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EXPERIMENTAL

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Volumetric capnography as a bedside monitoring of thrombolysis in major pulmonary embolism

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Abstract *Objective:* To describe the use of volumetric capnography, a plot of expired CO_2 concentration against expired volume, in monitoring fibrinolytic treatment of major pulmonary embolism. *Design and setting:* Two case reports in the emergency department of a teaching hospital. *Patients:* Two conscious and spontaneously breathing patients (69- and 31-year-old women) with major pulmonary embolism requiring thrombolysis. Decision for thrombolysis was based on the association of right ventricular afterload on echocardiography, with respiratory failure and hypotension in the first patient, and dyspnea and hemodynamically stable parameters in the second one. *Interventions:* Successive capnographic measurements were performed before, during, and after thrombolysis. Curves of volumetric capnography were obtained from a sidestream gas monitor with flow sensor and an arterial blood gas analysis for CO_2 partial pressure. *Measurements and results:* We calculated late deadspace fraction, previously suggested as the most effective capnographic parameter in the diagnosis of pulmonary embolism. Late deadspace fraction decreased in the two patients, respectively, from 64.4% to 1.1% and from 25.6% to 5.7% after thrombolysis, with a concomitant disappearance of right heart dysfunction signs on echocardiography. *Conclusions:* Volumetric capnography can monitor thrombolysis in major pulmonary embolism. Differences between volumetric capnography technology and the more traditional arterial to end-tidal CO_2 gradient are important to take into account for clinical application.

Keywords Capnography · Volumetric capnography · Pulmonary embolism · Major pulmonary embolism · Thrombolysis

Introduction

Major pulmonary embolism (MPE), defined as pulmonary embolism (PE) with arterial hypotension, cardiogenic shock, or right ventricular afterload [1], is characterized primarily by increased alveolar deadspace from unperfused but well ventilated lung regions. The mortality rate of MPE ranges from 10% to 25%, justifying the potential recourse to thrombolysis for rapid clot dissolution [2]. Monitoring the thrombolytic efficacy is essential but may require serial echocardiograms or pulmonary catheterizations, the later being invasive, and inconvenient for conscious and spontaneously breathing patients.

Volumetric capnography (VCap), the plot of expired CO_2 concentration against expired volume, is a bedside validated method for measuring airway and alveolar deadspace volumes, and appreciating the pulmonary ventilation-perfusion relationships [3, 4]. Because the performance of VCap in the diagnostic work-up for pulmonary embolism has been previously established [5, 6, 7], we hypothesized that it also applies in monitoring the clinical course during fibrinolytic treatment of MPE. The results of two first studied cases are presented here.

Material and methods

Volumetric capnography

VCap analysis is illustrated in Fig. 1. VCap displays the expired CO_2 as a function of the expired volume during one single breath, according to the work of Fletcher et al. [3] in 1981. The shape of the capnographic curve starts with a CO_2-free phase continues with an ascending transition phase and ends with a plateau phase which slope depends on the ventilation-perfusion mismatches. The slope is determined by least squares linear regression analysis for the end-expiratory plateau phase using at least the last 15% of the expired tidal volume. The end of the curve corresponds to the end-tidal CO_2 ($EtCO_2$). A vertical line surrounding the curvature of the second phase determines the airway deadspace (VD_{aw}). The arterial $PaCO_2$ value delimitates an upper horizontal line, the surface between this line and the plateau phase corresponding to the alveolar deadspace volume (VD_{alv}). The gradient between $PaCO_2$ and $EtCO_2$ traditionally represents the fraction of VD_{alv} on the tidal volume. Eriksson et al. [7] found that the extrapolation of the capnographic curve should cross the $PaCO_2$ horizontal line at a CO_2 value corresponding to 15% of the predicted total lung capacity ($E_{xp}CO_2^{15\%\ TLC}$) in healthy subjects, and in patients with obstructive lung diseases. He defined late deadspace fraction (Fd_{late}) as: $Fd_{late}=(PaCO_2-E_{xp}CO_2^{15\%\ TLC})/PaCO_2$, where TLC is estimated taking sex and height of the patient into consideration [8].

