

## EFFECTS OF ACUTE ISCHAEMIA INDUCED BY ATRIAL PACING ON CORONARY BLOOD FLOW IN DOGS\*

*R. Seabra-Gomes, A. F. Rickards, D. J. Parker*

The Department of Clinical Measurement. National Heart Hospital and Cardiothoracic Institute.  
London, U. K.

### SUMMARY

Five anaesthetized open chested dogs were studied by measuring left anterior descending (LAD) coronary blood flow, at rest, after atrial pacing and after Isoprenaline infusion. The LAD was then stenosed in order to reduce the hyperaemic response and then the study was repeated. During the control situation LAD flow was shown to increase with the increase in heart rate. Although the partial occlusion did not drop resting coronary flow, it actually fell under stress conditions to 68 % of the control values. The importance of this observation is that although one might expect flow in a stenosed vessel to increase to a maximum limited by the stenosis, this in fact does not happen. It appears that with increasing stress, local ischaemia produces a rise in coronary resistance. Such a mechanism may explain the occurrence of myocardial infarction without proximal occlusion of coronary vessels and may explain the discrepancy between the time course of myocardial infarction as observed following experimental coronary ligation and that seen in man.

When myocardial oxygen demand is increased there is a parallel increase in coronary blood flow under normal conditions (Katz e Feinberg 1958). In the presence of a flow limiting stenosis it has been assumed that coronary blood flow increases to a limit imposed by the stenosis and then can increase no further. If myocardial oxygen demand continues to increase a situation develops where the metabolic demands of the myocardium cannot be met and the myocardium therefore becomes ischaemic.

To examine whether this simple concept is true an experiment was designed whereby myocardial oxygen consumption was increased in the presence of a critical stenosis and the changes in coronary blood flow observed.

### MATERIALS AND METHODS

Five anaesthetised open chested mongrel dogs were studied. Fig 1 shows variables measured during the experiment. The proximal left anterior descending (LAD) coronary artery was dissected for about 2 cm just proximal to the origin of the diagonal

---

(\*) This Study was presented at the British Cardiac Society, Edinburgh 1976 and at a Joint Symposium of the French and European Society of Cardiology, Bordeaux 1976.

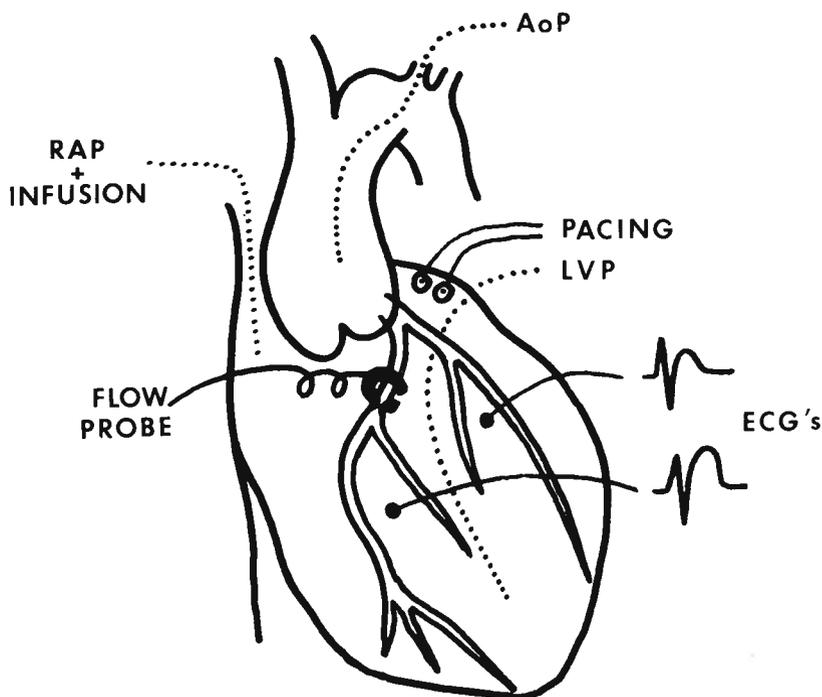


Fig. 1—*Experimental design. Three catheters were used, for mean right atrial pressure and isoprenaline infusion (RAP), mean aortic pressure (AoP) and left ventricular pressure and its first derivative (LVP). Electrodes were placed in LAD and circumflex territories*

