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REGIONAL DIFFERENCES IN THE TUNICA MEDIA OF THE UTERINE ARTERY OF DOMESTIC PIG (*Sus Scrofa Domesticus*): BASIS FOR UTERINE BLOOD FLOW REGULATION

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ABSTRACT

This study aimed at describing the structure of tunica media of the uterine artery of domestic pig, since this structure influences the pattern of blood flow and reproductive performance. Specimens were obtained from main trunk, broad ligament segment and the terminal portion of twelve healthy adult domestic pigs (*Sus scrofa domesticus*) age range 6 – 18 months. They were fixed in 10% formaldehyde solution, and routinely processed for paraffin embedding and sectioning. Seven micron thick sections were stained with Hematoxylin & Eosin, Mason's Trichrome and Weigert resorcin fuchsin counterstained with Van Gieson stains. Tunica media comprising predominantly smooth muscle occupied approximately fifty percent (50%) of the volume of the entire wall with vasa vasora present deep into its inner zone. It showed zonal and regional variation in that in the main trunk and broad ligament segments was divided into inner two thirds having predominantly circular smooth muscle orientation while outer third was preponderantly fibroelastic with longitudinally disposed smooth muscles. The terminal segment had only circular layer. Density of vasa vasora declined distally. The predominantly muscular tunica media of the uterine artery in pigs shows zonal and regional suggesting segmental differentiation of function. The main trunk of this artery, due to its additional longitudinal layer of smooth muscle may be involved in regulation of blood flow to the uterus depending on the functional demands of the uterus.

Key Words:

INTRODUCTION

The structure of vascular tunica media influences the pattern of blood flow by alteration of diameter and length (Davies 1995, Lee and Schmid-Schonbein 1996, Davis and Hill 1999). Structural organization of tunica media of the uterine artery is important in understanding its adaptations for uterine changes during the various phases of reproduction (Bulletti et al., 1988). Although distributing arteries are generally known to be muscular, they display subtle variations which depend on the target organ they supply (Segal, 2005). The demands of the uterus vary with its physiological state (Mueller et al., 2006). Accordingly, although structural adaptations are expected to underlie these physiological adjustments, they are hitherto not described. Further, adaptation of uterine artery is crucial for acceptable reproductive outcome (Goswamy and Steptoe, 1988). The structural correlates may also be important in the formulation of therapeutic interventions for some adverse reproductive outcomes (Guo-Tao et al, 2004). Domestic pigs (*Sus scrofa domesticus*) have widely been considered as suitable models in human translational research because of their close biological similarities with humans (Swindle, 2007).

This study therefore aimed at describing the structural organization of tunica media of the uterine artery in the domestic pig.

MATERIAL AND METHODS

Twelve young adult domestic pigs (*Sus scrofa domesticus*) aged 6 – 18 months were used in this study. All animals were nulliparous. Animals were purchased from livestock farmers in Ruiru, Thika and Kabete regions of central Kenya and only those certified by a veterinary doctor to be healthy were included in this study. All procedures were performed according to the *Guide for Care and Use of Laboratory Animals* (NIH publication, revised 2012). The animals were kept at least two together in stables with straw-saw dust ground and free access to an out-door pen during daytime. They were fed wetted, granulated full-fodder twice a day with other standard omnivorous diet and had free access to water. The stables were kept at 24°C and a light-dark cycle of 12/12 hours.

The animals were euthanized with intravenous sodium pentabarbitone 20 mg/ml and perfused with 10% formaldehyde solution. Abdominal and pelvic cavities were dissected to expose common iliac, internal iliac and uterine arteries. Five millimeter sections of the uterine artery were harvested from the following three regions, Main trunk (A - immediately after it is given off the internal iliac), Broad ligament (B - as it enters the broad ligament) and terminal (C - just before anastomosis with ovarian artery) [Figure 1]. The sections were routinely processed for paraffin embedding and sectioning. Seven micron thick sections were stained with Hematoxylin & Eosin, Mason's Trichrome and Weigert Elastin counterstained with Van Gieson stains. Sections were examined with light microscope at X100, 250 and 400. Representative micrographs were taken using digital camera.

RESULTS

Tunica media extending between the internal and the less distinct external elastic lamina bordering the adventitia (Figure 2 and 3A) occupied approximately fifty percent (50%) of the volume of the entire wall. It was predominantly muscular with scattered elastic fibers. There was notable regional variation in the main trunk and the broad ligament segments. They demonstrated zonation within the media with predominantly circular smooth muscle cells in the inner two thirds and longitudinally disposed smooth muscles in the outer portion of it forming approximately a third of the total medial thickness (Figures 3 C, 4 A, B). The longitudinal muscles were not continuous. They formed islands resembling *'taenia'* with fibroelastic fibres intervening between the islands. The terminal segment on the other hand, comprised of a single zone of circularly oriented smooth muscle in the tunica media (Figure 4 C).

