

**BALLOON-FREE GASTRIC TONOMETER COMBINED WITH THE EVALUATION
OF THE GASTRIC-TO-END-TIDAL CO₂ GAP IN CHILDREN**

Ph.D. Thesis

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List of publications

Original papers directly related to the thesis

- I. Király Á, Boda D, Tálosi Gy, Boda K. Intraoperative gastric tonometric examinations in children and infants with a new probe, combined with measurement of the endtidal PCO₂. *Pediatric Anesthesia* 2008; 18:501-507. [IF: 1.469]
- II. Szakál O, Király Á, Szűcs D, Katona M, Boda D, Tálosi Gy. Measurement of gastric-to-end-tidal carbon dioxide difference in neonates requiring intensive care. *The Journal of Maternal-Fetal and Neonatal Medicine* 2012; 25(9): 1791-1795 [IF: 2.071]

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INTRODUCTION

Because of their wide-ranging immaturity, prematures, term neonates and infants may undoubtedly be considered the most vulnerable population of patients. This period of life can be characterized by overall unsteadiness, with sudden and unusual reactions to different stimuli. Their reduced reserves and limited compensatory mechanisms, accompanied by their increased and altered reflex activity, predispose them to undergo rapid changes in their condition. This physiologically unstable state may be coupled with various diseases and/or special age-related diseases, such as congenital defects, necrotizing enterocolitis (NEC), the respiratory distress syndrome (RDS) or neonatal sepsis. In certain cases, they cannot be treated by conservative therapy, and surgical interventions may be required. The younger the patient, the higher is the risk of cardiovascular complications during anaesthesia and surgery

In spite of its immaturity at birth and the dynamic changes that occur throughout the further development of the patient, the cardiovascular system (in close conjunction with the respiratory system) forms a dynamic to-and-fro metabolic passage between the cells and the environment. A blood supply deterioration caused by hypovolaemia, sepsis or shock results in an early rearrangement of the circulation, diverting the blood flow from the splanchnic region towards organs of vital importance. During the recovery period, the splanchnic circulation is the last to be restored.

In view of the possible very rapid changes in the condition of these patients, there is a need for a reliable, not very expensive, complication-free, non-invasive and reproducible monitoring method with which to be able to follow the changes in their status and to predict the outcome of the disease. Monitoring should be started as early as possible and should be continued as long as required.

Apart from the discrepancies caused by the different sizes of the patients and tonometric probes currently available, gastrotonometry or gastric tonometry could meet these requirements. Boda et al. recently developed a balloon-free new generation of gastric tonometric sampling probes which can be applied even in the smallest population of patients. Gastric tonometry has proved to be a simple, sensitive, organ-specific and early detector of the condition of the splanchnic circulation and the oxygenation of the gastrointestinal organs. Deterioration of the gastrointestinal blood flow can be the first sign of an insufficiency of the systemic circulation. Splanchnic vasoconstriction is part of the redistribution process of the systemic circulation in response to generalized stress stimuli. In consequence of a reduction of

tissue oxygenation, cellular anaerobic metabolism results in the excessive production of carbon dioxide (CO₂) in the gastrointestinal mucosa. Measurement of the intragastric partial pressure of CO₂ (P_gCO₂) and calculation of its difference from the arterial partial pressure of CO₂ (P_aCO₂) may provide valuable information concerning the metabolic and circulatory conditions of the stomach and the splanchnic region.

In our studies, we set out to examine the feasibility and reliability of the new neonatal probes under paediatric surgical conditions and on critically ill, ventilated patients in the neonatal intensive care unit (NICU). Furthermore, we compared the P_{g-a}CO₂ gap (the difference of P_gCO₂ and P_aCO₂) with the P_{g-ET}CO₂ gap (the difference of P_gCO₂ and P_{ET}CO₂, the end-tidal partial pressure of CO₂), as an alternative, and investigated the relationship between increased P_{g-ET}CO₂ gap values and an unfavourable outcome.

AIMS AND QUESTIONS OF THE STUDIES

The usefulness of the novel gastric tonometric probe in paediatric patients has already been proven by earlier studies. We designed two prospective clinical investigations in order to support the applicability and reliability of the new neonatal gastric tonometric tool in extended fields: in the paediatric population under intraoperative conditions (study 1), and in low birth weight NICU patients in critical states (study 2).

