Experimental Fetal Transesophageal and Intracardiac Echocardiography Utilizing Intravascular Ultrasound Technology

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With the advent of cardiac interventions in human fetuses,[1-5] accurate guidance of interventional devices is critical and requires high-resolution definition of fetal cardiac anatomy. Guidance during initial cardiac interventions has been performed by transabdominal echocardiography.[1-5] However, fetal position, maternal obesity, or oligohydramnios can limit satisfactory imaging of these procedures by transabdominal echocardiography and an alternative fetal cardiac imaging tool would be helpful. Current development of fetoscopic surgical procedures with gas insufflation of the amniotic cavity for cardiovascular access requires imaging capabilities not attended by transabdominal and transvaginal imaging. The purpose of this study in fetal sheep was to define fetal cardiac anatomy by imaging with a 10 F-10 MHz intravascular ultrasound catheter (IVUC) from either a transesophageal or an intracardiac IVUC position.

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We studied a total of 19 Mixed-Western Breed fetal sheep between 90 and 140 days of gestation (term = 145 to 150 days). In 15 sheep, the ewe and her fetus were anesthetized with maternal intravenous injection of ketamine hydrochloride (10 to 20 mg/kg) and the ewe was positioned supine. Fetal head and neck were exteriorized through a maternal midline laparotomy and hysterotomy. The IVUC position was selected based on fetal size and the maximal tissue penetration of the imaging catheter. A transesophageal imaging position was chosen in 5 exteriorized small 90-day gestation fetuses (mean weight 580 g, range 510 to 700 g), because in these, the IVUC is too large to be placed into the heart. A right atrial imaging position was chosen in 10 exteriorized larger fetuses (130 to 140 days' gestation; mean weight 3,400 g, range 2,500 to 4,300 g), because in those, the penetration of the IVUC would not suffice to image the entire heart from the esophagus. In the latter group, the IVUC was inserted via vena sectio into the right jugular vein. In 4 nonexteriorized fetuses (95 to 100 days' gestation; mean weight 910 g, range 550 to 1,100 g), the IVUC was placed by a fetoscopic technique into the fetal esophagus. We used a commercially available intravascular ultrasound system with a 10 F-10 MHz IVUC (Boston Scientific Corporation, Sunnyvale, California). The IVUC consists of a fixed 10 MHz transducer and rotating mirror assembly. The ultrasound beam is reflected against the rotating mirror to create a 360° imaging plane perpendicular to the long axis of the catheter. Real-time images were obtained at 28 frames/s and recorded on super VHS videotape for subsequent off-line analysis. The tissue penetration for this catheter is 40 to 50 mm with axial resolution of 0.45 mm. After insertion into the fetal esophagus or jugular vein, the IVUC was advanced toward the heart. The screen image was rotated to display cardiac orientation in anatomic format with the cardiac apex pointing inferiorly. The fetal heart was imaged in 5 planes by advancing and withdrawing the IVUC within the esophagus or right atrium (Figure 1). Echocardiographic definition of cardiac anatomy and spatial relations were assessed.

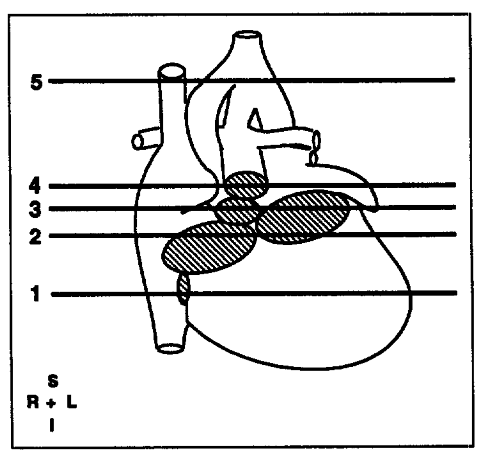

FIGURE 1. Imaging planes for fetal transesophageal and intracardial echocardiography. 1 = cardiac floor plane; 2 = 4-chamber plane; 3 = aortic valve plane; 4 = pulmonary valve plane; 5 = great vessel plane; I = inferior; L = left; S = superior; R = right.

