The adaptation of lung, chest wall and respiratory muscles during pregnancy: preparing for birth

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Short title: Pregnancy conditions the diaphragm for birth

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Abstract (/250)

Aim. A plethora of physiologic and biochemical changes occur during normal pregnancy. The changes in the respiratory system have not been as well elucidated, partly since radio-imaging are usually avoided during pregnancy. We aimed to use several non-invasive methods to characterize the adaptation of the respiratory system during the full course of pregnancy in preparation for childbirth.

Methods. Eighteen otherwise healthy women (32.3±2.8 years) were recruited during early pregnancy. Spirometry, opto-electronic plethysmography and ultrasonography were used to study changes in chest wall geometry, breathing pattern, lung and thoraco-abdominal volume variations and diaphragmatic thickness in the first, second and third trimester. A group of non-pregnant women were used as controls.

Results. During the course of pregnancy, we observed a reorganization of ribcage geometry, in shape but not in volume. In spite of the growing uterus, there was no lung restriction (forced vital capacity: 101±15 %predicted), but we did observe reduced ribcage expansion. Breathing frequency and diaphragmatic contribution to tidal volume and inspiratory capacity increased. Diaphragm thickness was maintained (first trimester: 2.7±0.8 mm; third trimester: 2.5±0.9 mm, p=0.187), possibly indicating a conditioning effect to compensate for the effects of the growing uterus.

Conclusions. Pregnancy preserved lung volumes, abdominal muscles and the diaphragm at the expense of rib cage muscles.

Keywords: diaphragm, opto-electronic plethysmography, pregnancy, position, ultrasound

New & Noteworthy: The non-invasive analysis of the kinematics of the chest wall and of the diaphragm during resting conditions in pregnant women revealed significant changes in the pattern of thoraco-abdominal breathing across the trimesters. Namely, concomitant to the progressive changes of chest wall shape, the diaphragm increased its contribution to both spontaneous and maximal breathing, maintaining its thickness despite its lengthening due to the enlarging uterus. These results suggest that during pregnancy the diaphragm is conditioned to optimize its active role provided during parturition.

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Introduction

The physiology of pregnancy is characterized by hormonal, cardiovascular, respiratory and muscular-skeletal changes which are associated with the modification of both the morphology and function of several organ systems(72). Both biochemical and mechanical pathways affect the anatomy and regulate the physiology of the respiratory system during normal pregnancy. The former includes increased levels of progesterone and relaxin that induces collagen loss, with consequent relaxation of ligaments and cartilage(28, 55). An example of the latter is the enlarging uterus, with cranial shift of viscera as its principal mechanical effect(2). The combination of these factors progressively influences the geometry and the dimensions of the chest wall in terms of increasing subcostal angle, as well as thoracic and abdominal perimeters(16, 17, 27, 44, 66).

The literature available is scant, outdated or based on antiquated or invasive techniques, with conflicting results. Furthermore, most studies deal with one aspect only, or exclusively consider the last trimester without following the progression of pregnancy. For example, lung volumes may be reported to be reduced, increased or to display no changes with gestation(17, 27, 29, 32, 35, 46, 50, 66, 72) The breathing pattern has been described as more thoracic(21, 27), although trans-diaphragmatic pressure has not been shown to change at the end of pregnancy(17, 21). Such apparently conflicting results, *i.e.* similar diaphragmatic force but reduced abdominal expansion, can be a consequence of the method used. For instance, in one study the respective displacement of only one thoracic and one abdominal point was measured.Moreover, the authors considered only the seated position, which is normally characterized by predominantly thoracic breathing(58).

Several studies have found that maximal inspiratory and expiratory pressures, being global indices of the forces developed by all the inspiratory and expiratory muscles, do not change with pregnancy(17, 27, 43). The capacity of the respiratory muscles to develop pressure therefore seems preserved, even though the geometry of the chest wall is significantly affected during pregnancy. Abdominal muscles lengthen and change their muscles insertions while preserving the force development(12, 26, 73). The diaphragm is shifted cranially at the end of pregnancy. This shift ranges from 1.5 to 4 cm and it was quantified in the first half of the 1900's using chest *X*-ray(47, 63, 66). Simultaneous changes in ribcage muscle function are less well elucidated.

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The diaphragm has both ventilatory and non-ventilatory (or expulsive) behaviours, including parturition. The former is accomplished by recruiting only fatigue-resistant (type S and FR) motor units, the latter by more fatigable motor units (type FInt and FF). During ventilatory behaviour the diaphragm develops ~10% of its total force-generating capacity(59), therefore having a large reserve of force generation and high levels of activation (22, 45). For these reasons, the diaphragm, together with abdominal muscles, is important also during the delivery stage when they have to contract forcefully, acting as a brace and being the "engine" that expels the foetus(8–10, 19, 57, 61).

Some decades ago, maternity would be prohibited for all women suffering from high-risk conditions. Recently, many institutions have changed their policies, and an increasing number of high-risk pregnancies are initiated and completed (18, 34, 36, 37, 49, 65, 71), leading to challenges that require a multi-disciplinary medical approach. For this reason, increased knowledge of the maternal physiological respiratory changes may help the physician to provide optimal care in these high-risk pregnancies. The present study would represent a first step towards understanding the physiological adaptation of lung, chest wall and respiratory muscles during normal pregnancy, also providing a base for future study of high-risk pregnancy.

The aim of this work was to characterize and progressively monitor changes of the respiratory system induced by pregnancy and to understand their mechanism and possible implications. We therefore undertook a longitudinal multidimensional study to investigate different aspects of the respiratory function, using non-invasive and accurate techniques, at each trimester of pregnancy in a group of primiparous women.

The different aspects comprised chest wall geometry, breathing pattern, lung and thoraco-abdominal volume variations, diaphragmatic thickness and motion in seated and supine position. In particular, we wanted to understand the net effect on the diaphragm of the progressively increased abdominal content, which may have two opposite effects: stretching and increased load.

Materials and Methods.

This is an observational, single-centre, longitudinal, controlled study approved by the Research Ethics Board of the IRCCS "Cà Granda Ospedale Maggiore Policlinico" (n: 2126; date: 17/10/2016), on otherwise healthy primiparous women. The inclusion criteria were: age>18 years, absence of chronic respiratory or other severe pathology; body mass index<25 $kg \cdot m^{-2}$.

A cohort of nulliparous women served as controls. All the recruited women signed a written informed consent form according to the Declaration of Helsinki.

Spirometry and lung volume subdivisions (total lung capacity, total gas volume and residual volume) were measured with body plethysmography (BPd-HD, nSpire Health, Longmont, CO, USA), while chest wall geometry, breathing pattern and thoraco-abdominal volumes were analysed using opto-electronic plethysmography (OEP, Smart System BTS, Milan, Italy).(14)

In OEP, infrared light is emitted and received by a set of cameras, and dedicated software is used to reconstruct the 3D coordinates of passive reflective markers (94 in seated position; 57 in supine position) placed on the trunk of the women, according to specific anatomical points. Various geometric parameters were computed starting from the 3D mesh of points to characterize the dimensions of the chest wall. These included subcostal angle, heights, diameters, perimeters, cross-sectional areas and volumes (figure 1). The volumes were also assessed in dynamic condition during quiet breathing (QB) and a slow vital capacity (SVC) manoeuvre. The ventilatory pattern (duty cycle, respiratory frequency, tidal volume and minute ventilation) was analysed during QB.

