Changes in blood volume distribution between legs and trunk during halothane anaesthesia†

G. B. DRUMMOND, D. W. PYE, F. J. ANNAN and P. TOTHILL

Summary
To assess the influence of halothane anaesthesia on the distribution of blood volume in supine humans, we used albumin labelled with 99mTc to measure blood volume distribution along the craniocaudal axis. We studied 6 volunteers in the supine position before, during and after anaesthesia with 1 % halothane and 66 % nitrous oxide. Using collimated detectors above and below the subject, counts were obtained from the legs, pelvis, abdomen, rib cage and head, with the arms excluded. During anaesthesia, the proportion of counts detected in the legs increased, but failed to achieve significance ($P = 0.059$). On recovery from anaesthesia, leg counts decreased significantly. Counts in the abdomen and rib cage decreased significantly during anaesthesia and the abdomen counts increased again on recovery ($P = 0.036$ for all changes). These results confirm other studies of the vascular effects of halothane, and do not support the hypothesis that blood volume redistributes from the legs to within the chest wall during anaesthesia.

It is generally accepted that anaesthesia with anaesthetic agents such as halothane is associated with a reduction in functional residual capacity (FRC) [1]. The mechanism of this reduction is debatable [2]. Some studies showed no change in the external dimensions of the rib cage and abdomen despite a reduction in FRC [3–5]. Movement of blood into the thorax could explain this discrepancy, and measurements of chest dimensions with CT imaging suggest that “tissue volume” of the chest contents increases to a variable degree during anaesthesia with artificial ventilation, supporting the possibility that intrathoracic blood volume increases during anaesthesia [6]. However, direct measurement of central blood volume did not support this possibility [5] and a more recent CT study of volunteers breathing spontaneously during halothane anaesthesia did not demonstrate changes in blood volume [7].

We undertook the present study to examine directly the distribution of blood in the trunk and legs, and thus assess the possibility that blood may move into either the rib cage or abdomen during anaesthesia. We tested the null hypothesis that anaesthesia would not alter blood distribution between the rib cage, abdomen and legs.

Key words

Subjects and methods
Six medically qualified male subjects volunteered and gave written consent for the study which was approved by the local Ethics of Research Committee. The subjects had a mean age of 31 (range 27–36) yr, mean weight 75 (SD 5; range 70–82) kg, mean height 180 (4; 173–185) cm and none was overweight (mean weight 95 % predicted, SD 8 %, range 84–105 %).

After taking potassium perchlorate 200 mg orally to prevent uptake of radionuclide by the thyroid, each subject fasted for 4 h before the study. Venous cannulae for blood sampling and drug administration were placed in the right and left forearms. The arms were then padded and placed within hollow cylindrical lead shields at the sides of the body to allow measurements from the trunk without counting activity from the arms. The subject lay supine on a horizontal scanning table with the arms supported at the sides of the body for at least 15 min. Before any radio-labelled albumin was administered, the subject was passed through the scanner with a linear external source (a plastic tube containing 99mTc solution set in the plane of the collimator) in the lower detector position, to measure the attenuation caused by the tissues of the trunk. These values were used to correct the trunk counts for attenuation. An injection of albumin 2 ml (TCK2, Sorin, Italy) labelled with approximately 80 Mbq of 99mTc was then administered into one venous cannula and flushed into the circulation with 10 ml of 0.9 % sodium chloride solution. After 10 min a venous blood sample was obtained from the other venous cannula and two
scans were performed (see below). Anaesthesia was then induced with methohexitone 100 mg i.v. (0.5 % solution containing 0.1 % lignocaine) and maintained with halothane and 67 % nitrous oxide in oxygen, administered from a tight fitting mask and a Magill breathing attachment. Initially up to 2 % halothane was given, an oropharyngeal airway was inserted and then the inspired concentration of halothane was reduced to 1 %. After 10 min of stable anaesthesia, two scans were performed. The subjects were then allowed to recover from anaesthesia and two additional scans were done. Another venous blood sample was then obtained. In one subject the bladder was emptied completely at the end of the procedure and the activity of the urine measured.

