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Fetal movements as a predictor of health

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Abstract

The key determinant to a fetus maintaining its health is through adequate perfusion and oxygen transfer mediated by the functioning placenta. When this equilibrium is distorted, a number of physiological changes, including reduced fetal growth, occur to favor survival. Technologies have been developed to monitor these changes with a view to prolong intrauterine maturity while reducing the risks of stillbirth. Many of these strategies involve complex interpretation, for example Doppler ultrasound for fetal blood flow and computerized analysis of fetal heart rate changes. However, even with these modalities of fetal assessment to determine the optimal timing of delivery, fetal movements remain integral to clinical decision-making. In high-risk cohorts with fetal growth restriction, the manifestation of a reduction in perceived movements may warrant an expedited delivery. Despite this, there has been little evolution in the development of technologies to objectively evaluate fetal movement behavior for clinical application. This review explores the available literature on the value of fetal movement analysis as a method of assessing fetal wellbeing, and demonstrates how interdisciplinary developments in this area may aid in the improvement of clinical outcomes.

Abbreviations: BPP, biophysical profile; cCTG, computerized cardiotocograph; CTG, cardiotocograph; FGR, fetal growth restriction; FHRV, fetal heart rate variability; SGA, small for gestational age; STV, short-term variation.

Introduction

The obstetrician's role in the antenatal period is principally early detection and management of maternal and fetal conditions that may influence the pregnancy outcome. In the third trimester, the main objective is to reduce the risk of stillbirth. Although some stillbirths are related to chromosomal or structural abnormalities, which may carry a poor prognosis irrespective of the timing of delivery, other pathologies may benefit from early detection.

In a large population-based cohort study of 2675 stillbirths from 1997 to 2003, 43% were attributable to fetal growth restriction (FGR) (1). If detected, a diagnosis of FGR may influence care and reduce the risk of stillbirth. In the past, FGR and small for gestational age (SGA) were

Key Message

The association between normal fetal movements and the physiological state in utero is clear. Its correlation with reassuring and pathological features of existing monitoring techniques support its clinical use, but this is dependent upon establishment of an accurate and objective assessment tool.

terms used almost interchangeably. Recently, there is an emerging concept that FGR may be diagnosed in a fetus whose biometry is within the normal percentiles, but where there is reduced growth velocity. This is a further challenge in the identification of FGR, and one that will require new screening strategies that do not rely on fetal biometry alone. Although fetal monitoring modalities have developed to help optimize the timing of delivery, perceived fetal movements remain crucial in that clinical decision-making.

Hypoxia

Adequate oxygenation of the fetal tissues is central to fetal wellbeing. The importance of fetal movements as a marker of health has been demonstrated in sheep models, with fetal behavior being reflective of fetal brain function. In acute onset hypoxemic intrauterine environments, movements are significantly reduced as a mechanism to conserve energy consumption (2). However, with prolonged stable hypoxemic exposure, fetal movements can return to normal patterns, presumably as part of a compensatory mechanism until the fetus becomes acidemic (3).

Physiology of fetal growth restriction

The physiological adaptations of the fetus during periods of hypoxemia are characterized by redistribution of blood flow away from the peripheries to the brain, heart and adrenals. Prolonged under-perfusion of the peripheral and hepato-enteric circulation results in tissue hypoxia and the accumulation of lactic acid, resulting in fetal acidosis. In the setting of placental insufficiency, acidemia is exacerbated by the reduced clearance of carbon dioxide. This brain-sparing response has been shown to affect fetal growth, Doppler blood flow and heart rate variability as well as fetal behavior. Understanding these physiological changes has facilitated the development of fetal monitoring techniques which aim to detect acute-on-chronic fetal compromise, and so to time delivery appropriately.

Our understanding of "at risk" babies is mainly derived from the monitoring of severely growth restricted fetuses. To understand the physiology of those at risk within the normal percentile range, it is important to appreciate fully the mechanisms involved in these severely compromised fetuses. Management of severe growth restriction is a delicate balance between the risks of iatrogenic preterm delivery and prolonging intrauterine maturity, with the risks of stillbirth and chronic acidemia to the fetus. In Europe, timing of delivery is largely based on Doppler investigations and fetal heart tracing, which identify hemodynamic decompensation and acidemia, respectively (4). However, in the USA, management is guided by the biophysical profile (BPP), a composite measure of the ultrasound assessment of amniotic fluid volume, fetal tone, breathing and movement, and fetal heart rate assessment (5). There is evidence that a reduction in fetal breathing and amniotic fluid volume resulting in an abnormal BPP score, is a late change that follows arterial and venous Doppler derangement (6). As such, its use may have a role in prolonging intrauterine maturity. While biophysical scoring is a composite measurement of physiological function, individual components of fetal movement have also been associated with fetal wellbeing.

