Contrast Echocardiographic Evaluation of Changes in Flow Velocity in the Right Side of the Heart

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SUMMARY We used contrast echocardiography to estimate changes in flow velocity at the tricuspid and pulmonic valve orifices, as reflected by varying angles of the moving linear contrast echoes. The validity of the method was established by catheterization and echocardiographic studies in 14 patients. Flow velocity at the tricuspid and pulmonic valve orifices was measured by means of an electromagnetic flow-velocity probe, and the contrast echocardiogram was recorded simultaneously. Instantaneous changes in contrast flow velocity as measured by the contrast echo angle correlated significantly with flow velocity changes measured by the probe at the tricuspid valve orifice (mean $r = 0.87$) and at the pulmonic valve orifice (mean $r = 0.92$).

In all 26 subjects (12 normals and 14 patients with heart disease) studied in the noninvasive laboratory, the effects of simple interventions that modify right-sided flow were observed. The contrast flow velocity at the tricuspid valve orifice in 12 normal subjects was $345 \pm 30$ mm/sec and was reproducible by repeated injections. The contrast flow velocity changed with respiration and heart rate, and was most rapid with inspiration. A 10% increase in heart rate resulted in a 45% average increase in contrast flow velocity. The contrast flow velocity began to increase immediately after 45° passive rapid elevation of both legs, and the maximal increase during this 5-second maneuver averaged 40%; thereafter, it gradually decreased and returned to the control level within 2 seconds after the legs were lowered to the horizontal position.

We conclude that the linear contrast echo obtained by contrast echocardiography is relatively easy to achieve, reliable and reproducible and that it facilitates evaluation of instantaneous changes in flow velocity in the right side of the heart, assuming that careful attention is given to the techniques of recording and measurement. Absolute flow velocity is more accurately measured for the pulmonary valve than for the tricuspid valve with this method. Changes in flow through either valve may be assessed by this means when interventions are applied.

KNOWLEDGE of flow velocity is clinically important in the evaluation of heart function. Flow velocity can be measured invasively and noninvasively, using, for example, the electromagnetic catheter-tip flow-velocity probe and the Doppler method. The latter method, however, presents technical problems for the measurement of flow velocity. Therefore, we developed a relatively simple and reliable technique for measuring flow velocity noninvasively, using M-mode contrast echocardiography.

Based on the principle underlying the contrast effect, we hypothesized that the particle (microbubble) moves midstream in the blood flow through either valve approximately parallel to the ultrasonic beam, producing a linear contrast echo. If the contrast echo is drawn as a straight line at a predetermined period of limited duration, it may be possible to use this line to determine flow velocity as the ratio of time and distance.

In this study we evaluated the usefulness of contrast echocardiography in calculating changes in flow velocity in the right side of the heart.

Materials and Methods

The present series consists of 12 normal male subjects (mean age 28 years, range 26–31 years) and 14 patients with heart disease (five males and nine females, mean age 40 years, range 28–55 years) who were diagnosed by cardiac catheterization (table 1). In the contrast technique, the participants received two to 10 injections that consisted of 1 ml of indocyanine green and 10 ml of saline into an antecubital vein over a period of one or several days. The linear contrast echo was recorded at the tricuspid or pulmonic valve orifice during quiet respiration. In theory, successful recording of the linear contrast echo depends primarily upon directing the ultrasonic beam so that it forms an almost 180° (0°) angle with the midstream blood flow through either valve. However, because the blood flow through the tricuspid valve orifice is multidirectional and the direction of the midstream blood flow may change with varying shapes of the right ventricle in different patients, it would not be as easy to determine a reasonable echo direction to ensure that the beam would parallel the midstream blood flow through the tricuspid valve orifice. We therefore selected the tip of the anterior leaflet of the valve as a suitable reference point that could be visualized in the parasternal four-chamber view by means of two-dimensional echocardiography using a
phased-array electrical sector scanner (Toshiba SSH-11A) or a mechanical sector scanner (Smith-Kline Instruments, EkoSector I). To direct the ultrasonic beam as nearly parallel to the long axis of the right ventricle as possible, a nonfocused, 13-mm-diameter, 2.25-MHz) transducer (Electronics for Medicine) was placed in the third or fourth intercostal space near the left sternal border and angled medially so that the tip of the tricuspid valve being recorded was the fastest anterior motion in the rapid-filling phase and the length of the linear contrast echo recorded was the longest possible. The interatrial septum13-16 at times was recorded below the valve.

