Multimodal Fetal Transesophageal Echocardiography for Fetal Cardiac Intervention in Sheep

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***Background*—**The overall performance of available mechanical intravascular ultrasound catheters for fetal transesophageal echocardiography during fetoscopic fetal cardiac interventions in sheep has been limited by radioelectronic interference, low system frame rates, and low acoustic outputs. Therefore, a more reliable device is desired for human fetoscopic surgical procedures.

***Methods and Results*—**We assessed the potential of a newly available 10-French phased-array intravascular ultrasound catheter for multimodal fetal transesophageal echocardiography in 5 fetal sheep between 78 and 98 days of gestation (term, 145 to 150 d). The intravascular ultrasound catheter was easily inserted through the mouth into the esophagus in all 5 sheep fetuses (mean weight, 600 g), and it permitted high-quality 2D imaging of the fetal heart in vertical imaging planes that were validated by MRI. Color Doppler and pulsed Doppler imaging permitted clear assessment of fetal cardiovascular flows and recording of velocity-time integral tracings of the fetal heart and great vessels. The vertical imaging planes were particularly useful to demonstrate interventional material inside the fetal heart and great vessels.

***Conclusions*—**Our early experience with the phased-array intravascular ultrasound catheter indicates that multimodal fetal transesophageal echocardiography has now become possible in these smallest of patients. **(*Circulation*. 2001;104:1757-1760.)**

Key Words: fetus ■ echocardiography ■ ultrasonics ■ valvuloplasty ■ surgery ■ catheterization ■ fetoscopy

Currently developed minimally invasive techniques in sheep for fetoscopic fetal cardiac catheterization use gaseous insufflation of the amniotic cavity for optimum fetal visualization and manipulation.[1–3] Because amniotic insufflation precludes conventional maternal transabdominal fetal echocardiography, fetal monitoring and guidance of interventional devices into the fetal heart during these entirely percutaneous procedures has relied on mechanical intravascular ultrasound catheters used as fetal transesophageal echo probes.[4,5] Unfortunately, these catheters carry several limitations that limit their application in the human fetus. The overall image quality suffers unpredictably from radioelectronic interference of the endoscopic equipment, and the low frame rate and low acoustic output of the mechanical catheters result in suboptimal temporal resolution and insufficient depth penetration. Accordingly, satisfactory imaging during experimental fetoscopic fetal cardiac catheterizations has been limited to the catheter near-field.[6] Because the mechanical ultrasound catheters also lack Doppler capabilities, an assessment of fetal hemodynamics was confined to observations of heart rate changes and ductus arteriosus size and oval foramen patency.[5] Because of these limitations, a more reliable device is desired for fetal cardiac intervention in humans. Therefore, we assessed the potential of a novel phased-array intravascular ultrasound catheter for multimodal fetal transesophageal echocardiography in sheep.

Methods

We studied a total of 5 ewes between 78 and 98 days of gestation (term, 145 to 150 d). Each ewe was sedated with an intravenous injection of ketamine hydrochloride (10 to 20 mg/kg) and positioned supine. After orotracheal intubation of the ewe, maternofetal anesthesia was performed by ventilation with 1% to 1.5% halothane in 50% oxygen. The uterus was exteriorized through a maternal midline laparotomy. After a minihysterotomy, the fetal head was exteriorized, and a commercially available 10-French phased-array intravascular ultrasound catheter (AcuNav, Acuson) was inserted into the fetal esophagus. Because the feasibility of percutaneous fetoscopic placement of a 10-French intravascular ultrasound catheter into the fetal esophagus has been shown before,[5] we preferred to use the more rapid and less expensive open operative approach for this study.

