

## Factors influencing the ocular pulse – the heart rate

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**Abstract.** Using pneumotometry combined with a Langham ocular blood-flow system, measurements of pulsatile ocular blood flow (POBF) were performed in eight ocular normotensive patients with implanted cardiac pacemakers, with the subjects assuming both the erect and the supine postures. Sequential measurements of POBF were made at pre-set values of heart rate over the physiological range between 60 and 120 beats/min at intervals of 10 beats/min. With patients in the supine position, measurements of cardiac output and stroke volume indices were also recorded by impedance cardiography. The mean pulse amplitude of the intraocular pressure (the ocular pulse) decreased as heart rate increased, and this change was statistically significant in both postures according to repeated-measures analysis of variance (erect:  $f=18.7$ ,  $P<0.0001$ ; supine:  $f=18.8$ ,  $P<0.0001$ ). As measured in supine patients following an increase in heart rate, the pulse amplitude decreased in parallel with a decline in stroke volume index ( $f=18.8$ ,  $P<0.0001$ ). Up to a level of 90 beats/min, the mean POBF increased with heart rate, but it declined above this rate in both erect and supine postures. At all heart rates, intraocular pressure was higher when subjects were supine than when they stood erect ( $f=4.3$ ,  $P<0.001$ ). At lower heart rates of 70 and 80 beats/min, ocular pulse volume and POBF were significantly lower in supine patients than in erect subjects (70 beats/min:  $t=3.89$ ,  $P<0.01$  vs;  $t=3.87$ ,  $P<0.01$ ; 80 beats/min:  $t=2.85$ ,  $P<0.05$  vs;  $t=2.87$ ,  $P<0.05$ ). We conclude that when the heart rate is under normal physiological drive, the decline in POBF that accompanies the act of lying down is determined both by the change in posture itself and by the fall in heart rate that is associated with it. These observations suggest a possible disadvantage inherent in the use of anti-glaucoma drugs that inter alia induce bradycardia.

### Introduction

We have previously shown that pulsatile ocular blood flow (POBF) decreases markedly in ocular normotensives and hypertensives assuming the supine posture [11] and in patients suffering from chronic open-angle glaucoma [12]. If this change is also reflected in total perfusion of the optic nerve head, which has both pulsatile and non-pulsatile components, then patients may be suffering from a damaging relative ischaemia during the hours when they are recumbent. Assumption of the supine position is accompanied by a rise in intraocular pressure (IOP) as well as a fall in heart rate [9], both of which may affect the circulation by reducing blood flow [1]. In an attempt to analyse further the relative contribution of the heart rate to POBF, measurements were made in patients with implanted cardiac pacemakers, whose pacing rates could be altered independently of posture. Additional information on cardiac output and stroke volume indices has also been obtained in supine subjects using the technique of impedance cardiography [2, 3].

### Subjects and methods

#### Subjects

Eight patients (four men and four women; mean age, 68.9 years) were recruited from the pacing clinic in the Department of Cardiology at Westminster Hospital. Each patient suffered from sick sinus syndrome and was fitted with a dual-chamber cardiac pacemaker (DDD) that enabled the variation of heart rate and atrio-ventricular (AV) delay. AV-sequential pacing was performed in all subjects for all measurements and a 'physiological' AV delay was chosen for each heart rate, as cardiac output may be affected by pacing mode and AV delay [7]. All patients gave their written consent to participate and the study was approved by the Ethics Committees of West Lambeth and Riverside East Health Authorities.

**Table 1.** Differences in ocular and systemic variables concerned in POBF as measured at various heart rates in erect vs supine posture in patients with implanted cardiac pacemakers