A typical capnographic appearance of moderate to severe pulmonary embolism is characterized with a flat plateau phase and an

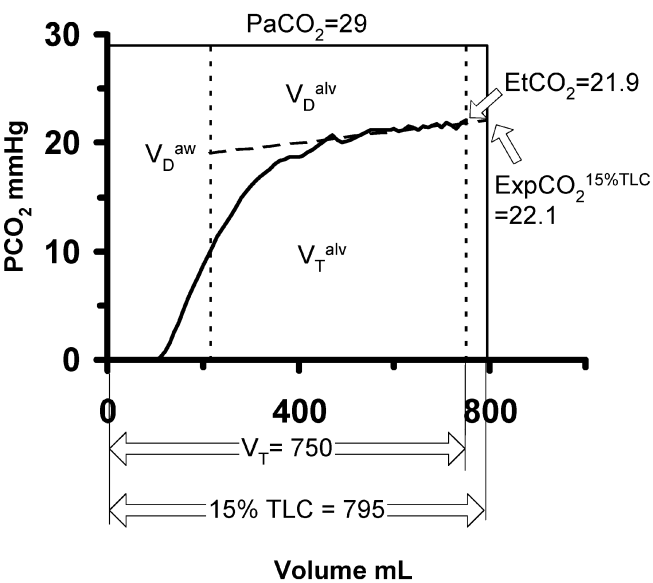

Fig. 1 Volumetric capnography and its different parameters, including alveolar deadspace (V_D^{alv}), airway deadspace (V_D^{aw}), and late deadspace fraction (Fd_{late}). Data are from patient 2 before starting thrombolysis. The arterial $PaCO_2$ is 29 mmHg and the end-tidal CO_2 is 21.9 mmHg; 15% of the predicted total lung capacity is 795 ml and the expired CO_2 partial pressure corresponding to this 795 ml volume ($E_{xp}CO_2^{15\%\ TLC}$) is 22.1 mmHg; Fd_{late} is calculated as (29–22.1)/29=23.8%. Tidal volume (V_T) is 750 ml

elevated $PaCO_2$–$EtCO_2$ gradient, as shown in Fig. 1. In these conditions the extrapolation of the curve fails to reach the $PaCO_2$ horizontal line. Since the VCap takes into consideration both the plateau phase curve pattern and the $PaCO_2$–$EtCO_2$ gradient, Fd_{late} has been found the most effective among the capnographic parameters for differentiating PE from other pulmonary illnesses [7]. Eriksson et al. [7] chose a cutoff value of 12% for Fd_{late}, patients with PE having higher values.

Time-based capnograms and respiratory flows were measured in this study by Datex-Ohmeda (GE Medical Systems, Information technology, Helsinki, Finland) CS/3 monitor, gas analyzer (M-COVX), and D-lite sensor (deadspace 9 cc) connected to the patient through a mouthpiece or a facial mask (deadspace 25 cc). Signals were synchronized at start of inspiration when CO_2-free fresh gas enters gas-sampling point practically parallel with the flow turning. Arterial $PaCO_2$ sample was collected slowly after 2 min stabilization period during capnographic registration. A breath of typical tidal volume, respiration rate, and $EtCO_2$ collected during arterial sampling was selected for analysis.

Patients and measurements

The first patient was a 69-year-old woman with dyspnea for 1 day before admission. She fainted shortly after admission. At that time her blood pressure was 88/43 mmHg, pulse rate 145/min, and respiratory rate 50/min. Echocardiography showed a systolic pulmonary arterial pressure (sPAP) of 50 mmHg, a paradoxical septal wall motion, and a right-to-left ventricular size ratio of 1.67. A 10-mg bolus of alteplase was immediately started, followed by 90 mg over a 2-h period. A control echocardiogram 12 h later showed a sPAP of 19 mmHg and the disappearance of right heart dysfunction signs. Lung scintigraphy confirmed segmental defects in the upper right and middle lung lobes. Her VCap was recorded during thrombolysis and repeated 5 and 24 h later.

