

The Lung Volume at Which Shunting Occurs with Inhalation Anesthesia

R. Dueck, M.D.,* R. J. Prutow, Ph.D.,† N. J. H. Davies, M.B.,‡ J. L. Clausen, M.D.,§ T. M. Davidson, M.D.¶

The relationship between functional residual capacity (FRC) and shunt development with halothane anesthesia in 18 nonobese surgical patients (age, 21-34 yr) was studied. FRC was measured by helium dilution, and intrapulmonary shunt was distinguished from ventilation-perfusion inequality by multiple tracer inert gas elimination analysis. Awake supine FRC was $34.6 \pm 6.6\%$ (mean \pm SD) of total lung capacity (TLC), and closing capacity (CC) was $29.8 \pm 5.3\%$ of TLC. Anesthesia, muscle paralysis, tracheal intubation, and mechanical ventilation produced an average $14.6 \pm 13.3\%$ FRC reduction to an average anesthesia FRC 29.8% of TLC ($P = 0.002$). Shunt increased from $1.2\% \pm 1.5\%$ awake to $8.6 \pm 8.3\%$ during anesthesia ($P = 0.005$). A nonlinear relationship was found between shunt and FRC/TLC so that anesthetized subjects with an FRC less than awake CC had an average $11.4 \pm 8.3\%$ shunt, whereas subjects with an FRC greater than CC had a $2.4 \pm 2.8\%$ shunt ($P = 0.025$). Nonsmokers developed shunt only if FRC was less than CC. Smokers showed a significantly higher shunt for a given (FRC - CC)/TLC compared to nonsmokers ($P < 0.001$). The slope of the regression of shunt on BMI (body mass index = weight/height²) showed a significant increase during anesthesia ($P = 0.005$), and smokers had a significantly higher slope compared to nonsmokers ($P = 0.001$). These findings suggest a gravity-dependent mechanism for intrapulmonary shunting during anesthesia. Therefore, shunting was due to dependent regional lung volume reduction associated with an FRC decrease to less than closing capacity. The enhanced intrapulmonary shunting in smokers may have been related to the increased dependent regional residual volume associated with smoking. (Key words: Anesthetics, volatile; halothane. Anesthetics, gases; nitrous oxide. Complications, pulmonary; obesity; smoking. Lung; atelectasis; closing capacity; functional residual capacity; shunting; volume.)

INHALATION ANESTHESIA is associated with reduced functional residual capacity (FRC) and impaired pulmonary gas exchange.^{1,2} This impairment is due to both increased intrapulmonary shunt and increased ventilation-perfusion (V_A/Q) inequality.² Computer assisted tomography (CAT) scans by Brismar *et al.*³ demonstrated dependent lung densities during halothane anesthesia. The

size of these densities showed linear correlation with the amount of intrapulmonary shunt, suggesting that anesthesia-induced shunting is caused by atelectasis.⁴

Earlier reports also showed significant correlation between FRC reduction and $P(A-a)O_2$ increase with halothane anesthesia.^{1,5} This led to the general hypothesis that FRC reduction during anesthesia results in airway closure and atelectasis. However, when Klineberg *et al.*⁶ intentionally reduced FRC with chest wall strapping in seated volunteers, they found only minimal shunting. This apparent difference between Klineberg's volunteer study and anesthesia studies in surgical patients, could have been due to: 1) volunteers studied in seated rather than supine position, 2) awake rather than anesthetized, paralyzed, intubated and mechanically ventilated conditions, and 3) either clinical or subclinical lung disease in surgical patients. We therefore wished to examine the relationship between FRC and shunting during halothane anesthesia in supine young surgical patients without symptoms or signs of lung disease.

Materials and Methods

Eighteen male surgical patients (age, 21-34 years) were selected on the basis of normal pulmonary history, physical exam, and chest radiograph. No subject was obese; body mass index (BMI = weight/height²) was always less than 30.0 kg/m^2 .⁷ Ten of the subjects were smokers (10-20 pack-yr). Approval of the protocol was obtained from the University Human Use Committee and written informed consent was obtained from each subject.

Pulmonary function tests consisting of static lung volumes and forced expiratory flow rates were determined in seated position in 17 subjects on the day before surgery. Fourteen subjects also had single breath nitrogen closing capacity (CC) tests in both the seated and supine position.⁸ Inspiratory and expiratory flow rates were limited to less than 0.5 l/s , as directed by the examiner and guided by a flowmeter signal displayed on a CRT screen mounted in front of the subject. Closing volume was determined as the volume expired after a change in slope of the alveolar plateau, and added to residual volume to obtain closing capacity. A minimum of two CC determinations were obtained from each subject in both positions.

All subjects received 10 mg diazepam premedication one hour prior to catheter insertion in a peripheral vein, radial and pulmonary artery (flow directed *via* antecubital vein), with the aid of bupivacaine 0.5% SC. A mixture of

* Associate Adjunct Professor of Anesthesiology.