We were the first to apply the novel gastric tonometric probe in this age group during surgical procedures. We wished to exploit the known benefits of the method: to assess the adequacy of ventilation and the splanchnic perfusion of the patients and to acquire information as to the severity of the disease.

We investigated the possibility of gaining therapeutic information in a semi-invasive manner, bypassing the risk of infection and vasoconstriction caused by the painful and often difficult blood sampling, and the considerable anaemia and haemodynamic changes that can occur in these small patients due to the significant blood loss caused by repeated blood samplings. In order to reduce the need for repeated blood sampling, we set out to examine and the possible usefulness of the P_{g-ET}CO₂ gap by using capnometric P_{ET}CO₂ values instead of P_aCO₂. We are not aware of previous studies of the diagnostic value of the P_{g-ET}CO₂ gap in this age group.

Both studies were approved by the Human Investigation Review Board of the University of Szeged. In every case, informed consent was obtained from the parents.

The main questions studied were the following:

Question I

Can the novel gastric tonometric probe developed for paediatric patients of all ages be used safely and reliably during paediatric surgical procedures (study 1) and in the population of smallest paediatric patients in the NICU (study 2)?

Question II

Is there any difference between the groups in terms of the $P_{ET}CO_2$ values during surgery (study 1) and in NICU patients (study 2)?

Question III

Is there any correlation between the P_aCO_2 and $P_{ET}CO_2$ values in the examined patients during surgery (study 1) and in NICU patients (study 2)?

Question IV

Does the respiratory dead-space of the patients exert any effect on the $P_{g-ET}CO_2$ gap?

Question V

Is there any difference between the groups in terms of the P_gCO_2 values during surgery (study 1) and in NICU patients (study 2)?

Question VI

Is there any difference between the groups in terms of the $P_{g-a}CO_2$ gap values during surgery (study 1) and in NICU patients (study 2)?

Question VII

Is there any difference between the groups in terms of the $P_{g-ET}CO_2$ gap values during surgery (study 1) and in NICU patients (study 2)?

Question VIII

Is there any correlation between the $P_{g-a}CO_2$ and $P_{g-ET}CO_2$ gaps during surgery (study 1) and in NICU patients (study 2)?

Question IX

Does the $P_{g-ET}CO_2$ gap relate to the severity of the disease?

STUDY 1

Study no. 1 was a prospective randomized study of the therapeutic value of the $P_{g-ET}CO_2$ gap beyond the already proven clinical reliability of the Boda probe under intraoperative circumstances in paediatric patients.

Patients and methods

The prospective study enrolled a total of 25 anaesthetized surgical patients: 19 elective and 6 acute cases. The 19 elective surgical patients were assigned to one or other of two groups according to their ages (group I and group II). Group III consisted of the acute surgical patients, independently of their ages.

Group I : Ten elective surgical patients younger than 2 years (age median: 11.2 months; range: 0.1-24)

Group II : Nine elective surgical patients older than 2 years (age median: 97.7 months; range: 29-261)

Group III : Six acute surgical patients independently from their age (age median: 98 months; range: 15-204)

Each patient in the study underwent general anaesthesia during the surgical intervention. Anaesthesia was induced with intravenously administered midazolam, fentanyl and ketamine or propofol. In order to establish optimum conditions for the endotracheal intubation, muscle relaxants (rocuronium or cisatracurium) were applied, and the level of muscle relaxation was monitored by an accelerometer throughout the procedure.

In the selection of the proper size of the intratracheal tubes, we followed the recommendations of internationally accepted guidelines. Seventeen of the examined patients were younger than 8 years, and they were therefore intubated with uncuffed tubes. In the case of the 8 patients older than 8 years, cuffed intratracheal tubes that could be passed with ease were inserted, but an important restriction was to have only minimally allowable gas leakage on ventilation.

During the surgical intervention, the patients were ventilated via a paediatric closed breathing circuit by a Dräger Julian ventilator (DrägerwerkAG, Luebeck, Germany) and for anaesthesia maintenance constant flow of a mixture of O_2 , N_2O and sevoflurane was administered.

CO₂ samples for determination of P_{ET}CO₂ could be delivered at the gas-sampling port of the endotracheal tube adapter in infants smaller than 4 kg, or at the CO₂ sampling port of the airway filter interconnecting the endotracheal tube and the breathing circuit in patients larger than 4 kg.