vessel. An electro magnetic flow meter was placed around this vessel. A catheter tipmanometer was introduced into the left ventricle through the left atrial appendage and two intramural electrodes were placed in the anterior descending territory in the area distal to an induced stenosis and away from this area in the circumflex territory. The information derived from the left ventricular pressure, anterior descending coronary flow and the two electrograms was recorded on an FM tape recorder played back into a Hewlett-Packard multi-channel recorder for later analysis. Myocardial oxygen consumption was increased by two manoeuvres. Firstly atrial pacing was performed using a bipolar electrode placed on the left atrial appendage and connected to a pacemaker capable of increasing the heart rate at increments of 30 beats between 210 and 300 beats per minute. Secondly an isoprenaline infusion starting at  $0.5\mu\text{g}/\text{Kg}/\text{m}$  and progressively increasing using a Harvard infusion pump, was used. The protocol demanded that following control measurements of flow and pressure, oxygen demand was increased firstly by using the pacing method, each one minute run consisting of 50 seconds of pacing followed by 10 seconds of switch off, the variables being measured in the immediate switch off period. This was necessary as the pacing artifact would otherwise interfere with the electro-magnetic flow probe and make measurements of flow unreliable. Secondly isoprenaline was infused and attempts made to record flow and pressure over the same range of heart rates as that obtained with atrial pacing. A critical stenosis was then produced in the anterior descending coronary artery just distal to the electro

magnetic flow probe by slowly tightening a linen thread. The degree of stenosis was estimated by calculating the hyperaemic response to a period of 10 second occlusion. This is shown in Fig 2. In the upper part of the panel the difference between the resting flow and a flow following a ten second occlusion of the anterior descending coronary artery in the unobstructed condition is shown and it is noted that the flow increased by a factor of 3.6 following the release of the clamp. In the lower part of the panel the same manoeuvre was undertaken following constriction of the artery by the linen thread. As the linen thread was being constricted it was important not to reduce the resting flow but only to reduce the hyperaemic response to a value of less than 1.5:1 over the resting flow. In this way although the resting flow was not changed, a critical stenosis was induced which in theory would allow a maximum flow through this vessel corresponding to the hyperaemic response. This value of 1.5:1 for the hyperaemic response corresponds in man to approximately a 90% stenosis.

Following induction of the stenosis the same manoeuvres to increase myocardial oxygen consumption were then used and the results which will be discussed compare the values obtained before and after the stenosis was induced.