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Dr. Kohl is a research fellow supported by educational Grant Ko 1484/1-1 of the German Research Society (DFG)/Bonn, Germany. Dr. Chou is partially funded by Grant F32 HL090969-01 from the National Institutes of Health, Bethesda, Maryland, and Dr. Hutchison is supported by a Fellowship of the R.L. McLaughlin Foundation, Toronto, Canada. Additional support was from the Boston Scientific Corporation Sunnyvale, California, Karl Storz Endoscopy America, Culver City, California, and grants from following institutions and individuals: Verein für das herzkranke Kind, Münster, Germany; MOET-Institute, San Francisco, California; Wilfried Vogeler, MD, Essen, Germany; and Deniz Kececioglu, MD, Münster, Germany.
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Manuscript received September 13, 1995; revised manuscript received and accepted November 20, 1995.

After each study, the anesthetized ewe and the fetus were killed with pentobarbital-sodium. The accuracy of transesophageal echocardiography (TEE) and intracardiac echocardiogram (ICE) for definition of fetal cardiac anatomy and procedure-related complications were evaluated at autopsy. Four fetuses were perfusion-fixed with 500 ml of 4% formalin via the umbilical vein, and their chests were sectioned horizontally to replicate the orientation of the echocardiographic imaging planes. The study protocol had been approved by the local committee on animal research and was performed according to institutional guidelines.

The IVUC was inserted successfully via the mouth into the esophagus in all 5 small and via the jugular vein into the right atrium in all 10 larger exteriorized fetuses. In 4 nonexteriorized fetal sheep, the IVUC was successfully inserted into the esophagus by the fetoscopic approach. Clear 2-dimensional echocardiographic images were obtained in all fetuses.

The cardiac floor plane defined at the junction between the inferior caval vein and the floor of the right atrium allowed in all fetuses TEE and ICE imaging of the coronary sinus throughout its entire course behind the left atrium to its right atrial mouth. The floor of both atria, ventricles, and the basal ventricular septum were defined from this view. In all ICE fetuses and in 3 TEE fetuses, the eustachian and thebesian valves were also imaged. By cranial withdrawal of the IVUC from the cardiac floor plane, a fetal 4-chamber plane was obtained by both ICE and TEE (Figure 2). This view allowed clear imaging of all atrial and ventricular cavities in all fetuses. The IVUC defined the lateral walls of the right atrium and ventricle better than those of the left atrium and ventricle. The moderator band was well identified in the right ventricle by both TEE and ICE in all fetuses. The integrity of the ventricular septum was less well defined by ICE than by TEE. Both mitral and tricuspid valves were imaged throughout their entire range of motion by both TEE and ICE in all fetuses. The pulmonary veins were displayed entering through a common confluence into the left atrium. Because of limited tissue penetration, shadowing, and poor lateral resolution in the far field of the IVUC, ICE did not allow clear imaging of the descending aorta. In contrast, TEE permitted high-resolution imaging of the entire thoracic aorta. The foramen ovale and the septum primum were seen in all fetuses. Further cranial withdrawal of the IVUC from the esophagus or right atrium produced the aortic valve plane (Figure 3) by both TEE and ICE in all fetuses. At this plane, the right ventricular outflow tract was observed as a circular structure in the most anterior position of the imaging plane. Immediately behind the right ventricular outflow tract, the aortic valve was normally wedged between the left and right atria. At the aortic valve level, fine manipulations of the IVUC were required to define all of the aortic valve leaflets that were visualized in all TEE and ICE fetuses. The pulmonary valve plane was reached by TEE and ICE by further cranial withdrawal of the IVUC from the aortic valve plane. Similar to the aortic valve, defining the pulmonary valve required precise adjustment of the catheter position. Because of their thinness, rapid motion, and distance from the IVUC, the leaflets of the pulmonary valve were the most difficult to image. Both TEE and ICE allowed excellent imaging of the pulmonary bifurcation. The spatial relation of the great arteries was defined in all fetuses by TEE and ICE from the junction between the superior caval vein and right atrium (great vessel plane) (Figure 4). The aortic arch lay almost parallel and immediately to the right of the pulmonary artery and the ductus in this plane. The continuity between main pulmonary artery, ductus arteriosus, and descending aorta was well defined by both techniques.

