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Intrapartum sonographic assessment of the fetal head flexion in protracted active phase of labor and association with labor outcome: a multicenter, prospective study

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American Journal of Obstetrics and Gynecology

Intrapartum sonographic assessment of the fetal head flexion in protracted active phase of labor and association with labor outcome: a multicentre, prospective study. --Manuscript Draft--

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| Manuscript Region of Origin: | ITALY |
| Abstract: | <p>Background</p> <p>To date no research has focused on the sonographic quantification of the degree of flexion of the fetal head in relation to the labor outcome in women with protracted active phase of labor.</p> <p>Objective</p> <p>To assess the relationship between the transabdominal sonographic indices of fetal head flexion and the mode of delivery in women with protracted active phase of labor.</p> <p>Study design</p> <p>Prospective evaluation of women with protracted active phase of labor recruited across three tertiary maternity units. Eligible cases were submitted to transabdominal ultrasound for the evaluation of the fetal head position and flexion, which was measured by means of the occiput-spine angle (OSA) in fetuses in non-occiput posterior (OP) position and by means of the chin-to-chest angle (CCA) in fetuses in OP</p> |

position. The OSA and the CCA were compared between women who had vaginal delivery vs those who had cesarean delivery. Cases where obstetric intervention was performed solely based on suspected fetal distress were excluded.

Results

129 women were included, of whom 43 (33.3%) had OP position. Spontaneous vaginal delivery, instrumental delivery and cesarean delivery were recorded in 66 (51.2%), 17 (13.1%) and 46 (35.7%) cases, respectively. A wider OSA was measured in women who had vaginal delivery compared to those submitted to cesarean delivery due to labor dystocia (126 + 14 vs 115 + 24, $p < 0.01$). At ROC curve the area-under-the-curve (AUC) was 0.675, 95%CI (0.538-0.812), $p < 0.01$, and the optimal OSA cut-off value discriminating between cases of vaginal delivery vs those delivered by cesarean delivery was 109 degrees. A narrower CCA was measured in cases who had vaginal delivery compared to those undergoing cesarean delivery (27 + 33 vs 56 + 28 degrees, $p < 0.01$). The AUC of the CCA in relation to the mode of delivery was 0.758, 95%CI (0.612-0.904), $p < 0.01$, and the optimal cut-off value discriminating between vaginal delivery and cesarean delivery was 33.0 degrees.

Conclusions

In women with protracted active phase of labor, the sonographic demonstration of fetal head deflexion in OP and in non-OP fetuses is associated with an increased incidence of cesarean delivery due to labor dystocia. Such findings suggest that intrapartum ultrasound may contribute in the categorization of the etiology of labor dystocia.

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Parma, 05/02/2020

To the Editor in Chief

American Journal of Obstetrics & Gynecology

Professor Roberto Romero

Dear Professor Romero,

We hereby enclose the revised version of our manuscript entitled "Intrapartum sonographic assessment of the fetal head flexion in protracted active phase of labor and association with labor outcome: a multicentre, prospective study." for consideration for publication in the American Journal of Obstetrics & Gynecology.

In this revised version we have addressed the Reviewers' comments and added a figure (Figure 5) showing the findings of a sub-analysis evaluating the relationship between the OSA and the sonographic indicators of head station in non-OP fetuses with favorable head flexion. Overall, we genuinely believe that the quality of the manuscript has improved and thank the Reviewers for their inputs.

The manuscript has been formatted according to the Journal Guidelines for Original Research articles.

This work is novel, has not been reported elsewhere and is not under consideration by another journal.

All the Authors have contributed significantly and are in agreement with the content of the manuscript.

There are no financial disclosures nor financial support or relationships that may pose potential conflict of interest.

Thank you in advance for your consideration.

Sincerely yours,

Andrea Dall'Asta

Tullio Ghi

1 **TITLE PAGE**

2 **Intrapartum sonographic assessment of the fetal head flexion in protracted active phase of labor**
3 **and association with labor outcome: a multicentre, prospective study.**

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25 **Condensation:**

26 The sonographic indicators of deflexed fetal head are associated with labor dystocia leading to
27 caesarean delivery in women with protracted active phase of labor.

28

29 **Short title:**

30 Intrapartum US in protracted active phase of labor.

31

32 **AJOG at a glance**

33 A.Why was the study conducted?

- 34 • To evaluate the relationship between the intrapartum sonographic indicators of fetal head
35 flexion and the mode of delivery in women with protracted active phase of labor.

36 B.What are the key findings?

- 37 • A wide occiput-spine angle and a narrow chin-chest angle are associated with an increased
38 incidence of vaginal delivery. A correlation between the occiput-spine angle and the
39 sonographic indicators of fetal head station was also demonstrated.

40 C.What does this study add to what is already known?

- 41 • The sonographic indicators of fetal head flexion are associated with labor dystocia leading
42 to cesarean delivery in women with protracted active phase of labor. The findings from this
43 study suggest that intrapartum ultrasound may contribute in the categorization of the
44 etiology of labor dystocia.

45

46 **Keywords**

47 Ultrasound in labor, labor dystocia, intrapartum care, caesarean delivery, instrumental delivery,
48 occiput-spine angle, chin-chest angle, angle of progression, head-perineum distance.

49

50 **Abstract**

51 **Background**

52 To date no research has focused on the sonographic quantification of the degree of flexion of the
53 fetal head in relation to the labor outcome in women with protracted active phase of labor.

54 **Objective**

55 To assess the relationship between the transabdominal sonographic indices of fetal head flexion
56 and the mode of delivery in women with protracted active phase of labor.

57 **Study design**

58 Prospective evaluation of women with protracted active phase of labor recruited across three
59 tertiary maternity units. Eligible cases were submitted to transabdominal ultrasound for the
60 evaluation of the fetal head position and flexion, which was measured by means of the occiput-
61 spine angle (OSA) in fetuses in non-occiput posterior (OP) position and by means of the chin-to-
62 chest angle (CCA) in fetuses in OP position. The OSA and the CCA were compared between women
63 who had vaginal delivery vs those who had cesarean delivery. Cases where obstetric intervention
64 was performed solely based on suspected fetal distress were excluded.

65 **Results**

66 129 women were included, of whom 43 (33.3%) had OP position. Spontaneous vaginal delivery,
67 instrumental delivery and cesarean delivery were recorded in 66 (51.2%), 17 (13.1%) and 46 (35.7%)
68 cases, respectively. A wider OSA was measured in women who had vaginal delivery compared to
69 those submitted to cesarean delivery due to labor dystocia (126 ± 14 vs 115 ± 24 , $p<0.01$). At ROC
70 curve the area-under-the-curve (AUC) was 0.675, 95%CI (0.538-0.812), $p<0.01$, and the optimal OSA
71 cut-off value discriminating between cases of vaginal delivery vs those delivered by cesarean
72 delivery was 109 degrees. A narrower CCA was measured in cases who had vaginal delivery
73 compared to those undergoing cesarean delivery (27 ± 33 vs 56 ± 28 degrees, $p<0.01$). The AUC of the

74 CCA in relation to the mode of delivery was 0.758, 95%CI (0.612-0.904), $p < 0.01$, and the optimal
75 cut-off value discriminating between vaginal delivery and cesarean delivery was 33.0 degrees.

76 **Conclusions**

77 In women with protracted active phase of labor, the sonographic demonstration of fetal head
78 deflexion in OP and in non-OP fetuses is associated with an increased incidence of cesarean delivery
79 due to labor dystocia. Such findings suggest that intrapartum ultrasound may contribute in the
80 categorization of the etiology of labor dystocia.

81 **Introduction**

82 Labor dystocia is estimated to account for approximately one third of all caesarean deliveries, the
83 vast majority being primary cesarean deliveries (1,2). Among these, arrest of dilatation in the first-
84 stage of labor is acknowledged to represent the most common indication (3,4). Such condition may
85 result from distinct but potentially coexisting mechanisms which include abnormalities of the
86 uterine contractions, malpositions or malpresentations of the fetal head and cephalopelvic
87 disproportion (5-13).

88 The progression of the first-stage of labor has been historically assessed by means of the norms of
89 active phase dilatation described by Friedman (14-26) and more recently re-evaluated by Zhang et
90 al. (1,27,28). These latter, which show a slow but progressive first-stage dilatation prior to 6 cm and
91 an overall slower course of labor compared to Friedman's sigmoid curve (14-17,23,25,26), are
92 currently endorsed for labor management by the American College of Obstetricians and
93 Gynecologists and by the Society for Maternal and Fetal Medicine (4,29). The active phase dilatation
94 is positively affected by the descent of the fetal head in the birth canal, and in normal labor a direct
95 correlation between the first-stage dilatation and the descent of the fetal head has been
96 demonstrated (30). The engagement and the progression of the fetal head through the birth canal
97 in the first-stage of labor are known to be to be influenced by the mechanism of head flexion –
98 which allow the shortest cephalic diameters to negotiate the maternal pelvis (5,6).

99 Available data suggests that ultrasound outweighs the digital examination in the assessment of the
100 fetal head station (31,32), progression and attitude, and ultrasound is currently endorsed as an
101 adjunct to the clinical evaluation in conditions of protracted active phase of labor and arrest of
102 dilatation (31). Under these circumstances, the sonographic indicators of the fetal head station
103 including the head-perineum distance (HPD) and the angle of progression (AoP) have been shown
104 to be more accurate than the digital examination in predicting the occurrence of cesarean delivery

105 (33-35). In an unselected group of women in the active phase of labor with occiput anterior and
106 occiput transverse fetuses the degree of fetal head flexion measured at transabdominal ultrasound
107 has been shown to be associated with the digital station and the likelihood of operative delivery
108 (36). Other sonographic studies have demonstrated that also in fetuses in occiput posterior (OP)
109 position the qualitative assessment of the fetal head deflexion is related to the chance of vaginal
110 delivery (37,38). To date no research has focused on the sonographic quantification of the degree
111 of flexion of the fetal head in relation to the labor outcome in women with protracted active phase
112 of labor. The aim of this study was to evaluate the relationship between the intrapartum ultrasound
113 indicators of malposition and malpresentation and the risk of obstetric intervention within a
114 selected cohort of women diagnosed with a protracted active phase of labor.

115 **Methods**

116 Study design

117 This was a prospective, observational study conducted between December 2018 and June 2020 and
118 including three maternity units in Italy (University Hospitals of Parma and Rome Tor Vergata and
119 Sant'Anna Hospital of Turin). A non-consecutive series of non-anomalous singleton term
120 pregnancies, with no history of previous uterine scar and with a protracted active phase of labor
121 was included. According to the local protocol of the participating Units, women diagnosed with
122 protracted active phase of labor are submitted to clinical examination by the senior Obstetrician
123 responsible for the patient care. For the present study, following the clinical diagnosis of protracted
124 active phase of labor intrapartum ultrasound was performed for research purposes also by five
125 investigators with dedicated training on ultrasound in labor (AD, TG, EDP, BM and GR) who were
126 not involved in the clinical management. The senior Obstetricians in charge for the labor care were
127 blinded to the ultrasound findings.

128 According to the protocol for the labor management adopted across the participating Units,
129 protracted active phase of labor was defined based on the ACOG/SMFM recommendations for the
130 safe prevention of the primary cesarean delivery (4). In details, a protracted active phase of labor
131 was defined in women ≥ 6 cm of dilatation with ruptured membranes who fail to progress despite 4
132 hours of adequate uterine activity or at least 6 hours of oxytocin administration with inadequate
133 uterine activity and no first-stage dilatation. In such cases, the arrest of dilatation requiring cesarean
134 delivery was defined following two more hours of oxytocin administration with no cervical change.
135 In the case of progression of the first-stage dilatation, obstetric intervention was indicated during
136 the first-stage in the event of the above criteria, while the diagnosis of arrest of labor in the second
137 stage was made in the event of a duration of the active phase of at least two hours in multiparous
138 women or three hours in nulliparous women, in accordance with the ACOG/SMFM

139 recommendations (4).With regards to instrumental vaginal delivery, the use of forceps is not
140 performed as part of routine clinical practice in the participating Units. Obstetric intervention – i.e.
141 cesarean delivery or vacuum extraction – due to suspected intrapartum fetal compromise
142 represented an exclusion criterion for the study. All the obstetric interventions were performed
143 according to a commonly shared management protocol when the criteria for arrest of dilatation or
144 arrest of labor in the second stage were fulfilled (4).

145 Clinical data including maternal age, ethnicity, body mass index, gestational at delivery, induced or
146 spontaneous labor, epidural analgesia, augmentation during labor, length of the first and of the
147 second stage of labor, head station and cervical dilatation at diagnosis of protracted active phase of
148 labor as well as mode of delivery, estimated blood loss, birthweight, 5 minutes APGAR and arterial
149 pH was collected from patient case notes.

150 Intrapartum ultrasound performed for research purposes

151 Portable ultrasound devices equipped with low frequency transabdominal probe were used for the
152 study purposes. The US measurements were performed on women lying in semirecumbent position
153 with an empty bladder. Transabdominal US was performed by placing the probe transversely over
154 the maternal suprapubic region to assess the position of the fetal head, while the flexion was
155 evaluated by tilting the probe by 90 degrees to the longitudinal plane. The position was defined
156 from the landmarks depicting fetal occiput and described as a clock face with 12 hourly divisions.
157 Positions >09:30 and <2:30 o'clock were classified as occiput anterior, while occiput transverse and
158 occiput posterior (OP) were defined in the case of occiput ≥ 02.30 and ≤ 03.30 o'clock or ≥ 08.30 h
159 and ≤ 09.30 o'clock and >03.30 and <08.30 o'clock, respectively (31,39).

160 Based on our experience no ultrasound parameter has the potential to objectively evaluate the
161 degree of head flexion for all the positions of the fetal occiput. The flexion of the fetal head was
162 quantitatively defined by means of the occiput-spine angle (OSA) for the fetuses in occiput anterior

163 and occiput transverse position and by means of the chin-to-chest angle (CCA) for the fetuses in OP
164 position. In details, the OSA was identified by the angle between a line tangent to the posterior
165 cervical spine and a second line tangent to the fetal occiput, as previously described (36) (Figure 1).
166 The CCA was defined as the angle identified by the intersection between one line through the
167 longest axis of the sternum and a second line through another straight structure represented by the
168 skin covering the inferior boundary of the oral cavity up to the chin (Figure 2).
169 Transperineal ultrasound was performed with the transducer placed in a transverse or longitudinal
170 position between the labia majora or more caudally at the level of the fourchette and allowed the
171 measurement of the sonographic indicators of fetal head station and descent. The head-perineum
172 distance (HPD) was assessed by placing the probe in the posterior fourchette and applying a gentle
173 but firm pressure on the perineum as previously described (40). The angle of progression (AoP) was
174 measured on the midsagittal image by drawing one line between calipers placed at the two points
175 identifying the long axis of the pubic symphysis; a second caliper line was then created on the frozen
176 image that extended from the most inferior portion of the pubic symphysis tangentially to the fetal
177 skull contour (41). All the measurements were obtained in the absence of uterine contractions
178 and/or maternal pushing efforts.

179 Endpoints

180 The primary outcome of the study was to evaluate the sonographic indicators of fetal head flexion,
181 i.e. the OSA and the CCA in fetuses in non-OP and in OP position, respectively, as measured at
182 diagnosis of protracted active phase of labor in relation to the mode of delivery and other labor
183 outcomes. Furthermore, we evaluated the relationship between the OSA and the CCA and the
184 transperineal sonographic indicators of fetal head descent.

185 Ethics approval

186 Ethics approval for this study was granted by the local Ethics Committee at the University Hospitals
187 of Parma (N 270/2018/OSS/UNIPR on 03/12/2018) and Rome Tor Vergata (N 17/Ob2 on
188 15/10/2017) and at the Sant'Anna Hospital of Turin (N 0061542 on 21/06/2017).

189 Statistical analysis

190 Statistical analysis was performed using SPSS version 20 (IBM Inc., Armonk, NY, USA). Normal or
191 abnormal distribution of continuous variables was evaluated by means of the Kolmogorov-Smirnov
192 and the Shapiro-Wilk tests and data were shown as mean \pm standard deviation or as median (range)
193 accordingly. Comparison of normally and non-normally distributed continuous variables included
194 the T test for independent sample and 2-tailed t test and the Mann-Whitney U-test, respectively.
195 Categorical variables were reported as number (percentage) and compared using the Chi-square or
196 Fisher exact test. Logistic regression analysis was used to control for potential confounding
197 variables, while the prediction of the mode of delivery by intrapartum sonographic parameters was
198 determined by receiver operating characteristic (ROC) curve analysis. $p < 0.05$ was considered as
199 significant. This study was conducted following the STROBE guidelines (42).

