ASSESSMENT OF AORTIC STENOSIS WITH SPECIAL REFERENCE TO DOPPLER ULTRASOUND

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Assessment of aortic stenosis with special reference to Doppler ultrasound

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ABSTRACT

The severity of left ventricular outflow obstruction, the left ventricular function and the occurrence of concomitant coronary artery disease are three important issues in the evaluation of patients with suspected aortic stenosis.

The systolic peak pressure gradient obtained by continuous wave Doppler echocardiography was compared with the peak to peak pressure gradient measured at cardiac catheterization in 58 consecutive patients. The two measurements agreed favourably; $r = 0.85$, SEE = 14 mm Hg.

The Doppler peak gradient was compared with the peak gradient measured at catheterization by simultaneous recordings in the left ventricle and ascending aorta in 26 patients. A close correlation was obtained; $r = 0.94$, SEE = 9.1 mm Hg.

Estimation of the mean systolic pressure drop across the valve from Doppler tracings of the same patients, using a simple formula $\Delta P_{\text{mean}} = 0.64 \times \Delta P_{\text{peak}}$, was compared with the invasive mean pressure gradient obtained by planimetry. The mean gradient was accurately estimated, $r = 0.91$, SEE = 7.6 mm Hg.

Aortic valve area measurements were obtained in 22 patients both by application of a modified Gorlin formula and by application of the continuity equation using the Doppler derived systolic pressure gradient and velocity integral as well as the stroke volume obtained by radionuclide angiography. The noninvasive valve area was compared with that obtained by invasive registrations and an excellent relationship was found; $r = 0.95$, SEE = 0.13 cm$^2$ by the Gorlin formula and $r = 0.94$, SEE = 0.14 cm$^2$ by the integration method.

Exercise ECG was used to estimate the occurrence of coexistent coronary heart disease in 35 patients. Patients with significant coronary lesions documented by angiography showed a lower mean working capacity, larger ST depressions and higher effort angina score during the exercise test than patients with no or only insignificant coronary obstructions.

Application of simultaneous ECG, phonocardiography and Doppler echocardiography were used to determine the interval between the QRS complex and the mitral valve opening (Q-MC) and the interval between the aortic valve closure and mitral valve opening (A2-MO). The ratio Q-MC/A2-MO correlated closely with the pulmonary capillary wedge pressure measured at catheterization; $r = 0.94$, SEE = 2.9 mm Hg, $n = 20$.

A reduction of invasive investigations in the evaluation of patients with aortic stenosis is suggested.

Key words: Aortic stenosis, aortic valve area, transvalvular pressure drop, coronary heart disease, pulmonary capillary wedge pressure, Doppler echocardiography, radionuclide angiography
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STUDY I - V
ABBREVIATIONS

CHD = Coronary heart disease
ET = Ejection time
PCWP = Pulmonary capillary wedge pressure
SV = Stroke volume
SVI = Systolic velocity integral
Vmax = Maximum velocity
Wmax = Maximum working capacity
WmaxN = Predicted normal Wmax
Wmax% = Wmax \cdot \frac{100}{WmaxN}
ABSTRACT

The severity of left ventricular outflow obstruction, the left ventricular function and the occurrence of concomitant coronary artery disease are three important issues in the evaluation of patients with suspected aortic stenosis.

The systolic peak pressure gradient obtained by continuous wave Doppler echocardiography was compared with the peak to peak pressure gradient measured at cardiac catheterization in 58 consecutive patients. The two measurements agreed favourably; \( r = 0.85, \text{SEE} = 14 \text{ mm Hg}. \)

The Doppler peak gradient was compared with the peak gradient measured at catheterization by simultaneous recordings in the left ventricle and ascending aorta in 26 patients. A close correlation was obtained; \( r = 0.94, \text{SEE} = 9.1 \text{ mm Hg}. \)

Estimation of the mean systolic pressure drop across the valve from Doppler tracings of the same patients, using a simple formula \( \Delta P_{\text{mean}} = 0.64 \times \Delta P_{\text{peak}}, \) was compared with the invasive mean pressure gradient obtained by planimetry. The mean gradient was accurately estimated, \( r = 0.91, \text{SEE} = 7.6 \text{ mm Hg}. \)

Aortic valve area measurements were obtained in 22 patients both by application of a modified Gorlin formula and by application of the continuity equation using the Doppler derived systolic pressure gradient and velocity integral as well as the stroke volume obtained by radionuclide angiography. The noninvasive valve area was compared with that obtained by invasive registrations and an excellent relationship was found; \( r = 0.95, \text{SEE} = 0.13 \text{ cm}^2 \) by the Gorlin formula and \( r = 0.94, \text{SEE} = 0.14 \text{ cm}^2 \) by the integration method.

