Hatle L, Angelsen B. Pressure velocity relationships. In: Doppler ultrasound in cardiology. Physical Principles and Clinical Applications. 2nd ed. Philadelphia: Lea & Febiger, 1985:202–204.

3. Laurent M, Leborgne O, Clement C, Foulgoc JL, Le Helloco A, Almange C, Leborgne P. Systolic intra-cavitary gradients following aortic valve replacement: an echo-Doppler study. *Eur Heart J* 1991;12:1098–1106.

4. Block PC, Powell WJ, Dinsmore RE, Goldblatt A. Coexistent fixed congenital and idiopathic hypertrophic subaortic stenosis. *Am J Cardiol* 1973;31:523–526.

5. Hatle L. Noninvasive assessment and differentiation of left ventricular outflow obstruction with Doppler ultrasound. *Circulation* 1981;64:381–387.

6. Sasson Z, Yock PG, Hatle LK, Alderman EL, Popp RL. Doppler echocardiographic determination of the pressure gradient in hypertrophic cardiomyopathy. *J Am Coll Cardiol* 1988;11:752–756.

7. Panza JA, Petrone RK, Fananazapir L, Maron BJ. Utility of continuous wave Doppler echocardiography in the noninvasive assessment of left ventricular outflow tract pressure gradient in patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 1992;19:91–99.

8. Sahn D, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. *Circulation* 1978;58:1072–1081.

9. Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, Reichek N. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am J Cardiol* 1986;57:450–458.

10. Criley JM, Lewis KB, White RI Jr, Ross RS. Pressure gradients without obstruction. A new concept of "hypertrophic subaortic stenosis." *Circulation* 1965;32: 881–887.

11. Thompson R, Ahmed M, Pridie R, Yacoub M. Hypertrophic cardiomyopathy after aortic valve replacement. *Am J Cardiol* 1980;45:33–41.

12. Wynne J, Braunwald E. The cardiomyopathies and myocarditides. In: Braunwald E, ed. Heart Disease. A Textbook of Cardiovascular Medicine. 3rd ed. Philadelphia: WB Saunders, 1988:1421–1428.

13. Smith N, McAnulty J, Rahmitoola S. Severe aortic stenosis with impaired left ventricular function and clinical heart failure: results of valve replacements. *Circulation* 1973;58:255–264.

14. Rastelli GC, Kirklin JW. Hemodynamic state early after replacement of aortic valve with ball-valve prosthesis. *Surgery* 1967;61:873–879.

15. Falicov RE, Resnekov L, Bharati S, Lev M. Mid-ventricular obstruction: a variant of obstructive cardiomyopathy. *Am J Cardiol* 1976;37:432–437.

16. Grose R, Strain J, Spindola-Franco H. Angiographic and hemodynamic correlations in hypertrophic cardiomyopathy with intracavitary systolic pressure gradients. *Am J Cardiol* 1986;58:1085–1092.

17. Raizner AE, Chahine RA, Ishimori T, Awdeh M. Clinical correlates of left ventricular cavity obliteration. *Am J Cardiol* 1977;40:303–309.

18. Nagata S, Nimura Y, Beppu S, Park YD, Sakakibara H. Mechanism of systolic anterior motion of mitral valve and site of intraventricular pressure gradient in hypertrophic obstructive cardiomyopathy. *Br Heart J* 1983;49:234–243.

19. Grose R, Maskin C, Spindola-Franco H, Yipintsoi T. Production of left ventricular cavity obliteration in normal man. *Circulation* 1981;64:448–455.

20. Harpole DH, Jones RH. Serial assessment of of ventricular performance after valve replacement for aortic stenosis. *J Thorac Cardiovasc Surg* 1990;99:645–650.

Paper VI

Cross-sectional Left Ventricular Outflow Tract Velocities Before and After Aortic Valve Replacement: A Comparative Study With Two-dimensional Doppler Ultrasound

Rune Wiseth, MD, Stein Samstad, MD, Ole Rossvoll, MD, Hans G. Torp, MS, Terje Skjaerpe, MD, and Liv Hatle, MD, *Trondheim, Norway*

To assess whether aortic valve replacement (AVR) results in changes in the flow velocity distribution in the left ventricular outflow tract (LVOT), 10 patients undergoing AVR for aortic stenosis were studied. By extracting velocity information from color flow maps as digital data, instantaneous cross-sectional velocity profiles were constructed. Velocity profiles obtained 1 to 3 days before AVR were compared with recordings made 3 months later. The LVOT velocity profiles were variably skewed both before and after surgery, and no systematic or uniform changes could be detected after AVR. The highest velocities were most often localized in the region from the center of the outflow tract diameter toward the septum both before and after surgery. At the time of peak flow the ratio of the maximum to the cross-sectional mean velocity was 1.38 ± 0.13 before and 1.39 ± 0.08 after AVR (NS), and the ratio of the maximum to the mean velocity time integral was 1.47 ± 0.10 before and 1.56 ± 0.10 after (NS). We conclude that AVR in patients with aortic stenosis does not result in a change in LVOT velocity profiles that will influence stroke volume estimates with the Doppler technique. (J AM SOC ECHOCARDIOGR 1993;6:279-85.)

