would be of use to know by pulsed Doppler echocardiography whether or not the origin of the murmur in question is consistent with a rheumatic process. When there has been no firm basis for the diagnosis of rheumatic fever, and pulsed Doppler echocardiography shows only a VSD, removal of the diagnosis of rheumatic fever and discontinuation of rheumatic fever prophylaxis may be considered.

In cases where the severity of VSD or MR may approach the surgical range, invasive studies are more appropriate, and there is usually less difficulty in distinguishing between VSD and MR. Questions may remain, however, especially if the VSD is of endocardial cushion type, with associated mitral abnormalities, or in situations where left ventricular angiography performed via the transatrial route is associated with so-called catheter induced mitral insufficiency.

Pulsed Doppler echocardiography is sensitive and specific in determining the origin of troublesome apical systolic murmurs due to VSD or MR, and in the situations discussed extends noninvasive ultrasound diagnosis beyond the capabilities of M-mode echocardiography.

References


The Pulsed Doppler Coronary Artery Catheter


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SUMMARY A new catheter which measures instantaneous changes in coronary artery blood flow velocity is described. The linear relationship between flow velocity measured with the catheter and volume flow through small arteries is documented with a correlation coefficient of $r = 0.99$. Coronary flow velocity has been measured from the proximal right and left coronary arteries and aortic ostia of saphenous vein bypass grafts in patients undergoing diagnostic coronary arteriography. The increase in coronary flow following injection of contrast media in normal coronary arteries is similar to the increase in coronary flow reported following near-maximum exercise. This increased flow response following injection of contrast media is severely limited by coronary artery stenosis and may provide a useful method for assessing hemodynamically significant stenosis in patients with coronary artery disease.

THE SYMPTOMS of coronary artery disease are usually precipitated by some type of hemodynamic stress. However, of all the laboratory techniques commonly used to assess the presence or severity of coronary artery disease, only the exercise electrocardiogram imposes a hemodynamic stress on the cardiovascular system. Since the symptoms of coronary artery disease presumably arise from an inability to adequately increase flow through stenosed coronary arteries, diagnostic tests which more clearly define the flow limiting characteristics of specific coronary artery lesions might be of considerable help in evaluating patients with this disease.

The significant increase in coronary blood flow that follows selective coronary artery injection of contrast media has been appreciated for several years. Initial studies were performed in acute, open-chest animal preparations.1-4 Recently, coronary blood flow measurements in patients undergoing cardiac catheterization have demonstrated a similar increase in coronary blood flow following selective coronary arteriography.5, 6

Gould et al., using an open-chest animal preparation, have demonstrated the potential usefulness of this flow response in assessing the critical nature of coronary artery stenosis.6 In their study, resting coronary flow was not decreased until the stenosis exceeded 85%. However, peak flow following selective coronary injection of contrast media was limited by a 50% stenosis. It was postulated that a quantitative measure of this post contrast media flow response would therefore provide a meaningful assessment of the flow limiting nature of a specific coronary artery lesion.

The clinical application of this contrast media-induced hyperemic response in man requires an easily applied method for measuring coronary artery blood flow. The method must also provide a measure of rapid changes in coronary blood flow since flow is constantly changing following injection of contrast media, and a prolonged steady state is never maintained during the hyperemic response phase. During the past 25 years, a variety of techniques for measuring coronary artery blood flow in conscious man have been
described. Basically these methods can be divided into 1) methods using diffusible gases; 2) methods utilizing diffusible substances that actively enter the cell; 3) measurement of coronary sinus blood flow by continuous thermodilution; and 4) methods to measure phasic coronary flow by means of videodensitometry or continuous wave Doppler. Each of the techniques poses individual advantages and disadvantages. Methods for measuring coronary blood flow in humans utilizing diffusible gases have been available for 25 years. This technique requires a steady coronary flow state plus catheterization of the coronary sinus. However, when combined with appropriate metabolic studies, it has provided significant data concerning normal and abnormal coronary blood flow. Rubidium and potassium are the most commonly used substances which actively enter the cell. This technique also requires a steady coronary flow state but catheterization of the coronary sinus is not required. Its accuracy depends on the fact that coronary flow and not cell permeability must be the rate-limiting variable. Measurement of coronary sinus blood flow by continuous thermodilution requires catheterization of the coronary sinus and is dependent on obtaining adequate mixing between the points of injection and sampling. However, relatively rapid changes in coronary flow may be measured with this technique. A major disadvantage of all three of these techniques is their inability to separate right and left coronary artery blood flow or to measure regional coronary blood flow. Rapid changes in regional coronary blood flow are probably most accurately assessed at the present time by roentgen videodensitometry. However the system required to obtain these data is extremely complex and not suitable for widespread research or clinical applications at the present time. The continuous wave Doppler technique requires a relatively simple system which could be used in any cardiac catheterization laboratory. However, because of catheter design, only coronary flow velocity at the proximal right or left coronary arteries is measured. Pressure is not recorded, and contrast media cannot be injected.

