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## *Transthoracic echocardiographic technique for aortic valve annular determination in adult sheep undergoing prosthetic valve implantation*

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## ABSTRACT

**Falkner P, Millner H, Nelson D, Rakow N, Shecterle LM, St. Cyr JA** *Transthoracic echocardiographic technique for aortic valve annular determination in adult sheep undergoing prosthetic valve implantation, Online Journal of Veterinary Research 9 (2) : 83-94, 2005.* The placement of prosthetic heart valves in sheep are commonly performed for pre-clinical investigation and studies have customarily implanted only one or two different valve sizes/study. Because of this intentional restriction in valve sizes for implantation, a reliable pre-operative determination of the animal's annulus is crucial to appropriately matching the prosthetic valve with the animal's measured annulus at the time of insertion. Without accurate pre-operative valve sizing, many animals are rejected/sacrificed at the time of surgery because of the valve-annular discrepancy. Transthoracic echocardiography can achieve a pre-operative annular assessment; however, adequate

evaluation and reproducibility of this necessary annular data has been lacking in adult sheep. The described transthoracic echocardiographic technique in adult sheep in this paper has provided reliable annular data prior to surgical prosthetic valve implantation. Further, additional cardiac structure and hemodynamic parameters from this echocardiographic assessment has also been found to be extremely beneficial.

**Key words:** echocardiography, valve's annulus, animal model, prosthetic valve implantation

## BACKGROUND

Prosthetic heart valves undergo both animal (pre-clinical) and subsequent clinical studies before obtaining Food and Drug Administration approval. Sheep are commonly accepted as an animal model for pre-clinical investigation and studies have customarily implanted only one or two different valve sizes/study. Because of this intentional restriction in available valve sizes for implantation, a reliable pre-operative determination of the animal's annulus is crucial to appropriately match the prosthetic valve with the animal's measured annulus at the time of insertion. Without accurate pre-operative valve sizing, many animals are rejected/sacrificed at the time of surgery because of valve-annular discrepancy. Echocardiography is commonly recommended for this pre-operative assessment; however, adequate evaluation and reproducibility of transthoracic echocardiography (TTE) in the determination of a valve's annulus has been lacking in adult sheep. Transthoracic echocardiography can also provide data on cardiac structures/anatomy, hemodynamic measurements, and evaluate myocardial contractility. This paper presents a TTE technique, which has produced reliable pre-operative data for adult sheep undergoing total aortic root replacement<sup>1</sup>.

## METHODS

Thirty adult sheep underwent pre-operative cardiovascular assessment in an awake, non-sedated state, using TTE. All animals were cared for and housed according to the United States Animal Welfare Act of 1996 (PL89-541), as

amended by the Animal Welfare Act of 1970 (PL91-579) and the 1976 Amendment to the Animal Welfare Act (PL94-279). The TTE aortic annular assessment performed pre-operatively was followed by a manual intra-operative direct annular measurement. There were two separate pre-operative sonographers, one performing 4 examinations. All imaging studies were performed using the GE Vivid 7 (GE Medical, Milwaukee, WI) ultrasound device with the M3S probe at a harmonic frequency of 1.6 MHz/3.2 MHz with the depth optimized for each animal. This TTE imagery provided ideal visualization. All digital images were stored on Medial Optical Disk for future analyses.

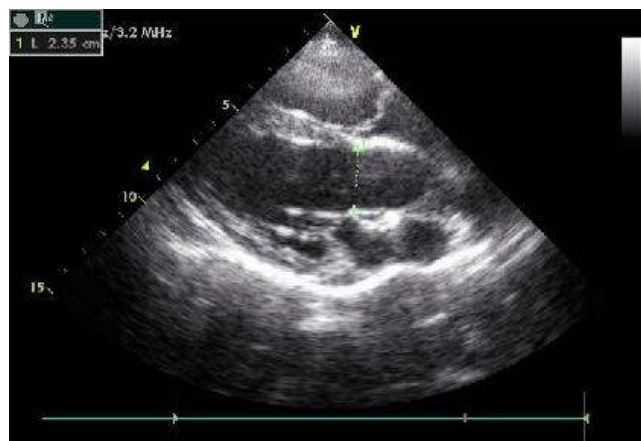


**Image 1-** Each adult non-sedated sheep was placed prone on a rectangular "blocking" pad for the ultrasound examination. The padded support allowed the animals to remain comfortable and cooperative by not having to support its own weight when either the right or left front leg was pulled forward for the desired position.