Doppler echocardiography is established as a valuable tool in assessing function of native and prosthetic aortic valves.[1-4] Measurement of flow velocities in the left ventricular outflow tract is an integral part of stroke volume estimate, necessary for cardiac output and valve area calculations.[1,5] When stroke volume is calculated as the product of the left ventricular outflow tract area and the velocity time integral, the spatial distribution of blood flow velocities is generally assumed to be uniform, and the velocities obtained from a pulsed Doppler sample volume are taken as representative for the whole cross-sectional area. A skewed or nonuniform velocity profile across the flow area would influence the accuracy of the Doppler-obtained stroke volume. The flow velocity distribution in the ascending aorta has been shown to be skewed,[6-8] whereas the flow velocity profile in the left ventricular outflow tract is less studied.[9] Recently our laboratory described a method for constructing velocity profiles based on digital data from two-dimensional Doppler flow maps.[9,10] With this technique, the velocity profile in the aortic annulus in normal subjects is demonstrated to be flat but slightly skewed with the highest velocities toward the septum.[9] To our knowledge there are no earlier studies published on the left ventricular outflow tract flow velocity distribution in patients with aortic valve disease. The aim of this study was to describe instantaneous cross-sectional velocity profiles in the left ventricular outflow tract in patients with aortic stenosis before and after valve replacement. Second, we would assess whether valve replacement results in changes in left ventricular outflow tract velocity distribution that could influence stroke volume and prosthetic valve area estimates with the Doppler echocardiographic technique.

From the Section of Cardiology and the Institute of Biomedical Engineering, University of Trondheim.

Reprint requests: Rune Wiseth, MD, Section of Cardiology, Department of Medicine, Regional Hospital, University of Trondheim, N-7006 Trondheim, Norway.

0894-7317/93 $1.00 + .10 27/1/43120

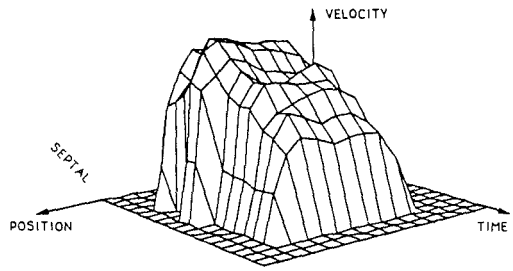


Figure 1 Three-dimensional plot of velocity distribution in left ventricular outflow tract close to the level of aortic annulus. Velocity is plotted against position in the left ventricular outflow tract diameter and against time. There are 20 msec intervals along the time axis and approximately 2 mm between each observation along the diameter axis.

PATIENTS AND METHODS

Patients

Ten patients, (seven women, three men) with a mean age of 63 years (range 50 to 74 years) were studied. All patients had pure or predominant aortic stenosis. Mean gradient was 63 ± 16 mm Hg (range 41 to 91 mm Hg) and valve area was 0.77 ± 0.14 cm^2 (range 0.57 to 1.00 cm^2). The patients were studied 1 to 3 days before and 3 months after surgery. A Medtronic-Hall 21 to 23 mm mechanical valve (Medtronic Inc., Minneapolis, Minn.) was implanted in five patients and five received a Carpentier-Edwards supraannular 23 to 27 mm bioprosthesis (Baxter Healthcare Corp., Edwards Div., Irvine, Calif.). All patients were in sinus rhythm at both examinations.

Methods

Three-dimensional, instantaneous cross-sectional velocity profiles were constructed by extracting velocity information from color flow maps as digital data by use of a method earlier described by our laboratory.[9,10] A VingMed CFM 700 (VingMed Sound A/S, Oslo, Norway) was used for ultrasound examination. This system has a mechanical, annular-array transducer. A 2.5 MHz transducer was used for Doppler and a 3 MHz transducer for imaging. In the color flow mode, a two-dimensional echocardiographic image is first constructed by a left-to-right sweep of the transducer. On the return sweep, velocity information is sampled.