† Assistant Professor of Anesthesiology.

‡ Fellow, Pulmonary Medicine. Present address: Anaesthesia, St. James Hospital, Sarsfeld Road, Balham, London SW12 8HW, United Kingdom.

§ Associate Professor of Medicine.

¶ Professor of Surgery.

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Address reprint requests to Dr. Dueck: Anesthesiology Service, V-125, 3350 La Jolla Village Drive, San Diego, California 92161.

six inert gases (sulphur hexafluoride, ethane, cyclopropane, enflurane, ether, and acetone) dissolved in tracer concentration in lactated ringers solution was infused through the iv catheter at 2.4 ml/min.

Awake studies were performed with the subjects supine, breathing 30% O₂ (balance N₂) via a mouthpiece (and with a noseclip). Mixed expired gas and arterial and mixed venous blood samples were obtained for multiple tracer inert gas and blood gas analysis after a minimum 30 min stable end-tidal CO₂ concentration. FRC was then determined in duplicate by the closed circuit helium dilution method, corrected for helium loss due to mass spectrometry sampling.

Anesthesia was induced and maintained with halothane 0.75–0.85% end-tidal concentration, with an FI_{O₂} of 0.30 and balance gas N₂ or N₂O (alternate studies, nine subjects in each group). Orotracheal intubation was facilitated with pancuronium 0.1 mg/kg iv. Mechanical ventilation was provided with tidal volumes of 10 ml/kg and respiratory rate adjusted to make minute volume equal to the awake value. Gas exchange and FRC measurements were repeated 45 min after anesthesia induction.

Inspired, end-tidal, and mixed expired gas concentrations of O₂, CO₂, halothane, N₂, and N₂O were measured with a Perkin Elmer model 1100A mass spectrometer. Expired minute volume was measured with a Med Science model 570 dry gas spirometer. Gas chromatographic analysis of mixed expired gas and arterial and mixed venous blood samples was used to determine retention and excretion of the six tracer gases.⁹ Distributions of ventilation and perfusion with respect to ventilation-perfusion ratio (V_A/Q) were derived from the retention and excretion data to distinguish the amount of intrapulmonary shunt (V_A/Q < 0.005) from V_A/Q inequality, as described by Wagner.¹⁰

STATISTICAL ANALYSIS

Measured variables are shown as mean ± SD. All lung volumes were referenced to seated total lung capacity (TLC) to standardize the findings for differences in patient size. The paired *t* test and analysis of variance were used to determine the significance of differences between awake seated and supine values, as well as between awake supine and anesthesia findings. The Mann-Whitney test was also used to compare shunt values in subjects with anesthesia FRC values less than and greater than awake CC. Linear regression and analysis of covariance was used to examine the relationships between shunt, FRC/TLC, and BMI. Multiple regression analysis was used to test for an effect of smoking and balance gas (N₂ vs. N₂O) on the above relationships.

Piece-wise linear regression of shunt on FRC/TLC was performed using maximum likelihood estimation, as de-

scribed in further detail in the "Appendix."^{11–13} This entailed dividing the data into two subsets, such that FRC/TLC was greater than and less than the transition point (point at which the slope changed). A straight line was fitted to each subset of data, requiring that the two lines join at the transition point. The position of the transition point was varied to determine the point at which the sum of residuals was minimized; hence the transition point was not predetermined. Likewise, the relationship of anesthesia shunt and FRC to awake CC was analyzed by using (FRC – CC)/TLC, instead of FRC/TLC, in the above linear and piece-wise linear regressions.

Results

The average age of the 18 subjects was 27.9 ± 4.0 (SD) years (range, 21–34 yr). BMI ranged from 19.9 to 28.1 kg/m², with a mean of 23.7 ± 2.5 kg/m². There were ten smokers who had a 10–20 pack-yr smoking history. There was no correlation between BMI, smoking history, and balance gas (N₂ vs. N₂O).

Pulmonary function tests showed normal forced expiratory flow rates in the 17 tested subjects.¹⁴ Static lung volumes in seated position were within normal limits in all but one subject with a low FRC. However, this subject also had a proportionately low TLC; hence the ratio FRC/TLC was within normal limits. This TLC-standardized seated FRC ranged from 40.5% to 58.0% (mean, 49.5 ± 5.5%) of TLC. Supine FRC was 23.3% to 46.2% of TLC (mean, 34.6 ± 6.6%). This was an average 30 ± 13% (14.6 ± 7.0% of TLC) less than the seated FRC.