200 **Results**

201 Overall, 129 women were included (Figure 3). The transabdominal and transperineal ultrasound
202 examination was successfully performed in all the eligible cases. Baseline and obstetrical features
203 of our cohort population are shown in Table 1. Spontaneous vaginal delivery occurred in 66 (51.2%)
204 women, while instrumental vaginal delivery and cesarean delivery were recorded in 17 (13.1%) and
205 46 (35.7%), cases, respectively. The mean length of the first and second stage of labor was $495 \pm$
206 171 minutes and 107 ± 52 minutes, respectively. No case of failed instrumental delivery requiring
207 emergency cesarean delivery was recorded. At diagnosis of protracted active phase of labor occiput
208 anterior, occiput transverse and OP positions accounted for 59 (45.8%), 27 (20.9%) and 43 (33.3%)
209 of the included cases.

210 Clinical and sonographic findings in fetuses in non-occiput posterior position are shown in Table 2a.
211 A wider OSA (126 ± 14 vs 115 ± 24 degrees, $p=0.006$) and AoP (118 ± 13 vs 104 ± 11 degrees, $p<0.001$)
212 and a shorter HPD (40 ± 5 vs 49 ± 9 mm, $p<0.001$) were measured in women who had vaginal delivery,
213 however only the OSA and the HPD proved to be independently associated with the mode of
214 delivery at logistic regression analysis ($p=0.007$ and $p=0.001$, respectively) (Table 3a). At ROC curve
215 the OSA was found to be associated with an area-under-the-curve (AUC) of 0.675, 95%CI (0.538-
216 0.812), $p<0.01$. The optimal cut-off value of the OSA discriminating between cases of VD vs those
217 delivered by CS was 109 degrees, and was associated with a 56.7% sensitivity, 87.5% specificity,
218 70.8% PPV and 79.0% NPV. When addressing the correlation between the OSA and the sonographic
219 indicators of fetal head station, the OSA showed a direct correlation with the AoP (Pearson's
220 correlation 0.449, $p<0.01$) but no correlation with the HPD ($p=0.15$). At visual analysis of the
221 scatter/dot charts (Figure 4), 9 cases in which the AoP of progression was not positively correlated
222 with the OSA were noted and labelled as outliers. Such cases showing a narrow AoP and a wide OSA
223 were all submitted to cesarean delivery and characterized by a lower maternal height (157 ± 7 vs

224 163±6 cm, p<0.01) and a higher ratio between the birthweight and the maternal height (22.6±1.6
225 vs 20.7±2.6, p=0.04) compared to the non-outlier cases.

226 When considering only the 62 non-OP fetuses with OSA width above 109 degrees – i.e. with
227 favorable head flexion –, such outlier cases accounted for 9/13 cesarean deliveries. Outlier cases
228 showed a higher ratio between the OSA and the AoP (1.45±0.19 vs 1.09±0.10, p<0.001) and a lower
229 ratio between the OSA and the HPD (2.60±0.46 vs 3.40±0.50, p<0.001) compared to non-outliers.
230 The distribution of the OSA/AoP ratio in relation to the mode of delivery showed a trend towards
231 an increased rate of CS with increasing OSA/AoP ratio (Figure 5a), while a trend towards an
232 increased rate of CS was noted with decreasing OSA/HPD ratio (Figure 5b). At ROC curve the
233 OSA/AoP ratio was found to be associated with an AUC for the prediction of cesarean delivery of
234 0.769, 95%CI (0.586-0.952), p=0.003, while the OSA/HPD ratio was associated with an AUC of 0.778,
235 95%CI (0.631-0.925), p=0.002. The optimal cut-off value of the OSA/AoP ratio discriminating
236 between cases of VD vs those delivered by CS was 1.20, and was associated with a 69.2% sensitivity,
237 87.8% specificity, 60.0% PPV and 91.5% NPV; the optimal cut-off value of the OSA/HPD ratio
238 discriminating between cases of VD vs those delivered by CS was 3.05, and was associated with a
239 69.2% sensitivity, 77.6% specificity, 45.0% PPV and 90.5% NPV.

240 The clinical and the sonographic findings in fetuses in OP position are shown in Table 2b. A narrower
241 CCA (27±33 vs 56±28 degrees, p=0.005) and a lower rate of induction of labor (22.2% vs 62.5%,
242 p=0.008) were found in women who had vaginal delivery. At logistic regression analysis CCA and
243 labor induction proved to be independently associated with the mode of delivery (p=0.008 and
244 p=0.007, respectively, Table 3b). At ROC curve the CCA was associated with an area-under-the-curve
245 (AUC) for the mode of delivery of 0.758, 95%CI (0.612-0.904), p<0.01. The optimal cut-off value of
246 the CCA discriminating between cases of VD vs those delivered by CS was 33.0 degrees, which was

247 associated with a 93.8% sensitivity, 63.0% specificity, 60.0% PPV and 94.4% NPV. No correlation was
248 found between the CCA and the AoP ($p=0.48$) nor the HPD ($p=0.98$).

249 **Discussion**

250 Principal findings

251 The results from this study conducted on a selected cohort of women with protracted active phase
252 of labor demonstrate that the degree of flexion of the fetal head as measured at transabdominal
253 ultrasound is related to the mode of delivery in OP as well as in non-OP fetuses, being head deflexion
254 associated with an increased risk of cesarean delivery due to labor dystocia. Furthermore, fetal head
255 station as measured at transperineal ultrasound by means of the HPD is independently associated
256 with the likelihood of vaginal delivery in non-OP fetuses. Finally, in non-OP fetuses the degree of
257 fetal head flexion correlates with the transperineal sonographic indicators of fetal head station.

258 Results in the context of what is known

259 The relationship of fetal head to spine – also referred to as “fetal attitude” – in the first-stage of
260 labor has traditionally been considered to impact on fetal head descent and ultimately on labor
261 outcome. Deflexed cephalic presentations are acknowledged to represent major determinants of
262 obstructed labor (7,8,36). According to the mechanics of the human labor the descent of the
263 presenting part through the birth canal is associated with a progressive flexion of the fetal head on
264 the chest (5). On this basis, previous data from an unselected population of non-OP fetuses
265 suggested that cephalic malpresentations in terms of deflexed fetal head are associated with a
266 higher clinical station and an increased likelihood of obstetric intervention secondary to intrapartum
267 dystocia (36). Consistently, a recent research conducted on 200 women found an increased
268 incidence of cesarean delivery in fetuses showing sonographic features of head deflexion (43). In
269 this study the degree of fetal head flexion was measured by means of the OSA in non-OP fetuses,
270 while in OP fetuses a qualitative assessment of the fetal attitude was performed. However, this
271 research did not include cases of labor dystocia, and the participating women were recruited at full
272 cervical dilatation and not during the first-stage of labor (43).

273 Some studies previously evaluated the risk of obstetric intervention secondary to labor dystocia in
274 relation to the position and the station of the fetal head at diagnosis of protracted active phase of
275 labor (33-35,44-47). Under these circumstances, an increased likelihood of cesarean delivery due to
276 labor dystocia was reported in fetuses with OP position and a high fetal station at transperineal
277 ultrasound as demonstrated by a long HPD and a narrow AoP. Our study has confirmed a similar
278 relationship between the sonographic indicators of fetal head station and the mode of delivery in
279 fetuses in non-OP position but not in those in OP position, among whom labor induction proved to
280 be independently associated with the likelihood of cesarean delivery.

281 Clinical implications

282 According to the recommendations of the International Society on Ultrasound in Obstetrics and
283 Gynecology, intrapartum ultrasound is indicated in conditions of first-stage dystocia (31). Based on
284 the findings from this study, the evaluation of the degree of flexion of the fetal head might be
285 incorporated in the sonographic evaluation of cases of protracted active phase of labor. However,
286 it is uncertain whether in such conditions the use of ultrasound can lead to an individualized
287 management in terms of increased augmentation in the case of favorable conditions in terms of
288 good head flexion and, conversely, anticipated caesarean delivery in the case of malpresentation
289 with or without malposition of the presenting part.

290 Research implications

291 Based on our results, we believe that also subtle degrees of deflexion of the fetal head may preclude
292 its descent through the birth canal by impairing the most favorable (suboccipito-bregmatic)
293 diameter of the fetal head to negotiate the pelvic inlet, thus leading to dystocia requiring cesarean
294 delivery (5,6).

295 Furthermore, this present study suggests that our ability in understanding the underlying cause of
296 protracted active phase of labor may be improved thanks to the use of ultrasound. The finding of

297 outlier cases requiring cesarean delivery due to labor dystocia and characterized by a high head
298 station (as witnessed by the narrow AoP and the long HPD) and no evidence of malposition and
299 malpresentation (i.e. non-OP position and wide OSA) may be interpreted in terms of cephalo-pelvic
300 disproportion. This hypothesis is supported by the fact that such cases were characterized by a lower
301 maternal height and by a higher birthweight-to-maternal height ratio in comparison to “non-
302 outliers”. We do envisage that in these conditions any attempt to perform an instrumental vaginal
303 delivery should be balanced against the risks of “true” obstructed labor. However, more research is
304 required in order to clarify whether the head circumference (48,49), the maternal height (50-53) or
305 other sonographic indices may be considered in the individualized management of the laboring
306 woman diagnosed with protracted active phase of labor in cases characterized by non-OP position,
307 wide OSA, narrow AoP and long HPD.

308 With regards to the degree of flexion of the fetal head in OP fetuses, ours is the first study describing
309 a quantitative parameter – i.e. the CCA – for the assessment of the degree of flexion of the fetal
310 head, which we show to be associated with a fair sensitivity and NPV in the prediction of CS due to
311 labor dystocia. The low specificity and positive predictive value of the CCA suggest that the degree
312 of flexion of the fetal head may vary across labor and may not represent the only determinant of
313 labor arrest in OP fetuses.

314 While we first describe the CCA as a sonographic indicator of flexion in OP fetuses, no correlation
315 could be demonstrated between the CCA and the AoP nor the HPD. This is likely to be dependent
316 on the different – and thus far unexplored – mechanics of the fetal head descent in OP compared
317 to the non-OP fetuses.

318 Strengths and limitations

319 This is the first study evaluating the sonographic indices of fetal head flexion which can be measured
320 on transabdominal ultrasound in women with protracted active phase of labor. Another strength is

321 that this study was prospectively conducted at three Units with dedicated expertise in intrapartum
322 ultrasound, which has allowed the collection of several ultrasound parameters within a selected
323 population of women at risk of cesarean delivery due to protracted active phase of labor.

324 With regards to the limitations, we acknowledge that our cohort was not powered for adverse
325 maternal and perinatal outcomes. Therefore, more research is warranted in order to understand
326 whether the deflexion of the fetal head in conditions of protracted active phase of labor impacts on
327 maternal and fetal outcomes other than on the mode of delivery. Another limitation is represented
328 by the fact that the measurement of the CCA may be challenging, and its intra- and inter-observer
329 reproducibility was not preliminary tested. However, it is important to note that all the research
330 scans were performed by a small number of investigators with expertise on ultrasound in labor,
331 therefore we believe that in such context a variability in the CCA measurements is highly unlikely.
332 Therefore, it is uncertain whether the use of such sonographic parameter can be easily implemented
333 outside the context of Units with expertise on ultrasound in labor such as those participating to this
334 present study. We acknowledge that additional malpresentations such as asynclitism, which are
335 known to impact the labor course (54-60), were not evaluated in this study. Such limitation needs
336 to be taken into account in a clinical context where different types of malpresentation may coexist
337 and contribute in determining a protracted active phase of labor.

338 Finally, the “non-consecutive” enrolment may be accounted as a potential source of bias, even
339 though we believe that the wide number of the enrolled patients together with the strict inclusion
340 criteria allow to overcome such potential limitation.

341 Conclusions

342 In conclusion, this work shows that within a selected cohort of women with protracted active phase
343 of labor, the evaluation of the sonographic indices of fetal head flexion is associated with the
344 incidence of labor dystocia leading to cesarean delivery in OP as well as in non-OP fetuses, while the

345 head station is related to the mode of delivery in non-OP but not in OP fetuses. This research
346 supports the sonographic assessment of the degree of flexion of the presenting part in conditions
347 of protracted active phase of labor, and suggest that intrapartum ultrasound may contribute in the
348 categorization of the etiology of the dystocia and support the individualized management of
349 conditions of protracted active phase of labor.

350 **Conflict of interest statement**

351 The Authors state no financial disclosures nor conflict of interest related to the content of this
352 research.

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511 2016 Sep 13.

Intrapartum sonographic assessment of the fetal head flexion in protracted active phase of labor and association with labor outcome: a multicentre, prospective study.

Reply to the Reviewers:

Reviewer #1: The manuscript has improved, and the authors have responded adequately to most comments.

Reviewer #1, POINT 1

A. I have some concerns related to line 221 to 231. Nine outliers (red spots indicating cesarean deliveries) in the scatter plots in figure 4 have been subjectively removed. In all 30 cesarean deliveries occurred in non-OP positions. Subjective removal of 30% and thereafter calculate prediction is not appropriate. The removed cases had only a modest difference in maternal height. The birth weight was not known at the time of decision of delivery mode, and should not be part of explaining why these cases were removed.

B. We thank the Reviewer for the comment. It is true that the “subjective removal” of outlier cases is not appropriate, however such attempt was made following on of the previous Reviewers’ comments, which we herein report:

“The authors may be the first to quantitate the sonographic angle of flexion, but the positive and negative predictive values (PPV and NPV) are not high enough to seem of much help to the clinician. For example, $30/86 = 35\%$ of fetuses in OA/OT position in this study were delivered by cesarean, whereas if the OSA was at least 108.5 degrees, the 70.8% PPV for vaginal delivery lowered this to about 29%. Not a big difference. The authors do acknowledge this in the Discussion, but it would help if they could provide insight as to why their findings nonetheless are of clinical importance. Is there anything to suggest that measuring these angles is an improvement over standard digital exams in managing labor?”

Reply: we thank again the Reviewer for this comment, which allows to further explain the main findings of the study. The Reviewer is correct in pointing out that the performance of the OSA cut-off is poor in discriminating fetuses who are likely to be delivered vaginally compared to those requiring cesarean delivery. However, when looking at the relationship between the OSA and the sonographic indicators of fetal head station (i.e. HPD and AoP, please see Figure 4) we demonstrate the existence of outlier cases characterized by a wide OSA – i.e. a good flexion of the fetal head – and a high station – i.e. narrow AoP and long HPD – and all delivered by cesarean. As

we state in the manuscript, by demonstrating a lower maternal height and a higher birthweight/maternal height ratio, we hypothesize that such discrepancy represents an indicator of cephalo-pelvic disproportion. On this basis, such outlier cases characterized by a wide OSA BUT a high station (narrow AoP, long HPD) do impact in reducing the AUC as well as the PPV for vaginal delivery of the cases with OSA >108.5 degrees. In the results section of the amended version of the manuscript we report a secondary analysis of the sensitivity, specificity, PPV and NPV for vaginal delivery in relation to the OSA cut-off value following the removal of the 9 outlier cases. In the analysis we demonstrate that a OSA >108.5° is associated with a 80.9% sensitivity, 87.5% specificity, 70.8% PPV and 92.5% NPV for vaginal delivery, with an overall rate of cesarean delivery as low as 7.5%. Therefore, we believe that the evaluation of the sonographic indicators of fetal head flexion and station does add an improvement in managing labor as this may allow to identify the etiology of the labor dystocia, ultimately leading to optimized management.”

It is also true that “The removed cases had only a modest difference in maternal height. The birth weight was not known at the time of decision of delivery mode, and should not be part of explaining why these cases were removed”, however we believe that the maternal height, the birthweight and their ratio can assist in supporting our hypothesis that those identified as outliers on the basis of the discrepancy between these usually paired sonographic findings (flexion and station) are delivered by cesarean because of cephalopelvic disproportion. Indeed, such cases all showed favorable degree of head flexion but unexpectedly the station was high and, interestingly, an increased mean birthweight and birthweight/maternal height ratio was eventually found. The paragraph was inserted in the amended version as we believe that such explanation can help the readers to better understand our point, but we are of course happy to amend the results section and remove it as requested. We e have added to the results section a further paragraph detailing the findings of the analysis evaluating the relationship between the sonographic indicators of head station (AoP and HPD) and the OSA in non-occiput posterior fetuses with favorable head flexion (i.e. with OSA wider than 109 degrees) in relation to the mode of delivery in outlier and non-outlier cases. As stated in the paragraph, the sub-analysis evaluating the ratios between the OSA and the sonographic indicators of head station allows to identify 9/13 (sensitivity 69%) cesarean deliveries performed within a selected cohort of fetuses with protracted active phase of labor but no apparent malpresentation, and in Figure 5 we clearly show a trend towards an increased frequency of cesarean delivery with increasing OSA/AoP ratio and with decreasing OSA/HPD ratio. Based on our

hypothesis, such findings support the concept that outlier cases represent a population characterized by a mismatch between the size of the birth canal and that of the fetus.