Variable	Posture	Heart rate (beats/min)						
		60	70	80	90	100	110	120
IOP (mmHg)	Erect	–	15.7 (1)	15.1 (1.1)	15.5 (1)	15.1 (1)	15.1 (0.9)	16 (0.9)
	Supine	19 (1.3)	18.9 (1.4)	18.9 (1.1)	18.4 (1.4)	18.3 (1.2)	18.5 (1.1)	17.8 (1.2)
Pulse amplitude (mmHg)	Erect	–	1.57 (0.16)	1.27 (0.11)	1.21 (0.12)	1.05 (0.1)	0.86 (0.11)	0.73 (0.08)
	Supine	1.5 (0.2)	1.51 (0.2)	1.46 (0.2)	1.34 (0.23)	1.11 (0.19)	1 (0.17)	0.84 (0.14)
Systolic BP (mmHg)	Erect	–	132.6 (8.3)	137 (6.3)	129.1 (7.5)	127.1 (6.5)	127.1 (9.8)	122 (6.1)
	Supine	121.8 (5.2)	127.8 (7.6)	129.6 (6)	128.5 (6.9)	126.5 (5.9)	129.9 (6)	127.9 (8.4)
Diastolic BP (mmHg)	Erect	–	87 (2.5)	90.6 (2.8)	90.1 (3.8)	90.1 (3.2)	91.6 (3)	90.6 (4.6)
	Supine	77.7 (1.8)	79.8 (2.1)	83.1 (1.9)	87.5 (2.1)	88.6 (2)	92.2 (1.7)	94.5 (3.6)

Data represent mean values  $\pm$ SEM. BP, Blood pressure

### Methods

With the subject standing, the cardiac pacing rate was adjusted to 70 beats/min. A constant rate of 60 beats/min could not be sustained, as patients's natural electrical heart activity tended to override their pacemakers. Measurements of POBF in the right eye were performed with subjects under local anaesthesia with 0.4% benoxinate using pneumotometry coupled to a Langham ocular blood-flow system as previously described [11, 12]. Heart rate and systemic blood pressure were recorded simultaneously by ECG and on a Takeda Medical UA-751 Digital blood-pressure meter. Subsequently, the pacing rate was adjusted in turn to 80, 90, 100, 110 and 120 beats/min and the above measurements were repeated after each adjustment. At each pacing rate the AV delay was altered to reflect normal physiological changes. Before each series of measurements, a 2-min rest period was observed after the heart rate had been re-set.

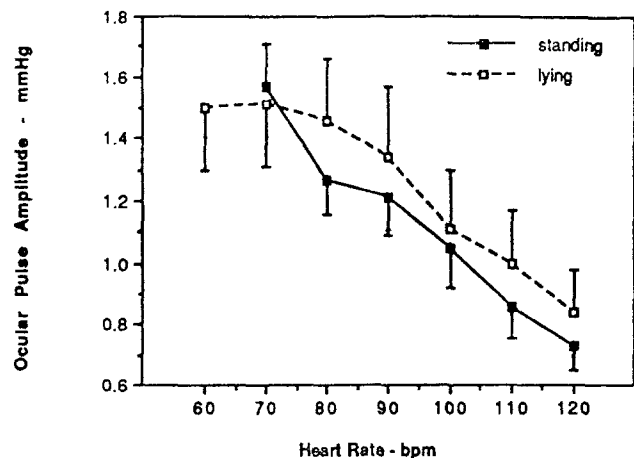
Subsequently, the subject relaxed supine for a period of 15 min after the pacing rate had been re-set to 60 beats/min, which was sustainable in this posture. The above sequence of measurements at each of the heart rates was then repeated in this position. Additionally, in supine patients, measurements of cardiac and stroke volume indices were made using an NCCOM3 (BoMed) Impedance Cardiograph [2, 3]. Following completion of the study, the pacing rate was re-set according to the patient's individual clinical requirements.

### Statistical analysis

Postural effects on the pulse amplitude of intraocular pressure, the single pulse volume for each bolus of blood entering the eye and POBF were compared by analysis of covariance and Student's paired *t*-test. For each posture, changes in cardiac output and stroke volume indices and in POBF, ocular pulse amplitude, IOP and mean systemic blood pressure were examined by repeated-measures analysis of variance. For the erect position, measurements were not obtainable in one patient at 70 and 80 beats/min and in another subject at 120 beats/min only.

### Results

The mean ( $\pm$ SEM) values obtained for variables concerned in POBF at different heart rates are shown in Table 1.



**Fig. 1.** Effect of heart rate on the mean pulse amplitude of intraocular pressure (ocular pulse) in the right eye. Vertical lines indicate the SEM

### Effects of altered heart rate

No alteration in IOP was significantly associated with a change in heart rate as measured in subjects assuming either posture. The mean pulse amplitude of the IOP (the ocular pulse) decreased significantly with increasing heart rate, regardless of the patients' posture (erect:  $f=18.7$ ,  $P<0.0001$ ; supine:  $f=18.8$ ,  $P<0.0001$ ; Fig. 1). The apparent non-linearity of the values obtained in supine patients was largely contributed by one of the subjects and, overall, was not statistically significant.