The second patient was a 31-year-old woman complaining of dyspnea for 3 days. On admission her blood pressure was 125/80 mmHg, pulse rate 120/min, and respiratory rate 26/min. Spiral computed tomography confirmed bilateral lobar and segmental pulmonary occlusions. Initial echocardiography showed a sPAP of 38 mmHg and the same right heart dysfunction signs as the previous patient. A 100-mg alteplase infusion was administered over a 2-h period. Echocardiography 12 h later was normal. VCap was measured seven times: twice before, twice during and three times after thrombolysis.

Neither of the two patients had bleeding complications.

Results

Patient 1

One hour after starting thrombolysis the patient's $PaCO_2$ was 37 mmHg and $EtCO_2$ 14.1 mmHg. The value for 15% of the predicted TLC was calculated as 765 ml, and $E_{xp}CO_2^{15\%\ TLC}$ was 13.3 mmHg. Fd_{late} corresponded to (37–13.3)/37 mmHg=64.4%. Fd_{late} was reduced to 21.9% 5 h after the end of thrombolysis and to 1.1%=(33–32.6)/33 mmHg the day thereafter. This Fd_{late} reduction parallels the decrease in the $PaCO_2$–$EtCO_2$ gradient related to VD_{alv} fraction reduction: this gradient was 22.9 mmHg at the beginning of thrombolysis, 11.3 mmHg 5 h later, and 2.7 mmHg the day thereafter. Figure 2 shows the

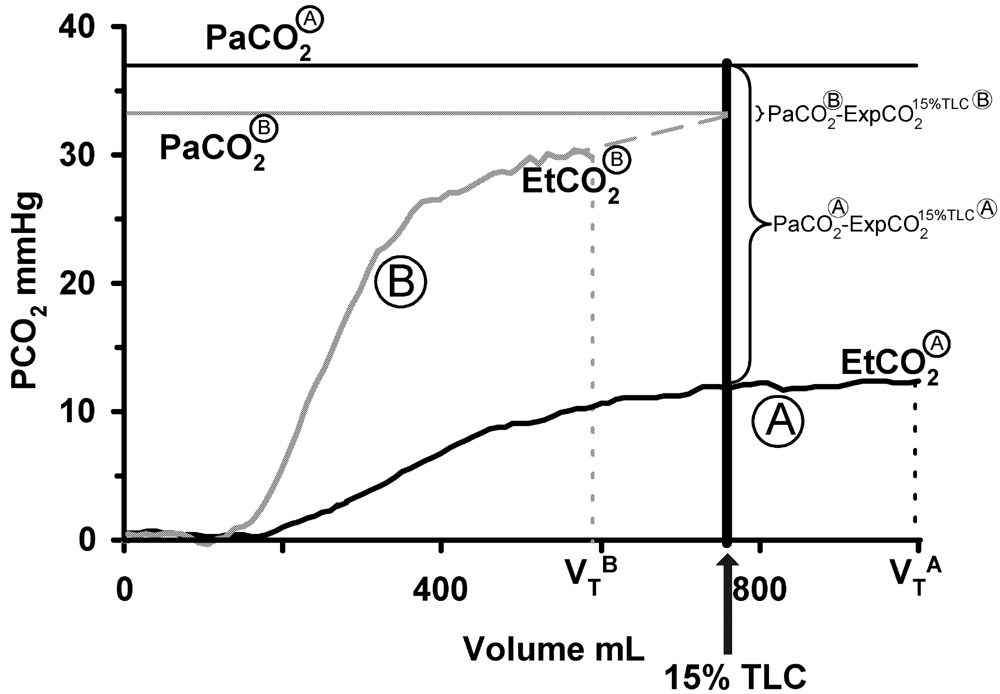

Fig. 2 Course of volumetric capnography measurement in patient 1, from beginning (*curve A*) to 24 h postthrombolysis (*curve B*). *Arrow* value for 15% of the predicted TLC (765 ml) used for Fd_{late} calculation. Note that the tidal volume of curve A (VT_A) is higher than 15% of the predicted TLC. The marked ranges (}) express Fd_{late} as the difference between $PaCO_2$ and $E_{xp}CO_2^{15\%\ TLC}$. Fd_{late} reduced from 64.4% at the beginning of thrombolysis to 1.1% on the day after, almost crossing the horizontal $PaCO_2$ line at the 15% of predicted TLC vertical line

capnographic curves of patient 1 at the beginning and 24 h after thrombolysis.