At autopsy, the existence and spatial orientation of all anatomic structures defined by fetal TEE and ICE were confirmed. No esophageal or gastric lesions were observed after TEE. In 2 fetuses during ICE, the floor of the right atrium was perforated when advancing the IVUC. In both fetuses, the resulting hemopericardium was observed during the study and confirmed at autopsy. With increased operator experience, no further perforations occurred in the remaining 8 fetuses. In all ICE fetuses, short episodes of IVUC-induced ectopic beats occurred, which cleared by catheter repositioning. In 2 fetuses after fetoscopic placement of the IVUC, forceps manipulation of the lower mandible resulted in local skin erosion and minor hematoma formation.

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This study in fetal sheep demonstrates that fetal cardiac anatomy can be defined by imaging with a 10 F-10 MHz IVUC. The IVUC permits accurate definition of fetal cardiac anatomy from a transesophageal imaging position in small midgestation fetuses and from an intracardiac right atrial imaging position in large late-gestation fetuses. Because fetal TEE was less invasive than ICE and was not associated with any significant complications in our study, it may serve as a useful monitoring tool for currently developed fetal cardiac and noncardiac interventions when transabdominal ultrasound is inadequate.[1–6] TEE may be as valuable in monitoring cardiac procedures in fetuses as it has been in children.[7] The IVUC can be placed into the fetal esophagus during either open or fetoscopic procedures and advanced toward the heart. Importantly, the size and penetration of the 10 F-10 MHz IVUC would permit fetal TEE in human fetuses between approximately 23 and 33 weeks' gestation. This period matches closely the time interval where most fetal cardiac interventions in human fetuses have been performed.[1–5] Intracardiac IVUC placement in late gestation fetuses as large as human neonates required fetal vessel dissection and was associated with right atrial perforation in 2 fetuses. Potentially, fetal ICE may also interfere with intracardiac streaming patterns, disrupting the return of oxygenated blood via the ductus venosus across the foramen ovale to the