Ocular pulse volume, derived from the pulse amplitude and the duration of its waveform, declined with increasing heart rate (erect:  $f=20$ ,  $P<0.0001$ ; supine:  $f=18.6$ ,  $P<0.0001$ ; Fig. 2). POBF demonstrated a curvilinear relationship with heart rate, the maximal values occurring at 90 beats/min in both erect and supine subjects (Fig. 3).

In supine patients, the cardiac index did not alter but the stroke volume index decreased significantly ( $f=15.7$ ,  $P<0.0001$ ) with increasing heart rate (Table 2).

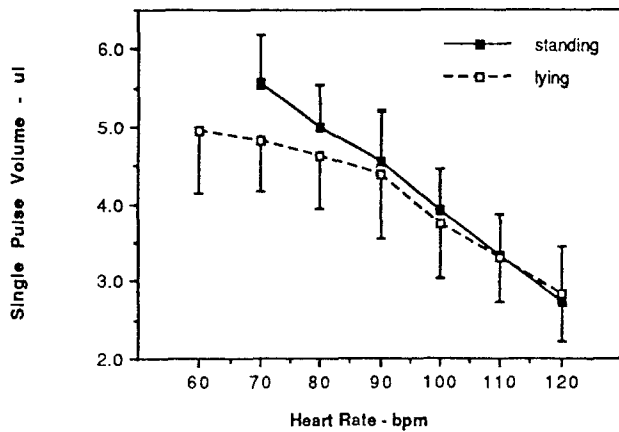


Fig. 2. Effect of heart rate on the mean volume of a single pulse (bolus) in the right eye. Vertical lines indicate the SEM

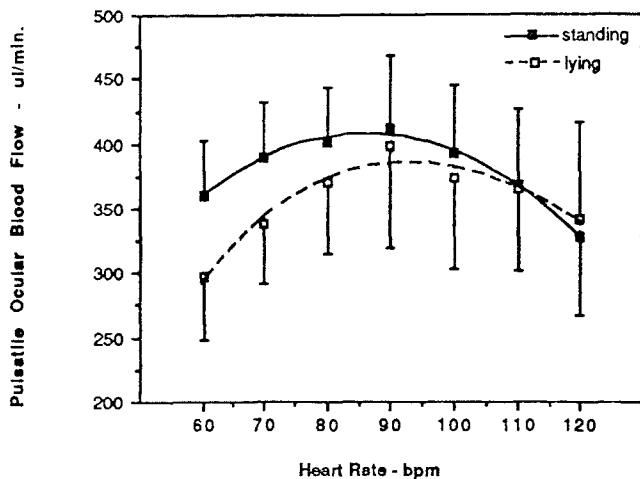


Fig. 3. Effect of heart rate on mean pulsatile ocular blood flow in the right eye. Vertical lines indicate the SEM

Moreover, increasing heart rate was associated with a rise in diastolic blood pressure alone and, therefore, with a resultant change in mean systemic blood pressure ( $f=3.92$ ,  $P=0.005$ ). Neither systolic nor diastolic blood pressure altered significantly in erect subjects.

#### Postural differences

IOP was significantly higher in supine subjects at all heart rates, but no overall significant differences in the

other parameters were attributable to posture as determined using analysis of covariance. However, at 70 and 80 beats/min, the single pulse volume, POBF and mean systemic blood pressure were significantly reduced in supine patients. The mean single pulse volume was reduced at 70 beats/min from  $5.57 \pm 0.61$  to  $4.82 \pm 0.66$   $\mu\text{l}$  ( $P < 0.01$ ) and at 80 beats/min from  $5 \pm 0.53$  to  $4.63 \pm 0.68$   $\mu\text{l}$  ( $P < 0.05$ ).

Similarly, the mean POBF was reduced at 70 beats/min from  $390 \pm 42$  to  $338 \pm 46$   $\mu\text{l}/\text{min}$  ( $P < 0.01$ ) and at 80 beats/min from  $401 \pm 42$  to  $370 \pm 55$   $\mu\text{l}/\text{min}$  ( $P < 0.05$ ). Differences noted at other heart rates were not statistically significant. Postural differences in the mean systemic blood pressure measured at these heart rates were: 70 beats/min  $102.9 \pm 3.7$  mmHg in erect patients vs.  $95.8 \pm 3.4$  mmHg in supine subjects ( $P < 0.05$ ); 80 beats/min,  $105.9 \pm 3.6$  mmHg in erect patients vs  $98.6 \pm 2.9$  mmHg in supine subjects ( $P < 0.05$ ).