Awake supine CC, 29.8 ± 5.3% of TLC, was not significantly different from seated CC. Supine CC was greater than FRC in two of the 14 subjects with CC measurements. There was no difference in CC for smokers versus nonsmokers (*P* = 0.25). The CC/TLC did not correlate with BMI, *r* = 0.42 (*P* = 0.14). Instead, between subject variation in CC/TLC was primarily due to variation in supine RV: CC/TLC = 0.133 + 0.793 · (RV/TLC), *r* = 0.81 (*P* = 0.004).

The average awake shunt value was 1.2 ± 1.5% of cardiac output (range, 0.0–6.4%). Ventilation-perfusion distribution for the V_A/Q range 0.005 < V_A/Q < 100.0 (nonshunt, nondeadspace) showed a log standard deviation (log SD) of blood flow 0.39 ± 0.10 (range, 0.26–0.58). There was no difference in shunt (*P* = 0.47) or log SD of blood flow (*P* = 0.25) for smokers versus nonsmokers.

Anesthesia produced an average 14.6 ± 13.3% FRC reduction relative to awake supine FRC (*P* = 0.02), or 5.0 ± 4.9% of TLC. The mean anesthesia FRC was 29.8 ± 6.7% of TLC (range, 17.3–43.2%). Eight of the 14 subjects with awake CC measurements showed FRC reduction to less than awake CC, to a mean value 28.7

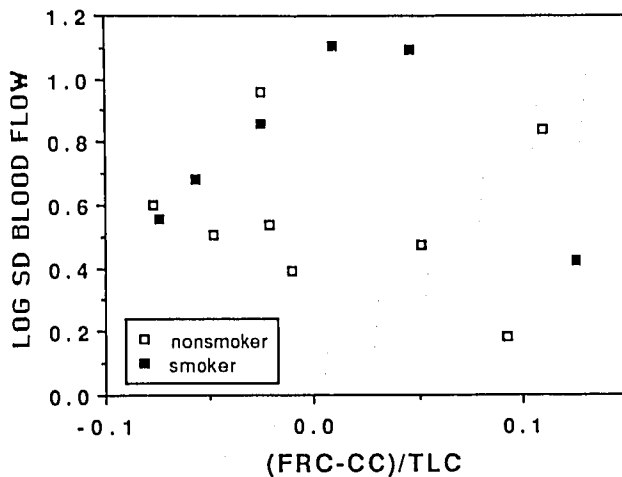


FIG. 1. The severity of V_A/Q inequality in terms of log SD of blood flow distribution during anesthesia is shown with respect to $(FRC - CC)/TLC$. The highest log SD values were seen at or near CC, especially in smokers.

$\pm 5.7\%$ of TLC. For the remaining six subjects the anesthesia FRC was $32.8 \pm 3.5\%$ of TLC.

Anesthesia shunt values ranged from 0.0 to 23.1%, with a mean of $8.6 \pm 8.3\%$. The eight subjects with anesthesia FRC less than awake supine CC had an average $11.4 \pm 8.3\%$ shunt, compared with $2.4 \pm 2.8\%$ shunt for the six subjects whose anesthesia FRC was greater than awake CC ($P = 0.025$, unpaired t test, or $P = 0.02$ by Mann-Whitney test).

Log SD of blood flow during anesthesia was 0.75 ± 0.32 , significantly greater than awake ($P < 0.001$). BMI and N_2O had no significant effect on log SD of blood

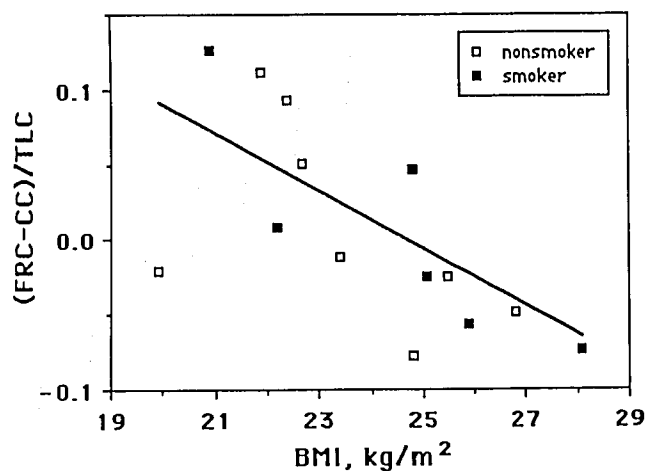


FIG. 2. Anesthesia $(FRC - CC)/TLC$ is plotted with respect to BMI. The regression equation is $(FRC - CC)/TLC = 0.47 - 0.019 \cdot BMI$, $r = -0.67$, $P = 0.009$. Smoking had no effect on this relationship. CC/TLC was independent of BMI ($r = 0.42$, $P = 0.14$) but showed significant correlation with RV/TLC ($r = 0.81$, $P = 0.004$).

