Dependence of Gorlin Formula and Continuity Equation Valve Areas on Transvalvular Volume Flow Rate in Valvular Aortic Stenosis

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Background Valve areas derived by the Gorlin formula have been observed to vary with transvalvular volume flow rate. Continuity equation valve areas calculated from Doppler-echo data have become a widely used alternate index of stenosis severity, but it is unclear whether continuity equation valve areas also vary with volume flow rate. This study was designed to investigate the effects of changing transvalvular volume flow rate on aortic valve areas calculated using both the Gorlin formula and the continuity equation in a model of chronic valvular aortic stenosis.

Methods and Results Using a canine model of chronic valvular aortic stenosis in which anatomy and hemodynamics are similar to those of degenerative aortic stenosis, each subject (n=8) underwent three studies at 2-week intervals. In each study, transvalvular volume flow rates were altered with saline or dobutamine infusion (mean, 10.3±5.1 flow rates per study). Simultaneous measurements were made of hemodynamics using micromanometer-tipped catheters, of ascending aortic instantaneous volume flow rate using a transit-time flowmeter, and of left ventricular outflow and aortic jet velocity curves using Doppler echocardiography. Valve areas were calculated from the invasive data by the Gorlin equation and from the Doppler-echo data by the continuity equation. In the 24 studies, mean transit-time transvalvular volume flow rate ranged from 80±33 to 153±49 mL/min (P<.0001). Comparing minimum to maximum mean volume flow rates, the Gorlin valve area changed from 0.54±0.22 cm² to 0.68±0.21 cm² (P<.0001), and the continuity equation valve area changed from 0.57±0.18 cm² to 0.70±0.20 cm² (P<.0001). A strong linear relation was observed between Gorlin valve area and mean transit-time volume flow rate for each study (median, r=.88), but the slope of this relation varied between studies. The Doppler-echo continuity equation valve area had a weaker linear relation with transit-time volume flow rate for each study (median, r=.51).

Conclusions In this model of chronic valvular aortic stenosis, both Gorlin and continuity equation valve areas were flow-dependent indices of stenosis severity and demonstrated linear relations with transvalvular volume flow rate. The changes in calculated valve area that occur with changes in transvalvular volume flow should be considered when measures of valve area are used to assess the hemodynamic severity of valvular aortic stenosis. (Circulation. 1994;89:827-835.)

Key Words • hemodynamics • valves • stenosis

Aortic valve area, calculated from invasive data by the Gorlin equation or from noninvasive data by the continuity equation, is a valuable index of hemodynamic severity in patients with valvular aortic stenosis. Traditionally, valve area has been considered a "flow-independent" measure of stenosis severity. However, recent evidence indicates that Gorlin valve areas vary with changes in transvalvular volume flow rate. Although an apparent increase in calculated valve area may represent a "true" increase in anatomic orifice area caused by flow-mediated distension of a nonrigid valve, Gorlin valve areas have also been observed to vary in in vitro models using fixed orifice areas. This phenomenon has been attributed to volume flow-mediated variability of the discharge coefficients used in the Gorlin equation.

Valve areas derived by both Gorlin and continuity equations are based on similar hydrodynamic principles. However, the continuity equation measures "effective" orifice area: the area of the vena contracta. In contrast, the Gorlin equation approximates "anatomic" valve area by assuming a coefficient of orifice contraction that is constant at varying transvalvular flow rates. In addition, the Gorlin equation assumes a constant coefficient of velocity, which accounts for energy dissipation caused by frictional loss and turbulence as pressure converts to velocity across the stenotic valve. Doppler-echo techniques measure transvalvular velocity directly, thus avoiding this assumption. As well, the mathematical formulation of the Gorlin equation contains a simplification of the temporal instantaneous pressure-flow relation that is not required with the continuity equation.

Continuity equation valve areas derived from Doppler-echo data are not free of assumptions. Flow in both the left ventricular outflow tract and the vena contracta are assumed to be laminar with flat velocity profiles. Thus, prestenotic and transvalvular velocities measured at one point are assumed to represent the mean spatial velocities across the left ventricular outflow tract and vena contracta, allowing calculation of prestenotic volume flow rate and vena contracta area. In addition, technical difficulties in accurate Doppler and two-dimensional data collection and analysis, most importantly, errors related to nonparallel Doppler/blood flow

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intercept angle and suboptimal imaging of maximal outflow tract diameter, are assumed to be minimal.

