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## Elective induction of labour in low risk nulliparous women at term: Caution is needed



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## ABSTRACT

The recently published ARRIVE trial demonstrated that “policies aimed at the avoidance of elective labour induction among low-risk nulliparous women at 39 weeks of gestation are unlikely to reduce the rate of caesarean delivery on a population level”. In this commentary we discuss some controversial aspects of the study that in our opinion may undermine its validity at wide population level.

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It has come a time in Obstetrics when the classical clinical management of low risk term pregnancy is about to be revolutionised. Indeed, we have grown up with the idea that a policy of labour induction should be mostly based on medical indication and reserved to those pregnancies with a recognized risk factor for adverse maternal or perinatal outcome [1,2].

The caveat against a wide medicalization of term gestations has been based upon evidence provided by a series of studies showing an increased risk of postpartum haemorrhage, caesarean delivery as well as costs for women submitted to induction, risks that were claimed as not acceptable if the induction was not clinically indicated [1,3–9]. Furthermore, obstetric interventions had also been associated with an increased incidence of late preterm delivery [10], with substantial impact of on perinatal morbidity. Finally, a general perception of “limited satisfaction” of the antenatal care has been reported in those women submitted to induction of labour [11,12].

More recently, the negative burden of labour induction has been hampered by studies which have shown that the increased risks of labour induction hold true only if we compared induction vs spontaneous onset of labour but not vs expectant management [12–18].

Among these, one RCT found no difference in the caesarean section rate nor in the incidence of short-term adverse maternal or neonatal outcomes in women aged 35 or above undergoing elective induction at 39 weeks compared to those submitted to expectant management [16].

Furthermore, available evidence has consistently shown that the safest gestational age for delivery in terms of perinatal outcome is around 39 weeks [9].

And finally a revolutionary approach in the pregnancy care seems now on its way after the recent publication on the New England Journal of Medicine of the ARRIVE trial by Grobman et al. [19]. In this extraordinarily large multicentric randomised trial conducted on behalf of Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network, nulliparous women who were at 38 weeks 0 days to 38 weeks 6 days of gestation were randomly assigned to induction at 39 weeks 0 days to 39 weeks 4 days or to expectant management. The primary outcome was a composite of perinatal death or severe neonatal

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complications; the principal secondary outcome was caesarean delivery. A total of 3062 women were assigned to labour induction, and 3044 were assigned to expectant management. The primary outcome occurred in 4.3% of neonates in the induction group and in 5.4% in the expectant-management group but this difference was not statistically significant (relative risk, 0.80; 95% confidence interval [CI], 0.64–1.00). On the other hand, the frequency of caesarean delivery (18.6% vs. 22.2%; relative risk, 0.84; 95% CI, 0.76 to 0.93) and that of hypertensive disorders of pregnancy (9.1% vs. 14.1%; relative risk, 0.64; 95% CI, 0.56 to 0.74;  $P < 0.001$ ) was significantly lower in the induction group than in the expectant-management group. Based on the study findings the Authors conclude that “policies aimed at the avoidance of elective labour induction among low-risk nulliparous women at 39 weeks of gestation are unlikely to reduce the rate of caesarean delivery on a population level”.

Before the findings of this study are passively incorporated in the standard obstetric practice of western countries, we would like to discuss some controversial aspects of the ARRIVE trial that in our opinion may undermine the external validity of the study at wide population level. The key misunderstanding of the ARRIVE study is that we are dealing with a high-risk group of pregnant women and not with a low risk of nulliparous women as claimed by the Authors and explicitly mentioned in the title. Indeed, the vast proportion of obese women in both arms of the trial as the mean body mass index of the entire population (above 30 kg/m<sup>2</sup> in both arms) cannot simply be licensed as a demographic characteristic of the study cohort but should be emphasized as a major risk factor for obstetric and perinatal complications. The high prevalence of obesity is the most plausible explanation for the unexpected burden of hypertensive disorders in the last two or three weeks of pregnancy provided that up to 38 weeks all the randomized women had been confirmed to have normal blood pressure. Indeed, 9.1% of the patients induced at 39 weeks and 14.1% of those managed expectantly developed de novo hypertension. On this basis, the Authors concluded that a policy of elective induction of labour of low risk nulliparous women allegedly implies a significant decrease of hypertensive disorders of pregnancy, which are among the secondary outcomes of the study. On this ground, we would rephrase saying that a policy of elective delivery at 39 weeks among obese women might reduce the incidence of hypertension manifesting beyond 38–39 weeks. Additionally, we would also speculate that the differences in the prevalence of hypertensive disorders at the time of delivery may account for the significant difference in the rate of caesarean delivery and the borderline significant difference in the incidence of primary composite outcome. If we take for granted that obese women with hypertension at term gestation have a higher risk of caesarean delivery and of perinatal events compared with their normotensive counterpart, here it is explained why the policy of induction at 39<sup>+0</sup> to 39<sup>+4</sup> weeks yielded a lower rate of these outcomes.

In other words, the two arms of the ARRIVE trial were almost comparable at randomization (36 and again 38 weeks) but not at delivery because in the expectant management group the prevalence of hypertensive disorders was significantly higher compared to the induction group. Such disproportionate presence of obese women in the whole study cohort might also account for the borderline improvement in the overall perinatal outcome and in the significant reduction of some neonatal events which were documented in the induction arm compared with the standard care one [19]. Obesity itself is widely acknowledged as a major risk factor for adverse perinatal outcome independently from the association with hypertensive disorders or preeclampsia [3], whose presence in the ARRIVE trial was excluded at least up to 38 weeks. A recent retrospective study on a large cohort of pregnant women has shown a significant decrease in perinatal mortality among women with body mass index higher than 30 who were electively induced before

term compared with those managed expectantly [20]. The high prevalence of overweight and obese women in the ARRIVE trial [19] may also explain why the prevalence of composite adverse perinatal outcome was substantially higher (5.4 vs 3.5%) compared to that hypothesized by the Authors before commencing the study. Again, this gives further strength to our belief that the study group enrolled for this RCT is not a low risk one, therefore a more plausible title for this paper should be “Labour Induction versus Expectant Management in Obese Nulliparous Women”.

One additional demographic parameter which is worth being commented is represented by the maternal age, whose negative association with the success rate of labour induction was demonstrated in previous studies from Western Countries [4]. In a large population-based study conducted on a wide cohort of Swedish women and evaluating the risk factors associated with post-term pregnancy and caesarean section following labour induction in singletons, maternal age above 35 years was associated with an over two-fold higher risk of caesarean section compared to a reference population aged between 20 and 24 years [21]. The reported median maternal age within the ARRIVE cohort was lower compared to former data [22], and this may further explain the favourable effects of induction of labour within a population mainly represented by obese women of young age.

On this ground, we are skeptical that the results of the ARRIVE study may become fully applicable to a truly low risk population of nulliparous women at term and we do believe that demographic parameters should be considered together with the pregnancy-related risk factors – on an individual basis – when considering the option of induction of labour [5,23]. Nonetheless, the ARRIVE trial has demonstrated that a policy of universal induction of labour at 39 completed weeks within a population of overweight and obese women is undoubtedly advantageous in reducing the caesarean section rate and the risk of adverse perinatal outcome and then should be considered as a possible standard of care in this particular clinical setting.

### Key message

Demographic parameters and obstetric risk factors should be evaluated on an individual basis when considering the option of elective induction of labour in low risk pregnancies at term gestation.

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