The amount of radioactive tracer administered and the activity of the blood samples obtained at the start and end of the procedure were measured. The subjects were scanned by moving the table in a horizontal plane between two NaI crystal detectors mounted above and below the table [8]. The subjects were scanned in an axial direction, from foot to head, by moving the table at 1 cm s⁻¹ and the outputs from the upper and lower detectors summed and recorded over every 2 s, that is for each 2 cm of movement. The collimation of the detectors was adjusted to 2 cm width.

The mean values of duplicate scans were used for analysis and separated into counts from the legs, pelvis, abdomen, rib cage and head. These parts of the body were defined by bony landmarks which were noted in each subject as distances from the feet to allow separation of the counting periods. The rib cage was defined to include only that part above the dome of the diaphragm, so that rib cage activity did not include activity from the abdominal organs contained within the lower rib cage. The margins were as follows: 20 cm caudal to anterior superior iliac spine (leg–pelvis); anterior superior iliac spine (pelvis–abdomen); 4 cm cephalad to lower edge of xiphisternum (abdomen–rib cage); and 2 cm cephalad to suprasternal notch (rib cage–head).

All counts were corrected for nucleonics deadtime and for radionuclide decay. A further correction was made for tissue attenuation. This assumed that the radionuclide was distributed uniformly through the body cross section, which was taken to be rectangular. The results from the transmission scan were used to estimate the effective tissue thickness for the pelvis, abdomen and rib cage. Leg thickness was assumed to taper uniformly along its length with a taper fitted to calf and thigh thickness measurements made on each subject using callipers. The head was assumed to have a fixed thickness of 12 cm.

For each section of the body (leg, pelvis, abdomen, rib cage, and head), the counts in each section were expressed as a fraction of the total counts detected into that period of the study, after subtraction of the activity detected in the pelvis (because of the influence of urinary ⁹⁹ᵐTc on these counts). This allowed the counts in each body section to be expressed as a proportion of the counts in the body. The changes in the proportion of counts in the leg, abdomen and rib cage from awake to anaesthesia, and from anaesthesia to recovery, were tested with the Wilcoxon paired rank sum test. Changes in total counts, from the start to the end of the study, were tested using a paired t test. We used a statistical package (Minitab version 8.2, MS DOS version 6, GA-486 US computer).

Results

Activity profiles in the awake and anaesthetized state are shown for a representative subject in figure 1. Despite the limited resolution of the detectors, it is clear that during anaesthesia there was increased activity in the lower legs and in the head, with less activity in the upper pelvis and lower abdomen. The same general pattern of change was seen in the other five subjects. In later scans in all subjects, a distinct spike of activity in the pelvis became progressively more obvious. This was presumed to be cumulation in the urine, after liberation of the pertechnetate from albumin and subsequent urinary excretion, and confirmed by the demonstration of 3.7 % of the administered dose in urine in the subject in whom this was measured. In this subject, the “spike” of counts on the profile scan at the level of the bladder, relative to the tissues cephalad and caudal to this, was similar to that noted in all other subjects. Counts in the different compartments for each subject, before, during and after anaesthesia, are shown in table 1. There was a slight but significant increase in total counts detected, from before anaesthesia to after anaesthesia, of about 6 % (P < 0.05). The increase in activity detected in the pelvis was much greater, accounting for 40 % of the entire increase in counts. The counts from the pelvis were not analysed further, as it was clear they were in part associated with urinary accumulation as well as radionuclide activity in the blood.

The proportional activity of each compartment in each subject, for each measurement period, is shown in figure 2. The mean values for the legs, abdomen and rib cage, and the mean changes in activity between before, during and after anaesthesia, are given in table 2.

The counts in the legs increased on induction of
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anaesthesia, but this change was not statistically significant ($P = 0.059$). However, on recovery the counts decreased significantly. The counts in the abdomen changed in the opposite direction, that is they decreased during anaesthesia and increased after recovery. Rib cage activity also decreased on induction of anaesthesia, but on recovery there was no significant change in activity.

Blood volume was calculated from the activity of the blood samples obtained 10 min after administration of albumin. In one subject the value obtained was inexplicably very large. In the other subjects the blood volume estimates were systematically greater, by about 25 %, than the values estimated from height and weight [9] (table 3).