C. Lines 229-242

D. Paragraph removed: “An inverse correlation between the OSA and the HPD (Pearson’s correlation -0.566, $p < 0.01$) and a stronger correlation between the OSA and the AoP (Pearson’s correlation 0.693, $p < 0.01$) were demonstrated following the removal of the 9 outliers from the non-OP dataset. Furthermore, following the removal of the 9 outlier cases a OSA width > 108.5 degrees showed 80.9% sensitivity, 87.5% specificity, 70.8% PPV and 92.5% NPV for the mode of delivery and an overall 7.5% rate of cesarean delivery.”

Paragraph added: “When considering only the 62 non-OP fetuses with OSA width above 109 degrees – i.e. with favorable head flexion –, such outlier cases accounted for 9/13 cesarean deliveries. The distribution of the OSA/AoP ratio in relation to the mode of delivery showed a trend towards an increased rate of CS with increasing OSA/AoP ratio (Figure 5a), while a trend towards an increased rate of CS was noted with decreasing OSA/HPD ratio (Figure 5b). At ROC curve the OSA/AoP ratio was found to be associated with an AUC for the prediction of cesarean delivery of 0.769, 95%CI (0.586-0.952), $p = 0.003$, while the OSA/HPD ratio was associated with an AUC of 0.778, 95%CI (0.631-0.925), $p = 0.002$. The optimal cut-off value of the OSA/AoP ratio discriminating between cases of VD vs those delivered by CS was 1.20, and was associated with a 69.2% sensitivity, 87.8% specificity, 60.0% PPV and 91.5% NPV; the optimal cut-off value of the OSA/HPD ratio discriminating between cases of VD vs those delivered by CS was 3.05, and was associated with a 69.2% sensitivity, 77.6% specificity, 45.0% PPV and 90.5% NPV.”

Reviewer #1, POINT 2

A. The authors say that cases showing a narrow AoP and a wide OSA were all submitted to cesarean delivery. Were the responsible clinicians aware of the ultrasound findings when deciding delivery mode? I suppose that they were blinded to the ultrasound findings.

B. As stated in the methods section (lines 127-128), “The senior Obstetricians in charge for the labor care were blinded to the ultrasound findings.” Thank you.

C. No change has been made to the manuscript.

D. No change has been made to the manuscript.

Reviewer #1, POINT 3

A. Predictive calculation should be based on all cases. Revise the discussion part accordingly.

B. Please see our Reply to the POINT 1. The results section has been amended.

C. No change has been made to the manuscript.

D. No change has been made to the manuscript.

Reviewer #1, POINT 4

A. In accordance with table 2, 30 women were delivered by cesarean, but I can only count 27 red spots in figure 4. Please explain.

B. We thank the Reviewer for this very smart comment. The Reviewer is correct in pointing out this, however there is no mistake. We have gone through our dataset again, and have concluded that the apparent absence of some dots in the scatter/dot chart can be explained by the overlapping of some cases among the non-outliers. We have of course happy to share our dataset should you have any further concern. Thank you.

C. No change has been made to the manuscript.

D. No change has been made to the manuscript.

Reviewer #1, POINT 5

A. The authors explain much better how the angles were measured. The authors say "It is important to acknowledge that a straight plane can identify only one tangent line". To my best knowledge, this is not correct or at least a very uncommon use of the word tangent. A tangent line is defined as a line which locally touches a CURVE at one and only one point. This could easily be corrected in the manuscript by saying that the chin-chest angle was defined as the angle identified by a line through the sternum and a second line through the straight structure represented by the skin covering the inferior boundary of the oral cavity up to the chin.

B. The Reviewer is correct in pointing out the actual definition of tangent line. The methods section has been amended consistently with the Reviewer's suggestion.

C. Lines 166-169

D. "The CCA was defined as the angle identified by the intersection between one line through the longest axis of the sternum and a second line through another straight structure represented by the skin covering the inferior boundary of the oral cavity up to the chin"

Reviewer #1, POINT 6

A.Line 212-213; Too many decimals are used. The angles and distances cannot be measured as OSA (126.2+14.4 vs 114.5+23.6 degrees, $p=0.006$) and AoP (117.5+12.7 vs 104.0+10.7 degrees, $p<0.001$) and a shorter HPD (39.7+5.2 vs 49.0+9.4 mm, $p<0.001$). Please remove the imprecise decimals throughout the manuscript.

B.This has been done as requested. Thank you.

C.See decimals changes in the results section and in the tables. Thank you.

D. See decimals changes in the results section and in the tables. Thank you.

Reviewer #2: This is an paper is original in its conception: namely defining the degree of head extension (non OP) and flexion (OP) deliveries and the relationship with vaginal, assisted vaginal or Cesarean delivery. Indices OSA (non OP) and CCA (OP) appear to be related to Cesarean where they denote fetal head extension. It seems that intrapartum ultrasound was undertaken in the late first and second stages of labour, based on a diagnosis of prolonged labour. This does introduce a potential difficulty as the timing or stage of ultrasound assessment in relation to delivery was not standardized, that said studies of this type in a delivery ward are notoriously difficult to undertake so this should be kept in mind.

Reply: we thank the reviewer for such comment. It is true that that we standardized the timing of the US assessment at the diagnosis of protracted active phase of labor but not at delivery, which could represent a potential limitation of the study, however it has to be acknowledged that this sort studies are difficult to be conducted in a clinical setting.

Reviewer #2, POINT 1

A.The authors report predictive value cut-offs and AUCs for OSA and CCA however I wonder how robust these are in the context of a selected, non consecutive population? The authors might wish to comment on this.

B.We thank the Reviewer for this comment. It is true that the “non-consecutive” enrolment may represent a limitation of the study, therefore this has been listed among the limitations in the revised version of the manuscript. The “non-consecutive” enrolment was dependent upon the fact that the study investigators were not always available to perform the ultrasound examination at the time of the diagnosis of protracted active phase of labor, which may be accounted as a source of bias also for randomized trials. On balance, we believe that the wide number of the enrolled patients and the strict inclusion criteria allow to overcome such potential limitation, therefore we believe that the “non-consecutive” enrolment does not impact on the robustness of our findings.

C.Lines 348-350

D.Finally, the “non-consecutive” enrolment may be accounted as a potential source of bias, even though we believe that the wide number of the enrolled patients together with the strict inclusion criteria allow to overcome such potential limitation.

Reviewer #2, POINT 2

A. Furthermore, while the OSA has been previously described, as far as I can see, the CCA hasn't, so there is little known about the reproducibility and variability of the technique: this knowledge is normally a pre-requisite before developing predictive models.

B. The Reviewer is correct in pointing out that the reproducibility of the measurement of the CCA was not tested, as we have acknowledged in the limitations section. However, it is important to note that all the research scans were performed by a small number of study investigators with expertise in ultrasound in labor, therefore we believe that in such context a variability in the CCA measurements is highly unlikely.

C. Lines 337-339

D. However, it is important to note that all the research scans were performed by a small number of investigators with expertise on ultrasound in labor, therefore we believe that in such context a variability in the CCA measurements is highly unlikely.

Reviewer #2, POINT 3

A. Figure 2(b) shows CCA being measured, however the fetal head appears either oblique or asynclitic: would the authors comment on the variability of the measurement in these circumstances? Furthermore, I am not clear if the posterior or anterior sternal aspect should be used to lay the chest line.

B. Thank you for this comment. As we state in the discussion (“Additionally, we acknowledge that complex malpresentations such as asynclitism, among whom some are known to impact on the labor outcome regardless of the additional sonographic parameters (54-60), were not evaluated”), we agree that the asynclitism of the fetal head may impact on the measurement of the sonographic indicators of fetal head flexion, however in a clinical context of protracted active phase of labor different types of malpresentation may coexist and impact on the fetal head descent. The variability of the measurement of the CCA in OP fetuses with co-existent asynclitism was not evaluated in this present study, and it is not clear how this may further affect the labor course. We have further commented on this in the limitation section, and we have amended Figure 2 by providing a new US picture of an OP fetus with synclitic head.

With regards to the technique for the measurement of the CCA, we now state in the methods section that “...The CCA was defined as the angle identified by the intersection between one line through the longest axis of the sternum and a second line through another straight structure represented by the skin covering the inferior boundary of the oral cavity up to the chin”. One line

only can be identified through the longest axis of the sternum, and lines parallel to such line can be used to lay the chest line either on the anterior or the posterior sternal aspect, with no difference in the measurement of the CCA. Thank you.

C.Lines 367-374

D.Such limitation needs to be taken into account in a clinical context where different types of malpresentation may coexist and contribute in determining a protracted active phase of labor.

Reviewer #2, POINT 4

A.On page 19, line 154-155: "Transabdominal US was performed by placing the probe transversely over the maternal suprapubic region to assess the position and the flexion of the fetal head." but I guess that for the OSA and CCA measurements, the probe was placed in plane with the long axis of the fetus (longitudinally?).

B.Yes, the reviewer is correct in pointing out that the sonographic indicators can be measured on a longitudinal axis and not on a transverse plane. The methods section was amended accordingly. Thank you.

C.Lines 154-156

D."Transabdominal US was performed by placing the probe transversely over the maternal suprapubic region to assess the position of the fetal head, while the flexion was evaluated by tilting the probe by 90 degrees to the longitudinal plane."

Table 1 – Features of the included cases.

| | |
|--|---|
| Maternal age, years Mean \pm SD | 32.9 \pm 4.9 |
| Ethnicity n (%) | Caucasian 107 (82.9%) African 7 (5.4%) Asian 15 (11.6%) |
| Parity n (%) | Nulliparous 116 (89.9%) |
| Maternal height, cm Mean \pm SD | 164 \pm 11 |
| Booking BMI, kg/m² Mean \pm SD | 23.6 \pm 3.5 |
| Term pregnancy BMI, kg/m² Mean \pm SD | 28.3 \pm 4.3 |
| Gestational age at delivery, weeks^{+days} Mean \pm SD | 40 ⁺¹ \pm 1 ⁺⁰ |
| Occiput position at diagnosis n (%) | OA 59 (45.7%) OT 29 (22.5%) OP 41 (31.8%) |
| Digital station at diagnosis, cm Median (range) | -2 (-4 – +1) |
| Cervical dilatation at diagnosis, cm Median (range) | 8 (6 – 9) |
| Occiput-spine angle, degrees Mean \pm SD | 122 \pm 19 |
| Chin-chest angle, degrees Mean \pm SD | 38 \pm 34 |
| Angle of progression, degrees Mean \pm SD | 111 \pm 14 |
| Head-perineum distance, mm Mean \pm SD | 43 \pm 8 |
| Mode of delivery n (%) | SVD 66 (51.2%) VE 17 (13.1%) CS 46 (35.7%) |
| Birthweight, grams Mean \pm SD | 3492 \pm 411 |
| Umbilical artery pH Mean \pm SD | 7.24 \pm 0.09 |
| Apgar at 5 minutes Median (range) | 9 (7 – 10) |
| Estimated blood loss, mls Mean \pm SD | 500 (50 – 2000) |
| Labor induction n (%) | Yes 34 (26.4%) |
| Epidural in labor n (%) | Yes 117 (90.7%) |
| Length of first stage of labor, minutes Mean \pm SD | 495 \pm 171 |
| Length of second stage of labor, minutes Mean \pm SD | 107 \pm 52 |

| | |
|--|--|
| <i>Length of labor, minutes</i> <i>Mean \pm SD</i> | <i>587 \pm 193</i> |
|--|--|

Table 2 – Demographic features, transperineal and transabdominal ultrasound parameters at diagnosis of protracted active phase of labor and outcomes in the vaginal delivery and in the cesarean delivery group in fetuses a) in non-occiput posterior (n=86) and b) in occiput posterior (n=43) position.

a)

| | Vaginal delivery | Cesarean delivery | p value |
|---|--|--|----------------|
| | N 56 (65.1%) | N 30 (34.9%) | |
| Maternal age, years <i>Mean ± SD</i> | 32.4 ± 4.2 | 33.7 ± 5.2 | 0.20 |
| Ethnicity <i>N (%)</i> | Caucasian 47 (83.9%) African 2 (3.96%) Asian 7 (12.5%) | Caucasian 21 (70.0%) African 3 (10.0%) Asian 6 (20.0%) | 0.27 |
| Parity <i>N (%)</i> | Nulliparous 53 (94.6%) | Nulliparous 29 (96.7%) | 0.67 |
| Maternal height, cm <i>Mean ± SD</i> | 164 ± 6 | 161 ± 7 | 0.03 |
| Booking BMI, kg/m² <i>Mean ± SD</i> | 22.8 ± 3.8 | 24.8 ± 3.4 | 0.02 |
| Term pregnancy BMI, kg/m² <i>Mean ± SD</i> | 27.3 ± 4.6 | 29.6 ± 4.2 | 0.03 |
| Gestational age at delivery, weeks^{+days} <i>Mean ± SD</i> | 40 ⁺⁰ ± 1 ⁺⁰ | 40 ⁺⁰ ± 0 ⁺⁶ | 0.72 |
| Digital station at diagnosis, cm <i>Median (range)</i> | -2 (-3 – -1) | -2 (-4 – +1) | 0.29 |
| Cervical dilatation at diagnosis, cm <i>Median (range)</i> | 8 (6 – 9) | 8 (6 – 9) | 0.57 |
| Occiput-spine angle, degrees <i>Mean ± SD</i> | 126 ± 14 | 115 ± 24 | 0.006 |
| Angle of progression, degrees <i>Mean ± SD</i> | 118 ± 13 | 104 ± 11 | <0.001 |
| Head-perineum distance, mm <i>Mean ± SD</i> | 40 ± 5 | 49 ± 9 | <0.001 |
| Birthweight, grams <i>Mean ± SD</i> | 3476 ± 397 | 3503 ± 311 | 0.74 |
| Labor induction <i>N (%)</i> | Yes 12 (21.4%) | Yes 6 (20.0%) | 0.88 |
| Epidural in labor <i>N (%)</i> | Yes 54 (96.4%) | Yes 27 (90.0%) | 0.23 |

b)

| | <i>Vaginal delivery</i> | <i>Cesarean delivery</i> | <i>p value</i> |
|---|--|---|-----------------------|
| | <i>N 27 (62.8%)</i> | <i>N 16 (37.2%)</i> | |
| <i>Maternal age, years Mean \pm SD</i> | 31.6 \pm 5.4 | 33.3 \pm 5.7 | 0.34 |
| <i>Ethnicity N (%)</i> | Caucasian 23 (85.2%) African 2 (7.4%) Asian 2 (7.4%) | Caucasian 16 (100.0%) African 0 (0.0%) Asian 0 (0.0%) | 0.27 |
| <i>Parity N (%)</i> | Nulliparous 8 (29.6%) | Nulliparous 1 (6.2%) | 0.07 |
| <i>Maternal height, cm Mean \pm SD</i> | 163 \pm 5 | 162 \pm 6 | 0.47 |
| <i>Booking BMI, kg/m² Mean \pm SD</i> | 24.4 \pm 0.9 | 24.0 \pm 1.0 | 0.55 |
| <i>Term pregnancy BMI, kg/m² Mean \pm SD</i> | 29.5 \pm 2.1 | 29.5 \pm 2.0 | 0.99 |
| <i>Gestational age at delivery, weeks^{+days} Mean \pm SD</i> | 40 ⁺¹ \pm 1 ⁺³ | 40 ⁺³ \pm 0 ⁺⁶ | 0.52 |
| <i>Digital station at diagnosis, cm Median (range)</i> | -2 (-3 – -1) | -3 (-3 – -2) | 0.15 |
| <i>Cervical dilatation at diagnosis, cm Median (range)</i> | 8 (6 – 9) | 7 (6 – 9) | 0.29 |
| <i>Chin-chest angle, degrees Mean \pm SD</i> | 27 \pm 33 | 56 \pm 28 | 0.005 |
| <i>Angle of progression, degrees Mean \pm SD</i> | 108 \pm 16 | 92 \pm 14 | 0.06 |
| <i>Head-perineum distance, mm Mean \pm SD</i> | 42 \pm 6 | 43 \pm 4 | 0.68 |
| <i>Birthweight, grams Mean \pm SD</i> | 3537 \pm 524 | 3493 \pm 446 | 0.78 |
| <i>Labor induction N (%)</i> | Yes 6 (22.2%) | Yes 10 (62.5%) | 0.008 |
| <i>Epidural in labor N (%)</i> | Yes 21 (77.8%) | Yes 15 (93.8%) | 0.17 |