The different assumptions underlying the Gorlin and continuity equations may have potential implications when valve area measurements are made at different transvalvular volume flow rates. The purpose of this study was to investigate the effects of changing transvalvular volume flow rate on aortic valve areas derived simultaneously by both the Gorlin and the continuity equations. A canine model of chronic valvular aortic stenosis, in which anatomy and hemodynamics are similar to those of degenerative aortic stenosis, was used in which pressure, volume flow rate, and Doppler-echo data could be acquired simultaneously during controlled variations in transvalvular volume flow rate.

Methods

All studies were approved by our institutional Animal Care Committee and were performed in accordance with National Institutes of Health guidelines.

Chronic Valvular Aortic Stenosis Model

Using a previously described protocol,19 8 adult mongrel dogs (weight, 18 to 24 kg) of either sex were tranquilized with thiamylal sodium (18 mg/kg) and anesthetized with halothane-diethyl ether azoate in 95% O2/5% CO2. After intubation, positive-pressure ventilation was delivered with a constant volume respirator at 20 ml/kg and 20 breaths per minute. Transfemoral arterial and venous polyethylene catheters were placed for hemodynamic monitoring, arterial sampling, and fluid administration. The ECG and arterial pressure were monitored continuously. Hypothermia was induced with direct surface cooling by ice water immersion and was monitored continuously by rectal temperature. Low molecular weight dextran (1 g/kg) was administered between 35°C and 25°C to reduce platelet aggregation. Cooling was terminated at 25°C to allow for thoracotomy and circuitary arrest.

Under sterile technique, a right thoracotomy was performed at the fourth interspace, and the pericardium was incised. The anterior parietal pericardium was excised to be used later to cover the obstructing masses used in creating valvular stenosis. Transthoracic aorta was induced at 21°C and was achieved by in- and outflow occlusion of the great vessels followed by cardioplegia with cold Young’s solution injected into the aortic root. An S-shaped aortotomy was performed, and three subcoronary obstructing masses were sutured with 3.0 Ti-CRON (Davis & Geck, Danbury, Conn) into each sinus of Valsalva, inferior to the coronary ostia, against the leaflet base and belly.20 The masses were created by rolling Teflon felt into small cylinders (8 to 9 mm in length by 5 to 6 mm in diameter), which were then covered with excised parietal tissue to avoid in vivo thrombus formation on their external surfaces. During placement of the masses, care was taken not to damage or distort the aortic cusps or obstruct the coronary ostia. The aortotomy was subsequently closed, and direct surface rewarming was initiated by rotation of the subject on a plastic sheet in a 40°C water bath. Resuscitation was achieved by manual massage and intravenous calcium chloride (300 mg). When necessary, epinephrine and electrical defibrillation also were used.

Implantable 16-mm nonconstricting transit-time flow probes (Transonics, Ithaca, NY) were placed around the ascending aorta during rewarming. A subcutaneous pocket was created to allow access to the implantable cable during follow-up studies. The chest was closed at 30°C, and active rewarming continued to 35°C. Recovery was monitored for 5 days after surgery. Gentamicin (2 mg/kg per day) and ampicillin (50 mg/kg per day) were given routinely for 3 days; intramuscular analgesia (buprenorphine 0.0125 mg/kg) was given routinely for 2 days and then as required for apparent discomfort.

With time, the pericardial covered masses fused to the aortic side of the leaflets at the basal flexion line, creating subcoronary valvular stenosis. In addition to decreased leaflet mobility, the leaflets began thickened but without commissural fusion. The Teflon felt masses were located in a similar position to the calcific deposits that are commonly observed in clinical degenerative aortic stenosis, with the masses simulating fibrocalsific changes (Fig 1). Progressive left ventricular hypertrophy developed during the 6- to 8-week follow-up. There was no evidence of congestive heart failure.

