



## Biophysical Validation of Intra-Abdominal Pressure and Transurethral Method

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### Abstract

**Objective:** The increase in intra-abdominal pressure (IAP) is a well-documented phenomenon, directly associated with pathophysiological changes in all organic systems, increasing morbidity and mortality. The gold standard for its determination is the transurethral method (TM), which still today is surrounded by controversy. The purpose of the study is to, through physical principles, demonstrate IAP, validate TM and explain the variables that influence IAP.

**Materials and Methods:** Development of a biophysical formulation, based on mechanics of fluids, to explain IAP, TM and its variables. Validation of the principles formulated in a non-living animal model, where all components that generate the IAP were determined. Determination of: IAP by TM, intra-gastric and direct method; gastric, bladder and abdominal areas and volumes; weight of all abdominal structures.

**Results:** IAP values obtained by the several methods are within the limits described for the species with average values between 2.31 and 7.14 mmHg.

Determination of the areas and strength of all anatomical structures allowed the replacement of values in the biophysical formulation and calculation of IAP. The mathematically calculation of IAP confirms the theoretical definition of IAP.

This value when compared with the direct readings per sensor showed no statistical differences ( $P < 0.05$ ). IAP determination by direct method also showed no differences in the five body positions ( $P = 0.765$ ). Indirect methods revealed statistically significant differences from the direct method only in the Trendelenburg and reverse Trendelenburg. Breathing, muscle contraction, body position and water manometer position influence IAP measurement by indirect methods.

Using digital treatment of images and using pixels analysis algorithms, it is also possible to determine bladder and gastric surface area, in average  $6.17 \cdot 10^{-3} \pm 5.05 \cdot 10^3 \text{ m}^2$  and  $3.55 \cdot 10^{-2} \pm 1.65 \cdot 10^{-2} \text{ m}^2$  respectively.

**Conclusion:** This study improves the knowledge of the application of the direct and indirect methods to accesses IAP. The biophysical principles explain the formation of IAP and prove the accuracy of TM, explaining the variables which affect it.

**Keywords:** Biophysical formulation; Intra-abdominal pressure; Transurethral method

### Introduction

The intra-abdominal pressure (IAP) is a state of pressure in the abdominal cavity which is determined by body mass index, posture, wall's muscle activity and respiration. The IAP is directly influenced by a variety of factors, such as volume of the organs, bones, content of the abdominal area and degree of elasticity of the abdominal wall. Because they directly change volume or accumulate fluid or gas, these structures are likely to change the IAP in acute, sub-acute and chronic forms [1,2]. Abdominal cavity is bounded cranially by the diaphragm and caudally connected with the pelvic cavity. Dorsally, it is delimited by the lumbar vertebrae, muscles and lumbar part of the diaphragm. The side walls are formed by abdominal muscles, peritoneum, caudal ribs, iliac wings and its muscles. The ventral portion is bordered mainly by abdominal muscles and the peritoneum [3,4].

The IAP is an important clinical parameter with great impact on the patient's prognosis when exists abdominal hypertension [5]. The IAP value is also used to determine abdominal perfusion pressure (APP) which is an accurate predictor of visceral perfusion in patients. The calculation of the APP is performed by subtracting the value of IAP to the mean arterial pressure (MAP) [6–8]. APP and IAP are both clinical parameters used to classify the abdominal hypertension degree. The abdominal hypertension is a measure of high abdominal pressure, with multifactorial cause in patients in critical condition. This is a well-documented phenomenon, and it is directly associated with pathophysiological changes in all organic systems [9]. These changes, when continuously verified, cause the compartmentalization syndrome, leading to increased morbidity and mortality. Despite their low incidence, 0.9 to 12 %, the mortality rate is very high, 50-80%, depending on the studied population [2,10,11].

Several methods have been used in the past to determine IAP by direct and indirect methods [12]. Direct IAP measurement is used as a reference to indirect methods [13,14] and can be measured with a solid microtransducer placed in the abdominal cavity [15]. Due to the disadvantages of direct monitoring and of the invasive procedure itself, the indirect techniques have been the most used. Being the transurethral method (TM) the most applied and considered the gold standard for evaluation of abdominal hypertension [12,16–18]. However, the IAP measurement by TM continues to generate some controversy due to the large number of variables that can affect the measurement, questioning its reproducibility [12,19–23]. The indirect methods like TM and intra-gastric manometry (MI) already have been clinically validated in humans, dogs, cats and pigs [14,17,24–28].

Pressure is the action of one or more forces on a given area, by the action of liquids, gases or solids [29]. The branch of physics which involves the study of fluids, their pressures and forces applied to them is the mechanics of fluids [30,31]. With the TM being based solely on columns of fluid, validation, interpretation and scientific explanation must be based on physical principles of mechanics of fluids [32].

On the literature review undertaken, no other study uses the principles of physic to explain IAP, variables and TM. The aim of this study was to perform an overlap of principles, based on laws of fluids mechanics, which would explain the IAP formation, validate TM and explain the variables that influence it in clinical routine. All the variables of the formulation were determined in a non-living dog model in order to prove the veracity of the biophysical model. After determining the values of each variable in the biophysics formulation, the IAP was calculated and compared with its direct measurement.

## Materials and Methods

The methodology used in this study was chosen because of the difficulty of eradicating some of the variables that influence IAP and all the ethical issues linked to experimentation. Using an analytical approach the study was realized in a non-living dog model of the abdominal cavity. This model allowed the eradication of the described variables that influence IAP: abdominal and gastric contraction, micturition reflex and breathing [5,19,26,33–37].

The IAP measurement was performed on a population of twenty-nine dogs cadavers admitted for necropsy in the Pathology Department at the Faculty of Veterinary Medicine, Lusofona University, Portugal. The studied population comprises, 14 males and 15 females, with an average weight of  $12.04 \pm 5.67$  kilograms (kg) (Adam CPW plus 150, USA). All the animals used in the study were not purposely euthanized for it. IAP measurements were carried out before necropsy. All anatomical and morphometric organs measurements were carried out under the normal procedure for necropsy. Necropsy was realized by general technique with: external examination; body cavity opening and evaluation; gastrointestinal, abdominal viscera, tongue, thyroids, trachea, lung, heart, eye and brain removal with individual examination; all the findings were registered in an individual report [38].

The inclusion criteria consisted in the absence of abdominal disease that would affect the abdominal cavity and its organs, which was confirmed by necropsy. All dogs' cadavers that demonstrated disease affecting the abdominal cavity and its organs were excluded from the study. To avoid changes in tissue tension and elasticity, the study was performed immediately after cadaver's entry into the service of pathological anatomy. Only dogs dead within 24 hours were used and kept under correct refrigeration. Cadavers which showed marked tension and elasticity alterations were also eliminated from the study. The population of 29 dogs was selected after a rigorous and careful evaluation and application of the selection criteria.

IAP measurements were performed using three different methods: the direct method and two indirect methods, TM and IM. The measurements with the three methods were carried out in five different anatomical positions: lateral, ventral, dorsal, trendelenburg and reverse trendelenburg (45 degree angle).

## Direct IAP measurements

Direct IAP measurement was performed through an intra-peritoneal catheter, using a CODMAN (Codman, Johnson & Johnson) sensor. The sensor was initially connected to the transducer, and then calibrated to zero, having as reference the atmospheric pressure. Then, the sensor was inserted into the catheter, until its entrance into the abdominal cavity; a minute was allowed for the pressure to stabilize before the commencement of readings [15,32].

## Indirect IAP measurements

The IAP measurement by the TM was made by the closed technique [39]. The IAP was measured by means of a urinary catheter, connected by two systems of three-way stopcock to a drainage system of urine, a metric column and a system of saline solution. The bladder was emptied and a standard volume of sterile solution, 0.5 to 1 ml/kg of 0.9% saline solution (Ecoflac Isotonic solution 0,9%, Braun) was instilled into the bladder in order to obtain a physiological distension (excessive saline solution on the bladder may incorrectly raise the measurement of IAP [27,40,41]). The zero point of the metric scale of the column should be leveled to the level of the patient's pubic symphysis. After achieving a balance between the two columns of fluid, the IAP value was the meniscus of saline solution in the metric scale [40]. The technique for measuring IAP by IM is similar to that described for the TM, but it uses the stomach instead of the bladder. For this, a standard nasogastric tube was placed, positioned at stomach level. All existing fluid was removed using the tube and a standard amount of saline solution was inserted (50 ml per animal - the same amount which is used in humans). This solution amount was used as reference because there is not any literature reference to the quantity which should be used in dogs. The pressure was obtained after allowing the balance between the metric column of saline solution and the gastric fluid [12]. The measurements were performed consecutively in the various positions, by three consecutive times and all values were recorded in a database (Excel, Microsoft Office Home and Student 2010, USA). These values were obtained in centimeters of water and then converted to millimeters of mercury (mmHg) by multiplication of 0.736. At the end of the IAP measurements, animals were subjected to necropsy. During the necropsy, the position of all catheters was confirmed to validate the readings accuracy.