Table 3 – Logistic regression analysis for intrapartum clinical, transperineal and transabdominal ultrasound parameters at diagnosis of protracted active phase of labor and mode of delivery (vaginal delivery vs cesarean delivery) a) for fetuses in non-occiput posterior position and b) for fetuses in occiput posterior position.

a)

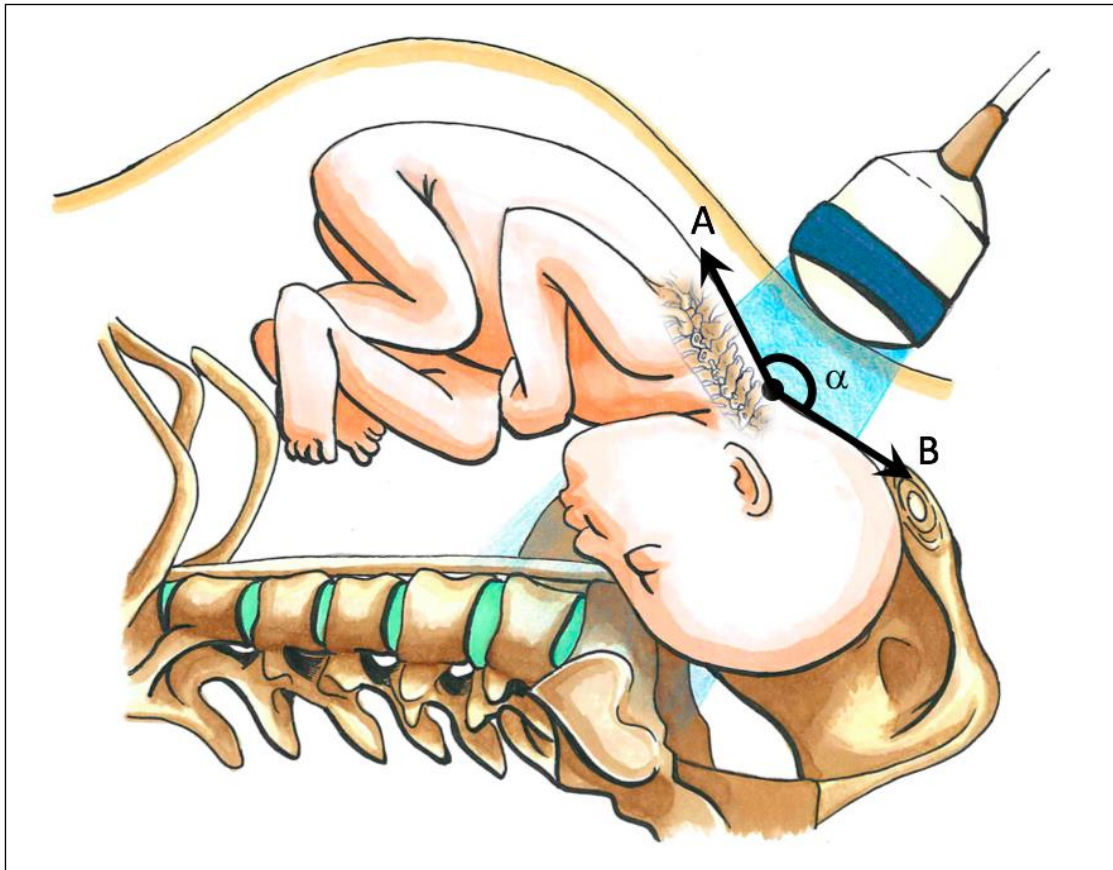
| <i>Variable</i> | <i>Adjusted OR</i> | <i>(95%CI)</i> | <i>p</i> |
|---------------------------|--------------------|----------------|----------|
| <i>Maternal height</i> | 1.020 | 0.897-1.158 | 0.766 |
| <i>Booking BMI</i> | 0.997 | 0.567-1.752 | 0.992 |
| <i>Term pregnancy BMI</i> | 1.418 | 0.877-2.293 | 0.155 |
| <i>OSA</i> | 0.921 | 0.868-0.977 | 0.007 |
| <i>AoP</i> | 1.052 | 0.962-1.150 | 0.266 |
| <i>HPD</i> | 1.305 | 1.116-1.525 | 0.001 |

b)

| <i>Variable</i> | <i>Adjusted OR</i> | <i>(95%CI)</i> | <i>p</i> |
|---------------------------|--------------------|----------------|----------|
| <i>Induction of labor</i> | 9.316 | 1.800-48.198 | 0.008 |
| <i>CCA</i> | 1.035 | 1.010-1.062 | 0.007 |

Figure 1 – Attitude in fetuses in non-occiput posterior position as measured by means of the occiput-spine angle (OSA): a) graphic representation of the OSA and b) sonographic view of a flexed fetal head showing a wide OSA.

a)



b)

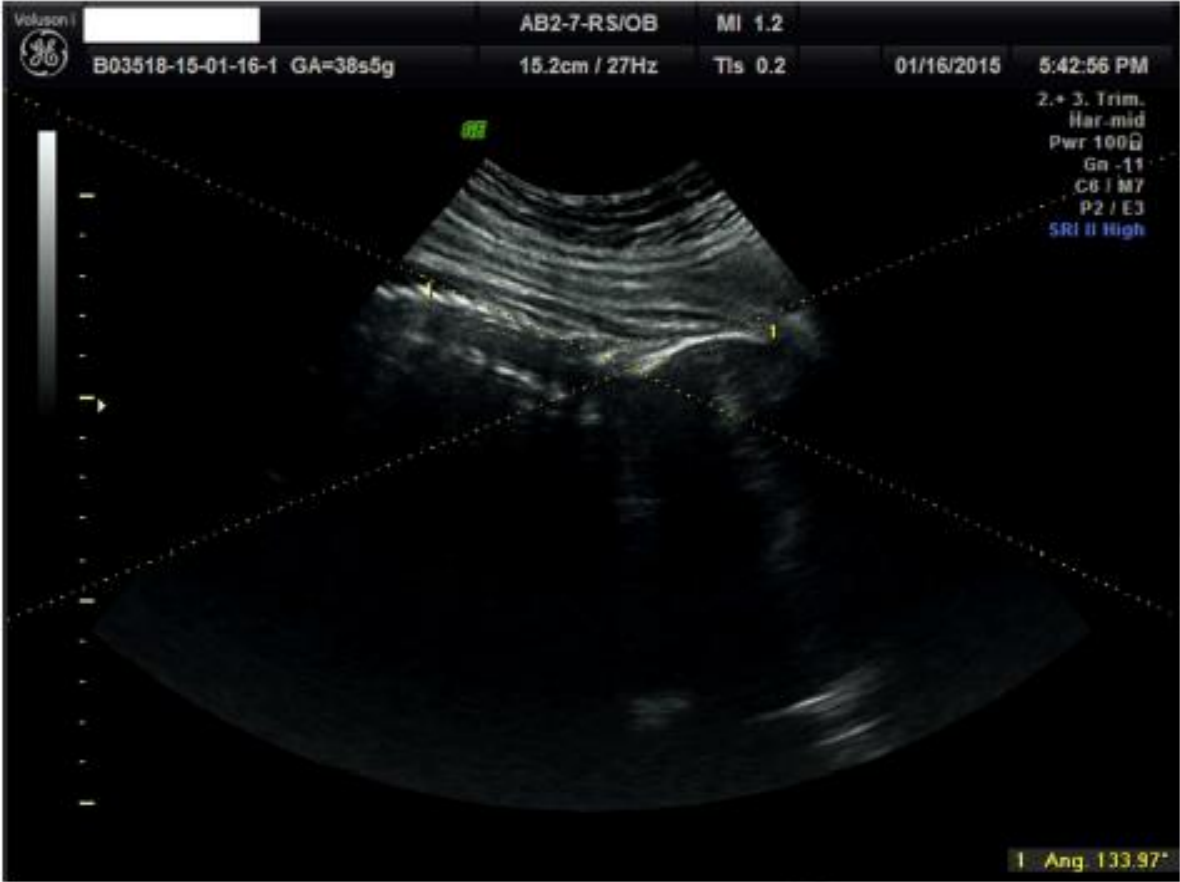
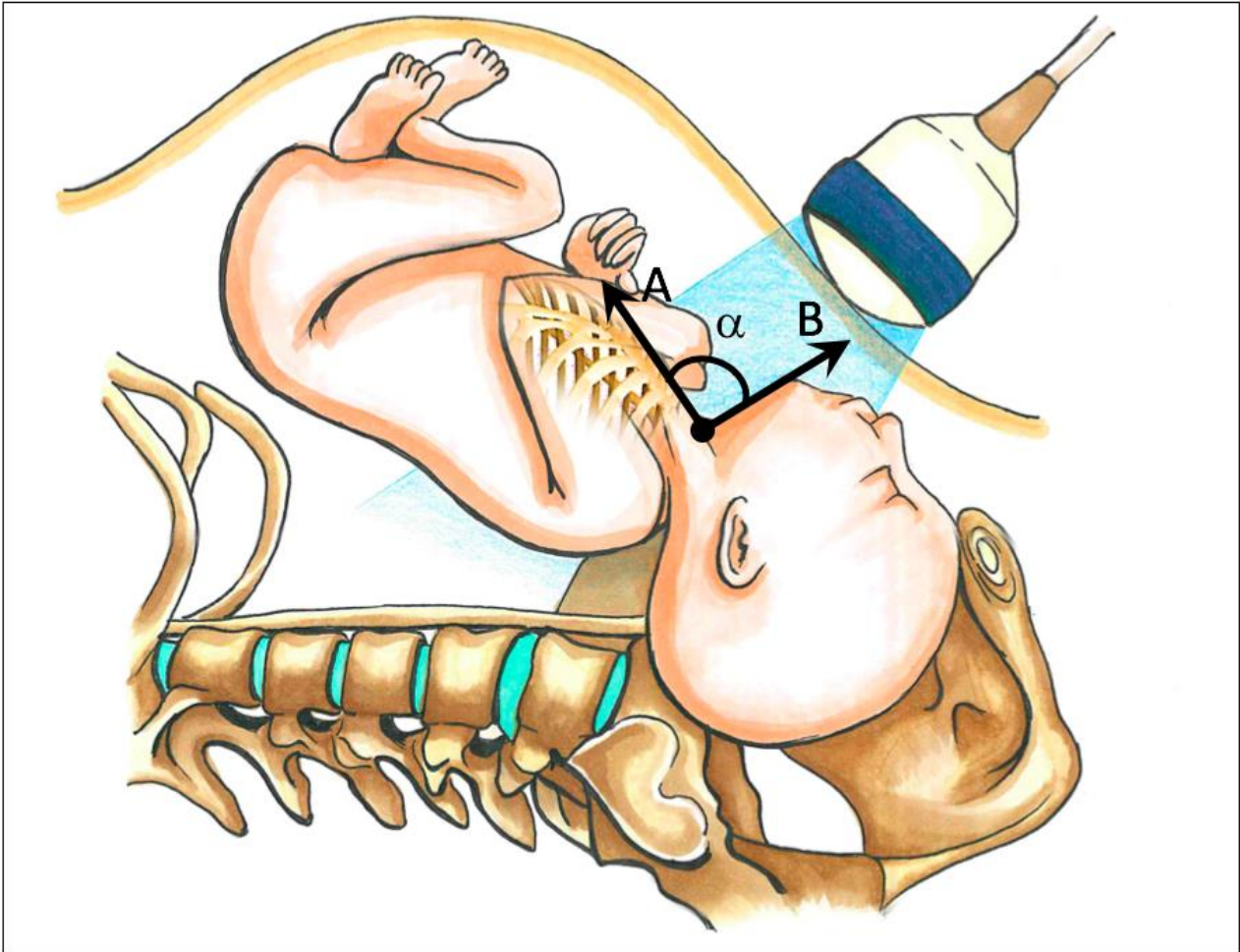


Figure 2 – Attitude in fetuses in occiput posterior position as measured by means of the chin-to-chest angle (CCA): a) graphic representation of the CCA and b) sonographic view of a deflexed fetal head showing a CCA between 45 and 90 degrees (A: line tangent to the longest axis of the sternum; B: line tangent to the skin covering the inferior boundary of the oral cavity up to the chin).

a)



b)

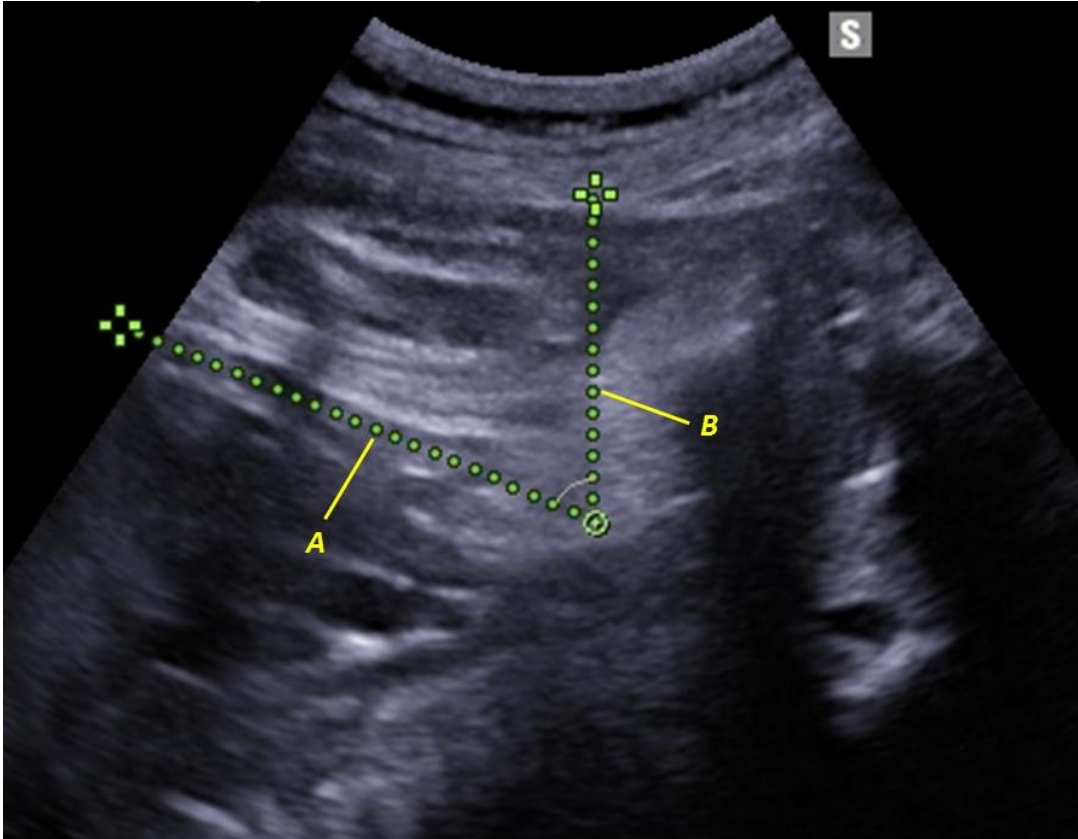


Figure 3 – Flow chart (according to STROBE guidelines) (33) for inclusion of cases.

