Variations in right and left coronary blood flow in man with and without occlusive coronary disease

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The relation of angiographically recognized coronary occlusion to regional myocardial blood flow has not been studied adequately in spite of its clinical significance. This is particularly important, as revascularization procedures, based on angiographic studies, are being performed with increasing frequency. To compare the severity of reduction in flow to the severity of coronary occlusion, regional myocardial blood flow (⁸⁵Kr washout) was measured in 34 patients. Selective coronary arteriograms were obtained using the Sones technique, and occlusions were graded as a percentage of luminal diameter. Of 26 right coronary arteries for which satisfactory arteriograms and coronary blood flow measurements were obtained, 16 were normal and 10 had significant stenosis (> 50%). Dominant right coronary arteries appeared to have high flows (67 ± 6 ml min⁻¹ per 100 g muscle) and a greater incidence of occlusion (10 of 20) than nondominant arteries, which had less flow (41 ± 2 ml min⁻¹ per 100 g muscle) and a lower incidence of occlusion (1 of 8). Coronary blood flow in 16 normal left coronary arteries was 84 ± 5 ml min⁻¹ per 100 g muscle and in 15 with 50 per cent or greater occlusion, 68 ± 3 ml min⁻¹ per 100 g muscle. Though coronary blood flow appeared reduced when lesions of both the right and left coronary arteries were present, a critical reduction was seen only when occlusion was > 90 per cent.

Coronary angiography is an accepted technique for the assessment of the severity of coronary artery disease. Whether the degree of coronary arterial stenosis on angiography quantitatively implies a reduction of myocardial blood flow to the area supplied by the vessel has not been adequately studied. A greater than 50 per cent reduction in the luminal diameter of a given coronary artery on angiography is thought to be significant (Abrams and Adams, 1969; Gensini and Buonanno, 1968), though we are not sure as to its effects on regional myocardial blood flow. Thus, the implications of any degree of stenosis in terms of coronary blood flow are unclear. Myocardial surgical revascularization procedures are performed with the notion that this procedure will augment the regional flow. It, therefore, appears important to determine whether the degree of angiographically demonstrated occlusion is proportional to the reduction in regional coronary blood flow. The purpose of this report is to establish normal values for right and left coronary

blood flow in patients with and without occlusive disease of the coronaries, and an attempt is made to correlate the degree of stenosis with the flow.

Clinical data

Regional myocardial blood flow measurements and selective coronary arteriography were performed in 34 patients, whose ages ranged from 32 to 63 years. Similar premedications were given to all patients (pentobarbitone sodium and pethidine) to assure their co-operativeness and to avoid high heart rates caused by apprehension. Patients who were in an unsteady state, as from vomiting, hypotension, or tachycardia, were excluded. Coronary arteriograms were obtained in multiple oblique projections, using the Sones technique (Sones and Shirey, 1962). Glyceryl trinitrate was not used in any of the patients before or after the arteriography or the coronary blood flow measurement. At least two of the authors evaluated the lesions independently. Coronary arterial occlusion was graded as a percentage of luminal diameter. Coronary blood flow was estimated by selective injections of ⁸⁵Kr into the right and left coronary arteries, with measurements of 'washout' made by praecordial counting equipment (Herd *et al.*, 1962; Ross *et al.*, 1964; Klein, Cohen, and Gorlin, 1965). At least 5 minutes elapsed between completion of the angiographic studies and the ⁸⁵Kr flow measurements. The

