The Effect of a Progressive Decrease in the Circulating Blood Volume of the Dog on the Transthoracic Impedance

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Abstract. The correlations between the haemodynamic and transthoracic electrical impedance changes resulting from a progressive reduction in the circulating blood volume were studied in four intact mongrel dogs artificially ventilated with a mixture of halothane in nitrous oxide-oxygen. The cardiac output of the dogs was measured by both the electrical impedance and the fibre optic dye dilution techniques. It was found that significant correlations existed between the blood loss and the arterial blood pressure, the maximum first derivative of the transthoracic impedance, the Heather Index, the transthoracic impedance, the maximum rate of change of aortic pressure and the cardiac stroke work. There was also a good correlation between the dye and impedance cardiac output values, the impedance value always being higher than the corresponding dye value. The correlation between the Heather Index and the PEP/LVET ratio and $1/PEP^2$ varied markedly from dog to dog.

Key words: Thoracic impedance, Haemorrhage, Systolic time intervals.

Introduction

The availability of a fibre optic densitometer (Polanyi, 1975) led us to investigate the changes in cardiac output in the dog as a result of a progressive reduction in the circulating blood volume using both the dye dilution and the electrical impedance method of Kubicek et al., (1966) and to compare the changes observed in the transthoracic impedance waveforms with the corresponding changes seen in as many haemodynamic variables as possible. The following measurements were performed: heart rate; aortic blood pressure; stroke volume and cardiac output by the dye dilution and electrical impedance methods; left ventricular stroke work; maximum rate of rise of the aortic blood pressure; the area under the aortic pressure curve during active systole; the maximum rate of change of the transthoracic impedance $(dZ/dt)_{max}$; the transthoracic impedance Z_o; the ratio of the pre-ejection period to left ventricular ejection time PEP/LVET; the reciprocal of the pre-ejection period squared $1/PEP^2$; the diastolic interval and the Heather Index.

Methods

Four unselected mongrel dogs of either sex and weighing 19.7–27 kg were premedicated with acepromazine (0.2–0.4 mg per kg) intramuscularly. They were anaesthetised 30 to 60 minutes later with thiopentone sodium (25 mg per ml, 0.5 ml per kg) intravenously. The trachea was intubated with a 9–11 mm cuffed endotracheal tube and anaesthesia maintained with 1.0–1.5% halothane in nitrous oxide/oxygen (60/40). Intermittent positive pressure ventilation was provided by a Manley ventilator (Hutchinson Blease Ltd.) with a non-rebreathing system, at an inflation pressure of 20–25 cm water. The minute volume of ventilation was adjusted in each case to maintain the arterial carbon dioxide tension within physiological limits. The body temperature was maintained at $37\,°C \pm 1.5\,°C$.

Following the induction of anaesthesia, a polyethylene cannula (Bardic, 18) was introduced into the left femoral artery for the withdrawal of blood. A catheter-tip micro-pressure transducer (Millar Instruments Inc. Model PC-350) was introduced into the ascending aorta via the right femoral artery for the measurement of the aortic pressure. An atmospheric pressure reference was obtained during the previous calibration of the transducer in water at 37 °C. A thermistor temperature probe (Light Laboratories Ltd., size 5F) was placed in the right femoral vein to monitor body temperature. Two catheters were advanced into the ascending aorta via the right carotid artery and placed approximately 20 mm from the aortic valve. One was a fluid-filled nylon catheter (5F, Portex

Ltd.) and the other was a 7F fibre optic catheter having a fluid-filled lumen. Placement of each catheter was achieved by temporarily connecting each to an external pressure transducer (Bell and Howell Ltd., Type 4-327-L221) and using the resulting pressure signal to determine entry, firstly into the left ventricle, with subsequent withdrawal into the ascending aorta. The fibre optic catheter was then connected to a fibre optic densitometer (Schwarzer in-vivo Hemoreflectometer IVH 3). The 5F nylon catheter was connected to a conventional densitometer cuvette (Waters Instruments Inc., Model DC-410) and then to a constant rate withdrawal syringe (Sage Instruments). The output signal from the densitometer was taken to an analogue cardiac output computer (Waters Instruments Inc., Model DCR-702). A fluid-filled nylon catheter (5F, Portex Ltd.) was placed in the left ventricle via the left carotid artery for dye injection. This was connected to a powered injector (Contraves AG) set to deliver a dose of indocyanine green dye and 5 ml of saline wash. It was triggered by the preceding R-wave of the lead II ECG after a delay of approximately 300 ms. A similar catheter was placed in the right ventricle via the left jugular vein for pressure measurements and connected to an external pressure transducer (Bell and Howell Ltd., Type 4-327-L221). The position of each catheter was verified by pressure tracings and re-checked at autopsy.