Study Protocol

After aortic stenosis induction, each subject underwent simultaneous Doppler-echo examinations and cardiac catheterization at 2-week intervals for a total of three studies per subject (6-week follow-up). General anesthesia with 1% halothane was used to avoid subject discomfort and activity during the study. A high-fidelity, dual-sensor micromanometer pressure catheter (Millar SPC 780C, Houston, Tex) with sensors 5 cm apart was calibrated and inserted via the carotid artery and advanced across the aortic valve under fluoroscopic guidance. The catheter was manipulated to avoid left ventricular sensor entrapment and to obtain artifact-free aortic pressure tracings and was used to measure simultaneous aortic and left ventricular pressures. Aortic regurgitation was detected by color-flow Doppler in all subjects when the catheter straddled the aortic valve. In only 1 subject was the regurgitation moderate in severity. The remaining subjects had either trivial or mild aortic insufficiency. Volume flow rates were measured by accessing the flow probe cable through an incision in the subcutaneous pocket and connecting to the flowmeter (Transonics T101D). The flow probe was factory calibrated (maximum error, ±15% of absolute volume flow; repeatability, ±2%), and adequate signal strength was verified at each study. Instantaneous volume flow measurements, left ventricular and aortic pressures, and a lead II ECG were recorded simultaneously into a PDP-11 computer with analog to digital conversion at 200 Hz.

ECG data were acquired with either an ATL Ultramark 6 (Advanced Technology Laboratories, Bothell, Wash) or Acuson 128 XP/10 instrument (Acuson, Mountain View, Calif) and a Ving-Med SD-100 Doppler instrument (Vingmed Inc, Allendale, NJ). Video images were recorded on half-inch VHS tape for later analysis. Left parasternal long-axis views of the left ventricular outflow tract were obtained in the left lateral decubitus position. Spectral pulsed Doppler data were col-
Invasive and Doppler-echo data were analyzed using an off-line analysis system (MicroSonic, Indianapolis, Ind) by an independent observer unaware of the invasive data (Fig 2). Left ventricular outflow tract diameter (LVOTd) was measured from the left parasternal long-axis view in midsystole parallel to the valve plane and immediately adjacent to the aortic leaflet insertion into the annulus. Left ventricular outflow tract cross-sectional area (CSALVOT) was calculated by assuming a circular shape such that
\[
CSALVOT = \pi \times (\text{LVOTd}/2)^2
\]
At least three high-quality Doppler left ventricular outflow tract and transvalvular velocity curves were traced and the average systolic velocity time integral determined for each profile (VTILVOT, VTILVOT). Stroke volume was calculated as
\[
SV = \text{VTILVOT} \times \text{CSALVOT}
\]
Mean transvalvular volume flow rate was derived by dividing stroke volume by the systolic ejection time. Peak instantaneous transvalvular pressure gradient (\(\Delta P_{\text{max}}\)) was calculated using the peak transvalvular velocity (\(V_{\text{max}}\)) and the simplified Bernoulli equation
\[
\Delta P_{\text{max}} = 4 \times (V_{\text{max}})^2
\]
Mean transvalvular pressure gradient (\(\Delta P_{\text{mean}}\)) was obtained by averaging the instantaneous pressure gradients calculated over
Altman.23 maximum was techniques defined transvalvular and least-squares using linear regression. The least-squares linear regression analyses and Pearson’s correlation coefficients.

Results Agreement of Doppler-Echo and Invasive Measurements of Transvalvular Volume Flow Rate and Valve Area

Simultaneous mean transvalvular volume flow rate derived by ascending aortic transit-time flow probe and Doppler-echo left ventricular outflow tract measurements compared well over a transit-time flow range of 29 to 250 mL/s (n=247, r=.84, SEE=24 mL/s) (Fig 4). Doppler-echo mean transvalvular volume flow rates tended to slightly overestimate transit-time volume flow rates (mean difference, 18±24 mL/s; P<.0001), with a 95% limit of agreement ranging from -30 to +66 mL/s of transit-time flow rate.