An index of the velocity of shortening of the diaphragm was calculated as the ratio of abdominal volume variation at rest to inspiratory time and to cross-sectional area at the xiphoidal level(53, 62, 70).

An index of velocity of shortening of ribcage muscles was calculated as the ratio of ribcage volume variation at rest to inspiratory time and to the cross-sectional area obtained as the mean between the cross-sectional area at xiphoidal and louis angle level (6).

The SVC was split into its components: inspiratory capacity (IC) and expiratory reserve volume (ERV). The thoraco-abdominal volume contributions at QB, SVC, IC and ERV were also computed.

Finally, we used ultrasound measurements (US) to dynamically evaluate the diaphragm (Hawk 2102 EXL, BK Medical). We used a 12MHz linear probe (B-mode) to measure the thickness of the diaphragm (DT) as the distance between two echogenic layers, the pleural and peritoneal membranes. Measurements were performed at end-inspiration and end-expiration and the difference between the two was divided by the value at end-expiration. The resulting ratio was defined as the diaphragmatic thickening fraction (TF). The displacement of the dome of the diaphragm was defined as the maximal excursion (i.e. the difference between end-expiration and end-expiration) on the vertical axis of the tracing (M-mode, 5 MHz convex probe).

The measurements were performed at the end of the first (T_1), second (T_2) and third (T_3) trimester of pregnancy in all the included pregnant women.

Opto-electronic plethysmography and US were performed in all experimental sessions by single operators: an expert bioengineer and an experienced echographist, respectively. They were performed in both seated and supine positions to enable analysis of postural effect

Statistical analysis

To evaluate the effect of the progression of pregnancy on all the acquired parameters, a one-way Analysis of Variance (ANOVA) or a Friedman ANOVA on ranks for repeated measures was performed if the parameter was normally or non-normally distributed, respectively, with trimester of pregnancy as independent variable. At each trimester, to evaluate the difference between nulliparous and primiparous women, a one-way or a Kruskall-Wallis ANOVA on ranks was performed if the parameter was normally or non-normally distributed, respectively, with pregnant status as independent variable. The global effect of posture was tested using a t-test or a Mann-Whitney Rank Sum Test if the parameter was normally or non-normally distributed, respectively, with posture as independent variable (SigmaStat version 11.0; Systat Software, San Jose, Calif., USA). For all the parameters, the median, 25th and 75th percentile of the changes between third and first trimester were calculated (Excell, Microsoft Office Professional Plus 2016, Santa Rosa, Calif., USA).

Differences were regarded as significant for p values <0.05.

Data were reported as median, 25th and 75th percentiles in the text, table and figures.

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Some of these data were collected for the first time and this was the reason for reporting absolute values, in order to provide reference values.

When planning the study, we could find no relevant published data on which to base a sample size calculation since available data were either measured with different and/or invasive techniques or reported with conflicting results. Although there are many studies evaluating both the primary outcome of the present study (diaphragm thickness assessed by US) and the secondary one (abdominal volume variations assessed by OEP), these methodologies have not been used before in pregnancy. In addition, when designing the study, the expected difference induced by pregnancy on the diaphragm was difficult to determine because we did not know which of the two opposite effects (stretching or conditioning) would prevail. The effect size was therefore uncertain because of lack of previous studies. Because the main interest was the longitudinal change during pregnancy in each subject, a pilot study would have delayed the start of the study by at least 6 months. There were, therefore, no data on which to base a proper power analysis. In addition, post-experiment power calculation is shown to be fundamentally flawed (33). The use of repeated measures tests, however, enables detection of significant differences in the mean or median effect of treatment(s) within individuals beyond what can be attributed to random variation of the repeated treatments.

Results

The protocol was applied to 39 subjects: 18 primiparous and 21 nulliparous women with a mean age difference of six years. Anthropometric data and gestational age were reported in table 1. The primiparous women gained in average 6.5 kg until the 31st week of pregnancy.

Lung and chest wall volumes during maximal manoeuvre. The absolute value of vital capacity did not change with the progression of pregnancy. This was both when the manoeuvre was forced, as measured by spirometry, and slow, as measured by OEP, and in both postures. Forced vital capacity remained within predicted values in all three trimesters (figure 2). Similarly, IC and ERV of the lung were both stable and not restricted with increasing maturation. Neither IC nor ERV of the chest wall changed across the considered trimesters, with the exception of ERV in the supine position at T_3 that was lower than in controls (online supplement: figures 1-2). Absolute lung volumes remained unaffected by the progression of pregnancy (online supplement: figure 3). Abdominal ERV did not change in the three trimesters in seated ($p=0.584$) position.

Chest wall geometry. With increasing gestation, chest wall geometry showed modifications at both thoracic and abdominal levels. As expected, all the abdominal geometrical parameters progressively increased. In particular chest wall volume increased by 4.46 litres at T_3 (online supplement: figure 4). In contrast, the ribcage changed in shape (diameters, perimeters, cross-sectional areas and costal angle progressively increased but height decreased) while the volume remained constant (figure 3). Because total chest wall volume increased by 4.46 litres at T_3, assuming an average density equal to 1, the 6.5 kg of weight gained was therefore mainly located in the trunk (~69%), mostly in the abdomen (~65%), with 31% in the extremities.

Breathing pattern during quiet breathing. Minute ventilation of primiparous women was higher than the nulliparous group in the supine position in all trimesters but only slightly at T_3 in the seated position. Respiratory rate increased slightly in the seated position at T_2 and T_3, but not in the supine position, compared to T_1 while tidal volume remained unchanged in both postures (figure 4). Within the duration of a single breath, duty cycle represented the percentage of inspiratory time. Duty cycle did not differ with the progression of pregnancy either in seated (T_1: 39.7%, T_2: 39.8%, T_3: 40.5%; p= 0.584) or supine (T_1: 40.9%, T_2: 40.7%, T_3: 41.2%; p= 0.926) position, being similar to nulliparous women (seated: 40.3%, supine: 41%; p= 0.922 and 0.683, respectively).

Thoraco-abdominal contribution. At rest and during the maximal manoeuvre, breathing tended to be shifted toward the abdomen with increasing gestation. The abdominal contribution in pregnant women was generally greater at T_3 compared to the other two trimesters and to the nulliparous in both postures. Of note, the abdominal contribution of ERV became negative at T_3 in supine position (figure 5). The ribcage contribution, being complementary to the abdominal one, changed consequently (online supplement: figure 5).