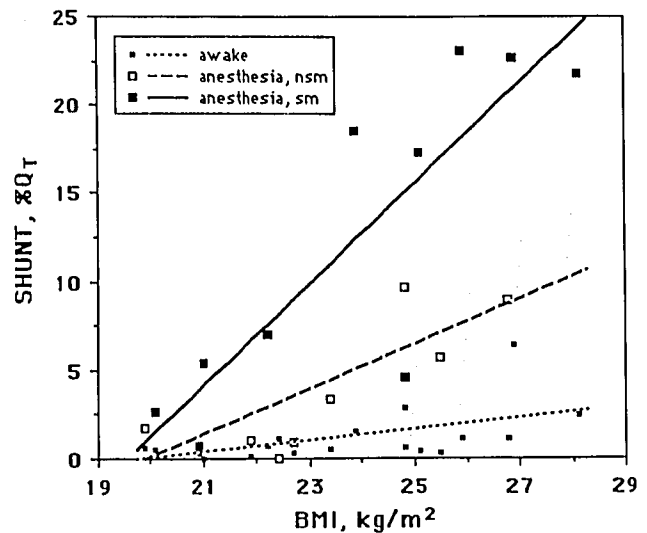


FIG. 3. Relationship between shunt and BMI. Analysis of covariance showed a significant increase in slope from awake to anesthetized, $r = 0.005$. In addition, the change in slope was significantly greater for smokers versus nonsmokers, $P = 0.001$. The regression equations are: 1) awake: shunt = $-6.8 + 0.33 \cdot BMI$, $r = 0.54$, $P = 0.02$; 2) anesthesia (nonsmokers): shunt = $-28.5 + 1.38 \cdot BMI$, $r = 0.81$, $P = 0.02$; 3) anesthesia (smokers): shunt = $-55.5 + 2.84 \cdot BMI$, $r = 0.86$, $P = 0.002$.

flow, but smokers had a log SD of blood flow of 0.89 ± 0.30 , compared to 0.56 ± 0.25 for nonsmokers ($P = 0.03$). Log SD of blood flow was highest when FRC/TLC was at or near CC/TLC , as shown in figure 1.

We found an inverse correlation between FRC/TLC and BMI: 1) $FRC/TLC = 0.731 - 0.010 \cdot (BMI)$, $r = -0.46$ ($P = 0.06$) for awake seated, 2) $FRC/TLC = 0.652 - 0.013 \cdot (BMI)$, $r = -0.51$ ($P = 0.03$) for awake supine, and 3) $FRC/TLC = 0.647 - 0.015 \cdot (BMI)$, $r = -0.54$ ($P = 0.02$) for anesthesia. Analysis of covariance showed no significant difference in slope for the three regression lines (F ratio = 0.55), but the elevations were significantly different for all three ($P = 0.001$). Neither smoking nor N_2O had an effect on the regressions.

Regression of the anesthesia $(FRC - CC)/TLC$ on BMI was also significant, $r = -0.67$ ($P = 0.009$), as shown in figure 2. Smoking did not influence this relationship ($P = 0.6$). Note that FRC was less than CC if BMI was greater than 24.7 kg/m^2 .

We found significant correlation between shunt and BMI for both awake and anesthesia conditions, as shown in figure 3. Note that anesthesia values have been subdivided into smoker and nonsmoker groups. There was a significant increase in the slope of the regression from awake to anesthetized ($P = 0.005$), as well as a significantly higher slope during anesthesia for smokers versus nonsmokers ($P = 0.001$). This difference in slope suggests a synergistic interaction between the effects of BMI, smok-

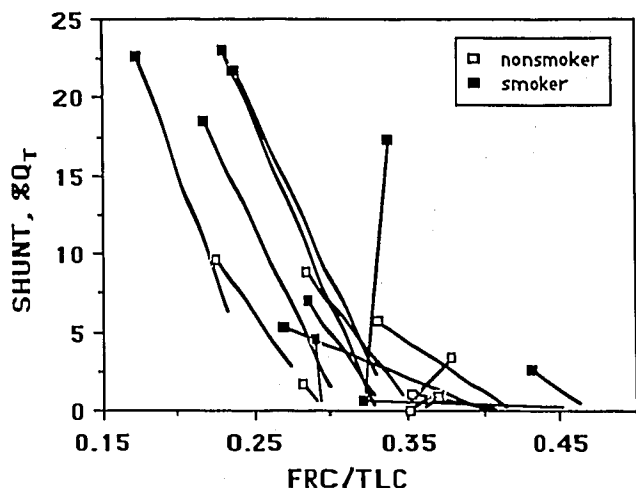


FIG. 4. The change in shunt from awake (beginning of each line) to anesthetized (open or closed square) is plotted with respect to FRC/TLC. Note that there was very little effect of FRC reduction until FRC/TLC was less than 0.30, i.e., less than awake supine CC.

ing, and anesthesia. Addition of balance gas (N_2 vs. N_2O) did not improve the regressions.

