# Coronary Blood Flow Measured by the Xenon-133 Washout Technique

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## SUMMARY

**Coronary blood flow was measured by the radioactive xenon ($^{133}$Xe) washout technique in 13 subjects: 6 controls, 5 patients with coronary artery disease and 2 patients who had undergone aortocoronary saphenous vein bypass grafts. The method did not discriminate between normal subjects and patients with coronary artery disease, but may be useful to the study of blood flow in coronary bypass grafts. In 2 patients changes in coronary flow were associated with a change in the patient's clinical status.**


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Myocardial ischaemia occurs when myocardial oxygen demand exceeds the available supply. Myocardial oxygen consumption is related to heart rate, ventricular ejection time, myocardial contractility and systolic tension in the ventricle.[1-3] Oxygen supply depends on arterial oxygen content and coronary blood flow—these, in turn, are related to velocity of aortic blood flow, the duration of diastole, the aorta-left ventricular pressure gradient and the length and diameter of the coronary arteries.

There are several methods for measurement of coronary blood flow in man.[4-8] Tracer techniques are effective if the coronary circulation is isolated from other segments of the vascular bed and this can be achieved by selective injection of radioactive xenon ($^{133}$Xe) into the coronary arteries. The gas is taken up by viable myocardium and the washout curve is a function of coronary blood flow, the volume of myocardium in which the gas is distributed and the blood-tissue partition coefficient of xenon.[7] The gas is eliminated from the lungs so that recirculation is unimportant.

We have measured coronary blood flow in 13 patients using the $^{133}$Xe washout technique to assess the value of the method and to study the relationship between the extent and distribution of coronary artery narrowing and obstruction and coronary blood flow.

## PATIENTS AND METHODS

Thirteen patients were studied. The patients were divided into 3 groups.

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**Group 1—normal coronary arteries:** Six patients had a clinical history suggestive of angina pectoris, but coronary angiography showed that the coronary arteries were normal. One patient had hypertrophic (non-obstructive) cardiomyopathy, the others had no haemodynamic abnormality.

**Group 2—coronary artery disease:** Selective coronary angiography showed a proximal obstruction of 70% or more involving one or more major coronary artery(ies) in 5 patients.

**Group 3—coronary artery vein bypass grafts.** Two patients with coronary artery disease (CAD) had undergone the operation of aortocoronary saphenous vein bypass grafting 3 and 5 months before this study.

No patient was receiving coronary vasodilator drugs or drugs which act on the autonomic nervous system at the time of study, although selective injection of contrast medium used for cine angiocardiography alters coronary blood flow.[6,9]

Premedication consisted of 10 mg diazepam and 50 mg pethidine. Routine left heart catheterisation was performed through a percutaneous puncture of the femoral artery. Pressures were recorded by means of a Statham P23 Db bonded strain gauge and an Electronics-for-Medicine DR-16 photographic recorder with electronic analogue differentiating circuit with minimal phase lag or distortion. The mid-chest level was used as the zero reference for pressure measurements.

Left ventriculography was performed in the right anterior oblique (RAO) position by using a slow injection of 50 ml 76% Urografin. Selective left and right coronary angiography was performed by means of the Judkins technique with cine filming at 32 frames per second on Gevapan 36 film in multiple oblique views. A Philips 15-cm image intensifier and Arriflex 35-mm camera were used.[10,11]