The digital velocity information in each sample volume is color coded and superimposed on the two-dimensional image as a flow map. The data from the most recently recorded flow-tissue images are stored in a digital replay memory.[11] Governed by custom software (Transdisp, Vingmed Sound), the contents of the digital memory can be transferred via a parallel interface to an external computer for further processing. Combined echo and flow map recordings were done from the apex with the patient in a left lateral decubitus position. A slightly modified standard apical four-chamber view was used to clearly visualize the outflow tract. To minimize movement of the heart, the records were done in held midexpiration. Velocity information was sampled along a line approximately perpendicular to the assumed flow direction at a distance of 0.5 to 1.0 cm proximal to the aortic valve or prosthesis to construct velocity profiles from the level of the outflow tract where the sample volume is placed in pulsed Doppler recordings. The instrument was set to an electrocardiogram-triggered mode, where the two-dimensional image and color sector were updated once per heart cycle. The start of the transducer sweep was triggered with adjustable delays in 20 msec intervals from the R wave in the electrocardiogram. The delay interval was increased 20 msec for each consecutive beat and, to overlap a full systole, 12 to 18 sequential flow maps (each requiring 50 msec for updating and each delayed 20 msec to the former) were needed. Inherent in this velocity sampling technique is the fact that the transducer needs time to sweep across the flow sector, resulting in a time distortion in the color flow map. With pulsatile flow this distortion will make a flat velocity profile appear skewed. To correct for the time distortion, a linear interpolation was done between sequentially delayed flow maps.[9,10] By this triggering technique and postprocessing procedure, velocities with known timing relative to the R wave in the electrocardiogram were available and instantaneous cross-sectional velocity-profiles could be constructed.[9,10,12] Velocity distributions were visualized in three-dimensional plots with velocity against time and diameter as demonstrated in Figure 1.

As a semiquantitative assessment of the velocity distribution, the ratio of the maximum to the cross-sectional mean velocity at the time of peak flow and the maximum to the mean velocity time integral were compared at the two recordings. Finally, the relative position of the maximal velocity in the outflow tract diameter was noted.

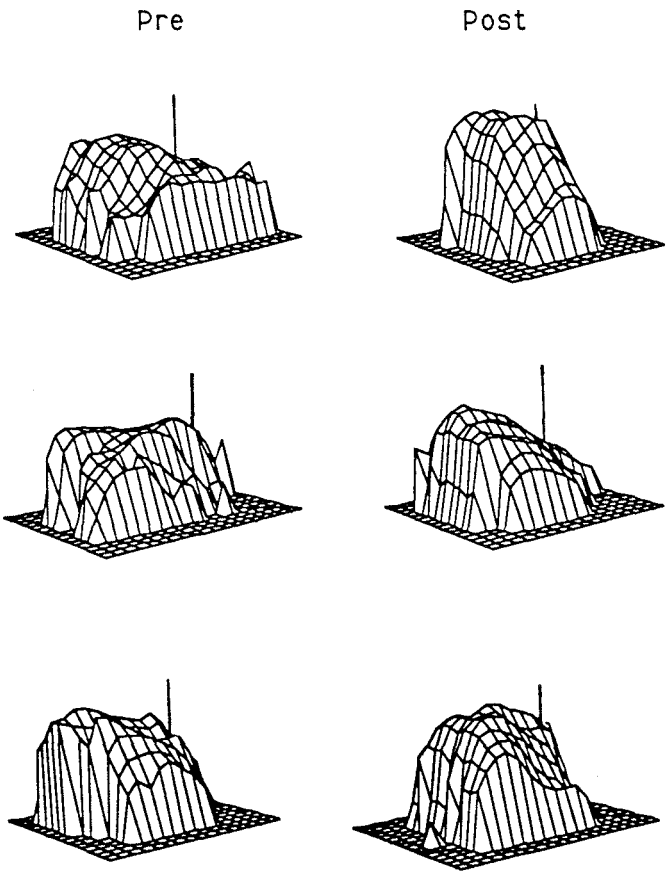


Figure 2 Examples of velocity profiles in left ventricular outflow tract before and after aortic valve replacement in three patients. No systematic or uniform changes in velocity distribution were found after valve replacement. (For definition of axes, see Figure 1.)

