Recommendations and guidelines for perinatal practice

Guidelines for the management of postterm pregnancy*

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Abstract

A pregnancy reaching 42 completed weeks (294 days) is defined as postterm (PT). The use of ultrasound in early pregnancy for precise dating significantly reduces the number of PT pregnancies compared to dating based on the last menstrual period. Although the fetal, maternal and neonatal risks increase beyond 41 weeks, there is no conclusive evidence that prolongation of pregnancy, *per se*, is the major risk factor. Other specific risk factors for adverse outcomes have been identified, the most important of which are restricted fetal growth and fetal malformations. In order to prevent PT and associated complications routine induction before 42 weeks has been proposed. There is no conclusive evidence that this policy improves fetal, maternal and neonatal outcomes as compared to expectant management. It is also unclear if the rate of cesarean sections is different between the two management strategies. After careful identification and exclusion of specific risks, it would seem appropriate to let women make an informed decision about which management they wish to undertake. There is consensus that the number of inductions necessary to possibly avoid one stillbirth is very high. If induction is preferred, procedures for cervical ripening should be used, especially in nulliparous women. Close intrapartum fetal surveillance should be offered, irrespective of whether labor was induced or not.

Keywords: Birth weight; body mass index; postterm pregnancy; ultrasound.

Abbreviations

PT	postterm
GA	gestational age
US	ultrasound
LMP	last menstrual period
BMI	body mass index
SB	stillbirth
IUGR	intrauterine growth restriction
PNM	perinatal mortality
BW	birth weight
NNM	neonatal mortality
SGA	small for gestational age
NICU	neonatal intensive care unit
MAS	meconium aspiration syndrome
CS	cesarean section
CRL	crown rump length
BPD	biparietal diameter
FL	femur length
RCT	randomized controlled trial
SR	systematic review
NNT	number needed to treat
CTG	cardiotocography
NST	non-stress test
AF	amniotic fluid
AFI	amniotic fluid index
EDD	expected date of delivery
IVF	*in-vitro* fertilization

Introduction

According to FIGO [4] and ACOG [3], a pregnancy lasting 42 weeks or more is defined as postterm (PT). Epidemiological studies have shown that after 41 weeks, the rate of fetal, maternal and neonatal complications increase. As such, management of this condition remains a matter of concern for most clinicians. Many national scientific societies have produced guidelines that are likely to be influenced by the characteristics of the local health systems. The aim of this document is to offer recommendations based on available evidence. This document particularly emphasizes the findings of published studies after 1990 to allow for more recent changes in obstetric practice, new surveillance tests, induction techniques and advances in neonatal care. The reported level of evidence follows the criteria suggested by ACOG.

Prevalence and etiology

The prevalence of PT is commonly reported as 4–10%. In Europe, the prevalence estimates range from 0.8% to 8.1% [112]. This wide variation is likely to be the consequence of different policies of labor induction and methods for assessing gestational age (GA). Ultrasound (US) dating of pregnancy is more accurate than that based upon the last menstrual period (LMP) and the use of routine US dating significantly reduces the rate of PT. When pregnancies are routinely dated by US and in the absence of a policy of induction only 7% of the pregnancies progress beyond 294 days and 1.4% beyond 301 days [63]. The etiology of PT is largely unknown, but both fetal abnormality (e.g., anencephaly) and placental sulphatase deficiency can be associated with prolongation of pregnancy. It has also been suggested that some genetic factors [56], fetal gender [28] and a high pre-pregnancy body mass index (BMI) can contribute to an increased risk for PT [88].

Diagnosis

The diagnosis is overtly simple: pregnancy duration beyond 42 weeks from the LMP. Unfortunately, even in the presence of regular menstrual cycles, the true GA is different from the estimated GA in a significant number of cases. The most accurate method for assessing GA is fetal biometry performed by US in early pregnancy.

Complications of postterm pregnancy

Fetal

Many epidemiological studies based on birth registries have been published [15, 22, 25, 29, 30, 46, 47, 49, 50, 71, 87], but the findings are somewhat inconsistent. In five studies, a significant increase in stillbirth (SB) has been observed [15, 29, 50, 71, 87], in particular if the SB risk as a function of ongoing pregnancies rather than SB rate per 1000 total births is used [25]. In two studies, increased SB rate has only been observed in nulliparous women [47, 50], whereas four other studies [15, 22, 30, 49] have suggested that risk factors, such as intrauterine growth restriction (IUGR) and fetal malformations outweigh the contribution of prolonged pregnancy to the risk of SB. The weakness of most epidemiological studies is that they do not describe the causes of death. Furthermore, epidemiological data are often drawn from large and distant secular periods. The latter do not take into account the advances in modern obstetrics, particularly in pregnancy dating and fetal assessment. The contribution of poor access and inequity of care is also often overlooked especially because an increasing migrant population and with racial differences exist in SB rates [11, 104]. The conclusions of epidemiological studies may vary according to whether the authors have included risk factors other than GA. The most important independent risk factor for SB is IUGR, which is associated with SB in 52% of the cases at any GA

[33] and when unrecognized, is the cause of 10% of perinatal mortality (PNM) in Europe [78].