Samples for P_gCO₂ measurement were delivered by Boda balloonless gastric tonometric probes after a 10-minute equilibration period. The examination tools were introduced nasally in every case, because of the need for firm fixation during the surgical procedures. The correct gastric positions of the probes were confirmed by the correct CO₂ curves on the capnograph monitor following the 10-minute equilibration period. For the determination of P_{ET}CO₂ and P_gCO₂, the same equipment was used (Sidestream Microcap Handheld Capnograph, Oridion Medical Ltd, Jerusalem, Israel).

In 6 cases, simultaneously with the P_{ET}CO₂ and P_gCO₂ measurements, arterialized capillary blood samples were obtained for blood gas analysis. The PCO₂ content of arterialized blood samples was determined with an ABL700 instrument (Radiometer, Copenhagen, Denmark).

Statistical analysis

The relationships between the measured P_{ET}CO₂ and P_gCO₂ in the study groups were examined by linear regression analysis. Pearson's correlation coefficient and *p* values were also calculated. To examine the agreement between the measurements, Bland - Altman analysis was performed. The bias (defined as the mean difference between values), the precision (defined as the standard deviation (SD) of the bias) and the limits of agreement (defined as the bias ± 2 SD) were determined for the groups.

Since there were multiple measurement data from each patient for the various PCO₂ values, we used a two-way mixed-model repeated-measurements analysis of variance (ANOVA) with groups as between-subject factor and time as within-subject factor for the comparison of the different groups. This method is a generalization of the two-sample *t*-test, where both group differences and the individual within-subject variations in time can be modelled.

SPSS 15.0 for Windows (SPSS for Windows Rel. 15.0, SPSS Inc., Chicago, Illinois, USA) was applied for the statistical calculations.

STUDY 2

Study 2 was a prospective study of the applicability of the novel gastric tonometric probe and the therapeutic value of the $P_{g-ET}CO_2$ gap under the circumstances of intensive care in low body weight neonatal ventilated patients.

Patients and methods

The 44 ventilated patients of the neonatal intensive unit were assigned to two groups independently from their ages according to the severity of their diseases (characterized by CRIB scores):

Group 1: Nine patients with their SCRIB scores ≤ 10 (gestational age: 32.1 ± 3.7 weeks; body weight: 1833 ± 885 g)

Group 2: Thirty five patients with their SCRIB scores >10 (gestational age: 30.9 ± 6.9 weeks; body weight: 1871 ± 1281 g)

The patients were investigated throughout their full stay in the NICU. Each of them was ventilated and sedated to meet their demands. For the determination of the sizes of the uncuffed tubes to be used for intratracheal intubation, we followed the recommendations of internationally accepted guidelines, in accordance with gestational age and body weight, similarly as in study 1.

The observed neonates were ventilated with SLE 2000, SLE 2000 HFO or SLE 5000 ventilators in conventional modes (synchronized intermittent mandatory ventilation and continuous mandatory ventilation) according to the requirements of their conditions. The need for other types of ventilation, such as high-frequency oscillation, was a criterion for exclusion from the study. The patients involved in the study were assigned to one or other of two groups. The 35 neonates (all survivors) with their CRIB scores lower than 10 were delegated to group 1, while group 2 consisted of 9 patients in severe condition with CRIB scores higher than 10 (2 out of 9 survived).

The treatment followed the local protocols, but the routine administration of H_2 receptor blockers was omitted. Three types of PCO_2 measurements were made in each patient, the ventilator setting parameters remaining unchanged.

$P_{ET}CO_2$ was measured on samples obtained from the gas-sampling port of the intratracheal tube adapter. Each measurement lasted for at least 4 minutes and the highest measured value was accepted. $P_{ET}CO_2$ was measured with a Sidestream Microcap Handheld Capnograph (Oridion Medical Ltd, Jerusalem, Israel).

P_gCO_2 levels were examined with the use of Boda's gastric tonometric probes, inserted orally or nasally. To ease the introduction, a flexible guide wire was used in the probe. Both were well lubricated with symethicon. The positions of the probes were considered gastric if correct CO_2 curves were obtained on the capnograph monitor after the 10-minute of equilibration period. Gastric tonometric measurements were performed after the appropriate equilibration interval had passed, and measurements were also made with the Sidestream Microcap Handheld Capnograph.