To direct the beam parallel to the flow through the pulmonic valve orifice, the transducer was placed in the third or fourth intercostal space and angled superiorly so that the direction of the ultrasonic beam paralleled the long axis of the main pulmonary artery as imaged by two-dimensional echocardiography and the recorded length of the linear contrast echo was again the longest possible. In this echo direction, no multiple echoes just below the pulmonic valve were recorded in systole and the rapid posterior motion of the tip of the valve in the early ejection phase was recorded.

In the invasive flow-velocity technique, flow velocity was measured in all 14 patients with a Millar electromagnetic catheter-tip flow-velocity probe that had a flexible guide approximately 4 cm long distal to the flow sensor, and was inserted through the antecubital or saphenous vein into the tricuspid or pulmonic valve orifice, respectively. To record the flow-velocity curve at the tricuspid valve orifice, the tip of the guide was manipulated to touch the right ventricular wall so that the sensor was positioned in the tricuspid valve orifice and the maximal and biphasic forward flow-velocity patterns during the diastolic phase could be recorded. To record the flow-velocity curve at the pulmonic valve orifice, we positioned the catheter so that the sensor was positioned in the pulmonic valve orifice and the maximal forward flow-velocity pattern during the systolic phase could be recorded.

To determine the relationship between the flow velocities as measured by the two techniques, flow velocity was determined invasively in 10 patients; simultaneously, the linear contrast echo at the tricuspid valve orifice was measured and right ventricular pressure was recorded. In the other four patients, flow velocity and the linear contrast echo at the pulmonic valve orifice were measured simultaneously, and right ventricular pressure was recorded at the same time.

The linear contrast echo that appeared within 120 msec after tricuspid valve opening was used to determine the linear contrast echo angle (O) (fig. 1). A 120-msec duration was thought to be appropriate for this determination, because during this period, acceleration of flow velocity was evidenced in our flow-velocity tracings (fig. 2). We therefore assumed that 120 msec represented the most rapid filling phase of the right ventricle.

The following method was used to calculate contrast flow velocity as measured by the contrast echo angle (fig. 1). A horizontal line (b) was drawn through the point of tricuspid valve opening; at the point where the fastest linear contrast echo trace that is straight and longer than 1.5 cm crosses this horizontal line, the trace was extrapolated upwards (c). In our experience,
FIGURE 1. Schema showing the method for measurement of the flow velocity by the linear contrast echo angle. A horizontal line is drawn through the position of tricuspid valve (TV) opening. Within 120 msec after tricuspid valve opening, the peak flow velocity is calculated as a/b mm/sec. IAS = interatrial septum.

A length of 1.5 cm permits accurate extrapolation. Then a line (a) perpendicular to (b) was constructed, thereby creating a triangle in which (b) is the duration (sec), (a) is the distance (mm) and (c) is the extrapolation trace of the fastest echo. The extrapolation to give (c) may be any arbitrary distance because the ratio of (a):(b) (i.e., angle \( \Theta \)) is constant. To express the linear contrast echo angle simply, in terms of flow velocity, we used the ratio obtained by multiplying the quotient of a/b by one unit of flow velocity. In other words, contrast flow velocity can be expressed as a/b mm/sec.

Similar to the measurement of the contrast echo angle at the tricuspid valve orifice, the contrast echo angle (\( \Theta \)) at the pulmonic valve orifice was also measured within 120 msec of pulmonic valve opening (fig. 3). Again, acceleration of flow velocity was evidenced in our flow-velocity tracings (fig. 4) and 120 msec was assumed to represent the most rapid ejection phase of the right ventricle. Pulmonic valve contrast flow velocity was calculated in a manner similar to tricuspid valve contrast flow velocity, by constructing the triangle. To obtain pulmonic valve contrast flow velocity, however, the echo trace is extrapolated downward (c) and line (a) is drawn perpendicular to line (b) to cross trace (c). Then contrast flow velocity can be expressed as the ratio of (a):(b): a/b mm/sec.

Damping, rejection and gain were controlled during contrast echo recording. The changes in contrast flow velocity were investigated under different respiration and heart rate conditions, as well as during a transient volume increase induced by 5-second, 45° passive rapid elevation of both legs.