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^{85}Kr injections were performed by the technique previously described by Herd *et al.* (1962) and later modified by Ross *et al.* (1964), Klein *et al.* (1965), and others (Burke *et al.*, 1969). Flows were calculated by the formula

$$F = \frac{K \times \lambda \times 100}{P}$$

where F represents coronary blood flow in ml min^{-1} per 100 g myocardium, λ the partition coefficient of ^{85}Kr (1.0), P the specific gravity of myocardium (1.050), and K ($K = \frac{\log C_1 - \log C_2}{0.4343 (T_2 - T_1)}$) the rate constant derived from

the semilogarithmic replot of the 'washout' curve. Background radiation present before the ^{85}Kr injection was subtracted from each curve. 1 ml ^{85}Kr saturated saline was injected into the coronary ostium; the catheter was then rapidly flushed and withdrawn into the aortic root. Expired air was collected into a bag to reduce background activity. When background counts had fallen to 10 per cent or less of the peak counts of the previous injection, a second measurement was made. In the majority of the patients, right and left coronary blood flow was measured in duplicate. Most flows were measured with the patient in the left anterior oblique position, though there were no differences when flows were obtained in the

right anterior oblique. The electrocardiogram and aortic blood pressure were monitored continuously to ensure that no major disturbances in heart rate or blood pressure occurred during the measurement. We have been able to measure normal and low flows using this method in dogs subjected to experimental myocardial infarction (Burke *et al.*, 1969) when complete occlusion was verified at necropsy. The sensitivity of this method in low flow states was shown to be adequate in this study by being able repetitively to measure both normal (average = 90 ml min^{-1} per 100 g muscle) and low (25 ml min^{-1} per 100 g muscle) flows. Fig. 1 shows typical flows before and after coronary occlusion in the dog. Further, repeated measurements of coronary blood flow in this study for the same coronary artery showed no significant variation. Coronary blood flow was measured twice or more in 22 patients in the same artery. Fig. 2 shows good reproducibility of coronary blood flow at all levels ($r = 0.9$). Previous authors (Holmberg *et al.*, 1967) have also been able to show reproducible coronary blood flow using isotope techniques. Statistical analysis of coronary flows, their means and standard errors, and Student's t test were computed (Batson, 1956). The least squares fit of the linear transform of hyperbolic function used to predict coronary blood flow at any given patency was used as suggested by Bliss and James (1966).

There has been considerable controversy as to the use

FIG. 1 Coronary blood flow before and after total occlusion in a dog.

FIG. 2 Relation between two consecutive blood flow measurements.

of the word 'significant' lesion. Any lesion causing 50 per cent or greater occlusion is considered significant by many (Abrams and Adams, 1969; Gensini and Buonanno, 1968). The purpose of this study, as stated previously, is to establish the significance of the 'significant' lesion. Thus, for purposes of comparison, lesions of > 50 per cent lumen reduction are called significant in this article.

Results

Some typical flow measurements and arteriograms are shown in Fig. 3 and 4. Fig. 3 shows flows and corresponding arteriograms from a patient with angiographically normal coronary arteries. Fig. 4 shows an abnormal left coronary arteriogram with a 95 per cent occlusion of the left anterior descending coronary artery. There is correspondingly reduced flow in this vessel. The right coronary artery appears diseased but has a normal flow. When significant lesions are present, as in Fig. 5 which shows an occlusion of the proximal left anterior descending coronary artery, there may still be a normal

FIG. 3 Normal coronaries and normal coronary blood flow in a patient.

FIG. 4 Abnormal coronary arteriogram with 95 per cent occlusion of left anterior descending artery (upper panel) with low flow, probably through collaterals.

flow. The right coronary artery of this patient has no significant lesions ($< 50\%$) and also had a normal flow.

Fourteen patients had normal right and left coronary arteriograms. The remaining 20 had occlusions 50 per cent or greater, except for 2 who had insignificant (20%) narrowing of the right coronary artery.

Coronary blood flow measurement was successful in 27 out of 29 right coronary arteries examined. They were divided into dominant (20) and nondominant (9) by their angiographic appearance, distribution, and calibre, before knowledge of coronary blood flow values (James, 1961). Significant occlusions ($> 50\%$) appeared to be more commonly present in the dominant right coronary arteries (Fig. 6) than in the nondominant. The values of mean coronary blood flow and standard error of the mean

for each coronary were as follows: the flow for the normal dominant right coronary artery was $67 \pm 6 \text{ ml min}^{-1}$ per 100 g muscle and was significantly less for nondominant right coronary artery ($41 \pm 2 \text{ ml min}^{-1}$ per 100 g muscle, $P < 0.005$). Dominant right coronary artery with disease had a lower mean flow of $60 \pm 7 \text{ ml min}^{-1}$ per 100 g muscle, which was not a significant difference when compared to dominant right normals, though when lesions were 90 per cent or greater, coronary blood flow appeared to fall critically (Fig. 7). However, when lesions were significant but less severe (60 to 90% occlusions), the flows appeared normal.

