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Integration of inspiratory and expiratory intra-abdominal pressure: a novel concept looking at mean intra-abdominal pressure

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Abstract

Background: The intra-abdominal pressure (IAP) is an important clinical parameter that can significantly change during respiration. Currently, IAP is recorded at end-expiration (IAP_{ee}), while continuous IAP changes during respiration (Δ IAP) are ignored. Herein, a novel concept of considering continuous IAP changes during respiration is presented.

Methods: Based on the geometric mean of the IAP waveform (MIAP), a mathematical model was developed for calculating respiratory-integrated MIAP (i.e. $MIAP_{ri} = IAP_{ee} + i \cdot \Delta IAP$), where 'i' is the decimal fraction of the inspiratory time, and where Δ IAP can be calculated as the difference between the IAP at end-inspiration (IAP_{ei}) minus IAP_{ee}. The effect of various parameters on IAP_{ee} and MIAP_{ri} was evaluated with a mathematical model and validated afterwards in six mechanically ventilated patients. The MIAP of the patients was also calculated using a CiMON monitor (Pulsion Medical Systems, Munich, Germany). Several other parameters were recorded and used for comparison.

Results: The human study confirmed the mathematical modelling, showing that MIAP_{ri} correlates well with MIAP ($R^2 = 0.99$); MIAP_{ri} was significantly higher than IAP_{ee} under all conditions that were used to examine the effects of changes in IAP_{ee}, the inspiratory/expiratory (I:E) ratio, and Δ IAP ($P < 0.001$). Univariate Pearson regression analysis showed significant correlations between MIAP_{ri} and IAP_{ei} ($R = 0.99$), IAP_{ee} ($R = 0.99$), and Δ IAP ($R = 0.78$) ($P < 0.001$); multivariate regression analysis confirmed that IAP_{ee} (mainly affected by the level of positive end-expiratory pressure, PEEP), Δ IAP, and the I:E ratio are independent variables ($P < 0.001$) determining MIAP. According to the results of a regression analysis, MIAP can also be calculated as

$$MIAP = -0.3 + IAP_{ee} + 0.4 \cdot \Delta IAP + 0.5 \cdot \frac{I}{E}.$$

Conclusions: We believe that the novel concept of MIAP is a better representation of IAP (especially in mechanically ventilated patients) because MIAP takes into account the IAP changes during respiration. The MIAP can be estimated by the MIAP_{ri} equation. Since MIAP_{ri} is almost always greater than the classic IAP, this may have implications on end-organ function during intra-abdominal hypertension. Further clinical studies are necessary to evaluate the physiological effects of MIAP.

Introduction

The intra-abdominal pressure (IAP) is an important clinical parameter with major prognostic impact [1,2]. An unrecognised pathological increase in IAP eventually leads to intra-abdominal hypertension (IAH) and

abdominal compartment syndrome (ACS) [3,4], which result in significant morbidity and mortality [5]. Thus, recognition and reliable measurement of IAP are the first important steps for prevention and management of IAH and ACS in critically ill patients [6].

Assuming no respiratory movement, the IAP would be relatively constant and primarily determined by body posture and anthropomorphy (e.g. body mass index) [3,7].

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The IAP may be affected by conditions influencing intra-abdominal volume and abdominal compliance (C_{ab}) [3,8,9]. Further, the complex interaction between intra-abdominal volume and C_{ab} during respiration (Figure 1) may significantly [10] and frequently (12 to 40 changes per minute) change the IAP (Figure 2), with more intense effects during positive-pressure mechanical ventilation or the presence of positive end-expiratory pressure (PEEP) [10-12].

According to the current consensus definitions of the World Society of the Abdominal Compartment Syndrome (WSACS), the IAP should be measured at end-expiration (IAP_{ee}) [13], referred to as the 'classic IAP' throughout the text. However, the IAP_{ee} is only a single component of an ever-changing trend and thus does not incorporate a considerable portion of this IAP trend (Figure 2). The objectives of this study were to develop and validate a novel IAP measurement concept to consider IAP changes during respiration and to identify independent variables influencing IAP within this novel concept.