In an attempt to measure rapid changes in coronary artery blood flow following a variety of different interventions, including selective coronary artery injection of contrast media, a system has been developed which measures phasic coronary artery flow velocity at the time of routine diagnostic coronary arteriography. The initial report of this system described its evaluation in animals. The system has also been used as a flowmeter in acute and chronically instrumented animal preparations. This report discusses the potential application of the system when evaluating patients with coronary artery disease and defines coronary flow response to contrast media in normal coronary arteries, arteries with varying degrees of atherosclerosis and in patent saphenous vein bypass grafts.

**Method**

Because of the desire to measure right and left coronary artery blood flow on a moment-to-moment basis when assessing coronary flow response to a variety of interventions, a pulsed Doppler system has been developed. This system has several advantages over the previously described continuous wave Doppler system. A single crystal can be used as both transmitter and receiver. Thus the transducer is small enough to mount on the tip of a standard Sones coronary catheter without distorting the configuration of the catheter. Pressure may be recorded simultaneously with coronary artery flow velocity, and contrast media, saline, or any desired pharmacologic agent may be injected directly into the coronary artery while recording phasic coronary artery flow velocity. The pulsed Doppler system also employs range gating which allows the operator to measure flow velocity at a desired distance away from the tip of the catheter, thereby decreasing artifacts resulting from catheter induced turbulence.

**Catheter Design**

Figure 1 is a cross-sectional diagram of the tip of the catheter. The transducer is piezoelectric ceramic crystal material with a resonance frequency of 20 MHz. The crystal is circular with an outer diameter of 1.6 mm and a central hole of 0.5 mm in diameter. Two #40 gauge nylon clad copper wires are soldered to the front and back sides of the crystal. The transducer is epoxied to the 1.7 mm tip of a standard #8 French Sones catheter. The wires are passed back through the lumen of the catheter and care is taken to keep all five holes (one end hole and four side holes) free of epoxy to provide maximum smoothness. The two wires are brought out from the lumen through a single hole in the side of the proximal luer-lok fitting and are connected to a coil wound around the catheter. The coil and connections are secured with epoxy and covered with heat shrinkable tubing. A primary coil which connects to the electronic equipment is slipped over the catheter and is free to rotate around the insulated secondary coil. This transformer coupling technique provides electrical isolation between the patient and the instrumentation as well as the mechanical freedom necessary.

**Figure 1.** Cross-sectional diagram of the tip of the pulsed Doppler coronary artery catheter.
for catheter manipulation. The proximal end with the transformer disassembled and distal tip of the catheter are illustrated in figure 2.