Velocity of shortening. During quiet breathing, the estimated velocity of shortening of the diaphragm increased in seated position at T_3 (0.28 ml/sec·cm^{-2}, p<0.05; T_1:0.22 ml/sec·cm^{-2} and T_2:0.22ml/sec·cm^{-2}); while it did not change in supine position (T_1: 0.35 ml/sec·cm^{-2}; T_2: 0.37 ml/sec·cm^{-2} and T_3: 0.36 ml/sec·cm^{-2}; p=0.148). The estimated velocity of shortening of ribcage muscles at T_3 (seated: 0.42 ml/sec·cm^{-2}; supine 0.21 ml/sec·cm^{-2}) became lower than T_1 (seated: 0.53 ml/sec·cm^{-2}, p<0.05; seated: 0.25 ml/sec·cm^{-2}, p=0.06).

Ultrasound measurements. The thickness of the diaphragm, the thickness fraction and the excursion of the diaphragmatic dome remained constant and within the range of nulliparous women along the three trimesters of pregnancy (figure 6).

Postural effect. Changing body position had similar effects on primiparous and nulliparous women. Passing from seated to supine position, minute ventilation decreased (p=0.016 and p<0.001, respectively); IC_{CW} increased (p<0.001 and p=0.011) while ERV_{CW} decreased (p<0.001 in both groups). A significant increment occurred in the abdominal contribution to tidal volume (p<0.001 in both groups), to SVC_{CW} (p=0.019 and p=0.006, respectively in primiparous and nulliparous) and to IC_{CW} (p<0.001 and p=0.011, respectively), while the abdominal contribution to ERV_{CW} was reduced (p<0.001 in both groups). In all women, the thickness of the diaphragm was 33% less in the supine compared to the upright position ($p<0.001$ and $p=0.007$), while the thickness fraction decreased only in the nulliparous group ($p=0.033$). All the other parameters measured both supine and upright were unaffected by the changing of posture.

The differences of all the considered parameters between the first and the third trimesters of pregnancy were also computed (online supplement: Table 1).

Discussion

In the present study, an original and comprehensive description of the respiratory changes with the evolution of pregnancy, using non-invasive measurements, was provided. Our main findings suggested that a reorganization of the ribcage geometry, in shape but not in volume, occurred during pregnancy. This process may driven by the slow mechanical force developed by the growing uterus and be mediated by pregnancy-induced hormonal changes. The new thoracic shape compensated for the enlarging uterus so that the lung was not restricted and space was accommodated for the abdominal expansion. The abdominal contribution to inspiration increased, at rest and during maximal capacity. In spite of the stretching effect of the cranial shift of viscera, diaphragm thickness was not diminished.

Pregnancy affects the respiratory system through two pathways, chemical and mechanical. The hormones (28, 55), *per se*, stimulate respiratory rate to increase (25). They also induce collagen loss with consequent joint relaxation(30). This, combined with the mechanical effect of the enlarging uterus, produce an upward bucket-handle shift centred in the xiphoidal process and a reduction of ribcage height. In accordance, we found the ribcage to change in shape, but not in volume. In this way, the lung was not restricted and space was accommodated for the abdominal expansion. The progressive geometrical changes of the thoraco-abdominal wall during gestation had different effects on the respiratory muscles. Breathing remained invariantly abdominal in the supine position, whereas the contribution of the abdomen increased in the seated position in the last trimester of pregnancy. This observation was in contrast with the findings of previous studies where breathing became more thoracic (14, 18). This conflicting result might be explained by the different methods used to measure thoraco-abdominal volume: the previous studies used two magnetometers, therefore deducing the volume variations by the displacement of only one thoracic and one abdominal diameter. In contrast, OEP allowed precise measurements of thoraco-abdominal volumes by considering a dense mesh of points from the clavicles to the iliac crest, according to anatomical points.

A didactic simplification of the actions of the diaphragm and rib cage muscles on the chest wall is that during inspiration, abdominal and ribcage expansion reflects diaphragm and inspiratory rib cage muscle action, respectively, while expiration is passive at rest and driven purely by the elastic recoil of the respiratory system (5, 69). Conversely, expiration is active during vital capacity manoeuvres, with expiratory ribcage and abdominal muscle contraction, the former contributing to reduce ribcage and the latter the abdominal volume, respectively. The results of the present study, namely the reduced contribution at T_3 of rib cage to volume variations, during both spontaneous breathing and maximal manoeuvre, suggest that the action of the ribcage muscles was reduced during pregnancy. This was presumably due to the altered orientation of the ribs that shortened rib cage muscle length, thereby reducing the contractile force. It has been reported that a 10% variation of the angle between ribs and vertebrae may lead to a 5% change in the force and work developed by intercostal muscles (54). In addition, at high lung volumes the orientation of the ribs also has a negative impact on the pleural pressure fall produced by a given cranial force applied to the ribs. This alteration in the pattern of rib motion is independent of muscle length and further inhibits rib cage muscle function. (67, 68)

By contrast, abdominal muscles lengthen with pregnancy(73). We found that they increased their contribution during maximal expiration in the upright position, as indicated by the increased abdominal contribution at T_3 during the expiratory vital capacity manoeuvre. This happened in spite of diaphragm stretching that presumably developed greater passive tension, resulting therefore in a reduced transmission of intra-abdominal pressure (P_{AB}) to the pleural cavity during abdominal muscle contraction.

ERV did not change throughout pregnancy in either the supine or the upright postures consistent with a constant lung volume at end expiration and with passive expiration during tidal breathing.

The enlarging uterus drives the pregnancy-induced changes on the diaphragm by affecting fibre length and abdominal pressure (3, 24).

It is known that the human pregnant uterus is contained in the pelvic cavity during the first trimester of pregnancy and it expands into the abdomen during the second and third trimesters. As a consequence, there is a reduction of the abdominal cavity, a marked increase of the pelvic cavity and a cranial shift of part of the abdominal organs determining diaphragmatic lengthening(2). If a material is stretched, it decreases its dimension transversal to the direction of stretching, therefore becoming thinner according to Poisson's ratio(56). The increasing abdominal pressure is applied uniformly to the abdominal surface of the diaphragm. This expands the operating length of the diaphragm during change of posture. Indeed, we showed that diaphragm thickness at end-expiration was reduced to one third compared to the upright position in both groups of women. In spite of the high inter-individual variability, the ultrasound technique was able to detect this important thinning effect of posture even on nulliparous women whose abdominal volume was significantly lower than pregnant women. In contrast, we hypothesize that the unchanged diaphragm thickness at end-expiration that we measured over pregnancy (i.e., under conditions of progressive diaphragm lengthening by the enlarging uterus), might actually be associated with an increased end-expiratory thickness (if measured at the same length). rather than to the variability introduced by measurement error, in order to progressively preserve resting muscle thickness.

The pregnancy-induced increase of ΔP_{AB} would infer an increased diaphragm inspiratory load and therefore, because the diaphragm is stretched, eccentric contraction during inspiration(52). Over time eccentric contraction of the diaphragm during tidal breathing would tend to increase diaphragm strength (23, 48), representing a form of muscle conditioning, which would be beneficial during parturition. However, in the absence of measurements of Pdi during a max inspiratory effort (Pdi max) across trimesters such observations remain mainly speculative. For ethical reasons, we did not use invasive methods in the present study.