Doppler-echo continuity equation and Gorlin equation valve areas also correlated (n=247, r=.74, SEE=0.13 cm²) despite a small range of Gorlin valve areas from 0.17 to 1.09 cm² and despite changing volume flow rates (Fig 4). Valve area measurements by continuity equation were slightly greater than Gorlin equation valve areas (mean difference, 0.05±0.14 cm²; P<.0001), with a 95% limit of agreement of -0.23 to +0.33 cm².

Effects of Changing Volume Flow Rate on Valve Area Determination

In the 24 studies, mean transit-time transvalvular volume flow rate varied from 80±33 mL/s to a maximum of 153±49 mL/s (P<.0001). Simultaneous Doppler-echo volume flow rate demonstrated a similar range from 94±26 to 166±48 mL/s (P<.0001). Over the range of mean volume flow rates from minimum to maximum values, Gorlin equation valve areas varied from 0.54±0.22 to 0.68±0.21 cm² (P<.0001), whereas Doppler-echo continuity equation valve areas varied from 0.57±0.18 to 0.70±0.20 cm² (P<.0001). The absolute change ranged from -0.02 to 0.43 cm² (mean, 0.14 cm²) for Gorlin valve areas and from -0.09 to 0.36 cm² (mean, 0.14 cm²) for Doppler-echo continuity equation valve areas. The percent increase in calculated valve areas from the minimum to maximum transvalvular volume flow rate ranged from -3% to 99% (mean, 33%) by Gorlin equation and -14% to 111% (mean, 30%) by continuity equation, with an increase in transvalvular flow rate ranging from 9% to 218% (mean, 103%). Equally, the percent decrease in calculated valve areas from the maximum to the minimum transvalvular volume flow rate ranged from -3% to 50% (mean, 22%) by Gorlin equation and -17% to 53% (mean, 19%) by continuity equation, with a decrease in transit-time transvalvular volume flow rate ranging from 8% to 69% (mean, 47%).

Minimum and maximum Doppler-echo mean transvalvular volume flow rate varied from 89±26 to 177±41 mL/s (P<.0001). Over this range, Gorlin and Doppler-echo continuity equation valve areas also varied from 0.54±0.22 to 0.66±0.22 cm² (P<.0001) and 0.54±0.19 to 0.76±0.19 cm² (P<.0001), respectively.

Data are expressed as mean±1 SD. Doppler-echo and invasive transvalvular volume flow rates and valve areas were compared using least-squares linear regression analyses and calculation of the standard error of the estimate. Correlations were described by Pearson’s correlation coefficient. Agreement between techniques was assessed by the method described by Bland and Altman.23 Doppler-echo and invasive data at minimum and maximum mean transvalvular volume flow rate for each study were compared using a Student’s paired t test. A P value <.05 was considered significant. Valve areas calculated by Gorlin or Doppler-echo continuity equation were compared with volume flow rate using least-squares linear regression analyses and Pearson’s correlation coefficients.

Fig 3. Typical hemodynamic recordings collected at 200 Hz on a PDP-11 computer in one subject at two different volume flow rates. The ECG recording is displayed on top, instantaneous volume flow rate in the middle, and left ventricular (LV) and aortic (Ao) pressures at the bottom. The left recordings demonstrate the hemodynamics at one flow rate. The right recordings display the hemodynamics at a larger volume flow rate during dobutamine infusion. ∆Pmax indicates maximum instantaneous pressure gradient; ∆Pmean, mean pressure gradient; and SV, stroke volume.

the period of flow. Aortic valve area (Doppler AVA) was calculated using the continuity equation,2 2 such that

\[ \text{Doppler AVA} = \frac{(\text{VTI}_{LVOT}/\text{VTI}_{AO}) \times \text{CSA}_{LVOT}}{} \]

Doppler-Echo Data Reproducibility

Interobserver variability was calculated for absolute continuity equation valve area measurements by two observers each measuring 3 to 5 beats from 17 separate interventions. Intraobserver variability was calculated for one observer repeating the measurements at a 1-week interval. Variability was described by the 95% limits of agreement.23 Intraobserver and interobserver variability was small at ±0.10 cm² and ±0.11 cm², respectively.