Retrospective cohort studies with exclusion of complications and careful monitoring of maternal and fetal well-being have been published [5, 7, 57, 63, 106]. They all conclude that in uncomplicated PT there is no increase of SBs or PNM. Although these studies are smaller and prone to weakness of this particular methodology, the importance of careful monitoring is emphasized [48]. However, two prospective hospital-based cohort studies have recently [42, 66] made contradictory observations regarding PNM rates, possibly reflecting differences in prenatal care between the two centers. Further, large prospective studies should be performed with uniform criteria for defining maternal and fetal complications. However, due to the relatively low prevalence of PT-related complications, very large studies would be required, decreasing the likelihood that they would be ever carried out.

The pathophysiological basis for the increased fetal risk in uncomplicated PT is unclear, although it has long been suggested that an underlying tendency for placental senescence exists in PT. Fetal growth appears to be unaffected until 43 weeks of gestation [26] and uncomplicated PT pregnancies do not appear to show differences in umbilical artery Doppler indices [58], fetal heart rate patterns [59] or cord blood nucleated red blood cell counts [76].

Maternal

A significant increase in the rate of maternal complications in PT is reported in all studies [7, 15, 49, 57, 63, 71, 106]. The most common are dysfunctional labor, shoulder dystocia, obstetric trauma and post-partum hemorrhage. These complications are associated with increased birth weight (BW) (>4000 g) and macrosomia (>4500 g) which is observed in 22% and 4% of newborns, respectively, at 41 weeks [63]. It has also been suggested that induction of labor can further increase the risk of labor complications [7, 42], although increased cesarean section (CS) rate has only been observed in nulliparous, but not multiparous women [20]. Even though maternal anxiety can increase when pregnancy progresses beyond term, two studies [57, 108] have suggested that women do not perceive this as a significant medical problem.

Neonatal

Mortality   A higher rate of NM is reported in some [20, 22, 46, 50, 71], but not in other studies [15, 30, 49, 63]. Where evaluated, both small for gestational age (SGA) and major congenital malformations appear to increase this risk [22, 30].

Neonatal complications   Neonatal complications include low Apgar scores, acidemia, admission to neonatal intensive care unit (NICU), meconium aspiration syndrome (MAS), clavicular fracture and Erb's palsy. Meconium stained liquor is a physiological finding in fetal life and should not be regarded as a neonatal complication. The frequency of meco-

nium stained liquor increases with advancing GA and is thought to be a consequence of fetal gut maturation [6]. Occasionally, meconium stained liquor is the consequence of chronic fetal hypoxemia that is reported to occur in 30% of IUGR fetuses [60]. MAS, on the other hand, is potentially a life threatening condition, which is thought to occur when acute hypoxemia during labor causes fetal gasping in the presence of meconium stained liquor [23]. There is also considerable evidence that meconium aspiration may occur before labor, but only manifest as MAS once delivery has occurred [81, 94]. Apgar scores are reported in six studies [20, 22, 42, 49, 63, 71]. The difference in low Apgar scores (<7) between term and PT newborns was not significant in all the studies. In one study low Apgar and acidemia were more frequently observed after induction than after spontaneous onset of labor [42]. Birth trauma is significantly more frequent in PT and is probably associated with increased BW.

The increased risks of fetal, maternal and neonatal complications depend on many factors. Fetal size, parity and the presence of malformations all play important roles. In cases of reduced fetal size, complications due to fetal hypoxemia are significantly increased. On the other hand, in cases with a normally functioning placenta and large fetal size or macrosomia, the risk of traumatic delivery is increased [61, 80].

Management

Two management strategies are recommended [3]. The first is to prevent the prolongation of pregnancy by inducing labor and the second is expectant treatment under close surveillance, with active management by induction of labor or CS only when specifically indicated. In either case, correct assessment of GA is crucial to avoid unnecessary interventions.