Both awake and anesthesia shunt showed significant inverse correlation with FRC/TLC: $r = -0.66$ ($P = 0.003$) and $r = -0.72$ ($P = 0.0007$), respectively. However, the increase in shunt produced by anesthesia did not correlate with change in FRC, whether related to awake supine FRC, $r = -0.46$ ($P = 0.06$) or to TLC, $r = -0.29$ ($P = 0.25$). The reason for this is shown in figure 4. There was little shunt development if FRC/TLC remained above 0.30 but a pronounced increase in shunt occurred if FRC/TLC decreased below 0.30.

This obvious change in the relationship between shunt and FRC at an FRC/TLC of approximately 0.30 led us to question whether nonlinear regression was more appropriate. Indeed linear regression yielded a negative shunt for FRC/TLC greater than 0.395, which is not physiologic. We therefore applied piece-wise linear regression to anesthesia shunt on FRC/TLC. This required determination of the two slopes of the regression line, as well as shunt and FRC/TLC at the transition point. The resulting fit is shown in figure 5. The transition point occurred at an FRC/TLC of 0.306 ± 0.018 (SE), which was not significantly different from CC/TLC, 0.298 ± 0.053 (SD).

Piece-wise linear regression of awake shunt on awake supine FRC/TLC is also shown in figure 5. The transition point was at 0.29 ± 0.01 (SE), not different from the anesthesia transition value. However, the awake shunt was only $20 \pm 15\%$ of anesthesia shunt for the same FRC/TLC.

Linear regression of anesthesia shunt on $(FRC - CC)/TLC$ showed significant correlation for both smokers,

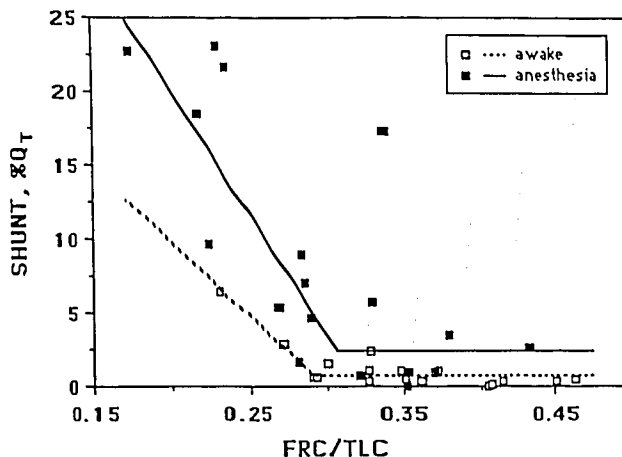


FIG. 5. Relationship between shunt and FRC/TLC. Piece-wise linear regression of shunt on FRC/TLC during anesthesia showed a marked increase in shunt if FRC was less than 30% of TLC. Awake shunt for a given FRC/TLC was $20 \pm 15\%$ of the corresponding anesthesia shunt. The regression equation for the anesthesia shunt is:

$$\text{shunt} = 2.4 - 166 \cdot (0.306 - \text{FRC}/\text{TLC}), \text{ for } \text{FRC}/\text{TLC} < 0.306;$$

$$\text{shunt} = 2.4, \text{ for } \text{FRC}/\text{TLC} > 0.306.$$

$r = -0.94$ ($P = 0.005$), and nonsmokers, $r = -0.85$ ($P = 0.008$). Analysis of covariance showed significantly higher slope ($P = 0.01$) and elevation ($P = 0.0002$) for smokers compared to nonsmokers. Again, the linear fit yielded a negative shunt for higher $(FRC - CC)/TLC$ values. We therefore used piece-wise linear regression for anesthesia shunt on $(FRC - CC)/TLC$, as shown in figure 6. The transition point for nonsmokers was at $(FRC - CC)/TLC = 0.010 \pm 0.010$ (SE), consistent with a

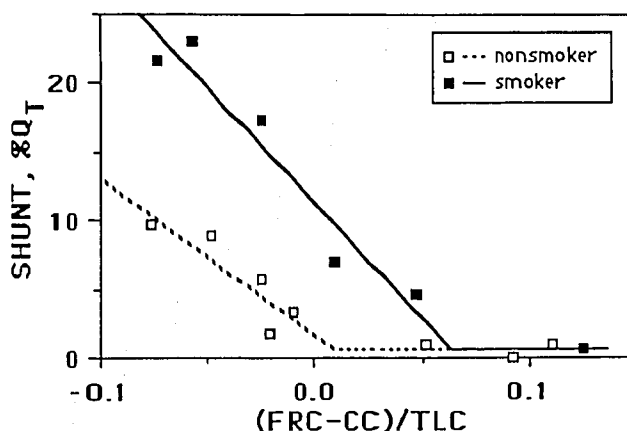


FIG. 6. The relationship between anesthesia shunt and $(FRC - CC)/TLC$ is compared for smokers versus nonsmokers using piece-wise linear regression. The shunt for a given lung volume was significantly greater for smokers compared to nonsmokers ($P < 0.001$). FRC was determined during anesthesia and referenced to awake CC and TLC.