Four disposable Mylar tape electrodes, each having an aluminium strip along its mid-line (3M type M 6001) were placed around the dog in order to measure its transthoracic impedance, the skin under the electrodes having been closely shaved and smeared with Cambridge electrode jelly. Two electrodes were placed around the neck and two around the thorax, the innermost at the level of the xiphisternum. The outermost pair of electrodes was fed with a constant sinusoidal current of approximately 4 mA r. m. s. at 100 kHz from an impedance cardiograph (Instrumentation for Medicine Inc., Model 304A). The innermost pair of electrodes was connected to the input of the impedance cardiograph. A 1 ml sample of arterial blood was taken from the dog and the haematocrit determined using a Hawksley microcentrifuge. The specific resistance of the blood was then read-off from a previously prepared graph relating the specific resistance and haematocrit for canine blood, Geddes and da Costa (1973).

The impedance stroke volume was calculated from the equation of Kubicek et al. (1966): $SV_z = p (L^2/Z_0^2)$ LVET $(dZ/dt)_{max}$, where SV_z is the impedance stroke volume in ml, p is the specific resistance of the dog's blood at 100 kHz in ohm-cm, I is the shortest distance in cm between the innermost pair of band electrodes, Z_0 is the basal thoracic impedance in ohms, LVET is the left ventricular ejection time in seconds, and $(dZ/dt)_{max}$ is the height of the systolic peak of the dZ/dt tracing in ohms per second above the baseline. LVET was measured from the crossing of the baseline by the systolic upstroke

of the dZ/dt tracing to the incisura of the aortic pressure waveform. The impedance cardiac output was calculated as the product SV_z x heart rate.

The cardiac output was also estimated by the dye dilution technique with the injection of 1 ml of indocyanine green dye (1.25 mg per ml) into the left ventricle. Sampling of the blood was performed simultaneously by withdrawing blood at a rate of 20 ml per minute from the aortic catheter through the densitometer cuvette. The cardiac output in litres per minute was automatically calculated on the associated analogue computer. Additionally, the arterial concentration of dye was measured with the fibre optic densitometer operating with a time constant of 0.2 s. The resulting dye dilution curve was plotted on a flat bed potentiometric chart recorder together with the lead II ECG on a second channel. The dye curve exhibited notches corresponding with each stroke ejection. This was confirmed from the position of the R-waves of the ECG. After each experiment had ended, the fibre optic densitometer was calibrated by immersing the tip of the fibre optic catheter in a sample of the dog's blood containing a known amount of dye and magnetically stirred. The cardiac output values from the analogue computer were only used as a check on the cardiac output during the experiment and have not been included in the statistical analysis.

The following signals were displayed on an ink jet recorder (Mingograf Type 81) at a paper speed of 100 mm per second: the change in the thoracic impedance ΔZ; the rate of change of the thoracic impedance dZ/dt; the aortic blood pressure; the right ventricular pressure and the lead II ECG. The value of the basal thoracic impedance Z_0 was read from the digital display of the impedance cardiograph.

A set of recordings was taken after each successive withdrawal of 50—80 ml of blood to a total of 375 to 755 ml. From the six waveforms the following variables were obtained: heart rate; systolic, diastolic, mean and pulse pressure in the aorta; $(dZ/dt)_{max}$; the R-$(dZ/dt)_{max}$ interval; the Heather Index, i.e. $(dZ/dt)_{max}$ divided by the (R-$(dZ/dt)_{max}$) interval; the left ventricular ejection time LVET; the pre-ejection period PEP (Q-wave to notch interval minus LVET); $1/PEP^2$; diastolic interval (notch to the following Q-wave, Weisdorf and Spodick, 1976); R-R interval; systolic area (area under the aortic pressure waveform during systole and above end-diastolic pressure); cardiac output and stroke volume from planimetry of the fibre optic dye dilution curve, $\dot{Q}_{dye}$ and SV_{dye}; cardiac output and stroke volume by the impedance technique, $\dot{Q}_z$ and SV_z; stroke work (SV_{dye} x mean aortic pressure, Kappagoda and Linden, 1976) and the total systemic resistance (mean aortic pressure/$\dot{Q}_{dye}$).

