Brief Rapid Communication

Fetoscopic Direct Fetal Cardiac Access in Sheep
An Important Experimental Milestone Along the Route to Human Fetal Cardiac Intervention

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Background—Fetal cardiac interventions by direct ultrasound-guided approaches or open fetal cardiac surgery have been fraught with technical difficulties, as well as with significant maternal and fetal morbidity in humans. Therefore, the purpose of our study in sheep was to assess the feasibility and potential of fetoscopic direct fetal cardiac access.

Methods and Results—In 15 anesthetized pregnant ewes (88 to 109 days of gestation; term, 145 days), 3 to 4 trocars were percutaneously placed in the uterus. Using videofetoscopic equipment, we assessed the feasibility of achieving direct fetal cardiac access. Minimally invasive direct fetal cardiac access by operative fetoscopy was achieved in 10 of the 15 fetal sheep. In 7 fetuses, the approach was successfully tested for fetal cardiac pacing (n=5) or antegrade fetal cardiac catheterization (n=2). Access was not achieved in 5 fetuses because of bleeding complications (n=2) or because the fetoscopic setup could not be established (n=3). All but 2 fetal sheep were alive at the end of the procedure. Acute fetal demise resulted from maternal hypotension or kinking of the fetal inferior caval vein by sternal suspension. Six ewes continued gestation; 3 of these went to term, with a normal fetal outcome. Two ewes died from septicemia 3 and 7 days after the procedure, and 1 ewe aborted 1 month after the procedure.

Conclusions—Minimally invasive direct fetal cardiac access by operative fetoscopy is feasible in fetal sheep. The fetoscopic approach carries important potential for fetal cardiac pacing, antegrade fetal valvuloplasties, and resection of fetal intrapericardial teratomas in human fetuses. (Circulation. 2000;102:1602-1604.)

Key Words: fetus ■ fetoscopy ■ thoracotomy ■ stenosis ■ valves ■ pacing ■ valvuloplasty

Direct access to the fetal heart to perform fetal cardiac pacing or balloon valvuloplasty has been attempted by direct ultrasound-guided approaches or open fetal surgery.1–7 The direct percutaneous ultrasound-guided approaches for these procedures have had a low technical success rate,7 and open fetal surgery for pacemaker insertion has been accompanied by significant maternal morbidity and fetal demise (M.R. Harrison, MD, and P. Zielinsky, MD, personal communications, 2000). Therefore, the purpose of our study in pregnant sheep was to assess the feasibility and potential of a minimally invasive fetoscopic approach to achieve direct fetal cardiac access. Our early experience indicates that fetoscopic direct fetal cardiac access is feasible and carries important potential for antegrade valvuloplasties, cardiac pacing, and the resection of fetal pericardial tumors in human fetuses.

Methods

Operative Approach

Fifteen anesthetized pregnant ewes (88 to 109 days of gestation; term, 145 days) were placed in the supine position, intubated, and ventilated with 100% oxygen and 1.5% to 2% halothane. Three to four 5-mm trocars were percutaneously inserted into the amniotic cavity, avoiding maternal laparotomy and hysterotomy.8 Videofetoscopic equipment (Karl Storz GmbH) was used for low-pressure insufflation of the amniotic cavity and fetal visualization. After percutaneous intra-amniotic access, fetal posturing was attempted in a fashion that avoided traction or compression of the umbilical cord but would, at the same time, be useful in achieving direct fetal cardiac access by a subxiphoid operative approach.9

We assessed the technical success rate of minimally invasive fetoscopic direct fetal cardiac access. In 5 fetuses, we tested its utility for pacing lead insertion, and in 3, for antegrade fetal cardiac catheterization. We studied the incidence and causes of bleeding complications, as well as the technical difficulties of the procedure. The study protocols were approved by the local committee on animal research and were performed according to institutional guidelines.

Results

Fetoscopic direct fetal cardiac access through a subxiphoid thoracotomy was achieved in 10 of the 15 fetal sheep. Fetoscopic insertion of a screw-in electrode into the cardiac apex followed by successful ventricular capture could be achieved in 3 of these fetuses.
achieved in 5 fetal sheep. In 3 of these, the pacing lead was secured and the chest incision was closed. The pacing wires were connected to a neonatal pacemaker system that was subcutaneously implanted into the maternal abdomen. Antegrade fetal cardiac catheterization was achieved in 2 of 3 attempts. After the diaphragmatic surface of the fetal heart was exposed, the left or right ventricle was punctured under fetoscopic visualization, and a 16-gauge needle was advanced into the respective ventricle (LV). The shaft is oriented toward the fetal left ventricular outflow tract to facilitate placement of a 0.014-inch guidewire and a balloon catheter across the aortic valve antegrade (in this acute study, the pericardium was widely removed to gain familiarity with the fetoscopic view of the heart). The black arrows indicate the course of the left anterior coronary artery.