Further studies should be designed to deeply explore the diaphragm during pregnancy in terms of length, thickness, electrical activity, action, force and their relationships to determine if the preserved diaphragmatic thickness. Based on the results of the present study, we propose a length adaptive mechanism and/or a conditioning effect resulting in the development of higher force or simply counterbalancing the decreased abdominal compliance (15).

An additional limitation of this study was the lack of follow-up after delivery. Future studies should address the duration of any observed changes and adaptations that we have found. The study has, however, several strengths, namely: a) the multidimensional parameters that have been measured in order to investigate different aspects of the pregnancy-induced changes on the respiratory function; b) the repeated measurements at each trimester of pregnancy in the entire cohort, by single operators and in the same experimental session, therefore allowing concentration of the effect of the treatments rather than the differences between individuals; c) the use of accurate and non-invasive techniques without the use of any ionizing radiation (not compatible with the condition); d) the detailed analysis of eupnoea that can be a landmark for high-risk pregnancy when the condition of the mother does not allow maximal manoeuvres; and e) the results depending only by the pure effects of pregnancy without other co-factors like obesity, because of the small weight gain in the cohort of pregnant women.

The localized increased abdominal mass in the primiparous women might be compared to ascites. The mechanical effects of ascites on respiratory muscles are well elucidated, thanks to a series of animal studies (39–42). However, in such canine model the acute effects of ascites developed over a couple of hours are studied, rather than months as during pregnancy. Acute ascites starts to have important respiratory effects after 200 mL/kg, in terms of reduced ability of both the diaphragm (39) and the abdominal muscles (41) to generate pressure, partially compensated by an increased force exerted by the parasternal intercostal muscles on the ribs (40, 42). These effects are opposite to the changes that we found during the progression of pregnancy. In addition, the threshold of 200 mL/kg would amount in 10 L of liquid for a woman of 50 kg like the primiparous. At birth, the amniotic fluid is ~ 1 L (13), the placenta is ~ 0.5 L (51) with an average baby of ~ 3.5 L. At the end of pregnancy, therefore, the amount of load/liquid in the abdomen is roughly 5 L. This estimation was supported by the 4.2 L of absolute abdominal volume increment that we found at T_3, being far below the threshold quantity to induce respiratory problems in ascites. In addition, large volume (range: 3.5-13 L) paracentesis changed neither the strength of inspiratory muscles nor thoraco-abdominal kinematics in eight cirrhotic patients, although decreasing their overload and activation (20). It appears, therefore, that the effects of pregnancy on the respiratory muscles are different from those of ascites.

The study has potential clinical implications. The co-contraction of the diaphragm and abdominal muscles, a sort of "inspiratory-expulsive manoeuvre", plays a fundamental role in the phase of baby expulsion, when the woman is asked to take deep inspirations followed by pushes, with intrauterine pressure increasing up to ~19 kPa (8). If the glottis is closed, this manoeuvre is called “close-glottis” or “Valsalva” pushing. Alternatively, the “open-glottis” pushing(9, 10, 57) implies no breath holding and slow exhalation so that P_{AB} increases to a lesser extent to avoid harmful consequence. The latter may be an ineffective strategy, in spite of the effort of the mother, because part of P_{AB} may be transmitted to the thorax through the relaxed diaphragm with possible wasting of the expulsive driving pressure and intrathoracic pressure rise to hamper venous return.

We have previously shown that expulsive manoeuvres can also be performed by simultaneous contraction of diaphragm and abdominal muscles with open glottis, so that pleural pressure does not rise and almost all P_{AB} contributes to the expulsive force, therefore more efficiently, with blood shifting in the order of 5 ml/cmH_2O increase in P_{AB} (4, 7).

We can speculate that the length adaptive mechanism and/or the conditioning effect is established to preserve the diaphragm from pregnancy-induced changes in a way to have an active role during parturition by contributing to the expulsive force, resisting the upward displacement and minimizing the raise in pleural pressure. In addition, our results helped to explain, at least in part, why upright positions are considered safer and suitable for more effective pushing (57, 61). The supine position seemed to hinder the action of abdominal muscles during forced expiration at T_3 because ERV was lower and entirely accomplished by ribcage muscles with paradoxical outward motion of the abdomen indicating less efficient action of the abdominal muscles.

Future studies should address which is the most efficient strategy and positioning of pushing that maximizes the expulsive effect of the respiratory muscles.

In conclusion, the physiological and structural adaptations of the chest wall that occur during pregnancy preserve lung volumes as well as diaphragm and abdominal muscle function at the expense of ribcage strength. Knowledge of these normal physiologic changes during pregnancy may be helpful for the clinician dealing with high-risk pregnancies.

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Conflict of interest: nothing to declare.

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Figure legend

Figure 1: Geometrical parameters computed starting from the 3D mesh of points: antero-posterior diameters (A: as the distance between the anterior and posterior central markers placed at the same vertical level), medio-lateral diameters (B: as the distance between the two extreme markers at the same vertical level on the frontal plane), perimeters (D: obtained by summing the 3D distances of all the contiguous markers placed at the same vertical level) and cross-sectional areas (E: calculated by summing the areas of the triangles, each formed by two contiguous markers and the centre of gravity of all the markers positioned at the same vertical level).

They were measured at two different vertical thoraco-abdominal levels: xiphoid process and *umbilicus*.

In addition, the subcostal angle (C: computed considering the three central markers in correspondence of xiphoid and the two lateral markers defining the subcostal line), the height of the ribcage (C: as the distance between the clavicle and the lower costal margin), of the abdomen (C: as the distance between the lower costal margin and the iliac crest) and the volumes enclosed by the mesh of points of the chest wall and its two compartments, namely the ribcage and the abdomen (F: through a triangulation of the 3D coordinates of the markers and the Gauss theorem) were also calculated.

Figure 2: Median and interquartile range (whiskers above and below the box) of spirometric forced vital capacity expressed as absolute values (a) and percentage predicted (b), slow vital capacity measured with opto-electronic plethysmography in seated (c) and supine (d) position during the first (T_1), the second (T_2) and the third (T_3) trimester of pregnancy. The short-dashed grey line and the grey area represent the median and the interquartile range, respectively, of the predicted values (a and b) or of the *nulliparous* women (c and d).

Figure 3: Median and interquartile range (whiskers above and below the box) of antero-posterior diameter (a), medio-lateral diameter (b), perimeter (d) and cross-sectional area (e) measured at xiphoidal level as well as the height of the ribcage (c), its volume (f), the subcostal angle (g) and explicative schematic diagram summarizing the ribcage geometrical changes during the first (T_1), the second (T_2) and the third (T_3) trimester of pregnancy. The short-dashed grey line and the grey area respectively represent the median and the interquartile range of *nulliparous* women.

*, **, ***: $p<0.05, 0.01, 0.001$ *vs* T_1; °, °°, °°°: $p<0.05, 0.01, 0.001$ *vs* T_2; ▪, ▪▪, ▪▪▪: $p<0.05, 0.01, 0.001$ *vs* *nulliparous* women.