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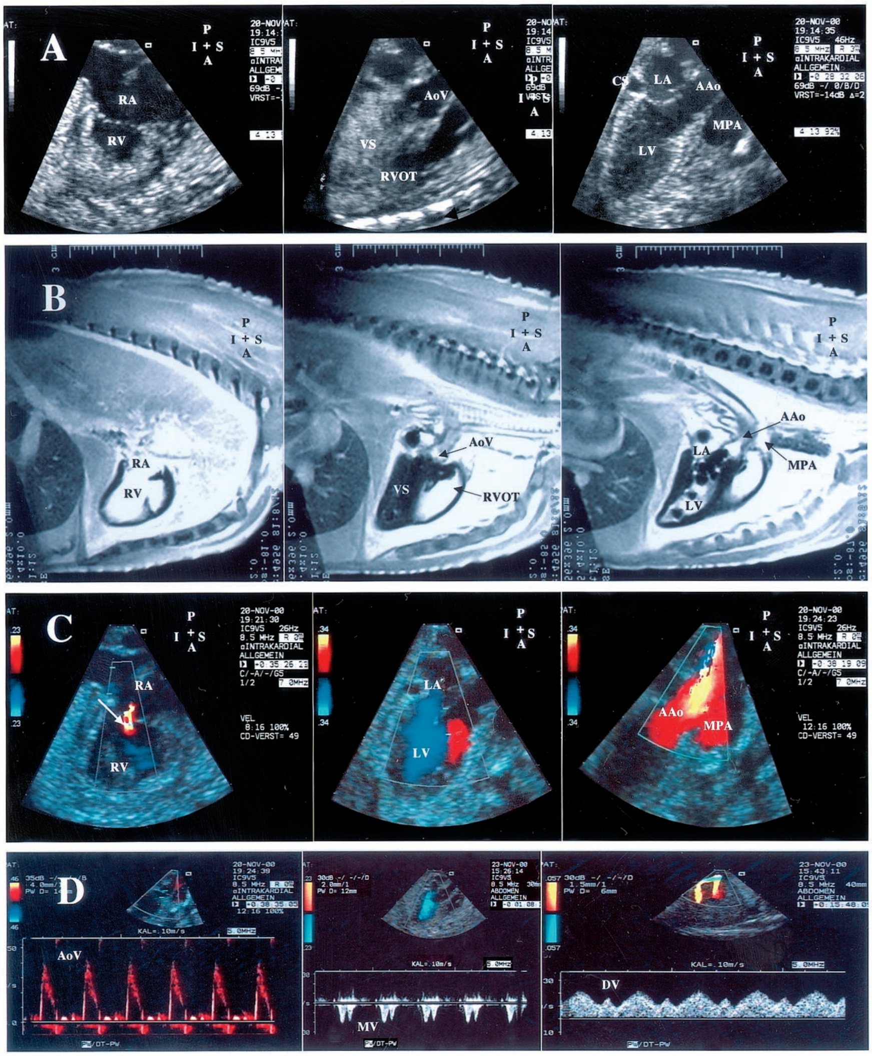

Figure 1. Fetal transesophageal echocardiography in a fetal sheep weighing 300 g using the phased-array intravascular ultrasound catheter. A, Two-dimensional echocardiographic demonstration of fetal cardiac anatomy in vertical planes. B, Magnetic resonance images replicating the vertical fetal transesophageal imaging planes. C, Color Doppler imaging during fetal transesophageal echocardiography showing mild tricuspid regurgitation (left), left ventricular inflow (middle), and aortic and pulmonary systolic ejection (right). D, Pulsed Doppler interrogation allows us to obtain clear velocity time integral recordings of the cardiac valves, great vessels, and even the umbilical circulation. A indicates anterior; P, posterior; I, inferior; S superior; RA, right atrium; RV, right ventricle; VS, ventricular septum; RVOT, right ventricular outflow tract; AoV, aortic valve; LV, left ventricle; LA, left atrium; AAo, ascending aorta; MPA, main pulmonary artery; MV, mitral valve; and DV, ductus venosus.

The catheter permits 2D real-time imaging and Doppler imaging and is tipped with a frequency agile 5.5 to 10 MHz vector phased-array ultrasound transducer. Tissue penetration ranges between 2 mm to >10 cm. The catheter is linked to commercially available ultrasound platforms (Acuson). In contrast to the previously used mechanical intravascular ultrasound system (Insight II, Boston Scientific), which displayed fetal cardiac anatomy in horizontal imaging planes, this novel catheter provides vertical planes. Therefore, one objective of our study was to describe and validate the transesophageal echocardiographic definition of fetal cardiac anatomy and spatial relationships in this new imaging format. In 3 fetuses, transesophageal ultrasound guidance of interventional devices that were introduced via the umbilical vein, right jugular vein, or direct ventricular puncture was tested and compared with the horizontal imaging technique of the mechanical intravascular ultrasound catheter. In addition, in all fetuses, the feasibility of pulsed and color Doppler interrogation of the fetal heart and great vessels was assessed.

After each study, the anesthetized ewe and the fetus were killed with a potassium chloride overdose. To validate the novel vertical fetal transesophageal imaging planes, 2 fetuses weighing 300 and 600 g, respectively, were perfusion-fixed with 500 mL of 4% formalin via the umbilical vein. In these fetuses, T1-weighted, 3D, gradient echo sequence MRI followed by multiplane reconstruction (PRIMA 1.0 Tesla, General Electric, Neu Isenburg, Germany) replicating the vertical transesophageal imaging planes was performed. The study protocol had been approved by the local Committee on Animal Research and was performed according to institutional guidelines.