Movement patterns

Fetal movement patterns are determined by neurological development of the fetus and its metabolic state. Early studies have shown that behavioral states of the normal fetus change throughout gestation, with periods of quiescence ranging on average from six minutes in the second trimester, up to 37 min in the late third (7). It has been suggested that the reduction in movements is due to improved coordination due to neurological maturity, in addition to reduced amniotic fluid and intrauterine space (8). Movement patterns also alter diurnally, with demonstrably increased fetal activity during the evening compared with that during the day (9).

Fetal movements and outcome

Numerous studies have shown that fetal movement provides an important measure of fetal health. Of women perceiving decreased fetal movements, 25% have poor perinatal outcomes, and more than half of stillbirths are preceded by decreased fetal movements (10). However, within a low-risk population, the detection rate of growth-restricted fetuses in response to a reduced perception of fetal movements, remains low. Although this may reflect the inter-patient subjectivity of quantifying movements, the correlation of perception and concurrent "true" movements detected by ultrasound is at best modest, with concordance as low as 37%, and false-positive rates of up to 30% (11). Moreover, in keeping with the data seen with biophysical profiling, a perceived reduction of movements is often a late sign which can already signify irreversible fetal compromise (12).

Currently, the only practical modality of quantifying fetal movements is through maternal perception. There is no consensus regarding the clinically significant lower threshold of movements; accordingly, the Royal College of Obstetricians and Gynaecologists does not recommend the quantification of movement through the use of kick charts (13).

When we consider the evidence from both animal and human studies, it is clear that fetal movement patterns are still not well defined. While a reduction in movements may represent an acute hypoxic episode, the restoration of movements may represent either a resolution of the hypoxia or the onset of a stable, chronic hypoxia. This is of critical importance in the management of antenatal patients: are we currently being falsely reassured by the return of movements? Moreover, would longitudinal quantification of these movements aid in reducing stillbirths? Currently, the only practice supported by strong evidence for screening of FGR is fetal biometry and Doppler studies (14). However, although this allows detection of those babies which are SGA, i.e. a size less than the 5th or the 10th percentile, the majority of term stillbirths are within the normal weight percentiles (15). This poses an important dilemma that there is currently no strategy to tackle: how do we determine "at risk" fetuses that are not meeting their growth potential but who lie within two standard deviations of the mean? These are truly growth-restricted fetuses that are failing to meet their growth potential secondary to a pathological process, as opposed to being simply SGA. Arguably, the former is the cohort that is most at risk. This cohort of patients may be falsely reassured following an ultrasound scan with conventional parameters. The capability to objectively characterize movement patterns may aid our understanding of normality and allow detection of fetuses at risk, who can then be offered further antenatal surveillance and organization of a timely delivery.

Existing methods for assessing fetal health

Cardiotocography (CTG)

Cardiotocography is a well-established method of monitoring fetal wellbeing. Its underlying principle is that compensatory changes of heart rate patterns can be predictive of fetal hypoxia. Four features are typically described in the interpretation of a CTG trace; each of these will be discussed below in terms of their relation to fetal wellbeing.

Fetal heart rate variability (FHRV). Antenatal electronic fetal monitoring of FHRV is an important predictor of fetal wellbeing in SGA pregnancies (16). Profound reductions in FHRV are thought to represent acute fetal compromise. Unlike clinical assessment of FHRV on a traditional CTG, which has well acknowledged intra-observer variability and which does not alter perinatal mortality (17), computerized CTG (cCTG) produces objective measures of FHRV based on the Dawes–Redman criteria previously published (18). One such measure, short-term variation (STV), is a statistical summary measure of the variation in inter-beat intervals of a 3.75-s epoch of averaged fetal heart rate recordings, excluding pronounced accelerations and decelerations. Reduction of STV to below 3 ms within 24 h of delivery has been shown to be predictive of an increased risk of metabolic acidosis and early neonatal death (16). Although there is a clear correlation between fetal acidosis and a reduction in fetal movements (19), the use of movement as an objective measure for detecting acidosis has not been translated into clinical use. As such, interpretation of cCTG based on STV remains essential for prenatal surveillance of fetuses with suspected FGR to detect acute fetal distress requiring delivery (14). STV is recognized to be lower in FGR fetuses than in control groups, even while remaining above the critical threshold of 3 ms, with a positive predictive value for acidemia of 77% (20); attempts to better predict fetal acidemia outside the context of acute fetal distress are being made by further cCTG characterization of the accelerative capacity of the fetal heart rate (20,21).