Patient 2

Considering a predicted TLC of 795 ml, Fd_{late} values were 25.6% and 23.8% 1 h before and at the beginning of thrombolysis, respectively, confirming stable baseline values. Fd_{late} was reduced to 1.4% after 50 min of thrombolytic treatment and to 1.8% at the end of the 2-h alteplase regimen. Fd_{late} stabilized to −1.3%, −3.6%, and 5.7%, respectively, 12, 36, and 60 h after thrombolysis. The $PaCO_2$–$EtCO_2$ gradient decreased as follows: 5.9 and 7.1 mmHg before thrombolysis, 2.4 and 2 mmHg during thrombolysis, 0.1, 1.2, and 2.4 mmHg after thrombolysis.

Discussion

This report shows that Fd_{late} measured by VCap can monitor the improvement in pulmonary vascular obstruction during thrombolysis for MPE. The normalization of echocardiographic signs of pulmonary dysfunction coupled with a significant decrease in the Fd_{late} ratio shows thrombolytic efficacy in two spontaneously breathing patients. The improvement in Fd_{late} during and after thrombolysis was markedly affected by the reduction in $PaCO_2$–$EtCO_2$ gradient.

One study and two case reports previously assessed the role of capnography in MPE requiring thrombolysis by using information from the $PaCO_2$–$EtCO_2$ gradient [9, 10, 11]. This gradient increases in the case of MPE, firstly because unperfused but well ventilated lung regions are unable to eliminate CO_2, and secondly because right ventricular failure decreases the CO_2 transport to the lungs [12, 13]. Wiegand et al. [11] showed a high intraindividual correlation (R^2=0.77–0.98) between the changes in the $PaCO_2$–$EtCO_2$ gradient and the changes in pulmonary arterial pressure in 12 mechanically ventilated patients with MPE, demonstrating that capnography was a reliable noninvasive alternative to pulmonary catheterization in monitoring the efficacy of thrombolysis. The two other case reports shared the same encouraging results [9, 10], but only one patient in these three reports was breathing spontaneously, a clinical condition associated with less stable respiratory pattern and less extensive embolic burden.

VCap is based on solid physiological principles developed by Fletcher and associates [3, 14] in the early 1980s. The technique allows a breath-by-breath calculation of deadspace volumes and gives information on the ventilation-perfusion relationship thanks to the slope of the plateau phase. VCap is considered a gold standard for measuring deadspace [15], and several investigators have reported its role in the diagnostic work-up for a clinical suspicion of PE [5, 6, 16]. Fd_{late} is another VCap parameter that uses the extrapolation of the capnographic curve to differentiate patients with PE from those with obstructive lung diseases [7, 17]. Moreover, a recent study showed that the diagnostic performance of Fd_{late} was significantly better than the $PaCO_2$–$EtCO_2$ gradient in a group of 45 outpatients with a suspicion of PE, as assessed by a receiver operating characteristic curve analysis (87.6% vs. 75.9%, p=0.02) [16]. We therefore hypothesized that Fd_{late} is more appropriate in clinical conditions associated with potential false-positive $PaCO_2$–$EtCO_2$ gradients, such as in apprehensive and rapidly breathing patients or in cases of PE combined with chronic obstructive pulmonary disease [18, 19].

Physicians caring for patients with MPE currently use several methods to evaluate the effect of thrombolysis: (a) clinical signs of arterial hypotension, cardiogenic shock or right ventricular overload, (b) pulmonary catheterization, (c) serial echocardiography, and (d) lung scintigraphy or angiography. Fd_{late} provides advantages over these being a noninvasive, low-cost bedside measurement even for spontaneously breathing patients, which provides rapid information of the thrombolytic efficacy as shown in this study (Fig. 2). Fd_{late} may also complete or precede changes in the clinical vital signs assessment (e.g., blood pressure, heart rhythm, urinary output). Finally, VCap is a more easily repeatable technique than serial echocardiography.

VCap thus promises results in monitoring thrombolysis of spontaneously breathing patients with MPE. This validated noninvasive bedside technique can improve patient care by providing rapid information on the therapeutic efficacy and completing the clinical signs assessment.

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