Analysis of Invasive Hemodynamic Data

Invasive hemodynamic data were averaged from all cardiac cycles collected over the 30- to 60-second period during which the Doppler-echo data were also recorded (Fig 3). Stroke volume was determined by integrating the systolic area under the flow curve for each beat. Mean transvalvular volume flow rate was derived by dividing stroke volume by the systolic ejection time. The greatest instantaneous difference between left ventricular and aortic pressures over the ejection period was defined as the maximum pressure gradient. The mean pressure gradient was calculated by averaging the instantaneous positive pressure gradients from the crossovers of left ventricular and aortic pressures to end ejection, defined by the transit-time flow probe as zero flow crossover. Anatomic valve area was calculated using the Gorlin equation (Gorlin AVA)¹

\[ \text{Gorlin AVA} = \frac{\text{SV}}{44.3 \times \sqrt{\text{ΔP}_{\text{mean}}}} \]

Statistical Analysis

Data are expressed as mean±1 SD. Doppler-echo and invasive transvalvular volume flow rates and valve areas were compared using least-squares linear regression analyses and calculation of the standard error of the estimate. Correlations were described by Pearson’s correlation coefficient. Agreement between techniques was assessed by the method described by Bland and Altman.23 Doppler-echo and invasive data at minimum and maximum mean transvalvular volume flow rate for each study were compared using a Student’s paired t test. A P value <.05
Flow Dependence of Valve Area in Aortic Stenosis

Linear Relation of Transvalvular Volume Flow Rate and Gorlin Equation Valve Area

Valve area calculations were performed at 10.3±5.1 (range, 2 to 19) different volume flow rates per study. In the 23 studies with at least three separate volume flow rates, Gorlin valve area had a strong linear relation with transit-time volume flow rate, with a median correlation coefficient of .88 (range, .22 to .97) (Fig 5). Only 2 of 23 studies had correlation coefficients less than .60, 1 of which included only four volume flow rates. The slope of the regression line derived from the percent increase in Gorlin valve area, calculated from the valve area at the smallest mean transvalvular flow rate, versus percent increase in transit-time mean flow rate, calculated from the smallest flow rate in each study, ranged from −0.05 to 4.27 (median slope, 0.28) (Fig 6). Thus, the median slope predicts a 22% change in valve area for a doubling in mean transit-time volume flow rate.

Similarly, Gorlin equation valve area also demonstrated a linear relation with Doppler-echo volume flow rate with a median correlation coefficient of .72 (range, −.38 to .97) (Fig 5). Correlation coefficients were greater than .60 in 13 of the 23 studies with greater than three volume flow rates.

Linear Relation of Transvalvular Volume Flow Rate and Doppler-Echo Continuity Equation Valve Area

Continuity equation valve area correlated linearly with transit-time volume flow rate with median correlation coefficient of .51 (range, −.39 to .97) and with 9 of the 23 studies having coefficients greater than .60 (Fig 5). The slopes of the regression line derived for percent increase in Doppler-echo continuity equation valve area, calculated from the valve area at the smallest mean transvalvular flow rate, versus percent increase in transit-time mean flow rate, calculated from the smallest flow rate in each study, ranged from −0.14 to 5.48 (median slope, 0.22) (Fig 6). Thus, the median slope predicts a 22% change in valve area for a doubling in mean transit-time volume flow rate.

Continuity equation valve areas had a strong linear relation with Doppler-echo volume flow rates (Fig 5). The median correlation coefficient was .85 (range, .13 to .98), with 16 of the 23 studies with at least three volume flow rates having coefficients greater than .60.

Intersubject and Intrasubject Temporal Variability for Changes in Valve Area With Changes in Transvalvular Volume Flow Rate

The slopes of the regression line for percent increase in valve area from the smallest mean transvalvular flow rate versus percent increase in transvalvular transit-time volume flow rate demonstrated marked variability both between subjects and temporally within a subject. The mean slopes for the 8 subjects, derived by averaging the three studies performed in each subject, had a standard deviation of ±0.41 for Gorlin equation valve areas and ±0.69 for continuity equation valve areas (intersubject variability). The average standard deviation of the slopes from the three studies in each subject was ±0.45 for Gorlin equation valve areas and ±0.71 for continuity equation valve areas (intrasubject temporal variability).

