Experimental Validation of Doppler Echocardiographic Measurement of Volume Flow Through the Stenotic Aortic Valve

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In aortic stenosis, evaluation of aortic valve area by the continuity equation assumes that the volume of flow through the stenotic valve can be measured accurately in the left ventricular outflow tract. To test the accuracy of Doppler volume-flow measurement proximal to a stenotic valve, we developed an open-chest canine model in which the native leaflets were sutured together to create variable degrees of acute aortic stenosis. Left ventricular and aortic pressures were measured with micromanometer-tipped catheters. Volume flow was controlled and varied by directing systemic venous return through a calibrated roller pump and back to the right atrium. Because transaortic volume flow will not equal roller pump output when there is coexisting aortic insufficiency (present in 67% of studies), transaortic flow was measured by electromagnetic flowmeter with the flow probe placed around the proximal descending thoracic aorta, just beyond the ligated arch vessels. In 12 adult, mongrel dogs (mean weight, 25 kg), the mean transaortic pressure gradient ranged from 2 to 74 mm Hg, and transaortic volume flow ranged from 0.9 to 3.2 L/min. In four dogs, electromagnetic flow that was measured distal to the valve was accurate compared with volume flow determined by timed collection of total aortic flow into a graduated cylinder (n = 24, r = 0.97, electromagnetic flow = 0.87 Direct + 0.13 L/min). In eight subsequent dogs, electromagnetic flow was compared with transaortic cardiac output measured by Doppler echocardiography in the left ventricular outflow tract as circular cross-sectional area [π(D/2)^2] × left ventricular outflow tract velocity-time integral × heart rate. Agreement of the two methods was good (n = 52, r = 0.91, y = 1.00x + 0.03 L/min), and in individual dogs, directional changes in volume flow as measured by both methods were in agreement. We conclude that Doppler echocardiographic measurement of volume flow proximal to the stenotic valve is accurate in this canine model of acute valvular aortic stenosis. (Circulation 1988;78:435–441)

The continuity equation has been proposed as a means to determine stenotic aortic valve area by data from Doppler echocardiography. Several clinical studies have shown reasonable agreement between valve areas determined by data from the Doppler continuity-equation and valve areas determined at catheterization by the Gorlin formula, but moderate scatter of the data has been noted. Although valve areas determined at catheterization are used as the reference standard, there are a number of potential sources of error when invasive transaortic pressure gradient and volume-flow measures are made in the clinical setting, and the Gorlin formula itself has inherent limitations. Thus, it remains unclear whether disagreement between valve areas determined by the two methods are due to inaccuracies of Doppler echocardiography, errors in the standard of reference, or both.

The continuity equation requires accurate measurement of both the high-velocity aortic jet and the volume of blood flow through the stenotic aortic valve. Experimental and clinical studies of aortic stenosis have shown that invasive transaortic pressure gradients correlate closely with simultaneous
Doppler pressure gradients calculated from aortic jet velocities by the modified Bernoulli equation.\textsuperscript{12–23} These studies confirm that the high-velocity aortic jet can be recorded accurately.

However, validation of the other component of the continuity equation, that is, transaortic volume flow, has been more difficult.\textsuperscript{24} In animal models and patients with intracardiac shunts, volume flow can be measured by Doppler echocardiography at several different intracardiac sites where flow is undisturbed and laminar, where the spatial profile of flow velocities is relatively blunt, and where the cross-sectional area of flow can be measured.\textsuperscript{25–27} This method has been applied with success in adult patients without aortic stenosis.\textsuperscript{28,29} In aortic stenosis, however, volume flow cannot be measured in the ascending aorta because of nonlaminarity of flow downstream from the stenosis. Potentially, volume flow could be measured in the pulmonary artery or across the mitral valve. Unfortunately, these approaches are limited by technical factors. Imaging of the lateral wall of the pulmonary artery is often inadequate for diameter measurement, and accurate measurement of mitral annulus diameter is limited by the high prevalence of annular calcification in adults with aortic stenosis.\textsuperscript{24} Furthermore, neither pulmonary artery nor transmitral flow is equivalent to transaortic volume flow if coexisting aortic insufficiency is present as is found in 80% of adults with predominant aortic stenosis.\textsuperscript{2–24}