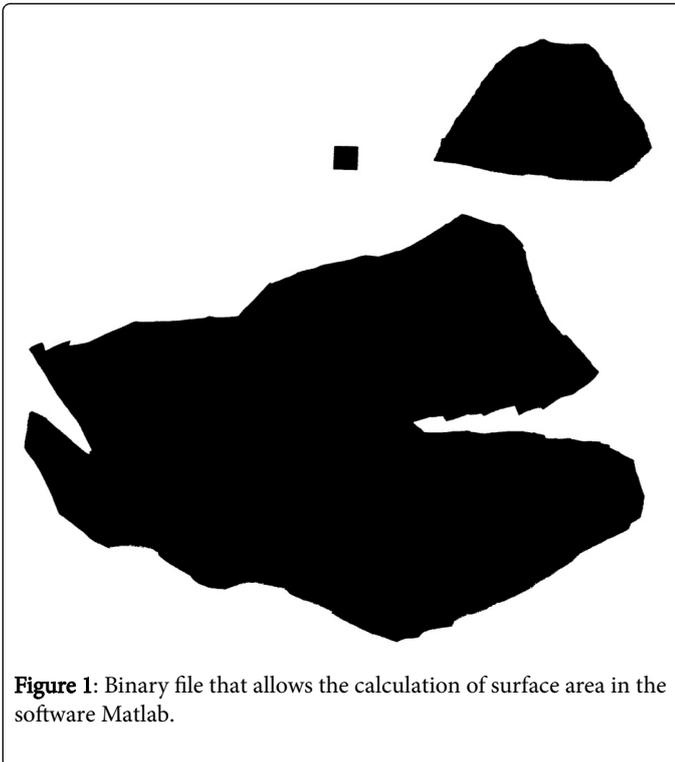
## Morphometric determinations

During the necropsy procedure all organic structures were weighed individually in order to obtain the values to insert in the biophysical formulation. All abdominal viscera were weighted, as well as the lateral wall of the abdomen (skin and muscles), the bladder, and stomach. The force was calculated according with the Newton's second law, which corresponds to the multiplication of mass by gravitational acceleration [42]. The organic volumes were established through the Archimedes principle [43].

## Stomach and bladder area

To determine bladder and stomach surface areas, a sagittal dieresis of cavitory organs was performed to obtain a flat surface. The organs were extended and placed in a white tray next to a black paper square with 1 centimeter wide; a digital photography was taken, covering the entire surface area of the organ and the scale. Through the digital treatment of images and using pixels, analysis algorithms, was possible to determine organs surface area [44]. This type of methodology is

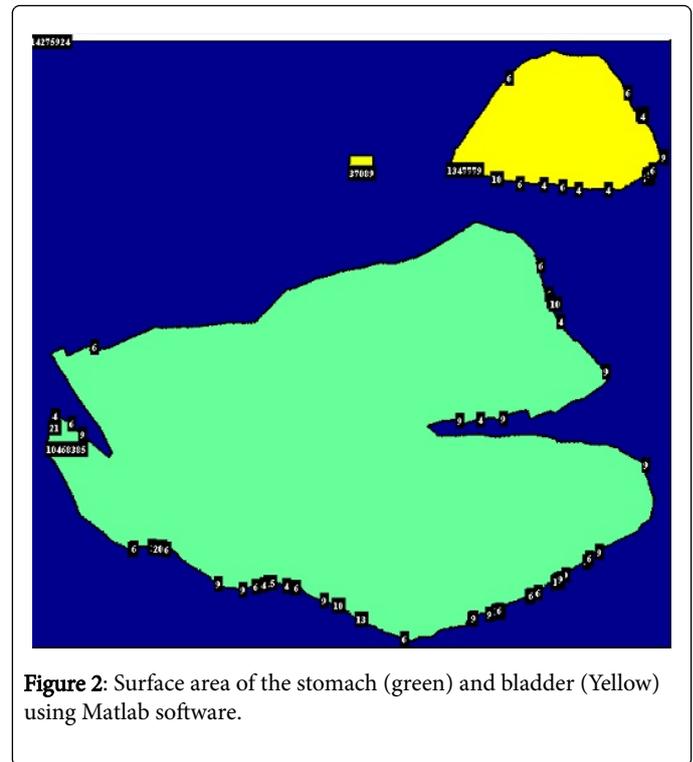
used for the measurement of skin lesions surface areas in chronic wounds [44]. The analysis of digital image and calculation of surface area was performed by using the program Matlab (R2015a, USA). Using the `imshow` function, it is possible to represent an image in a binary format (bitmap), with two colors only: black and white sorted by pixels (value 0: black color and value 1: white color) (Figure 1). Through the `regionprops` function, which measures and delimits regions of the image, and using Matlab functions to determine areas, it was possible to determine the area of the digital image (Figure 2).



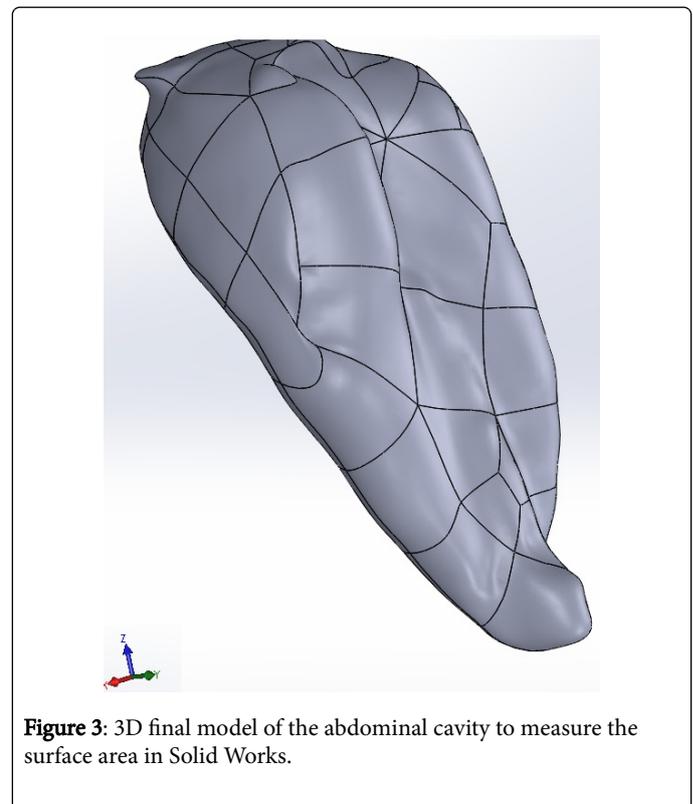
**Figure 1:** Binary file that allows the calculation of surface area in the software Matlab.

### Body surface area and abdominal cavity surface area

The body surface area (BSA) determination was calculated using the formula:  $BSA (m^2) = K \times \text{body weight (grams)}^{2/3} \times 10^{-4}$ , with the constant (K) for dogs being 10.1 [45,46]. In this study, for abdominal cavity surface area (ACSA) determination we resorted to tomographic exam (CT) of the abdominal cavity. Exams were performed using a General Electric CT HI Speed LX/I scanner (United Kingdom), and they show constant thickness of cut, between 1 and 3 millimeters. The exams were assessed regarding the presence of all anatomical limits. Processing the digital images of the CT using a software of medical imaging, Osirix® (Pixmeo Sarl, Swiss), through segmentation processes of the abdominal cavity we set up 3D models. Abdominal Cavity 3D modeling was performed using the Solid Works software (Dassault Systems, US). This type of program allows determining volume and surface area in just a few steps. With these 3D models it was possible to determine the volume and surface area (Figure 3) [47].



**Figure 2:** Surface area of the stomach (green) and bladder (Yellow) using Matlab software.



**Figure 3:** 3D final model of the abdominal cavity to measure the surface area in Solid Works.

### Mechanics of fluids

The TM uses a system of communicating vessels which allows communication between the bladder and a water column, metrically divided in centimeters of water [12]. The fluid contained in the bladder

is under the influence of the physical Pascal principle, which establishes that any change in pressure in a fluid in equilibrium is transmitted to all points of the liquid and to the walls of the container [12,30,31]. This means that, any change in pressure in the abdominal cavity is transmitted to the fluid contained in the bladder as well as to the system of vessels that establishes communication with the water column. Whenever a reading is performed, there is a point of balance in which the pressure of the fluid in the bladder is equal to the pressure in the water column. In this moment the principles of hydrostatic are verified, since the number of particles per volume unit is constant; there is no relative velocity of the particles of the fluid; and the forces of the fluid on the walls of the vessels that contain it are perpendicular [30,31]. Through hydrostatics principles, physical pressure definition, Newton's laws applications and trigonometry concepts, an overlap of principles was created, permitting to obtain IAP taking into account the various variables that affect it. To determinate the total pressure values was used the atmospheric pressure at the sea level, 101 325 Pa and the constant value of gravity acceleration of 9.80665 m/s<sup>2</sup> [30,31,42].

### Statistics

The data were analyzed using the SPSS program (Statistical Package for the Social Sciences, version 2010), which compared all variables. Analysis of variance (ANOVA) was used to identify significant differences between the mean values of the groups. The values were expressed as average ± standard deviation and in the statistical tests of mean comparisons, the differences were considered statistically significant when P<0.05. The correlation test of Pearson's was used to analyze the relations and the variables strength. The correlation degree between the variables was better if closer to one. To evaluate if the weight influences the IAP, the linear regression test was used, considering that the regression model predicted the variable if P<0.05.