Figure 4: Median and interquartile range (whiskers above and below the box) of minute ventilation, respiratory rate and tidal volume in seated (a, c, e, respectively) and supine position (b, d, f, respectively) during the first (T_1), the second (T_2) and the third (T_3) trimester of pregnancy. The short-dashed grey line and the grey area respectively represent the median and the interquartile range of *nulliparous* women.

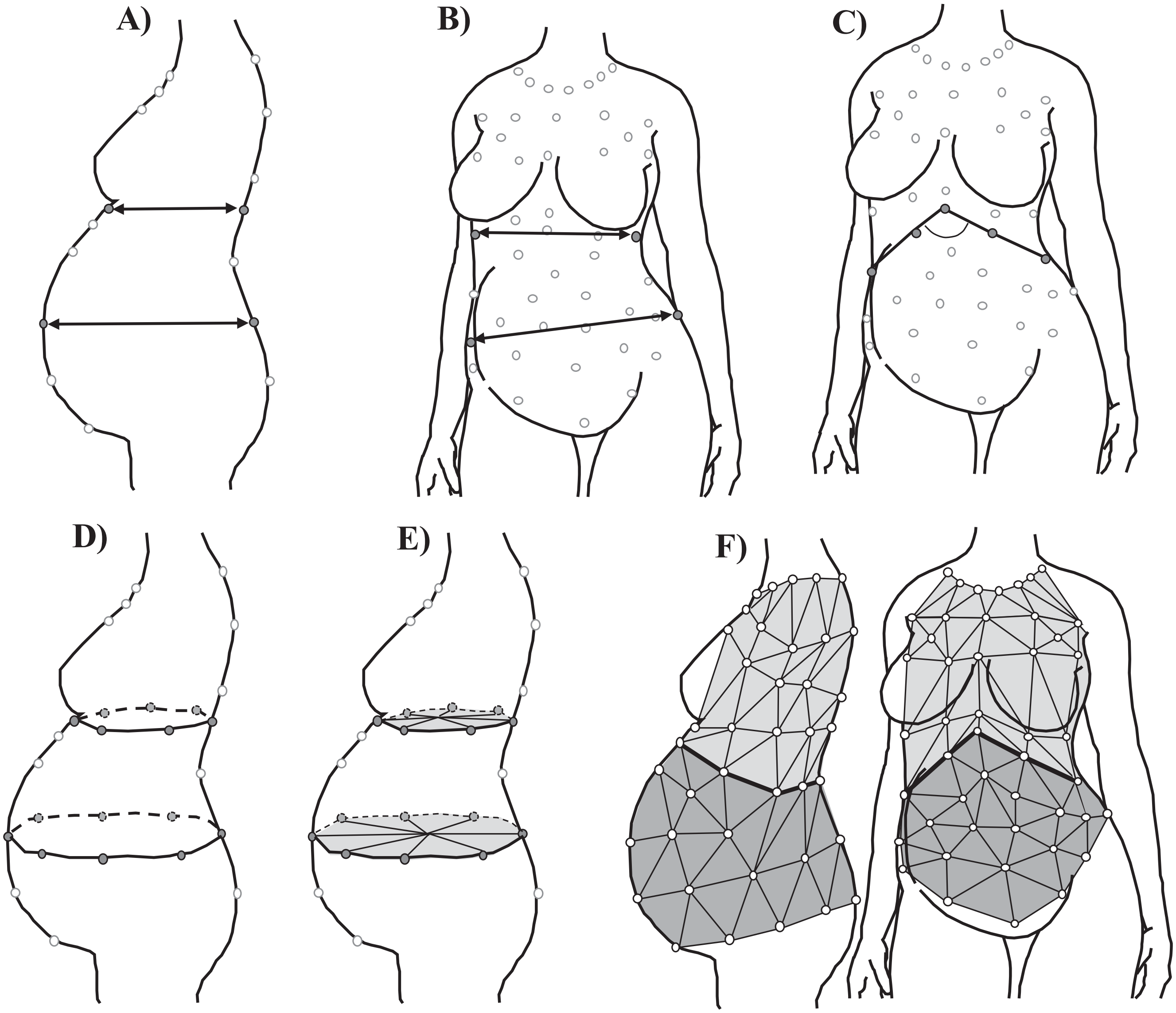
*: $p< 0.05$ *vs* T_1; ▪: $p< 0.001$ *vs nulliparous* women.

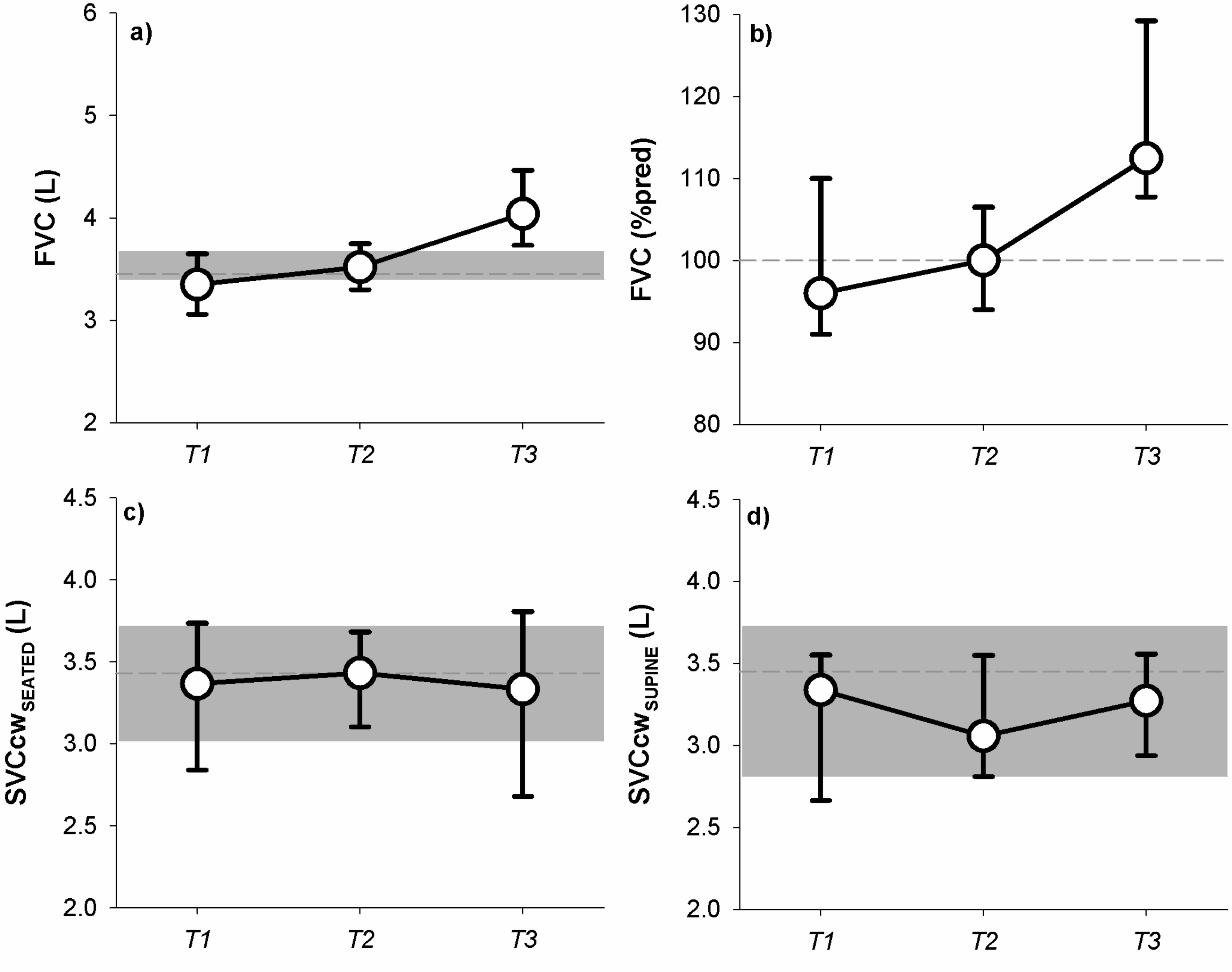
Figure 5: Median and interquartile range (whiskers above and below the box) of the abdominal percentage contribution to the tidal volume (V_T), slow vital capacity (SVC), inspiratory capacity (IC) and expiratory reserve volume (ERV) in seated (a, c, e, g, respectively) and supine position (b, d, f, h, respectively) during the first (T_1), the second (T_2) and the third (T_3) trimester of pregnancy. The short-dashed grey line and the grey area respectively represent the median and the interquartile range of *nulliparous* women.