Instrumentation

The pulsed Doppler system used in this study has been previously described. The basic principle of this technique is outlined in figure 3. A single piezoelectric crystal is used as both transmitter and receiver. The master oscillator frequency of 20 MHz is pulsed at a repetition frequency of 62.5 KHz. Each pulse is approximately one microsecond in width and therefore contains 20 cycles of the master oscillator frequency. These acoustic tone bursts (transmit pulses) are propagated into the blood or surrounding tissue, where they are reflected by the various structures encountered (blood cells, vessel wall, etc.). The acoustic signals returning to the crystal are separated in time according to the distance of each reflecting structure. Therefore, by adjusting an electronic time delay (adjustable receiver gate), one can select signals reflected from structures a specific distance away from the transducer. These reflected signals are amplified and compared in phase and frequency with a signal from the master oscillator. The result of the processing is the difference in frequency (Doppler shift) between the master oscillator and the signals reflected from the flow sensitive region as defined by the adjustable receiver gate. The relationship between the Doppler shift and absolute velocity is noted in the equation of figure 3. C (velocity of sound in blood) and f (transmitter frequency) are both constant. Therefore, if the catheter is in a stable position and the angle θ remains constant, Δf or Doppler shift frequency is linearly related to blood flow velocity (V). The parameters chosen (master oscillator frequency = 20 MHz and pulse repetition frequency = 62.5 KHz) allow velocities up to 100 cm/sec to be recorded at a distance up to 1.2 cm from the catheter tip. The system is directionally sensitive so that flow reversals are properly displayed, and since zero frequency shift corresponds to zero flow, excellent zero stability is achieved.

Calibration

The experimental validation of the relationship between volume flow and Doppler shift measured from the tip of the Sones catheter was obtained using the femoral artery of an anesthetized dog. The tip of the catheter was inserted through the carotid artery, passed down the descending aorta and into the femoral artery. A long segment of the femoral artery was dissected free and all branches were ligated. The tip of the catheter was then positioned longitudinally in the proximal end of the isolated segment of femoral artery and the range gate adjusted to record the maximum velocity signal. The distal end of the isolated segment was then cannulated with flexible polyethylene tubing. Varying levels of volume flow through the artery were obtained by adjusting a pinch clamp on the cannula. Volume flow was measured by the graduated cylinder and stopwatch technique, and volume flow and mean Doppler shift were measured simultaneously at varying levels of flow.

The relationship between the amount of contrast media injected into the coronary artery and the subsequent increase in coronary artery flow was evaluated in a conscious, chronically instrumented dog. Through a left thoracotomy a pulsed Doppler, cuff type, flow probe was placed on the mid-circumflex coronary artery and a Konigsberg pressure gauge positioned in the apex of the left ventricle. Two weeks after surgery, under light sedation and local anesthesia, a cut down was performed on the left carotid artery, a Sones catheter passed to the ascending aorta and positioned in the proximal circumflex artery. Flow response in the circumflex artery was then recorded with selective injection of 0.5, 1, 2, 3, 4, 5 and 6 cc of Renografin-76. After obtaining the dose-response data, the catheter was advanced until its tip was immediately proximal to the cuff flow meter. Contrast media (6
cc) was then injected and, at the time of maximum hyperemic response, the catheter was removed from the artery.

**Clinical Evaluation**

The catheter has been used in fifty-eight patients undergoing diagnostic cardiac catheterization and coronary arteriography. All necessary diagnostic data were acquired by conventional techniques. Coronary arteriography was performed by the Sones technique, and patients were heparinized at the onset of the procedure with sodium heparin, 5,000 units. After completing the diagnostic procedure, the pulsed Doppler catheter was inserted through the brachial arteriotomy and advanced to the ascending aorta. The tip of the catheter was then positioned in the ostium of the right or left coronary artery or a saphenous vein bypass graft. The techniques used to position the pulsed Doppler catheter are similar to those used in manipulating the standard Sones catheter. Small test injections were used to verify the position of the catheter tip. After obtaining a stable position, the range gate was adjusted to record the maximum velocity signal. Usually, minor changes in position of the tip of the catheter, combined with adjustment of the range gate, were required to obtain the maximum flow velocity signal. When the optimal velocity signal was obtained Renografin-76 was injected into the coronary artery. The amount injected was sufficient to opacify the artery completely and uniformly when viewed under fluoroscopy. This was usually 3–5 cc. Phasic and mean coronary blood flow velocity, aortic pressure and ECG were recorded continuously before, during, and after injection of the contrast media. (Aortic pressure was not recorded for 3–4 seconds during the injection of contrast media since the stopcock was switched from the pressure transducer to the injection syringe.) All data were recorded on both strip chart recorder and FM tape recorder. The latter allowed playback at variable speeds for data analysis. The former was used during each study to assess flow velocity waveform quality and to verify a stable baseline. Two or more angiographic injections were obtained in each artery, and cine films were obtained with each injection of contrast media.