### Results

#### Biophysical principles formulation

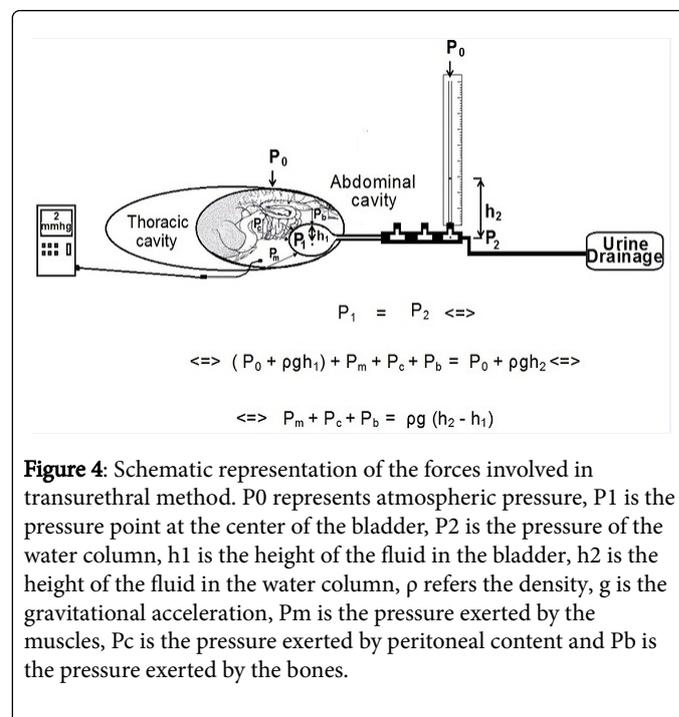
This section of results was obtained by deduction and it was based on the physics principles, mechanics of fluids and hydrostatic applications. The following formulas were written in an attempt to explain IAP and its measurement by TM (Figure 4):

The IAP theoretical definition is the pressure within the abdominal cavity. In this study was used a non-living animal model, and so breathing and muscle contraction were not represented. Therefore IAP is the sum of the muscles pressure (P<sub>m</sub>), pressure of the entire peritoneal content (P<sub>c</sub>) and the pressure exerted by the bones themselves (P<sub>b</sub>) in ACSA [30,31]:

The pressures schematic representations in TM are represented in Figure 4. The pressure inside the bladder is represented by P<sub>1</sub> and represents the pressure of the fluid. This fluid is connected with the metric system of the water column being the letter P<sub>2</sub> the pressure in the water column. According with the Pascal's principle, the pressure of a fluid is transmitted to the all fluid [30,31]:

According to the Hydrostatic fundamental law, when there is an hydrostatic equilibrium, the pressure of a liquid equals the atmospheric pressure, plus the product of the density with gravitational acceleration (g) and liquid height (h) [30,31]. However, for the specific example of TM, the bladder cannot be considered a rigid container. It is subject to the pressure of the muscles (P<sub>m</sub>), pressure of the entire peritoneal

content (P<sub>c</sub>) and pressure exerted by the bones themselves (P<sub>b</sub>) (Figure 4, equation 3). Thus, the formulation of the equilibrium can be represented as follows for P<sub>1</sub> and P<sub>2</sub>:



**Figure 4:** Schematic representation of the forces involved in transurethral method. P<sub>0</sub> represents atmospheric pressure, P<sub>1</sub> is the pressure point at the center of the bladder, P<sub>2</sub> is the pressure of the water column, h<sub>1</sub> is the height of the fluid in the bladder, h<sub>2</sub> is the height of the fluid in the water column, ρ refers the density, g is the gravitational acceleration, P<sub>m</sub> is the pressure exerted by the muscles, P<sub>c</sub> is the pressure exerted by peritoneal content and P<sub>b</sub> is the pressure exerted by the bones.

In short, according to connected vessels theorem, which is based on Stevin's law, the pressure exerted by the muscles and by the peritoneal content to the bladder wall is proportional to the difference between water columns heights, since the density of the liquid and gravity are constant.

Through the overlap of biophysical principles we are trying to prove that:

Direct Intra-abdominal pressure measured (IAP) = P<sub>1</sub> (Point at the center of the bladder) = P<sub>2</sub> (Point in the fluid column) (Equation 5)

In order to prove the veracity of the overlapping principles undertaken, all variables required for the calculation of IAP in a dog cadaver model were determined, such as the measurement of the pressure by direct and indirect methods.

#### Values obtained for Intra-abdominal Pressure

**Direct method:** The pressure measurements by direct sensor in the abdominal cavity provided very constant readings in every position. In lateral decubitus, average pressures were 3.07 ± 3.04 mmHg; in ventral, 2.31 ± 3.38 mmHg; in dorsal, 1.93 ± 3.44 mmHg; in trendelenburg position, 2.35 ± 3.22 mmHg; finally, in reverse trendelenburg position, 2.24 ± 3.29 mmHg (Table 1). The comparison of IAP direct values in the different positions showed no statistically significant differences between them (P=0.765).

Position	Lower limit	Upper limits	Mean ± Standard Deviation
Lateral	0.00	13.00	3.07 ± 3.04
Ventral	- 2.00	13.00	3.31 ± 3.38

Dorsal	0.00	14.00	1.93 ± 3.44
Trendelenburg	-2.00	13.00	2.34 ± 3.22
Reverse trendelenburg	-3.00	13.00	2.24 ± 3.52

**Table 1:** Means values of IAP direct measurement in mmHg.

**Transurethral method:** Pressure measurements by TM provided variable readings, especially in positions with an inclination angle (trendelenburg and reverse trendelenburg). In lateral decubitus, pressure averages were  $4.52 \pm 3.12$  mmHg; in ventral,  $3.59 \pm 2.94$  mmHg; in dorsal,  $3.40 \pm 3.43$  mmHg; in trendelenburg position,  $2.57 \pm 3.14$  mmHg; finally, in reverse trendelenburg position,  $4.55 \pm 2.98$  mmHg (Table 2).

Position	Lower limit	Upper limits	Mean ± Standard Deviation
Lateral	0.29	13.99	4.52 ± 3.12
Ventral	0.00	11.55	3.59 ± 2.94
Dorsal	0.00	12.65	3.40 ± 3.43
Trendelenburg	0.00	11.25	2.57 ± 3.14
Reverse trendelenburg	0.00	11.18	4.55 ± 2.98

**Table 2:** IAP Mean values by TM in mmHg.

The comparison of the values of IAP in the various positions showed no statistically significant differences between them ( $P=0.091$ ).

**Intra-gastric Manometry Method:** The pressure measurements by IM provided quite inconstant readings, especially in inclined planes. In lateral decubitus, average pressures were  $4.73 \pm 2.16$  mmHg; in ventral,  $3.04 \pm 1.55$  mmHg; in dorsal,  $2.59 \pm 1.99$  mmHg; in trendelenburg position,  $7.14 \pm 2.72$  mmHg; finally, in reverse trendelenburg position,  $0.11 \pm 0.28$  mmHg (Table 3).

Position	Lower limit	Upper limits	Mean ± Standard Deviation
Lateral	1.47	10.67	4.73±2.16
Ventral	0.00	5.37	3.04±1.55
Dorsal	0.00	9.19	2.59±1.99
Trendelenburg	0.96	12.00	7.14±2.72
Reverse trendelenburg	0.00	0.88	0.11 ± 0.28

**Table 3:** IAP Mean values by IGM in mmHg.

The comparison of values of IAP in the various positions showed statistically significant differences between them ( $P=0.0001$ ).

### Variables value for calculating IAP

After necropsy, all variables required for the IAP calculations were determined; the average values are shown in Table 4. The average weight of the viscera was  $1.53 \pm 0.77$  Kg, which represents an average strength of  $14.95 \pm 7.57$  Newton (N), by application of the Newton second law (strength is equal to the product of the body mass by gravity acceleration) [30,31]. The average weight of the abdominal muscles and skin was  $0.27 \pm 0.16$  Kg, which represents strength of  $2.59 \pm 1.52$  N.

Parameter	Lower limit	Upper limits	Mean ± Standard Deviation
Weight	4.00	25.00	12.04 ± 5.67
Weight of the skin and muscles	0.09	0.73	1.53 ± 0.77
Weight of the bowels	0.47	3.34	0.27 ± 0.16
Strength of the skin and muscles	0.88	7.15	2.59 ± 1.52
Strength of the bowels	4.60	32.70	14.95 ± 7.57
Bladder volume	$1.00 \times 10^{-5}$	$6.00 \times 10^{-5}$	$1.08 \times 10^{-4} \pm 1.21 \times 10^{-4} \text{ m}^3$
Bladder surface area	$1.30 \times 10^{-3}$	$2.73 \times 10^{-2}$	$6.17 \times 10^{-3} \pm 5.05 \times 10^{-3}$
Abdominal cavity surface area	0.05	0.16	$9.69 \times 10^{-2} \pm 2.93 \times 10^{-2}$
Abdominal volume	$1.00 \times 10^{-3}$	$6.00 \times 10^{-3}$	$2.15 \times 10^{-3} \pm 1.17 \times 10^{-3}$
Stomach surface area	$9.40 \times 10^{-3}$	$8.52 \times 10^{-2}$	$3.55 \times 10^{-2} \pm 1.65 \times 10^{-2}$
Stomach volume	$1.00 \times 10^{-5}$	$3.70 \times 10^{-3}$	$1.16 \times 10^{-3} \pm 1.01 \times 10^{-3}$
Body surface area	0.25	0.86	0.52 ± 0.17

**Table 4:** Lower and upper limit, mean and standard deviation from the variables used to IAP calculation.

The bladder surface area values were calculated using the computational calculation program Matlab, with average values of  $6.17 \times 10^{-3} \pm 5.05 \times 10^{-3} \text{ m}^2$ . The bladder average volume was  $1.08 \times 10^{-4} \pm 1.21 \times 10^{-4} \text{ m}^3$ . For the stomach morphometric values it showed average values of surface area of  $3.55 \times 10^{-2} \pm 1.65 \times 10^{-2} \text{ m}^2$  and average volume of  $1.16 \times 10^{-3} \pm 1.01 \times 10^{-3} \text{ m}^3$  (Figure 2).