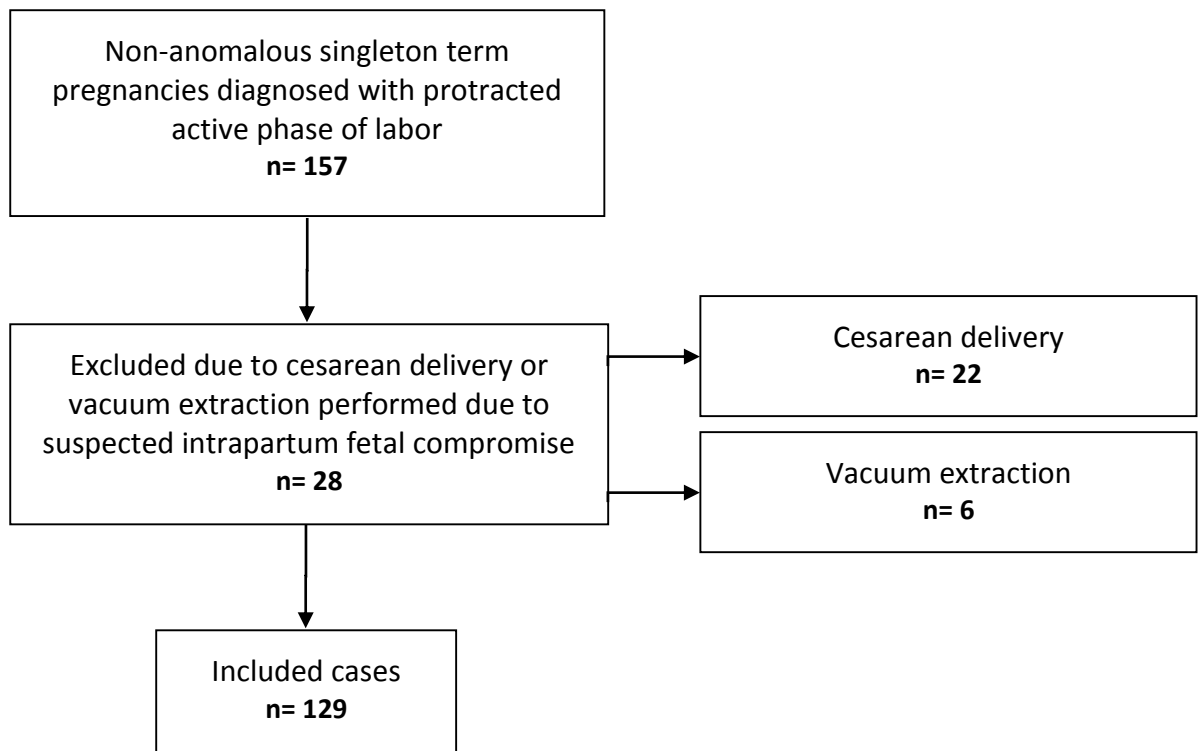
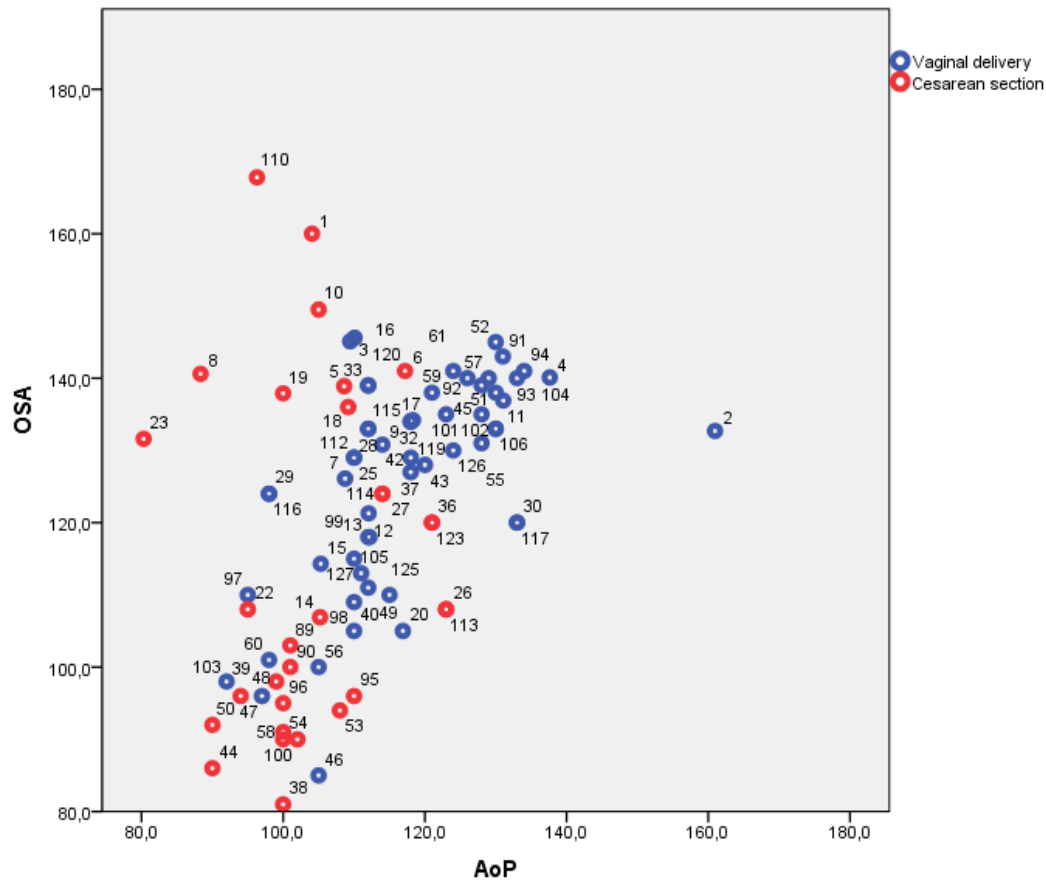


Figure 4 – Scatter/dot charts demonstrating the correlations a) between the occiput-spine angle (OSA) and the angle of progression (AoP) and b) between the OSA and the head-perineum distance (HPD) in fetuses in non-occiput posterior position.

Outliers corresponding to the case numbers 1, 5, 6, 8, 10, 18, 19, 23 and 110.

a)



b)

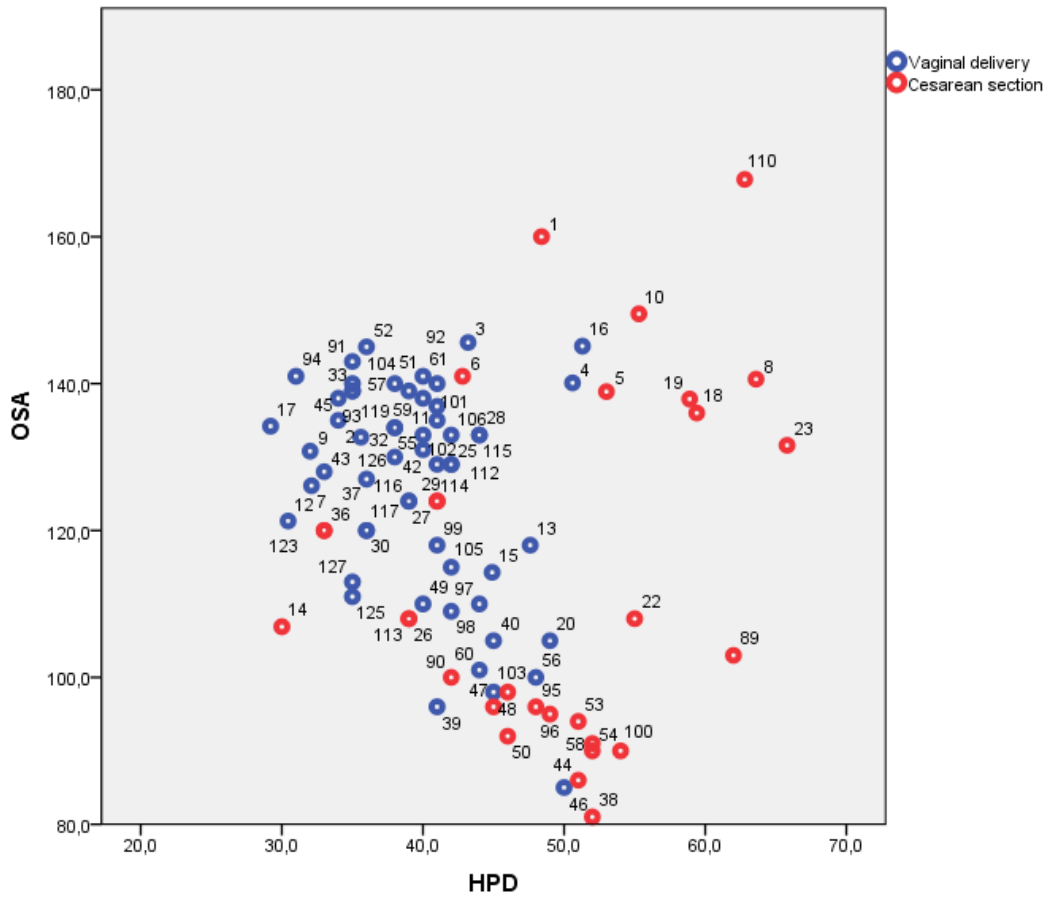
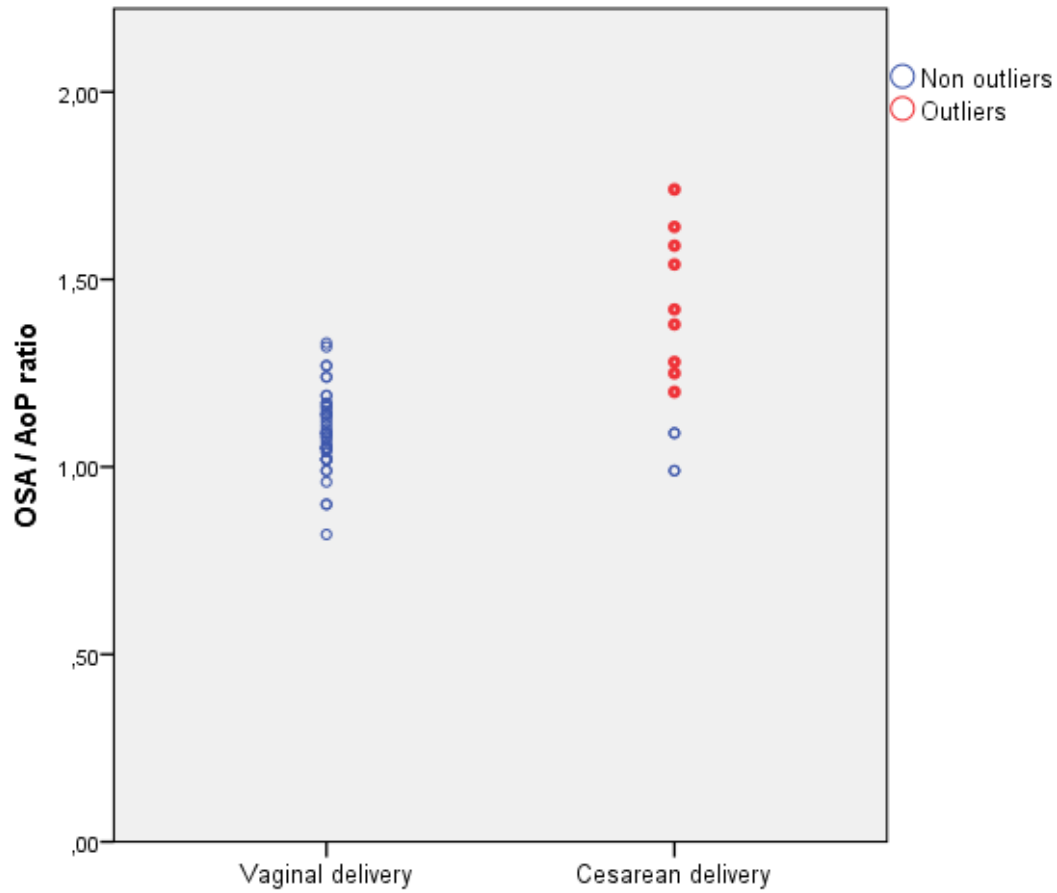
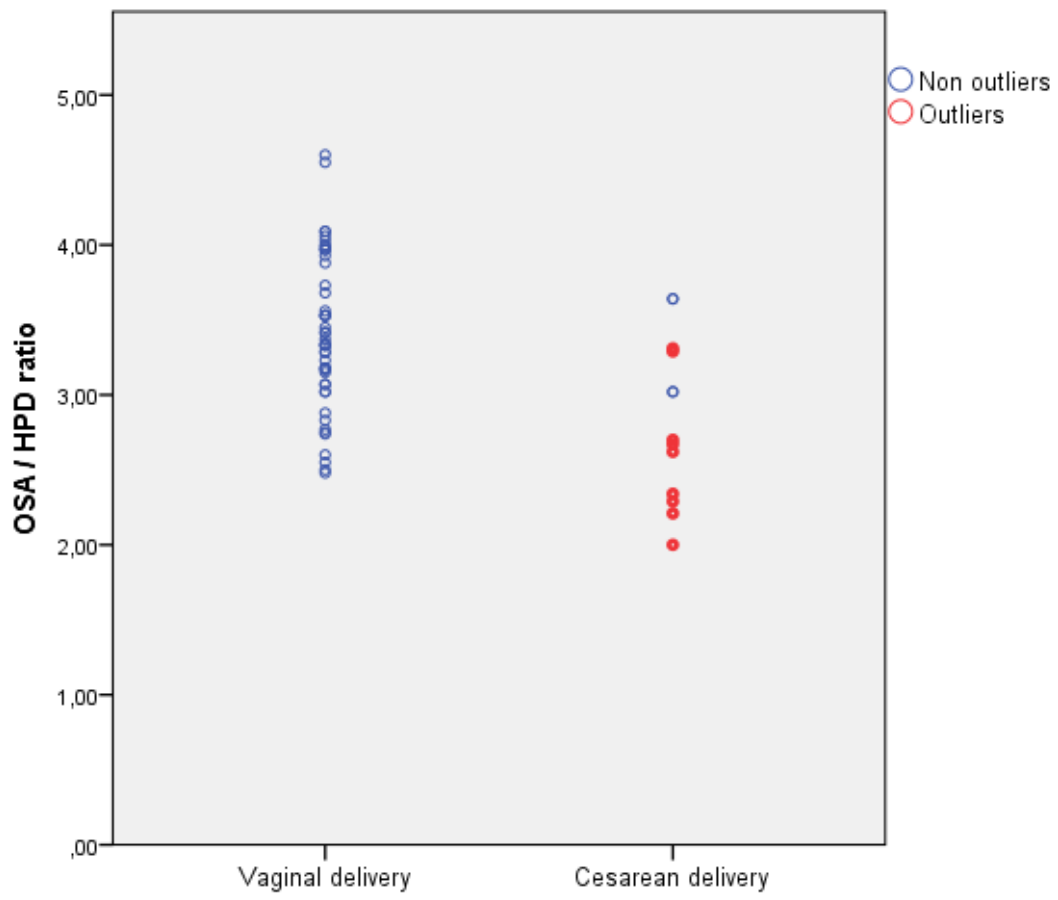


Figure 5 – Distribution of the occiput-spine angle (OSA)-to-angle of progression (AoP) ratio (Figure 5a) and of the OSA-to-head perineum distance (HPD) ratio (Figure 5b) in relation to the mode of delivery in outlier and non-outlier cases in cases with OSA >109 degrees.

a)



b)



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Each author is required to submit a signed Statement of Authorship upon submission. This applies to all submission types including Editorials, Letters to the Editor, etc.

Date: 01/12/2020 Manuscript # (if available): _____

Manuscript title: **Intrapartum sonographic assessment of the fetal head flexion in protracted active phase of labor and association with labor outcome: a multicentre, prospective study.**

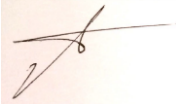
Corresponding author: Prof Tullio Ghi

Authors may either sign the same form or submit individually

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MAQINA PAVJOLA


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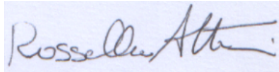
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Typed or CLEARLY Printed Name: **Guido Menato**



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1 **TITLE PAGE**

2 **Intrapartum sonographic assessment of the fetal head flexion in protracted active phase of labor**
3 **and association with labor outcome: a multicentre, prospective study.**

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24

25 **Condensation:**

26 The sonographic indicators of deflexed fetal head are associated with labor dystocia leading to
27 caesarean delivery in women with protracted active phase of labor.

28

29 **Short title:**

30 Intrapartum US in protracted active phase of labor.

31

32 **AJOG at a glance**

33 A. Why was the study conducted?

- 34 • To evaluate the relationship between the intrapartum sonographic indicators of fetal head
35 flexion and the mode of delivery in women with protracted active phase of labor.

36 B. What are the key findings?

- 37 • A wide occiput-spine angle and a narrow chin-chest angle are associated with an increased
38 incidence of vaginal delivery. A correlation between the occiput-spine angle and the
39 sonographic indicators of fetal head station was also demonstrated.