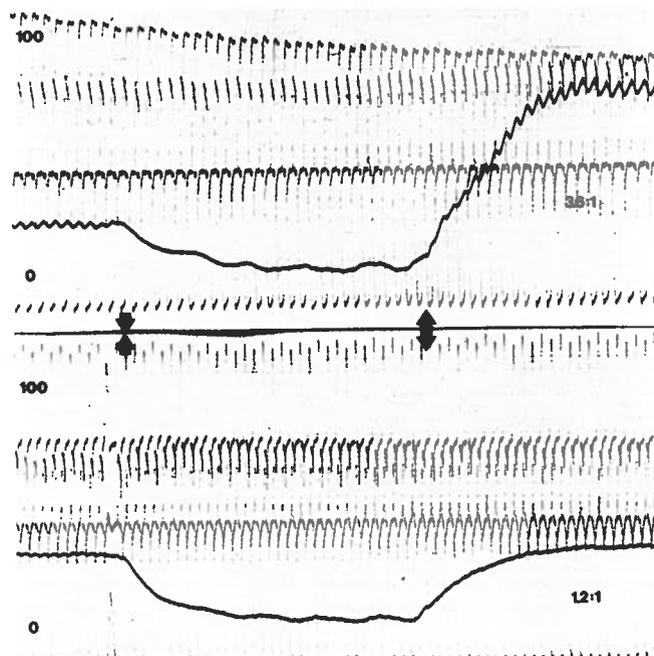


Fig. 2—Recordings of ECG of the LAD electrogram, LV pressure and its first derivative and mean LAD coronary blood flow, to show an example of the hyperaemic response in one dog. On the top part is the nonobstructed vessel, the response to a 10 second occlusion is 3.6:1. On the lower part with the LAD obstructed the hyperaemic response is 1.2:1

## RESULTS

Mean resting left anterior descending coronary blood flow in the five animals was  $26 \pm 4$  ml/m before the stenosis was induced and  $25 \pm 3$  ml/m after the ligation. The hyperaemic response before stenosis averaged 3.6:1 and after the ligation

averaged 1.4:1. Fig 3 shows the results obtained with atrial pacing and isoprenaline infusion in 5 animals. Atrial pacing in the control situation produced a progressive and significant increase in coronary blood flow from the resting value of 26 ml/m up to 48 ml/m but following the induction of the coronary stenosis flow actually decreased from the resting value of 25 ml/m to an average of 17 ml/m. This difference was statistically significant. With Isoprenaline infusion although the heart rate is not as accurately controlled, the same trend is seen with the flow progressively falling with increased heart rate in the presence of a critical stenosis. During atrial pacing small but insignificant rises were seen in left ventricular end diastolic pressure following the application of the stenosis and these were not observed with Isoprenaline. There were no obvious changes in left ventricular systolic function.

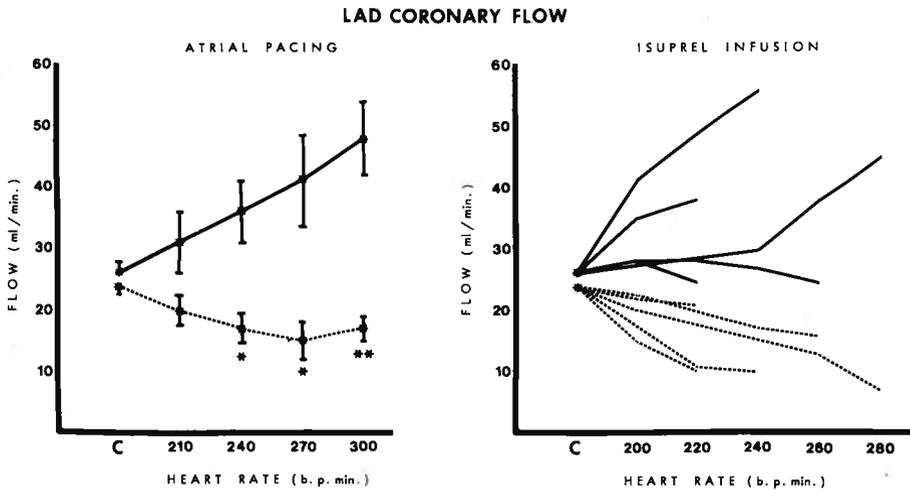


Fig. 3 — Values of the LAD coronary flow plotted against heart rate, in response to Atrial Pacing and Isoprenaline infusion. The dotted line represents the blood flow in the obstructed LAD. C = control heart rates. \*  $p < .05$  \*\*  $p < .01$ . (Means  $\pm$  ISD plotted for atrial pacing test, individual values in each animal for isoprenaline)

## DISCUSSION

The factors controlling myocardial blood flow with increasing heart rate are complex. In the presence of an unobstructed vessel increasing myocardial consumption has been shown to increase coronary flow by reduction of coronary vascular resistance without changes in coronary driving pressure (Katz & Feinberg 1958; Maxell et al 1958). We had expected that in the presence of a flow limiting stenosis that flow would increase to a value dictated by the degree of stenosis and then increase no further, myocardial ischaemia then supervening. However we were surprised to note that consistently in all our experiments flow actually decreased compared with the resting value. It appeared therefore that coronary vascular resistance in the territory beyond the stenosis was showing an increase, presumably related to ischaemia.