Echocardiographic tracings were made on a Smith-Kline ultrasonoscope (Ekoline 20-A) interfaced with an Electronics for Medicine VR-12 strip-chart recorder. All recordings were made at a paper speed of 100 mm/sec.

Results

The linear contrast echo that appeared within 120 msec of tricuspid and pulmonic valve opening was almost a straight line and its angle (\( \Theta \)) could be measured accurately (figs. 1 and 3). The linear co-
contrast echo angles were steeper than the opening slopes of the tricuspid and pulmonic valves.

In 10 patients, we recorded the contrast echo at the tricuspid valve orifice simultaneously with the flow-velocity curve obtained by the probe at the same orifice. Figure 2 shows representative simultaneous recordings of the contrast echo at the tricuspid valve orifice, right ventricular pressure, and flow velocity obtained by the probe at the tricuspid valve orifice. The peak flow velocity can be evaluated by the height of the curve. The pattern is very similar to the tricuspid valve motion. By comparison, where the flow-velocity curve is higher, the ratio of a/b is greater, whereas when the flow-velocity curve is lower, the ratio of a/b is smaller (fig. 2). Instantaneous changes in contrast flow velocity and flow velocity as measured by the probe during the simple physiologic maneuvers of respiration and elevation of both legs to increase right ventricular flow were observed. Figure 5 shows representative instantaneous changes in contrast flow velocity as determined by the contrast echo angle and simultaneously recorded flow velocity, measured by the probe, during 5 second, 45° passive rapid elevation of both legs (case 1). Contrast flow-velocity changes coincided with changes in flow velocity measured by the probe. We investigated the relationship between flow-velocity changes as measured by the contrast echo angle and the probe and found a good correlation between the two measurements (table 1; mean r = 0.87). Figure 6 shows typical examples of these measurements and their relationships. Figures 6A and B show two of five patients in whom probe values were higher than the contrast echo measurements, figure 6C shows one of two patients in whom the two values were almost equivalent and figure 6D

**Figure 3.** Method for measurement of the flow velocity by the linear contrast echo angle at the pulmonic valve (PV) orifice. A horizontal line is drawn at the position of pulmonic valve opening. Within 120 msec after pulmonic valve opening, the peak flow velocity is calculated as a/b mm/sec.

**Figure 4.** Simultaneous recordings of the contrast echo at the pulmonic valve orifice, right ventricular pressure (RVP) and flow velocity (FV) obtained by the probe at the same orifice in one patient with atrial fibrillation. Vertical and horizontal lines are drawn through the point of pulmonic valve opening. Flow velocity changed according to the different preceding RR interval, and the two panels show flow-velocity changes in atrial fibrillation. For explanation of the triangles, see figure 3. When the flow-velocity curve is higher, the ratio of a/b is greater (right), whereas when the flow-velocity curve is lower, the ratio of a/b is smaller (left).
Figure 5. Instantaneous changes in flow velocity measured at the tricuspid valve orifice by the contrast echo angle and simultaneously recorded with flow velocity measured by the probe before, during and after elevation of both legs in patient 1 (see figure 6A).

shows one of three patients in whom value measured by the contrast echo was higher than the probe value. The difference between the measurements obtained by the two procedures was less than 30% in all patients but the one shown in figure 6D.

Simultaneous recordings of the contrast echo and intracardiac pressure and flow velocity measured invasively at the pulmonic valve orifice during the different RR intervals in all four patients with atrial fibrillation showed good correlation (mean $r = 0.92$) between the instantaneous changes in contrast flow velocity and flow velocity measured by the probe at the pulmonic valve orifice (table 1). The findings in case 11 are illustrated in figure 7. The value measured at the pulmonic valve orifice was in better agreement with the flow velocity value than that measured at the tricuspid valve orifice. Figure 4 is a representative simultaneous recording of the contrast echo at the pulmonic valve orifice, right ventricular pressure, and flow velocity obtained by the probe at the pulmonic valve orifice in the same patient with atrial fibrillation. Flow velocity changed according to the different preceding RR intervals.

In 12 normal subjects, variability of the contrast flow velocity was within 10% when each subject was assessed two to 10 times over a period of one or several days.