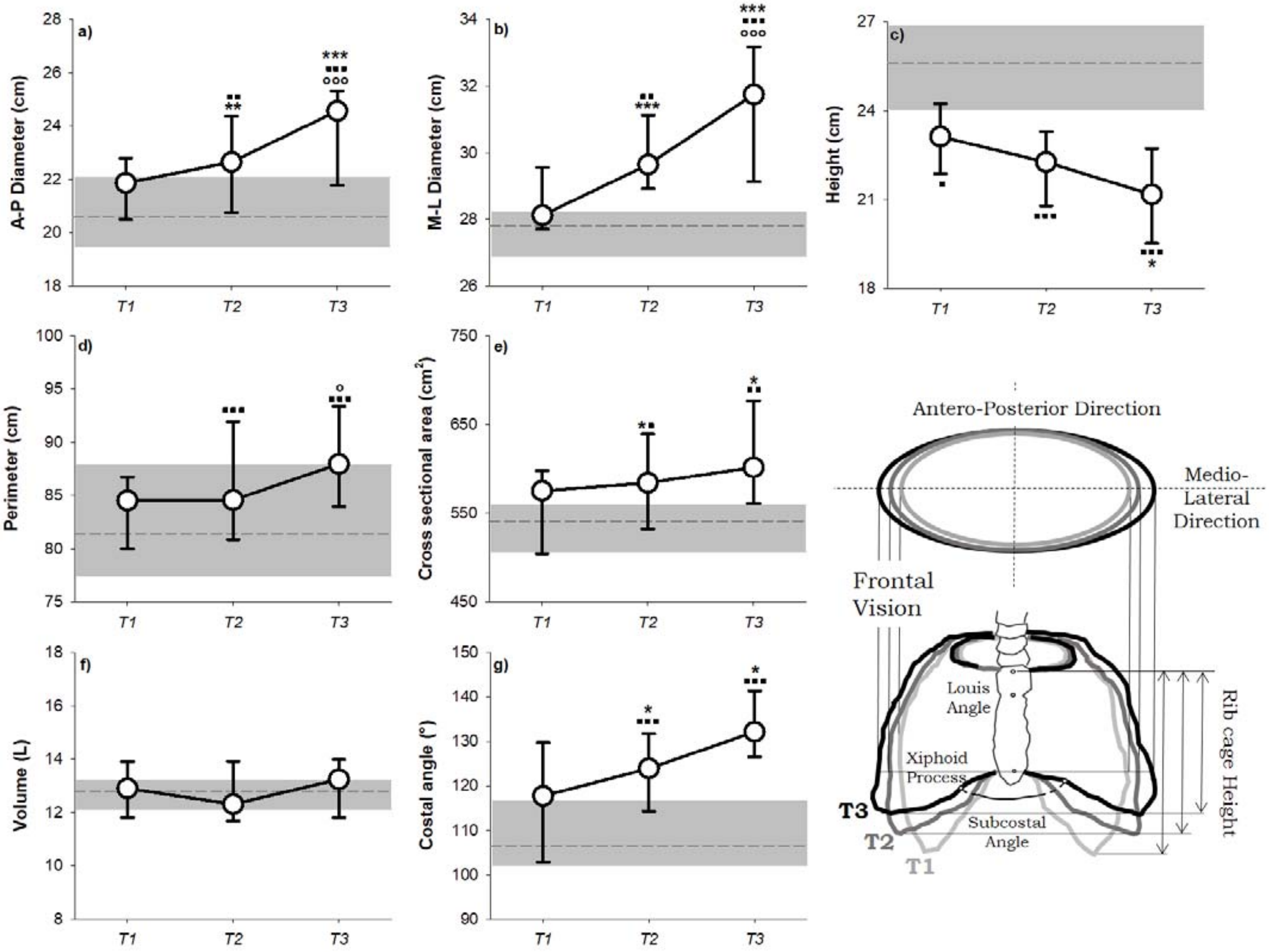
*,***: $p<0.05, 0.001$ *vs* T_1; °,°°°: $p<0.05, 0.001$ *vs* T_2; ▪,▪▪,▪▪▪: $p<0.05, 0.01, 0.001$ *vs nulliparous* women.