Baseline fetal heart rate. The baseline fetal heart rate fluctuates under the influence of centrally mediated sympathetic and parasympathetic tones. The rate can alter with increasing gestational age as these two systems mature at different rates and between different fetal behavioral states (22). Diurnal variation in FHRV is also seen, as well as a certain amount of intrinsic variability (23). Increases in normal values for STV are seen with advancing gestational age with lower rates of increase in FGR fetuses (21). Ultrasound CTG studies (24) and fetal magnetocardiogram studies (25) demonstrate that the relative time spent in each fetal behavioral state is unchanged between normally grown and growth-restricted fetuses. This suggests that autonomic dysregulation of FHR control, even when not acutely distressed, underlies the observed differences in FHR variation between these groups. Whether this represents a loss of autonomic control or an inability of the fetal heart to respond to autonomic control has yet to be demonstrated.

Accelerations. Fetal heart accelerations are an indication of normal neurological function, mediated through the somatic nervous system. In a study investigating the association of accelerations with fetal movements, 52 fetuses under CTG surveillance were simultaneously scanned by ultrasound. The study demonstrated that 99.6% of large accelerations and 82.4% of small accelerations were associated with concurrent fetal movements (26). Conversely, the absence of accelerations has been

noted during fetal sleep cycles. This physiological phenomenon may reflect the parasympathetic dominance during periods of rest.

Decelerations. Late decelerations are typically associated with fetal distress. Schifrin et al. demonstrated with the use of concurrent real time ultrasonography that late decelerations occurring following a normal CTG trace with a stable baseline and variability may be strongly suggestive of fetal breathing movements (27). Fetal breathing is an important component of biophysical profiling and is typically associated with fetal wellbeing (5). The findings support previous observations that isolated decelerations with a normal baseline and variability are not usually associated with an adverse outcome (28).

Doppler ultrasonography

Doppler ultrasound provides valuable information on the impedance to blood flow through vessels. In the setting of placental insufficiency and FGR, changes are first seen in the umbilical artery that is reflective of high placental impedance. However, this typically only manifests after 30% of the placenta is affected (29). As a compensatory mechanism, blood is preferentially redirected to the brain that is reflected in lower impedance to flow in the middle cerebral arteries. Late changes are reflected in the venous system as demonstrated by changes in flow velocity pattern of the ductus venosus. Its compromise (demonstrated by "a" wave reversal) reflects altered cardiac function as a result of altered shunting of oxygenated blood from the umbilical vein into the fetal heart, and is predictive of poor prognosis.

The understanding of the sequence of Doppler changes reflecting hemodynamic compensation in early growth-restricted fetuses has gradually evolved to improve neonatal outcome (30). However, management strategies to prolong intrauterine maturity of late FGR are less clear, in part because sub-critical failure of placental function may not result in Doppler changes or severe growth restriction.

Biophysical profile

Investigators have previously correlated Doppler changes with BPP to improve surveillance for high-risk babies (31). In a large cohort of 987 patients, Crimmins et al. found that all biophysical parameters became abnormal in severely growth-restricted fetuses at <34 weeks' gestation, with hemodynamic redistribution and changes in venous Dopplers. In the less severe group involving patients at >34 weeks' gestation, but also exhibiting cerebrovascular redistribution on Doppler, they demonstrated that BPP changes were generally a late feature, with normal findings still seen within a week of stillbirth. These results suggest that the biophysical parameters that were assessed in this high-risk cohort may have been such a late feature that they were not clinically useful in the prevention of stillbirth. This supports the use of current management strategies based on Doppler techniques as the most predictive of adverse outcome.

However, complex Doppler investigations are typically only performed in specialized units and once FGR is suspected. Bardakci et al. compared the performance of the umbilical artery Doppler with a modified BPP score in fetuses at >36 weeks' gestation (32). The data suggest that the detection of adverse perinatal outcomes was superior with BPP compared with umbilical artery Doppler. This either suggests that more comprehensive Dopplers than just those of the umbilical artery are essential for surveillance of late fetal distress, or that the sensitivity of the BPP may be improved with gestational maturity.