Methods

Part A: mathematical model

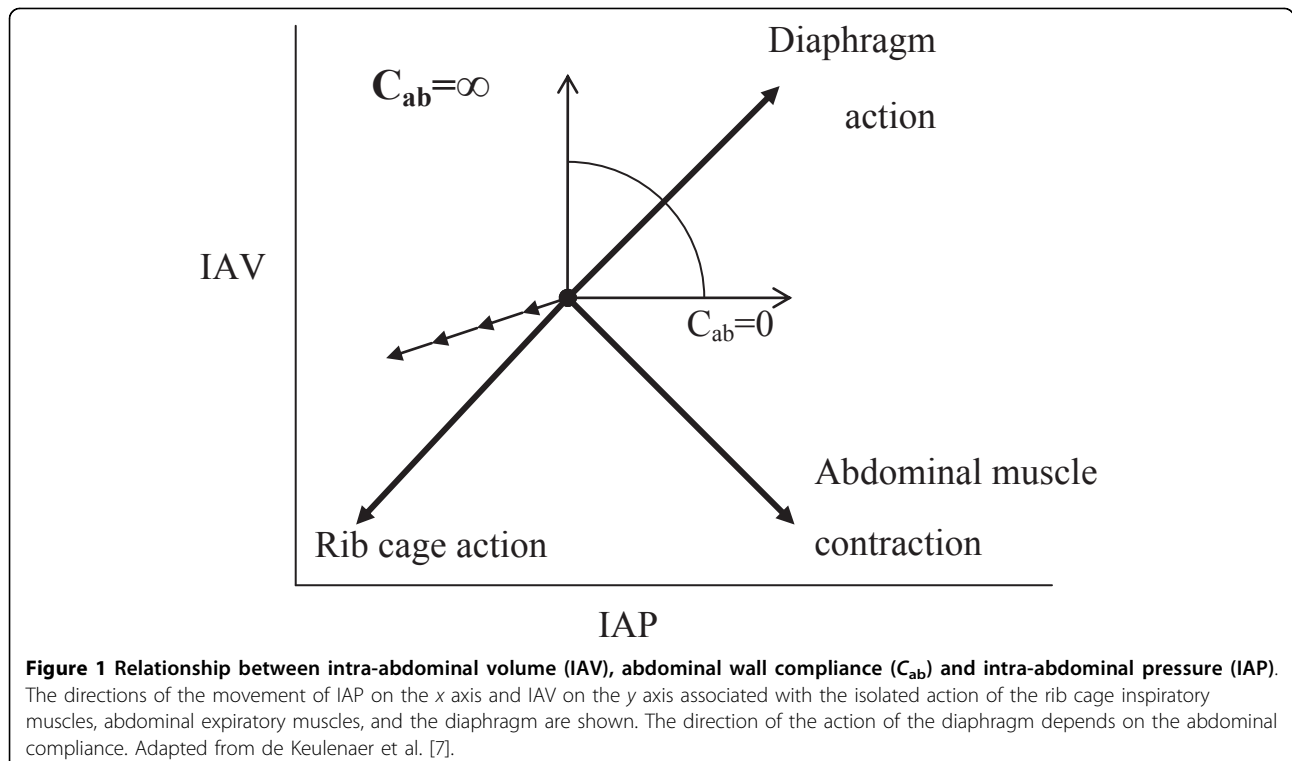
A set of numerous IAP values occurs for a patient during a single respiratory cycle. The central tendency of a set of values can be calculated by the mathematical function of the 'mean'. In determining the mean IAP, the arithmetic mean for IAP_{ee} and the end-inspiratory IAP (IAP_{ei}) was

described previously [14], calculated by dividing the sum of the values by the number of values. However, employing the arithmetic mean for the IAP waveform is mathematically incorrect. Instead, the mean of a waveform can be calculated by the 'geometric mean' function. The geometric mean is calculated by dividing the area under the waveform in a definite interval (i.e. the definite integral of the waveform) by the value of the definite interval [15]. Therefore, the mean IAP (MIAP) for a sample IAP waveform between the times (T_0) and (T) in Figure 2 can be calculated as follows:

$$MIAP_{ri} = \left(\frac{1}{T - T_0} \right) \cdot \int_{T_0}^T IAP(t) dt, \quad (1)$$

where ' $MIAP_{ri}$ ' is the respiratory-integrated MIAP, ' $T - T_0$ ' is the time interval for a full respiratory cycle, and ' $IAP(t) dt$ ' is the IAP at each time point (t). The result would be a time-weighted mean for the IAP waveform. This is closely analogous with the critically important cardiovascular concept of mean arterial blood pressure [16-18], which is the geometric mean of the arterial blood pressure waveform [19,20]. Equation 1 may be simplified as follows (see the addendum [21]):

$$MIAP_{ri} = IAP_{ee} + i \cdot \Delta IAP, \quad (2)$$



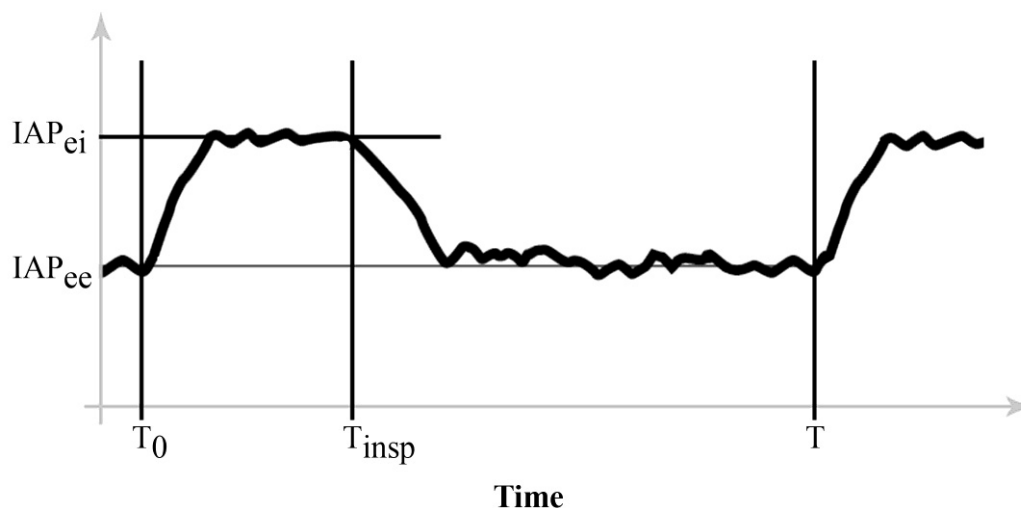


Figure 2 Effect of respiration on intra-abdominal pressure (IAP). T_0 , start of inspiration; T_{insp} , inspiratory time; T , total respiration time; IAP_{ee} , end-expiratory IAP; IAP_{ei} , end-inspiratory IAP.

where ' i ' is the decimal fraction of the inspiratory time in a respiratory cycle and can be calculated from the inspiratory/expiratory ($I:E$) ratio ($i = I / (I + E)$; $0 < i < 1$) and $\Delta IAP = IAP_{ei} - IAP_{ee}$. Since IAP_{ee} , i , and ΔIAP can be assumed to be independent, a computerised iteration can be used for a set of values for each parameter to determine their effect on $MIAP_{ri}$ and to compare the $MIAP_{ri}$ with the classic IAP.