For the left coronary artery, 31 were visualized adequately and had satisfactory flow measurements. Sixteen patients had normal coronary arteries. In 15 abnormal left coronary systems studied, a left anterior descending coronary artery

FIG. 5 Abnormal coronary arteriogram (occlusion of left anterior descending artery) and yet normal coronary blood flow in the corresponding vessel.

FIG. 6 Incidence of disease in dominant and non-dominant right coronary artery (RCA) and in the left coronary artery (LCA) system.

lesion was present in all but one, with 6 patients having anterior descending and circumflex coronary artery lesions. The normal group had a mean flow for the left coronary artery of $84 \pm 5 \text{ ml min}^{-1}$ per 100 g muscle. In the diseased group, coronary blood flow was lower ($68 \pm 4 \text{ ml min}^{-1}$ per 100 g muscle, $P < 0.01$). This reduction, however, was not as low as expected compared with the degree of stenosis (Fig. 8). When lesions were 90 per cent or greater, a critical reduction in coronary blood flow was seen. It was further noted that when lesions were significant but not critical (50 to 90%), coronary blood flow was maintained at near normal levels under the conditions of the study.

Fig. 7 and 8 graphically depict the relation which was found to exist between coronary blood flow and the percentage patency in the right and left coronary arteries, respectively. Since regional coronary flows are not done frequently in most diagnostic laboratories, an attempt was made to calculate flow for a

FIG. 7 Graph showing patency versus flow in the right coronary artery. Patency is plotted on the horizontal axis and flow represented on the vertical axis, e.g. 90 per cent occlusion will be expressed as 10 per cent patency. Open circles represent 100 per cent patency or no disease in dominant vessels and closed circles 100 per cent patency in non-dominant vessels. Solid squares show diseased vessels. Note the only diseased nondominant vessel (x) has only 20 per cent occlusion. The curved line connecting open triangles represents the linear transform of the hyperbolic function.

FIG. 8 Graph showing patency versus flow for the left coronary artery. Open circles show 100 per cent patency for the left coronary and its branches and closed circles represent significant disease. The remainder of the legend to this figure is the same as for Fig. 7.

given patency level. Using the given data points, a least squares fit of the linear transform of the hyperbolic function (Bliss and James, 1966),

$$F = \frac{AP}{P+B}$$

was calculated (F = coronary blood flow, P = percentage patency, and A and B are constants). This function fulfils two necessary criteria. First, such a function predicts the theoretical condition of zero blood flow at zero percentage patency. In reality, this condition may not apply because of collateral blood flow. Second, at 100 per cent P , this function predicts a coronary blood flow which is not significantly different from that determined experimentally. The constants A and B were determined and the following equations apply to right and left coronary blood flow, respectively:

$$F_R = \frac{(69.10) P}{P + (4.27)}$$

$$F_L = \frac{(83.94) P}{P + (4.01)}$$

Thus, for any determined degree of patency, it becomes possible to predict a corresponding blood flow.

Discussion

The normal values for coronary blood flow reported in this study are in agreement with those of Ross *et al.* (1964) and others (Klein *et al.*, 1965; Pitt, Friesinger, and Ross, 1969; Albert *et al.*, 1970; Cannon, Dell, and Dwyer, 1972). The left coronary artery system has two components, and patency of one major vessel may have contributed to the higher than expected coronary blood flows obtained in the involved artery. Despite this technical problem, a reduced coronary blood flow in the left system was seen when lesions were of critical degree.