The values calculated for the body surface area were  $0.52 \pm 0.17 \text{ m}^2$ , and the values of the ACSA were  $9.69 \times 10^{-2} \pm 2.93 \times 10^{-2} \text{ m}^2$ . The abdominal cavity showed an average volume of  $2.15 \times 10^{-3} \pm 1.17 \times 10^{-3} \text{ m}^3$  (Table 4).

## Calculation of IAP by overlapping principles

With the determination of all variables conducted in each individual, the values were replaced on the overlap of principles for determining the premise, equation 5. The IAP calculation according with the principles created was carried out using the values obtained in the lateral decubitus position.

### P1 pressure calculation

The P1 pressure was calculated at the bladder central point (Figure 4). It is a pressure with several components: hydrostatic pressure of the fluid; pressure exerted by the skin and muscles (Pm); pressure exerted by viscera (Pc); pressure exerted by bone component (Pb). The sum of these pressures is exercised in the ACSA. Thus the pressure at P1 is provided by equation 3:

In the specific case of lateral decubitus, pressure exerted by the muscles and skin is calculated by the force exerted by them per unit of area, in this case the abdominal cavity (ACSA). The pressure exerted by viscera (Pc) is equal to the force exerted by the weight of the viscera on the area (ACSA) and the pressure exerted by bones (Pb) is approximately zero, because the weight is resting on the table. The average results calculated for P1 were  $101694.83 \pm 300.78$  Pascal (Pa) (Table 5).

Parameter	Lower limit	Upper limits	Mean $\pm$ Standard Deviation
P <sub>1</sub>	101580.4 2	101809.2 4	101694.83 $\pm$ 300.78
P <sub>2</sub>	101716.6 6	102021.0 3	101838.67 $\pm$ 400.08
Direct Pressure more P <sub>0</sub>	101588.3 9	101898.3 2	101766.34 $\pm$ 407.39

**Table 5:** P<sub>1</sub> and P<sub>2</sub> values calculated by the overlap principle and direct pressure of IAP more atmospheric pressure (lower and upper limit, mean and standard deviation).

### P2 pressure calculation

The calculation of the total pressure in P<sub>2</sub> is obtained by the hydrostatic fundamental law. The pressure of the column of fluid is equal to the sum of the atmospheric pressure plus the product of the density of the liquid, with the gravitational acceleration and the height of the column of fluid [30,31]. Thus the value of the pressure P<sub>2</sub> is given by equation 4:

The P<sub>2</sub> average results calculated were  $101926.84 \pm 415.44$  Pa (Table 5).

### Comparison of the values obtained by overlapping principles

Comparing the values calculated for P<sub>1</sub> and P<sub>2</sub>, it was found that the values did not show statistically significant differences between them (P=0.07). By comparing the values calculated for P<sub>1</sub> and P<sub>2</sub> with the direct measurement of the sensor of IAP (equation 5), it was determined that these did not show statistically significant differences between them either (P=0.192). This means that the IAP direct values are identical to the values calculated for P<sub>1</sub> (point inside the bladder) and P<sub>2</sub> (point in the water column). The Pearson's correlation coefficient was used to check the strength of the association of

variables and it resulted in a high correlation between the variable P<sub>1</sub> and P<sub>2</sub> (cc. 0,737), an average correlation between P<sub>2</sub> and IAP, measured directly by sensor (cc. 0,342), and a lower correlation between the P<sub>1</sub> and the IAP directly measured (cc. 0.02). The correlation levels are significant for the level 0.01, bilaterally.

### Variables that influence IAP measurement

There are several variables described in the literature which can influence the measurement of IAP by increasing or decreasing it. For all these variables, this study tried to explain and confirm their influence using biophysical formulations.

### Physiological and morphological individual characteristics

Weight is one of the variables described in the literature as leading to increased IAP. Usually we get higher IAP values in obese patients [26,48]. In this study, it was found that IAP and weight were statistically associated (P=0.04), despite showing a low degree of correlation (cc. 0.23). Applying the overlap of principles to test this variable, it was demonstrated how the weight affects the IAP:

Pressure, according to its definition, is the result of quotient between the force (F) applied per unit area (A) [30,31]. The force, according to the second Newton's Law, corresponds to the multiplication of mass by gravitational acceleration [31,42]. If the live weight of the animal increases, the mass of all tissues increases, with a proportional increase of the mass of visceral content (Mc), abdominal muscles (Mm) and bone mass (Mb). This increase leads to a bigger force exerted by each component (Fc, Fm, Fo) per unit of abdominal area.

If all parameters depend on mass rise, and since the density ( $\rho$ ) and the gravitational acceleration (g) are constant, the differential between fluids column heights will necessarily have to be higher (Figure 5).

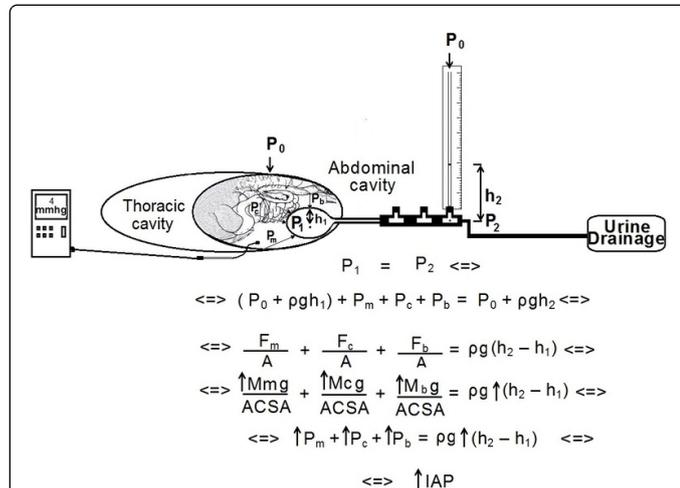
So the increased value of P<sub>1</sub> and P<sub>2</sub> necessarily leads to an increase IAP because equation 5.

Another physiological variable described in the literature which can lead to changes in IAP values is the abdominal muscles contraction. The abdominal muscles contraction works as an external force applied to the abdomen and elevates the IAP [35,49]. The abdominal muscles contraction in humans can increase an average strength supplement in the abdominal region of 46.4 Kg [50]. If we use the formulation of biophysical principles to IAP calculation, with additional strength of abdominal contraction of 10 Kg (strength exercised in the abdomen) the average results are  $102830.25 \pm 476.09$  Pa (Figure 6).

Comparing these hypothetical IAP outcomes with the IAP values in the studied population, where there was not abdominal contraction ( $101694.83 \pm 300.78$  Pa), the differences determined are statistically significant (P=0.0005).

The co-activation of the diaphragm and abdominal muscles in respiratory movements is another variable that may also affect IAP [49,51]. In order to prove the influence of respiration in IAP values, an intermittent positive pressure was held in the thoracic cavity until a pressure of 10 mmHg was reached in order to mimic the moment of inspiration. This pressure was obtained by endotracheal intubation and manual ventilation. IAP measurements mimicking a thoracic inspiration pressure showed average values of  $102019.19 \pm 568.30$  Pa. If we compare these values with the values of IAP obtained by the direct method in lateral decubitus ( $101743.36 \pm 407.39$  Pa), they show

statistically significant differences ( $P=0.038$ ). Physiologically, the inspiratory movements cause changes in abdominal and chest cavities volumes. The diaphragm delimits the thoracic cavity of the abdominal cavity and its movements cause a change of area during inspiration and expiration movements (Figure 7).