**Image 2-** Anatomically, the cardiac window in adult sheep is easily visualized due to the heart's position directly under the alopecic area of the axilla, which eliminates shearing of the animal and any additional stress caused by shearing.

Echocardiographic measurements were obtained using a 2D right parasternal long axis view of the aortic valve/root area. Two to three, three-second cine loops, visualizing the valve in mid to late systole, were recorded with no less than 3 heart cycles/loop.



**Image 3-** The ultrasound's measurement package calipers were used to measure the AA size between the two hyper-echoic annular points at the level of the valve's leaflet attachments. An average of 3 separate measurements of this long axis determined the annular size of the aortic valve. Commonly, at least one measurement was taken from each loop; however, in those cases where only 2 cine loops were acquired two measurements were taken from each loop.

At the time of surgical implantation of the prosthetic valve, a manual measurement of the animal's native aortic valve's annulus was performed using valve sizers (Medtronic, Inc.), which were inserted following removal of the valve leaflets. The manual intra-operative annular measurement was then compared to the pre-operative TTE evaluation.

## RESULTS

The right parasternal long axis view provided an accurate and reproducible visualization of the aortic valve's annulus, assessment of the native aortic and mitral valves, aortic root area, aortic outflow tract, ascending aorta, cardiac size (including chamber dimensions), ventricular/septal contractility, and hemodynamic parameters (data not shown). Furthermore, hemodynamic findings aided in both the short and long term management of these sheep (long term management not discussed).

Pre-operative awake TTE assessment of the aortic valve annulus versus intra-operative manual measurement data were assessed in 30 adult sheep undergoing total root aortic replacement. The following distribution of the animal's native aortic valve annuli measured pre-operatively by TTE revealed: 19-21 mm (n=8), 23-25 mm (n=20), and  $\geq 27$ mm (n=2). The TTE pre-operative evaluation compared to the intra-operative manual measurement demonstrated a comparison accuracy of at least 60%. This comparison between pre-operative TTE and intra-operative measurement when considering a  $\pm 1$  valve size lance, increased the accuracy to 93%. Only 2 of the 30 implanted valves revealed a  $> 1$  valve size difference when comparing TTE to the intra-operative manual measurement.

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## DISCUSSION

Various animal models have been utilized for pre-clinical assessment of valve prostheses prior to human clinical trials; however, over the past decade a sheep model has universally been accepted as a reliable model for both short and long-term pre-clinical prosthetic valve evaluation. Historically, non site-specific implantation was routinely performed. Today, orthotopic placement of an investigative prosthesis in animals, mimicking the human setting, has not been deemed mandatory, but highly recommended, in order to obtain a more accurate pre-clinical physiological assessment of the experimental prosthesis prior to human trials<sup>2</sup>.

Pre-operative aortic annular measurement along with myocardial functional assessment provides valuable information for orthotropic, site-specific prosthetic heart valve implantation. In the past, reliable echocardiographic images and hemodynamic data in the adult sheep have been difficult due to the lack of animal cooperation and a small viewing window due to chest wall/rib anatomy. Brown et al. advocated surgical resection of rib(s) at the time of implantation, thereby providing a viewing window for echocardiographic measurements postoperatively<sup>3</sup>. Obviously, the echocardiographic window described by Brown et al, which was created at the time of surgery was not present for a pre-operative evaluation; therefore, negating any future intra- and post-operative comparisons. Our presented technique produced reproducible data without having the animal undergoing surgical resection of rib(s), allowing the ability to perform pre- and post-operative comparisons.

The importance of our TTE technique cannot be over emphasized; however, a learning curve was found during this study, with more accurate assessments obtained as the study progressed. Our technique was originally designed and developed to provide the necessary information of the animal's native valve annulus for an appropriate fit of the implanted prosthesis at the time of surgery. This alone reduces the number of sacrificed animals at the time of implantation due to annular-prosthesis mismatch. Further, a transthoracic echocardiographic examination can also assess cardiac structural and functional parameters in a non-stressful situation, providing data for current and subsequent therapeutic management. Therefore, our technique could be not only important in prosthetic valve implantation, but more importantly as a diagnostic tool in the field of veterinary cardiovascular medicine.

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