Stroke volume has been measured accurately from dimensions and velocities recorded in the left ventricular outflow tract (LVOT) in patients without aortic stenosis.\textsuperscript{29} Fluid dynamic considerations suggest that when blood is ejected across a discrete stenotic orifice, flow proximal (upstream) to the stenosis will be relatively laminar and normal in velocity with a blunt flow-velocity profile, especially if the area of flow converges (as it does in the outflow tract).\textsuperscript{9,30,31} Clinical observations indicate that LVOT flow is undisturbed and normal in velocity in aortic stenosis. Thus, in applying the continuity equation to patients with aortic stenosis, we\textsuperscript{24} and others\textsuperscript{1} have measured transaortic volume flow in the LVOT, just proximal to the stenotic valve. However, comparisons of Doppler echocardiographic and invasive transaortic volume-flow measures in clinical patients with aortic stenosis have been somewhat disappointing.

Unfortunately, it is difficult to ascertain to what degree the disagreement between the two methods is due to shortcomings in the experimental method as opposed to limitations in the standard of reference. There are many potential sources of error in transaortic volume-flow measurement by Fick or thermodilution techniques (which can be used in the absence of coexisting aortic insufficiency) or by angiographic techniques (needed when aortic insufficiency is present), and the inherent accuracy of these techniques is only about ±10%.\textsuperscript{32,33} In addition, many adults with aortic stenosis have both aortic insufficiency and mitral regurgitation. Although not always clinically significant, these conditions do preclude exact measurement of transaortic volume flow in the cardiac catheterization laboratory.

Therefore, the purpose of this study was to develop an in vivo model of valvular aortic stenosis in which transaortic volume flow can be varied and measured directly and then to test the accuracy of Doppler echocardiographic measurement of volume flow proximal to the stenotic valve.

**Materials and Methods**

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

**Surgical Preparation and Instrumentation**

Twelve adult mongrel dogs ranging in weight from 20 to 31 kg (mean, 25 kg) were anesthetized with sodium thiopental (18 mg/kg i.v.). After endotracheal intubation, anesthesia was maintained with halothane and 100% oxygen. Ventilation before cardiopulmonary bypass surgery was controlled by a Harvard constant-volume ventilator (South Natick, Massachusetts) adjusted to provide an arterial oxygen tension greater than 100 mm Hg. The electrocardiogram was recorded from peripheral limb leads. The heart was exposed by a median sternotomy, and after systemic heparinization (3 mg/kg), perfusion cannulas were inserted into the left carotid artery and superior and inferior venae cavae. Two Millar micromanometer-tipped catheter transducers (Houston, Texas) were used to measure arterial and left ventricular pressures. Arterial pressure was measured by an 8F catheter positioned in the ascending aorta. Left ventricular pressure was measured by a 7F catheter that was inserted into the left ventricle through the left atrial appendage.

In this model, volume flow was controlled and varied by directing systemic venous return through a calibrated roller pump (Edward A. Olson, Ashland, Massachusetts) and back to the right atrium. The extracorporeal system consisted of a Bentley BOS-5 pediatric bubble oxygenator (Irvine, California), Q-110 cardiectomy reservoir, Tygon tubing, and the roller pump. The system was primed with lactated Ringer’s solution, 6% Macrodex (Dextran 70), and fresh homologous blood. Blood return to the extracorporeal circuit was augmented as needed by cannulating the femoral arteries bilaterally and connecting them to a second roller pump, which returned blood to the cardiectomy reservoir. All animals were perfusion-cooled to a mean rectal temperature of 28°C before the induction of cardioplegic arrest and creation of valvular aortic stenosis. A cold, potassium, cardioplegic solution, administered through the aortic root (Plasma-Lyte A, Travenol Laboratories, Deerfield, Illinois), was used for myocardial protection during ischemia.
Valvular aortic stenosis was created through an ascending aortotomy. Two (in four dogs) or three (in eight dogs) aortic commissures were sutured together with pledgeted sutures to create varying degrees of aortic stenosis. Aortic cross-clamp time averaged 30 minutes. Hearts that failed to convert spontaneously to sinus rhythm were electrically defibrillated. Cardiotonics, including calcium chloride, epinephrine, and sodium bicarbonate, were given as needed to establish a physiological postischemic hemodynamic and blood-gas profile.