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Application of simultaneous ECG, phonocardiography and Doppler echocardiography were used to determine the interval between the QRS complex and the mitral valve opening (Q-MC) and the interval between the aortic valve closure and mitral valve opening (A2-MO). The ratio Q-MC/A2-MO correlated closely with the pulmonary capillary wedge pressure measured at catheterization; \( r = 0.94, \text{SEE} = 2.9 \text{ mm Hg}, n = 20. \)

A reduction of invasive investigations in the evaluation of patients with aortic stenosis is suggested.

Key words: Aortic stenosis, aortic valve area, transvalvular pressure drop, coronary heart disease, pulmonary capillary wedge pressure, Doppler echocardiography, radionuclide angiography
The present study is based on the following papers, which will be referred to by their Roman numerals.


INTRODUCTION

Evaluation of patients with suspected aortic stenosis
Several factors have to be taken into consideration in the evaluation of patients with aortic stenosis, particularly the severity of outflow obstruction, left ventricular performance and concomitant coronary heart disease. An accurate assessment is crucial since surgery may be life-saving.

The systolic pressure gradient across the valve is a measure of obstruction to flow. The systolic pressure gradient is, however, also dependent on left ventricular stroke volume, i.e. the systolic flow across the valve. Patients with a compromised left ventricular function may show a low gradient despite a small valve area. The aortic valve area is thus an important entity and it should be calculated in all patients in whom there is any doubt about the severity of the lesion. Left ventricular performance may be assessed by measuring the ejection fraction, stroke volume or cardiac output, and the pulmonary capillary wedge pressure.

The occurrence of concomitant significant coronary heart disease is another major issue. There are conflicting reports regarding the prevalence of coronary heart disease in patients with aortic stenosis and the significance of coronary atheromatosis in this setting is disputed (1-11). Angina pectoris is a frequent complaint in patients with aortic stenosis both with and without angiographic evidence of obstructive coronary artery lesions. On the other hand, a negative history of effort related chest pain does not rule out significant coronary obstructions even if this combination is rare (1-11).

A noninvasive procedure to screen patients with suspected aortic valve lesions in respect to the severity of obstruction, left ventricular function and concomitant coronary disease is thus desirable. In addition, the accuracy of the noninvasive procedures should allow the use of invasive methods to be minimized. The advent of Doppler ultrasound is an important step in this direction (12).
The Doppler principle

The Doppler effect was described in the first half of the 19th century by Christian Johann Doppler (1803-1853). It applies to all wave-forms including sound. Several illustrations have been used to exemplify this phenomenon. One example is a row boat; when the boat is stationary a certain frequency of the sea waves is felt in the boat. If the boat is rowed against the waves a sensation of increased wave frequency is experienced, while the opposite is true when the boat is rowed in the other direction. The difference in frequency felt when the boat is moving and not moving is the Doppler shift or the Doppler frequency. The Doppler frequency can be used to calculate the velocity of the boat provided that the frequency of the waves is known.

In Doppler echocardiography a transducer emits ultrasound with a known frequency (usually 1-10 MHz). The moving blood cells act as reflectors and the velocity of the blood corpuscles can be calculated from the Doppler equation,

$$ v = \frac{c \cdot \Delta f}{2 \cdot f \cdot \cos \alpha} $$

$v$ = velocity of the blood  
$c$ = velocity of sound in tissues  
$\Delta f$ = the frequency shift of reflected ultrasound  
$f$ = ultrasound frequency  
$\alpha$ = angle of incidence between the ultrasonic beam and velocity vectors of the moving blood

A small angle of incidence between the blood flow and the ultrasonic beam is critical to obtain accurate estimation of the flow velocity. In aortic stenosis as well as in other valvular lesions, it is usually possible to obtain a transducer position with an angle less than 15°, which gives a cosine of more than 0.95. It is, however, of the utmost importance to try many different transducer positions to minimize the angle.
The Bernoulli equation

This equation is essential in Doppler echocardiography because it denotes the relation between the difference in blood velocity and the pressure difference between the two sides of an obstructive lesion (13).