A multiple cross-correlation computer program was used to determine the correlation between the individual pairs of variables and the level of significance of the correlation coefficients. Fisher's Z-transform was em-

ployed to investigate whether there was any significant difference between the correlation for the various dogs for a given variable and also to combine the set of four correlations according to Brookes and Dick (1969).

Results

Tables 1 and 2 list the correlation coefficients together with their respective level of significance found for the variables in each of the four dogs, and Table 3 details the comparison of the impedance and dye dilution cardiac output measurements. The amount of blood lost correlated well with the systolic, diastolic and mean aortic blood pressures and variably with the heart rate and pulse pressure. It also correlated well with the thoracic impedance Z_o, $(dZ/dt)_{max}$, and the Heather Index — all of these quantities diminishing with an increasing blood loss. Both the impedance and dye cardiac outputs and stroke volumes had a strong negative correlation with the blood loss. The stroke work also showed a strong negative correlation with the blood loss as would be expected since it depends upon both the mean aortic blood pressure and the stroke volume. There was no significant correlation between the amount of the blood loss and the total systemic resistance. The use of Fisher's Z-transformation confirmed that there was no significant

Table 1. Comparison of the blood loss with various haemodynamic variables. The table shows the correlation coefficients (r) for each dog, together with their level of significance and the mean correlation coefficients ($\bar{r}$) for the group of 4 dogs

Dog Number	ONE r_1	TWO r_2	THREE r_3	FOUR r_4	$\bar{r}$ (By z-transform)
Blood loss v Heart Rate	−0.532 x	+0.748 xx	+0.631 x	+0.936 xxx	+0.556
Blood loss v Systolic B. P.	−0.920 xxx	−0.899 xxx	−0.865 xxx	−0.932 xxx	−0.904
Blood loss v Diastolic B. P.	−0.935 xxx	−0.879 xxx	−0.805 xxx	−0.949 xxx	−0.899
Blood loss v Mean B. P.	−0.929 xxx	−0.888 xxx	−0.829 xxx	−0.946 xxx	−0.902
Blood loss v Pulse B. P.	−0.131	−0.106	−0.934 xxx	−0.772 xx	−0.638
Blood loss v LVET	−0.805 xxx	−0.863 xxx	−0.888 xxx	−0.878 xxx	−0.860
Blood loss v 1/PEP^2	−0.799 xxx	−0.597 x	−0.839 xxx	−0.620 x	−0.744
Blood loss v PEP/LVET	+0.811 xxx	+0.499	+0.601 x	+0.761 xx	+0.683
Blood loss v Diastolic Interval	+0.731 xx	−0.708 xx	−0.452	−0.853 xxx	−0.340
Blood loss v R-R Interval	+0.517	−0.766 xx	−0.630 x	−0.934 xxx	−0.565
Blood loss v Systolic Area	−0.762 xx	−0.549	−0.877 xxx	−0.924 xxx	−0.812
Blood loss SV$_Z$	−0.978 xxx	−0.940 xxx	−0.909 xxx	−0.890 xxx	−0.942
Blood loss v $\dot{Q}_Z$	−0.966 xxx	−0.942 xxx	−0.844 xxx	−0.884 xxx	−0.923
Blood loss v $\dot{Q}_{dye}$	−0.832 xxx	−0.878 xxx	−0.794 xx	−0.845 xx	−0.841
Blood loss v Stroke Work	−0.952 xxx	−0.895 xxx	−0.851 xxx	−0.961 xxx	−0.922
Blood loss v Total Systemic Resistance	+0.163	−0.274	+0.341	−0.375	+0.259