Maximum manometric transaortic pressure gradients ranged from 2 to 120 mm Hg, averaging 34 mm Hg. Mean pressure gradients ranged from 2 to 74 mm Hg, averaging 19 mm Hg. Distortion of aortic leaflet diastolic coaptation by the pledgeted sutures resulted in coexisting aortic insufficiency in 67% (eight of 12) of studies. Aortic insufficiency as assessed by pulsed-Doppler flow mapping was mild in five and moderate in three animals. Thus, this model resulted in predominant aortic stenosis, usually accompanied by aortic regurgitation, with hemodynamics similar to those observed in patients with valvular aortic stenosis.

Because roller-pump output does not equal transaortic flow when there is coexisting aortic insufficiency, transaortic volume flow was measured with an electromagnetic (EM) flowmeter (ZWF-4RD, Zepeda Instruments, Seattle, Washington). Volume-flow measurement by EM flowmeter may be influenced by turbulence and is inaccurate when the flow profile is skewed across the vessel lumen. Theoretical considerations suggest that flow should relaminarize and develop a relatively symmetric profile of velocities approximately five-vessel diameters distal to the stenosis. Therefore, an appropriately sized cuff-type flow probe was placed around the proximal descending thoracic aorta (about five-aortic diameters distal to the valve), and all branch vessels proximal to the flow probe were ligated. At the end of each experiment, the flow probe and attached aorta were explanted and calibrated by timed collection of saline at several known flow rates.


To ensure that EM transaortic volume-flow measurement was accurate in this open-chest model, a timed-collection technique was used in the first four dogs. A Gortex graft was anastomosed end-to-side to the descending aorta distal to the flow probe. Then, the descending aorta was cross-clamped below the graft, and timed collection of total aortic blood flow into a graduated cylinder was performed simultaneously with EM aortic volume-flow measurement (Figure 1). This procedure was repeated at several different roller-pump rates for each animal.

Part 2. Doppler and Two-Dimensional Echocardiography Transaortic Volume Flow

In the remaining eight dogs, Doppler and two-dimensional echocardiographic data were recorded in open-chest animals at several different volume-flow rates, beginning approximately 1 hour after suturing the aortic leaflets, with simultaneous EM-flow curves. Invasive measures of aortic stenosis severity for these eight dogs are shown in Table 1, with valve areas calculated by the Gorlin formula. Two-dimensional echocardiographic images of the LVOT were obtained with the transducer placed directly on the epicardial surface of the heart, oriented perpendicular to the long axis of the outflow tract, with a commercial echocardiographic instrument (ATL-600, Advanced Technology Laboratories, Bothell, Washington). Real-time images were recorded on ½-in. VHS videotape. The transducer then was placed directly on the cardiac apex, and flow in the LVOT was recorded with

![FIGURE 1. Schematic of aortic stenosis model, part 1. Timed collection of aortic blood flow was compared with transaortic flow measured by electromagnetic (EM) flowmeter. See text for details. LA, left atrium; LV, left ventricle; RA, right atrium.]

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**Table 1. Severity of Aortic Stenosis Measured by Doppler and Two-Dimensional Echocardiography (Group 2)**

<table>
<thead>
<tr>
<th>Dog</th>
<th>Maximum ΔP (mm Hg)</th>
<th>Mean ΔP (mm Hg)</th>
<th>AVAS (cm²)</th>
<th>AI (0–4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>6–20</td>
<td>3–10</td>
<td>0.6</td>
<td>1 +</td>
</tr>
<tr>
<td>6</td>
<td>6–41</td>
<td>4–26</td>
<td>0.5</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>12–26</td>
<td>9–12</td>
<td>0.4</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>21–40</td>
<td>15–24</td>
<td>0.3</td>
<td>1 +</td>
</tr>
<tr>
<td>9</td>
<td>61–120</td>
<td>35–74</td>
<td>0.2</td>
<td>1 +</td>
</tr>
<tr>
<td>10</td>
<td>5–25</td>
<td>3–18</td>
<td>0.4</td>
<td>2 +</td>
</tr>
<tr>
<td>11</td>
<td>31–63</td>
<td>19–39</td>
<td>0.3</td>
<td>1 +</td>
</tr>
<tr>
<td>12</td>
<td>8–21</td>
<td>6–14</td>
<td>0.4</td>
<td>1 +</td>
</tr>
</tbody>
</table>

