In this era of minimally invasive surgery, it is generally accepted, and usually true, that minimally invasive procedures are better for patients and provide better outcomes compared with conventional open surgery. However, with the exception of ultrasound-guided procedures that can be performed through a single small trocar, minimally invasive surgery in the fetus has thus far proved disappointing, due primarily to uterine membrane rupture and the associated complications. In this issue of the Journal, Professor Thomas Kohl and his team from the German Center for Fetal Surgery & Minimally Invasive Therapy in Giessen present a long-awaited update of their experience with fetoscopic repair of myelomeningocele (MMC). With publication of these two manuscripts, one can now ask whether the era of fetoscopic repair of MMC and perhaps other anatomical fetal anomalies has arrived. I believe not.

As prologue, Professor Kohl has been performing fetoscopic procedures for repair of MMC for over 10 years and has a series of at least 81 patients. Aside from technical reports in review articles on fetoscopic surgery, he has published two manuscripts describing five of these patients, without outcome analysis. The largest report of his experience thus far has come from Verbeek et al., describing 19 patients on whom his fetal surgical team in Bonn operated. That report documented high rates of fetal death, iatrogenic hemorrhage, premature rupture of membranes, persistent hindbrain herniation and complications of prematurity, and was accompanied by an editorial by Dr David Shurtleff stating that ‘the extremely high complication rates for mother and infant in this study and the principle of primum non nocere indicate that at this time it is unethical to pursue intrauterine endoscopic myelomeningocele repair in humans until the procedure has been perfected in animals.’ Undaunted, Professor Kohl completed his pilot study of 30 patients in Bonn, and now reports a retrospective series of a subsequent 51 patients operated between July 2010 and June 2013 in Giessen using an approach which has been shaped by his experience. Thus, it would seem that, by this point, the procedure should be optimized and standardized, and its results should be clear.

Since a third study, on neurological outcomes, was deemed not to have sufficiently long postnatal follow-up to make its documentation suitable for publication, one is left to evaluate the results of a maternal–fetal surgical procedure without postnatal fetal outcomes, and to read a description of the technique without data on its efficacy. Nevertheless, there are several clear observations that can be made. First, the procedure continues to be extremely technically challenging. It requires three or more 5-mm trocars and an average of 3 hours of partial amniotic carbon dioxide insufflation (PACI). In 35/51 cases the procedure required 200–315 min, with a maximum PACI time of 275 min. In contrast, the average skin-to-skin operating time for the open surgical procedure at my institution is 78.5 ± 11 min. This is of concern, as even relatively brief periods of PACI have been documented experimentally to cause significant fetal acidosis and the effects of prolonged anesthesia on the neurological outcome of the fetus are unknown. In Professor Kohl’s experimental assessment of PACI, he applied it to six fetal lambs at relatively low pressure, for periods of less than 80 min, and observed the sheep for abnormal neurological symptoms after birth, with a final readout of simple brain histology to conclude that it appeared safe. Second, the procedure continues to be accompanied by an extremely high rate of amniotic fluid leakage, at a mean gestational age of 30 weeks. This is not surprising, as the use of three 5-mm trocars for prolonged operative procedures has been associated universally with high rates of chorioamniotic membrane separation and premature rupture of membranes (PROM), with their attendant risks of chorioamnionitis and oligohydramnios. The low rate of membrane separation reported by Professor Kohl is likely to be the result of assessment in a cursory manner. Although he makes a point of stating that ‘Coverage of the trocar insertion defects within the chorioamniotic membranes has been one of the most important accomplishments during the development of the fetoscopic technique’, Professor Kohl does not describe the device he uses to achieve this, and to my knowledge has not published on this topic. Third, the procedure for coverage of the MMC defect is clearly still evolving, which usually suggests that it may be problematic. The procedure consists of removal of the pathologic tissues followed by placement of one to three patches of either GoreTex and collagen or collagen alone. The choice of these procedures is difficult to ascertain as Professor Kohl fails to describe key components. For instance, it is not clear whether he removes all epithelial elements from the placode, or whether the placode is untethered distally. Failure to do either may compromise neurological function in the future due to postnatal dermoid formation or progressive loss of neurological function with growth. The greatest concern with his technique is whether a watertight seal is achieved consistently, because only a watertight closure will prevent...
the deleterious effects of amniotic fluid on exposed neural tissue and prevent cerebrospinal fluid leakage through the defect to reverse hindbrain herniation. There are no data on reversal of hindbrain herniation from which to draw and there is the disturbing result of two postnatal deaths from severe brain-stem dysfunction attributed to Chiari-II malformation – a phenomenon not observed after open fetal surgery, in which some degree of reversal of the Chiari malformation is seen almost universally. Adding to this concern, there is usually no skin closure performed, resulting in an exposed, non-epithelialized patch at birth.

If Professor Kohl truly expects this approach to gain acceptance over open fetal surgery, which has been subjected to the most rigorous of outcome analyses, it is time for the data on surgical and neurological assessment of this cohort – which I believe to be currently available – to be published. This should include documentation of the status of the hindbrain, rate of ventriculoperitoneal shunting and clear criteria by which it was performed, anatomical vs observed level of neurological function, ambulatory status and, ultimately, bowel, bladder and cognitive function. Most importantly, this should be reported by third-party observers to remove the potential for investigator bias.

The Management of Myelomeningocele Study (MOMS) trial11 set a clear standard for the comparison of other techniques for prenatal closure of myelomeningocele. While there can be no argument that, outcomes being equal, a fetoscopic approach avoids the maternal morbidity of hysterotomy, the MOMS trial demonstrated that open fetal surgery could be performed in experienced centers with acceptable maternal morbidity and morbidity of prematurity. Many of the arguments raised by Professor Kohl and his team against open fetal surgery are likely to have been made because maternal morbidity was reported frankly and comprehensively in the MOMS trial. For instance, maternal postoperative oxygen requirement was reported as pulmonary edema, and reported maternal complications, such as placental abruption and uterine dehiscence, were all observed only at the time of delivery and were not clinically important. The reality is that: (1) the rate of clinically significant membrane-related issues (i.e. PROM and amniotic fluid leakage) is significantly lower after open fetal surgery than after fetoscopic repair; (2) the average gestational age at delivery is significantly lower after open surgery than after fetoscopic repair (34.1 and 34.3 weeks in MOMS trial and post-MOMS experience, respectively, vs 32.9 for fetoscopy); (3) the average duration of postoperative hospitalization is longer after fetoscopic repair (7.2 days vs 4.2 days); and, most importantly, (4) the neurological outcome of fetuses which underwent fetoscopic repair has not been reported and remains a major question given the issues raised above.

Professor Kohl and his colleagues should be acknowledged for providing some account of their substantial experience with fetoscopic repair of myelomeningocele. However, to justify the benefits of what amounts to avoidance of hysterotomy, and improved maternal cosmesis to their patients, they are obligated to demonstrate rigorously at least equal postnatal neurological outcomes to those achieved after open fetal surgical repair. Until they do, this is best viewed as an ongoing example of human experimentation.

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