The effects of IAP_{ee} on $MIAP_{ri}$ and the classic IAP were examined through a gradual increase of IAP_{ee} from 12 to 25 mmHg, with steps of 1 mmHg (Figure 3). For each IAP_{ee} , a range of possible $MIAP_{ri}$ values was calculated according to Equation 2 with an $I:E$ ratio of 4:1 and an ΔIAP of 8.16 mmHg for the maximum $MIAP_{ri}$, and an $I:E$ ratio of 1:4 and an ΔIAP of 1 mmHg for the minimum $MIAP_{ri}$. Because previous studies have shown a correlation between ΔIAP and IAP_{ee} , the ΔIAP was increased 10% for each 1 mmHg increase in the IAP_{ee} .

The effects of the $I:E$ ratio on $MIAP_{ri}$ and the classic IAP were examined by a gradual increase in the $I:E$ ratio from 1:4 to 4:1 with steps of 0.5 (Figure 4). The amount of IAP_{ee} was held constant (19 mmHg). For each $I:E$ ratio, a range of possible $MIAP_{ri}$ values was calculated with an ΔIAP of 7 mmHg for the maximum $MIAP_{ri}$ and an ΔIAP of 2 mmHg for the minimum $MIAP_{ri}$.

The effects of ΔIAP on $MIAP_{ri}$ and the classic IAP were examined by a gradual increase in ΔIAP from 1 to 5 mmHg, with steps of 0.5 mmHg (Figure 5). The amount of IAP_{ee} was held constant (19 mmHg). For each ΔIAP , a range of possible $MIAP_{ri}$ values was calculated with an $I:E$ ratio of 4:1 for the maximum $MIAP_{ri}$ and an $I:E$ ratio of 1:4 for the minimum $MIAP_{ri}$.

Each of the abovementioned data sets was assumed to be a unique case, and the values shown in Figures 3,4,5 should not be considered as a trend in changes that can be obtained in a single patient.

Part B: human pilot study

In six ICU patients that were mechanically ventilated with Evita XL ventilators (Draeger, Lubeck, Germany), the mean IAP was automatically calculated as the geometrical mean ($MIAP$) via a balloon-tipped nasogastric tube connected to a CiMON monitor (Pulsion Medical Systems, Munich, Germany). The $MIAP_{ri}$ was also calculated according to Equation 2. Data were collected on respiratory settings, plateau and mean alveolar pressures (P_{plat} , P_{mean}), PEEP, and dynamic compliance (calculated as the tidal volume (TV) divided by ($P_{plat} - PEEP$)). The C_{ab} was calculated as TV divided by ΔIAP . The thoraco-abdominal index of transmission (TAI) was calculated as ΔP_{alv} ($= P_{plat} - PEEP$) divided by ΔIAP , in which P_{alv} is the alveolar pressure.

The effects of IAP_{ee} on $MIAP_{ri}$ were examined by a gradual increase in PEEP from 0 to 15 cmH₂O, with steps of 5 cmH₂O during a best-PEEP manoeuvre (20 measurements at each PEEP level in five patients, resulting in 80 measurements). The effects of ΔIAP on $MIAP_{ri}$ were examined by a gradual increase in TV from 250 to 1,000 ml, with steps of 250 ml during a low-flow pressure-volume loop (20 measurements at each TV level in five patients, resulting in 80 measurements). The effects of $I:E$ ratio on $MIAP_{ri}$ were examined by a gradual increase in the $I:E$ ratio from 1:2 to 2:1, with steps of 0.5 during a recruitment manoeuvre (9 measurements at each $I:E$ ratio in one patient, resulting in 45 measurements).

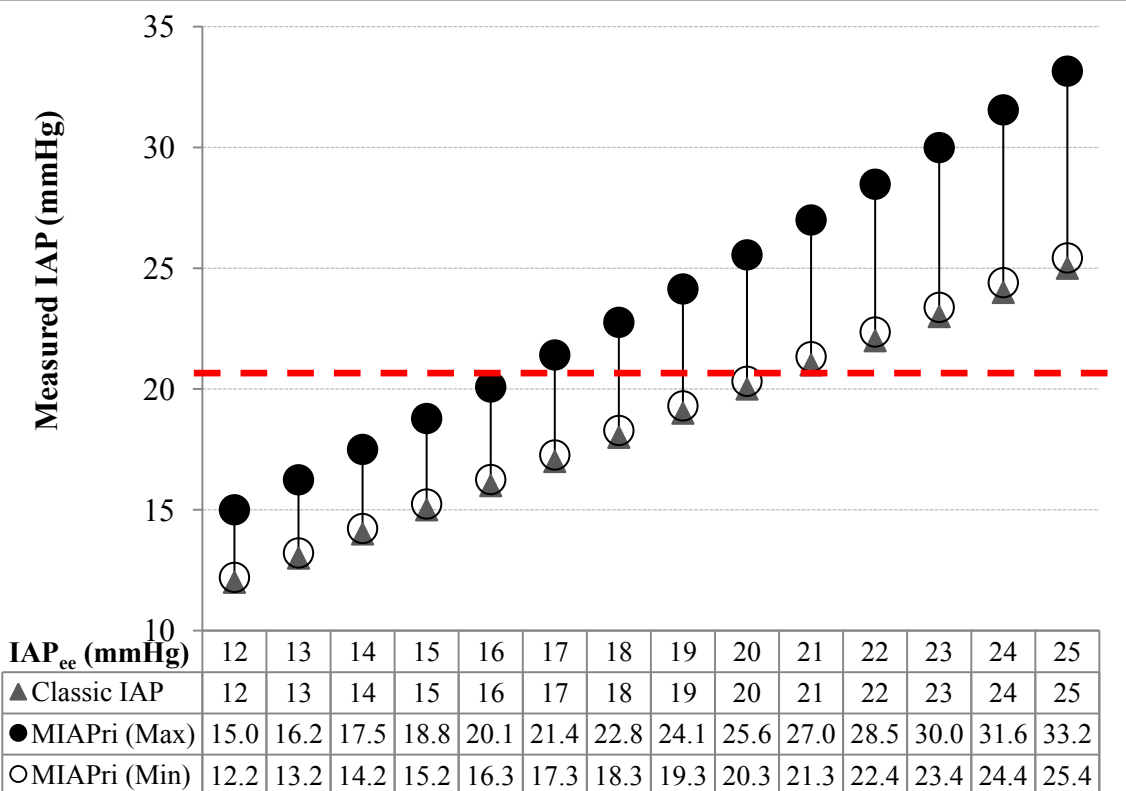


Figure 3 Mathematical modelling of IAP measurements for various end-expiratory IAP values (IAP_{ee}). The classic (IAP_{ee}) and novel ($MIAP_{ri}$) methods were used to measure the IAP. The dashed line represents the ACS threshold. The lines connecting the Max and Min $MIAP_{ri}$ values represent the range of possible $MIAP_{ri}$ values.