Table 1 Comparison of hemodynamic and flow parameters at the preoperative and postoperative examinations

	Before surgery	After surgery	*p* value
Heart rate (beats/min)	62 ± 8	66 ± 6	NS
LVET (msec)	322 ± 23	298 ± 29	NS
V max (cm/sec)	87 ± 12	98 ± 19	NS
V mean (cm/sec)	64 ± 12	71 ± 14	NS
VTI max (cm)	15.6 ± 3.0	17.5 ± 3.3	NS
VTI mean (cm)	10.6 ± 2.4	11.3 ± 2.7	NS
V max/V mean	1.38 ± 0.13	1.39 ± 0.08	NS
VTI max/VTI mean	1.47 ± 0.10	1.56 ± 0.10	NS

LVET, Left ventricular ejection time; V max, maximum velocity at time of peak flow; V mean, mean velocity at time of peak flow; VTI max, maximum velocity time integral; VTI mean, mean velocity time integral.

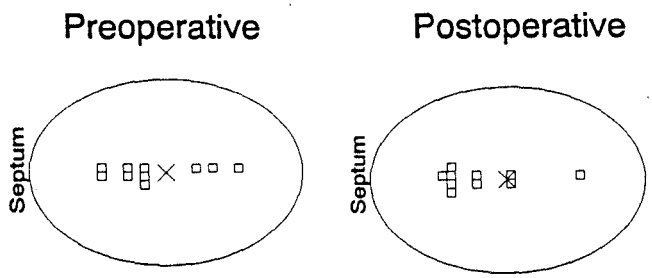


Figure 3 The highest velocities in the outflow tract were most often localized in the region from the centrum of the outflow tract toward the septum.

Reproducibility

At both examinations the whole recording sequence was repeated, resulting in a total of 40 separate recordings. Five of those were technically inadequate. Accordingly, repeatability could be analyzed from 15 paired recordings obtained within a few minutes of each other and is expressed as the absolute difference between repeated analyses in per cent of the mean value. Repeat analyses of the same recordings were also performed.

Statistics

All values are presented as mean ± SD. Paired data were compared by use of a two-tailed paired *t* test. A p value <0.05 was considered statistically significant.

RESULTS

Data obtained at the preoperative and the postoperative recordings are compared in Table 1. Heart rate was similar at the two recordings. Left ventricular ejection time tended to be shorter while the maximum velocity at the time of peak flow and the maximum velocity time integral tended to increase after surgery, although these differences did not reach statistical significance. The left ventricular outflow tract velocity profiles were variably skewed both before and after surgery. When comparing the preoperative and postoperative profiles, no systematic or uniform changes could be detected after aortic valve replacement. Figure 2 shows velocity profiles at the two recordings from three different patients. The localization of the highest velocities showed individual variation; however, in most patients they were found in the region from the centrum of the outflow tract diameter toward the septum both at the preoperative and postoperative recordings (Figure 3). The ratio of the maximum to the cross-sectional mean velocity at the time of peak flow and the ratio of the maximum to the mean velocity time integral did not significantly change from the preoperative to the postoperative recordings (Table 1).

At 3 months, abnormal (paradox) septal movement (defined as the septum moving away from the posterior wall during systole) in an M-mode recording was present in one patient only. The velocity profiles in this patient did not differ compared with the rest. In this particular patient, the ratio of the maximum to the mean velocity was 1.24 before surgery and 1.26 after surgery; the ratio of the maximum to the mean velocity time integral was 1.48 before surgery and 1.43 after.

Prosthesis Type

None of the parameters studied differed significantly according to the type of prosthesis implanted. In patients with a bioprosthesis the ratio of the maximum to the mean velocity at the time of peak flow was identical at the two recordings (1.35 at both); in patients with mechanical valves this ratio was 1.41 ± 0.16 before surgery and 1.42 ± 0.05 after. The ratio of the maximum to the mean velocity time integral was 1.44 ± 0.09 before and 1.52 ± 0.05 after surgery in patients with bioprostheses compared with 1.5 ± 0.11 before and 1.59 ± 0.12 after surgery in the group with mechanical valves.

Reproducibility

The variability between two separate recording sequences for the maximum velocity was 9.4%, for mean velocity 11.8%, for the maximum and mean velocity time integral 18.1% and 14.8%, respectively,

and for the ratio of the maximum to the mean velocity and ratio of maximum to the mean velocity time integral 5.0% and 11.3%, respectively. When repeated analyses were performed on the same recordings, the variability was between 5.6% to 8.6% for all parameters.