The number of stars indicate the significance level, i. e. the probability of getting this high a value of the correlation coefficient from random data. xxx, xx, x represent the probability $P < 0.001$, $P < 0.01$, $P < 0.05$ respectively

Table 2. Comparison of haemodynamic variables with those derived from the transhoracic impedance variation. The table shows the correlation coefficients (r) for each dog, together with their level of significance and the mean correlation coefficients ($\bar{r}$) for the group of 4 dogs

Dog Number	ONE r_1	TWO r_2	THREE r_3	FOUR r_4	$\bar{r}$ (By z-transform)
Blood loss v Z_0	+0.980 xxx	+0.805 xxx	+0.960 xxx	+0.920 xxx	+0.943
Blood loss v $(dZ/dt)_{max}$	−0.974 xxx	−0.939 xxx	−0.940 xxx	−0.962 xxx	−0.956
Blood loss v Heather Index	−0.960 xxx	−0.915 xxx	−0.965 xxx	−0.880 xxx	−0.943
Blood loss v (R-dZ/dt)	+0.598	+0.919 xx	+0.758 x	+0.720 x	+0.777
$(dZ/dt)_{max}$ v SV_{dye}	+0.749 xx	+0.945 xxx	+0.927 xxx	+0.842 xxx	+0.888
Heather Index v SV_{dye}	+0.972 xxx	+0.960 xxx	+0.943 xxx	+0.868 xxx	+0.949
$(dZ/dt)_{max}$ v Stroke Work	+0.859 xxx	+0.952 xxx	+0.904 xxx	+0.937 xxx	+0.917
Heather Index v Stroke Work	+0.910 xxx	+0.962 xxx	+0.885 xxx	+0.887 xxx	+0.917
$(dZ/dt)_{max}$ v LVET	+0.795 xxx	+0.875 xxx	+0.783 xx	+0.884 xxx	+0.834
Heather Index v LVET	+0.762 xx	+0.866 xxx	+0.833 xx	+0.810 xx	+0.821
$(dZ/dt)_{max}$ v PEP/LVET	−0.789 xxx	−0.514	−0.638 x	−0.806 xx	−0.698
Heather Index v PEP/LVET	−0.782 xxx	−0.523	−0.659 xx	−0.737 xx	−0.685
$(dZ/dt)_{max}$ v $1/PEP^2$	+0.737 xx	+0.727 xx	+0.847 xx	+0.679 x	+0.765
Heather Index v $1/PEP^2$	+0.786 xxx	+0.731 xx	−0.842 xx	+0.666 x	+0.772
SV_{dye} v Diastolic Interval	−0.748 xx	−0.902 xxx	+0.705 xx	+0.910 xxx	+0.576
SV_{dye} v LVET	+0.622 x	+0.809 xx	+0.833 xx	+0.872 xxx	+0.794
Systolic Area v SV_{dye}	+0.600 x	+0.842 xxx	+0.774 xx	+0.922 xxx	+0.800
Systolic Area v SV_Z	+0.807 xxx	+0.744 xx	+0.876 xxx	+0.934 xxx	+0.851
SV_Z v SV_{dye}	+0.758 xx	+0.947 xxx	+0.898 xxx	+0.955 xxx	+0.905
$\dot{Q}_Z$ v $\dot{Q}_{dye}$	+0.788 xxx	+0.941 xxx	+0.908 xxx	+0.931 xxx	+0.904

The number of stars indicate the significance level, i. e. the probability of getting this high a value of the correlation coefficient from random data. xxx, xx, x represent the probability $P < 0.001$, $P < 0.01$, $P < 0.05$ respectively

difference ($P = 0.05$) between the four dogs for the correlation coefficients listed in Tables 1 and 2 except for the following: blood loss v Z_0, heart rate, (R-dZ/dt)$_{max}$) and R-R interval; blood loss v systolic area; SV_{dye} v diastolic interval.