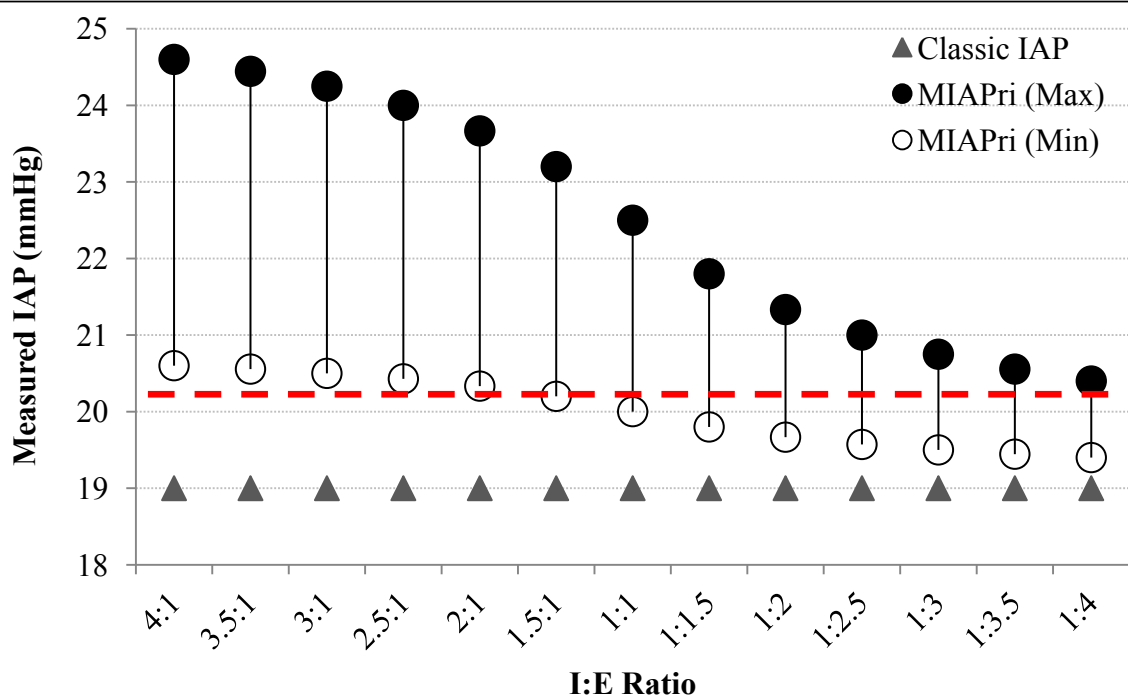


Figure 4 Mathematical modelling of IAP measurements for a constant 19 mmHg end-expiratory IAP (IAP_{ee}) and various $I:E$ ratios. The $MIAP_{ri}$ values were calculated for various $I:E$ ratios. The classic (IAP_{ee}) and novel ($MIAP_{ri}$) methods were compared. For each $I:E$ ratio, a range of possible $MIAP_{ri}$ values was calculated according to various ΔIAP values. The dashed line represents the ACS threshold.

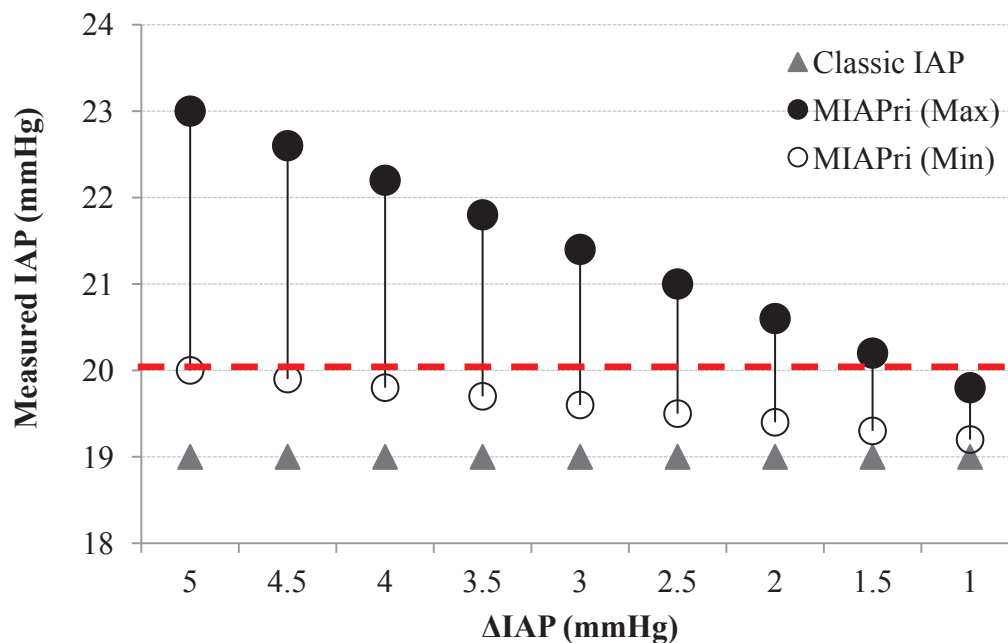


Figure 5 Mathematical modelling of IAP measurement for a constant 19 mmHg end-expiratory IAP (IAP_{ee}) and various ΔIAP . The classic (IAP_{ee}) and novel ($MIAP_{ri}$) methods were used to measure the IAP. The $MIAP_{ri}$ values were calculated for each ΔIAP . A range of possible $MIAP_{ri}$ values for each ΔIAP was calculated according to various $I:E$ ratios. The dashed line represents the ACS threshold.