transition point at CC. For smokers the transition point was at $(FRC - CC)/TLC = 0.064 \pm 0.010$. The curves shown for smokers and nonsmokers were significantly different ($P < 0.001$). However, as discussed in the "Appendix," we could not determine whether the difference was due to a difference in slope and/or transition point. Replacement of CC by RV in the above analysis yielded similar results in that smokers had significantly more shunt for given $(FRC - RV)/TLC$ compared to nonsmokers ($P = 0.003$).

Discussion

We demonstrated substantial shunt development with halothane anesthesia in patients whose FRC was less than awake CC. Smokers had significantly more shunt for a given $(FRC - CC)/TLC$, compared with nonsmokers. In addition, the slope of the regression of shunt on BMI was significantly higher during anesthesia compared to awake, and the slope was significantly higher for smokers compared to nonsmokers. These findings suggest a synergistic interaction between anesthesia, smoking, and body weight.

The magnitude of anesthesia shunt in our nonsmokers was comparable to the values seen in young healthy volunteers by Marshall *et al.*¹⁵ and by Rehder *et al.*¹⁶ Smokers had shunt values similar to those reported by Price *et al.*¹⁷ The increased V_A/Q inequality in our anesthetized nonsmokers was essentially the same as that reported for supine volunteer subjects by Rehder *et al.*¹⁶

Our observation that anesthesia shunt correlated with lung volume contrasts with two recent studies of intentional FRC reduction in awake volunteers. Klineberg *et al.*⁶ showed little or no shunt with 30% FRC reduction induced by chest strapping in the seated position. This difference could conceivably be explained by the seated position because our subjects showed a 30% awake FRC reduction simply due to reclining to the supine position. However, Tokics *et al.*¹⁸ also showed no shunt or V_A/Q changes with an average 21.5% supine FRC reduction induced by thoracoabdominal restriction in awake subjects. Their mean restricted FRC/TLC of 0.304 was essentially the same as our anesthesia value. These findings suggest that anesthesia shunt and V_A/Q changes are probably not simply due to FRC reduction.

The 15% FRC reduction with anesthesia in our surgical patients was comparable to earlier findings.^{1,5} However, change in shunt did not show linear correlation with FRC reduction, which contrasts with the correlation between FRC and $P(A-a)O_2$ changes demonstrated by Hickey *et al.*¹ and Hewlett *et al.*⁵ It is likely, therefore, that the increased $P(A-a)O_2$ in their subjects was due to the combined effects of increased V_A/Q inequality and shunting. This is consistent with the report by Hedenstierna *et al.*⁴ who showed

direct correlation between anesthesia shunt and amount of dependent lung density but no correlation between V_A/Q inequality and lung density.

Piece-wise linear regression of shunt on FRC/TLC , as well as shunt on $(FRC - CC)/TLC$ (figs. 5 and 6), provided the most direct evidence for a quantitative relationship between FRC, CC, and shunting. Nonlinear regression was indicated because a simple linear regression yielded a negative (nonphysiologic) shunt for the highest FRC/TLC values. The two slopes as well as the position of the transition point for the piece-wise linear regression ($FRC/TLC = 0.306$) were not predetermined but instead were all derived as unknowns in the regression equation. Furthermore, the increased V_A/Q inequality at or near CC (fig. 1) and the marked increase in shunting if FRC was less than CC were consistent with earlier findings by Bergman and Tien¹⁹ and by Weenig *et al.*²⁰ They showed increased $P(A-a)O_2$ at anesthesia lung volumes less than CC. We therefore conclude that the similarity of the transition point in the regression of shunt on FRC/TLC and the mean value of CC/TLC was not coincidental.

Closing capacity is in part determined by dependent airway closure, and in part by dynamic flow limitation in dependent airways.^{21,22} Both flow limitation and intermittent airway closure would be consistent with the increased amount of V_A/Q inequality with anesthesia FRC/TLC at or near CC/TLC , as shown in figure 1. Furthermore, rapid uptake of high inspired concentrations of soluble anesthetic gases, such as N_2O , could induce or enhance absorption atelectasis in regions with either intermittent airway closure or flow limitation. However, we did not show a significant difference in shunt with N_2O versus N_2 breathing, implying that absorption atelectasis was not an important factor in shunt development. Recent studies by Forkert *et al.*²³ showed marked reduction of N_2O uptake in dependent regions during a breath-hold at lung volumes less than CC. They interpreted their findings as a progressive increase in airway closure when lung volume decreased from closing capacity to residual volume. This interpretation is consistent with the increasing V_A/Q inequality as anesthesia FRC was reduced to CC/TLC , followed by increasing shunt as FRC was reduced from CC toward RV.