\[ p_1 - p_2 = 1/2 \rho (v_2^2 - v_1^2) + \rho \frac{d}{dt} \int_1^2 ds + R(v) \]

flow acceleration viscous friction

Suffix 1 denotes the position prior to the obstruction and suffix 2 post the obstruction.

\[ p_1 = \text{pressure prior to obstruction} \]
\[ p_2 = \text{pressure post to obstruction} \]
\[ \rho = \text{mass density of blood per unit volume} \]
\[ v_1 = \text{velocity prior to obstruction} \]
\[ v_2 = \text{velocity in the jet} \]

The second term on the right side of the equation represents the pressure drop caused by changes of the velocity with time. The last term represent viscous losses. It has been shown (12-13) that the two last paragraphs can be omitted when the equation is applied to the pressures and dimensions found in stenotic valve disease. Since the velocity prior to a stenosis is small compared with the velocity in the jet it can also be neglected in most cases with obstruction localized to the valvular plane. The equation can then be written,

\[ \Delta p = 4 (V_{\text{max}})^2 \]

\[ \Delta p = \text{pressure drop across the stenosis} \]
\[ V_{\text{max}} = \text{maximal velocity in the jet} \]

The validity of the simplified equation has been tested by several authors (12-17) and Hatle and Angelsen (18) have presented a detailed discussion on this subject in their excellent textbook.
AIMS OF THE STUDY

To evaluate the applicability of Doppler ultrasound for quantification of pressure difference across the valve in patients with suspected aortic stenosis.

To evaluate a simple method to estimate the mean pressure difference in aortic stenosis from Doppler tracings.

To noninvasively estimate the aortic valve area by combining Doppler echocardiography and radionuclide angiography in patients with aortic valve disease.

To evaluate the usefulness of the standard exercise test to identify coexistent coronary heart disease in patients with aortic stenosis.

To noninvasively estimate the pulmonary capillary wedge pressure in patients with aortic stenosis.
PATIENTS

Study I
In this study 58 consecutive patients were included. They were referred for evaluation of suspected aortic stenosis. Nineteen patients had significant aortic regurgitation and three of them also had mitral regurgitation according to angiography. No patient was excluded on grounds of imperfect Doppler recordings.

Studies II, III
Twenty-six consecutive patients examined for suspected aortic stenosis were included. There were 15 patients with pure aortic stenosis or only minimal aortic regurgitation, 8 had stenosis with moderate or moderately severe regurgitation and 3 had severe regurgitation. Of the 26 patients, 14 had mitral regurgitation, which was moderate in 2 and minimal in 12. No patient included in Studies II and III was recruited from Study I. Four patients were excluded in Study III as they did not fully complete the invasive protocol of the study.

Study IV
In this study, 35 patients were included, mainly those participating in Study I. However, patients with aortic or mitral regurgitation were excluded.

Study V
Twenty consecutive patients were included, 18 of them from Studies II and III.
METHODS

Cardiac catheterization
In all studies the pressure curves were recorded by liquid filled catheters connected to mechanoelectrical transducers interfaced with an UV recorder and calibrated against a hydrostatic standard. Cardiac output was measured by the direct Fick method. No premedication was given. The following systolic pressure differences were calculated:

a) the peak to peak gradient which is the difference between the peak systolic pressure in the left ventricle and the peak systolic pressure in the aorta,

b) the peak pressure difference which is the largest instantaneous systolic pressure difference,

c) the mean gradient which is the difference between the mean systolic pressure in the left ventricle and the mean systolic pressure in the ascending aorta. It was calculated by integrating the area between the left ventricle and the aortic pressure recordings (19).

A single catheter was used in Study I and this catheter was positioned in the left ventricle and subsequently a pull-back procedure was performed. Two catheters were used in Studies II and III, one catheter was positioned with the tip in the left ventricle and the other in the ascending aorta.

In Study V, the wedge position of the catheter was confirmed by typical phasic waveform and fluoroscopic determination of the site of the catheter tip. The mean pulmonary capillary wedge pressure was obtained by electronic damping of the signal.

Cineangiography
Left ventriculography and aortography were performed in the 45° right and 45° left anterior oblique projections. Left ventricular end-diastolic and end-systolic volumes were calculated using a computer system with a biplane ellipsoid method, or in cases with a deformed ventricular cavity, a biplane integration method. The stroke volume was calculated as the difference between them (20). The severity of aortic and
mitral regurgitation was assessed as described by Dexter and Grossman (19). Left ventricular motion score (LVMS) was calculated visually according to the motion of different wall segments (21). The left ventricle was thereby divided into seven segments according to the American Heart Association (22). The motion of each segment was graded as follows: normal motion = 0, hypokinesia = 1, akinesia = 2, dyskinesia = 3 points. By adding these points LVMS was obtained.