Statistical analysis was performed using SPSS software. Pearson correlation analysis and Bland and Altman analysis were performed. For comparisons between $MIAP_{ri}$ and IAP_{ee} at different levels of IAP_{ee} (PEEP), TV, and $I:E$ ratio, a two-tailed paired Student's t -test was performed. Data are expressed as the mean with the standard deviation (SD), unless specified otherwise. A P value below 0.05 was considered statistically significant. The local EC and IRB approved the study, and informed consent was obtained from next of kin.

Results

Part A: mathematical modelling

According to Equation 2, three major independent parameters determine the $MIAP_{ri}$: IAP_{ee} , $I:E$ ratio, and ΔIAP . Therefore, for each IAP_{ee} , the $MIAP_{ri}$ depends on two other factors (Figure 3). For IAP_{ee} values between 16 and 20 mmHg, the classic IAP remained below the ACS threshold (dashed line in Figure 3); however, the $MIAP_{ri}$ was able to exceed the ACS threshold. Furthermore, as seen in Figures 4 and 5, the classic IAP was continuously below the ACS threshold, but different ranges of probable $MIAP_{ri}$ values were above the ACS threshold. By changing the $I:E$ ratio, the $MIAP_{ri}$ values changed with dissimilar intensities (e.g. when the $I:E$ ratio decreased from 4:1 to 3.5:1, the intensity of changes in the $MIAP_{ri}$ values was less than that when the $I:E$ ratio decreased from 1.5:1 to 1:1;

Figure 4). Furthermore, for a constant IAP_{ee} , higher values for either the $I:E$ ratio or ΔIAP were found to be capable of causing a wider range of possible $MIAP_{ri}$ values (Figures 4 and 5). Mathematically, for all instances in which the ΔIAP was greater than 0 mmHg, the $MIAP_{ri}$ was larger than the classic IAP (see the addendum) [21].

Part B: human pilot study

Six mechanically ventilated patients (three severely burned patients and three surgical ICU patients) were studied. The male-to-female ratio was 2:1. Table 1 summarises the baseline patient demographics.

Regression analysis and Bland and Altman analysis

In total, 205 paired $MIAP$ and $MIAP_{ri}$ measurements were performed with an identical statistical mean of 12.2 ± 3.8 mmHg. Figure 6A shows an excellent correlation between the $MIAP$ and $MIAP_{ri}$ ($R^2 = 0.99$, $P < 0.001$). Analysis according to Bland and Altman showed a bias and precision of 0 and 0.2 mmHg, respectively, with small limits of agreement ranging from -0.4 to 0.5 mmHg (Figure 6B). The percentage error was 3.5%.

Effect of IAP_{ee} , $I:E$ ratio, and ΔIAP on $MIAP_{ri}$

Gradually increasing PEEP from 0 to 15 cmH₂O resulted in an increase in $MIAP_{ri}$ from 11.7 ± 4.1 to 13.1 ± 4.2 mmHg ($P < 0.001$). Meanwhile, IAP_{ee} increased from 9.9 ± 3.4 to 11.9 ± 3.7 mmHg ($P < 0.001$). Moreover, a gradual increase in the $I:E$ ratio from 0.5 (1:2) to 2 (2:1)

Table 1 Patient characteristics at baseline

Parameter	Mean ± SD
Age	59.5 ± 14.4
SAPS-II	43.5 ± 11.6
APACHE-II	21.8 ± 8.6
SOFA	9.5 ± 4
BMI (kg/m ²)	28.6 ± 4.7
IAP _{ei} (mmHg)	15.3 ± 3.7
IAP _{ee} (mmHg)	11.1 ± 2.8
ΔIAP (mmHg)	4.3 ± 1.3
MIAP (mmHg)	12.9 ± 3
IBP (mmHg)	12 ± 3
TV (ml)	608 ± 117
TV (ml/kg)	7.2 ± 1.2
RR (/min)	17.7 ± 2.1
P _{plat} (cmH ₂ O)	28 ± 4.1
PEEP (cmH ₂ O)	9.2 ± 3.3

SAPS, simplified acute physiology score; APACHE, acute physiology and chronic health evaluation; SOFA, sequential organ failure assessment; BMI, body mass index; IAP_{ei}, end-inspiratory IAP; IAP_{ee}, end-expiratory IAP; MIAP, mean IAP; IBP, intra-bladder pressure; TV, tidal volume; RR, respiratory rate; P_{plat}, plateau airway pressure; PEEP, positive end-expiratory pressure.

caused an increase in MIAP_{ri} from 10.8 ± 2.6 to 12.9 ± 2.9 mmHg ($P < 0.001$), while IAP_{ee} increased from 9.7 ± 2.3 to 10.4 ± 2.5 mmHg ($P < 0.001$). In addition, gradually increasing TV from 250 to 1,000 ml led to an increase in ΔIAP from 2.1 ± 1.1 to 5.7 ± 2.3 ($P < 0.001$). This increase in ΔIAP resulted in an increase in MIAP_{ri} from 11.6 ± 4 to 13.1 ± 4.3 mmHg ($P < 0.001$), while IAP_{ee} increased from 10.7 ± 3.6 to 10.9 ± 3.5 mmHg ($P = \text{NS}$). The MIAP_{ri} was significantly higher than IAP_{ee} at each PEEP level, $I:E$ ratio, and TV (Figure 7A,B,C; $P < 0.001$).