The main trunk was composed of spindle-shaped smooth muscle cells arranged in concentric layers ranging from 25 to 35. All smooth muscle cells were invested with a thin external lamina and a narrow layer of delicate collagenous fibrils (Figure 3 B). Vasa vasora penetrated outer zone of tunica media. They were made of single layer of cells and resembled blood capillaries. The vasa vasora appeared to branch from arterioles within the tunica

adventitia (Figure 3 D). The external elastic lamina (EEL) was not obviously discernible at media-adventitial junction in the broad ligament and terminal segments but was prominent in the main trunk segment.

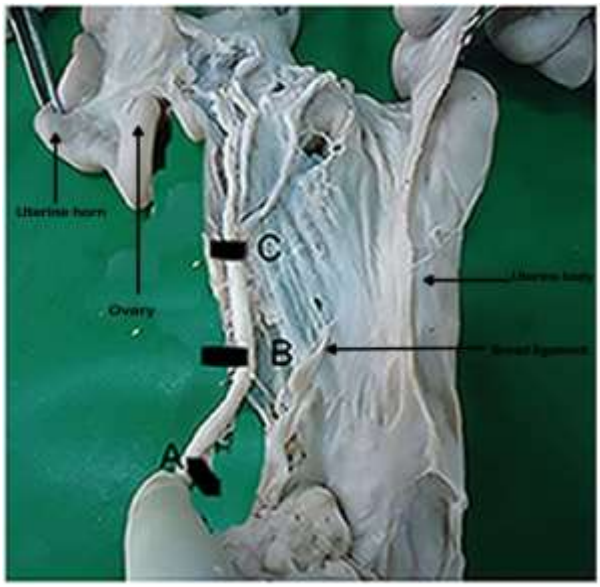

Figure 1: Macrograph of the uterus and uterine artery showing sites where specimens were taken from A: Main trunk, B: Broad ligament and C: Terminal segments

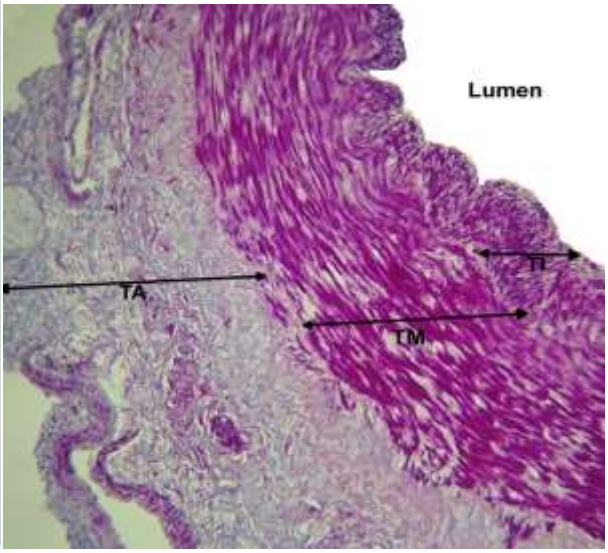

Figure 2: Photomicrograph of the uterine artery of domestic pig showing the arterial tunics; tunica intima (TI), tunica media (TM) and tunica adventitia (TA) [Masson's Trichrome stain, at X100].