Aortic valve area
The aortic valve area was calculated according to Gorlin and Gorlin (23):

\[
AVA = \frac{SV}{ET \cdot 44.5 \sqrt{\Delta P_{\text{mean}}}}
\]

AVA = aortic valve area
SV = stroke volume
ET = ejection time
\(\Delta P_{\text{mean}} = \text{mean systolic gradient}

Both the Fick (or net) and the cineangiographic (or total) stroke volume were used in the calculations of the valve area.

Coronary angiography
Coronary angiography was carried out according to Judkins' technique (24). Obstruction of a coronary vessel resulting in a decrease of the transsectional area by more than 75% was regarded as a significant stenosis. Calculation of myocardial coronary obstruction score is a method employed to estimate the degree of arterial obstruction, and it includes an evaluation of the myocardial mass subserved by the stenotic vessel (21). The maximal score is 15 which indicates occlusion of all coronary arteries.

Routine ECG. A 12-lead ECG (aVL, I, -aVR, II, aVF, III, and V1-6) was recorded using a direct writing ECG-recorder (Mingograph, Siemens Elema).
Phonocardiography. Phonocardiography was recorded together with the ECG and Doppler recording. A 500-1000 Hz filter was used.

Exercise test. A standard exercise ECG test was performed (25). Maximum working capacity (Wmax) according to Strandell (26) was calculated and compared with the predicted normal maximum working capacity (WmaxN) (Linderholm, unpublished observations). Wmax as a percentage of WmaxN has been used as an index of physical performance (Wmax%). ST depression during exercise was measured as the difference between ST levels during maximum work and at rest. The ratio 100 x ST depression/ Wmax% was used as an index of coronary insufficiency (CI-index). Effort angina during the exercise test was recorded and an effort angina score was defined. 0 = No angina during or after the exercise test, 1 = Typical or atypical angina during exercise but no angina after exercise, 2 = Typical or atypical angina during exercise which disappears within 5 minutes after exercise, 3 = Typical or atypical angina during exercise which persists for more than 5 minutes after exercise.

Doppler echocardiography. Continuous wave Doppler examinations were performed using a Pedof system with a 2.0 MHz nonimaging transducer (Vingmed A/S). Flow velocities up to 6 m/s corresponding to a pressure difference of approximately 140 mm Hg can be measured with this equipment. Spectral frequency analysis was not available for these studies.

In Studies I and IV the investigations were performed prior to the invasive investigation, usually one day before. In Studies II, III and V the examinations were carried out within one hour of the subsequent invasive procedure. Some patients have been examined simultaneously by noninvasive and invasive methods.

The maximal flow velocity was recognized by listening to an audio signal of alternating pitch from the loudspeaker in the apparatus (the higher the pitch, the higher the velocity) and observing recorded velocity profiles.

Doppler gradients. The simplified Bernoulli formula was used to calculate the peak pressure gradient from the recorded peak velocity in Studies I-V (13).
Estimation of pulmonary capillary wedge pressure

Combined ECG, phonocardiogram and Doppler amplitude recordings were applied to record the Q-MC and A2-MO intervals. The Q-MC was measured as the interval between the onset of the QRS complex and the top of the amplitude signal of the mitral valve closure. The A2-MO interval was measured as the interval between the onset of the second heart sound and the beginning of the amplitude signal of the mitral valve opening. These intervals as well as the quotient Q-MC/A2-MO were compared with the mean capillary wedge pressure measured at catheterization.

Systolic velocity integral (SVI). The area under the maximum velocity recording was manually integrated to obtain the systolic velocity integral. This measure represents the distance covered by the stroke volume per beat.

Analysis of flow in aortic stenosis indicates that the velocity profile is flat (18). The aortic valve area can therefore also be calculated as the relation between stroke volume and systolic velocity integral (SV/SVI).

Radionuclide angiography

A non-geometric attenuation-corrected technique was used to determine absolute left ventricular end-diastolic and end-systolic volumes from ECG-gated blood pool studies (27).