40 C. What does this study add to what is already known?

- 41 • The sonographic indicators of fetal head flexion are associated with labor dystocia leading
42 to cesarean delivery in women with protracted active phase of labor. The findings from this
43 study suggest that intrapartum ultrasound may contribute in the categorization of the
44 etiology of labor dystocia.

45

46 **Keywords**

47 Ultrasound in labor, labor dystocia, intrapartum care, caesarean delivery, instrumental delivery,
48 occiput-spine angle, chin-chest angle, angle of progression, head-perineum distance.

49

50 **Abstract**

51 **Background**

52 To date no research has focused on the sonographic quantification of the degree of flexion of the
53 fetal head in relation to the labor outcome in women with protracted active phase of labor.

54 **Objective**

55 To assess the relationship between the transabdominal sonographic indices of fetal head flexion
56 and the mode of delivery in women with protracted active phase of labor.

57 **Study design**

58 Prospective evaluation of women with protracted active phase of labor recruited across three
59 tertiary maternity units. Eligible cases were submitted to transabdominal ultrasound for the
60 evaluation of the fetal head position and flexion, which was measured by means of the occiput-
61 spine angle (OSA) in fetuses in non-occiput posterior (OP) position and by means of the chin-to-
62 chest angle (CCA) in fetuses in OP position. The OSA and the CCA were compared between women
63 who had vaginal delivery vs those who had cesarean delivery. Cases where obstetric intervention
64 was performed solely based on suspected fetal distress were excluded.

65 **Results**

66 129 women were included, of whom 43 (33.3%) had OP position. Spontaneous vaginal delivery,
67 instrumental delivery and cesarean delivery were recorded in 66 (51.2%), 17 (13.1%) and 46 (35.7%)
68 cases, respectively. A wider OSA was measured in women who had vaginal delivery compared to
69 those submitted to cesarean delivery due to labor dystocia (126.2 ± 14.4 vs 114.5 ± 23.6 , $p < 0.01$). At
70 ROC curve the area-under-the-curve (AUC) was 0.675, 95%CI (0.538-0.812), $p < 0.01$, and the optimal
71 OSA cut-off value discriminating between cases of vaginal delivery vs those delivered by cesarean
72 delivery was 108.5 degrees. A narrower CCA was measured in cases who had vaginal delivery
73 compared to those undergoing cesarean delivery (27.2 ± 32.9 vs 56.2 ± 27.7 degrees, $p < 0.01$). The AUC

74 of the CCA in relation to the mode of delivery was 0.758, 95%CI (0.612-0.904), $p < 0.01$, and the
75 optimal cut-off value discriminating between vaginal delivery and cesarean delivery was 33.0
76 degrees.

77 **Conclusions**

78 In women with protracted active phase of labor, the sonographic demonstration of fetal head
79 deflexion in OP and in non-OP fetuses is associated with an increased incidence of cesarean delivery
80 due to labor dystocia. Such findings suggest that intrapartum ultrasound may contribute in the
81 categorization of the etiology of labor dystocia.

82 **Introduction**

83 Labor dystocia is estimated to account for approximately one third of all caesarean deliveries, the
84 vast majority being primary cesarean deliveries (1,2). Among these, arrest of dilatation in the first-
85 stage of labor is acknowledged to represent the most common indication (3,4). Such condition may
86 result from distinct but potentially coexisting mechanisms which include abnormalities of the
87 uterine contractions, malpositions or malpresentations of the fetal head and cephalopelvic
88 disproportion (5-13).

89 The progression of the first-stage of labor has been historically assessed by means of the norms of
90 active phase dilatation described by Friedman (14-26) and more recently re-evaluated by Zhang et
91 al. (1,27,28). These latter, which show a slow but progressive first-stage dilatation prior to 6 cm and
92 an overall slower course of labor compared to Friedman's sigmoid curve (14-17,23,25,26), are
93 currently endorsed for labor management by the American College of Obstetricians and
94 Gynecologists and by the Society for Maternal and Fetal Medicine (4,29). The active phase dilatation
95 is positively affected by the descent of the fetal head in the birth canal, and in normal labor a direct
96 correlation between the first-stage dilatation and the descent of the fetal head has been
97 demonstrated (30). The engagement and the progression of the fetal head through the birth canal
98 in the first-stage of labor are known to be to be influenced by the mechanism of head flexion –
99 which allow the shortest cephalic diameters to negotiate the maternal pelvis (5,6).

100 Available data suggests that ultrasound outweighs the digital examination in the assessment of the
101 fetal head station (31,32), progression and attitude, and ultrasound is currently endorsed as an
102 adjunct to the clinical evaluation in conditions of protracted active phase of labor and arrest of
103 dilatation (31). Under these circumstances, the sonographic indicators of the fetal head station
104 including the head-perineum distance (HPD) and the angle of progression (AoP) have been shown
105 to be more accurate than the digital examination in predicting the occurrence of cesarean delivery

106 (33-35). In an unselected group of women in the active phase of labor with occiput anterior and
107 occiput transverse fetuses the degree of fetal head flexion measured at transabdominal ultrasound
108 has been shown to be associated with the digital station and the likelihood of operative delivery
109 (36). Other sonographic studies have demonstrated that also in fetuses in occiput posterior (OP)
110 position the qualitative assessment of the fetal head deflexion is related to the chance of vaginal
111 delivery (37,38). To date no research has focused on the sonographic quantification of the degree
112 of flexion of the fetal head in relation to the labor outcome in women with protracted active phase
113 of labor. The aim of this study was to evaluate the relationship between the intrapartum ultrasound
114 indicators of malposition and malpresentation and the risk of obstetric intervention within a
115 selected cohort of women diagnosed with a protracted active phase of labor.

116 **Methods**

117 Study design

118 This was a prospective, observational study conducted between December 2018 and June 2020 and
119 including three maternity units in Italy (University Hospitals of Parma and Rome Tor Vergata and
120 Sant'Anna Hospital of Turin). A non-consecutive series of non-anomalous singleton term
121 pregnancies, with no history of previous uterine scar and with a protracted active phase of labor
122 was included. According to the local protocol of the participating Units, women diagnosed with
123 protracted active phase of labor are submitted to clinical examination by the senior Obstetrician
124 responsible for the patient care. For the present study, following the clinical diagnosis of protracted
125 active phase of labor intrapartum ultrasound was performed for research purposes also by five
126 investigators with dedicated training on ultrasound in labor (AD, TG, EDP, BM and GR) who were
127 not involved in the clinical management. The senior Obstetricians in charge for the labor care were
128 blinded to the ultrasound findings.

129 According to the protocol for the labor management adopted across the participating Units,
130 protracted active phase of labor was defined based on the ACOG/SMFM recommendations for the
131 safe prevention of the primary cesarean delivery (4). In details, a protracted active phase of labor
132 was defined in women ≥ 6 cm of dilatation with ruptured membranes who fail to progress despite 4
133 hours of adequate uterine activity or at least 6 hours of oxytocin administration with inadequate
134 uterine activity and no first-stage dilatation. In such cases, the arrest of dilatation requiring cesarean
135 delivery was defined following two more hours of oxytocin administration with no cervical change.
136 In the case of progression of the first-stage dilatation, obstetric intervention was indicated during
137 the first-stage in the event of the above criteria, while the diagnosis of arrest of labor in the second
138 stage was made in the event of a duration of the active phase of at least two hours in multiparous
139 women or three hours in nulliparous women, in accordance with the ACOG/SMFM

140 recommendations (4).With regards to instrumental vaginal delivery, the use of forceps is not
141 performed as part of routine clinical practice in the participating Units. Obstetric intervention – i.e.
142 cesarean delivery or vacuum extraction – due to suspected intrapartum fetal compromise
143 represented an exclusion criterion for the study. All the obstetric interventions were performed
144 according to a commonly shared management protocol when the criteria for arrest of dilatation or
145 arrest of labor in the second stage were fulfilled (4).

146 Clinical data including maternal age, ethnicity, body mass index, gestational at delivery, induced or
147 spontaneous labor, epidural analgesia, augmentation during labor, length of the first and of the
148 second stage of labor, head station and cervical dilatation at diagnosis of protracted active phase of
149 labor as well as mode of delivery, estimated blood loss, birthweight, 5 minutes APGAR and arterial
150 pH was collected from patient case notes.

151 Intrapartum ultrasound performed for research purposes

152 Portable ultrasound devices equipped with low frequency transabdominal probe were used for the
153 study purposes. The US measurements were performed on women lying in semirecumbent position
154 with an empty bladder. Transabdominal US was performed by placing the probe transversely over
155 the maternal suprapubic region to assess the position and the flexion of the fetal head. The position
156 was defined from the landmarks depicting fetal occiput and described as a clock face with 12 hourly
157 divisions. Positions >09:30 and <2:30 o'clock were classified as occiput anterior, while occiput
158 transverse and occiput posterior (OP) were defined in the case of occiput ≥ 02.30 and ≤ 03.30 o'clock
159 or ≥ 08.30 h and ≤ 09.30 o'clock and >03.30 and <08.30 o'clock, respectively (31,39).

160 Based on our experience no ultrasound parameter has the potential to objectively evaluate the
161 degree of head flexion for all the positions of the fetal occiput. The flexion of the fetal head was
162 quantitatively defined by means of the occiput-spine angle (OSA) for the fetuses in occiput anterior
163 and occiput transverse position and by means of the chin-to-chest angle (CCA) for the fetuses in OP

164 position. In details, the OSA was identified by the angle between a line tangent to the posterior
165 cervical spine and a second line tangent to the fetal occiput, as previously described (36) (Figure 1).
166 The CCA was defined as the angle identified by the intersection between one line tangent to one
167 straight structure represented by the longest axis of the sternum and a second line tangent to
168 another straight structure represented the skin covering the inferior boundary of the oral cavity up
169 to the chin (Figure 2).

170 Transperineal ultrasound was performed with the transducer placed in a transverse or longitudinal
171 position between the labia majora or more caudally at the level of the fourchette and allowed the
172 measurement of the sonographic indicators of fetal head station and descent. The head-perineum
173 distance (HPD) was assessed by placing the probe in the posterior fourchette and applying a gentle
174 but firm pressure on the perineum as previously described (40). The angle of progression (AoP) was
175 measured on the midsagittal image by drawing one line between calipers placed at the two points
176 identifying the long axis of the pubic symphysis; a second caliper line was then created on the frozen
177 image that extended from the most inferior portion of the pubic symphysis tangentially to the fetal
178 skull contour (41). All the measurements were obtained in the absence of uterine contractions
179 and/or maternal pushing efforts.

180 Endpoints

181 The primary outcome of the study was to evaluate the sonographic indicators of fetal head flexion,
182 i.e. the OSA and the CCA in fetuses in non-OP and in OP position, respectively, as measured at
183 diagnosis of protracted active phase of labor in relation to the mode of delivery and other labor
184 outcomes. Furthermore, we evaluated the relationship between the OSA and the CCA and the
185 transperineal sonographic indicators of fetal head descent.

186 Ethics approval

187 Ethics approval for this study was granted by the local Ethics Committee at the University Hospitals
188 of Parma (N 270/2018/OSS/UNIPR on 03/12/2018) and Rome Tor Vergata (N 17/Ob2 on
189 15/10/2017) and at the Sant'Anna Hospital of Turin (N 0061542 on 21/06/2017).

190 Statistical analysis

191 Statistical analysis was performed using SPSS version 20 (IBM Inc., Armonk, NY, USA). Normal or
192 abnormal distribution of continuous variables was evaluated by means of the Kolmogorov-Smirnov
193 and the Shapiro-Wilk tests and data were shown as mean \pm standard deviation or as median (range)
194 accordingly. Comparison of normally and non-normally distributed continuous variables included
195 the T test for independent sample and 2-tailed t test and the Mann-Whitney U-test, respectively.
196 Categorical variables were reported as number (percentage) and compared using the Chi-square or
197 Fisher exact test. Logistic regression analysis was used to control for potential confounding
198 variables, while the prediction of the mode of delivery by intrapartum sonographic parameters was
199 determined by receiver operating characteristic (ROC) curve analysis. $p < 0.05$ was considered as
200 significant. This study was conducted following the STROBE guidelines (42).

201 **Results**

202 Overall, 129 women were included (Figure 3). The transabdominal and transperineal ultrasound
203 examination was successfully performed in all the eligible cases. Baseline and obstetrical features
204 of our cohort population are shown in Table 1. Spontaneous vaginal delivery occurred in 66 (51.2%)
205 women, while instrumental vaginal delivery and cesarean delivery were recorded in 17 (13.1%) and
206 46 (35.7%), cases, respectively. The mean length of the first and second stage of labor was $495 \pm$
207 171 minutes and 107 ± 52 minutes, respectively. No case of failed instrumental delivery requiring
208 emergency cesarean delivery was recorded. At diagnosis of protracted active phase of labor occiput
209 anterior, occiput transverse and OP positions accounted for 59 (45.8%), 27 (20.9%) and 43 (33.3%)
210 of the included cases.

211 Clinical and sonographic findings in fetuses in non-occiput posterior position are shown in Table 2a.
212 A wider OSA (126.2 ± 14.4 vs 114.5 ± 23.6 degrees, $p=0.006$) and AoP (117.5 ± 12.7 vs 104.0 ± 10.7
213 degrees, $p<0.001$) and a shorter HPD (39.7 ± 5.2 vs 49.0 ± 9.4 mm, $p<0.001$) were measured in women
214 who had vaginal delivery, however only the OSA and the HPD proved to be independently associated
215 with the mode of delivery at logistic regression analysis ($p=0.007$ and $p=0.001$, respectively)(Table
216 3a). At ROC curve the OSA was found to be associated with an area-under-the-curve (AUC) of 0.675,
217 95%CI (0.538-0.812), $p<0.01$. The optimal cut-off value of the OSA discriminating between cases of
218 VD vs those delivered by CS was 108.5 degrees, and was associated with a 56.7% sensitivity, 87.5%
219 specificity, 70.8% PPV and 79.0% NPV. When addressing the correlation between the OSA and the
220 sonographic indicators of fetal head station, the OSA showed a direct correlation with the AoP
221 (Pearson's correlation 0.449, $p<0.01$) but no correlation with the HPD ($p=0.15$). At visual analysis of
222 the scatter/dot charts (Figure 4), 9 cases in which the AoP of progression was not positively
223 correlated with the OSA were noted and labelled as outliers. Such cases showing a narrow AoP and
224 a wide OSA were all submitted to cesarean delivery and characterized by a lower maternal height

225 (157±7 vs 163±6 cm, $p<0.01$) and a higher ratio between the birthweight and the maternal height
226 (22.6±1.6 vs 20.7±2.6, $p=0.04$) compared to the non-outlier cases. An inverse correlation between
227 the OSA and the HPD (Pearson's correlation -0.566, $p<0.01$) and a stronger correlation between the
228 OSA and the AoP (Pearson's correlation 0.693, $p<0.01$) were demonstrated following the removal
229 of the 9 outliers from the non-OP dataset. Furthermore, following the removal of the 9 outlier cases
230 a OSA width >108.5 degrees showed 80.9% sensitivity, 87.5% specificity, 70.8% PPV and 92.5% NPV
231 for the mode of delivery and an overall 7.5% rate of cesarean delivery.

232 The clinical and the sonographic findings in fetuses in OP position are shown in Table 2b. A narrower
233 CCA (27.2±32.9 vs 56.2±27.7 degrees, $p=0.005$) and a lower rate of induction of labor (22.2% vs
234 62.5%, $p=0.008$) were found in women who had vaginal delivery. At logistic regression analysis CCA
235 and labor induction proved to be independently associated with the mode of delivery ($p=0.008$ and
236 $p=0.007$, respectively, Table 3b). At ROC curve the CCA was associated with an area-under-the-curve
237 (AUC) for the mode of delivery of 0.758, 95%CI (0.612-0.904), $p<0.01$. The optimal cut-off value of
238 the CCA discriminating between cases of VD vs those delivered by CS was 33.0 degrees, which was
239 associated with a 93.8% sensitivity, 63.0% specificity, 60.0% PPV and 94.4% NPV. No correlation was
240 found between the CCA and the AoP ($p=0.48$) nor the HPD ($p=0.98$).

241 **Discussion**

242 Principal findings

243 The results from this study conducted on a selected cohort of women with protracted active phase
244 of labor demonstrate that the degree of flexion of the fetal head as measured at transabdominal
245 ultrasound is related to the mode of delivery in OP as well as in non-OP fetuses, being head deflexion
246 associated with an increased risk of cesarean delivery due to labor dystocia. Furthermore, fetal head
247 station as measured at transperineal ultrasound by means of the HPD is independently associated
248 with the likelihood of vaginal delivery in non-OP fetuses. Finally, in non-OP fetuses the degree of
249 fetal head flexion correlates with the transperineal sonographic indicators of fetal head station.