ΔP, pressure change; AVAS, area of valvular aortic stenosis; AI, aortic insufficiency.
conventional pulsed Doppler with a sample volume of 9 mm in axial dimension. The LVOT-velocity curve was recorded close to the stenotic valve but just proximal to the region where flow began to accelerate into the stenotic jet (Figure 2). Care was taken to record flow velocity in a region where mapping across the outflow tract suggested that the profile of velocities was uniform.

Data Analysis

The electrocardiogram, left ventricular and aortic pressures, and EM transaortic flow curves were recorded simultaneously at 100 mm/sec on an eight-channel Hewlett-Packard Physiologic Recorder (model 7788A, Palo Alto, California). Stroke volume was calculated from the area under the EM-flow curve with the postmortem flow probe calibration for each dog. Cardiac output was calculated by multiplying stroke volume by heart rate. All values were averaged from five to 10 representative cardiac cycles.

The Doppler echocardiographic data were analyzed with a DataVue System (MicroSonics, Indianapolis, Indiana) with a digitizer board and video overlay system. With the parasternal long-axis image, LVOT diameter was measured in midsystole just below the aortic valve leaflets, from the leading edge of the left septal endocardium to the leading edge of the basal anterior mitral leaflet. The average diameter was calculated from five to 10 beats, and circular cross-sectional area (CSA) was calculated as $\pi(D/2)^2$. In a subset of studies, average LVOT cross-sectional area was determined directly by planimetry of short-axis images from three to five beats. The velocity-time integral (VTI), planimetered as the outer border of the pulsed-Doppler spectral display, was averaged from five to 10 beats. Stroke volume (SV) was calculated as $SV = CSA \times VTI$, and cardiac output was determined by multiplying stroke volume by heart rate (Figure 3).

Doppler echocardiographic and EM measurements of volume flow were determined independently. Methods were compared by linear regression, and Pearson’s correlation coefficients were calculated.

Results

1. Electromagnetic Flow and Directly Measured Transaortic Volume Flow

Transaortic cardiac output measured by EM flowmeter for 24 data points from four studies correlated closely with transaortic flow by timed-volumetric collection, in the range of 0.4–2.4 l/min. As shown in Figure 4, the regression line closely parallels the line of identity with a small positive y-intercept ($r=0.97, y=0.87x+0.13$ l/min, SEE = 0.12 l/min). When the distal aorta was cross-clamped, a steady state could not be achieved in these dogs at flow rates higher than 2.5 l/min.

2. Doppler and Two-Dimensional Echocardiography Transaortic Volume Flow

Figure 5 shows the correlation between Doppler and EM transaortic cardiac output in aortic stenosis, cardiac output ranging from 0.9 to 3.2 l/min. This corresponds to an output varying from 36 to 128 ml/min/kg body wt. The regression line ($r=0.91$, $y=1.00x+0.03$ l/min, SEE = 0.25 l/min) closely approximates the line of identity. The results are similar when stroke volume by the two methods is compared ($r=0.88$, $y=0.97x+1.45$ ml, SEE = 2.42 ml), ranging from 5.1 to 25.9 ml. Higher flow rates could not be achieved in these dogs with acute aortic stenosis because higher roller-pump rates resulted in an acute increase in left ventricular end-diastolic pressure, left ventricular systolic dysfunction and dilatation, and right ventricular distension and failure.