Coronary blood flow was measured in each artery after the corresponding coronary arteriogram had been made. Fifteen measurements were made in duplicate. A solution of 0,5-1 mCi $^{133}$Xe dissolved in 2 ml normal saline was injected into each coronary artery; 5 ml flushing solution was used and the catheter promptly withdrawn from the coronary ostium. The myocardial clearance curve of $^{133}$Xe was recorded with a collimated scintillation detector with rate meter and a direct-writing recorder. The curves were digitised manually and analysed as an exponential function by means of a Wang 700 series programmable calculator and plotter-printer. Myocardial blood flow was calculated[6,12-14] for each coronary artery from the formulae of Ross *et al.*[6]:

$$Q_i\ (t) = Q_i\ (0)\ e^{-kt}$$

$$k = \frac{F}{V.\lambda}$$

$$F_{100} = \frac{k\ (\lambda.100)}{\rho}\ \text{ml/min/ 100 g}$$

where $Q_i$ = quantity of indicator,
$k$ = rate constant,
$F$ = flow,
$\lambda$ = partition coefficient of xenon,
$\rho$ = specific gravity of myocardium,
$V$ = volume of myocardium.

## RESULTS

Measurements of coronary blood flow were compared with the clinical status of the patient and the corresponding coronary arteriogram (Table I). Resting coronary blood flow varied in normal subjects (LCA = 43,8 ± 13,2 ml/min/100 g; RCA = 45,8 ± 22,5 ml/min/100 g). There was not a significant difference in patients with coronary artery disease (LCA = 65,1 ± 25,4 ml/min/100 g, NS; RCA = 44,5 ± 10,2 ml/min/100 g, NS) and this confirmed previous reports.[6,15] A large coronary flow was observed in 1 patient with isolated subtotal (90%) disease of the left anterior descending coronary artery. Measurements of blood flow in coronary vein grafts were also similar to those previously reported (30,3 - 76,0 ml/min/100 g).[16]

There was no correlation between abnormal coronary anatomy and coronary blood flow except in 1 patient who had had a triple aortocoronary saphenous vein bypass graft operation. In him, angiography showed large grafts to the left anterior descending and circumflex coronary arteries with good distal perfusion: the flow measurements were 74,0 ml/min/100g and 76,0 ml/min/100 g myocardium respectively. The graft to the distal segment of the right coronary artery supplied a small area of the diaphragmatic surface of the heart and there was slow clearance of angiographic contrast medium from this graft: coronary blood flow was 47,1 ml/min/100 g.

The flow measurements were not reproducible in all patients. In 5 estimations duplicate flow measurements were clearly different: this finding may have been due to a technical fault or to a change in the patient's myocardial oxygen supply and clinical status. Two patients showed a significant reduction in coronary blood flow during the second measurement in the same coronary artery: it is interesting that this was accompanied by angina pectoris in each patient and (reversible) ventricular fibrillation occurred during the immediately succeeding (contralateral) coronary angiogram.

## DISCUSSION

Resting coronary blood flow per 100 g of viable myocardium is similar in normal subjects and in patients with coronary disease and myocardial hypertrophy, although