The acid-base parameters (pH, HCO_3^- , BE, PO_2 and PCO_2) were obtained from the blood gas analysis of umbilical artery blood samples or arteriolized capillary blood samples with an ABL 700 instrument (Radiometer, Copenhagen, Denmark).

Two more data were calculated from the results of the measurements: the $P_{g-a}CO_2$ gap and the $P_{g-ET}CO_2$ gap. The dead-space ventilation fraction was estimated via the equation: dead-space volume / tidal volume = $(P_{a-ET}CO_2) / P_aCO_2$.

Statistical analysis

As there were multiple measurement data from each patient for the various PCO_2 values, we used a two - way mixed - model repeated - measurements ANOVA for the comparison of the two groups. For the comparison of the PCO_2 gap values in the groups, a three-way mixed-model ANOVA was used, with the groups as between-subject factor, gaps as within-subject factor and time as within-subject factor. The various PCO_2 values and PCO_2 gap values were compared using Bland - Altman analysis for multiple measurements per individual, and the correlation recommended for repeated measurements was used for the comparison of the characteristics of the neonates in the two groups of patients with unpaired Student's *t*-tests.

RESULTS (in the sequence of the main questions studied)

Result I

Study 1. Apart from 2 cases, the gastric tonometric probes could be introduced with ease. In one case, the probe stopped at a certain point of the oesophagus and could not be

passed further. In the other case, the probe could not be passed through the pharynx. There were no further technical difficulties during the measurements.

Study 2. The oral or nasal introduction manoeuvres of the tonometric probes proved facile in all cases. There were no difficulties, unintended side-effects or serious complications during the introduction procedure or the repeated measurements.

Result II

Study 1. In spite of the differences between the ages of the group I and II patients, their $P_{ET}CO_2$ levels were nearly identical (mean difference 0.10 mmHg and $p = 0.96$), whereas the result in group III differed significantly from those for the elective surgery cases (mean differences: 1.9 mmHg and 2.0 mmHg, $p = 0.03$ and 0.031 , respectively).

When groups I and II were combined, their $P_{ET}CO_2$ levels differed significantly from that for group III (mean difference 1.94, $p = 0.014$)

Study 2. There were no significant differences in $P_{ET}CO_2$ between the groups of NICU patients with conditions of different severity, nor when either group I or group II was compared with the overall group ($p = 0.05$).

Result III

Study 1. Arterialized capillary blood samples were taken simultaneously with the $P_{ET}CO_2$ and P_gCO_2 measurements under intraoperative circumstances in only 6 cases. In these cases, the average \pm SD of the differences between the arterialized blood and end-tidal CO_2 value was 2.38 ± 2.23 mmHg. The difference between the two parameters was statistically not significant ($p = 0.35$).

Study 2. In each group of examined NICU patients, $P_{ET}CO_2$ proved to be lower than P_aCO_2 . There was a significant correlation ($p < 0.001$) between each pair of P_aCO_2 and $P_{ET}CO_2$ ($r = 0.631$). This correlation did not reveal a closer connection than that found between the gastric and systemic PCO_2 levels.

Result IV

- Study 1. The fraction of dead-space ventilation was not calculated during this study. In the 6 intraoperative cases where simultaneous arterialized capillary PCO₂ measurements were performed, the average \pm SD of the differences between P_{ET}CO₂ and P_aCO₂ was 2.38 ± 2.23 mmHg (not statistically significant: $p = 0.35$).
- Study 2. In the low body weight NICU patients, a dead-space of 0.176 ± 0.223 was observed. The dead-space was significantly higher in group 2 (0.236 ± 0.098 versus 0.155 ± 0.143 , $p = 0.022$). We also compared the smaller (weight < 1500 g, $n = 13$) and larger (weight > 2500 g, $n = 15$) patients. In this comparison, the dead-space was higher in the case of the low birth weight neonates (0.194 ± 0.115 versus 0.146 ± 0.141), but the difference was non-significant ($p = 0.069$). In each NICU patient group, the P_{ET}CO₂ was significantly lower than P_aCO₂, and as a consequence the P_{g-ET}CO₂ gap was significantly higher than the P_{g-a}CO₂ gap. In the cases of P_gCO₂ and both gaps, there was a significant difference between groups 1 and 2.