![Figure 3](http://circ.ahajournals.org/)

**Figure 3.** Left panel: Two-dimensional echocardiogram for LVOT diameter (D) measurement. Circular cross-sectional area (CSA) was calculated as shown. Ao, aorta; LV, left ventricle; LA, left atrium. Right panel: Pulsed-Doppler recording of LVOT velocity showing the velocity-time integral (VTI). Flow curve is inverted; SV, stroke volume.
Flowmeter (y axis) measurement

Doppler from short-axis images just of Doppler level (n = valvular aortic stenosis cardiac with test), measurements the two rather than by supravalvular flow volume models of directional of a was shown in change in in changes aortic volume were not variation for of variation between repeat o20 we to direction (x axis) and electromagnetic flow (x axis) of electromagnetic flow (x axis) for three of the animals. Directional changes in flow were mainly due to changes in the velocity-time integral, with little change in LVOT diameter or cross-sectional area.

Cross-sectional areas calculated from long-axis LVOT-diameter measurements were not different from cross-sectional areas planimetered directly from short-axis images just below the aortic valve level (n = 15, 2.74 vs. 2.78 cm², p = NS by paired t test), with a mean coefficient of variation between the two methods of 5%. The mean coefficient of variation for repeat LVOT-diameter measurements (n = 29) was only 2%. Use of directly measured rather than calculated-LVOT area does not change the cardiac output results.

Discussion

In this study, we developed an animal model of acute valvular aortic stenosis to judge the accuracy of Doppler echocardiographic measurement of volume flow proximal to the stenotic valve. Previous models of acute aortic stenosis used obstructions created by supravalvular constriction or plication of a sinus of Valsalva, neither of which resembles the pathological process seen clinically. Accordingly, we created stenosis at the valvular level by suturing the leaflets together so that the anatomy, hemodynamics, and subvalvular flow patterns were similar to the clinical disease. We avoided stainless steel clips, which would interfere with Doppler recordings.

Our method resulted in acute valvular aortic stenosis with an appropriate range of pressure gradients and valve areas. Valve areas determined by the Gorlin formula were calculated as an index of stenosis severity, although the limitations of this measurement make it unsuitable as a reference standard for validation of noninvasive valve area determinations. In addition, mild or moderate coexisting aortic insufficiency occurred in the majority of cases as is seen commonly in the clinical disease. Although aortic stenosis in adult patients most often is due to a rigid calcified valve and although the leaflets are thin but "fused" in this model, subvalvular hemodynamics should be similar in both situations. A model of chronic aortic stenosis has been described that results in rigid, thickened aortic valve leaflets, which is more similar to calcific aortic stenosis; however, we chose a model of acute aortic stenosis to control, vary, and measure cardiac output accurately.

A disadvantage of the acute model was that it neither results in the changes in left ventricular mass or geometry that would be expected with chronic disease, nor does it mimic the clinical pattern of valve calcification that potentially could result in an abnormal prestenotic flow profile. Although the model with acute aortic stenosis also limited the range of flow rates that could be achieved, the range of flow rates studied includes the normal flow rate for a dog (approximately 100 ml/kg/min) and encompasses low flow rates, which are most important clinically.

Volume flow was varied in this model with a roller pump that returned systemic venous blood to the right atrium. Transaortic volume flow was measured by EM flowmeter because if coexisting aortic

![Figure 4](http://circ.ahajournals.org/)

**Figure 4.** Plot of direct (x axis) and electromagnetic flow (y axis) measurement of transaortic volume flow distal to the stenotic aortic valve.

![Figure 5](http://circ.ahajournals.org/)

**Figure 5.** Plot of electromagnetic flow (x axis) and Doppler LVOT cardiac output (CO) (y axis).

![Figure 6](http://circ.ahajournals.org/)

**Figure 6.** Plot of directional changes in cardiac output (CO) measured by Doppler (y axis) compared with electromagnetic flow (x axis) in three representative studies.

For individual dogs, directional changes in transaortic volume flow generally were accompanied by similar directional changes in Doppler volume flow as shown in Figure 6 for three of the animals. Directional changes in flow were mainly due to changes in the velocity-time integral, with little change in LVOT diameter or cross-sectional area.
When insufficiency is present, roller-pump output will differ from transaortic volume flow. The EM flow probe was placed approximately five-vessel diameters distal to the aortic valve for both practical reasons (ascending aortotomy needed to create valvular stenosis) and theoretical considerations (effect of turbulence and skewed velocity profile on flow probe accuracy). Thus, the accuracy of cardiac output measured by EM flowmeter was validated in comparison with direct, timed collection of transaortic blood flow. However, in the presence of severe aortic insufficiency, the theoretical possibility that flow in the descending aorta will not equal transaortic flow if the ascending aorta acts as a capacitor cannot be excluded with certainty.