250 Results in the context of what is known

251 The relationship of fetal head to spine – also referred to as “fetal attitude” – in the first-stage of
252 labor has traditionally been considered to impact on fetal head descent and ultimately on labor
253 outcome. Deflexed cephalic presentations are acknowledged to represent major determinants of
254 obstructed labor (7,8,36). According to the mechanics of the human labor the descent of the
255 presenting part through the birth canal is associated with a progressive flexion of the fetal head on
256 the chest (5). On this basis, previous data from an unselected population of non-OP fetuses
257 suggested that cephalic malpresentations in terms of deflexed fetal head are associated with a
258 higher clinical station and an increased likelihood of obstetric intervention secondary to intrapartum
259 dystocia (36). Consistently, a recent research conducted on 200 women found an increased
260 incidence of cesarean delivery in fetuses showing sonographic features of head deflexion (43). In
261 this study the degree of fetal head flexion was measured by means of the OSA in non-OP fetuses,
262 while in OP fetuses a qualitative assessment of the fetal attitude was performed. However, this
263 research did not include cases of labor dystocia, and the participating women were recruited at full
264 cervical dilatation and not during the first-stage of labor (43).

265 Some studies previously evaluated the risk of obstetric intervention secondary to labor dystocia in
266 relation to the position and the station of the fetal head at diagnosis of protracted active phase of
267 labor (33-35,44-47). Under these circumstances, an increased likelihood of cesarean delivery due to
268 labor dystocia was reported in fetuses with OP position and a high fetal station at transperineal
269 ultrasound as demonstrated by a long HPD and a narrow AoP. Our study has confirmed a similar
270 relationship between the sonographic indicators of fetal head station and the mode of delivery in
271 fetuses in non-OP position but not in those in OP position, among whom labor induction proved to
272 be independently associated with the likelihood of cesarean delivery.

273 Clinical implications

274 According to the recommendations of the International Society on Ultrasound in Obstetrics and
275 Gynecology, intrapartum ultrasound is indicated in conditions of first-stage dystocia (31). Based on
276 the findings from this study, the evaluation of the degree of flexion of the fetal head might be
277 incorporated in the sonographic evaluation of cases of protracted active phase of labor. However,
278 it is uncertain whether in such conditions the use of ultrasound can lead to an individualized
279 management in terms of increased augmentation in the case of favorable conditions in terms of
280 good head flexion and, conversely, anticipated caesarean delivery in the case of malpresentation
281 with or without malposition of the presenting part.

282 Research implications

283 Based on our results, we believe that also subtle degrees of deflexion of the fetal head may preclude
284 its descent through the birth canal by impairing the most favorable (suboccipito-bregmatic)
285 diameter of the fetal head to negotiate the pelvic inlet, thus leading to dystocia requiring cesarean
286 delivery (5,6).

287 Furthermore, this present study suggests that our ability in understanding the underlying cause of
288 protracted active phase of labor may be improved thanks to the use of ultrasound. The finding of

289 outlier cases requiring cesarean delivery due to labor dystocia and characterized by a high head
290 station (as witnessed by the narrow AoP and the long HPD) and no evidence of malposition and
291 malpresentation (i.e. non-OP position and wide OSA) may be interpreted in terms of cephalo-pelvic
292 disproportion. This hypothesis is supported by the fact that such cases were characterized by a lower
293 maternal height and by a higher birthweight-to-maternal height ratio in comparison to “non-
294 outliers”. We do envisage that in these conditions any attempt to perform an instrumental vaginal
295 delivery should be balanced against the risks of “true” obstructed labor. However, more research is
296 required in order to clarify whether the head circumference (48,49), the maternal height (50-53) or
297 other sonographic indices may be considered in the individualized management of the laboring
298 woman diagnosed with protracted active phase of labor in cases characterized by non-OP position,
299 wide OSA, narrow AoP and long HPD.

300 With regards to the degree of flexion of the fetal head in OP fetuses, ours is the first study describing
301 a quantitative parameter – i.e. the CCA – for the assessment of the degree of flexion of the fetal
302 head, which we show to be associated with a fair sensitivity and NPV in the prediction of CS due to
303 labor dystocia. The low specificity and positive predictive value of the CCA suggest that the degree
304 of flexion of the fetal head may vary across labor and may not represent the only determinant of
305 labor arrest in OP fetuses.

306 While we first describe the CCA as a sonographic indicator of flexion in OP fetuses, no correlation
307 could be demonstrated between the CCA and the AoP nor the HPD. This is likely to be dependent
308 on the different – and thus far unexplored – mechanics of the fetal head descent in OP compared
309 to the non-OP fetuses.

310 Strengths and limitations

311 This is the first study evaluating the sonographic indices of fetal head flexion which can be measured
312 on transabdominal ultrasound in women with protracted active phase of labor. Another strength is

313 that this study was prospectively conducted at three Units with dedicated expertise in intrapartum
314 ultrasound, which has allowed the collection of several ultrasound parameters within a selected
315 population of women at risk of cesarean delivery due to protracted active phase of labor.

316 With regards to the limitations, we acknowledge that our cohort was not powered for adverse
317 maternal and perinatal outcomes. Therefore, more research is warranted in order to understand
318 whether the deflexion of the fetal head in conditions of protracted active phase of labor impacts on
319 maternal and fetal outcomes other than on the mode of delivery. Another limitation is represented
320 by the fact that the measurement of the CCA may be challenging, and its intra- and inter-observer
321 reproducibility was not preliminary tested. Therefore, it is uncertain whether the use of such
322 sonographic parameter can be easily implemented outside the context of Units with expertise on
323 ultrasound in labor such as those participating to this present study. Additionally, we acknowledge
324 that complex malpresentations such as asynclitism, among whom some are known to impact on the
325 labor outcome regardless of the additional sonographic parameters (54-60), were not evaluated.

326 Conclusions

327 In conclusion, this work shows that within a selected cohort of women with protracted active phase
328 of labor, the evaluation of the sonographic indices of fetal head flexion is associated with the
329 incidence of labor dystocia leading to cesarean delivery in OP as well as in non-OP fetuses, while the
330 head station is related to the mode of delivery in non-OP but not in OP fetuses. This research
331 supports the sonographic assessment of the degree of flexion of the presenting part in conditions
332 of protracted active phase of labor, and suggest that intrapartum ultrasound may contribute in the
333 categorization of the etiology of the dystocia and support the individualized management of
334 conditions of protracted active phase of labor.

335 **Conflict of interest statement**

336 The Authors state no financial disclosures nor conflict of interest related to the content of this
337 research.

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1 **TITLE PAGE**

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2 **Intrapartum sonographic assessment of the fetal head flexion in protracted active phase of labor**
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5 **and association with labor outcome: a multicentre, prospective study.**

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25 **Condensation:**

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3 26 The sonographic indicators of deflexed fetal head are associated with labor dystocia leading to
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5 27 caesarean delivery in women with protracted active phase of labor.
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10 29 **Short title:**

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13 30 Intrapartum US in protracted active phase of labor.
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18 32 **AJOG at a glance**

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21 33 A. Why was the study conducted?

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23 34
 - To evaluate the relationship between the intrapartum sonographic indicators of fetal head

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25 flexion and the mode of delivery in women with protracted active phase of labor.
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28 36 B. What are the key findings?

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31 37
 - A wide occiput-spine angle and a narrow chin-chest angle are associated with an increased

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33 incidence of vaginal delivery. A correlation between the occiput-spine angle and the

34 38
35 sonographic indicators of fetal head station was also demonstrated.
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39 40 C. What does this study add to what is already known?

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41 41
 - The sonographic indicators of fetal head flexion are associated with labor dystocia leading

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43 to cesarean delivery in women with protracted active phase of labor. The findings from this

44 42
45 study suggest that intrapartum ultrasound may contribute in the categorization of the

46 43
47 etiology of labor dystocia.
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54 46 **Keywords**

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57 47 Ultrasound in labor, labor dystocia, intrapartum care, caesarean delivery, instrumental delivery,
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59 48 occiput-spine angle, chin-chest angle, angle of progression, head-perineum distance.
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50 **Abstract**

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3 **Background**

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6 To date no research has focused on the sonographic quantification of the degree of flexion of the
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8 fetal head in relation to the labor outcome in women with protracted active phase of labor.

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10 **Objective**

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13 To assess the relationship between the transabdominal sonographic indices of fetal head flexion
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15 and the mode of delivery in women with protracted active phase of labor.

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18 **Study design**

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21 Prospective evaluation of women with protracted active phase of labor recruited across three
22
23 tertiary maternity units. Eligible cases were submitted to transabdominal ultrasound for the
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25 evaluation of the fetal head position and flexion, which was measured by means of the occiput-
26
27 spine angle (OSA) in fetuses in non-occiput posterior (OP) position and by means of the chin-to-
28
29 chest angle (CCA) in fetuses in OP position. The OSA and the CCA were compared between women
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31 who had vaginal delivery vs those who had cesarean delivery. Cases where obstetric intervention
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33 was performed solely based on suspected fetal distress were excluded.

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36 **Results**

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39 129 women were included, of whom 43 (33.3%) had OP position. Spontaneous vaginal delivery,
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41 instrumental delivery and cesarean delivery were recorded in 66 (51.2%), 17 (13.1%) and 46 (35.7%)
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43 cases, respectively. A wider OSA was measured in women who had vaginal delivery compared to
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45 those submitted to cesarean delivery due to labor dystocia (126±14 vs 115±24, p<0.01). At ROC
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47 curve the area-under-the-curve (AUC) was 0.675, 95%CI (0.538-0.812), p<0.01, and the optimal OSA
48
49 cut-off value discriminating between cases of vaginal delivery vs those delivered by cesarean
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51 delivery was 109 degrees. A narrower CCA was measured in cases who had vaginal delivery
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53 compared to those undergoing cesarean delivery (27±33 vs 56±28 degrees, p<0.01). The AUC of the
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74 CCA in relation to the mode of delivery was 0.758, 95%CI (0.612-0.904), $p < 0.01$, and the optimal
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75 cut-off value discriminating between vaginal delivery and cesarean delivery was 33.0 degrees.

56 **Conclusions**

77 In women with protracted active phase of labor, the sonographic demonstration of fetal head
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78 deflexion in OP and in non-OP fetuses is associated with an increased incidence of cesarean delivery
79 due to labor dystocia. Such findings suggest that intrapartum ultrasound may contribute in the
80 categorization of the etiology of labor dystocia.

81 **Introduction**

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3 82 Labor dystocia is estimated to account for approximately one third of all caesarean deliveries, the
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5 83 vast majority being primary cesarean deliveries (1,2). Among these, arrest of dilatation in the first-
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8 84 stage of labor is acknowledged to represent the most common indication (3,4). Such condition may
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11 85 result from distinct but potentially coexisting mechanisms which include abnormalities of the
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13 86 uterine contractions, malpositions or malpresentations of the fetal head and cephalopelvic
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15 87 disproportion (5-13).

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18 88 The progression of the first-stage of labor has been historically assessed by means of the norms of
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21 89 active phase dilatation described by Friedman (14-26) and more recently re-evaluated by Zhang et
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23 90 al. (1,27,28). These latter, which show a slow but progressive first-stage dilatation prior to 6 cm and
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26 91 an overall slower course of labor compared to Friedman’s sigmoid curve (14-17,23,25,26), are
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28 92 currently endorsed for labor management by the American College of Obstetricians and
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31 93 Gynecologists and by the Society for Maternal and Fetal Medicine (4,29). The active phase dilatation
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33 94 is positively affected by the descent of the fetal head in the birth canal, and in normal labor a direct
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36 95 correlation between the first-stage dilatation and the descent of the fetal head has been
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39 96 demonstrated (30). The engagement and the progression of the fetal head through the birth canal
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41 97 in the first-stage of labor are known to be to be influenced by the mechanism of head flexion –
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44 98 which allow the shortest cephalic diameters to negotiate the maternal pelvis (5,6).

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46 99 Available data suggests that ultrasound outweighs the digital examination in the assessment of the
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49 100 fetal head station (31,32), progression and attitude, and ultrasound is currently endorsed as an
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52 101 adjunct to the clinical evaluation in conditions of protracted active phase of labor and arrest of
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54 102 dilatation (31). Under these circumstances, the sonographic indicators of the fetal head station
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57 103 including the head-perineum distance (HPD) and the angle of progression (AoP) have been shown
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59 104 to be more accurate than the digital examination in predicting the occurrence of cesarean delivery
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105 (33-35). In an unselected group of women in the active phase of labor with occiput anterior and
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106 occiput transverse fetuses the degree of fetal head flexion measured at transabdominal ultrasound
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107 has been shown to be associated with the digital station and the likelihood of operative delivery
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108 (36). Other sonographic studies have demonstrated that also in fetuses in occiput posterior (OP)
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109 position the qualitative assessment of the fetal head deflexion is related to the chance of vaginal
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130 delivery (37,38). To date no research has focused on the sonographic quantification of the degree
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111 of flexion of the fetal head in relation to the labor outcome in women with protracted active phase
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1812 of labor. The aim of this study was to evaluate the relationship between the intrapartum ultrasound
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2113 indicators of malposition and malpresentation and the risk of obstetric intervention within a
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2314 selected cohort of women diagnosed with a protracted active phase of labor.
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115 **Methods**

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116 Study design

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117 This was a prospective, observational study conducted between December 2018 and June 2020 and
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118 including three maternity units in Italy (University Hospitals of Parma and Rome Tor Vergata and
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119 Sant'Anna Hospital of Turin). A non-consecutive series of non-anomalous singleton term
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120 pregnancies, with no history of previous uterine scar and with a protracted active phase of labor
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121 was included. According to the local protocol of the participating Units, women diagnosed with
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1822 protracted active phase of labor are submitted to clinical examination by the senior Obstetrician
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21 responsible for the patient care. For the present study, following the clinical diagnosis of protracted
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24 active phase of labor intrapartum ultrasound was performed for research purposes also by five
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27 investigators with dedicated training on ultrasound in labor (AD, TG, EDP, BM and GR) who were
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30 not involved in the clinical management. The senior Obstetricians in charge for the labor care were
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33 blinded to the ultrasound findings.

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3629 According to the protocol for the labor management adopted across the participating Units,
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39 protracted active phase of labor was defined based on the ACOG/SMFM recommendations for the
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42 safe prevention of the primary cesarean delivery (4). In details, a protracted active phase of labor
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45 was defined in women ≥ 6 cm of dilatation with ruptured membranes who fail to progress despite 4
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48 hours of adequate uterine activity or at least 6 hours of oxytocin administration with inadequate
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51 uterine activity and no first-stage dilatation. In such cases, the arrest of dilatation requiring cesarean
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54 delivery was defined following two more hours of oxytocin administration with no cervical change.

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5735 In the case of progression of the first-stage dilatation, obstetric intervention was indicated during
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60 the first-stage in the event of the above criteria, while the diagnosis of arrest of labor in the second
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63 stage was made in the event of a duration of the active phase of at least two hours in multiparous
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66 women or three hours in nulliparous women, in accordance with the ACOG/SMFM

139 recommendations (4).With regards to instrumental vaginal delivery, the use of forceps is not
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140 performed as part of routine clinical practice in the participating Units. Obstetric intervention – i.e.
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141 cesarean delivery or vacuum extraction – due to suspected intrapartum fetal compromise
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142 represented an exclusion criterion for the study. All the obstetric interventions were performed
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143 according to a commonly shared management protocol when the criteria for arrest of dilatation or
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144 arrest of labor in the second stage were fulfilled (4).

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145 Clinical data including maternal age, ethnicity, body mass index, gestational at delivery, induced or
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146 spontaneous labor, epidural analgesia, augmentation during labor, length of the first and of the
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147 second stage of labor, head station and cervical dilatation at diagnosis of protracted active phase of
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148 labor as well as mode of delivery, estimated blood loss, birthweight, 5 minutes APGAR and arterial
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149 pH was collected from patient case notes.