DISCUSSION

In this study blood velocity distribution in the left ventricular outflow tract close to the aortic annulus was studied in patients with aortic stenosis immediately before and 3 months after valve replacement. A newly developed technique based on digital data extracted from sequentially delayed electrocardiographic-triggered two-dimensional Doppler flow maps was used. With this technique no uniform qualitative or quantitative changes could be demonstrated in velocity distribution in the outflow tract after aortic valve replacement. The flow velocity distribution in the left ventricular outflow tract in patients with aortic stenosis and aortic prosthesis is of considerable clinical relevance because pulsed Doppler recordings in the outflow tract are necessary for estimation of cardiac output and valve area in these patients. In aortic stenosis the continuity equation is well validated against invasive methods[1,13,14] and is widely accepted for assessing severity of native aortic stenosis. In patients with aortic valve prostheses, however, the continuity equation is less validated and its accuracy in evaluating prosthetic valve area remains undetermined.[4,15,16] Several factors might contribute to the continuity equation being less reliable in aortic prostheses compared with native valves; a less uniform velocity pattern in the outflow tract after valve replacement could be one. According to our study, this should not be the case. Our findings suggest that the limitations and sources of error inherent in the Doppler technique in volume flow estimates in the outflow tract are similar before and after aortic valve replacement. This assumption may not be valid in the early postoperative period when a more hyperdynamic circulatory state (with increased heart rate and a shorter left ventricular ejection time) is present.[17] These altered hemodynamics might result in different velocity patterns in the outflow tract compared with the findings 3 months after surgery in this study.

A nonuniform, skewed velocity profile was found both in aortic stenosis and after valve replacement, with the highest velocities typically located from the center of the outflow tract toward the septum. These findings are in accordance with results from normal subjects studied by the same technique[9] and with data from a peroperative Doppler study analyzing the velocity distribution in the proximal aorta 1 to 2 cm above normal valves.[8] In these studies the maximal velocities were found toward the septum[9] and rightward toward the anterior aortic wall.[8]

Mathison et al.[8] discussed the relation of the velocity distribution in the aorta to the genesis of aortic valve calcification, inasmuch as this calcification usually occurs first at the site of the commissure of the right coronary and the noncoronary cusp. They concluded that the jet directed toward this cusp may cause damage to it. The method used in the present study gives the opportunity to study left ventricular outflow tract velocity patterns in various categories of aortic valve disease.

Knowledge of left ventricular outflow tract velocity distribution after aortic valve replacement may have implications for what is the optimal implantation technique for prosthetic valves. Segadal and Matre[6] studied blood velocity distribution in the ascending aorta 6 to 7 cm above the valve in patients undergoing open heart surgery. In patients with normal aortic valves, a skewed peak systolic velocity profile with the highest velocity along the left posterior wall was found, and during systole a clockwise rotation of the maximum velocities was demonstrated. In patients with Medtronic-Hall tilting disc valves, where the major orifice was directed posteriorly and to the right, the velocity profile in the ascending aorta was skewed in the opposite direction of normal.[6] A clockwise, helical rotation of the flow vector is also described in the proximal ascending aorta in normal subjects.[8] With the finding in the present study that the outflow tract velocity distribution in patients with aortic valve prostheses principally shows the same patterns as in normal subjects,[9] it can be anticipated that with the disc valves the deviation from normal flow pattern in the ascending aorta will depend on the orientation of the major orifice of the prosthesis. Whether this could influence prosthesis hemodynamics is not known, but there are data indicating that hemodynamics of aortic disc valves are influenced by the orientation of the major orifice.[18]

With a nonuniform velocity distribution in the outflow tract, recording of the maximum velocities will result in an overestimation of stroke volume. In normal subjects this overestimation was calculated to

about 15%.[9] The present study indicates the possibility of an even larger overestimation in patients with aortic valve disease. However, when the sample volume is positioned in the left ventricular outflow tract it will not necessarily record the highest velocities; furthermore, the velocities recorded may to some extent be underestimated by the angle between the ultrasound beam and the flow direction. This could explain the acceptable correlations demonstrated between invasive and noninvasive methods in calculating cardiac output and valve area in patients with aortic valve prostheses.[4,19] Nevertheless, the nonuniformity of velocity profiles (demonstrated also in patients with aortic stenosis or an aortic prosthesis) may result in a variable overestimation of stroke volume and valve area, and care should be taken to try to obtain a mean value by scanning across the outflow tract.

Limitations of the Study

In this study the velocity distribution was evaluated in only one plane without a complete mapping of velocities in the outflow tract. Accordingly, the highest velocities might have been missed at least in some cases. The velocity profiles were constructed from only one sequence of time-gated recordings in each patient. In each patient two separate recordings were done, and velocity profiles obtained from pairs of recording sequences were similar. Velocity data were lost at the start and at the end of ejection; accordingly, the computed velocity-time integrals are imprecise concerning absolute values. These limitations, however, were the same at both recordings and should not influence the comparison of velocity profiles before and after surgery.