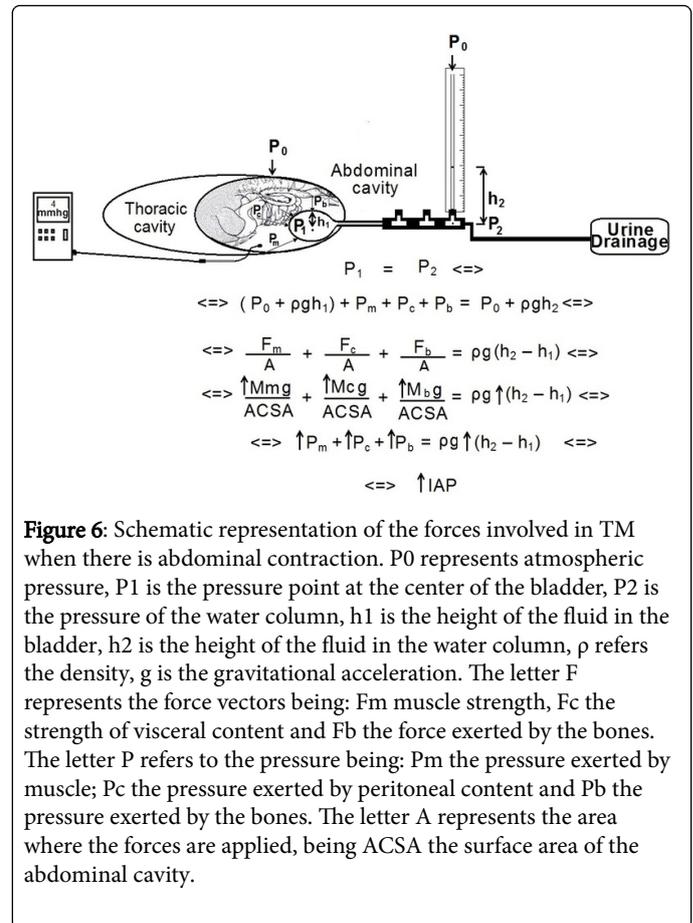
**Figure 5:** Schematic representation of the forces involved in TM when there is increased weight. P0 represents atmospheric pressure, P1 is the pressure point at the center of the bladder, P2 is the pressure of the water column, h1 is the height of the fluid in the bladder, h2 is the height of the fluid in the water column,  $\rho$  refers the density, g is the gravitational acceleration. The letter F represents the force vectors being: Fm muscle strength, Fc the strength of visceral content and Fb the force exerted by the bones. The letter P refers to the pressure being: Pm the pressure exerted by muscle; Pc the pressure exerted by peritoneal content and Pb the pressure exerted by the bones. The letter A represents the area where the forces are applied, being ACSA the surface area of the abdominal cavity.

In inspiration, lungs increase in volume, with the diaphragm being caudally moved, causing the reduction, for a brief moment, of the area of the abdominal cavity. Thus, according to the overlap of principles:

Increased value of P1 and P2 necessarily leads to an increase of IAP, by equation 5. During expiration, the diaphragm is cranially displaced, causing an increase in the abdominal area. Since pressure and area are inversely proportional, it leads to a momentary decrease of IAP:

### Body Position during measurements

It is documented that IAP values can be changed due to the body position; in humans there are IAP variations in the trendelenburg and reverse trendelenburg positions [52]. In this study, the comparison of the direct IAP values in the different body positions showed no statistic significant differences between them ( $P=0.765$ ). However, the comparison of IAP measured by indirect methods revealed that TM and IM showed statistically significant differences in the trendelenburg and reverse trendelenburg positions ( $P>0.05$ ).



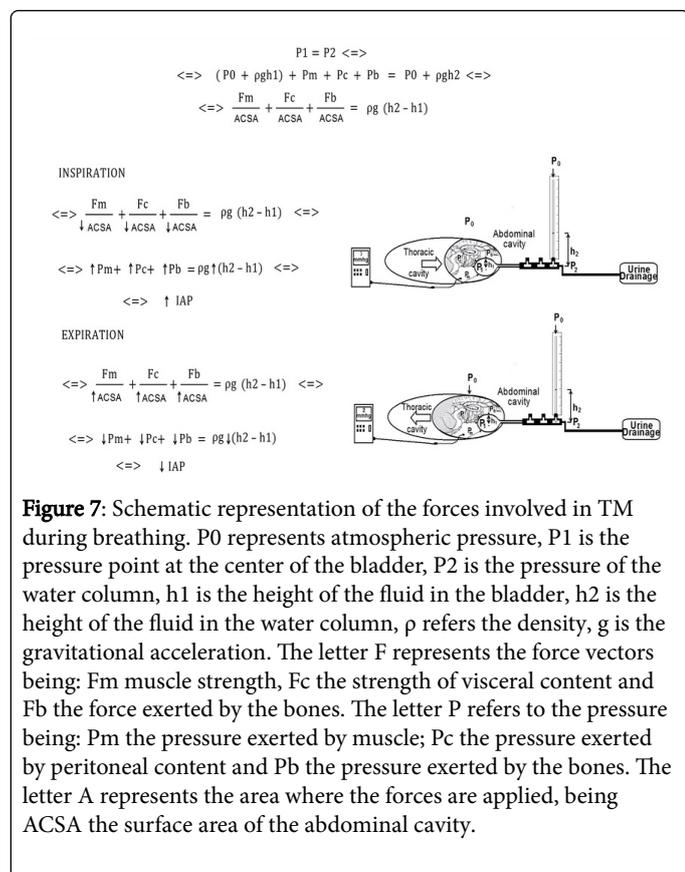
**Figure 6:** Schematic representation of the forces involved in TM when there is abdominal contraction. P0 represents atmospheric pressure, P1 is the pressure point at the center of the bladder, P2 is the pressure of the water column, h1 is the height of the fluid in the bladder, h2 is the height of the fluid in the water column,  $\rho$  refers the density, g is the gravitational acceleration. The letter F represents the force vectors being: Fm muscle strength, Fc the strength of visceral content and Fb the force exerted by the bones. The letter P refers to the pressure being: Pm the pressure exerted by muscle; Pc the pressure exerted by peritoneal content and Pb the pressure exerted by the bones. The letter A represents the area where the forces are applied, being ACSA the surface area of the abdominal cavity.

This fact seems to be directly related with Hydrostatic principles and with the movement of the fluid in the columns. According to the formulation of biophysical principles, if the IAP measurement is performed in ventral decubitus, the balance is reflected as previously referred in Figure 4. By cranially tilting the body (trendelenburg position) or caudally tilting the body (reverse trendelenburg position) a new balance of pressures will be created. The new balance of pressures is related with the tilting angle (angle  $\Theta$ ), which leads to the variation of the fluid forces.

By increasing the angle  $\Theta$ , to move to a trendelenburg position, we are automatically changing the balance of hydrostatic pressure on the water manometer. In this new equilibrium, we have a new condition where we have to take in account the inclination angle in the water column. Thus, by increasing the angle we have increased the height of the column of fluid in P2, showing the two components. We hence have the pressure exerted by the column of fluid along the column L (Figure 8) and the component of pressure exerted by fluid contained in the water manometer.

These two components lead to an increase in the hydrostatic pressure and to the movement of fluid towards the bladder. According to the biophysical principles:

To perform the calculation of the height, h3, component (Figure 8) we have to use the trigonometric calculation, the overlap being:



**Figure 7:** Schematic representation of the forces involved in TM during breathing. P<sub>0</sub> represents atmospheric pressure, P<sub>1</sub> is the pressure point at the center of the bladder, P<sub>2</sub> is the pressure of the water column, h<sub>1</sub> is the height of the fluid in the bladder, h<sub>2</sub> is the height of the fluid in the water column, ρ refers the density, g is the gravitational acceleration. The letter F represents the force vectors being: F<sub>m</sub> muscle strength, F<sub>c</sub> the strength of visceral content and F<sub>b</sub> the force exerted by the bones. The letter P refers to the pressure being: P<sub>m</sub> the pressure exerted by muscle; P<sub>c</sub> the pressure exerted by peritoneal content and P<sub>b</sub> the pressure exerted by the bones. The letter A represents the area where the forces are applied, being ACSA the surface area of the abdominal cavity.

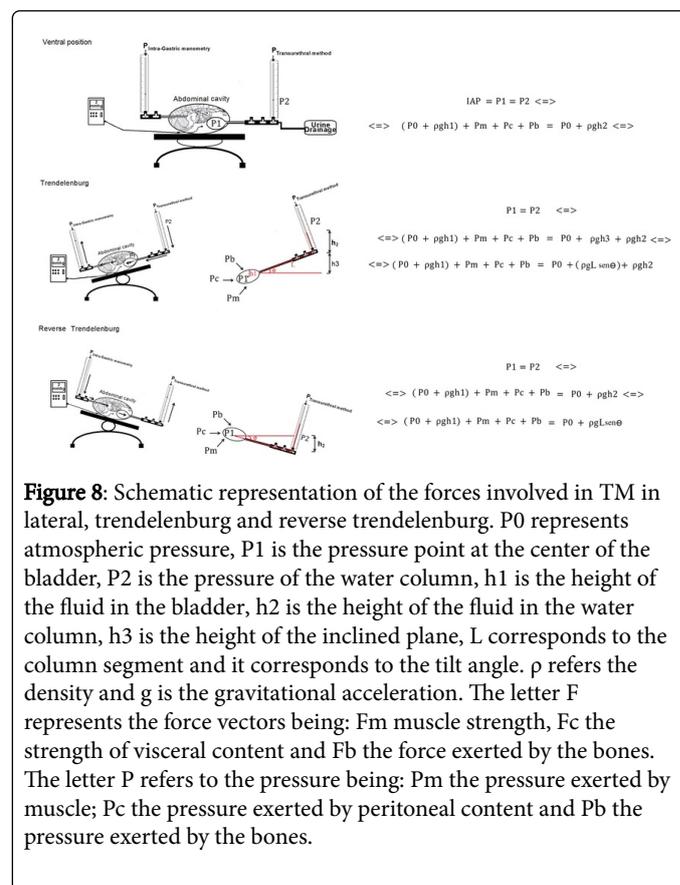
In this new equilibrium condition, the pressure exerted by peritoneal content to the bladder also decreases, since the weight force is being applied in the diaphragm. These factors, consequently lead to a displacement of the fluid to the bladder, leading to an underestimation of the reading on the water manometer (Figure 8) showing average results of  $2.57 \pm 3.14$  mmHg.