The classic IAP of patients was below the IAH grade I threshold; however, the MIAP_{ri} significantly exceeded the threshold in several instances ($P < 0.001$; Figure 7).

Univariate analysis

Univariate Pearson regression analysis showed significant correlations between MIAP_{ri} and IAP_{ei} ($R = 0.99$), IAP_{ee} ($R = 0.99$), ΔIAP ($R = 0.78$), and C_{ab} ($R = -0.74$); between IAP_{ei} and IAP_{ee} ($R = 0.96$), ΔIAP ($R = 0.86$), and C_{ab} ($R = -0.73$); between IAP_{ee} and ΔIAP ($R = 0.7$) and C_{ab} ($R = -0.73$); between ΔIAP and ΔP_{alv} ($R = 0.79$) and C_{ab} ($R = -0.58$); and finally between TAI and C_{ab} ($R = -0.8$) ($P < 0.001$). Figure 8A,B,C shows some regression plots.

Multivariate regression analysis

Analyses showed that the IAP_{ee} (mainly affected by PEEP), ΔIAP, and $I:E$ ratio were independent variables defining the MIAP (Table 2). According to the regression analysis in our sample population, the MIAP can also be calculated from the following simplified formula ($P < 0.001$), in which 'I' and 'E' are elements of the $I:E$ ratio:

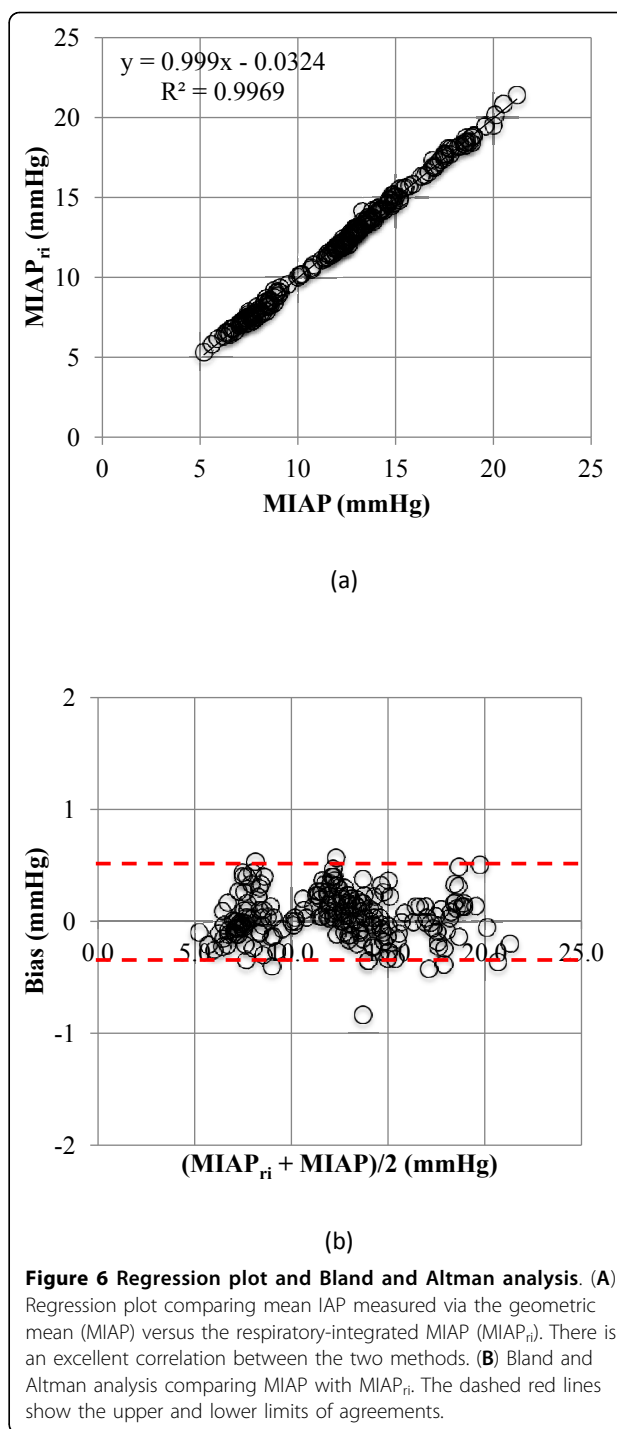
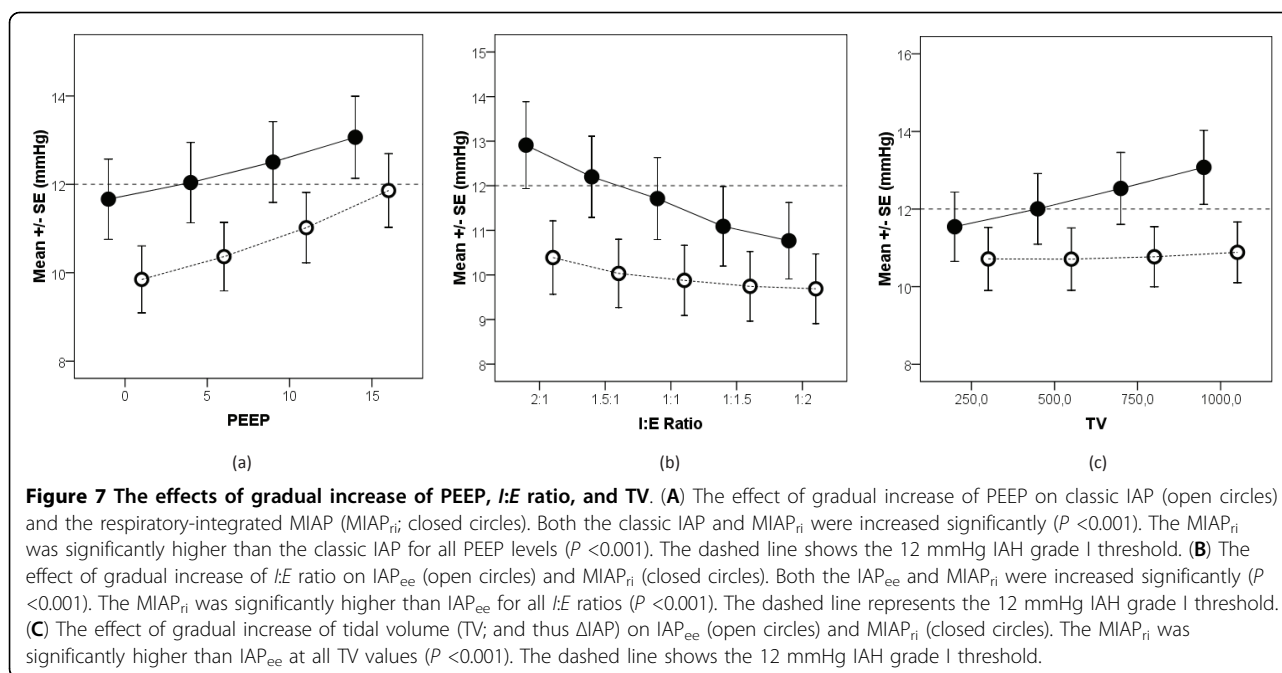