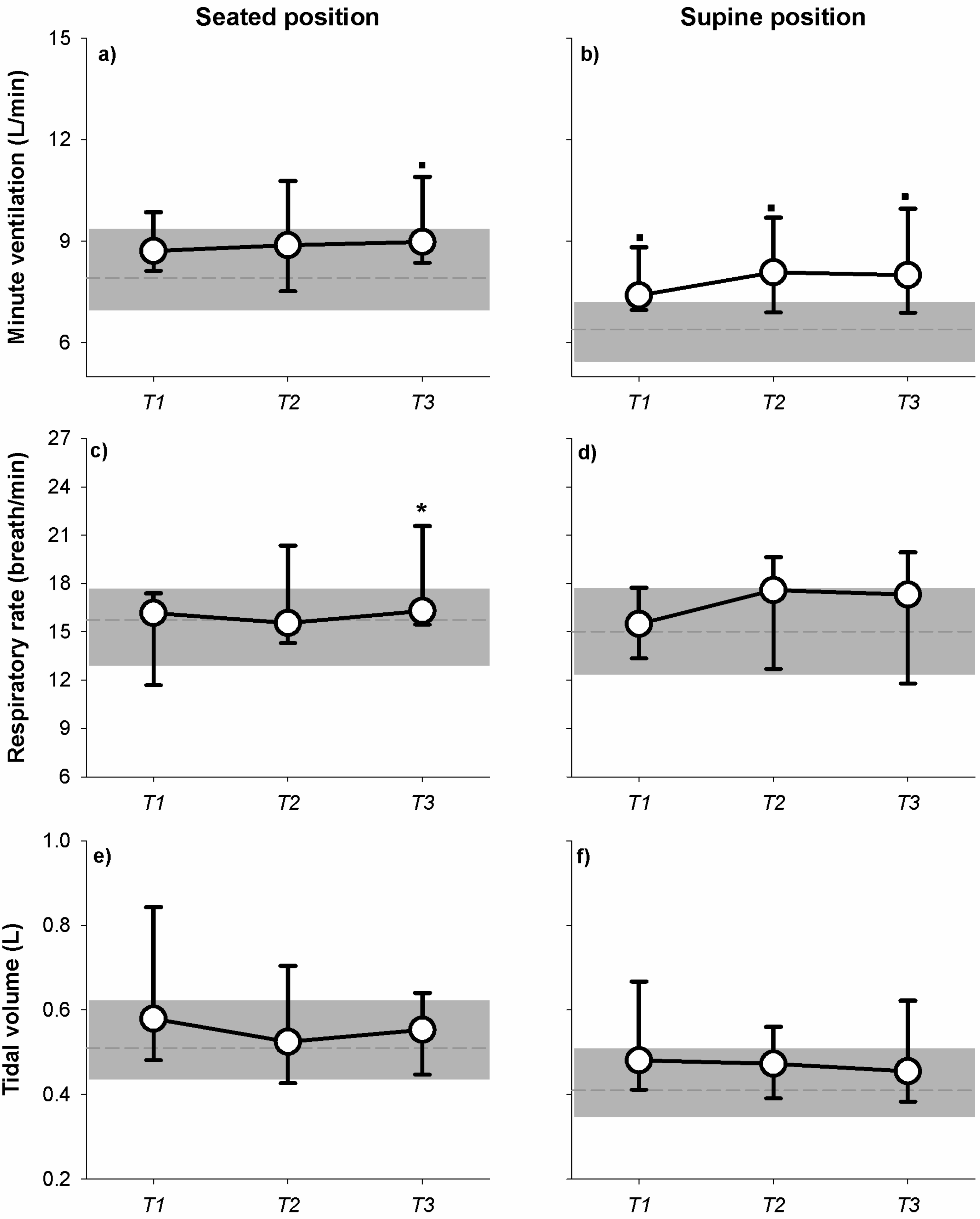
Figure 6: Median and interquartile range (whiskers above and below the box) of the thickness, thickness fraction and the dome excursion of the diaphragm in seated (a, c, e, respectively) and supine position (b, d, f, respectively) during the first (T_1), the second (T_2) and the third (T_3) trimester of pregnancy. The short-dashed grey line and the grey area respectively represent the median and the interquartile range of *nulliparous* women.

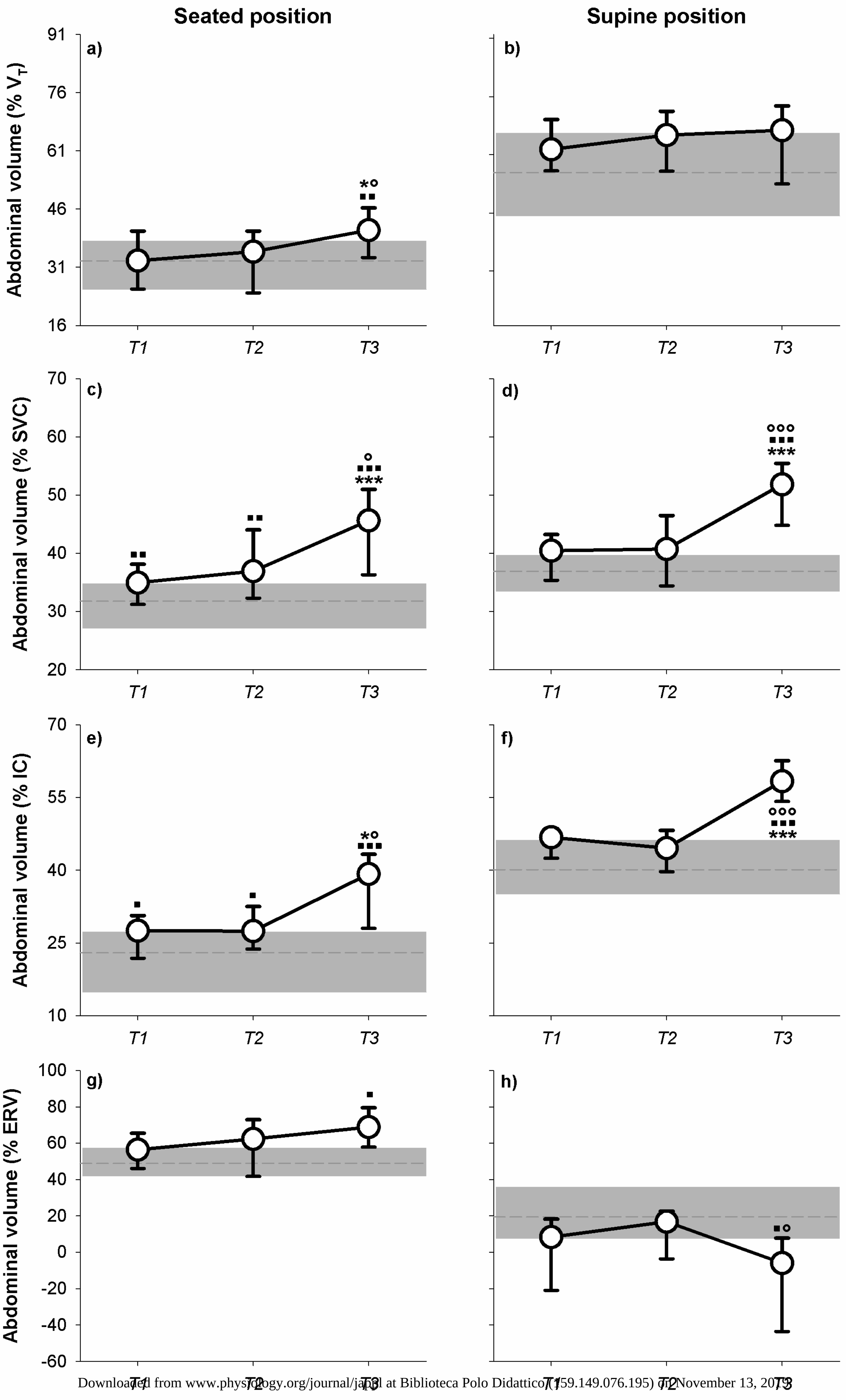
*,***: $p<0.05, 0.001$ *vs* T_1; °,°°°: $p<0.05, 0.001$ *vs* T_2; ▪,▪▪,▪▪▪: $p<0.05, 0.01, 0.001$ *vs nulliparous* women.


