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Editorial II

Forty years of closing volume

The fundamental features of 'airway closure' were described in a landmark paper by Dollfuss and colleagues,[1] published 40 years ago in 1967. This paper showed a tracing of exhaled gas composition, related to lung volume. The subject first exhaled to residual volume and then inhaled a small quantity of an insoluble gas, followed by normal air, filling the lungs to total lung capacity (TLC). In the following slow expiration, the expected alveolar plateau showed an inflexion, with an increase in the tracer gas concentration as lung volume approached the end of expiration, that is, residual volume. The interpretation was that the lung emptied unevenly. The change in tracer gas concentration indicated that the final part of the exhaled gas came from parts of the lung that had received more of the initial inspirate: the principle of 'first in, last out' (Fig. 1). Indications that a decrease in lung volume would reduce ventilation of portions of the lung, and could in some circumstances cause hypoxaemia, had already been reported: in dogs with the thorax open[2 3] and in man during active expiration.[4] At first, the exact mechanism of the phenomenon of airway closure was unclear. A series of elegant experiments slowly unravelled the relative contributions of transpulmonary pressure and airway collapsibility, and the relationship between changes in airway patency and lung mechanics.[5–7] Better methods, with high resolution of lung images, have supported and extended the original concept. For example, inhaling a bolus of labelled particles that remain in the lung can provide an image of the patchy pattern of ventilation in asthma.[8]

In the following 40 yr, the concept of airway closure was applied in a number of important and disparate ways, as knowledge of lung biology advanced. At first, closing volume (CV) was considered useful to study lung disease caused by smoking or air pollution, as a marker of small airway damage which could not be detected by simple spirometry. For example, a large study of smokers found that although only 11% had abnormal spirometry, 44% of them had abnormal CVs.[9] Initial enthusiasm waned as it became clear that, although sensitive, the measure was poorly reproducible and not predictive,[10] perhaps partly because it was as much a marker of inflammation of the small airways as it was of structural damage,

Interest shifted, and a lot of research reported on the relationship between airway closure and impairment of gas exchange. A seminal study had already shown that posture affected lung efficiency in that recumbency increased the difference in nitrogen partial pressure between tissues and alveolar gas.[11] This observation was interpreted using knowledge of the behaviour of inert gases, new at the time, that laid the foundation for much of our understanding of gas exchange, the effects of matching between ventilation and perfusion, and many of the methods we now use. In lung units that are poorly ventilated, not only is the oxygen tension low, but the nitrogen tension is high. Blood leaving these units increases the arterial nitrogen tension and thus provides a clear, if indirect, sign that lung units with low ventilation/perfusion ratios must be present. Such conditions could occur if airway closure were to occur during tidal breathing, in other words when closing capacity was greater than functional residual capacity, as might occur in the supine position, in pregnancy,[12] obesity,[13] with ageing,[14] voluntary reduction of lung volume,[15] after abdominal surgery,[16] and in heart failure.[17] Later, the direct evidence of airway closure reinforced the initial deductions. Since oxygenation is impaired during anaesthesia, and studies had been published about that time showing how FRC was reduced by anaesthesia, the relationship between CV and impaired oxygenation during anaesthesia was also studied.[18] Applying positive end-expiratory pressure during anaesthesia to increase lung volume did indeed improve oxygenation,[19 20] but the effect was only seen in those with poor oxygenation, and was not very marked: an increase from 10.3 to 13.6 kPa by 15 cm H_2O PEEP![20]

A third stage of interest in airway closure has now developed, along with the understanding of how the lung and airways may be damaged by the process of ventilation itself. When lung inflation starts from residual volume, the lung tissue that is inflating will not include those parts where airways are closed. At the start of inflation, the lung is functionally 'smaller', and the quantity of participating tissue progressively increases as the airways open. Thus, the mechanical properties change, and this may be seen as an inflexion, or change of slope, on the pressure–volume plot.[6 21] This can also be detected as a change in airway resistance[22] and as sounds in the airway.[23] The airway opening occurs in a stepwise manner, indicating a hierarchical pattern of airway opening.[24] The pressure–volume relationship of the respiratory system of anaesthetized patients shows how airways re-open over a large range of pressures, probably up to 20 cm H_2O.[25] The successive re-opening of these airways, even in normal lungs