On the reverse trendelenburg position the opposite happens. In this new condition of balance, the fluid contained in the bladder and the fluid contained in column L increase their height, leading to an increase in pressures hydrostatic. The increase of the forces exerted by the column of liquid, such as the increase of forces exerted by visceral content in the cranial surface of the bladder, lead to an increase of P<sub>2</sub> to average values of  $4.55 \pm 2.98$  mmHg.

### Variables depending on the operator

The manometer leveling in TM to the pubic symphysis level is described as being able to change the IAP measurement [21]. The biophysics formulation which explains this phenomenon is very similar to what happens when we change the position for trendelenburg or reversed trendelenburg. If we increase the height of the water manometer compared to the iliac crest, the value of IAP is underestimated. This happens because when we increase the water column height we prompt an increase in the hydrostatic pressure leading to a fluid motion into the bladder. If we lower the water manometer in relation to the iliac crest, we decrease the height fluid column and in particular the pressure in the column. Thus the pressure in the bladder will be higher and will trigger a fluid motion in the

direction of the water column causing an overestimate of IAP (Figure 9).

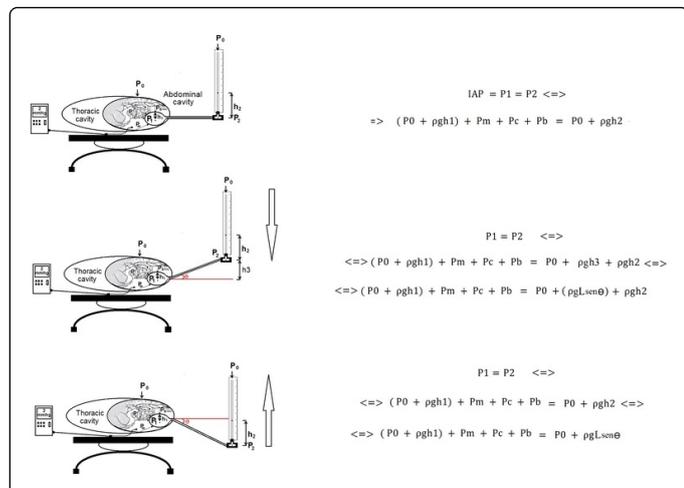


**Figure 8:** Schematic representation of the forces involved in TM in lateral, trendelenburg and reverse trendelenburg. P<sub>0</sub> represents atmospheric pressure, P<sub>1</sub> is the pressure point at the center of the bladder, P<sub>2</sub> is the pressure of the water column, h<sub>1</sub> is the height of the fluid in the bladder, h<sub>2</sub> is the height of the fluid in the water column, h<sub>3</sub> is the height of the inclined plane, L corresponds to the column segment and it corresponds to the tilt angle. ρ refers the density and g is the gravitational acceleration. The letter F represents the force vectors being: F<sub>m</sub> muscle strength, F<sub>c</sub> the strength of visceral content and F<sub>b</sub> the force exerted by the bones. The letter P refers to the pressure being: P<sub>m</sub> the pressure exerted by muscle; P<sub>c</sub> the pressure exerted by peritoneal content and P<sub>b</sub> the pressure exerted by the bones.

The operator could also influence the IAP measurement, with the choice of residual volume instilled into the bladder [23]. The objective of the instillation of a residual volume in the bladder is to introduce the minimum physiological quantity of fluid that could allow the balance with the manometer, reflecting the IAP. The instillation of a large residual volume (V<sub>u</sub>) in the bladder will increase its volume of fluid, causing an increase of the exerted forces (F<sub>u</sub>) without changing area (A<sub>u</sub>). These changes lead to an increase of hydrostatic pressure in the bladder (P<sub>u</sub>). The hydrostatic pressure can also be calculated by the result of the quotient between the force (F) applied per unit area (A) [30,31]. The changes that take place in the bladder will be transmitted to the fluid and will cause an increase in the volume of the water manometer (V<sub>2</sub>), rendering an increase in hydrostatic pressure. According to the overlapping principles we can translate this fact as follows:

Through the pressure definition, force submitted per unit area and with the application of Newton's second law [42], we have the following equilibrium

As the pressure exerted by the muscles, peritoneal content and bone structure (P<sub>m</sub>, P<sub>c</sub>, P<sub>b</sub>) is constant, atmospheric pressure cancels itself and we are left with the following expression:



**Figure 9:** Schematic representation of the forces involved when the reference of the metric scale of the pressure manometer is leveled and not leveled (above and under the anatomical reference). P0 represents atmospheric pressure, P1 is the pressure point at the center of the bladder, P2 is the pressure of the water column, h1 is the height of the fluid in the bladder, h2 is the height of the fluid in the water column, h3 is the height of the inclined plane, L corresponds to the column segment and the  $\theta$  corresponds to the tilt angle.  $\rho$  refers the density and g is the gravitational acceleration. The letter F represents the force vectors being: Fm muscle strength, Fc the strength of visceral content and Fb the force exerted by the bones. The letter P refers to the pressure being: Pm the pressure exerted by muscle; Pc the pressure exerted by peritoneal content and Pb the pressure exerted by the bones.

Applying the definition of density, which is the result of the division of mass by volume, the following expression is determined:

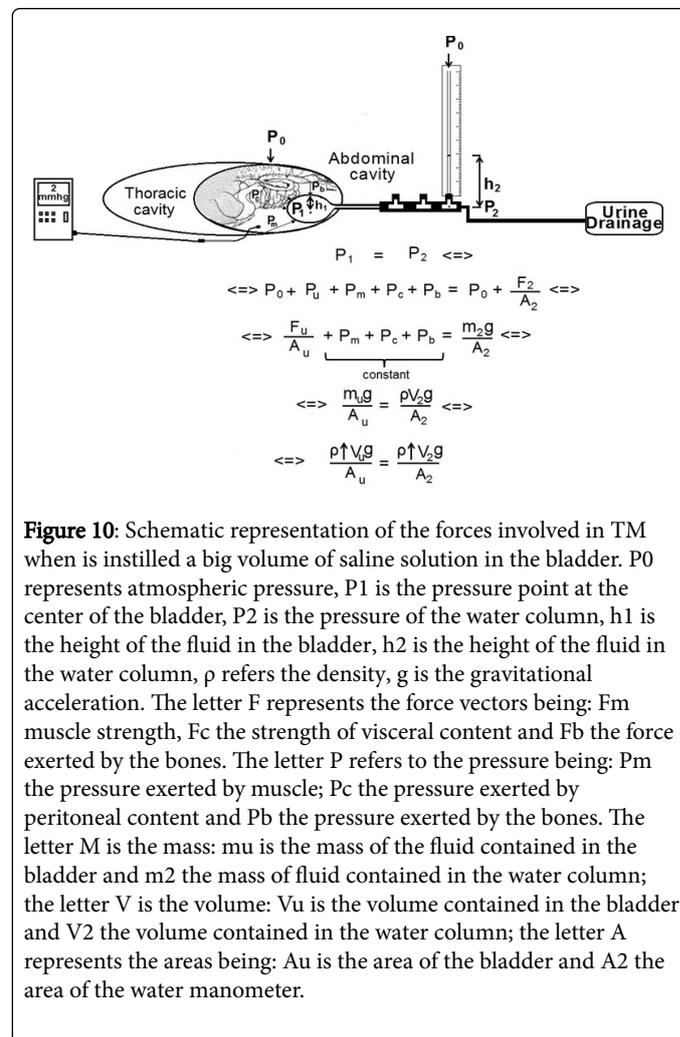
Thus, the instillation of a large volume to the bladder ( $V_u$ ) causes an overestimate IAP, because it leads to an increase in  $V_2$ , since all other elements remain constant (Figure 10). If we place a residual volume in the bladder of 5 ml/kg, approximately 5 times more than what is described in the literature, and use the overlapping principles to determine the IAP, we obtain average results of  $219340.1 \pm 56109.7$  Pa. These results show statistically significant differences ( $P < 0.05$ ), when compared to the measurements performed with 1 ml/kg, and displayed an overestimation in IAP values approximately two times more.

## Discussion

The importance of monitoring the IAP is well documented, as are the pathophysiological changes derived from the abdominal hypertension. It is a clinical setting with great impact on the patient prognosis, causing remarkable changes in all organic systems [53–57]. These changes, when verified, produce the syndrome of compartmentalization, which has a quite high mortality rate, 50-80% [10,11].

Due to this fact, the monitoring and reliable IAP measurement acquires particular importance in intensive care units. From direct and indirect monitoring methods, the TM is the most widely used due to low cost, very practical usage, allowing the continuous and isolated pressures readings, being a minimally invasive method, in comparison with the direct method, and presenting a good correlation of values

when compared with the direct measurement [12,16–18]. However, due to the variables that influence it, it continues today to generate controversy, calling into question its reproducibility [12,19–21,23,58].