A)
B)
C)
D)
E)
F)


a)
FVC (L)
6
5
4
3
2
T1
T2
T3
b)
FVC (%pred)
130
120
110
100
90
80
T1
T2
T3
c)
SVCcw SEATED (L)
4.5
4.0
3.5
3.0
2.5
2.0
T1
T2
T3
d)
SVCcw SUPINE (L)
4.5
4.0
3.5
3.0
2.5
2.0
T1
T2
T3


a)
A-P Diameter (cm)
18
20
22
24
26
28
T1
T2
T3
**
***
ooo
b)
M-L Diameter (cm)
26
28
30
32
34
***
***
ooo
c)
Height (cm)
18
21
24
27
*
d)
Perimeter (cm)
75
80
85
90
95
100
o
e)
Cross sectional area (cm²)
450
550
650
750
*
*
*
f)
Volume (L)
8
10
12
14
16
18
g)
Costal angle (°)
90
100
110
120
130
140
150
*
*
Antero-Posterior Direction
Medio-Lateral Direction
Frontal Vision
Louis Angle
Xiphoid Process
Subcostal Angle
Rib cage Height
T3
T2
T1


Seated position
Supine position
Minute ventilation (L/min)
15
12
9
6
a)
b)
T1
T2
T3
Respiratory rate (breath/min)
27
24
21
18
15
12
9
6
c)
d)
*
Tidal volume (L)
1.0
0.8
0.6
0.4
0.2
e)
f)



Seated position
Supine position
Abdominal volume (% V_T)
91
76
61
46
31
16
a)
b)
*°
▪▪
T1
T2
T3
Abdominal volume (% SVC)
70
60
50
40
30
20
c)
d)
°
▪▪▪
***
°°°
▪▪▪
***
▪▪
Abdominal volume (% IC)
70
55
40
25
10
e)
f)
*°
▪▪▪
▪
°°°
▪▪▪
***
Abdominal volume (% ERV)
100
80
60
40
20
0
-20
-40
-60
g)
h)
▪°

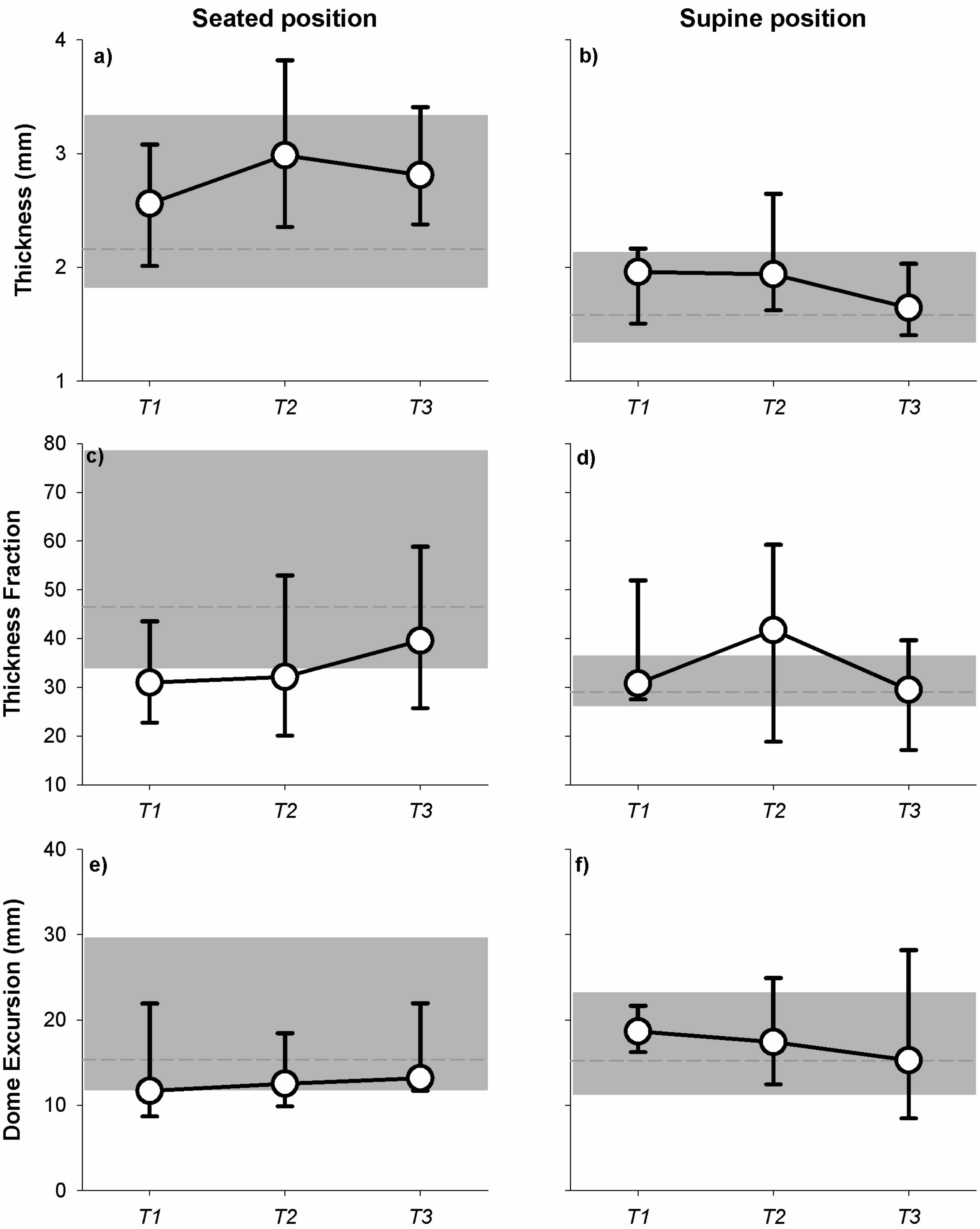

Seated position
Supine position
Thickness (mm)
Thickness Fraction
Dome Excursion (mm)
a)
b)
c)
d)
e)
f)
4
3
2
1
80
70
60
50
40
30
20
10
40
30
20
10
0
T1
T2
T3

Table 1: Anthropometric data and gestational age at each trimester of pregnancy. Data are reported as median, 25th and 75th percentiles (p25 and p75, respectively).

	Nulliparous females			**Primiparous females**											
				1st trimester				*2nd trimester*				*3rd trimester*			
	median	**p25**	**p75**	**median**		**p25**	**p75**	**median**		**p25**	**p75**	**median**		**p25**	**p75**
age (years)	26.0	25.0	26.3	32.0	§	31.0	33.5	-				-			
height (m)	1.69	1.63	1.72	1.63		1.60	1.65	-				-			
weight (kg)	57.0	54.8	63.3	57.2		53.8	62.3	59.2	***	57.6	65.0	62.3	*** °°°	60.1	69.4
BMI (kg/m^2)	20.1	19.2	22.4	21.4		20.2	22.9	22.4	***	21.3	23.3	23.4	*** °°°	22.8	25.9
gestational age (weeks)	-			15.0		13.8	17.0	21.0		21.0	22.0	31.5		31.0	32.0

BMI: body mass index computed as weight/height^2

*** : $p<0.001$ vs 1st trimester; °°° : $p<0.001$ vs 2nd trimester; §: $p<0.05$ vs *nulliparous*