We also found that the anesthesia shunt was significantly higher than the awake shunt for a given FRC/TLC (fig. 5). The mechanism(s) responsible for this difference may be related to several important earlier observations. First, there is direct correlation between anesthesia shunt and amount of increased lung density in dependent regions.⁴ Second, anesthesia decreases dependent regional lung volume, whereas nondependent lung volume may actually be increased.^{24,25} In addition, inhaled anesthetics may impair hypoxic pulmonary vasoconstriction in atelectatic regions.²⁶

The location of the dependent regional volume reduction and atelectasis during anesthesia suggests a gravity-dependent mechanism.^{3,24,25} This was supported by the significant increase in slope of the regression between shunt and BMI shown in figure 3. Roussos *et al.*²⁷ showed increased disparity of dependent and nondependent regional lung volume with voluntary diaphragm relaxation. Froese and Bryan²⁸ demonstrated cephalad displacement of dependent portions of the diaphragm with anesthesia and paralysis. Krayer *et al.*,²⁹ however, found cephalad diaphragm displacement in only four of eight anesthetized-paralyzed subjects, but internal ribcage volume did decrease significantly. These findings support the hypothesis that chest wall relaxation is a significant factor in FRC reduction, and more specifically, that chest wall relaxation may be responsible for dependent regional volume reduction during anesthesia.

An additional mechanism that could reduce dependent regional volume is an increase in dependent pulmonary blood volume. Whether total thoracic blood volume changes with anesthesia is uncertain.^{29,30} However, this mechanism would explain the fact that reduction in internal chest wall dimensions accounted for only one-half of the FRC reduction induced by anesthesia in Krayer's subjects.²⁹ Alternatively, the difference between N₂ washout and chest cage volume changes could have been due to gas trapping. This is consistent with helium dilution studies by Don *et al.*,³¹ who demonstrated an increased volume of trapped gas in patients whose anesthesia FRC was less than their awake closing capacity.

Dependent regional airway closure and gas trapping could also have been responsible for the enhanced V_A/Q inequality in our smokers whose FRC was at or near CC, and for their enhanced shunting with respect to (FRC - CC)/TLC. Smokers are presumably more susceptible to airway closure and/or atelectasis at low lung volume because of focal inflammation and wall thickening in membranous and respiratory bronchioles.^{32,33} These changes generally remain difficult to detect until they reach advanced severity because flow rate in small airways is relatively low. However, the early changes induced by smoking result in increased dependent regional residual volume.³⁴ This is consistent with the direct correlation of awake CC/TLC and RV/TLC, as well as the inverse correlation between anesthesia shunt and both (FRC - CC)/TLC and (FRC - RV)/TLC in our subjects.

The relationship between anesthesia shunt and (FRC - CC)/TLC in our study was based on awake control CC measurements. It is unclear whether CC remains the same as awake or is changed during anesthesia. Rehder *et al.*²² speculated that increased elastic recoil of the lung or changes in airway transmural pressure might decrease CC, whereas changes in airway tone or surface forces might either increase or decrease CC. Gilmour *et al.*³⁵ showed

increased CC with mechanical ventilation in awake subjects, but halothane anesthesia had no effect. Hedenstierna *et al.*³⁶ also showed no change in CC with iv thiopental and fentanyl anesthesia. Both studies were performed with the resident gas (single breath N₂) method. Juno *et al.*,³⁷ however, used the foreign gas bolus (FGB) method and showed significant CC reduction with anesthesia, which raised the question of whether the difference between these reports was due to methodologic rather than anesthetic variables. It has been suggested that the FGB test is better suited for conditions in which it is not possible to provide a vital capacity breath equal to the awake control.²² However, Tokics *et al.*¹⁸ recently demonstrated CC reduction due to chest wall strapping, using the single breath N₂ test. Both methods are therefore able to show CC reduction during restricted lung volume conditions. Unfortunately, this does not resolve the issue of whether it was appropriate to use awake control CC values, or whether we should have obtained anesthetized CC values, because the latter may not reflect airway closure, which led to the anesthesia-induced alteration in lung mechanics.

Juno *et al.*³⁷ speculated that the anesthesia CC reduction was either due to increased elastic recoil of the lung or due to atelectasis. These two mechanisms are not mutually exclusive. Douglas *et al.*³⁸ found increased flow rate and increased quasistatic recoil pressure at low lung volume during chest wall strapping in awake subjects. They attributed the increased flow rate to a vagally mediated decrease in airway resistance, which was diminished by ipratropium, a vagolytic bronchodilator. Both the reduction in anesthesia CC and the reduction in airway resistance at restricted lung volume could be explained by increased elastic recoil of the lung through an increase in vagal tone. A mechanism linking lung elastic recoil and vagally mediated tone was recently suggested by Crawford *et al.*,³⁹ who observed a reduction in elastic recoil with iv atropine.