Discussion

This canine model of valvular aortic stenosis, which mimics the anatomy and hemodynamics of degenerative aortic valve stenosis, has provided a setting to investigate intensively the effects of altered volume flow rate on aortic valve areas calculated simultaneously using the Gorlin equation and Doppler-echo continuity equation. We observed that a change in transvalvular volume flow rate resulted in a change in calculated valve area using either invasive measurements with the Gorlin equation or Doppler-echo measurements with the continuity equation.

Only a modest correlation (r=.74) was observed between simultaneous Gorlin and continuity equation valve areas. This is not surprising for several reasons. First, valve areas derived by the two equations are conceptually different. The continuity equation calculates effective orifice area, whereas the Gorlin equation uses a constant to derive anatomic valve area. Additionally, variability of the discharge coefficients incorporated in the Gorlin constant and a small error in
mathematical formulation of the Gorlin equation may result in further discrepancy between valve area measurements.\textsuperscript{15,17,24} Second, valve area is derived from individual measurements of either pressure and flow or velocity and outflow tract dimension, each associated with error in measurement accuracy. Third, small discrepancies in valve area measurements may affect significantly the calculated correlation coefficient over the narrow range of stenotic valve areas studied (0.17 to 1.09 cm\textsuperscript{2} by Gorlin equation). Importantly, the 95% limits of agreement of continuity and Gorlin equation valve areas were small and less than the reported accuracy of the Gorlin equation.\textsuperscript{14}

**Effects of Altered Volume Flow Rate on Gorlin Equation Valve Areas**

Several previous studies have documented changes in Gorlin valve areas for stenotic native aortic valves induced by changes in volume flow rate both in vitro\textsuperscript{25} and in patients.\textsuperscript{7,12} In studies in which mean transvalvular flow rates were available, Gorlin valve areas were observed to increase 19% to 50% with a 50% increase in transvalvular volume flow rate. Similarly, 5% to 22% increases in Gorlin valve area have been observed with 50% increases in transvalvular flow rate for native and stenotic bioprosthetic valves in vitro.\textsuperscript{14,17,25} The current canine model of chronic valvular aortic stenosis resulted in a mean valve area change of comparable magnitude (17%) with a 50% increase in volume flow rate. Additionally, a 24% decrease in Gorlin valve area was demonstrated with a 50% decrease in transvalvular flow rate.

The change in Gorlin equation valve areas may result in part from a “true” change in anatomic area. Video images of in vitro pulsatile flow models have documented that valve orifice area does increase with increasing volume flow rate.\textsuperscript{14,25-28} Presumably because greater flow-mediated forces are delivered to a nonrigid valve.\textsuperscript{13} However, elaborate in vitro studies using inflexible orifices also have documented changes in Gorlin valve areas with altered volume flow rate.\textsuperscript{14,15} Two components of the Gorlin constant, the coefficients of velocity and orifice contraction, have been found to vary with volume flow rate\textsuperscript{15} in addition to orifice area, eccentricity, and inlet geometry.\textsuperscript{24} Assuming that these coefficients are constant despite varying flow conditions results in changes in Gorlin valve area that may not represent actual changes in anatomic valve area. Presumably, increases in volume flow rate may affect the discharge coefficients directly or may indirectly modify their value by altering valve geometry. However, it seems unlikely that the changes in Gorlin valve area that we observed were due solely to changes in discharge coefficients, because similar changes were observed for valve areas calculated by the continuity equation.