**Figure 10:** Schematic representation of the forces involved in TM when is instilled a big volume of saline solution in the bladder. P0 represents atmospheric pressure, P1 is the pressure point at the center of the bladder, P2 is the pressure of the water column, h1 is the height of the fluid in the bladder, h2 is the height of the fluid in the water column,  $\rho$  refers the density, g is the gravitational acceleration. The letter F represents the force vectors being: Fm muscle strength, Fc the strength of visceral content and Fb the force exerted by the bones. The letter P refers to the pressure being: Pm the pressure exerted by muscle; Pc the pressure exerted by peritoneal content and Pb the pressure exerted by the bones. The letter M is the mass:  $m_u$  is the mass of the fluid contained in the bladder and  $m_2$  the mass of fluid contained in the water column; the letter V is the volume:  $V_u$  is the volume contained in the bladder and  $V_2$  the volume contained in the water column; the letter A represents the areas being:  $A_u$  is the area of the bladder and  $A_2$  the area of the water manometer.

This study tries to explain IAP phenomenon, as well as validate and increase the TM understanding allowing better clinicians' procedures in order to obtain more reliable results.

The methodology used in this study was chosen because of three reasons: 1 - The difficulties linked to human and animal experimentation and ethical issues; 2 - The difficulty of creating an artificial model of the abdominal cavity; and 3- The difficulty of eradicating some of the variables described that influence the measurement of IAP. To achieve the study main objectives, it was decided to use an animal cadaver model, in order to eliminate some of the variables described as having influence on the measurement of IAP, thus achieving greater control of variables. Therefore, these variables: abdominal contraction, micturition reflex, bladder volume and respiration will not be present [19,33,35]. Like this we have an anatomical model of the abdominal cavity with scale and similarities to humans. The main difference between the abdominal cavity of dogs and humans is the orientation of the organs because animals walk in prone position. This fact can influence abdominal compliance which affects IAP. These and other differences lead to different values of IAP between species. However the cavity type, the anatomical constituents

and the abdominal pressure definition is similar. This type of study has many advantages, since it allows the elimination of variables that are identified in the literature as being liable for influencing IAP measurements [5,33–37].

The normal values of IAP for the human species are between 0.2-12.2 mmHg and the normal range for dogs is between 0-3.75 mmHg, although it can reach values of 11.25 mm Hg in animals undergoing ovariectomy [28,40,59]. Recently it was founded in dogs higher average IAP values ( $5.9 \pm 1.0$  mmHg) than those previously described [27]. Even with this study being performed on cadavers, the IAP values obtained by direct methods are within the limits described for the species in all positions. Nevertheless the IAP values obtained can be considered low. Lower IAP values in this study can be due to loss of tissue tension, the non-existence of respiratory movements and a complete absence of abdominal muscles contraction. It is documented that only the variable muscle contraction may lead to a decrease in 25% of IAP if exists neuromuscular blocking in abdominal surgery [60]. The effect of respiratory movements in IAP was studied by Wilson et al. [51] concluded that there is a rise in IAP during inspiration proportional to the depth of inspiration. He also concluded that no rise of IAP occurs in normal expiration [51]. As in this study there are no respiratory movements will be any change in IAP, independently of the physiological mechanism.

The fact that IAP values in cadavers are similar to live animals is directly linked with the definition of IAP, which is nothing more than a pressure state. The pressure state of the abdominal cavity is determined by body mass index, posture, muscular activity of the wall and breath [1,8,61]. This definition of IAP is precisely the reason why in this study was decided to carry out a cadaver study.

The IAP values obtained by indirect methods (TM and IM), when compared with the values obtained by the direct method, revealed no statistically significant differences ( $P < 0.05$ ) in the lateral, dorsal and ventral positions. From the indirect methods used, the TM presented the higher correlation values, when compared with the direct method, such as described in the literature [62]. The fact that IM shows worst correlation values with the direct method may be due to gastric contents not being completely liquid which obviously influence the reading. In studies performed *in vivo*, this could also be explained by the fact that peristaltic contractions may influence the measurement [12]. The use of the IM in spite of TM is because the first one does not interfere with the production of urine and so has no risk of infection [12].

The determination of the individual morphometric parameters in each cadaver, within the scope of the necropsy, had a crucial importance in order to obtain the required values to biophysical principles. Body surface area calculated values were  $0.52 \pm 0.17$  m<sup>2</sup>, the ACSA values were  $9.69 \times 10^{-2} \pm 2.93 \times 10^{-2}$  m<sup>2</sup> and the abdominal cavity showed an average volume of  $2.15 \times 10^{-3} \pm 1.17 \times 10^{-3}$  m<sup>3</sup> (Table 4). For the direct calculation of pressures, one of the most important factors is the area. This is because the definition of pressure is the result of the forces exerted per unit area [29]. The ACSA hence assumes crucial importance in the physical determination of IAP. The ACSA determination was performed using methods of three-dimensional modelling by tomographic exams. These techniques have some associated error, when compared with the actual structures, with literature describing errors between 2.9 % and 4.95 %, an error considered quite low [63–65]. This type of methodology was adopted due to the difficulty of accurately measuring an organic cavity.

The physical determination of viscera and organic cavities dimension, like volume and surface area, sometimes is a challenge in the several fields of medicine [66-71]. There are many techniques that were developed over the time to this end: direct measured of the organ with a tape [71,72]; transfer the structure to paper to measure the surface area [71,73]; measuring the amount of liquid that fills a cavity [66,70,74]; applying Arquimedes principle to define a volume [43,75]; mathematical formulas based on organic structures and other techniques [69–72,75]. The measurement of surface areas of the stomach and bladder also present an increased difficulty. The determination of these areas was important because the indirect methods use this surface area to determine the IAP. In order to determine these measures, with the smallest error associated, a technique of image processing and calculation by mathematical software was adopted [44]. Using this type of method it was possible to determine bladder and gastric surface area,  $6.17 \times 10^{-3} \pm 5.05 \times 10^{-3}$  m<sup>2</sup> and  $3.55 \times 10^{-2} \pm 1.65 \times 10^{-2}$  m<sup>2</sup> respectively of all the dogs.

With the determination of surface areas carried out and in order to carry out the calculation of the pressure values, we are only missing the determination of forces exerted. To establish the forces exerted values, the use of the cadaver model was fundamental. In this type of model, the only forces present are the exerted by the weight of the structures. Thus, to obtain another crucial parameter for the IAP determination, the weight determination of all abdominal structures was conducted and, through the Second Newton's law, the results were converted into forces exerted.

The determination of all the required morphometric values allowed the replacement of the variables on the biophysical formulation (equation 1, 2, 3, 4 and 5). Thus we were able to compare pressure values calculated with pressure values determined by direct and indirect method. It was found that the calculated pressure value for the point P1 (equation 3 - point inside the bladder) did not show statistically significant differences ( $P = 0.07$ ) with the pressure point P2 (equation 4 - point in the water column). This means that the pressure inside the bladder, exercised by the entire abdominal content, is identical to the pressure value demonstrated by the water manometer. Comparing the values calculated for P1 and P2 with the direct measurement of the IAP sensor (equation 1), it was determined that there were not statistically significant differences between them ( $P = 0.192$ ). In other words, the direct determination by IAP sensor is identical to the IAP calculated in point P1, which is also identical to the IAP calculated in the point P2 (TM). To assess the association strength between variables, the correlation coefficient was calculated and it was found: a high correlation between the variable P1 and P2 (cc. 0.737); an average correlation between P2 and the IAP measured directly by sensor (cc. 0.342); and a lower correlation between the P1 and the IAP measured directly (cc. 0.02). The mathematical calculation of IAP confirms the theoretical definition of IAP by the first time [2].

These results also demonstrate that TM can be used for measurement of IAP being this physically explained. The variations obtained between P1, P2 and the values of direct IAP obtained by sensor, may be explained by the difficulties in calculating some of the morphometric parameters. Some of these parameters we were only able to determine by resorting to computational calculation, and there is an error associated to it. This error might have influenced a lower P value, maintaining however its statistical significance. In addition to this, other reasons that may explain the low value of P are the size of the population, the error associated with the determination of forces

and weight of the structures. The use of cadavers also can lead to physical changes such as the loss of tension in the abdominal wall, urinary or gastric, influencing the study of IAP. Despite the cadavers show physical changes of tissues, pressure continues to be a physical state, determined by the forces exerted per unit area at a given moment [29]. The clinical definition of IAP is a state of pressure in the abdominal cavity which is determined by body mass index, posture, wall's muscle activity and respiration [2,52]. In this study only will not be present muscle contraction and respiration so IAP is the result of the strength exerted by the body mass index in ACSA.

The validation of the overlap of principles in the application of the TM enabled its application in the explanation of the variables described in the literature as influencing the measurement of IAP. One of the physiological variables that is described as an influence to IAP is the weight of the individual [26,48]. In this study we found that IAP and weight are associated, there being statistical association of variables according to the linear regression model ( $P=0.04$ ), showing however a low degree of correlation ( $cc, 0.23$ ). The result obtained is in agreement with data reported in the literature, but the values presented in studies of Varela [26] and Rader [48] showed a greater statistical correlation]. This may be due to the type of model used in the study. The cadaver models have no muscular contraction, or variations submitted by breathing as the live animals used in those studies. However, even so, it appears that as the weight increases there is also an increase in IAP values. In physical terms, and using the overlap of principles to explain this fact, it is easy to conclude that if the force of the weight increases and if the ACSA remains relatively constant, it will cause a proportional increase in IAP (Figure 5).