Assessment of fetal movements

Maternal sensation

Despite the development of ultrasound scanning and Doppler technologies, maternal perception remains the most common method of quantifying movement as a marker of fetal health. Reduced movements have been associated with poor outcome in terms of growth restriction and stillbirth, with the UK Confidential Enquiry into Stillbirths and Deaths in Infancy indicating that 16% of all stillbirths are preceded by a reduction of perceived activity (33). When the outcome measures are broadened to consider neonatal outcomes such as intrauterine growth restriction in addition to stillbirths, the incidence of reduced fetal movements is found to be even greater, experienced by 25% of those who subsequently delivered with an adverse outcome (10).

Unfortunately, our comprehension of fetal movement patterns still does not provide clear guidance on the quantification of perceived movements which can be classified as "normal" or "safe". In fact, the advice of a minimum threshold of 10 fetal movements per 12-h period that often forms the basis for counseling patients, originated from data involving high-risk populations who were studied as inpatients on wards (34). This is problematic both in itself, being based on a skewed population, and also due to the confounding effects of psychological impact while a hospital inpatient. Despite the lack of consensus in clinical guidelines, "kick counting" has been established as a common method of screening high-risk patients in many healthcare settings. However, in a major study involving 68 000 women

randomized to counting or not, no significant difference in outcomes for the two groups were observed. The authors concluded that once perceived movements were reduced, it was often too late to save the baby (35).

Cardiotocograph

Rayburn et al. investigated overall CTG interpretation in comparison with perceived fetal movements quantified by the mother (36). In 206 high-risk individuals, they found that 97% of women with an active fetus had normal CTG parameters. Moreover, in the presence of reduced fetal movement with an abnormal CTG, the outcomes were invariably poor. However, in larger populations where CTG is used in the setting of triaging women who present with reduced movements, Valentin et al. report a poor concordance between perceived movements and abnormal CTG findings; with 84% found to have reassuring CTGs (12). Although it is not clear from the data whether the sequence of natural events are reduced movements prior to heart rate changes, or vice versa, their use in conjunction has a good sensitivity when both are abnormal.

Actograph

Due to the significant time involved with performing movement characterization using ultrasound, there have been efforts to find alternative tools to analyze fetal movements. During the 1980s, an actograph function was introduced to fetal heart rate monitoring by CTG. The actograph separates high-frequency Doppler signals, indicative of the fetal heart rate, from low-frequency signals, indicative of fetal movements. A number of early studies showed promising results of capturing major fetal movements, reporting a concordance of movements with concurrent real time ultrasonography of as high as 95% (37,38). However, in later studies, as actograph became more widely available and was incorporated into most CTG devices, it was reported that false-positive rates were unacceptably high and the authors urged caution in its clinical use (39). Currently, the actograph is not widely used in either clinical or research settings.

Ultrasound and BPP

Given that Manning first proposed the BPP as an important technique in the assessment of wellbeing in 1979, it is surprising that technology to objectively quantitate and potentially qualitatively analyze different types of movement in relation to fetal health has not progressed as quickly as other modalities of fetal monitoring. Ultrasound remains the gold standard in total quantification, and although numerous groups have comprehensively characterized fetal movement patterns (40,41), the most common clinical application of using movement as a component of antenatal surveillance remains the BPP or a modified variant.

The BPP describes five parameters which reflect normal function and perfusion to different organ systems; the underlying principle that hypoxia to any of those systems can be detected on scan and heart rate tracing, with a composite score to reflect overall fetal wellbeing [5]. Nageotte et al. compared the performance of BPP with a contraction stress test, an assessment performed to assess a CTG response to an iatrogenically induced uterine contraction, where a negative result was predictive of tolerance to labor. In their high-risk series, no significant difference was observed between the perinatal outcomes for those with a negative BPP from those with a negative contraction stress test (42). Although it is clear even from the early work that this ultrasound-based assessment has value in antenatal surveillance, its utilization has certainly been limited within Europe due to its negative performance as compared with fetal heart monitoring (43). As both CTG and BPP changes are reflective of neuroendocrine and neurophysiological responses to hypoxic stress, their similarity in performance seems plausible.