Result V

- Study 1. We obtained nearly identical P_gCO₂ values in groups I and II (mean difference 0.85 mmHg, $p = 0.45$), but the corresponding result in group III of acute patients differed significantly from those for the elective surgery cases (mean differences 7.8 mmHg and 8.66 mmHg, $p < 0.001$ and $p < 0.001$, respectively). When groups I and II were combined, their P_gCO₂ level differed significantly from that for group III (mean difference 8.81, $p < 0.001$).
- Study 2. P_gCO₂ was significantly higher in group 2 of severely ill NICU patients than in group 1, consisting of children in a better health state ($p < 0.05$).

Result VI

- Study 1. In the course of the study simultaneous arterialized capillary PCO₂ sampling could be performed in only 6 of the total of 25 cases. The differences between the P_{g-a}CO₂ values of the investigated groups could not be evaluated because of the low number of data.

Study 2. $P_{g-a}CO_2$ was significantly higher in group 2 (NICU patients in a more severe condition) than in group 1 (NICU patients with a better disease status) ($p < 0.05$)

Result VII

Study 1. Although $P_{ET}CO_2$ was higher in group III, $P_{g-ET}CO_2$ was still greater in the group of acute patients than in groups I and II. This difference proved to be significant ($p < 0.001$).

As the data for the two elective surgery groups did not differ significantly, Bland - Altman analysis was performed on the combined data for groups I and II, while the acute surgery cases were analysed separately. The comparison of the bias values between the elective surgical groups and the acute surgical group (i.e. the $P_{g-ET}CO_2$) revealed a significant difference ($p < 0.001$). Significant correlations were found between P_gCO_2 and $P_{ET}CO_2$ in each group (group I: $r = 0.59$, $p < 0.001$; group II: $r = 0.71$, $p < 0.001$; group III: $r = 0.39$, $p < 0.029$).

Study 2. In each NICU patient group, $P_{ET}CO_2$ was significantly lower than P_aCO_2 , and as a consequence, the $P_{g-ET}CO_2$ gap was significantly higher than the $P_{g-a}CO_2$ gap. P_gCO_2 and the $P_{g-ET}CO_2$ gaps were significantly higher in group 2 ($p < 0.01$).

Result VIII

Study 1. Since the $P_{g-a}CO_2$ gap could not be calculated as a result of the inappropriate number of arterialized capillary blood samplings, the correlations between the $P_{g-a}CO_2$ gap and $P_{g-ET}CO_2$ gap for the various groups could not be established.

Study 2. There was a significant correlation ($p < 0.001$) between the $P_{g-a}CO_2$ gap and the $P_{g-ET}CO_2$ gap ($r = 0.635$). During the examination of the relation of the two PCO_2 gaps, Bland - Altman analysis revealed an acceptable correspondence between the two methods (7.78 ± 6.34 mmHg, bias and precision).

Result IX

Study 1. The $P_{g-ET}CO_2$ gap in group I of elective surgical patients younger than 2 years was 6.12 ± 3.9 , and in group II, the elective surgical cases older than 2 years, was 5.37 ± 2.48 . The $P_{g-ET}CO_2$ gap was significantly higher (12.03 ± 5.87) in group III of acute surgical patients.

Study 2. The $P_{g-ET}CO_2$ gap for group 2, NICU patients with a worse health status, significantly exceeded that for group 1, NICU patients in a better condition (8.71 ± 10.89 and 2.53 ± 6.78 , respectively).

CONCLUSIONS (in the sequence of the main questions studied)

Conclusion I

Boda's novel gastric tonometric probe is a useful tool in the care of the smallest patients. It can reform gastric tonometric monitoring, and enhances the safety of paediatric and neonatal care under a broad range of circumstances. For these reasons, introduction of the device in everyday paediatric and neonatal monitoring practice is strongly recommended.

Conclusion II

Changes in end-tidal CO_2 levels did not seem to be dependent on age or the severity of the condition in our ventilated patients. In spite of the individually set ventilatory strategy, an elevation in $P_{ET}CO_2$ was found only in the acute surgical group of patients. The phenomenon could be explained only by external physical effects on the patients. Nonetheless, all ventilated patients should be monitored by continuous capnometry, and particularly those who are most susceptible to undergo rapid changes in their condition, or who are exposed to external stimuli. $P_{ET}CO_2$ monitoring indicates the effectiveness of ventilation, providing prompt warning sign of abrupt changes in the condition of the patient and furnishing the opportunity for other monitoring techniques, leading to more specific information on the patients' condition.