Measurements of flow in the right coronary artery, which is a 'one compartment' system, should be free of such technical disadvantages. The normal values for right coronary flow observed in this study differed from those found by Gorlin and coworkers (Klein *et al.*, 1965) who reported somewhat higher flow rates. Separating the right coronaries into 'dominant' and 'nondominant' was useful in explaining some of this variation (James, 1961; Asokan *et al.*, 1972). Our data suggest that the dominant right coronary artery has flows nearly equal to that found on the left, whereas, nondominant right coronary artery flow is consistently lower. Cannon has reported normal flows of 47 and 34 ml min^{-1} per 100 g muscle for right ventricle and right atrium, respectively (Cannon *et al.*, 1972). Our values for the nondominant right coronary artery

flow, 41 ± 2 ml min⁻¹ per 100 g muscle, appear in agreement with their study if one assumes that supply from the nondominant right coronary artery is principally to those structures.

It is widely known that the relation between symptoms of coronary disease and observed anatomical lesions has been inconsistent (Baroldi and Scomazzoni, 1967; Conti *et al.*, 1970; Holmberg *et al.*, 1967; Klocke *et al.*, 1968; Rowe *et al.*, 1969; Schwartz *et al.*, 1973; Soloff, 1972). Part of this problem may be related to varying flow states. Earlier studies using nitrous oxide have been unable to find good agreement between anatomical lesions and flow (Ross *et al.*, 1964). Information on coronary flow after exercise in a diseased vessel is also limited (Holmberg *et al.*, 1967). Conti *et al.* (1970) have measured regional flow after atrial pacing, and were able to show the poor correlation between anatomy and flow. Correlation was lacking when left anterior descending lesions were compared with estimates of left anterior descending flow by great cardiac vein sampling (Schwartz *et al.*, 1973). Since angina pectoris usually occurs during exertion at a time when myocardial oxygen demands are increased, flow measurements made after stress will be important. This is particularly important if the observed lesions were less than 90 per cent and flow measurements made at rest were not correspondingly low.

The limitations of flow measurements by isotope methods are well known and are indeed a major factor in the lack of correlation between stenosis and flow (Ross *et al.*, 1964; Klein *et al.*, 1965; Conti *et al.*, 1970). Further, another factor that limits the sensitivity of the method used in this study is the large volume of myocardium diffused by the right and left coronary artery injections. Since flow of isotope is dependent on the volume of myocardium under exploration, a normal flow could conceivably be shown in areas of reduced myocardial volume as the rate of disappearance of isotope will be unchanged. The use of large crystal gamma cameras might offer improved specificity in regional estimates of myocardial flow in the future. Further criticisms of flow measurements by this technique have been based on the non-homogeneity of coronary blood flow or the non-homogeneity of the isotope distribution (Klocke *et al.*, 1968). The fact that we are able to measure critical reductions in flow in experimental myocardial infarction after coronary occlusion using the same method answers at least some of the technical objections (Burke *et al.*, 1969; Harman *et al.*, 1966).

We conclude that little relation exists between coronary arteriography and coronary blood flow measurements. Implications of this finding are apparent when patients are selected for various

forms of treatment, including coronary artery surgery.