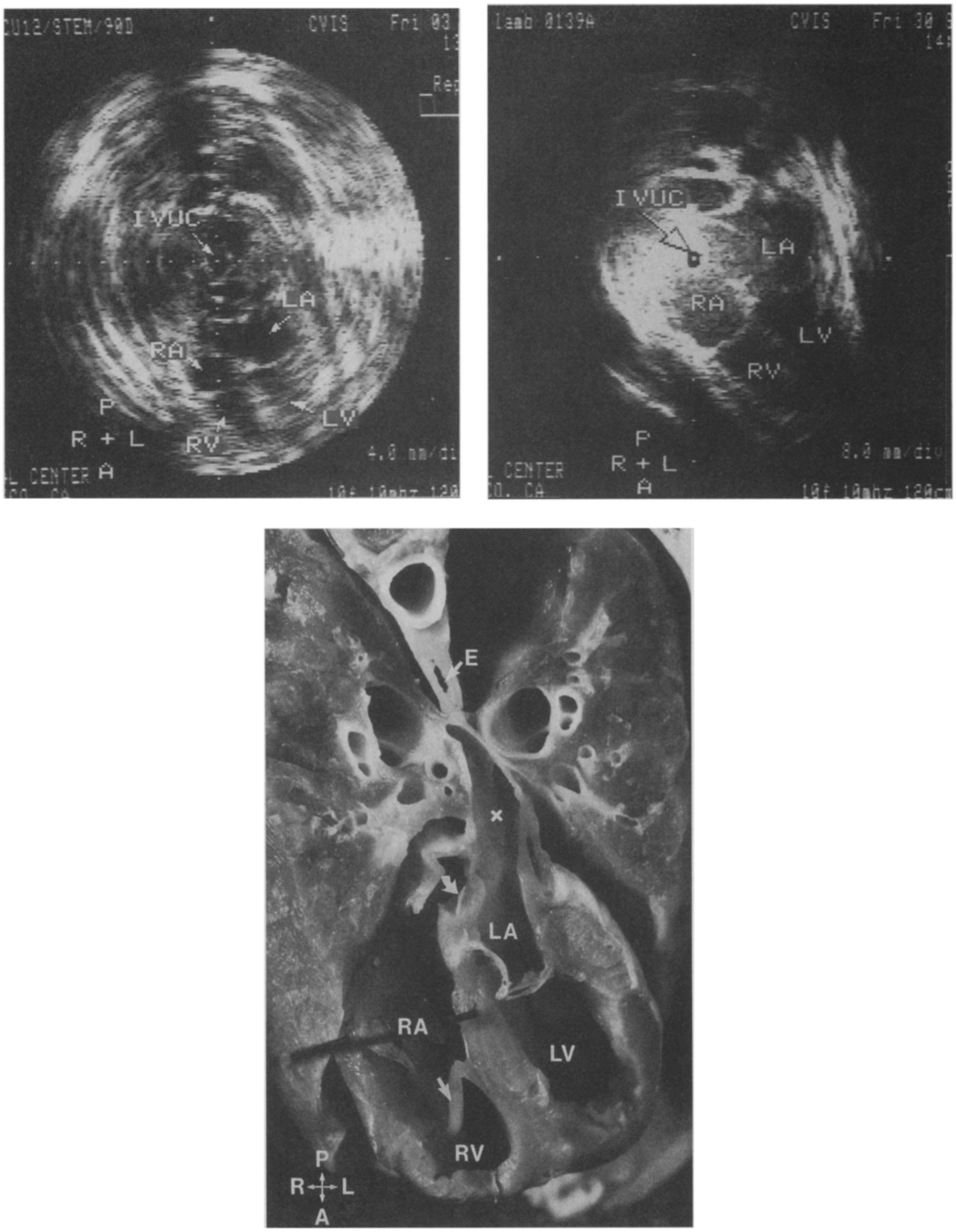

FIGURE 2. **Four-chamber plane.** ***Top left,*** **fetal transesophageal echocardiogram at 90 days' gestation;** ***top right,*** **fetal intracardiac echocardiogram (ICE) at 132 days' gestation;** ***bottom,*** **dissected specimen (132 days' gestation); transesophageal echocardiogram and ICE defined the lateral walls of the right atrium (RA) and ventricle (RV) better than the lateral walls of the left atrium (LA) and left ventricle (LV). Because the ventricular septum is positioned almost parallel to the ultrasound beam from the right atrial position, its integrity is less well defined by ICE. The mitral and tricuspid valves are seen throughout their entire range of motion. The pulmonary veins enter the left atrium through a common confluence (x). Both techniques identify such small structures as the foramen ovale, septum primum, or moderator band. A = anterior; E = esophagus; IVUC = intravascular ultrasound catheter; L = left; P = posterior; R = right.**

left heart. In addition, the 10 F IVUC may obstruct blood flow in the superior vena cava, predisposing the fetus to intraventricular hemorrhage. Because of the actual risk of right atrial perforation and the potential risks of interference with systemic and placental venous return to the heart, we currently cannot recommend performing fetal ICE in human fetuses until smaller imaging catheters with sufficient tissue penetration become available. The fetal semilunar valves were the most difficult structures to image due to their rapid motion, the slow frame rate of the imaging system, its limited tissue penetration, and decreased lateral resolution in the far field.[8] Despite these limitations, we believe that in the case of fetal