Results

Two-Dimensional Imaging

The intravascular ultrasound catheter was easily inserted through the mouth into the esophagus in all 5 sheep fetuses (mean weight, 600 g; range, 300 to 650 g) and permitted high-quality 2D imaging of all cardiac chambers, semilunar and atrioventricular valves, and supracardiac and infracardiac vessels (Figure 1A). The cardiac anatomy and spatial relationships were validated by MRI, which replicated the novel vertical imaging planes (Figure 1B). The inflow and outflow portions of both ventricles were displayed in great detail. The phased-array catheter permitted clear definition of the ventricular walls and the cardiac apex. Because of the mesocardiac position of the ovine heart, the ventricular septum was displayed as a vertical tissue plate. The foramen ovale, septum primum, coronary sinus, and Eustachian and Thebesian valves were visualized. The anterior and posterior mitral and the anterior and mural tricuspid valve leaflets were imaged throughout their entire range of motion. In contrast, the tricuspid valve septal leaflet was less well defined.

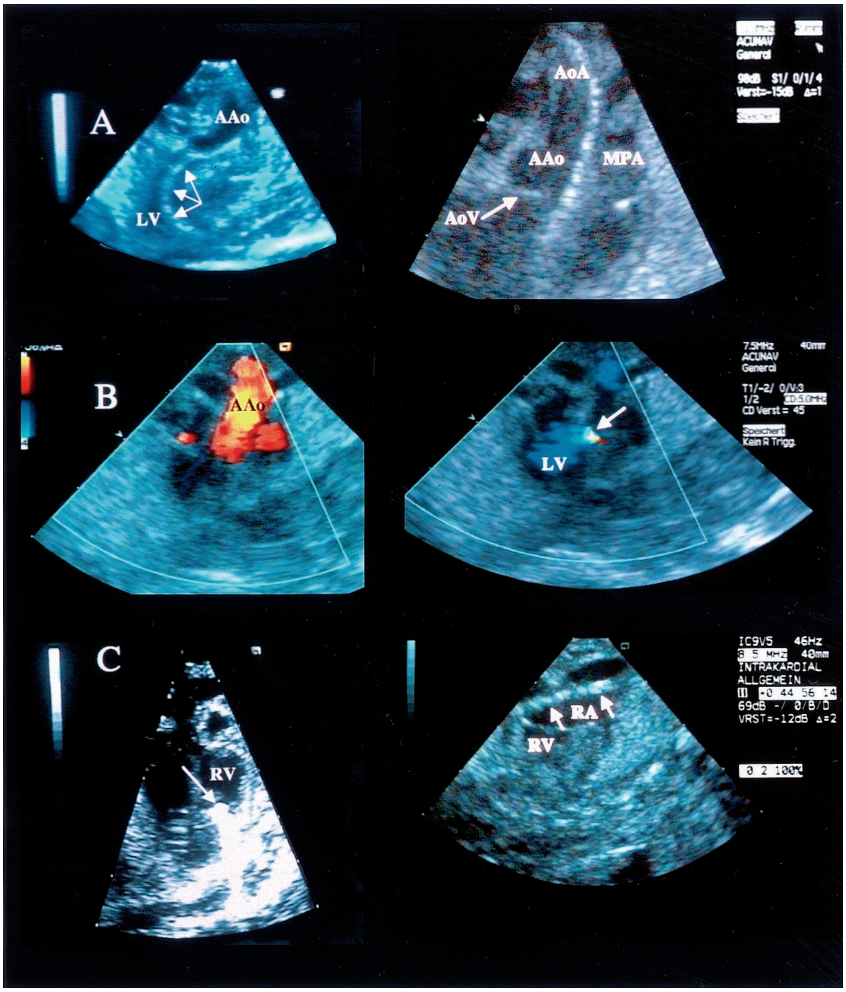

Figure 2. A, Fetal transesophageal imaging using the phased-array intravascular ultrasound catheter for retrograde cardiac catheterization through the umbilical artery. A 0.014-inch guidewire has been placed inside the left ventricle (left; arrows) and above the aortic valve (right). B, Documentation of iatrogenic aortic insufficiency (arrow) after retrograde cardiac catheterization in another fetus (systolic frame on left; diastolic frame on right). C, The high penetration of the catheter also permits visualization of intracardiac insertion of a needle shaft (arrow on left) from the anterior chest for direct transventricular fetal cardiac catheterization (left). In the near field, the catheter permits accurate monitoring of intracardiac insertion of interventional material through the caval veins (arrows on right). AAo indicates ascending aorta; AoA, aortic arch; AoV, aortic valve; MPA, main pulmonary artery; LV, left ventricle; RA, right atrium; and RV, right ventricle.