The contrast flow velocity was strongly affected by respiration. Figure 8 shows the contrast echo tracing at the tricuspid valve orifice in a normal subject during respiration. The contrast flow velocity changed during inspiration and expiration. Two vertical lines

Figure 6. Correlation between instantaneous changes in flow velocity measured at the tricuspid valve orifice by the probe and contrast echo angle during elevation of both legs in patients 1-4. Each dot represents one cardiac cycle.

Figure 7. Correlation between the instantaneous changes in flow velocity measured at the pulmonic valve orifice by contrast echo angle and the probe in patient 11. Each dot represents one cardiac cycle.
were drawn at the point of tricuspid valve opening. The contrast flow velocity is fast at deep inspiration and slow at maximal expiration. Figure 9 shows the changes in the heart rate and contrast flow velocity during deep respiration in the same subject. The contrast flow velocity changed with respiratory phase and heart rate. A 10% increase in heart rate produced a 45% average increase in contrast flow velocity, from the control value of 340 mm/sec to a value of 500 mm/sec. Similar results were obtained in all other normal subjects tested. The changes in contrast flow velocity were less than 5% compared with the control level when the subjects held their breath. At the shallowest respiration possible, changes in contrast flow velocity were less than 10% compared with the control level.

The contrast flow velocity at the tricuspid valve orifice in 12 normal subjects was 345 ± 30 mm/sec during the shallowest respiration possible. In each case, 45° passive rapid elevation of both legs for 5 seconds effected a change in contrast flow velocity. Figure 10 shows the relative changes in contrast flow velocity caused by passive rapid elevation of both legs. The premaneuver values were those recorded 3–5 seconds before leg elevation. One standard deviation of contrast flow velocity was calculated from each cardiac cycle of the 12 normal subjects. Contrast flow velocity began to increase immediately upon elevation of both legs, and the maximal increase during this maneuver averaged 40%. Thereafter, it gradually decreased and returned to the control level within 2 seconds after the legs were lowered to the horizontal position.

In four patients with atrial fibrillation (nos. 11–14), changes in flow velocity at the pulmonic valve orifice determined by the contrast echo angle correlated significantly with the preceding RR interval (r = 0.92, r = 0.91, r = 0.93, r = 0.91, mean r = 0.92). Patient 11 is illustrated in figure 11.

**Figure 8.** Contrast echo tracing at the tricuspid valve orifice in a normal subject during respiration. A vertical line is drawn at the point of tricuspid valve opening. For explanation of the triangles, see figure 1. Contrast flow velocity at deep inspiration is fast (the ratio of a/b is greater), whereas at maximal expiration, it is slow (the ratio of a/b is smaller).

**Figure 9.** Changes in contrast flow velocity and heart rate during respiration in a normal subject. Contrast flow velocity changed in relation to changes in heart rate and respiratory phase. Insp = inspiration; Exp = expiration.

**Figure 10.** Relative changes in contrast flow velocity due to 45° passive rapid elevation of both legs in 12 normal subjects. The line through each point denotes 1 standard deviation of contrast flow velocity for each cardiac cycle calculated from 12 normal subjects.
Discussion

Because knowledge of flow velocity is an important factor in the evaluation of heart function, it would be clinically useful to be able to estimate flow velocity noninvasively. Electromagnetic flowmeter probes of either the cannulating or the perivascular type have been used to evaluate intracardiac flow velocity. However, several disadvantages have been noted, and in many laboratories the electromagnetic catheter-tip flow velocity probe has been found to be superior.

Doppler methods are now available for evaluating flow velocity noninvasively. In particular, as regards the right heart, Kalman and co-workers reported a directional Doppler ultrasonic technique. However, the Doppler method is not free from technical problems, for example, when the Doppler beam is pointed in a direction different from intracardiac flow, the flow-velocity pattern obtained is not completely reliable.