It is essential that catheter tip position remain stable while data are recorded before and after injection of contrast media. Therefore, the following criteria were utilized to assure a stable position: 1) following injection of contrast media, flow velocity returned to preinjection baseline level; 2) the contour of the waveform did not change significantly throughout the period of observation; 3) similar response to injection of contrast media was obtained on at least two injections; 4) the coronary arterial system was adequately and uniformly opacified with each injection of contrast media; and 5) the visible orientation of the catheter tip did not change throughout the observation period. If all five of these criteria were met, the data were considered valid.

Data were then analyzed as follows: the time course and magnitude of the hyperemic response following selective injection of contrast media were defined for normal coronary arteries and for arteries with varying degrees of stenosis. The post hyperemic response in saphenous vein bypass grafts was also defined. The time from onset of injection to maximum increase in mean coronary artery velocity was measured in seconds. The magnitude of the hyperemic response was defined as the maximum increase in mean velocity of coronary blood flow following injection of contrast media and was expressed as a percent increase above baseline. All coronary arteries were viewed in both right and left anterior oblique projections, and the diameter of the stenosed region was compared with the nearest normal vessel diameter. Calipers were used to compare normal and abnormal segments, and stenoses were then classified as 25%, 50%, 75%, 95% and 100% reduction of the original diameter. If a significant difference existed between two views the average was used.

**Results**

**In Vivo Calibration**

Results of the in vivo calibration obtained from the dog femoral artery are illustrated in figure 4. Seven simultaneous measurements of Doppler shift (ordinate) and volume flow (abscissa) were obtained. The linear relationship between these two measurements is apparent with a correlation coefficient of 0.996.

Figure 5 is the dose-response curve. Percent increase in flow is noted on the ordinate while amount of contrast media injected is on the abscissa. Each data point represents the response to a single injection of contrast media. Maximum

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**Figure 4.** In vivo calibration of the pulsed Doppler catheter. The catheter was positioned in an isolated segment of the dog femoral artery. Volume flow (abscissa) was measured by the timed volume collection technique and recorded simultaneously with mean Doppler shift (ordinate) at seven different levels of flow.

**Figure 5.** In vivo dose-response curve obtained from a chronically instrumented dog. The amount of Renografin-76 injected in the circumflex artery is on the abscissa. The percent increase in circumflex blood flow following each injection is on the ordinate. The maximum hyperemic response occurs with 4 cc; larger amounts of Renografin-76 do not induce greater hyperemia. However, it is apparent that inadequate delivery of contrast media would result in an underestimation of the hyperemic response.
increase in flow occurs with 4 cc of Renografin-76, and there is no further increase in magnitude of flow response with larger amounts of contrast media. When 5 or 6 cc of contrast media were injected it could be seen refluxing back into the sinus of Valsalva. This also happens when one attempts to inject large amounts of contrast media into human coronary arteries. Because of the variable size of coronary arteries and partial reflux of large amounts of contrast media, the amount of contrast media required to produce uniform and complete opacification of the arterial system was accepted as the "maximum vasodilating dose" in humans. The flow response was found to be very reproducible in an individual subject but varied among different individuals even with normal coronary arteries (table 1). We have no definitive answer at this time as to why normal individuals vary in their response to contrast media.

Finally, there was no change in flow velocity waveform as measured by the cuff flow type meter, when the pulsed Doppler Sones catheter was withdrawn from the chronically instrumented dog's circumflex artery during maximum Renografin-76 induced hyperemia.

It should be pointed out that in patients only changes in flow velocity were measured and no attempt was made to quantify volume flow. These in vivo calibration results show that even if catheter position, crystal angle, and vessel diameter cannot be measured with sufficient accuracy to allow volume flow calculations, the instrument output is linear over a wide range of flows if the catheter position is stable during the measurement period. Changes in volume flow can thus be accurately evaluated under these conditions.