28 29 150 Intrapartum ultrasound performed for research purposes

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151 Portable ultrasound devices equipped with low frequency transabdominal probe were used for the
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152 study purposes. The US measurements were performed on women lying in semirecumbent position
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153 with an empty bladder. Transabdominal US was performed by placing the probe transversely over
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154 the maternal suprapubic region to assess the position of the fetal head, while the flexion was
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155 evaluated by tilting the probe by 90 degrees to the longitudinal plane. The position was defined
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156 from the landmarks depicting fetal occiput and described as a clock face with 12 hourly divisions.
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157 Positions >09:30 and <2:30 o'clock were classified as occiput anterior, while occiput transverse and
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158 occiput posterior (OP) were defined in the case of occiput ≥02.30 and ≤03.30 o'clock or ≥08.30 h
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159 and ≤09.30 o'clock and >03.30 and <08.30 o'clock, respectively (31,39).

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160 Based on our experience no ultrasound parameter has the potential to objectively evaluate the
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161 degree of head flexion for all the positions of the fetal occiput. The flexion of the fetal head was
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162 quantitatively defined by means of the occiput-spine angle (OSA) for the fetuses in occiput anterior
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163 and occiput transverse position and by means of the chin-to-chest angle (CCA) for the fetuses in OP
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164 position. In details, the OSA was identified by the angle between a line tangent to the posterior
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165 cervical spine and a second line tangent to the fetal occiput, as previously described (36) (Figure 1).
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166 The CCA was defined as the angle identified by the intersection between one line through the
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167 longest axis of the sternum and a second line through another straight structure represented by the
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168 skin covering the inferior boundary of the oral cavity up to the chin (Figure 2).
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169 Transperineal ultrasound was performed with the transducer placed in a transverse or longitudinal
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1870 position between the labia majora or more caudally at the level of the fourchette and allowed the
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2171 measurement of the sonographic indicators of fetal head station and descent. The head-perineum
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2372 distance (HPD) was assessed by placing the probe in the posterior fourchette and applying a gentle
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2673 but firm pressure on the perineum as previously described (40). The angle of progression (AoP) was
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2974 measured on the midsagittal image by drawing one line between calipers placed at the two points
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3175 identifying the long axis of the pubic symphysis; a second caliper line was then created on the frozen
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3476 image that extended from the most inferior portion of the pubic symphysis tangentially to the fetal
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3677 skull contour (41). All the measurements were obtained in the absence of uterine contractions
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3978 and/or maternal pushing efforts.
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4179 Endpoints

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4480 The primary outcome of the study was to evaluate the sonographic indicators of fetal head flexion,
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4781 i.e. the OSA and the CCA in fetuses in non-OP and in OP position, respectively, as measured at
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4982 diagnosis of protracted active phase of labor in relation to the mode of delivery and other labor
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5283 outcomes. Furthermore, we evaluated the relationship between the OSA and the CCA and the
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5484 transperineal sonographic indicators of fetal head descent.
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5685 Ethics approval

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186 Ethics approval for this study was granted by the local Ethics Committee at the University Hospitals
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3 of Parma (N 270/2018/OSS/UNIPR on 03/12/2018) and Rome Tor Vergata (N 17/Ob2 on
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6 188 15/10/2017) and at the Sant'Anna Hospital of Turin (N 0061542 on 21/06/2017).

189 Statistical analysis

190 Statistical analysis was performed using SPSS version 20 (IBM Inc., Armonk, NY, USA). Normal or
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13 abnormal distribution of continuous variables was evaluated by means of the Kolmogorov-Smirnov
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16 192 and the Shapiro-Wilk tests and data were shown as mean \pm standard deviation or as median (range)
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19 accordingly. Comparison of normally and non-normally distributed continuous variables included
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21 194 the T test for independent sample and 2-tailed t test and the Mann-Whitney U-test, respectively.
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24 195 Categorical variables were reported as number (percentage) and compared using the Chi-square or
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27 196 Fisher exact test. Logistic regression analysis was used to control for potential confounding
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30 variables, while the prediction of the mode of delivery by intrapartum sonographic parameters was
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33 198 determined by receiver operating characteristic (ROC) curve analysis. $p < 0.05$ was considered as
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65 199 significant. This study was conducted following the STROBE guidelines (42).

200 **Results**

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201 Overall, 129 women were included (Figure 3). The transabdominal and transperineal ultrasound
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202 examination was successfully performed in all the eligible cases. Baseline and obstetrical features
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203 of our cohort population are shown in Table 1. Spontaneous vaginal delivery occurred in 66 (51.2%)
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204 women, while instrumental vaginal delivery and cesarean delivery were recorded in 17 (13.1%) and
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205 46 (35.7%), cases, respectively. The mean length of the first and second stage of labor was $495 \pm$
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206 171 minutes and 107 ± 52 minutes, respectively. No case of failed instrumental delivery requiring
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207 emergency cesarean delivery was recorded. At diagnosis of protracted active phase of labor occiput
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208 anterior, occiput transverse and OP positions accounted for 59 (45.8%), 27 (20.9%) and 43 (33.3%)
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209 of the included cases.

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210 Clinical and sonographic findings in fetuses in non-occiput posterior position are shown in Table 2a.
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211 A wider OSA (126 ± 14 vs 115 ± 24 degrees, $p=0.006$) and AoP (118 ± 13 vs 104 ± 11 degrees, $p<0.001$)
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212 and a shorter HPD (40 ± 5 vs 49 ± 9 mm, $p<0.001$) were measured in women who had vaginal delivery,
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213 however only the OSA and the HPD proved to be independently associated with the mode of
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214 delivery at logistic regression analysis ($p=0.007$ and $p=0.001$, respectively) (Table 3a). At ROC curve
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215 the OSA was found to be associated with an area-under-the-curve (AUC) of 0.675, 95%CI (0.538-
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216 0.812), $p<0.01$. The optimal cut-off value of the OSA discriminating between cases of VD vs those
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217 delivered by CS was 109 degrees, and was associated with a 56.7% sensitivity, 87.5% specificity,
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218 70.8% PPV and 79.0% NPV. When addressing the correlation between the OSA and the sonographic
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219 indicators of fetal head station, the OSA showed a direct correlation with the AoP (Pearson's
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220 correlation 0.449, $p<0.01$) but no correlation with the HPD ($p=0.15$). At visual analysis of the
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221 scatter/dot charts (Figure 4), 9 cases in which the AoP of progression was not positively correlated
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222 with the OSA were noted and labelled as outliers. Such cases showing a narrow AoP and a wide OSA
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223 were all submitted to cesarean delivery and characterized by a lower maternal height (157 ± 7 vs
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224 163±6 cm, p<0.01) and a higher ratio between the birthweight and the maternal height (22.6±1.6
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225 vs 20.7±2.6, p=0.04) compared to the non-outlier cases.
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226 When considering only the 62 non-OP fetuses with OSA width above 109 degrees – i.e. with
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227 favorable head flexion –, such outlier cases accounted for 9/13 cesarean deliveries. Outlier cases
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228 showed a higher ratio between the OSA and the AoP (1.45±0.19 vs 1.09±0.10, p<0.001) and a lower
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229 ratio between the OSA and the HPD (2.60±0.46 vs 3.40±0.50, p<0.001) compared to non-outliers.
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230 The distribution of the OSA/AoP ratio in relation to the mode of delivery showed a trend towards
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231 an increased rate of CS with increasing OSA/AoP ratio (Figure 5a), while a trend towards an
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232 increased rate of CS was noted with decreasing OSA/HPD ratio (Figure 5b). At ROC curve the
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233 OSA/AoP ratio was found to be associated with an AUC for the prediction of cesarean delivery of
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234 0.769, 95%CI (0.586-0.952), p=0.003, while the OSA/HPD ratio was associated with an AUC of 0.778,
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235 95%CI (0.631-0.925), p=0.002. The optimal cut-off value of the OSA/AoP ratio discriminating
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3236 between cases of VD vs those delivered by CS was 1.20, and was associated with a 69.2% sensitivity,
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3237 87.8% specificity, 60.0% PPV and 91.5% NPV; the optimal cut-off value of the OSA/HPD ratio
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3238 discriminating between cases of VD vs those delivered by CS was 3.05, and was associated with a
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3239 69.2% sensitivity, 77.6% specificity, 45.0% PPV and 90.5% NPV.
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41 The clinical and the sonographic findings in fetuses in OP position are shown in Table 2b. A narrower
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441 CCA (27±33 vs 56±28 degrees, p=0.005) and a lower rate of induction of labor (22.2% vs 62.5%,
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4742 p=0.008) were found in women who had vaginal delivery. At logistic regression analysis CCA and
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4943 labor induction proved to be independently associated with the mode of delivery (p=0.008 and
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5244 p=0.007, respectively, Table 3b). At ROC curve the CCA was associated with an area-under-the-curve
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5445 (AUC) for the mode of delivery of 0.758, 95%CI (0.612-0.904), p<0.01. The optimal cut-off value of
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5746 the CCA discriminating between cases of VD vs those delivered by CS was 33.0 degrees, which was
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247 associated with a 93.8% sensitivity, 63.0% specificity, 60.0% PPV and 94.4% NPV. No correlation was
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248 found between the CCA and the AoP ($p=0.48$) nor the HPD ($p=0.98$).
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249 **Discussion**

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250 Principal findings

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251 The results from this study conducted on a selected cohort of women with protracted active phase
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252 of labor demonstrate that the degree of flexion of the fetal head as measured at transabdominal
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253 ultrasound is related to the mode of delivery in OP as well as in non-OP fetuses, being head deflexion
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254 associated with an increased risk of cesarean delivery due to labor dystocia. Furthermore, fetal head
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255 station as measured at transperineal ultrasound by means of the HPD is independently associated
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256 with the likelihood of vaginal delivery in non-OP fetuses. Finally, in non-OP fetuses the degree of
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257 fetal head flexion correlates with the transperineal sonographic indicators of fetal head station.
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258 Results in the context of what is known

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259 The relationship of fetal head to spine – also referred to as “fetal attitude” – in the first-stage of
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260 labor has traditionally been considered to impact on fetal head descent and ultimately on labor
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261 outcome. Deflexed cephalic presentations are acknowledged to represent major determinants of
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262 obstructed labor (7,8,36). According to the mechanics of the human labor the descent of the
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263 presenting part through the birth canal is associated with a progressive flexion of the fetal head on
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264 the chest (5). On this basis, previous data from an unselected population of non-OP fetuses
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265 suggested that cephalic malpresentations in terms of deflexed fetal head are associated with a
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266 higher clinical station and an increased likelihood of obstetric intervention secondary to intrapartum
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267 dystocia (36). Consistently, a recent research conducted on 200 women found an increased
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268 incidence of cesarean delivery in fetuses showing sonographic features of head deflexion (43). In
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269 this study the degree of fetal head flexion was measured by means of the OSA in non-OP fetuses,
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270 while in OP fetuses a qualitative assessment of the fetal attitude was performed. However, this
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271 research did not include cases of labor dystocia, and the participating women were recruited at full
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272 cervical dilatation and not during the first-stage of labor (43).
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273 Some studies previously evaluated the risk of obstetric intervention secondary to labor dystocia in
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274 relation to the position and the station of the fetal head at diagnosis of protracted active phase of
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275 labor (33-35,44-47). Under these circumstances, an increased likelihood of cesarean delivery due to
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276 labor dystocia was reported in fetuses with OP position and a high fetal station at transperineal
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277 ultrasound as demonstrated by a long HPD and a narrow AoP. Our study has confirmed a similar
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278 relationship between the sonographic indicators of fetal head station and the mode of delivery in
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279 fetuses in non-OP position but not in those in OP position, among whom labor induction proved to
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280 be independently associated with the likelihood of cesarean delivery.
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281 Clinical implications

282 According to the recommendations of the International Society on Ultrasound in Obstetrics and
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283 Gynecology, intrapartum ultrasound is indicated in conditions of first-stage dystocia (31). Based on
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284 the findings from this study, the evaluation of the degree of flexion of the fetal head might be
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285 incorporated in the sonographic evaluation of cases of protracted active phase of labor. However,
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286 it is uncertain whether in such conditions the use of ultrasound can lead to an individualized
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287 management in terms of increased augmentation in the case of favorable conditions in terms of
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288 good head flexion and, conversely, anticipated caesarean delivery in the case of malpresentation
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289 with or without malposition of the presenting part.
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43 Research implications

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291 Based on our results, we believe that also subtle degrees of deflexion of the fetal head may preclude
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292 its descent through the birth canal by impairing the most favorable (suboccipito-bregmatic)
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293 diameter of the fetal head to negotiate the pelvic inlet, thus leading to dystocia requiring cesarean
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294 delivery (5,6).

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295 Furthermore, this present study suggests that our ability in understanding the underlying cause of
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296 protracted active phase of labor may be improved thanks to the use of ultrasound. The finding of
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297 outlier cases requiring cesarean delivery due to labor dystocia and characterized by a high head
1 station (as witnessed by the narrow AoP and the long HPD) and no evidence of malposition and
298 2 malpresentation (i.e. non-OP position and wide OSA) may be interpreted in terms of cephalo-pelvic
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299 5 malpresentation (i.e. non-OP position and wide OSA) may be interpreted in terms of cephalo-pelvic
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300 7 disproportion. This hypothesis is supported by the fact that such cases were characterized by a lower
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301 10 maternal height and by a higher birthweight-to-maternal height ratio in comparison to “non-
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302 12 outliers”. We do envisage that in these conditions any attempt to perform an instrumental vaginal
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303 15 delivery should be balanced against the risks of “true” obstructed labor. However, more research is
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304 17 required in order to clarify whether the head circumference (48,49), the maternal height (50-53) or
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305 20 other sonographic indices may be considered in the individualized management of the laboring
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306 22 woman diagnosed with protracted active phase of labor in cases characterized by non-OP position,
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307 25 wide OSA, narrow AoP and long HPD.
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308 28 With regards to the degree of flexion of the fetal head in OP fetuses, ours is the first study describing
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309 31 a quantitative parameter – i.e. the CCA – for the assessment of the degree of flexion of the fetal
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310 33 head, which we show to be associated with a fair sensitivity and NPV in the prediction of CS due to
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311 35 labor dystocia. The low specificity and positive predictive value of the CCA suggest that the degree
36 37
312 38 of flexion of the fetal head may vary across labor and may not represent the only determinant of
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313 41 labor arrest in OP fetuses.
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314 44 While we first describe the CCA as a sonographic indicator of flexion in OP fetuses, no correlation
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315 46 could be demonstrated between the CCA and the AoP nor the HPD. This is likely to be dependent
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316 49 on the different – and thus far unexplored – mechanics of the fetal head descent in OP compared
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317 51 to the non-OP fetuses.
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318 Strengths and limitations

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319 56 This is the first study evaluating the sonographic indices of fetal head flexion which can be measured
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320 59 on transabdominal ultrasound in women with protracted active phase of labor. Another strength is
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321 that this study was prospectively conducted at three Units with dedicated expertise in intrapartum
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322 ultrasound, which has allowed the collection of several ultrasound parameters within a selected
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323 population of women at risk of cesarean delivery due to protracted active phase of labor.
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324 With regards to the limitations, we acknowledge that our cohort was not powered for adverse
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1325 maternal and perinatal outcomes. Therefore, more research is warranted in order to understand
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1326 whether the deflexion of the fetal head in conditions of protracted active phase of labor impacts on
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1327 maternal and fetal outcomes other than on the mode of delivery. Another limitation is represented
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1328 by the fact that the measurement of the CCA may be challenging, and its intra- and inter-observer
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229 reproducibility was not preliminary tested. However, it is important to note that all the research
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230 scans were performed by a small number of investigators with expertise on ultrasound in labor,
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231 therefore we believe that in such context a variability in the CCA measurements is highly unlikely.
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232 Therefore, it is uncertain whether the use of such sonographic parameter can be easily implemented
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333 outside the context of Units with expertise on ultrasound in labor such as those participating to this
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334 present study. We acknowledge that additional malpresentations such as asynclitism, which are
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335 known to impact the labor course (54-60), were not evaluated in this study. Such limitation needs
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336 to be taken into account in a clinical context where different types of malpresentation may coexist
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Conclusions

166 In conclusion, this work shows that within a selected cohort of women with protracted active phase
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345 head station is related to the mode of delivery in non-OP but not in OP fetuses. This research
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346 supports the sonographic assessment of the degree of flexion of the presenting part in conditions
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347 of protracted active phase of labor, and suggest that intrapartum ultrasound may contribute in the
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348 categorization of the etiology of the dystocia and support the individualized management of
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349 conditions of protracted active phase of labor.
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350 **Conflict of interest statement**

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351 The Authors state no financial disclosures nor conflict of interest related to the content of this
352 research.

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- 460 Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) Statement:
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