Red blood cell labelling in vivo was accomplished by intravenous administration of stannous pyrophosphate followed after 20 minutes by administration of 740 MBq technetium-99m pertechnetate. Left ventricular depth (d) in the left anterior oblique 45° projection was measured, and used according to a previously described technique for attenuation correction (27). In accordance with previous reports (28) and our own experience an attenuation coefficient (µ) of 0.13 cm⁻¹ was used.

Each cardiac cycle was divided into 24 frames with ECG-gating and data were collected using a Portacamera IIc (General Electric) with a high resolution parallel hole collimator interfaced with a Gamma 11 computer system (Digital Equipment Corporation) for 10 minutes in the LAO 45° projection with the patients in the supine position. Approximately 500 to 1000 cardiac cycles were collected depending on the actual heart rate. No arrhythmia rejection was used.
Regions of interest were manually drawn around the left ventricle in the end-diastolic and the end-systolic frames, with a manually drawn postero-lateral region in the end-systolic frame for background correction.

Immediately before data collection in the LAO 45° view a 10 ml venous blood sample was drawn from the patients arm contralateral to the injection site. The blood sample was contained in a Petri dish and the activity was counted with the same gammacamera equipment for 3 minutes to obtain the specific activity in the blood, corrected for background in the field and also corrected for decay to midtime of the sampling from the left anterior oblique view. Left ventricular stroke volume (SV) was thereafter calculated according to the formula:

\[
SV = \frac{1}{e^{-\mu d}} \left( \text{end-diastolic counts} - \text{end-systolic counts} \right) \times 1.8 \times 10^6 \frac{\text{counts in blood sample}}{\text{cycles collected}} \times \text{frame time}
\]

The procedure was previously validated against stroke volume determination by cineangiography and there was close agreement between the two methods in line with previous reports (29, 30).

Noninvasive calculations of aortic valve area

Calculations of the aortic valve area from noninvasive data was accomplished by two different approaches. A modified Gorlin equation derived by results from Study II was used,

\[
\text{AVA} = \frac{\text{SV}}{(\text{ET} \times 71.2 \times \text{Vmax})}
\]

Furthermore, according to the continuity equation (31-33):

\[
\text{AVA} = \frac{\text{SV}}{\text{SVI}}
\]

AVA = aortic valve area

SV = stroke volume

ET = left ventricular ejection time

SVI = systolic velocity integral
RESULTS AND DISCUSSION

Quantification of the transvalvular pressure difference (Studies I, II)

Study I was carried out to examine the applicability of systolic pressure difference estimation by Doppler ultrasound in a consecutive series of patients with aortic stenosis. The peak gradient calculated from the Doppler recordings was compared with the peak to peak gradient measured at catheterization. Noninvasive and invasive pressure gradients showed an acceptable correlation, \( r = 0.85, \text{SEE} = \pm 14 \text{mm Hg} \). The Doppler peak gradient exceeded the invasive peak to peak gradient in some patients. Although it was realized that the peak to peak gradient and the Doppler peak gradient were conceptually different the possibility of a large difference between the two pressure differences was not fully appreciated. On the other hand, there was an obvious underestimation of the pressure difference in several patients with severe stenosis. The patients were examined in 1982 and 1983. The number of reports in the literature at that time was limited and only involved small series of patients and children (who are more easily examined). In addition, patients had often been excluded because of unsatisfactory Doppler recordings (34, 35).

In 1985, when Studies II and III were performed it was apparent that a more refined invasive procedure had to be adopted. A dual catheter technique was used and the Doppler gradient was compared with the instantaneous peak gradient measured at catheterization. A correlation \( r = 0.94, \text{SEE} = \pm 9.1 \text{mm Hg} \) was obtained in Study II. A difference of up to 48 mm Hg between the peak and the peak to peak gradient was also observed. Differences of this magnitude have also been reported by Krafchek (36). Since Hatle's (12) original report numerous studies have been reported, and today Doppler ultrasound is a generally accepted method to estimate the peak gradient in aortic stenosis (37-40). In most studies comparisons have been made with gradients measured by fluid filled catheters. However, the accuracy of the reference method must also be considered. The fidelity of a fluid filled catheter pressure measurement systems and the presence of catheter induced artefacts are thus important considerations. Oscillations may lead to errors in estimation of peak and mean pressure gradients. When a single catheter
study is performed, it is necessary to superimpose the aortic tracing onto the recording from the left ventricle and small errors in the timing may result in large differences in the gradients. In addition, measurement of the gradient is based on nonsimultaneous beats. Ideally, simultaneous registrations from the left ventricle and the ascending aorta using micromanometer-tipped catheters should be undertaken. Simultaneous invasive and Doppler recordings would seem ideal, but the Doppler investigation may be hindered by difficulties in getting the patient in an optimal position in the catheterization laboratory. Smith et al (40) even reported closer correlations between noninvasive and invasive data when the noninvasive tests were carried out at a separate time in the noninvasive laboratory. Of course, this only holds true if the patient is in a stable hemodynamic condition. Some of the discrepancies between Doppler and invasive measurements reported may thus be explained by inaccuracies in the reference method. A perfect Doppler recording might even render a better measurement of the pressure difference than that achieved by a pull-back procedure using a fluid filled catheter.