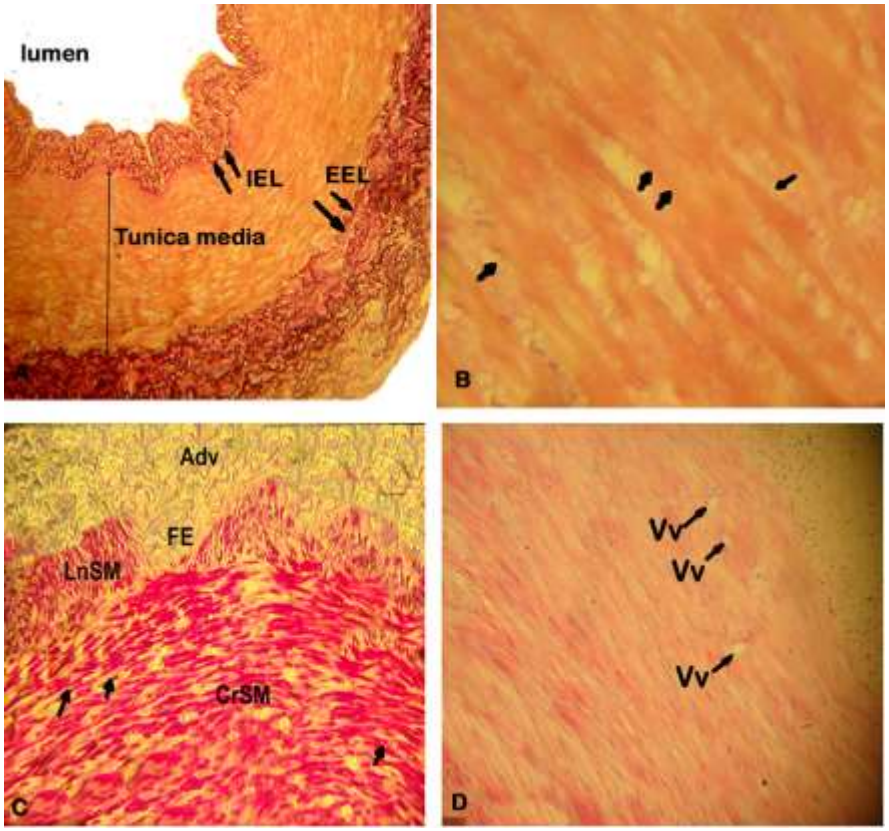

Figure 3 A – D: Photomicrograph of structure of tunica media in uterine artery of domestic pig. A: The extent of the tunica media between the Internal Elastic lamina, IEL and External elastic lamina, EEL. Weigert's Resorcin-Fuschscin conterstained with Van Gieson stain, X100. B. Higher magnification of tunica media with population of smooth muscle cells and fibroelastic components. Note a layer of delicate collagenous fibrils surrounding the muscles, (arrows). Hematoxylin and Eosin stain, X400. C: Zonation of the tunica media with circular smooth muscle CrSm and the longitudinal smooth muscles, LnSm. Note the vasa vasora (arrows). Hematoxylin and Eosin stain, X100. D: Tunica media with vasa vasora, (Vv). Note the variable dimensions of the vasa vasora. Hematoxylin and Eosin stain, X100.