**Technical Problems**

In the first 4 fetuses, up to 3 adjacent incisions were necessary to identify the correct subxiphoid site for direct fetal cardiac access. In 3 of these fetuses, this problem resulted in bleeding complications from the superior epigastric, internal thoracic, or intercostal arteries; this forced us to abandon the procedure in 2 of the fetuses. In the remaining 2 fetuses, direct cardiac access was ultimately achieved.

In 3 other fetuses, direct fetal cardiac access was precluded by anterior membranous division of the amniotic cavity which, in our experience, makes it technically impossible to establish the fetoscopic setup. All but 2 fetal sheep survived direct fetal cardiac access. In these 2, acute fetal demise resulted from poor uterine blood flow during a period of anesthesia-induced maternal hypotension and from kinking of the fetal inferior caval vein after fetal sternal suspension for improved cardiac exposure.

In 7 fetuses that were terminated after acute procedures, the incision lengths varied between 8 and 20 mm. Six of the 15 ewes were allowed to continue gestation. Three of these went to term and had a normal fetal outcome. In one of the long-term survivors, the pacing lead was still correctly inserted into the cardiac apex, and successful capture at a low threshold was achieved during VVI stimulation. In a second survivor, the pacing lead had entirely dislodged from the fetus. Two ewes died from septicemia 3 and 7 days after the procedure. In their fetuses, adequate apical position of pacing leads was confirmed at autopsy. One ewe aborted 1 month after the procedure for unclear reasons; an appropriately grown fetus with a completely healed thoracotomy site was found at autopsy. In both the long-term survivors and the fetuses that survived the procedure for weeks, the thoracotomy scars grew in length and measured between 40 and 60 mm at autopsy. The underlying tissues were completely healed, and only minor, functionally inconsequential pericardial adhesions were found.

**Discussion**

This study demonstrates that fetoscopic direct fetal cardiac access is feasible in fetal sheep. This novel approach carries important potential for cardiac pacing and the dilatation of severe semilunar valvar obstructions in human fetuses, as was illustrated by our ability to achieve pacing lead insertion and antegrade fetal cardiac catheterization when using this access route. Compared with open fetal surgery, fetoscopic direct fetal cardiac access may be more favorable because it avoids maternal laparotomy, hysterotomy, and fetal exteriorization, which have been accompanied by substantial decreases in fetoplacental blood flow and a poorer outcome in human fetuses with noncardiac lesions. The most difficult operative step in achieving fetoscopic direct fetal cardiac access was precisely defining the correct incision site; this must be correct to within a few millimeters. The xiphoid process is very soft and could not, with confidence, be identified by touch with the laparoscopic instruments. This tactile difficulty was aggravated by the fact that visual orientation using anatomical landmarks becomes extremely difficult in the highly magnified fetoscopic field. Both problems, therefore, resulted in the need for repetitive incisions and bleeding complications in our initial studies, which are unacceptable for human fetal procedures.

Fortunately, with greater operative experience, precise definition of the incision site was reliably and repeatedly achieved by ultrasound-guided marking of the xiphoid process or by suspension of the lower third of the fetal sternum. Either procedural modification permitted us to achieve fetoscopic direct fetal cardiac access in sheep fetuses weighing as little as 350 g, and they may permit cardiac interventions in similarly sized human fetuses at <20 weeks of gestation. In particular, fetuses with severe semilunar valvar obstruction may benefit from such timely intervention, because valvar dilatation early in fetal life may ameliorate the progressive development of ventricular hypoplasia, myocardial fibrosis, and endocardial fibroelastosis of the affected side of the heart.
Compared with retrograde fetal cardiac access by transumbilical fetal cardiac catheterization,\textsuperscript{14} the antegrade approach leaves the fetoplacental circulation unharmed and may, therefore, be more favorable for valvar dilatation in fetuses in heart failure. Fetuses with life-threatening heart failure from therapy-refractory congenital complete heart block or large pericardial tumors may also be saved by fetal pacemaker insertion or tumor resection.

Although our study shows that fetoscopic pacing lead insertion and antegrade catheterization can be achieved in sheep, it also leaves no doubt that substantial changes in design and further miniaturization of interventional equipment, as well as tailoring the operative techniques to the human anatomy, will be necessary before these complex procedures can be performed in humans. For example, fetoscopic fetal cardiac pacing will require the development of leads to eliminate the excessive force on the tiny fetal hearts exerted by currently available neonatal pacing leads. Similarly, antegrade fetal cardiac catheterization will require special sheaths, catheters, and fixation devices. Those who undertake these procedures will need an understanding of both the obstetric problems and the complex cardiac anatomy they will encounter.

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