The mean gradient (Study II)
The mean gradient describes the degree of pressure drop throughout systole, and it is usually included in hydraulic orifice formulas. The area between the left ventricular and aortic pressure curves is integrated to determine the mean gradient. The corresponding Doppler gradient can be calculated by transferring the velocity curve to a pressure drop curve by applying the Bernoulli equation. This is a burdensome procedure involving numerous measurements of the instantaneous velocities at short intervals throughout systole. The instantaneous velocities then have to be squared and the resulting pressure drop curve plotted. The mean pressure difference can then be obtained by planimetry. Good correlation has been reported (36-41) between invasive and noninvasive measurements of the mean pressure gradient. The complicated procedure involved has, however, stimulated an interest in finding a simpler method of assessment. Zhang et al (41) reported a formula in which the peak and mean velocity were included: \[ \Delta p_m = 8 V^2_m \left[ V_p/(V_p + V_m) \right] \] where \( \Delta p_m \) is the mean gradient, \( V_p \) is the peak systolic velocity, and \( V_m \) is the mean systolic velocity. We observed that in
most patients the plotted pressure drop curve had a configuration very similar to a sine wave. Applied to a pressure drop curve this means that the mean pressure gradient is equivalent to $2/\pi$ multiplied by the peak gradient according to basic trigonometric principles. Others (33, 41) have considered the velocity curve to be symmetrical for practical purposes. Our results showed that there was no significant difference between the mean gradient obtained by planimetry at catheterization and that obtained by multiplying the peak gradient by $2/\pi$.

Of course the curves cannot invariably be regarded as a sine wave. In theory it may be triangular at one extreme and rectangular at the other, resulting in a mean pressure gradient ranging between $1/3$ and 1 of the peak gradient. These hypothetical situations were not encountered in our material and do not seem to represent a major problem. Moreover, a simplification should indeed be simple.

A possibility to modify the Gorlin equation is also given by the simple relation between mean and peak pressure gradient. When $0.64 \times 4(V_{\text{max}})^2$ is substituted for $\Delta p$ mean, the equation is transformed to: $AVA = SV/(ET \times 71.2 \times V_{\text{max}})$, a formula very similar to that suggested by Ohlsson et al (42).

Determination of aortic valve area (Study III)
The Gorlin equation was used to calculate the aortic valve area from invasive data. Stroke volumes measured by left ventriculography were used since aortic regurgitation was a frequent finding in our patients. In the absence of significant mitral regurgitation this method gives the actual flow across the aortic valve. In the noninvasive study both the modified Gorlin equation and the integration method were used. In both stroke volume was obtained by radionuclide angiography, which like cineangiography gives the total stroke volume. Close correlations with the invasive data were obtained, $r = 0.95$, SEE = $\pm 0.13$ cm$^2$ by the modified Gorlin equation and $r = 0.94$, SEE = $\pm 0.14$ cm$^2$ by the integration method. The two noninvasive tests gave almost identical results, $r = 0.98$, SEE = $\pm 0.09$ cm$^2$. More important, all patients with an aortic valve area of less than 1 cm$^2$ by the invasive study were identified by both the noninvasive procedures.
There are some previous reports of valve area calculations in which Doppler ultrasound was used to measure the mean gradient or the SVI (or both). The principal difference between these studies is the method chosen to estimate the stroke volume. Skjærpe et al (31), Zhang et al (32) and Zoghbi et al (33) used a combined echo and Doppler ultrasound method to calculate the stroke volume. The stroke volume can be estimated from the flow through pulmonary annulus, mitral annulus and through the aortic annulus directly below the obstruction. When stroke volume is calculated using flow through the mitral valve, patients with significant aortic and/or mitral regurgitation has to be excluded, since the actual aortic flow is needed.