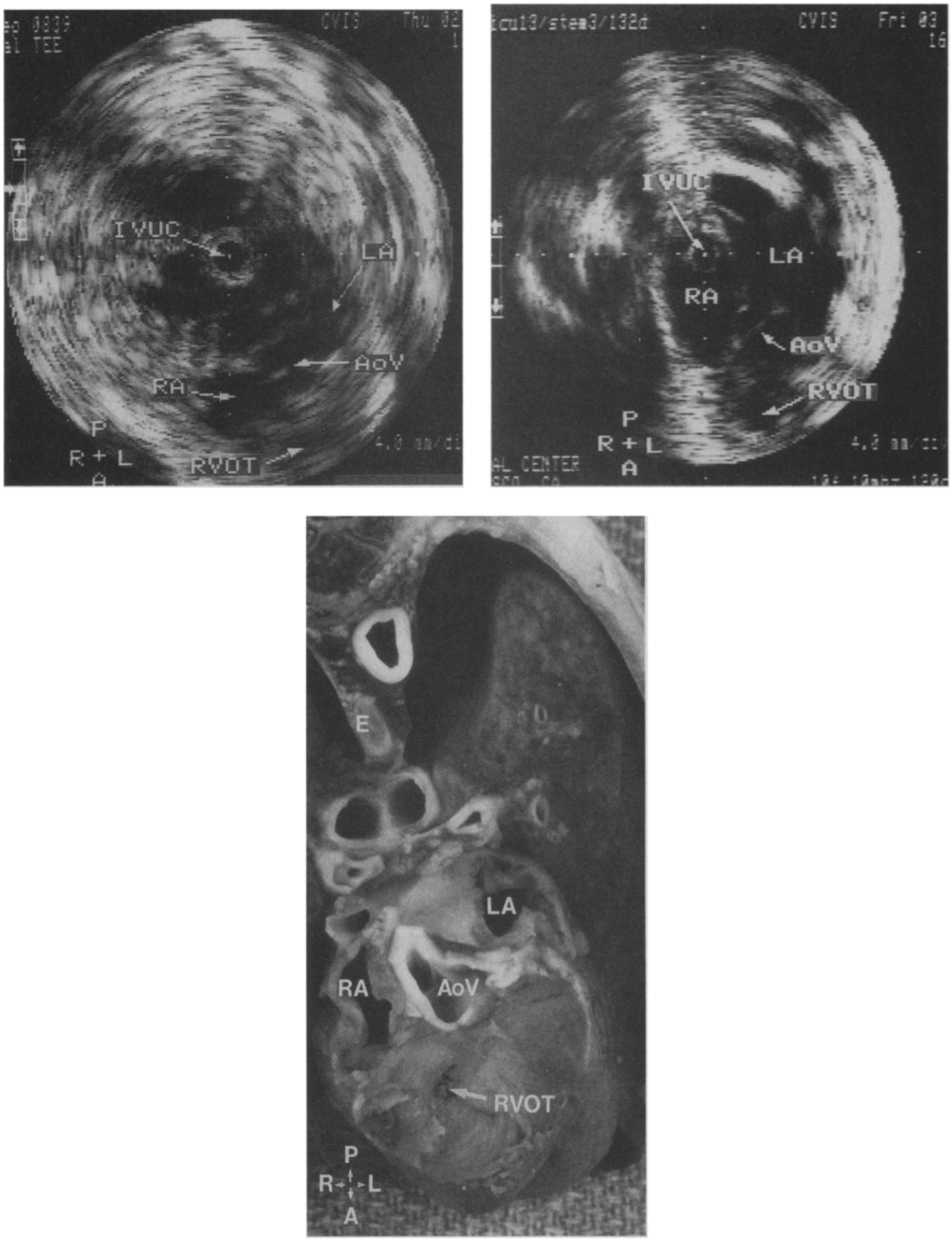

FIGURE 3. Aortic valve plane. *Top left,* fetoscopic fetal transesophageal echocardiogram in a 90-day-old fetus weighing 550 g; *top right,* fetal intracardiac echocardiogram (ICE) at 132 days' gestation; *bottom,* dissected specimen (132 days' gestation). At this plane, the right ventricular outflow tract (RVOT) is imaged as a circular structure in the most anterior position of the imaging plane. Immediately behind the right ventricular outflow tract and to the left of the right atrial appendage, the aortic valve (AoV) is seen wedged between the left (LA) and right (RA) atria. Fine manipulations of the intravascular ultrasound catheter (IVUC) were required to define all of the aortic valve leaflets. Abbreviations as in Figures 1 and 2.

aortic or pulmonary valve stenosis, the thickness and decreased motility of the dysplastic valve leaflets will facilitate their visualization by TEE and ICE. In addition, the ventricular septum was less well defined by ICE because it was almost coaxial to the ultrasound beam from the right atrial position. A comparison between conventionally used fetal echocardiographic techniques with the new imaging approaches is needed to further define the strengths and weaknesses as well as the safety of fetal TEE and ICE in more detail. Further reduction in IVUC size, lower frequencies, pulsed Doppler capabilities, and softer blunt-tipped catheters would be welcomed for performing TEE in human fetuses.

In conclusion, this study in fetal sheep demonstrates that fetal cardiac anatomy can accurately be defined from a transesophageal imaging position in