The large number of volume flow rates performed in this study allowed us to assess the relation between changes in valve area and changes in transvalvular volume flow rate. Previous in vitro flow models have described a linear relation for normal native aortic and bioprosthetic orifice areas measured by video analysis\textsuperscript{25,27} or calculated by the Gorlin equation.\textsuperscript{17} Similarly, a linear relation has been described for small numbers of in vitro stenotic native aortic and bioprosthetic orifice areas also measured by video analysis\textsuperscript{26,27} or by the Gorlin equation.\textsuperscript{14} However, results have been inconsistent.\textsuperscript{28} The current study provides strong evidence for a linear relation of Gorlin valve areas and transvalvular flow rate in vivo. The slope of the Gorlin valve area–flow relation was observed to vary both between subjects and...
temporally within the same subject. Most likely, the area-flow relation for a given valve is determined by its precise anatomy and geometry, which would be expected to differ between subjects and within subjects as the valve response (inflammation, fibrosis, etc) evolved after stenosis induction.

Effects of Altered Volume Flow Rate on Continuity Equation Valve Areas

In this study, Doppler-echo continuity equation valve areas also were flow dependent with changes similar in magnitude to those measured by the Gorlin equation. In a previous in vitro study,27 continuity equation valve areas were observed to parallel volume flow–mediated increases in video-imaged orifice areas for 12 native and bioprosthetic aortic valves, 5 of which were stenotic. However, there was a tendency for the continuity equation to underestimate imaged orifice areas at higher flow rates and to overestimate them at lower flow rates. In a clinical study of patients with asymptomatic aortic stenosis,28 a 22% increase in exercise-induced volume flow rate resulted in a 9% increase in continuity equation valve area. Another smaller study failed to demonstrate an increase in continuity equation valve areas with a 26% increase in volume flow rate induced by dobutamine infusion despite an increase in simultaneous Gorlin equation valve areas.

Several possibilities might explain these discordant observations. First, the stenotic valves in our study were characterized by thickened, stiff leaflets without commissural fusion. Postmortem examination demonstrated that although orifice areas were reduced, greater cusp excursion could be induced by manually applying a greater force through the valve leaflets from below. In essence, there was stiffness of the body of the leaflets but flexibility at the base. Thus, the actual orifice area would be expected to change with alterations in volume flow rate as flow-mediated forces fluctuated. Similarly, patients with asymptomatic aortic stenosis may have a degree of valve flexibility accounting for exercise-induced increases in continuity equation valve areas. In contrast, patients with symptomatic stenosis8 may have immobile, heavily calcified, nonflexible valves. These observations support the intriguing hypothesis that the onset of symptoms in aortic stenosis may be predicted by valve rigidity, indicated by the lack of increase of continuity equation valve areas with increases in volume flow rate.30 In this situation, continuity equation valve areas could theoretically remain constant whereas Gorlin equation valve areas change as a result of flow-mediated perturbations in the coefficient of velocity.

The linear relation between continuity equation valve areas and mean transit-time transvalvular volume flow rates was weaker than that observed for Gorlin valve areas. This probably results primarily from measurement variability of Doppler-echo continuity equation valve area measurements. The 0.14-cm² mean change in continuity equation valve areas during a study approaches the 95% limits of agreement for reproducibility of valve area measurements in this model (±0.11 cm²). Additionally, when continuity equation valve areas are compared with Doppler-echo transvalvular volume flow rates, thereby eliminating differences in Doppler-echo and transit-time volume flow determinations, the median correlation coefficient increases to .85. In vitro studies have suggested that continuity equation valve areas, derived by invasive pressure and flow measures in bioprosthetic valves in vitro, are linearly related to transvalvular flow.17 The current study demonstrates that in vivo, Doppler-echo derived continuity equation valve areas also have a linear relation with transvalvular volume flow rate.

Potential Limitations

Lack of Absolute Standard of Reference

In this study, we cannot determine with certainty whether the observed changes in calculated valve areas by both Gorlin and continuity equations represent true increases in anatomic orifice area or reflect changing flow dynamics. No "gold standard" measurement of anatomic valve area exists in vivo to which the observed valve area changes can be compared. Further, flexibility of the valve leaflets limits accurate postmortem anatomic measurement to the precise forces and conditions applied to the leaflets at the time of inspection. Of note, the changes in both Gorlin and continuity equation valve areas were similar in direction and magnitude. While the possibility of flow-mediated variability in the Gorlin constant cannot be excluded, Doppler-echo con-
Doppler-Echo Assessment of Volume Flow Rate

The presence of a large proximal flow acceleration region in the left ventricular outflow tract may complicate volume flow measurements used in calculating valve area by continuity equation. If the pulsed Doppler sample volume is positioned too close to the stenotic valve, sampling of accelerated velocities in the proximal flow convergence can lead to erroneous flow measurements and an overestimation of valve area by continuity equation. However, we used a 5-mm-length sample volume and excluded velocity profiles with spectral broadening, thus minimizing the potential to measure velocities within this region.