Figure 6 Regression plot and Bland and Altman analysis. (A) Regression plot comparing mean IAP measured via the geometric mean (MIAP) versus the respiratory-integrated MIAP (MIAP_{ri}). There is an excellent correlation between the two methods. (B) Bland and Altman analysis comparing MIAP with MIAP_{ri}. The dashed red lines show the upper and lower limits of agreements.

$$MIAP_{ri} = -0.3 + IAP_{ee} + 0.4 \cdot \Delta IAP + 0.5 \cdot \frac{I}{E}$$

Discussion

A novel concept of IAP measurement based on the geometric mean of the IAP waveform was presented. The



independent parameters determining the IAP in this concept were defined. The human pilot study validated the mathematical modelling with an excellent correlation. A significant difference was observed between the classic IAP and the MIAP_{ri} in our clinical study.

The human study confirmed that MIAP_{ri} is as accurate as an automated geometric MIAP calculation by a CiMON monitor. More importantly, the higher the MIAP or IAP_{ee}, the higher the Δ IAP since Δ IAP acts as an indirect marker of C_{ab} . The Δ IAP is correlated with ΔP_{alv} or is thus inversely correlated with dynamic compliance. As well, the higher the C_{ab} , the lower the TAI. The human study confirmed the predictions of the mathematical modelling in which IAP_{ee} (affected by different PEEP settings), Δ IAP, and *I:E* ratio were recognised as the major independent determinants of MIAP_{ri}. We also showed that in patients with IAH and under mechanical ventilation, the IAP may be influenced by ventilator settings.

The critical difference between the MIAP_{ri} and the classic IAP near the ACS threshold in our mathematical modelling, as well as the significantly higher MIAP_{ri} than the IAP_{ee} around the IAH threshold in our human study, calls for future studies. The dissimilar intensity in MIAP_{ri} changes under changes in the *I:E* ratio in Figure 4 may implicate the existence of critical points in the *I:E* ratio, wherein changing this ratio may cause a more intense change in the MIAP_{ri}. Furthermore, since MIAP_{ri} seems to be almost always larger than the classic IAP, relying only on the classic IAP may place some patients at risk of

silent IAH or ACS. Although the aim of the current study was not to address these implications clinically, these findings indicate that further investigations should be performed on respiratory manoeuvres to manage IAH in mechanically ventilated patients (e.g. decreasing the *I:E* ratio and/or the Δ IAP, or maintaining the *I:E* ratio in a predefined range).

A limitation of our study was the lack of data to evaluate the physiological difference between the MIAP_{ri} and the classic IAP. However, this study only aimed to prove the concept and to set the stage for further studies. Therefore, we believe that the lack of physiological data does not limit our findings. Nonetheless, further studies on the clinical effects of this concept are necessary before it can be introduced in clinical practice.

Conclusions

A novel concept MIAP_{ri} was presented to consider the IAP changes during respiration and was based on the geometric mean (MIAP) of the IAP waveform. An excellent correlation was observed between the results of the mathematical modelling and those obtained in real patients. Substantial differences were observed between the two IAP methods (the classic IAP measured at end expiration and the novel MIAP). Based on our findings, we believe that the novel concept of MIAP_{ri} may be a better representation for the pressure concealed within the abdominal cavity. Further clinical studies are necessary to reveal the physiological effects of this novel concept.