Conclusions

In patients with aortic stenosis the velocity profile in the left ventricular outflow tract is skewed both before and after valve replacement. The highest velocities are usually, but not invariably, located toward the septum both before and after surgery. The maximum velocity at peak flow and the maximum velocity time integral overestimated the mean values to the same extent before and after surgery. Accordingly, the limitations and sources of error inherent in the pulsed Doppler technique are likely the same before and after surgery in patients with aortic stenosis. The nonuniformity of velocity profiles demonstrated may influence stroke volume and valve areas estimates obtained by the pulsed Doppler technique. Further studies with sampling of velocity data from several imaging planes are required to construct more complete left ventricular outflow tract velocity profiles to allow for a more accurate validation of the Doppler estimates as well as correcting for the overestimation probably inherent in the method. Further studies are also required to study left ventricular outflow tract velocity distribution in various subgroups of aortic valve disease as well as at different hemodynamic states.

REFERENCES

1. Skjaerpe T, Hegrenaes L, Hatle L. Noninvasive estimation of valve area in patients with aortic stenosis by Doppler ultrasound and two-dimensional echocardiography. Circulation 1985;72:810-8.
2. Kapur KK, Fan P, Nanda NC, Yoganathan AP, Goyal RG. Doppler color flow mapping in the evaluation of prosthetic mitral and aortic valve function. J Am Coll Cardiol 1989;13:1561-71.
3. Burstow DJ, Nishimura RA, Bailey KR, et al. Continuous wave Doppler echocardiographic measurement of prosthetic valve gradients. A simultaneous Doppler-Catheter correlative study. Circulation 1989;80:504-14.
4. Rothbart RM, Castriz JL, Hardings LV, Russo CD, Teague SM. Determination of aortic valve area by two-dimensional and Doppler echocardiography in patients with normal and stenotic bioprosthetic valves. J Am Coll Cardiol 1990; 15:817-24.
5. Ihlen H, Amlie JP, Dale J, et al. Determination of cardiac output by Doppler echocardiography. Br Heart J 1984; 51:54-60.
6. Segadal L, Matre K. Blood velocity distribution in the human ascending aorta. Circulation 1987;76:90-100.
7. Paulsen PK, Hasenkam JM, Stodkilde-Jorgensen H, Albrechtesen O. Three-dimensional visualizations of velocity profiles in the ascending aorta in humans. A comparative study among normal aortic valves, St. Jude Medical and Starr-Edwards Silastic Ball valves. Int J Artif Organs 1988;11:277-92.
8. Mathison M, Furuse A, Asano K. Doppler analysis of flow velocity profile at the aortic root. J Am Coll Cardiol 1988;12:947-54.
9. Rossvoll O, Samstad S, Torp HG, et al. The velocity distribution in the aortic annulus in normal subjects: a quantitative analysis of two-dimensional Doppler flow maps. J Am Soc Echocardiogr 1991;4:367-78.
10. Samstad SO, Torp HG, Linker DT, et al. Cross sectional early mitral flow velocity profiles from colour Doppler. Br Heart J 1989;62:177-84.
11. Linker DT, Johansen E, Torp H, Angelsen BAJ. Practical considerations and design of a digital system for acquisiton of two-dimensional ultrasonic and flow data. Echocardiography 1988;5:485-94.
12. Samstad SO, Torp HG, Matre K, Rossvoll O, Segadal L, Piene H. Instantaneous cross-sectional flow velocity profiles: a comparative study of two ultrasound Doppler methods ap-

plied to an in vitro pulsatile flow model. J AM SOC ECHOCARDIOGR 1990;3:451-64.
13. Otto CM, Pearlman AS, Comess KA, Reamer RP, Janko CL, Huntsman LL. Determination of the stenotic aortic valve area in adults using Doppler echocardiography. J Am Coll Cardiol 1986;7:509-17.
14. Oh JK, Taliercio CP, Holmes DR, et al. Prediction of the severity of aortic stenosis by Doppler aortic valve area determination: prospective Doppler-catheterization correlation in 100 patients. J Am Coll Cardiol 1988;11:1227-34.
15. Chambers J, Coppack F, Deverall P, Jackson G, Sowton E. The continuity equation tested in a bileaflet aortic prosthesis. Int J Cardiol 1991;31:149-54.
16. Chafizadeh ER, Zoghbi WA. Doppler echocardiographic assessment of the St. Jude Medical prosthetic valve in the aortic position using the continuity equation. Circulation 1991; 83:213-23.
17. Wiseth R, Hegrenaes L, Rossvoll O, Skjaerpe T, Hatle L. Validity of an early postoperative baseline Doppler recording after aortic valve replacement. Am J Cardiol 1991;67:869-72.
18. Olin CL, Bomfim V, Halvazulis V, Holmgren AC, Lamke BJ. Optimal insertion technique for the Bjørk-Shiley valve in the narrow aortic ostium. Ann Thorac Surg 1983;36:567-76.
19. Ihlen H, Mølstad P. Cardiac output measured by Doppler echocardiography in patients with aortic prosthetic valves. Eur Heart J 1990;11:399-402.