Gestational age assessment

The most precise and reproducible method for assessing GA is fetal biometry by US in early pregnancy [21, 75, 96]. US has proved to be more accurate than GA assessment based on the LMP even in women with regular menstrual cycles [54, 91, 95]. Moreover, fetal biometry was shown to be very accurate even in *in-vitro* fertilization (IVF) pregnancies, when the time of embryo transfer is known [82, 86, 99]. The prevalence and need for induction of PT pregnancies has been reduced significantly after the introduction of routine US dating [12, 16, 31, 35]. Adverse effects of adjusting the GA according to US have not been reported [97, 98]. In the first trimester pregnancies are dated according to the crown-rump length (CRL). In the second trimester the biparietal diameter (BPD) may be used alone or in combination with femur length (FL). The accuracy of CRL for dating is superior to that of 2nd or 3rd trimester biometry [53]. Therefore, early US scanning should be routinely performed, and US biometry should be used to date pregnancy, irrespective of the degree of concordance with LMP-based GA. If there is a discrepancy in GA assessment in subsequent US exami-

nations, revision of the GA is not warranted; other explanations, such as IUGR or accelerated growth should be considered.

In conclusion, before choosing any kind of management it is fundamental that the GA is accurately assessed. US biometry in early pregnancy is the best available method and the subsequent management of PT pregnancy should be performed on the basis of the US adjusted GA. However, it must be remembered that even the best method has a small margin of error.

Routine induction vs. expectant management

The target of avoiding the prolongation of the pregnancy at or beyond 42 weeks is to prevent or reduce fetal, maternal and neonatal complications. All eight randomized controlled trials (RCTs) published since 1990 compared routine induction of labor before 42 weeks and expectant management [17, 36, 39, 44, 45, 51, 68, 79]. The three most recent meta-analyses are evaluated in this document [38, 84, 107] as well as observational prospective [8, 10, 52], retrospective case/control [13, 73, 102] or retrospective cohort [41, 89, 111] studies. Although a case-control study must be retrospective, a cohort study can be either prospective or retrospective.

Randomized controlled trials

Perinatal mortality   No significant differences in PNM have been reported in the published RCTs. In the largest and most influential RCT, no neonatal deaths were observed after exclusion of congenital abnormalities [39]. Although there were two SBs in the expectant arm of the study, both were of SGA babies (BW ≤10 centile) that were not diagnosed prenatally.

Cesarean section   No differences in CS rates were reported in seven out of eight RCTs. In one study there was a significantly lower CS rate in the induction group [39]. One possible explanation for this finding was published four years later [40] by the same authors in a secondary analysis of data from the same RCT. In the expectant management group 554 (32.4%) women were actually induced with a CS rate of 33.6%, whereas in the expectant non-induced group the CS rate was 20.1%. The CS rate was higher in nulliparous women irrespective of allocation and was highest (42%) among nulliparous women randomized to expectant management, but required induction of labor. In contrast to the Canadian study, the majority of RCTs reported a significant reduction in CS for either abnormal intrapartum fetal heart rate patterns or poor labor progress in both treatment and control groups, when spontaneous labor ensued. The Canadian multicenter PT pregnancy trial has been criticized for the methodology and the conclusions [64].

Neonatal morbidity   No differences in neonatal morbidity were reported in seven RCTs. Only one study found a small but significant increase in MAS and shoulder dystocia in the expectant management group [36].

Systematic reviews (SRs) and meta-analysis

The principal task of a meta-analysis is to pool data from different RCTs. The possible limitations of SRs and meta-analysis have been extensively examined and discussed [27, 34, 74, 93]. The three available SRs on PT management are influenced by two types of potential bias: >50% of all RCTs were published before 1990 [38, 84, 107] making homogeneity of the studies a problem and the Canadian multicenter PT pregnancy [39] study represents the major contributor to the pooled cases in all SRs, despite concerns regarding the consistency of the findings in this study (see above).

The results for perinatal outcome are contradictory with one SR showing improvement [38] and the other two no reduction in PNM [84, 107].

Two SRs reported lower CS rates in the induction group [38, 107] whilst the third showed no difference between groups [84].

In two reviews a lower prevalence of MAS was observed in the induction group [38, 107].

One method by which homogeneity may be improved is to only include into SRs the RCTs published after 1990. The obvious reason for this is that modern obstetrics has changed over the last decades in terms of the introduction of routine US and fetal surveillance. However, the inclusion of the Canadian multicenter PT pregnancy which accounts for some 60% of cases will significantly influence the results of a meta-analysis [39]. Wennerholm et al. [107] performed a sub-analysis after exclusion of the Canadian trial [51] and found no significant differences in CS rate. Due to the very small PNM rates, estimates are that a definitive study would require randomization of between 16,000 [38] and 30,000 [39] pregnancies. At present no such studies exist, and they will presumably never be performed.