We compared flow-velocity measurements simultaneously obtained by using the probe and by the echo angle. At the pulmonic valve orifice, we observed very good agreement in terms of absolute value and relative changes during the different RR intervals in all four patients with atrial fibrillation when the values were obtained by the two procedures (fig. 7). However, at the tricuspid valve orifice, the absolute values obtained by these two procedures were different in some patients. This may be explained by greater technical difficulties in positioning the catheter at the tricuspid valve orifice, which, to measure velocity, should be facing the midstream blood flow. Differences in flow-velocity values obtained by the two procedures may be further explained by the principles of measurement of contrast flow velocity. Measurement of flow velocity by the contrast echo angle is based on the hypothesis that the particle (microbubble) that produces the contrast effect moves approximately parallel to the ultrasonic beam. When a microbubble is moving parallel to the beam, it may be possible to determine the absolute flow-velocity value. By comparison, if a microbubble is not moving completely parallel with the ultrasonic beam, the absolute value cannot be measured.

We assumed that flow direction in the early ejection phase at the pulmonic valve orifice is directly in parallel with the main pulmonary artery. Therefore, we directed the ultrasonic beam parallel to the main pulmonary artery as imaged by two-dimensional echocardiography. In all cases studied in this series, a linear contrast echo longer than 3.5 cm was recorded within 120 msec of pulmonic valve opening. As the main pulmonary artery in this series was angiographically estimated to be 4 cm long, a linear contrast echo longer than 3.5 cm was a good indication that the beam was directed approximately parallel to the midstream blood flow through the valve in the early ejection phase in every case.

We assumed that flow through the tricuspid valve orifice in the rapid filling phase is multidirectional and that the direction of midstream blood flow can differ with various shapes of the right ventricle. Therefore, it would not be as easy to determine a reasonable ultrasound direction to ensure that the beam would be parallel to the midstream blood flow. We directed the beam as parallel as possible to the long axis of the right ventricle and decided that the tip of the anterior leaflet of the valve would be a more suitable point of reference at which to direct the beam as it moves most rapidly facing the ultrasonic beam. Recording this fastest motion of the valve could be a good indicator of the most rapid flow facing the ultrasonic beam.

We considered that one possible reason for the poor tricuspid flow correlation, compared with pulmonary flow correlation, with flow-velocity measured by the catheter method may be the difference in blood flow pattern through these two orifices. At the pulmonic valve orifice, the blood flow from the right ventricle into the pulmonary artery is mostly laminar. However, the blood flow through the tricuspid valve from the right atrium to the right ventricle may be multidirectional and may not always be directed straight ahead. Therefore, the geometry of the pulmonary artery during recording is much more likely to provide a parallel relationship of the ultrasonic beam with the midstream blood flow than that of the tricuspid valve.

As we used a nonfocused, 13-mm-diameter transducer with a near field of 68 mm, the length of the recorded linear contrast echo may be changed by the duration of the microbubble within the beam as well as by the speed of the microbubble. Therefore, a longer contrast echo may be recorded when the beam is directed completely parallel to the direction of the microbubble movement than when the beam is at an angle to the microbubble. If the line of microbubble movement is at a large angle to the ultrasonic beam, (i.e., if microbubble movement cannot be considered to be even approximately in parallel with the beam), probably only a very short linear contrast echo or no evident echo motion will be recorded. Therefore, it is necessary not only to direct the beam at the tip of each valve, but also to record a longer contrast echo within 120 msec of the valve opening. In our experience,
when we recorded the linear contrast echo at the tricuspid valve orifice where the ultrasonic beam was directed as described previously, the length of the echo was 2.4 ± 0.6 cm in 60 cases (22 cases in this study and additional 38 cases in another series) who showed a well-defined linear contrast echo. In the 10 patients in whom the flow velocity was recorded simultaneously with the echo trace, the shortest linear contrast echo was 1.5 cm (two cases). However, even in these two cases, flow velocity was underestimated by 29% and 27% when the catheter method was used. Therefore, we considered 1.5 cm the minimum length required to calculate flow velocity using our method. While the absolute value of flow velocity cannot be measured in this situation, it is possible to evaluate the relative changes in flow velocity. In fact, instantaneous changes in contrast flow velocity agreed well with values obtained by the probe (fig. 6). We concluded that the linear contrast echo measurement represents a reliable alternative to the catheter method.

Accurate recording of the linear contrast echo tracings is severely hampered when the ultrasonic beam is incorrectly angled. In fact, in about half of 45 patients in another series, in whom the linear contrast echo was recorded at the pulmonic valve orifice, it was extremely difficult to position the beam correctly for reasons such as the proximity of the pulmonary artery to the chest wall, which yielded unclear echo tracings. However, in the four patients with dilated pulmonary arteries in the present study, no such problem existed, as the pulmonic valve could easily be located for echocardiographic investigation. By comparison, it was easier to position the beam correctly at the tricuspid valve, and distinct linear contrast echoes were therefore relatively simple to achieve. Indeed, a well-defined linear contrast echo was obtained in more than 80% of the additional 45 patients mentioned above.