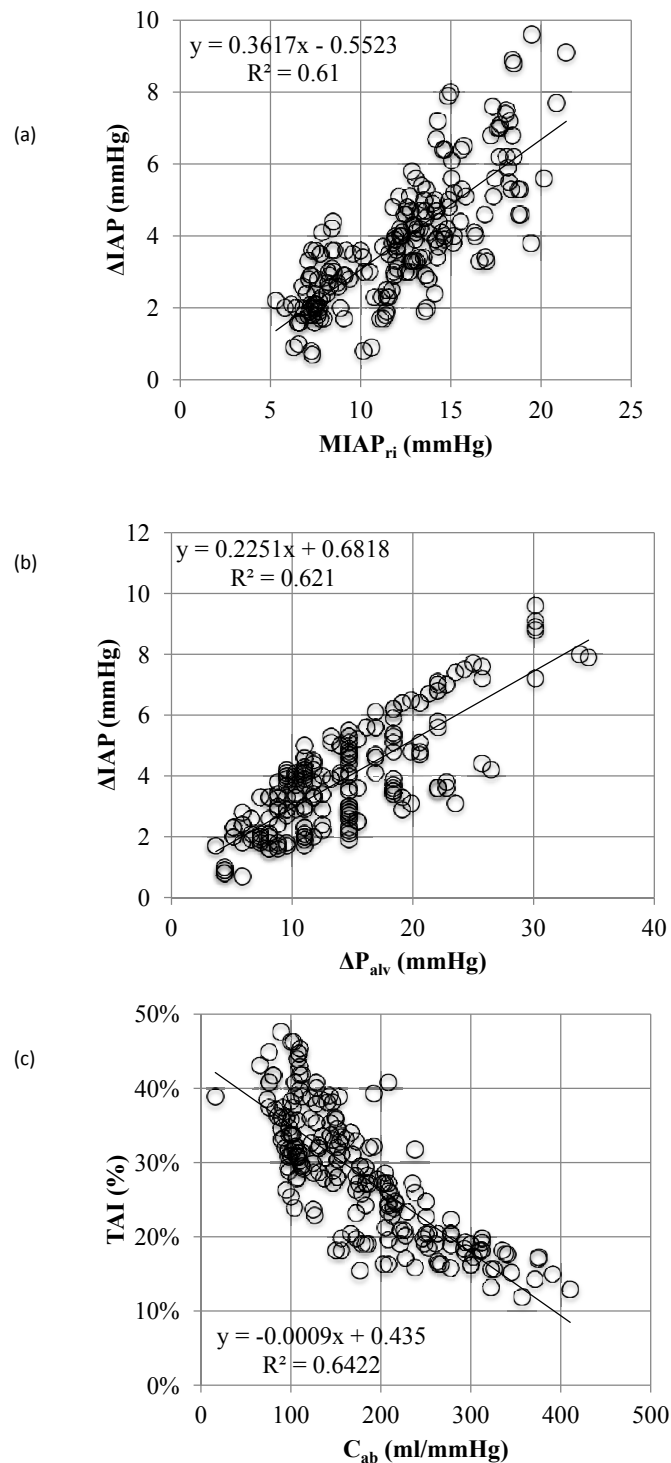


Figure 8 Linear regression plots. (A) Linear regression plot showing the respiratory-integrated mean intra-abdominal pressure ($MIAP_{ri}$) in relation to ΔIAP ($= IAP_{ei} - IAP_{ee}$, where IAP_{ei} is the end-inspiratory IAP and IAP_{ee} is the end-expiratory IAP). (B) Linear regression plot showing the respiratory changes of intra-abdominal pressure (ΔIAP) in relation to ΔP_{alv} ($= P_{plat} - PEEP$, where P_{alv} is the alveolar pressure, P_{plat} is the plateau alveolar pressure, and PEEP is the positive end-expiratory pressure). (C) Linear regression plot showing the relation between the thoraco-abdominal index of transmission (i.e. $TAI = \Delta P_{alv} / \Delta IAP$) and the abdominal wall compliance (i.e. $C_{ab} = TV / \Delta IAP$).

Table 2 Multiple regression analysis looking for independent variables influencing MIAP

Model	Unstandardized coefficients		Standardized coefficients			95.0% Confidence interval for B	
	B	Standard error	Beta	t	Significance	Lower bound	Upper bound
(Constant)	-0.27	0.20		-1.4	0.164	-0.66	0.11
PEEP	0.01	0.00	0.01	2.1	0.040	0.00	0.01
ΔP_{alv}	0.01	0.01	0.02	1.5	0.133	0.00	0.02
I:E ratio	0.48	0.04	0.04	12.3	0.000	0.40	0.56
IAP _{ee}	0.99	0.01	0.86	144.6	0.000	0.98	10.01
Δ IAP	0.35	0.03	0.16	11.3	0.000	0.29	0.41
TAI	0.00	0.00	0.01	1.1	0.259	0.00	0.01
C _{ab}	0.00	0.00	-0.01	-1.6	0.105	0.00	0.00

PEEP, positive end-expiratory pressure; P_{alv} , alveolar pressure; I:E ratio, inspiratory-to-expiratory ratio; IAP_{ee}, end-expiratory IAP; TAI, thoraco-abdominal index of transmission; C_{ab}, abdominal wall compliance.

Addendum

See additional file 1.

Additional material

Additional file 1: Mathematical model for calculation of mean intra-abdominal pressure, taking into account integration of inspiratory and expiratory intra-abdominal pressure.

Abbreviations

ACS: abdominal compartment syndrome; C_{ab}: abdominal compliance; IAH: intra-abdominal hypertension; IAP: intra-abdominal pressure; IAP_{ee}: end-expiratory IAP; IAP_{ei}: end-inspiratory IAP; MIAP: mean intra-abdominal pressure (geometrical mean); MIAP_{ri}: respiratory-integrated mean intra-abdominal pressure; P_{alv} : alveolar pressure; P_{mean} : mean airway pressure; P_{plat} : plateau airway pressure; PEEP: positive end-expiratory pressure; TAI: thoraco-abdominal index of transmission; TV: tidal volume; WSACS: World Society of the Abdominal Compartment Syndrome.

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Authors' contributions

SA and MLNGM planned the study and were responsible for the design, coordination, and drafting the manuscript. SA developed the mathematical model for MIAP calculation and performed the theoretical analyses. MLNGM performed the data collection and statistical analysis for the human pilot study. Both authors read and approved the final manuscript.

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SA is a veterinary surgeon (DVM, DVSc) and a medical research consultant in laboratory animal researches in the field of trauma, haemorrhage, critical care, and anaesthesia. MLNGM is a former president and treasurer of the World Society of the Abdominal Compartment Syndrome and is the ICU and High Care Burn Unit Director of the Department of Intensive Care in Ziekenhuis Netwerk Antwerpen Stuivenberg.

Competing interests

MLNGM is a member of the medical advisory board of Pulsion Medical Systems, Munich, Germany.

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