### Flow Response to Contrast Media

The response of coronary artery flow velocity was similar in right and left coronary arteries and patent saphenous vein bypass grafts. The response in a normal left coronary artery is illustrated in figure 6. The peak response occurs 10–12 seconds following injection and is 200% above baseline flow velocity. A similar response in a normal right coronary artery is seen in figure 7. The time course and magnitude of the flow response are similar. The response in a patent saphenous vein bypass graft to the distal right coronary artery is seen in figure 8. Again the magnitude of the response is similar. However, the time from injection to peak response is slightly longer.

The effect of coronary artery stenosis on peak flow response is summarized in table 1. Flow response was measured in the right coronary artery in ten patients. In five patients having 0–50% stenosis of the right coronary artery the mean peak flow response was 131% (range 94–215%) while in five patients with 75–100% stenosis the mean peak response was 14% (range 0–33%).
Flow response was measured in the left coronary artery in 18 patients. None of these had left main coronary artery stenosis. In ten, both the left anterior descending and circumflex arteries had 0-50% stenosis. In this group, the mean peak response was 158% (range 40-283%). In four patients, one of the major branches (left anterior descending or circumflex) had 0-50% stenosis while the other major branch had 75-100% stenosis. In this group the mean peak response was 61.5% (range 29-133%). Four patients had 75-100% stenosis in both the left anterior descending and circumflex branches. In this group, the mean peak response was 41% (range 10-65%).

Flow response was measured through patent saphenous vein bypass grafts in seven patients. Three grafts were to the distal right, one to the left anterior descending and three grafts were a Y configuration to both right and left anterior descending. The mean peak flow response in the seven grafts was 193% (range 111-380%).

The time to peak response was similar throughout the native coronary circulation with the majority reaching maximum flow response ten to twelve seconds following the injection. Peak flow response through bypass grafts was slightly delayed, peaking fourteen to sixteen seconds after the injection.

Flow response was measured in the left coronary artery in 18 patients. None of these had left main coronary artery stenosis. In ten, both the left anterior descending and circumflex arteries had 0-50% stenosis. In this group, the mean peak response was 158% (range 40-283%). In four patients, one of the major branches (left anterior descending or circumflex) had 0-50% stenosis while the other major branch had 75-100% stenosis. In this group the mean peak response was 61.5% (range 29-133%). Four patients had 75-100% stenosis in both the left anterior descending and circumflex branches. In this group, the mean peak response was 41% (range 10-65%).
Discussion

This report describes a new technique for measuring coronary artery blood flow velocity and changes in flow velocity following selective coronary artery injection of contrast media in man. The reliability and potential usefulness of these data is dependent on the relationship between blood flow velocity as measured with the pulsed Doppler catheter and actual volume flow. The theoretical relationship between volume flow and flow velocity is illustrated in figure 3. If flow velocity is to remain linearly related to volume flow over a wide range of flow, diameter of the vessel must remain constant. With this technique, it is not possible to measure coronary artery diameter during the peak hyperemic response, and therefore it is not possible to be absolutely sure that vessel diameter has not changed. However, the following observations suggest that significant changes in diameter do not occur in the ostia and proximal coronary arteries at the time of maximum hyperemic response.

The wall of the aorta at the ostia of both the right and left main coronary arteries is relatively rigid and not readily subject to change in size or shape. Studies determining the compliance properties of epicardial coronary arteries in dogs have demonstrated relatively small changes in radius with large changes in intraluminal pressure. Patel and Janicki found a 5% increase in radius with an increase in static pressure from 109 to 139 mm Hg while Douglas and Greenfield found a 10% increase in radius when static pressure increased from 70 to 120 mm Hg. The change in radius was only 3.7% when the change in pressure (i.e., 50 mm Hg) was applied dynamically rather than in a static condition. Finally, it will be noted in figures 6-8 that arterial pressure has returned to within 5 mm Hg of baseline at the time of maximum hyperemic flow response. Thus any decrease in arterial dimensions secondary to decrease in arterial pressure would be negligible. The maximum decrease in diameter that might be anticipated would be 2-3% and would not significantly alter the relationship between volume flow and flow velocity over the range of flows presented in this report.