Another variable which is described to influence the IAP is the abdominal muscles contraction [35,49]. The abdominal pressure corresponds, in biophysical terms, to an increase of the force exerted in the same area (Figure 6). Mimicking a strength of abdominal contraction of 10 Kg, the IAP values obtained had statistically significant differences ( $P=0.0005$ ), comparing with normal values (Figure 6). The detrusor muscle contraction, responsible for the urination reflex, may also influence the IAP values, acting identically yet in the fluid contained in the bladder. In the study conducted by Johna and collaborators in 1999, they compared the IAP measurements obtained by direct measurement with the TM. They concluded that the values obtained by TM had a higher baseline pressure, when compared with the values of IAP obtained by direct measurement [19]. Johna and their collaborators explained this fact with the activity of the detrusor muscle. The triggering of the functioning of the muscle could be caused by instillation of saline solution into the bladder, its rate of infusion or even its temperature. The detrusor muscle contraction due to the urination reflex is one of the facts that may lead to changes in IAP due to increase of force exerted. The influence of muscular contraction in the measurement of IAP can often be detected. In muscles, there is a period of contraction and another of muscle relaxation and this fact is demonstrated in the IAP through maximum and minimum values in a short timeframe [19].

In the literature it is described how the IAP suffers an increase during inspiration proportional to its depth [51,76]. Chieveley-Williams et al. [51] conducted a study on patients under assisted ventilation and concluded that the bladder pressure and central venous pressure imparted a reflection of respiratory muscles when the support pressure was reduced. In this study, the IAP results obtained with a thoracic pressure of 10 mmHg, when compared with the values

obtained without thoracic pressure, revealed statistically significant differences ( $P=0.038$ ). These results are in agreement with the literature, being registered higher IAP values during inspiration. This fact, in biophysical terms, and applying the overlap of principles, is easy to explain since there is a variation in the abdominal area during respiration movements. Hence, the increase or decrease in the abdominal area, depending on the time of breathing, causes a change in the IAP (Figure 7).

Most patients in intensive care unit (ICU) are nursed with an head-of-bed elevation to reduce the risk of ventilator-associated pneumonia and pressure ulcers [77]. Measuring IAP via the bladder in the supine position is still the accepted standard method but sometimes these measurements are made with head-of-bed elevation [78]. Another factor which could influence the IAP values is the patient position. The patient position may lead to over or underestimation IAP values, according with the study of Yi et al. [58], who showed that the elevation of the head 30 to 45° in patients in critical condition increases the values of IAP. In cats it is also described that the body position can affect the IAP measurements when used the ventral decubitus in comparison with the lateral position [26]. In our study, the comparison of direct IAP values in the various positions did not show statistically significant differences between them ( $P=0.765$ ). This fact leads to the conclusion that there is no changes in IAP when position changes. However, in all studies that reported differences of IAP due to body position, indirect methods of measurement were used. As it has already been mentioned, the indirect methods are dependent on a water column and thus of the principles of mechanics of fluids [26,52,58]. These principles allow the explanation of the results obtained. The comparison of the direct method, the TM and IM did not show statistically significant differences in the lateral, ventral and dorsal positions, but showed differences in the positions of trendelenburg and reverse trendelenburg. In these two positions, when we moved to the inclination of the stretcher according to an angle of 45 ° a movement of the fluid column contained on the manometer could be observed. This fact is directly related to the height of the column of fluid that influences the balance of pressures. The new balance of pressures happens because, when a tilt angle is imposed (angle  $\Theta$ ), the forces subjected on the fluids will change due to the change of height (Figure 8). The overlap of principles helps explain what happened and calculate the new equilibrium point. Thus, in trendelenburg position, the height of the water manometer increases, causing an increase in pressure. This increase in pressure causes a fluid displacement in the direction of lower pressure, which corresponds, in this case, to the bladder. This study revealed this fact because in trendelenburg position the IAP was much lower ( $2.57 \pm 3.14$  mmHg) than the values obtained in the normal position ( $4.52 \pm 3.12$  mmHg), meaning it was underestimated. In reverse trendelenburg position, our study revealed that it showed slightly overestimated IAP ( $4.55 \pm 2.98$  mmHg) since the exact opposite occurs. Since the IAP measurement was carried out simultaneously by three methods, it was quickly noted that, by changing the tilt of the table, the fluid contained in the manometers would accompany the tilt submitted. This movement of fluid was incorrectly translated as pressure variation because the direct sensor pressure did not change. This fact leads to the conclusion that there is no change of IAP according to the position when it is used the direct method. Using indirect methods in inclined positions it is not possible to obtain a reliable IAP value. Indirect methods should only be used in the lateral or dorsal position.

Another common error in the IAP measurement, by indirect methods based on columns of fluids, consists in air bubbles moving in

the manometer and its wrong positions, leading to measurement errors [12]. Variations from -6 to +30 mmHg were reported in previous studies, some of which revealing a variation of reproducibility coefficient between 25 and 66% [20,79]. Soler Morejon and colleagues (2012) concluded that the manometer position has a crucial importance to correctly assess the IAP values [21]. The zero reference of the metric scale of the pressure manometer must be levelled at the measure of the iliac crest, to decrease the errors in results. If the pressure manometer is not well levelled it can lead to errors of over or underestimation values. This happens due to the creation of a different angle in the columns of fluids, leading to changes in hydrostatic balance (Figure 9). By increasing or lessening the angle, the water column height contained in the pressure transducer, it varies, causing an over or underestimation, in line with what happens in the trendelenburg and reverse trendelenburg position.

The choice of residual volume instilled into the bladder is another of the variables which can influence the measurement of IAP [23]. In human medicine, the volumes used for instillation into the bladder are not uniform, literature reports volumes of 50 to 250 ml of saline solution being used. The instillation of 50 ml in a not complacent bladder will increase the internal bladder pressure and overestimate the IAP [23]. With the determination of IVP (intravesical pressure), through the construction of volume curves, it was concluded that the use of volumes between 50 to 100 ml would not affect the measurement [80]. In dogs, the volume instilled in the bladder is between 0.5 and 1 ml/kg of saline solution being the value of 1 ml/kg the most commonly used [27,40]. According to the overlap of biophysical principles, the instillation of a large amount of residual fluid in the bladder will increase the pressure inside the bladder, due to excessive volume instilled (Figure 10). The volume instilled should be enough to allow physiological distension. By increasing the pressure in the bladder, because of an excessive volume instilled, the dynamic equilibrium with the water column will be higher. In this study, by mimicking the use of a quantity of fluid five times higher (5 ml/kg) than what is normally instilled into the bladder, we obtained values of IAP much higher than what is normally obtained through the TM. These values, when compared with the normal values, showed statistically significant differences. This fact can also be correlated with the loss of distensibility of tissue in cadavers, but the most plausible explanation is the instillation of a large volume of fluid in an area of limited distension.

The last variable described as being able to alter IAP is the abdominal surgery. In human medicine, it is described how the acute abdominal distension, after complex abdominal surgery, can result in gastric dilation leading to oliguria and increase of respiratory pressures [81]. In veterinary medicine, an increase in post-surgical IAP has also been identified in female dogs which had undergone ovariohysterectomy [28] and in female cats subjected to the same procedure [61]. The association of this variable with the increase in IAP may be linked to several aspects. All factors that alter the conditions and forces submitted within the abdominal cavity can lead to an increase in the IAP. In the case of surgery, visceral edema, abdominal pressure due to pain or even entrance of air in the abdominal cavity can lead to change in the IAP. If there is an edema or inflammation of any visceral component there is a change in the strength of the weight exerted, leading to an increase in IAP, as it is explained in Figure 5; if there is abdominal pressure due to pain or contraction of smooth muscles, there will be increase in IAP, as shown in Figure 6. Depending on the mechanism, all these factors can explain

the increase in IAP due to an increase in the forces on the same surface area.

Being the TM the most used method in veterinary and human clinical practice this study is going to improve its measurements. The IAP values obtained by direct method in this study in comparison with the values of the indirect methods remove all the doubts regarding the effect position. The position only changes the measurement of IAP if the clinics use the indirect methods. The indirect methods should not be used when the patient is lying with an angle. When the clinic use the indirect methods to obtain the IAP values he also need to now that the position of the water manometer is very important. Incorrect position increases or decreases the angle of the water column leading to under or over valuation of IAP. Muscle contraction is other important factor that needs to be absent to obtain reliable values of IAP. The measurement of IAP cannot be measured with abdominal or detrusor contraction because of all factors explained above. All these factors and the others described need to be evaluated by the clinic.

## Conclusions

The biophysical principles formulated, aiming to explain the TM and IAP physiology, offer additional information for a better implementation of the method and understanding of the results obtained, in intensive care units. The TM, being based on physical principles of the mechanics of fluids, allows its use for IAP measurement, but it implicates variables that affect it. The correct use of this knowledge will enable clinicians to gain a greater confidence on the obtained results and the diagnosis of cases of abdominal hypertension. This way, the application of therapeutic manoeuvres will be faster and enable a higher success rate. In addition to these facts, the biophysical formulation can be applied to more complex algorithms as to create alternatives for the IAP measurement.

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