The angle of the linear contrast echo is steeper than the opening slope of both the tricuspid and pulmonic valve (figs. 1 and 3). If the ultrasonic beam is directed approximately parallel to the microbubbles in midstream blood flow, the angle of the linear contrast echo made by these microbubbles may be taken as the velocity of midstream flow. On the other hand, although the tip of the tricuspid or pulmonic valve is positioned at the midstream at the beginning of valve opening, the tips are pushed away by the stream. Therefore, the opening slope of each valve cannot represent the actual midstream flow velocity and is less steep than the angle of the contrast echo.

Our method is relatively simple and reproducible. In 12 normal subjects, contrast flow velocity varied by 10% or less when assessed in each subject at least twice in a single day and also on different days. When these normal subjects held their breath while the contrast echo was being recorded, there was a difference of less than 5% between the echo angle at the beginning of the breath-holding exercise (control value) and the angles obtained during the subsequent 10 cardiac cycles. These results suggest satisfactory reproducibility and reliability.

To confirm the validity of our method, we evaluated contrast flow-velocity changes at the tricuspid valve orifice caused by respiration and elevation of both legs. Deep inspiration leads to decreased intrathoracic pressure and increased venous return. Using this well-established phenomenon of respiratory effect on the returning blood flow to the right ventricle, we evaluated the changes in contrast flow velocity during respiration. At first, we observed the effect of breath-holding on contrast flow velocity and found that there was at most a 5% variation from the control level. As expected, marked changes in contrast flow velocity occurred during deep respiration (figs. 8 and 9). The contrast flow velocity appeared to reflect changes in heart rate and phase of respiration very closely.

Next, we produced an increase in venous return by passive rapid elevation of both legs to determine its effect upon contrast flow velocity. In 12 normal subjects, the maximal increase averaged 40%. Even in the cardiac cycle that showed the greatest patient-to-patient difference, 1 standard deviation was still less than 20%. In addition, on return of both legs to the horizontal position, the contrast flow velocity returned to the control level within 2 seconds. These results strongly support the reliability of our method.

We considered the possibility that changes in contrast flow velocity may be induced by changes in the angle of the ultrasonic beam during respiration and elevation of both legs. If the angle of the ultrasonic beam is changed, for example, by body or chest wall motion during the maneuvers, contrast flow velocity may be changed. Therefore, before starting the maneuvers, we repeatedly recorded well-defined linear contrast echoes by directing the beam at the tip of the tricuspid valve as imaged by two-dimensional echocardiography, and measured the fastest possible angle of the contrast echo. Then, if the angle of the ultrasonic beam was changed in relation to the tricuspid valve during maneuvers, it is possible the contrast flow velocity could be decreased, because the angle between the ultrasonic beam and the moving microbubble could be greater than the premaneuver angle. However, during the maneuvers, only an increase in contrast flow velocity compared with the premaneuver level was noted. This suggests that contrast flow velocity may have been underestimated, even though the direction of the ultrasonic beam may not have changed markedly during the maneuvers.

By comparing the relative changes in contrast flow velocity induced by elevation of both legs with the pattern of the normal subjects (fig. 10), it was possible to evaluate right ventricular function in terms of flow velocity in patients with heart disease.

When we measured the contrast flow velocity at the pulmonic valve rather than the tricuspid valve, the velocity varied depending on the preceding RR interval. After a longer diastole, flow velocity was higher. In our four patients with atrial fibrillation, this relationship was very good and patient 11 gave a typical correlation of 0.92 (fig. 11).

We conclude that the linear contrast echo obtained by contrast echocardiography is relatively easy to
achieve, reliable and reproducible, and that it facilitates evaluation of instantaneous changes in flow velocity in the right side of the heart, assuming careful attention is given to the techniques of recording and measurement. Absolute flow velocity is more accurately measured for the pulmonary valve than for the tricuspid valve with this method. Changes in flow through either valve can be assessed by this means when interventions are applied.

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