#### Discussion

The results of the present study show that the pulsatile component of ocular blood flow is maximal at a heart rate of approximately 90 beats/min in both upright and supine patients. The curvilinear relationship found was such that at slower heart rates, which are usually encountered except in exercising subjects, assumption of the supine posture was accompanied by a fall in POBF. This is attributable partly to the change in posture and partly to the resultant decline in heart rate. Observations recorded using the Langham technique reflect only the IOP change produced by the entry of a bolus of arterial blood into the ocular circulation at systole. However, diastolic blood flow has been demonstrated in Doppler ultrasound studies of the ophthalmic artery [5], suggesting the existence of a non-pulsatile component of total ocular blood flow. The extent to which the changes we measured in various ocular and systemic parameters affect non-pulsatile flow and, therefore, the total amount of blood passing through the eye remains unclear.

Additional information from our results may provide a useful indication of the relative contributions of the pulsatile and non-pulsatile components, however, particularly with respect to any differences occurring at the higher and lower heart rates encountered in man. We showed that the diastolic blood pressure increases as the heart rate rises, and as previous ultrasound studies have demonstrated that non-pulsatile flow is present in

Table 2. Systemic variables measured by impedance cardiography in supine cardiac-paced patients

Variable <sup>a</sup>	Heart rate (beats/min)						
	60	70	80	90	100	110	120
Stroke volume index ( $\text{ml}/\text{m}^2$ )	54.1 (6.4)	46.1 (4.3)	40.2 (3.9)	39.9 (4.5)	35.3 (3.6)	32.9 (3.0)	29.5 (3.32)
Cardiac index ( $\text{l min}^{-1} \text{m}^{-2}$ )	3.25 (0.38)	3.23 (0.30)	3.22 (0.32)	3.59 (0.40)	3.51 (0.37)	3.61 (0.33)	3.54 (0.39)

Data represent mean values  $\pm$  SEM

<sup>a</sup> Variables were measured in terms of body surface area

diastole [5], it is possible that at the higher heart rates, this component is increased at the expense of the pulsatile component. This assertion is supported by the changes observed in the ocular pulse; as heart rate increased, the amplitude of the ocular pulse and the derived values of single pulse volume decreased in an essentially linear fashion. This suggests that as heart rate increases, there may be a shift from pulsatile to non-pulsatile flow. Pacing rates of >90 beats/min may be non-physiological, altering cardiac output [10] and further affecting the relationship between pulsatile and non-pulsatile blood flow.

At heart rates of <90 beats/min, the usual physiological state, the pulsatile ocular blood flow also falls. However, the present study shows that when the heart rate decreases, the diastolic blood pressure remains relatively low and, thus, the shift to non-pulsatile flow may not necessarily occur under these circumstances. This would suggest that when individuals are lying down and when the heart rate is lower, not only POBF but also total ocular blood flow is reduced.

The postural differences noted in POBF must still be explained, however. There is some evidence of a volume reduction of each bolus of blood entering the eye in supine as compared with erect subjects. This may be related to a number of factors. First, the reduction in blood pressure associated with the supine position, could affect the pulsatile flow, and second, a reduction in cardiac output and, particularly, in stroke volume may also be responsible for reduced POBF. For technical reasons, we could not measure stroke volume and cardiac indices in erect subjects in the present study, but a posture-related change in these parameters is a well-recognised phenomenon [4].

In conclusion, the present study demonstrated that POBF is affected by changes in the heart rate and reaches a peak value at approximately 90 beats/min in both erect and supine individuals. At rates lower than this, a significantly lower POBF is measured in supine subjects. We attempted to relate these observations to known physiological changes in the circulation and cardiac indices. These findings may be of importance in vascularly related ophthalmic disease such as glaucoma and ischaemic optic neuropathy. Our measurements provide information on the pulsatile component of total ocular blood flow, 90%–95% of which is choroidal [6, 8] and derived from the posterior ciliary circulation, and

which also supplies the optic nerve head. There are also implications for the therapeutic use of drugs such as beta-blockers, which reduce heart rate and cardiac output, thus potentially reducing pulsatile perfusion.

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