The correlations existing between the blood loss and the various time intervals were substantially different from dog to dog. As would be expected, the effect of an increasing blood loss was to reduce the left ventricular ejection time and the value of $1/PEP^2$ and thus increase the value of the PEP/LVET ratio. The systolic area of the aortic pressure waveform exhibited a strong negative correlation with the blood loss and the impedance and dye stroke volumes. Good correlations were found for

Table 3. Details of the comparison between cardiac outputs obtained simultaneously by the dye dilution and electrical impedance methods

Dog number and number of data point (n)	Mean of $\dot{Q}_z$ L/min	Mean of $\dot{Q}_{dye}$ L/min	Linear correlation coefficient (r) and level of significance	Regression line equation	Over-estimation of $\dot{Q}_z$ taking $\dot{Q}_{dye}$ as the standard
ONE (n = 14)	2.394	1.580	0.788 xxx	$\dot{Q}_{dye} = 0.453\ Q_z + 0.495$	51.518%
TWO (n = 12)	2.303	1.311	0.941 xxx	$\dot{Q}_{dye} = 0.935\ Q_z - 0.844$	75.667%
THREE (n = 14)	2.903	2.145	0.908 xxx	$\dot{Q}_{dye} = 1.001\ Q_z - 0.763$	35.337%
FOUR (n = 11)	3.922	2.318	0.930 xxx	$\dot{Q}_{dye} = 0.535\ Q_z + 0.216$	69.197%
Overall analysis (n = 51) pooled data from 4 dogs	2.842	1.831	0.847 xxx	$\dot{Q}_{dye} = 0.645\ Q_z - 0.002$	55.215%

the impedance and fibre optic stroke volumes and cardiac outputs.

There was little difference between the correlation coefficients for either $(dZ/dt)_{max}$ or the Heather Index and the dye stroke volume, $(dP/dt)_{aorta}$, LVET, PEP/ LVET, $1/PEP^2$ and the left ventricular stroke work.

Discussion

The impedance technique of Kubicek et al. (1966) offers a simple, non-invasive approach to the monitoring of changes occurring in the stroke volume and cardiac output of patients during anaesthesia (Hill and Lowe, 1973); Lenz et al., 1976) and intensive care. It can also be applied to outpatients and coronary care patients (Kubicek et al., 1974). However, it is indirect and care must be exercised in the interpretation of the results obtained. This study confirms that the impedance stroke volume and cardiac output values faithfully follow changes in these physiological variables in the dog when there is no valvular incompetence. The impedance values over-estimate in comparison with the corresponding dye values in the dog and this feature has been observed by others (Baker et al., 1975; Pate et al., 1975; Geddes and Baker, 1972). The mean over-estimate for our four dogs was 55.2%. Baker et al. (1974) suggested that the over-estimation by the impedance method may result from a contribution by the outputs of both ventricles to the impedance change, and this agrees with the findings of Geddes and Baker (1972). A similar over-estimate has been observed in neonates when comparing the nitrous oxide uptake and impedance cardiac output values (Costeloe et al., 1976). It appears that the degree of the over-estimate may relate in some way to thoracic size, since a good correlation and a good agreement of absolute values between the impedance and dye dilution cardiac outputs

in adult volunteers has been reported by Denniston et al. (1976).

The value of monitoring Z_0 has been confirmed in the present study, since it has been shown that Z_0 increases steadily with an increasing blood loss. Others have shown that Z_0 decreases with an accumulation of fluid in the thorax (Pommerantz et al., 1969, 1970; Van de Water et al., 1970). The method cannot distinguish the nature of the fluid involved, but a definite change in Z_0 is likely to be of clinical significance. It should be noted that Baker and Denniston (1975) have confirmed that within the presence of a marked reduction in Z_0, the values of SV_z and $\dot{Q}_z$ can be unreliable.

Both $(dZ/dt)_{max}$ and the Heather Index adequately followed the dye stroke volume and the left ventricular stroke work. Thus the simple monitoring of the peak value of dZ/dt would be a worthwhile addition to patient monitoring equiment. Quite apart from its ability to follow changes in heart output and work, the dZ/dt waveform can also be used to measure the left ventricular ejection time (Hill and Merrifield, 1976) and in conjunction with the ECG — which can be picked-up from the outermost impedance electrodes — to follow changes in the systolic time intervals of Weissler et al. (1968) and $1/PEP^2$ which has been shown to be a correlate of myocardial contractility (Reitan et al., 1972). It is also useful in demonstrating an impaired stroke ejection consequent upon extrasystoles (Kubicek et al., 1974).

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