The in vivo calibration curve was obtained from an artery comparable in size to the human proximal right and left main coronary arteries over the normal physiologic range of blood flow and confirms the linear relationship between volume flow and flow velocity. The magnitude of change in flow velocity following selective injection of contrast media in this study is also similar to the response noted in anesthetized animals when volume flow was measured with an electromagnetic flowmeter. This further supports the linear relationship between volume flow and flow velocity.

If the flow response to contrast media is to be a useful diagnostic adjunct in the assessment of ischemic heart disease, the increased flow response noted following the injection of contrast media should be comparable to changes in coronary flow following conventional physiologic stress.

Exercise is the most common, symptom producing, cardiovascular stress in patients with ischemic heart disease. Several studies have measured coronary blood flow at rest and during varying levels of exercise in normal subjects and in patients with coronary artery disease. In normal patients undergoing maximum supine exercise, coronary blood flow increased an average of 163% (range 94 to 270%) above resting control level, while in patients with angiographically documented coronary artery disease, the average increase in coronary flow was 110% (range 58 to 205%). It must be remembered that all of the techniques used to measure coronary blood flow in these studies probably measured changes in flow through both normal and diseased coronary arteries since none of the techniques are capable of selectively measuring regional coronary blood flow.

The maximum increase in mean coronary flow velocity following selective injection of contrast media in normal right coronary arteries was 131% and in normal left coronary arteries was 158%. These values are similar to the 163% increase in coronary blood flow noted during exercise in subjects without coronary artery disease and indicate that indeed selective injection of contrast media in human subjects produces an increase in coronary flow similar to that accompanying near maximum physical activity.

It is also apparent that this maximum flow response
produced by contrast media is progressively impaired by increasingly severe coronary artery stenosis. It is possible that this limitation in flow response as measured by the pulsed Doppler catheter may prove to be a useful way of determining the hemodynamic significance of lesions in the proximal and mid-right coronary artery. However, its usefulness in the left coronary system probably will be limited. Since the right coronary artery is a single vessel with relatively few branches before the acute margin, flow through a stenosis in this artery would be similar to flow at the ostium. In the left system, however, the division of the left main coronary artery into the left anterior descending and circumflex branches produces a much more complex relationship between flow through a stenosis in one of the branches and flow at the ostium of the left main coronary artery. Although there is a definite decrease in flow velocity response to contrast media in the presence of significant left anterior descending and circumflex stenosis, it is unlikely that this response will prove useful when attempting to assess the hemodynamic significance of specific lesions throughout the left coronary system.

Other techniques utilizing radioisotopes or videodensitometry may prove to be more helpful in assessing the hemodynamic significance of stenoses throughout the left coronary system. However, the data presented in this study describe the time course of the hyperemic response following injection of contrast media and identify the optimum time during the response to employ these other techniques.

Finally, this report describes the flow response in patent saphenous vein bypass grafts. Despite alterations in anatomy (i.e., caliber of the graft and angle formed between the aorta and origin of the graft) it is gratifying to note that the flow response is similar to that seen in normal vessels.

The ultimate role of the hyperemic response which follows the selective injection of contrast media in assessing the hemodynamic significance of specific coronary artery stenoses is yet to be determined. The major problem is our present inability to measure coronary blood flow in branches of the left coronary system. However, if this problem can be solved adequately, the data from this study indicate that selective injection of contrast media may be an easily applied and useful means of assessing coronary artery stenosis in patients.

The ultimate role of the pulsed Doppler catheter in assessing coronary artery stenosis also is not defined. This report demonstrates the ability of the system to record rapid changes in coronary blood flow velocity. More clinical utilization will be required to document its reliability and applicability. Although this study used contrast media as a stress, it is possible that a more uniform stress such as atrial pacing or isometric hand grip exercise might be more uniformly satisfactory as a stimulus for increased flow.

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