New technologies

Other approaches that have been trialed for fetal movement monitoring include magnetocardiograph recordings (a non-invasive technique in which changes in the magnetic field near the maternal abdomen due to the electrical activity of the fetal heart are acquired and interpreted) (44) and multi-Doppler sensor systems (45). However, neither of these techniques have been compared with concurrent ultrasound or maternal sensation.

More recently, the utilization of MRI in fetal medicine has aided the development of cine MRI. This technique allows accurate assessment of global fetal movements (46), even in late gestation, that may otherwise be limited with ultrasound. However, its use is limited to the research arena due to the resources needed, as well as the time-intensive post-capture analysis required.

Some studies have explored fetal movement monitors for maternal wear (47–50), but none of these systems is in routine clinical use. A number of studies have investigated the potential of measuring vibrations transmitted through the maternal abdomen as a predictor of fetal movements. Such systems have the advantages of being non-transmitting, usable in a home setting, and potentially low in cost. Mesbah et al. developed a fetal activity monitor based on accelerometers, being the first to

introduce a method to account for maternal movement artifact as a technique to improve specificity (47). Although their overall sensitivity was good at 76% when compared with real time ultrasonography, their specificity remained low at 56%. A similar study from Girier et al. (48), also involving an accelerometer-based system, reported a true detection rate of 62% and an average false detection rate of 40%, concluding that only large fetal movements are registered by an accelerometer system and that accelerometers are prone to signal artifacts due to maternal movement. Two groups have proposed fetal movement monitors based on capacitive acceleration sensors to detect oscillations of the maternal abdomen (49,50). Nishihara et al. (49) reported an 87.7% agreement between subjective maternal sensation and their sensor. Although using similar technology, Ryo et al. reported that their sensors were most effective in picking up gross fetal movements (with prevalence- adjusted bias-adjusted kappa values ranging between 0.69 and 0.83), but less effective in detecting breathing or isolated limb movements compared with ultrasound.

It is clear that all passive forms of fetal monitoring that record the physical signals of the fetus through the maternal abdomen are inferior to the gold standard of ultrasound. However, methods such as accelerometry or phonography have the advantage of capturing automated, longitudinal data in the out-of-hospital setting where it is most needed, even if they systematically under-recorded. These methods to record movement signals will only be optimized by the use of multiple sensors over the maternal abdomen in order to maximize the likelihood that movement is registered. However, the disadvantage of this is that undesirable artifacts that are not fetal in origin will naturally increase. How sensitive the signals are and the manner in they are processed is a key element in the performance of these types of devices, and accuracy levels can vary significantly between analysis techniques and sensing modality. Astute strategies to tackle this problem include the introduction of a reference sensor to identify and remove maternal movement artifacts. Complex signal processing and development of intricate algorithms will determine the successes of these devices in clinical practice. It is unrealistic to expect any one algorithm to provide a high yield in accurate detection of all movements; a compromise will have to be made between accuracy and the type of movement behaviors useful to discern.

Longitudinal, prospectively collected data from such devices could finally allow clinicians and researchers to reach a consensus on normal fetal movement patterns according to gestational age, and whether these will translate into a useful tool in our management of babies at risk of stillbirth.

Conclusion

Treatment options available in the field of fetal medicine are limited. The most important fundamental strategy to improve fetal health is determining the optimal time for delivery. The importance of such an approach is essential, especially for growth-restricted fetuses. The ability to detect and appropriately time delivery will determine whether a mother will take home a healthy but potentially iatrogenically premature baby, one with residual effects of chronic hypoxic starvation or, worse, be faced with delivery of a stillborn. It is clear that our management strategies have developed over the past 30 years, and although the indications for delivery have very recently been clearly defined in the small population of growth-restricted fetuses <32 weeks' gestation (30), the strategies for later gestations, where the burden of stillbirth is greater, is less clear. Moreover, even within this cohort, the detection is still reliant on direction from mothers reporting reduced fetal movements. The difficulties for this "late" group lie not only in consensus regarding the most appropriate monitoring techniques, but perhaps more importantly in identifying our target population, given that the babies most at risk, lie within the normal growth percentiles.

The evidence presented advocates that fetal movements have an important role in antenatal surveillance, but we are currently lacking the technology to utilize this important marker of wellbeing. There is an urgent need for new technologies, or better application of existing ones, to objectively assess fetal movements in the low-risk setting and to characterize how these may relate to fetal health. In doing so, it may become possible for us to improve management of FGR, more precisely determine optimal delivery timing and potentially reduce stillbirths.

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