However, Westbrooke *et al.*⁴⁰ showed increased elastic recoil of the lung, increased airway resistance, and FRC reduction during anesthesia with endotracheal intubation. Awake volunteer studies by Gal⁴¹ showed increased airway resistance during endotracheal intubation but no change in FRC (measured by body plethysmography). Bickler *et al.*⁴² demonstrated an average 23% reduction in helium dilution FRC with intubation during barbiturate anesthesia, whereas mask breathing subjects showed only a 3% reduction from awake. In addition, Bickler *et al.*⁴² showed significant correlation between decrease in FRC and increase in P(A-a)O₂. This difference in FRC response to intubation may have been due to either the barbiturate anesthetic or due to differences in methodology. A reduction in helium dilution FRC without a significant change in body box FRC would most likely be due to gas trapping, which could occur as a consequence of airway constriction due to intubation. This explanation is sup-

ported by the increased RV in Gal's awake intubation study.⁴¹ We therefore propose that reflex airway constriction due to endotracheal intubation may be an important factor in the FRC reduction and shunt development produced by general anesthesia.

In summary, we found significant intrapulmonary shunting with anesthesia if FRC was reduced below awake closing capacity. Shunt during anesthesia was directly proportional to BMI, and it showed a synergistic effect of BMI and smoking. This suggests a gravity-dependent mechanism for shunting, which in turn supports the hypothesis that dependent regional lung volume was reduced by chest wall relaxation. Furthermore, because smokers had a higher shunt for a given (FRC - CC)/TLC, and because variation in CC was related to residual volume, we speculate that the synergistic interaction between anesthesia, smoking, and BMI may have been due to increased dependent regional residual volume.

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Appendix

The details of the piece-wise linear regression of shunt on FRC/TLC, and (FRC - CC)/TLC are presented. The mathematical expression used was:

$$Y = a + b_{<} \cdot (c - X), \text{ for } X < c$$

$$Y = a - b_{>} \cdot (X - c), \text{ for } X > c$$

where Y denotes shunt and X denotes FRC/TLC, or (FRC - CC)/TLC. The four parameters to be determined (a , $b_{<}$, $b_{>}$, and c) represent the transition point at which the slope changes ($X = c$), the elevation at the transition point ($Y = a$ at $X = c$), and the slope of the line for $X < c$ (slope = $b_{<}$) and for $X > c$ (slope = $b_{>}$). Requiring that shunt be nonnegative and that it be a nonincreasing function of FRC/TLC required that the parameters a , $b_{<}$, and $b_{>}$ be nonnegative. The maximum-likelihood estimation of the parameters was determined using the quasi-Newton method, assuming either a Gaussian or Cauchy distribution of residuals.^{11,12} Use of the Cauchy distribution reduces the influence of potential outliers.

The unknown location of the transition point made the piece-wise linear model nonlinear in the parameters, thereby making possible more than one relative minimum of the function being minimized.¹³ To assure that the correct solution was obtained, we determined the maximum-likelihood estimate (for fixed c) as a function of c . Slope $b_{<}$ was significantly greater than slope $b_{>}$, which was not significantly different from zero. Therefore, we used the solutions corresponding to $b_{>} = 0$ in the results (figs. 5 and 6).

To determine whether the smoking effect indicated in figure 6 was significant, we considered the 5 parameter model:

$$Y = a + b \cdot (c - X), \text{ for } X < c$$

$$Y = a, \text{ for } X > c$$

for nonsmokers, and:

$$Y = a + (b + d) \cdot (c + e - X), \text{ for } X < c + e$$

$$Y = a, \text{ for } X > c + e$$

for smokers, where Y denotes anesthesia shunt and X denotes (FRC - CC)/TLC. The coefficients (d,e) are the increase in slope and transition point due to smoking. The best fit corresponded to $d = 52$, $e = 0.055$, with $SS = 33$. This was significantly different ($P < 0.001$) from the solution assuming no effect of smoking ($d = 0$, $e = 0$, $SS = 337$). The best fit 4 parameter models corresponded to $d = 0$, $e = 0.074$, $SS = 39$ and to $d = 111.8$, $e = 0$, $SS = 43$. These two solutions are the preferred solutions because neither is significantly different from the 5 parameter model. Both yield a significant smoking effect ($P < 0.001$) and both fit the data equally well. This analysis indicates that there is a significant smoking effect, which appears as an increase in slope ($d > 0$) and/or an increase in transition point ($e > 0$). In conclusion, smokers had significantly more shunt for a given (FRC - CC)/TLC, or equivalently, the same amount of shunt occurred in smokers at a significantly higher (FRC - CC)/TLC compared to nonsmokers.

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