Conclusion III

In each group of examined NICU patients, $P_{ET}CO_2$ proved to be lower than P_aCO_2 , though P_aCO_2 and $P_{ET}CO_2$ correlated significantly in the examined ventilated NICU patients. With the exception of certain circumstances, there is a good correlation between the concomitant P_aCO_2 and $P_{ET}CO_2$ values in paediatric patients. In these cases, $P_{ET}CO_2$ monitoring is a pain-free, blood-sparing and non-invasive way to estimate P_aCO_2 . However, blood gas sampling can not be omitted. Rapid and excessive changes or an irregular tendency of $P_{ET}CO_2$ are indications of the need for P_aCO_2 control.

Conclusion IV

Higher dead-space was calculated in the group of NICU patients in a more severe condition, and a non-significantly increased dead-space was found in the low birth weight neonates. Higher dead-space ventilation due to physiological developmental reasons or diseases leads to a greater difference between P_aCO_2 and $P_{ET}CO_2$, consequently giving rise to a divergence between the $P_{g-a}CO_2$ and $P_{g-ET}CO_2$ gaps.

Conclusion V

Significantly higher P_gCO_2 values were obtained in the acute surgical patients in the first study; similarly, higher P_gCO_2 results were found in group 2 of severely ill NICU patients. An elevation in P_gCO_2 may be a warning sign of a severe condition of paediatric patients or it may suggest an imminent worsening of their health status. In order to acquire more accurate information concerning the condition of the patient, evaluation of either the $P_{g-a}CO_2$ gap or the $P_{g-ET}CO_2$ gap is required.

Conclusion VI

The differences between the P_gCO_2 and P_aCO_2 values of the different groups could be evaluated only in study 2. In terms of the $P_{g-a}CO_2$ gap, there was a significant increase in group 2, comprising NICU patients in a more severe condition, as compared with the patients in better health. This provides support for the finding that widening of the $P_{g-a}CO_2$ gap is a good indicator of the severity of the splanchnic impairment and hence the worsening of the disease.

Conclusion VII

In study 1, the difference between $P_{ET}CO_2$ and P_gCO_2 was significantly greater in the group of acute patients, and in study 2 the $P_{g-ET}CO_2$ gap was significantly higher in group 2 of severely ill patients. We found that monitoring of the $P_{g-ET}CO_2$ gap, similarly to monitoring of the $P_{g-a}CO_2$ gap, provides a useful and sensitive indication of a splanchnic impairment and hence the worsening of the patient's condition. This method is more convenient, and causes no pain and blood loss as compared with monitoring of the $P_{g-a}CO_2$ gap.

Conclusion VIII

The potential correlation between the $P_{g-a}CO_2$ and $P_{g-ET}CO_2$ gaps could not be investigated in study 1. In study 2, we found a significant correlation between the $P_{g-a}CO_2$ gap and the $P_{g-ET}CO_2$ gap, and relation analysis of the data revealed an acceptable correspondence between the two methods. This result suggests that monitoring of the $P_{g-ET}CO_2$ gap can be an effective alternative to monitoring of the $P_{g-a}CO_2$ gap in neonatal patients.

Conclusion IX

The $P_{g-ET}CO_2$ gap results clearly indicates a significant increase in the acute surgical group in study 1, and in study 2 it also proved to be significantly higher in the group of severely ill patients. Our findings tend to support the assumption that the $P_{g-ET}CO_2$ gap may reflect the severity of the disease.

MAJOR FINDINGS OF THE THESIS

- I.* The clinical utility of Boda balloonless gastric tonometric probes under paediatric intraoperative circumstances was investigated for the first time in our study. It proved to be reliably and easily applicable in patients of different ages and with various surgical diseases, and the measurements provided useful information relating to the severity of the disease.
- II.* Gastric tonometric investigation of the $P_{g-ET}CO_2$ gap is also a well-applicable method in the course of paediatric surgical interventions and is informative as to the severity of the disease.
- III.* This was probably the first investigation of the clinical value of the $P_{g-ET}CO_2$ gap as compared with the $P_{g-a}CO_2$ gap in low body weight prematures and neonates. Measurements of the $P_{g-ET}CO_2$ gap with its advantages can be a good alternative to the $P_{g-a}CO_2$ gap investigations in this population of patients, but it can not completely eliminate the need for occasional blood gas samplings.

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