Observational studies

These are not homogenous with different study designs and study populations. The CS rates were significantly increased with induction of labor compared to spontaneous labor in six studies [8, 10, 13, 52, 73, 102], particularly in nulliparous women [41, 111]. Only one study [89] reports a lower CS rate in the induction group.

Numbers needed to treat (NNT)

The NNT to avoid one SB or perinatal death varies between studies. NNT ranges from 100 to infinity [38] and from 500 to >1000 [64]. These numbers are strongly dependent on the estimation of the fetal/neonatal risk. A more recent analysis presented the NNT according to GA [43]. It was estimated that the NNT is reduced with advancing GA from 527 inductions at day 287 to 195 inductions at day 302.

Conclusions

The findings are equivocal on the advantages or disadvantages of routine induction vs. expectant management. The individual RCTs report no differences in PNM, and only one of three SRs indicates a lower PM rate after routine induc-tion. Seven out of eight RCTs found no differences in CS rate after routine induction vs. expectant management. An increased rate of MAS with expectant management was found in one out of eight RCTs and two SRs. Maternal and neonatal traumatic complications are mainly a consequence of fetal macrosomia without evidence from RCTs [37] or SRs [83] that induction reduces the neonatal complication or CS rates. Therefore, both management strategies (routine induction or expectant management) are acceptable. The choice depends on the local capacities to diagnose the conditions with increased risks and to monitor the fetal well-being if expectant management is preferred.

Fetal assessment in the post-dates period

There is no agreement on a specific GA at which fetal monitoring should start. As the rate of fetal, maternal and neonatal complications are significantly increased beyond 41 weeks, it is reasonable to identify fetuses at high risk at that time.

Fetal

There are no specific fetal surveillance tests for PT pregnancy which are able to predict acute events (e.g., placental abruption or cord complications). The most commonly used tests are cardiotocography (CTG) non-stress test (NST), amniotic fluid (AF) volume assessment [amniotic fluid index (AFI) or deepest pocket], fetal biophysical profile, US estimation of fetal weight and Doppler studies on umbilical and fetal vessels.

Cardiotocography This is the most commonly used fetal surveillance test, despite the accepted limitations due to inter- and intra-observer variability. In order to overcome this problem, computer assisted evaluation of CTG has been used. Assessment of the fetal heart rate variability offers a reliable assessment of fetal hypoxemia and/or acidemia. It has been shown that reduced fetal heart rate variability on the computerized CTG is associated with fetal distress in labor and acidemia [105]. The observation of a reactive CTG or short-term variability >4 ms (computerized CTG) offers good negative predictive value for SB, except for unpredictable acute events (e.g., placental abruption or cord accidents).

Ultrasound fetal biometry US can predict SGA defined as BW below the 10th or the 5th percentile [70]. As SGA and IUGR are not synonyms, the observed US measurements should be compared with the expected curve of growth based on any previous scans in order to identify the degree of growth restriction. The recognition of IUGR and/or small fetal size identifies the most important risk factor for subsequent fetal and neonatal adverse outcomes. Non-reassuring fetal tests, before and during labor, are more frequently observed in cases of reduced fetal size [90] and rate of complications in labor is inversely correlated to the BW [85]. US biometry has limited value in diagnosing large or macrosomic fetuses because of the systematic error in estimated fetal

weight is about $\pm10\%$. As a consequence, the larger the fetus the larger the error will be in actual weight.

Amniotic fluid   AF volume evaluation is commonly performed in PT, usually with assessments of the AFI or the deepest pocket. Neither of the two methods reflects the actual AF volume [19]. Moreover, many studies have shown that the predictive value of the methods is poor in prolonged pregnancy [9, 18, 24, 65, 69].

Biophysical profile   This test is popular in the USA, but less so in Europe. Currently, there is insufficient evidence to support its use as a test of fetal well-being in high-risk pregnancies [55].

Doppler ultrasound   There is evidence that Doppler US of blood flow in the umbilical arteries improves management and outcome in high-risk pregnancies [67]. Although the routine use of Doppler US in low-risk pregnancies is not recommended, it is of established value in the evaluation of fetal well-being in cases of IUGR. Doppler US in fetal vessels (arterial and venous) assesses fetal adaptation to chronic hypoxemia. There is no evidence that fetal Doppler investigation is of value in timing delivery for the management of PT pregnancies.

There is no agreement on the optimal monitoring techniques or the interval at which these tests should be applied. The most commonly reported frequency is to do a test twice a week even without evidence that these tests improve outcome of PT pregnancy. US assessment of fetal size should not be performed at intervals <2 weeks. Assessment of fetal growth/size would appear to be critical to successful identification of high fetal/neonatal risk in PT pregnancies.