**Discussion**

These results do not support the hypothesis that blood volume decreases in the legs and increases in the rib cage or abdomen during inhalation anaesthesia. Several technical aspects of the study require consideration. The count rates were sufficiently high to ensure satisfactory reproducibility in successive measurements, and individual pairs of measurements made at each time showed little
variation. The use of mean measurements reduced this source of variability. The resolution and sensitivity of the scanner used for this study have been fully described elsewhere [8]. The resolution of the detectors, using 2-cm parallel collimators, varies according to the distance of the source from the detector and the energy of the source. With the settings and source energy used (chosen to limit the injected activity and hence the radiation dose) resolution would have been about 6 cm at the midline of the body. We corrected for tissue thickness, in the thoracic part of the scan, by obtaining a transmission scan before giving the isotope. This allows a correction to be made, but assumes that the radionuclide is distributed homogeneously. If more of the injected activity were in the centre of a mass of tissue such as the abdomen, the counts would be reduced more than if the blood were at the skin. Changes in the distribution of radionuclide within the body, such as might happen if blood were to move from central to superficial veins in the legs, may have contributed to a change in the total number of counts detected. These effects were minimized partly by the use of detectors above and below the subjects.

We could not measure activity in the arms as they were shielded so that activity in the rib cage and abdomen could be assessed. We consider the position of the subjects a better reflection of the usual conditions of anaesthesia than some of the CT studies that were carried out with the arms extended over the head [5, 6], although recent work suggests that this posture does not affect FRC, at least in the awake subject [7]. In addition, we did not include the counts from the pelvis because a proportion of this activity was not intravascular. Hence the estimation of “total activity” is clearly only a part of the true total, and the changes we noted with time may have been caused at least partly by changes in the arms.

The calculated blood volume was greater than expected (table 3). There was a consistent over-estimate of blood volume, relative to predicted, of 25%. We consider that the most likely reason is that the label tended to dissociate from albumin so that the volume of distribution of the label was greater than the intravascular volume. This was supported by our finding label in urine. Expression of counts as a proportion of the counts detected at that particular time was intended to correct for this loss from the circulating volume. Based on observed changes in counts and measured blood activity, we calculated that the mean change in blood volume in the legs after induction of anaesthesia was 70 ml, and the volume of blood in the rib cage and abdomen decreased by about 30 ml. However, this estimate depends on assumptions such as radioactive decay, corrections for nucleonic deadtime and attenuation by the tissues, and is only an approximation.

Because of the limited resolution of the detectors, analysis was done by summing the activity detected into relatively large lengths of the body, determined by reference to skeletal landmarks. The low resolution of dimensions implies that a true anatomical division between rib cage and abdomen was impractical, particularly as the average length of the “rib cage” was 14 cm. However, changes in diaphragm position on induction of anaesthesia are generally small, variable and of the order of 1–2 cm [10], and are unlikely to have greatly influenced the distribution of signals detected from the abdomen and rib cage.

We only studied six subjects. We were unable to assess, a priori, the sample size required as we had few data to do this. A study of 10 volunteers, using similar methods, was able to detect the effect of glyceryl trinitrate [11], but we had no prior reason to expect that similarly sized changes might occur in this study. We were also keen to limit, as much as possible, the number of subjects undergoing anaesthesia and receiving radionuclide. Krayer and co-workers estimated that there could be an increase of 300 ml in thoracic blood volume during anaesthesia [6]. Using assumptions similar to those used to estimate the possible volume shifts seen in this study, and the SD of the changes in activity from awake to anaesthesia that we observed, the standardized difference (twice the expected change/SD of the change) of such an increase is 6, and hence the power of the study exceeds 0.8. Consequently, it is apparent in retrospect that the present study should have been able to detect a change of this magnitude. In fact the changes, although small, were in the other direction.