TABLE I. CORONARY ARTERIOGRAPHIC AND CORONARY FLOW DATA

| | Age | Sex | Angina* | Dyspnoea* | Coronary arteriography (% obstruction) RCA | LAD | Circumflex | Coronary blood flow (ml/min/100 g) RCA 1 | RCA 2 | RCA Mean | LCA 1 | LCA 2 | LCA Mean | Grafts LAD | Grafts Circumflex |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Group 1. Control subjects** | | | | | | | | | | | | | | | |
| 1 | 59 | F | | | | | | — | — | — | 32,5 | 37,0 | 34,7 | | |
| 2 | 50 | F | | | | | | 60,6 | 77,9 | 69,2 | 29,4 | 54,8 | 42,1 | | |
| 3 | 55 | F | | | | | | 59,4 | — | 59,4 | 49,1 | — | 49,1 | | |
| 4 | 49 | F | | | | | | 20,4 | — | 20,4 | 24,6 | 39,0 | 31,8 | | |
| 5 | 39 | M | | | | | | — | — | — | 57,6 | 78,0 | 67,8 | | |
| 6 | 78 | M | | | | | | 30,3 | 38,1 | 34,2 | 34,8 | 39,7 | 37,2 | | |
| Mean ± 1 SD | | | | | | | | | | 45,8 ±22,5 | | | 43,8 ±13,2 | | |
| **Group 2. Coronary artery disease** | | | | | | | | | | | | | | | |
| 7 | 60 | M | 3 | 1 | | 90 | 90 | 31,7 | — | 31,7 | 39,6 | — | 39,6 | | |
| 8 | 43 | M | 3 | 1 | 100 | 100 | | 35,3 | 43,5 | 39,4 | 63,4 | 57,1 | 60,1 | | |
| 9 | 62 | M | 3 | 1 | | 90 | | 71,5 | 38,5 | 55,0 | 145,4 | 68,8 | 107,1 | | |
| 10 | 45 | M | 3 | 2a | 80 | 100 | 100 | 38,8 | 45,1 | 41,9 | 60,6 | 71,1 | 65,8 | | |
| 11 | 42 | M | 3 | 1 | 80 | 95 | 100 | 61,6 | 48,0 | 54,8 | 52,9 | — | 52,9 | | |
| Mean ± 1 SD | | | | | | | | | | 44,5± 10,2 | | | 65,1± 25,4 | | |
| **Group 3. Post-aortocoronary vein bypass grafts** | | | | | | | | | | | | | | | |
| 12 | 58 | M | 2a | 2b | 60 | 100 | 100 | 26,9 | — | 26,9 | 72,2 | — | 72,2 | 47,1 | 74,0 | 76,0 |
| 13 | 67 | M | 2a | 1 | 40 | 100 | 80 | — | — | — | 54,8 | 42,5 | 48,7 | — | 33,5 | 30,3 |
| Mean | | | | | | | | | | 26,9 | | | 60,5 | 47,1 | 53,8 | 53,2 |

* New York Heart Association grading at time of study.[30]

there is an abnormal response to exercise and to coronary vasodilators in patients with coronary artery disease.[6-8,15,17-20] Pacing-induced angina may cause a considerable increase in coronary flow; the increase may be due to increased flow in the normal adjacent non-ischaemic area as a compensatory mechanism or following the liberation of vasodilator substances from ischaemic tissue.[21] The concept of 'coronary steal' has also been suggested,[20,22,23] where vasodilatation of the resistance vessels in the non-ischaemic area in response to certain vasodilators shunts blood away from the ischaemic zone.

The measured rate of disappearance of $^{133}Xe$ is a function of coronary blood flow, the volume of myocardium and the partition coefficient of xenon; if coronary flow and myocardial volume are decreased proportionately, there is no change in the rate of disappearance and the apparently normal flow may be due to lack of perfusion of a fibrous or cold area of myocardium.[7] The $^{133}Xe$ method, made with a single praecordial counter, is often incapable of detecting areas of reduced blood flow.

We have observed that clinical symptoms may be accompanied by changes in the $^{133}Xe$ washout curve and that angiographically visible abnormalities in perfusion are usually confirmed by coronary blood flow measurement. The method is probably insensitive where there are small changes in regional coronary flow, and the problem of inhomogeneous perfusion is the most likely explanation for conflicting results.[20,24] We have been disappointed by the insensitivity of the $^{133}Xe$ washout technique in assessing regional abnormalities of myocardial perfusion, although it may be useful to study the effect of acute interventions (e.g. exercise or drugs) on myocardial blood flow[7,20] or for the serial study of aortocoronary saphenous vein bypass grafts. It does not measure coronary blood flow in absolute terms of ml/min.

Fibrotic areas of myocardium with reduced perfusion can be demonstrated by regional scintiscanning[25,27] or by macro-autoradiography in the animal laboratory.[28] Moreover, macro-autoradiography has shown that radioactivity is located primarily in the myocardium during the early portion of the xenon washout curve and later in epicardial fat. More sophisticated methods of measuring regional abnormalities of perfusion, such as the injection of $^{42}K$, require more extensive investigation and verification.[29]

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