ACTA UNIVERSITATIS NIDROSIENSIS FACULTATIS MEDICINAE

Series A: Dissertations

1. Knut Joachim Berg: EFFECT OF ACETYLSALICYLIC ACID ON RENAL FUNCTION. 1977.
2. Karl Erik Viken and Arne Ødegaard: STUDIES ON HUMAN MONOCYTES CULTURED *IN VITRO*. 1977.
3. Karel Bjørn Cyvin: CONGENITAL DISLOCATION OF THE HIP JOINT. 1978.
4. Alf O. Brubakk: METHODS FOR STUDYING FLOW DYNAMICS IN THE LEFT VENTRICLE AND THE AORTA IN MAN. 1978.
5. Geirmund Unsgaard: CYTOSTATIC AND IMMUNOREGULATORY ABILITIES OF HUMAN BLOOD MONOCYTES CULTURED IN VITRO. 1979.
6. Størker Jørstad: URAEMIC TOXINS. 1980.
7. Arne Olav Jenssen: SOME RHEOLOGICAL, CHEMICAL AND STRUCTURAL PROPERTIES OF MUCOID SPUTUM FROM PATIENTS WITH CHRONIC OBSTRUCTIVE BRONCHITIS. 1980.
8. Jens Hammerstrøm: CYTOSTATIC AND CYTOLYTIC ACTIVITY OF HUMAN MONOCYTES AND EFFUSION MACROPHAGES AGAINST TUMOUR CELLS *IN VITRO*. 1981.
9. Tore Syversen: EFFECTS OF METHYLMERCURY ON RAT BRAIN PROTEIN. 1983.
10. Torbjørn Iversen: SQUAMOUS CELL CARCINOMA OF THE VULVA. 1983.
11. Tor-Erik Widerøe: ASPECTS OF CONTINUOUS AMBULATORY PERITONEAL DIALYSIS. 1984.
12. Anton Hole: ALTERATIONS OF MONOCYTE AND LYMPHOCYTE FUNCTIONS IN RELATION TO SURGERY UNDER EPIDURAL OR GENERAL ANAESTHESIA. 1984.
13. Terje Terjesen: FRACTURE HEALING AND STRESS-PROTECTION AFTER METAL PLATE FIXATION AND EXTERNAL FIXATION. 1984.
14. Carsten Saunte: CLUSTER HEADACHE SYNDROME. 1984.
15. Inggard Lereim: TRAFFIC ACCIDENTS AND THEIR CONSEQUENCES. 1984.
16. Bjørn Magne Eggen: STUDIES IN CYTOTOXICITY IN HUMAN ADHERENT MONONUCLEAR BLOOD CELLS. 1984.
17. Trond Haug: FACTORS REGULATING BEHAVIORAL EFFECTS OF DRUGS. 1984.
18. Sven Erik Gisvold: RESUSCITATION AFTER COMPLETE GLOBAL BRAIN ISCHEMIA. 1985.
19. Terje Espevik: THE CYTOSKELETON OF HUMAN MONOCYTES. 1985.
20. Lars Bevanger: STUDIES OF THE Ibc (c) PROTEIN ANTIGENS OF GROUP B STREPTOCOCCI. 1985.
21. Ole-Jan Iversen: RETROVIRUS-LIKE PARTICLES IN THE PATHOGENESIS OF PSORIASIS. 1985.
22. Lasse Eriksen: EVALUATION AND TREATMENT OF ALCOHOL DEPENDENT BEHAVIOUR. 1985.
23. Per I. Lundmo: ANDROGEN METABOLISM IN THE PROSTATE. 1985.
24. Dagfinn Berntzen: ANALYSIS AND MANAGEMENT OF EXPERIMENTAL AND CLINICAL PAIN. 1986.
25. Odd Arnold Kildahl-Andersen: PRODUCTION AND CHARACTERIZATION OF MONOCYTE-DERIVED CYTOTOXIN AND ITS ROLE IN MONOCYTE-MEDIATED CYTOTOXICITY. 1986.
26. Ola Dale: VOLATILE ANAESTHETICS. 1986.
27. Per Martin Kleveland: STUDIES ON GASTRIN. 1987.