A possible explanation of this effect with the increasing heart rate in the presence of a stenosis is that as coronary blood flow is mainly diastolic, the stenosis is reducing the higher components of phasic flow during diastole which would normally contribute to the overall increase in flow with increasing heart rate. As the stenosis limits these

high velocity components and with the decreasing diastolic interval induced by increasing heart rate, flow might be expected to progressively fall beyond the stenosis. While this explanation is undoubtedly tenable for the Isoprenaline experiment it cannot be so for the atrial pacing experiment as the observations were made at the control heart rate immediately after the pacemaker had been switched off. In this immediate post-pacing interval the heart rate was not significantly different from control the diastolic interval was not measurably shorter than in the control state and it appeared that the decreased coronary flow was independent of the diastolic interval and independent of the limitation by the stenosis of the high velocity components of coronary flow. It is likely however that under normal conditions that the apparent increase in coronary vascular resistance is a function of both the decreasing diastolic interval, the limitation of the high velocity components by the stenosis in diastole and also a real increase in coronary resistance which seems to be associated with myocardial ischaemia.

This observation of a paradoxical decrease in flow to an ischaemic territory is consistent with observations made by others in man (Maseri et al. 1971) but the explanation is uncertain. However it is certain that an ischaemic rise in coronary resistance must be considered in addition to the classical hypothesis used to explain angina.

#### RESUMO

Fez-se o estudo do fluxo da artéria coronária descendente anterior em cinco cães anestesiados e com tórax aberto, em repouso, após *pacing* auricular e após infusão de Isoprenalina. A artéria foi depois parcialmente ocluída de modo a reduzir a resposta hiperémica, e o mesmo protocolo repetido.

Durante o período de controle o fluxo coronário aumentou com os aumentos da frequência cardíaca. Após a oclusão parcial da artéria coronária, embora o fluxo em repouso não se alterasse, a resposta ao aumento da frequência cardíaca traduziu-se numa redução do fluxo para 68 % do seu valor controle.

O facto mais importante destas observações, é que embora fosse de esperar que o fluxo dum vaso estenosado aumentasse até ao valor máximo imposto pela estenose, isto na realidade não acontece. Parece assim que, com um aumento da frequência cardíaca, a isquémia local produzirá uma subida da resistência dos vasos coronários. Tal mecanismo poderá explicar a ocorrência de enfarte do miocárdio sem oclusão proximal do vaso coronário, e a discrepância entre a evolução temporal do enfarte do miocárdio provocado experimentalmente e a observada na situação humana.

#### REFERENCES

- KATZ LN, FEINBERG H: The relation of cardiac effort to myocardial oxygen consumption and coronary flow. *Circulation Research* 6: 656, 1958.
- MASERI A, MANCINI P, L'ABBATE A, CONTINI C, PESOLA A: Alterations of regional myocardial perfusion during angina. In *Myocardial blood flow in man*, Edt. A. Maseri, *Minerva Medica*, p. 543, 1971.
- MAXWELL GM, CASTILLO CA, WHITE DH, CRUMPTON CW, ROWE GG: Induced tachycardia: its effect upon the coronary hemodynamics, myocardial metabolism and cardiac efficiency of the intact dog. *J Clin Invest* 37: 1413, 1958.

Adress for reprints: R. Seabra-Gomes  
Serviço de Cardiologia Médico-Cirúrgica  
Hospital de Santa Maria  
Lisboa - Portugal