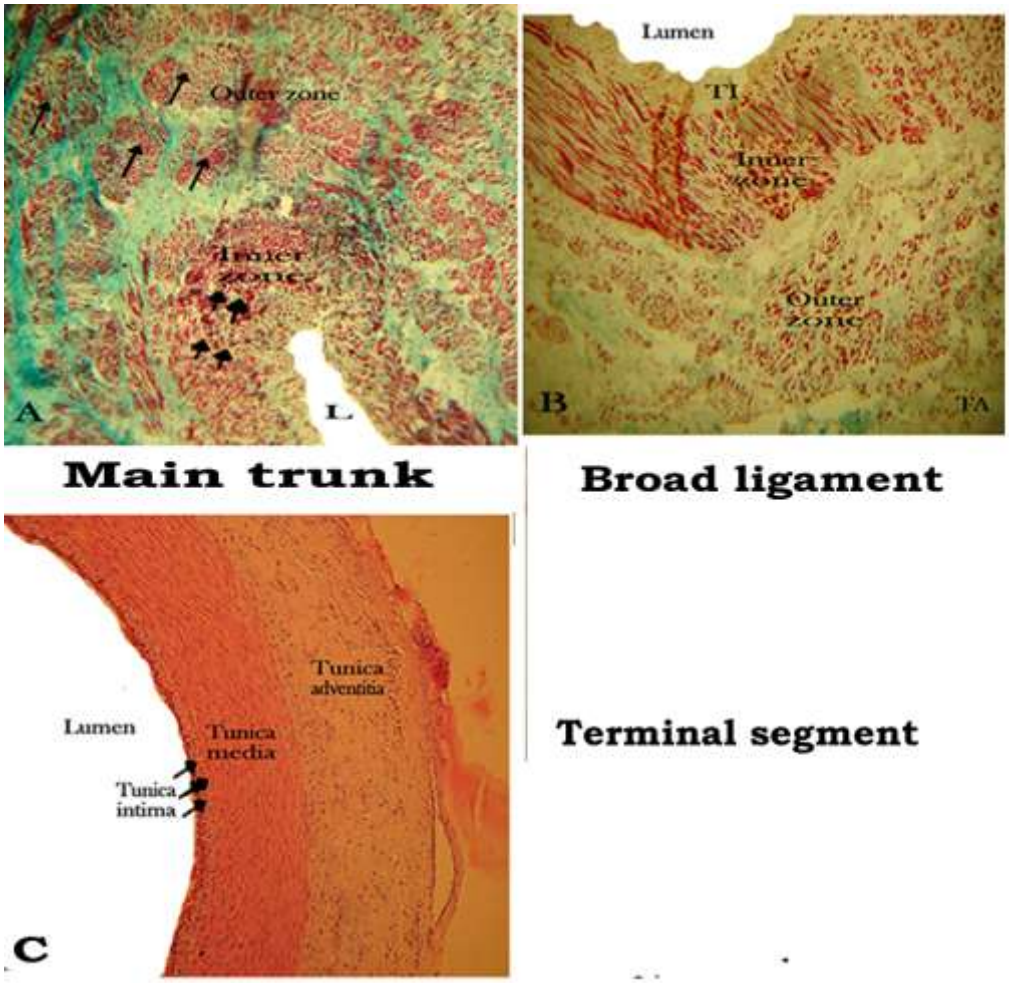

Figure 4 A – C: Photomicrograph showing regional changes in structure of tunica media of uterine artery of domestic pig: A: Zonation of the tunica media, note the outer zone of tunica media with longitudinally predisposed muscle fibres- arrows. Mason's Trichrome stain, X400. B: Zonation of the tunica media with circular muscle in the inner zone and longitudianal muscle in the outer zone. Notice that the muscles in the outer zone aren't as prominent as in the previous section Mason's Trichrome stain, X400. C: Terminal portion showing the tunica media. Notice the absence of zonation in this section. Mason's Trichrome stain, X400.

DISCUSSION

Tunica media was composed of predominantly smooth muscle cells typical of muscular arteries (Junqueira and Carneiro 2003, Megen et al., 2007). The smooth muscle cells adapt to changes in hemodynamic demands in two ways: through synthesis of extracellular matrix or by myogenic response (Sjolund et al., 1988, Joannidess et al., 1993, Davies et al., 1999). This response is necessary in maintaining column of blood flow within the artery thus playing a regulatory role (Johnson, 1989). Since the main trunk of the uterine artery experiences systolic pressure before the terminal segment, the myogenic response of smooth muscle may be useful in maintenance of column of blood throughout the entire length of uterine artery.

A remarkable finding of this study is that the tunica media of the main trunk and broad ligament segments comprised circular and longitudinal smooth muscle layers, similar to that of mesenteric, portal and femoral veins (Cohen and Wiley, 1977, Brown et al., 1982). In these sites, the arrangement regulates blood flow. A

similar arrangement is also found at the branching parts of arteries and is also believed to be involved in intra-arterial regulation of blood flow to the target organ (Novikov and Yal'tsev, 2002). Indeed, it has been advanced by some workers that the smooth muscles engage in relaxation, constriction of the uterine artery (Bodelsson and Stjernquist, 1992) and may play a role in a sphincter mechanism (Todd et al., 1980, Mitchell et al, 1998).

Longitudinal muscle response is greater than the circular muscle when tension is applied (Brown et al, 1982). It is possible that volumes of blood flowing to the uterus, during heavy peaks is associated with increased pressure on the uterine artery and thus need for it to have such an arrangement for an intra-arterial regulation mechanism. The presence of longitudinal muscle layer in the main trunk and broad ligament segments of the uterine artery, therefore, may be due to an increased turbulence at these points where the artery branches to supply the uterus and cyclically demands an increased blood flow during estrous. Pertinent to this suggestion is the finding that chronic trauma inflicted by pressure to an arterial wall may result in abnormal longitudinal muscles in the media (Inada et al., 1978). These forces decrease proximo-distally, with the broad ligament segment experiencing intermediate pressure and having sparse longitudinal muscle arrangement. The terminal segment may be exposed to milder pressure after blood has coursed a greater distance and distributed through arcuate arteries hence absence of longitudinal muscle. This observation is supported by ultrasonographic studies that show slower blood flow at the terminal end of the uterine arteries (Kouje, 2003).

In this study, vasa vasora that penetrated the tunica media were present in the main trunk and broad ligament segments but were missing in the distal segment. Existence of vasa vasora in an artery suggests arterial activeness in regulation of blood flow to the target organ such as the uterus (Chuncher and Somana, 2005) and its level of metabolic activities (Kachlick et al., 2007). Preferential presence of vasa vasora in the tunica media of the main and broad ligament trunks of the uterine artery suggests that these segments are important in regulation of blood flow. Vasa vasora were not seen in the tunica media of the terminal segment may be because of its reduced activeness in regulation of uterine blood flow.

In conclusion, the predominantly muscular tunica media of the uterine artery in pigs shows zonal and regional variation suggesting segmental differentiation of function. The main trunk of this artery, due to its additional longitudinal layer of smooth muscle may be involved in regulation of blood flow to the uterus depending on the functional demands of the uterus.

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