Then, using simultaneous volume flow measured by an EM flowmeter as the reference standard, we recorded Doppler echocardiographic data in the LVOT, just proximal to the stenotic valve, to calculate transaortic volume flow. There was good agreement between the two techniques both for the entire set of data points and for directional changes in transaortic volume flow in individual animals. Based on these data, we conclude that Doppler echocardiographic measurement of transaortic volume flow in aortic stenosis is accurate and that directional changes in volume flow can be followed with this technique.

However, several potential limitations of this study must be acknowledged. The Doppler method is based on both anatomic and hemodynamic assumptions. First, the LVOT is assumed to be circular, constant in size and shape during systole, and filled by forward flow. Review of short-axis, two-dimensional echocardiographic images of the LVOT in each study, the excellent agreement between calculated and planimetered LVOT cross-sectional areas, and color-Doppler flow echocardiograms in a subset of animals suggests that these assumptions are warranted. This method also assumes that flow in the LVOT is laminar, which is supported by the finding of a smooth velocity curve in the outflow tract, with a narrow band of velocities throughout systole. Finally, it is assumed that the three-dimensional flow velocity profile is blunt. Careful sampling across the outflow tract in two tomographic planes shows a relatively uniform profile of flow velocities in the region just below the stenotic valve, but more precise characterization of subvalvular fluid dynamics was not possible in our animal model.

One further assumption is that diameter and velocity are measured at the same anatomic location in the outflow tract. LVOT diameter was measured from long-axis images obtained with the ultrasound transducer oriented perpendicular to the septal endocardial edge and anterior mitral valve leaflet, thus taking advantage of more accurate axial resolution rather than lateral beam resolution. However, the outflow tract systolic velocity curve was recorded from an apical approach to orient the ultrasound beam parallel to flow. Thus, to ensure that these two measurements were taken at the same level in the outflow tract, diameter was measured just below the stenotic valve (where the outflow tract is circular), and the velocity curve was recorded with the sample volume as close as possible to the stenotic valve.

We found that outflow tract cross-sectional areas calculated from long-axis diameters were nearly identical to areas measured by planimetry of short-axis images. We believe the long-axis diameter approach is preferable. Alignment of short-axis images perpendicular to the outflow tract is more difficult, and misalignment can result in an oblique tomographic plane; the absence of long-axis reference points results in greater difficulty in acquiring the tomographic plane just below the aortic leaflets; and, even with the excellent image quality in this open-chest dog model, lateral beam resolution limits the certainty with which the lateral and medial edges of the outflow tract can be identified.

Other studies have demonstrated accurate measurement of antegrade transaortic volume flow by Doppler echocardiography both in the absence of valve disease and in the presence of aortic regurgitation. The current study provides evidence that this technique also is valid proximal to a stenotic aortic valve. Although our model provides no direct data regarding the underlying assumptions needed for accurate volume-flow measurement, results from in vitro models do support these assumptions, and the agreement between our Doppler and EM transaortic volume-flow measurements further suggests that these assumptions are warranted.

We conclude that in this animal model of aortic stenosis, with anatomy and hemodynamics similar to clinical aortic stenosis, Doppler echocardiographic measurement of transaortic volume flow proximal to the stenotic valve is accurate. In conjunction with data from other studies on the accuracy of Doppler velocities for determining pressure gradients in aortic stenosis, our findings support the validity of the Doppler continuity equation for calculating aortic valve area.

**Acknowledgments**

We thank Robert Thomas, Richard Tuck, and Andrew E. Luedtke for their technical assistance.

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KEY WORDS • aortic stenosis • stroke volume • valve area
Experimental validation of Doppler echocardiographic measurement of volume flow through the stenotic aortic valve.

_Circulation_. 1988;78:435-441
doi: 10.1161/01.CIR.78.2.435
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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