Ohlson et al (42) used a CO₂ rebreathing technique, which gives the effective (or net) stroke volume. This technique has the same limitations, the aortic flow being undervalued in patients with aortic regurgitation. It seems attractive to use the stroke volume through the aortic annulus because no patient needs to be excluded because of aortic or mitral regurgitation. Skjærpe et al (31), however, stress that this approach is difficult to handle and subject to significant errors.

Estimation of left ventricular stroke volume by radionuclide angiography has the same limitation in respect to mitral regurgitation. In our study there was a close correlation between stroke volume estimated by the isotope technique and left ventriculography, $r = 0.91$, SEE $+9.9$ ml. In addition, the ejection fraction is obtained and regional ventricular function can be assessed.

The present study concerned patients with aortic stenosis. Doppler examinations have shown that the so called isolated aortic stenosis is a rarity; most patients show some degree of concomitant regurgitation. A high percentage of leaking valves has been reported also in healthy individuals. There were only 4 out of the 26 patients who did not show either aortic or mitral regurgitation in Studies II and III. This has important implications for calculations of the aortic valve area as discussed previously. The diagnosis aortic regurgitation may be difficult and we believe that Doppler is the most sensitive method. However, quantification of valvular regurgitation is often difficult. Angio-
graphy has been regarded as the gold standard in many studies but when the severity of regurgitation is divided into four grades there is a considerable overlap (Croft et al, 43). Grading of aortic regurgitation with pulsed wave Doppler technique has been described (44-45) but the validity of these approaches is doubtful (46, 47). In our experience discrepancies between angiographic gradings and that of pulsed Doppler are often observed. Continuous wave Doppler has also been used for this purpose (48). There is still no optimal method for accurate quantification of regurgitant lesions.

The coexistence of coronary heart disease (CHD) (Study IV)
The reported prevalence of coronary heart disease in aortic stenosis shows considerable variation with figures ranging between 20-60% (49-55). In Study IV, 43% of the patients had significant CHD. This is in agreement with a larger study recently published from our hospital (49), where 37% of 221 patients with aortic valve disease had significant CHD.

It is controversial whether coronary angiography should be carried out in all patients despite the absence of angina pectoris (49-55). A screening procedure to identify patients with clinically significant CHD would be desirable. A standard ECG exercise test for this purpose was examined. The coronary insufficiency-index was able to separate patients with and without CHD fairly accurate. When an index ≥ 3 and an index < 3 was used to identify those patients with and without CHD, 11 out of 15 patients with CHD and 18 out of 19 without CHD could be identified. When the presence of angina at the exercise test was included the sensitivity of the test was somewhat enhanced. About 50% of the angiographies may be omitted when these criteria are used. On the other hand, approximately 15% of the patients with CHD would be missed which is not acceptable and our policy is to perform coronary angiography in all patients aged 40 years or more regardless of a history of angina.

Estimation of pulmonary capillary pressure in aortic stenosis (Study V)
An estimate of left ventricular performance is valuable and often achieved by combined evaluation of two-dimensional echocardiography,
radionuclide angiography, and left ventriculography. The pulmonary capillary wedge pressure provides an estimate of the left ventricular end-diastolic pressure. An abnormally elevated pulmonary capillary wedge pressure in the presence of other signs of depressed ventricular function, i.e. reduced cardiac output, ejection fraction, or stroke work indicates that contractility is probably impaired (56) However, a reduced ventricular compliance caused by e.g. hypertrophy may elevate the filling pressure while the end-diastolic volume remains normal (56). Despite these difficulties the pulmonary capillary wedge pressure might add information, particularly in patients with coexisting valvular lesions or ischemic myocardial injuries.

The A2-MO interval decreased and the Q-MC interval increased in patients with mitral stenosis when the degree of obstruction increased (57). Further studies showed that these intervals were useful for estimation of the pulmonary capillary pressure in valvular diseases other than mitral stenosis even if there are some conflicting results reported (58-63). In those studies, the intervals have been recorded using M-mode echocardiography. In Study V, the Doppler amplitude signal of the mitral valve was used, since in our experience the measurement points were more easily identified by Doppler than by M-mode echocardiography. The intervals were combined to a quotient

\[
\frac{Q - MC}{A2 - MO}
\]

which compared favourable with the mean pulmonary capillary wedge pressure at catheterization, \( r = 0.94 \), \( \text{SEE} = \pm 2.9 \text{ mm Hg} \). The method accurately separated those patients with a normal or near normal pulmonary capillary wedge pressure from those with an elevated wedge pressure.