Our observations are supported by others, who have used methods similar in principle to the present study. With gamma camera images of radiolabelled red cells, the influence of extradural anaesthesia and vasoactive agents can be measured. The results were consistent with the known effects of these procedures and agents. A gamma scintigram in one of these reports showed that 99mTc was lost from labelled erythrocytes and excreted in the urine [12], in a way similar to the loss from labelled albumin in our study. We performed preliminary studies and found that labelling erythrocytes did not give better retention of label compared with labelled albumin. We administered perchlorate to our subjects to prevent uptake of isotope by the thyroid gland. We were unable in preliminary studies to identify significant gastric uptake or excretion of the isotope which we had considered as another potential source of error.

Some of the labelled albumin may have left the circulation and entered extravascular spaces, such as the lung and splanchnic areas. The small progressive increase that was noted in total counts, detected over the whole time period of the study, would contribute to the increases noted from one state to the next.

Table 3 Measured blood volume and predicted volume [9]

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Measured volume</th>
<th>Predicted volume</th>
<th>Measured/predicted (%)</th>
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<tr>
<td>1</td>
<td>11.64</td>
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<tr>
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</tr>
<tr>
<td>Mean</td>
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<td>125</td>
</tr>
<tr>
<td>SD (excluding subject 1)</td>
<td>0.29</td>
<td></td>
<td>6</td>
</tr>
</tbody>
</table>
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(such as the increase in leg counts on induction of anaesthesia), and tend to conceal any decrease in counts from one state to the next. However, the changes noted occurred promptly on induction of anaesthesia and were reversed on recovery. In addition, the presence of a fixed fraction of tracer in a particular body site that did not respond to changes in blood volume distribution would tend to reduce the apparent changes seen. Consequently, we believe that loss of label from albumin would not influence our qualitative conclusions. Similarly, correction for tissue attenuation does not alter the direction of any of the changes in counts that were noted, but does allow the counts to be related more exactly to the activity of the labelled blood. Finally, it is possible that the changes noted were a result of prolonged recumbency and independent of anaesthesia. We feel that this is unlikely, in view of the reciprocal changes or trends that occurred on induction and recovery, and because we allowed our subjects to rest for 20 min before the study started.

The changes noted in the present study were of the same order of magnitude as those found when known vasoactive agents are used. For example, nitroglycerin, a known venodilator, causes a 9.6 % increase in counts from the calf [11]. During extradural anaesthesia, leg counts increase by 9.9 % [12]. The changes we found were of a similar order of magnitude and consistent with the expected response of the peripheral circulation to halothane [13, 14].

We performed this study to investigate the possibility, first suggested by Hewlett and colleagues [1], that the reduction in FRC noted during anaesthesia could be explained in part by movement of blood into the thorax. Direct measurements of limb volume showed only small changes after thiopentone, which were abolished by inhalation anaesthesia with spontaneous ventilation [15]. Despite decreases in FRC on induction of anaesthesia, early studies were unable to demonstrate a decrease in the external dimensions of the thorax and abdomen [3–5]. However, a subsequent study using a sensitive and accurate magnetometer reported changes in chest wall dimensions consistent with the expected decrease in lung volume when anaesthesia was induced in the supine position [16].

CT scanning has been used to estimate chest wall dimensions, with different estimates of thoracic blood volume. Krayer and colleagues found that although the volume of the chest wall and of the entire intrathoracic contents decreased, this was less than the decrease in FRC [6]. They suggested that the difference must have been predominantly blood accumulation in the thorax and estimated this to be about 300 ml, but the variation in this value was large with an SD of 410 ml. A subsequent study by these investigators, of volunteers breathing spontaneously during halothane anaesthesia, did not confirm these observations [7].

Studies of the effects of deliberately increasing fluid volume within the trunk do not support the possibility that fluid shifts can alter lung volume alone, without at the same time also affecting the dimensions of the chest or abdomen. Distension of the stomach with 1 litre of fluid caused an average reduction in lung volume of only 33 % of this volume, while at the same time the volume of the rib cage and abdomen increased by 66 % [17]. Similarly, displacement of 500 ml of blood from the legs into the chest and abdomen by inflating splints on the arms and legs caused a reduction in lung volume by only 40 % of the displaced volume, and an increase in external dimensions of about 60 % [18].

Such indirect findings support our conclusion that changes in blood volume distribution from the limbs to within the thorax are unlikely to contribute to the reduction in FRC that occurs during halothane anaesthesia in the supine subject.

References