Maternal

The main maternal complications that need to be excluded are carbohydrate intolerance and gestational hypertension. Ketonuria should be assessed as it may alter the results of well-being fetal tests [72]. Parity should also be taken in consideration as the SB risk is increased in nulliparous, but not in multiparous women [47]. When fetal macrosomia is suspected, maternal stature must be evaluated to assess the risk of traumatic delivery for both mother and newborn.

Counseling

After exclusion of high-risk groups, routine induction or expectant management can be offered. Information must be provided to the patient clearly documenting risks and benefits of both management strategies, and the number of inductions needed to avoid one SB (NNT) should be disclosed. Counseling should be informative and not directive. The choice of the patient must be respected. The terms used must be easily understood by the patients.

Induction

The success of labor induction is dependent on the characteristics of the cervix, commonly referred to as cervical ripeness. The most commonly used method for assessing the cervix is the Bishop's score, where a score ≤4 is considered to be unfavorable for labor induction. More recently the transvaginal US assessment of the cervix has been proposed as a method for more accurately predicting the success of induction measured by the risk of cesarean for failed induction [92, 100] or spontaneous onset of labor [62, 77, 92, 100, 103].

Cervical ripening

Cervical ripening should be used to improve the success rate of induction in a woman with unfavorable or ultrasonographically long cervix. Many methods have been proposed, such as mechanical (transcervical Foley catheter with or without saline infusion, sweeping of the membranes, laminaria tents) and pharmacological (PGE 2 or PGE 1).

Methods for induction

Oxytocin, with or without amniotomy and prostaglandin can be used for labor induction. However, the concurrent use of prostaglandins and oxytocin is associated with myometrial hyperstimulation leading to tachycardia, non-reassuring CTGs and uterine rupture. It is therefore advisable that in case of pharmacological induction, especially with prostaglandins, fetal heart rate should be routinely monitored.

How long to leave?

When expectant management is undertaken, two key dilemmas exist: what is the best surveillance test (see above) and how long to wait before intervention? When routine induction is not performed, 7% of pregnancies continue beyond 42 weeks, but only 1.4% reach 43 weeks [63]. Due to the frequent use of routine induction before 42 weeks and to the fact that the majority of the women deliver spontaneously before 42 weeks, the number of available studies considering the outcome after 294 days is limited [5, 9, 10, 17, 63, 66, 73, 79]. Pooling 3914 cases observed after 42 weeks with exclusion of complications (malformations, maternal diabetes, IUGR), only two cases of perinatal deaths are reported (0.05%). From four studies it is possible to calculate that there were only 238 pregnancies passing beyond 43 weeks, precluding any firm conclusions. It is not possible to give a specific GA at which an otherwise uncomplicated pregnancy should be induced.

Delivery

Close fetal surveillance should be offered during either spontaneous or induced labor. Although the use of amnioinfusion in case of meconium stained liquor for preventing MAS is

controversial [32], it may have some advantages in clinical settings with limited access to peripartum surveillance [1, 110].

Neonatal management

MAS often arises as a result of fetal hypoxemia and subsequent gasping. There is no indication for oropharyngeal or nasopharyngeal suctioning with delivery of the head in these babies [2, 101]. A recent meta-analysis of four studies of endotracheal intubation at birth to prevent morbidity and mortality in vigorous meconium-stained infants born at term shows no benefit from this technique [109]. However, there is limited evidence of benefit in meconium-stained neonates born in poor condition and there may still be an indication for routine endotracheal intubation in these cases.

Recommendations

Recommendation	Level
GA should be accurately assessed with US, preferably using CRL measurements in the 1st trimester	A
An assessment of the maternal and fetal condition is recommended at 41 completed weeks in order to identify specific risks	B
After 41 completed weeks, routine induction or expectant management can be offered.	A
If specific risks are present, a prompt delivery should be performed	B
Complete information about risks and benefits of the two management strategies should be given, including the number of labor induction needed to prevent one SB	B
If induction is undertaken, cervical ripening should be performed	B
If expectant management is preferred, close monitoring of fetal and maternal conditions is recommended	B
Intrapartum fetal monitoring is recommended during PT labor, irrespective of induction or spontaneous onset	B
Induction for suspected macrosomia is not recommended	A
Appropriate neonatological assistance at birth should be provided	B

Level of evidence (ACOG)

Level A: ''Based on good and consistent scientific evidence''
Level B: ''Based on limited or inconsistent scientific evidence''
Level C: ''Based primarily on consensus and expert opinion''

Acknowledgements

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