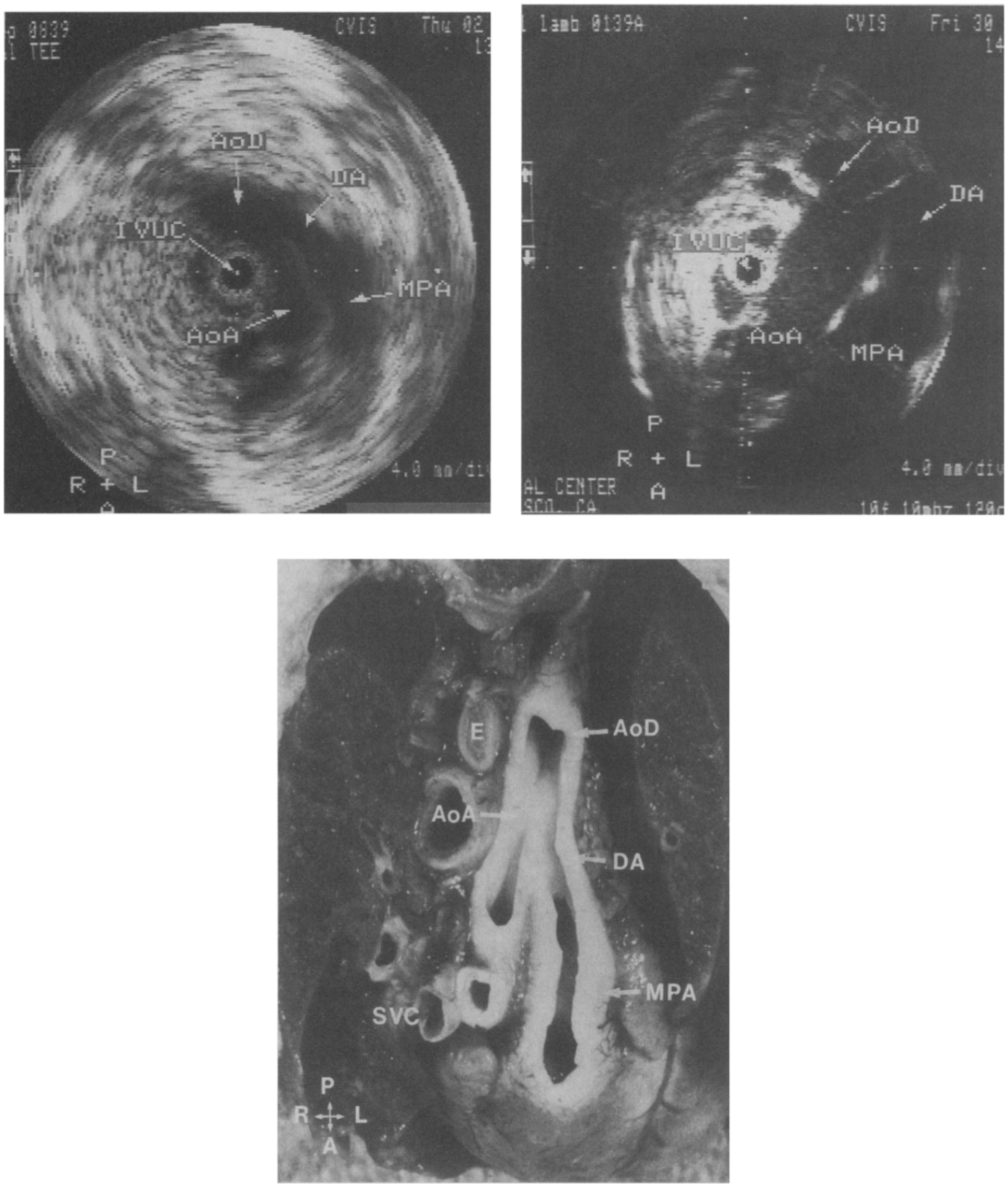

FIGURE 4. Great vessel plane. *Top left,* fetoscopic fetal transesophageal echocardiography (TEE) in 550 g fetal sheep; *top right,* fetal intracardiac echocardiography (ICE) at 132 days' gestation; *bottom,* dissected specimen (132 days' gestation). The main pulmonary artery (MPA) can be seen traveling in an anteroposterior direction to the left of the aortic arch (AoA). The main pulmonary artery continues through the ductus arteriosus (DA) into the descending aorta (AoD). SVC = superior vena cava; other abbreviations as in Figures 1 to 3.

small midgestation fetuses and from an intracardiac right atrial imaging position in large late-gestation fetuses. Because fetal TEE was less invasive than ICE and was not associated with any significant complications in our study, it has the potential to serve as an alternative fetal monitoring tool during fetal cardiac interventions when transabdominal ultrasound is inadequate.

Acknowledgment: We thank Christine Roman, Mario Trujillo, and Vincente G. Lapiz for expert technical assistance.

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