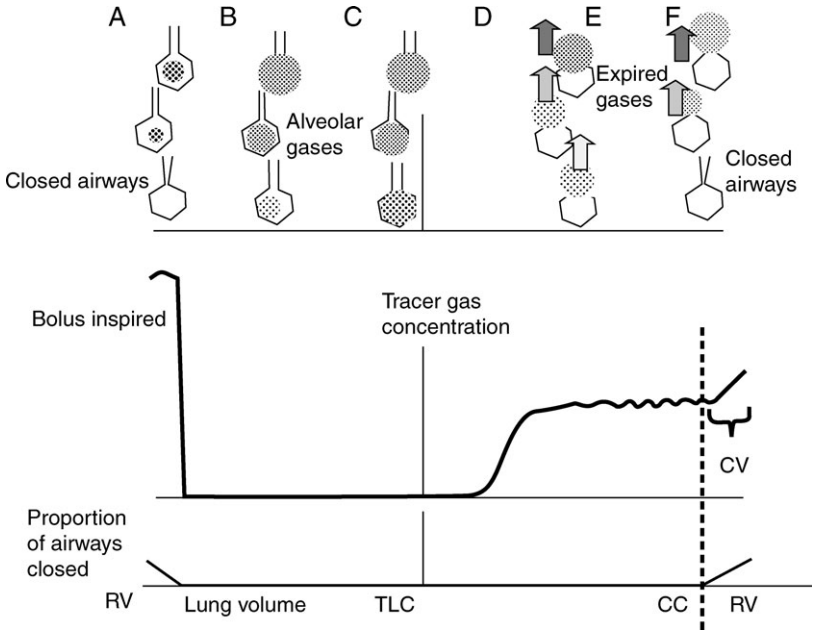

Fig 1 The proposed mechanism of the CV manoeuvre with a tracer gas. (A) The lung is at RV, and a bolus of tracer gas is inspired, which passes into lung regions served by airways that remain open. Lung regions with closed airway do not receive any tracer gas. (B) The tracer gas bolus is followed by unlabelled air. As this unlabelled air is inspired, it dilutes the tracer gas according to the regional ventilation pattern of the lung. Those regions that were closed have opened, and receive air. (C) TLC is reached. The alveoli that were open at RV contain tracer gas: the alveoli that were closed, and the airways, contain air only. (D) Expiration has started and airway gas containing no tracer is exhaled: this is dead space gas. (E) The 'alveolar plateau' contains slightly varying contributions from different lung regions (partly because of cardiac movement). The exhaled concentration represents this variation in contributions from different regions. (F) As airway closure starts, the lung regions that contain less or no tracer gas cease to contribute to expired gas. Consequently, the tracer gas concentration in the expired gas increases, as it now is only issuing from labelled lung regions. The lung volume at which airway closure starts is called closing capacity, and the difference between CC and RV is the CV.

ventilated at low lung volumes, leads to damage, and can be prevented by maintaining the lung volume and a normal end-expiratory volume.[26] The lung damage is also made worse if the inflation rate of mechanical ventilation is increased.[27] A picture has emerged of another mechanism of 'volutrauma' where repeated opening and closing of the airways is a damaging mechanism,[28] interacting with other damaging mediators,[29] just as excessive tidal volumes were proposed as harmful,[30] and can cause poor outcome even after a few hours of anaesthesia.[31]

During deflation, as the lung gets smaller, the number of airways contributing to the expired flow declines, and the flow is reduced. In patients with emphysema, who have increased CV and reduced lung recoil, expiratory flow limitation may be present. When this happens, incomplete expiration leads to lung hyperinflation and dyspnoea on exertion.[32 33] This flow limitation during expiration may be yet another mechanism of airway damage.[34] In animals, ventilation at low lung volumes causes disruption of the airway epithelium, disruption of alveolar attachments to the airways, and inflammation. The resistance of these airways increases, which is likely to make dynamic airway closure even more severe.[26] In many circumstances, changes in posture and variations in breathing pattern may 'share out' this damage in different parts of the lung. However, in the obese immobile patient receiving mechanical ventilation, flow limitation may occur in the same small airways for several hours, leading to damage.[35] Flow limitation is also evident in patients receiving intensive care.[36] One means of 'sharing out' the damage may be to vary the pattern of ventilation, which has been shown to prevent a progressive deterioration of lung function with standard ventilation.[37]

The concept of airway closure over the last 40 yr has been a valuable idea that we have been able to apply respiratory measurements to explain disease and provide solutions to clinical problems, by combining experiment and clinical investigation with more recent ideas of inflammation without losing sight, or understanding, of mechanical reality!

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