Because of their proximity to the imaging catheter and horizontal course, the pulmonary veins could not reliably be defined.

Placement of Interventional Devices

Because both ventricular outflow tracts were displayed vertically, 0.014-inch guidewires were demonstrated in a single imaging plane coursing through the respective valve and adjacent subvalvular and supravalvular areas (Figure 2). During attempts at transventricular fetal cardiac catheterization, the ultrasound catheter permitted the exact localization of blunt needle shafts that were placed onto the left ventricular epicardium and, subsequently, the visualization of the intracardiac alignment of these shafts with the left or right ventricular outflow tract.

Doppler Imaging

Color and pulsed Doppler imaging permitted clear assessment of fetal cardiovascular flows (Figures 1C and 1D). By adjusting the intraesophageal catheter position, pulsed Doppler interrogation at incidence angles below 10° allowed us to record good quality velocity-time integral tracings of all cardiac valves, the ascending aorta, aortic arch, bovine trunk, main and left pulmonary artery, ductus arteriosus, hepatic veins, ductus venosus, and umbilical vein. Because of their course and/or proximity to the ultrasound catheter, pulsed Doppler interrogation of the inferior caval vein, descending aorta, right pulmonary artery, pulmonary veins, and oval foramen at incidence angles below 45° was not possible.

Discussion

Our early experience with the novel phased-array intravascular ultrasound catheter in fetal sheep indicates that multimodal fetal transesophageal echocardiography for fetal cardiac intervention has now become possible in these smallest of patients. Because the soft-tipped, rounded catheter could be placed in sheep fetuses as small as 300 g without esophageal injury, it can be inferred that after incorporation of thermal sensors, the device also carries great potential for transesophageal echocardiographic monitoring during cardiac surgery in low-birthweight infants. For this patient group, no means of intraoperative echocardiographic monitoring is currently available.

Two-Dimensional Imaging and Placement of Interventional Devices

Because of its intraesophageal position, the phased-array catheter permits 2D imaging of the fetal heart in previously unattained detail and clarity in sheep fetuses as small as 300 g. In contrast to the previously used mechanical ultrasound catheters, the higher depth penetration of the phased-array catheter permits clear definition of even the anterior margins of the fetal heart and chest. This ability allows the physician to choose the appropriate cardiac entry site for direct transventricular fetal cardiac catheterization.[2] This antegrade approach aims to dilate severely obstructed fetal semilunar valves and is currently being tested by our group because it greatly reduces the technical requirements for interventional devices. Although the ultrasound catheter tip can be flexed substantially, we did not attempt fetal transgastric cardiac imaging to avoid injuring the delicate fetal esophagus and stomach.

Because the phased-array ultrasound catheter displays both ventricular outflow tracts longitudinally, the course of interventional devices through the respective semilunar valve and adjacent subvalvular and supravalvular areas can be better recognized during fetal cardiac catheterization than with using the mechanical imaging device. With the latter device, the horizontal imaging planes required constant catheter repositioning to deliver an interventional device into the fetal heart (Figure 2). In addition, because the phased-array technology permits electronic magnification of any chosen cardiac region of interest, steering interventional devices into the fetal heart can be monitored far more precisely than with the mechanical catheter, in which any increment in magnification was bought at the expense of image depth display.

Doppler Imaging

The phased-array catheter offers, for the first time, color Doppler and pulsed and continuous Doppler interrogation of the fetal heart from the esophagus, thus opening the door for detailed hemodynamic assessment during fetoscopic and open fetal cardiac interventions. By simple adjustments of the intraesophageal position of the device, low incidence angles can be achieved for most intracardiac and great vessel flow regions, thus providing the basis for accurate estimation of transvalvular pressure gradients and quantitation of valve regurgitation.

Limitations of the Device

Although the vertical imaging planes seem particularly useful for the dilation of semilunar valve obstructions, a number of fetal cardiac interventions might involve atrial septostomy or dilation of a restrictive oval foramen. The lack of transverse plane imaging might make visualization of the oval foramen more difficult. Therefore, further technical developments toward a biplane or multiplane device and the incorporation of thermal sensors are desired. To perform fetal transesophageal echocardiography in human fetuses as early as 16 weeks of gestation, a further reduction in catheter dimensions and even softer materials will be required.

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