We believe that the measurement points of the amplitude signals corresponds to the start and end of the flow through the mitral valve as indicated by the mean velocity signal. The exact relation to the pressure crossover of the left ventricular pressure curve and left atrium/pulmonary capillary wedge pressure curves remains to be clarified.
Accurate determination of the aortic systolic pressure drop can be achieved by Doppler ultrasound in most patients. Sophistication of the transducers/receivers and still better signal analysis can be expected. This may optimize the recordings in patients in whom difficulties in obtaining sufficient signals are encountered today. The colour Doppler system might make the exact area of interest simpler to identify and will speed up the examination. On the other hand, the single nonimaging transducers still will have its definite place in experienced hands. In our experience, it is often quicker to obtain good Doppler recordings when a single transducer is used, at least when compared to duplex transducers. According to wellknown psychological mechanisms (64), it is difficult to concentrate on two tasks simultaneously, i.e. both a 2D-picture and a high quality sound signal (Doppler).

Regarding stroke volume determination more refined methods for separate left and right ventricular output will be developed. Tickner et al (65) have developed a so called microbubble technique, which seems promising. This technique may also be applied for estimation of rightsided cardiac pressures.

Identification of patients with coronary heart disease in conjunction with aortic stenosis can be done with some degree of certainty applying the described work test procedure. It will be interesting whether the results reported in Study V will be validated in a larger group of patients with and without concomitant aortic regurgitation. Such a study is in progress.

Kemper et al (66) have injected $H_2O_2$ in the aortic root in dogs and have been able to evaluate regional wall perfusion. $H_2O_2$ or similar echogenic substances may be developed in the future for this purpose. Even echogenic "bubbles" injected on the venous side and passing through the pulmonary circulation to the left side of the heart have been described (67). Probably we will see further development in the field of echo "contrast".
The application of exercise nuclear angiography and myocardial scintigraphy to detect coronary heart disease in patients with aortic stenosis have been reported (68, 69) and further advancement can be expected with this technique. The applicability of digital subtraction angiography of coronary lesions is another interesting issue.

The use of Doppler in the evaluation of coronary circulation will be an expanding field. Gramiak et al (70) have recently published a study of Doppler examination of left coronary arterial blood flow. The introduction of colour Doppler system may even make diagnosis of significant coronary heart disease possible. At least central major obstruction may be identified. The combination of echo dimension measurements and Doppler velocity recordings to obtain coronary volume flow in analogy with stroke volume estimation may lead to further progress in the non-invasive estimation of coronary heart disease. However, coronary angiography is not likely to be fully replaced by noninvasive procedures.

When it comes to the evaluation of aortic regurgitation it is the colour Doppler system which will be most interesting. It is important, however, to realize that the same evaluation is available with conventional Doppler but the colour system may make it easier to detect a regurgitation and will probably speed up the investigation. Even if it is well known it is worth mentioning that the red "stream" coming towards you from the aortic valves (apical view) is not a volume of blood but blood velocity.
GENERAL SUMMARY AND CONCLUSIONS

The present study reports on noninvasive evaluation of patients with suspected aortic stenosis with emphasis on Doppler ultrasound. The degree of outflow obstruction can be satisfactorily evaluated as far as the peak gradient and the mean gradient are concerned. The determination of aortic valve area can be accomplished by combining radioisotope technique with Doppler tracings.

Noninvasive estimation of the pulmonary capillary wedge pressure seems to be a feasible procedure.

Today there is no generally accepted method to reduce the number of coronary angiographies. The method described may serve as a screening procedure but we feel that coronary angiography still have to be recommended as a part of the standard evaluation program.

It is important to realize that not all patients can be satisfactorily evaluated by noninvasive methods and therefore invasive procedures should be carried out whenever there is any remaining doubt about the severity of the valvular lesion.

It is suggested that the preliminary evaluation of patients with suspected aortic stenosis should include a standard ECG, a bicycle ergometer test, Doppler and two-dimensional echocardiography. These examinations make it possible to accurately estimate the pressure gradient and to make a fair assessment of the left ventricular function. Assessment of the valve area is also possible by Doppler and two-dimensional echocardiography alone, but radionuclide angiography is a useful approach. Before surgery, coronary angiography should probably be undertaken in patients aged 40 years or more.
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