References

- Abrams, H. L., and Adams, D. F. (1969). The coronary arteriogram: structural and functional aspects. (Parts I and II.) *New England Journal of Medicine*, **281**, 1276 and 1336.
- Albert, H., Moccetti, T., Senning, A., and Lichtlen, P. (1970). Zur Myokarddurchblutung nach rekonstruktiver Koronarchirurgie: Koronarflussmessung an Hand der Xenon-Myokard-Clearance-Methode. *Schweizerische Medizinische Wochenschrift*, **100**, 1749.
- Asokan, S. K., Fraser, R. C., Cundey, D. W., and Frank, M. J. (1972). Variations in human right coronary blood flow with and without occlusive disease. *Circulation*, **45**, Suppl. II, 127.
- Baroldi, G., and Scomazzoni G. (1967). *Coronary Circulation in the Normal and the Pathologic Heart*. Armed Forces Institute of Pathology, Washington, D.C.
- Batson, H. C. (1956). *An Introduction to Statistics in the Medical Sciences*. Burgess, Minneapolis.
- Bliss, C. I., and James, A. T. (1966). Fitting the rectangular hyperbola. *Biometrics*, **22**, 573.
- Burke, W. M., Asokan, S. K., Moschos, C. B., Oldewurtel, H. A., and Regan, T. J. (1969). Effects of glucose and non-glucose infusions on myocardial potassium ion transfers and arrhythmias during ischemia. *American Journal of Cardiology*, **24**, 713.
- Cannon, P. J., Dell, R. B., and Dwyer, E. M., Jr. (1972). Measurement of regional myocardial perfusion in man with xenon and a scintillation camera. *Journal of Clinical Investigation*, **51**, 964.
- Conti, C. R., Pitt, B., Gundel, W. D., Friesinger, G. C., and Ross, R. S. (1970). Myocardial blood flow in pacing-induced angina. *Circulation*, **42**, 815.
- Gensini, G. G., and Buonanno, C. (1968). Coronary arteriography: a study of 100 cases with angiographically proved coronary artery disease. *Diseases of the Chest*, **54**, 90.
- Harman, M. A., Markov, A., Lehan, P. H., Oldewurtel, H. A., and Regan, T. J. (1966). Coronary blood flow measurements in the presence of arterial obstruction. *Circulation Research*, **19**, 632.
- Herd, J. A., Hollenberg, M., Thorburn, G. D., Kopald, H. H., and Barger, A. C. (1962). Myocardial blood flow determined with Krypton⁸⁵ in unanesthetized dogs. *American Journal of Physiology*, **203**, 122.
- Holmberg, S., Paulin, S., Prerovsky, I., and Varnauskas, E. (1967). Coronary blood flow in man and its relation to the coronary arteriogram. *American Journal of Cardiology*, **19**, 486.
- James, T. N. (1961). *Anatomy of the Coronary Arteries*, p. 79. Paul B. Hoeber, New York.
- Klein, M. D., Cohen, L. S., and Gorlin, R. (1965). Krypton 85 myocardial blood flow: precordial scintillation versus coronary sinus sampling. *American Journal of Physiology*, **209**, 705.
- Klocke, F. J., Koberstein, R. C., Pittman, D. E., Bunnell, I. L., Greene, D. G., and Rosing, D. R. (1968). Effects of heterogeneous myocardial perfusion on coronary venous H₂ desaturation curves and calculations of coronary flow. *Journal of Clinical Investigation*, **47**, 2711.
- Pitt, A., Friesinger, G. C., and Ross, R. S. (1969). Measurement of blood flow in the right and left coronary artery beds in humans and dogs using the xenon technique. *Cardiovascular Research*, **3**, 110.

- Ross, R. S., Ueda, K., Lichtlen, P. R., and Rees, J. R. (1964). Measurement of myocardial blood flow in animals and man by selective injection of radioactive inert gas into the coronary arteries. *Circulation Research*, 15, 28.
- Rowe, G. G., Thomsen, J. H., Stenlund, R. R., McKenna, D. H., Sialer, S., and Corliss, R. J. (1969). A study of hemodynamics and coronary blood flow in man with coronary artery disease. *Circulation*, 39, 139.
- Schwartz, L., Froggatt, G., Covvey, H. D., Taylor, K., and Morch, J. E. (1973). Measurement of left anterior descending coronary arterial blood flow. *American Journal of Cardiology*, 32, 679.
- Soloff, L. A. (1972). Clinical significance of the angiographic demonstration of coronary atherosclerosis. *American Heart Journal*, 83, 727.
- Sones, F. M., and Shirey, E. K. (1962). Cine coronary arteriography. *Modern Concepts of Cardiovascular Disease*, 31, 735.
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