28. Audun N. Øksendal: THE CALCIUM PARADOX AND THE HEART. 1987.
29. Vilhjalmur R. Finsen: HIP FRACTURES. 1987.
30. Rigmor Austgulen: TUMOR NECROSIS FACTOR: A MONOCYTE-DERIVED REGULATOR OF CELLULAR GROWTH. 1988.
31. Tom-Harald Edna: HEAD INJURIES ADMITTED TO HOSPITAL. 1988.
32. Joseph D. Borsi: NEW ASPECTS OF THE CLINICAL PHARMACOKINETICS OF METHOTREXATE. 1988.
33. Olav F.M. Sellevold: GLUCOCORTICOIDS IN MYOCARDIAL PROTECTION. 1988.
34. Terje Skjærpe: NONINVASIVE QUANTITATION OF GLOBAL PARAMETERS ON LEFT VENTRICULAR FUNCTION: THE SYSTOLIC PULMONARY ARTERY PRESSURE AND CARDIAC OUTPUT. 1988.
35. Eyvind Rødahl: STUDIES OF IMMUNE COMPLEXES AND RETROVIRUS-LIKE ANTIGENS IN PATIENTS WITH ANKYLOSING SPONDYLITIS. 1988.
36. Ketil Thorstensen: STUDIES ON THE MECHANISMS OF CELLULAR UPTAKE OF IRON FROM TRANSFERRIN. 1988.
37. Anna Midelfart: STUDIES OF THE MECHANISMS OF ION AND FLUID TRANSPORT IN THE BOVINE CORNEA. 1988.
38. Eirik Helseth: GROWTH AND PLASMINOGEN ACTIVATOR ACTIVITY OF HUMAN GLIOMAS AND BRAIN METASTASES – WITH SPECIAL REFERENCE TO TRANSFORMING GROWTH FACTOR BETA AND THE EPIDERMAL GROWTH FACTOR RECEPTOR. 1988.
39. Petter C. Borchgrevink: MAGNESIUM AND THE ISCHEMIC HEART. 1988.
40. Kjell-Arne Rein: THE EFFECT OF EXTRACORPOREAL CIRCULATION ON SUBCUTANEOUS TRANSCAPILLARY FLUID BALANCE. 1988.
41. Arne Kristian Sandvik: RAT GASTRIC HISTAMINE. 1988.
42. Carl Bredo Dahl: ANIMAL MODELS IN PSYCHIATRY. 1988.
43. Torbjørn A. Fredriksen: CERVICOGENIC HEADACHE. 1989.
44. Rolf A. Walstad: CEFTAZIDIME. 1989.
45. Rolf Salvesen: THE PUPIL IN CLUSTER HEADACHE. 1989.
46. Nils Petter Jørgensen: DRUG EXPOSURE IN EARLY PREGNANCY. 1989.
47. Johan C. Ræder: PREMEDICATION AND GENERAL ANAESTHESIA IN OUTPATIENT GYNECOLOGICAL SURGERY. 1989.
48. M. R. Shalaby: IMMUNOREGULATORY PROPERTIES OF TNF-α AND RELATED CYTOKINES. 1989.
49. Anders Waage: THE COMPLEX PATTERN OF CYTOKINES IN SEPTIC SHOCK. 1989.
50. Bjarne Christian Eriksen: ELECTROSTIMULATION OF THE PELVIC FLOOR IN FEMALE URINARY INCONTINENCE. 1989.
51. Tore B. Halvorsen: PROGNOSTIC FACTORS IN COLORECTAL CANCER. 1989.
52. Asbjørn Nordby: CELLULAR TOXICITY OF ROENTGEN CONTRAST MEDIA. 1990.
53. Kåre E. Tvedt: X-RAY MICROANALYSIS OF BIOLOGICAL MATERIAL. 1990.
54. Tore C. Stiles: COGNITIVE VULNERABILITY FACTORS IN THE DEVELOPMENT AND MAINTENANCE OF DEPRESSION. 1990.
55. Eva Hofsli: TUMOR NECROSIS FACTOR AND MULTIDRUG RESISTANCE. 1990.
56. Helge S. Haarstad: TROPHIC EFFECTS OF CHOLECYSTOKININ AND SECRETIN ON THE RAT PANCREAS. 1990.
57. Lars Engebretsen: TREATMENT OF ACUTE ANTERIOR CRUCIATE LIGAMENT INJURIES. 1990.
58. Tarjei Rygnestad: DELIBERATE SELF-POISONING IN TRONDHEIM. 1990.
59. Arne Z. Henriksen: STUDIES ON CONSERVED ANTIGENIC DOMAINS ON MAJOR OUTER MEMBRANE PROTEINS FROM ENTEROBACTERIA. 1990.