The measurement of volume flow rate in the left ventricular outflow tract by Doppler-echo techniques assumes that the spatial velocity profile is flat, and thus the ratio of spatially averaged and maximum velocity approaches unity. Theoretically, variations in the spatial velocity profile from flow-mediated perturbations in boundary layer thickness could result in a discrepancy between Doppler-echo and transit-time measurements. However, experimental evidence supports the assumption of a flat velocity profile for both left ventricular outflow tract and transvalvular flow at different flow rates in valvular aortic stenosis. Discrepancy in Doppler-echo and transit-time volume flow rates may result in part from variability in the pulsed Doppler sample volume position within the outflow tract with optimization of Doppler recordings at different flow rates and measurement error in transit-time volume flow rate determination (accuracy, ±15%).

Relation to Clinical Disease

We used a model of chronic valvular aortic stenosis to investigate intensively the effects of altered volume flow rate on simultaneous Gorlin and continuity equation valve areas. This allowed avoidance of the risks of prolonged catheterization or administration of pharmacological agents to a population of patients with aortic stenosis and a high prevalence of coronary artery disease. While this model clearly has a valvular lesion that differs from degenerative valvular aortic stenosis on histological examination, the gross valve anatomy is similar, with thickened leaflets but without commissural fusion. The masses are in a similar location to the calcific deposits present in the clinical disease, and left ventricular hypertrophy develops in response to the outflow obstruction. The observed changes in Gorlin valve area with changes in transvalvular flow rate were of similar magnitude to those described in patients with valvular aortic stenosis. This suggests that the observed relation of transvalvular volume flow rate with valve area derived either by Gorlin or Doppler-echo continuity equation accurately reflects expected phenomena in the clinical disease.

In this model, the severity of stenosis created was in the range of severe aortic stenosis for human subjects.

However, several observations suggest that flow dependence of either valve area technique will occur over the spectrum of mild to severe aortic stenosis. First, we did not observe a relation between the initial valve area and the slope of the valve area–transvalvular volume flow rate relation in our experimental model. In addition, both in vitro and in vivo studies have demonstrated flow dependence of Gorlin and continuity equation valve areas in the presence of milder degrees of stenotic native aortic valves and bioprostheses.

Clinical Implications

The absolute changes in valve area calculated by both Gorlin and continuity equations are small, and the clinical importance of these observations is as yet undetermined. It appears unlikely that the 0.14-cm² change in valve area observed with Gorlin and continuity equations would have a significant effect on clinical decision making. However, this also represents a mean 33% and 30% increase in valve area, respectively, with a mean doubling in transvalvular volume flow rate, and a mean 24% and 20% decrease in valve area, respectively, with a halving of transvalvular flow rate. Should further study demonstrate that observed percent changes in valve area are maintained at larger valve areas, flow dependence of calculated valve areas may have significant effects on clinical decision making. In accordance with current clinical experience, both Gorlin and continuity equation valve areas may be difficult to interpret in patients with reduced transvalvular flow associated with left ventricular dysfunction (coronary artery disease, cardiomyopathy). Clinical decision making may be further complicated when symptom etiology is unclear. Importantly, significant variability was observed in the response of individual valves to changing volume flow rate. Large increases in calculated areas were observed with some valves, whereas others appeared relatively rigid.

Conclusions

In this chronic model of valvular aortic stenosis, valve areas derived by either the Gorlin equation or the Doppler-echo continuity equation were flow-dependent indices of stenosis severity. Changes in transvalvular volume flow rate resulted in linear changes in Gorlin and continuity equation valve areas. This relation has potential clinical implications for the assessment of hemodynamic severity using either technique in patients with degenerative valvular aortic stenosis.

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