Spinal Angulation: A Limitation of the Fetal Lamb Model of Myelomeningocele.

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Public Summary:
The prevalence of spina bifida in large animal species is extremely rare. Therefore, in order to study spina bifida in a large animal model the defect must be created through chemical or surgical intervention. Currently, several research groups have used retinoic acid to induce spina bifida in small animals, but this approach will not work in large animal species due to the large quantities of retinoic acid needed to create the defect. Our laboratory creates spina bifida in fetal sheep by surgically creating the defect. However, since this is a surgical technique, variations can be made in the defect creation that can potentially effect study outcomes. In this study we created the spina bifida defect in 31 fetal lambs. 10 of these animals received repair with an extracellular patch material and 21 received repair with the same patch material seeded with placental stem cells. After the lambs were born we assessed their motor function and performed postmortem magnetic resonance imaging. From these images we analyzed the degree of boney spinal angulation and the amount of bone removed around the defect that was generated by the surgical creation of the defect. When we compared motor function to the degree of angulation in the spine and to the amount of bone removed in the defect there was a significant correlation in both instances. However, when lambs that have severe deformity, defined as greater than 60 degrees of angulation, are removed from the data set, the correlation is no longer significant. Thus, lambs with severe deformity, that were created by removal of too much bone during the defect creation, can be excluded from our studies so that they do not compromise the results of the different treatments.

Scientific Abstract:
INTRODUCTION: The surgically induced fetal lamb model is the most commonly used large animal model of myelomeningocele (MMC) but is subject to variation due to surgical technique during defect creation. MATERIAL AND METHODS: Thirty-one fetal lambs underwent creation of the MMC defect, followed by defect repair with either an extracellular matrix (ECM) patch (n = 10) or ECM seeded with placental mesenchymal stromal cells (n = 21). Postnatal hindlimb function was assessed using the Sheep Locomotor Rating (SLR) scale. Postmortem magnetic resonance imaging of the lumbar spine was used to measure the level and degree of spinal angulation, as well as cross-sectional area of remaining vertebral bone. RESULTS: Median level of angulation was between the 2nd and 3rd lumbar vertebrae, with a median angle of 24.3 degrees (interquartile range 16.2-35.3). There was a negative correlation between angulation degree and SLR ($r = -0.44$, $p = 0.013$). Degree of angulation also negatively correlated with the normalized cross-sectional area of remaining vertebral bone ($r = -0.75$, $p < 0.0001$). DISCUSSION: Surgical creation of fetal MMC leads to varying severity of spinal angulation in the ovine model, which affects postnatal functional outcomes. Postnatal assessment of spinal angulation aids in standardization of the surgical model of fetal MMC repair.