

The heritability of vessel size of the pampiniform plexus as a means to assess the genetic component of varicocele

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Summary

Ultrasonography of each testicle was used to capture a coronal-sagittal image of the veins of the pampiniform plexus (PP) and the testicular artery of 239 boars at approximately 6 months of age. Three to 10 vessels of the PP were used to derive the average area of right PP vessels (AAR) and the average area of the left PP vessels (AAL) and the standard deviation for each testicle for each boar. Within boar ratios, as well as boar to population ratios of vessel size were then calculated to identify boars with suspect varicocele. Suspect varicocele was defined as vessel area 1.5 times larger than the other testicle within a boar or compared to the average vessel size for that testicle in the population. Utilizing the within boar ratio, 34% of boars presented with suspect varicocele, with 85% of the varicocele occurring in the left testicle PP. Heritability estimates from a sire model were 0.39 and 0.34 for AAR and AAL, respectively. These moderate heritability estimates suggest that varicocele could be selected against in breeding programs to potentially improve boar semen quality.

Introduction

Tortuous dilated veins and/or vascular lesions of the pampiniform plexus are vascular abnormalities called varicocele, and an association with male infertility has been reported (Jarow, 2001). The majority of reported varicoceles are located on the left side of the scrotum and this predominance is explained by the right angle insertion and long course of entry of the left testicular vein into the left renal vein (Sabanegh & Agarwal, 2012). Varicocele impairs testicular function by causing the counter current heat exchange of the pampiniform plexus to be less efficient. The testicle with varicocele tend to have a higher than normal temperature caused by warm abdominal blood not properly cooling prior to entering the testicle (Hsiung *et al.*, 1991).

In men with infertility and reduced semen parameters, the most common physical abnormality identified were varicoceles (Sigman & Jarow, 1997; Sigman & Howards, 1998). A study examined the reproductive tracts of culled boars whose semen quality was considered poor for at least 5 weeks prior to culling. Varicoceles were found in 22% of these boars (Ubeda *et al.*, 2014). Ultrasonography has been used to identify varicocele in the live boars and 23.4% of the adult boars measured were reported to have varicocele. The boars with varicocele showed a significant increase in sperm morphology abnormalities and a significant effect on sperm membrane integrity (Kleve-Fled *et al.*, 2015).

Several studies have documented varicocele incidence in first-degree relatives of men with known varicocele to evaluate the familial risk. A significant 3 to 8-fold increase in varicocele was reported when compared to control populations for first-degree relatives examined (Gökçe *et al.*, 2010; Raman *et al.*, 2005). However, the degree to which genetics plays a role in varicocele in swine is unknown. Consequently, the objective of this study was to estimate preliminary heritability for average left and right side pampiniform plexus area in boars.

Methods and Materials

A total of 239 boars at approximately 6 months of age from the Nebraska Index Line at the University of Nebraska- Lincoln research farm were measured via ultrasonography and used in the analysis. The first set, measured in 2016, consisted of 127 boars from 16 sires with an average of 7.9 boars per sire. The second set, measured in 2017, consisted of 112 sons from 11 of the previously measured boars for an average of 10.2 boars per sire.

Ultrasonography of each side of the scrotum was performed using an Ibex EVO ultrasound (E.I. Medical Imaging, Loveland, CO) with a linear endorectal probe (L6E). The transducer was orientated toward the lower half of the testicle at approximately a 45° angle capturing a coronal-sagittal image of the veins of the pampiniform plexus and the testicular artery. All images were compiled into a collage in Bioquant image system (Bioquant Image Analysis Corp., Nashville, TN). The Bioquant image system was then used to measure the area (mm²) of 3 to 10 vessels of the pampiniform plexus to derive the average area of right PP vessels (AAR) and the average area of the left PP vessels (AAL) and the standard deviation for each testicle. A within-boar ratio was then produced for each testicle (AAL of boar X / AAR of boar X) and was repeated for the right testicle to assess differences in vessel size between an individual boar's testicles. Individual boars were then compared against the entire population for the year they were measured with the ratio (AAL of boar X / AAL of the population) and was repeated for the right testicle. If a boar's average vessel area was more than 1.5 times larger than the opposing plexus, or 1.5 times larger than the average for the population, those vessels were considered suspect varicocele.

A Welch's t-test was used to test if a significant difference existed between AAL and AAR vessel size for all boars sampled. A sire model was used to estimate variance components of pampiniform plexus vessel size for both the left and right side. Fixed effects included weight at time of measurement, finishing pen (concatenation of finishing room and pen), and year of measurement, with the random effect of sire. The model was implemented in R (R Core Team, 2015). The heritability of AAR and AAL was then calculated as the sire variance multiplied by 4 divided by the summation of sire and residual variance.

Results and Discussion

Summary statistics for AAR and AAL are presented in Table 1. AAL had a larger average vessel size than AAR ($P < 0.001$). This was in agreement with previous literature that have reported left testicle PP vessels being larger in diameter and most commonly found with varicocele (Sabanegh & Agarwal, 2012). Utilizing the within boar ratio, 34% of boars presented with suspect varicocele, with 85% of the varicocele occurring in the left testicle PP. The reported percentage

of boars described as having varicocele in this study was slightly higher than that of previous studies. This could be due to different thresholds used as a means to categorize boars as suspect varicocele as this was not well described in the previous studies (Kleve-Fled *et al.*, 2015; Ubeda *et al.*, 2014). Only 11% of boars were labeled suspect varicocele when compared to the entire population. There was considerable variation between boars in this population for both AAR and AAL and this may explain why when individual boars were compared to the overall population, not as many boars were considered suspect.

Variance components and heritability estimates are presented in Table 2. Both AAR and AAL were found to be moderately heritable, although variance components are associated with large standard errors. Heritability estimates of varicocele in boars, or any other species, is non-existent. However, in humans a higher incidence of varicocele occurring in some families has been reported (Gökçe *et al.*, 2010; Raman *et al.*, 2005).

Although the data currently available is limited, there are future plans to continue to measure boars from this genetic line in order to increase the sample size. Though sample size was small, this study does demonstrate that PP vessel size is a heritable trait, which could allow for its use in selection programs. Selecting against varicocele has the potential to improve semen quality, as previous studies have shown varicocele to be associated with infertility and poor semen quality (Jarow, 2001; Kleve-Fled *et al.*, 2015; Ubeda *et al.*, 2014).

Table 1. Summary statistics of the average area of right pampiniform plexus vessels (AAR) & the average area of the left pampiniform plexus vessels (AAL) from 239 boars at the University of Nebraska-Lincoln.

	AAR, mm ²	AAL, mm ²
Average	7.20*	8.69*
Standard Deviation	2.68	2.99
Minimum	1.86	2.86
Maximum	19.64	20.49

* indicates a significant difference (p<0.001)

Table 2. Variance component and heritability (SE) estimates for AAR¹ & AAL².

	AAR, mm ²	AAL, mm ²
Sire variance	0.70 (0.83)	0.75 (0.86)
Residual variance	6.52 (2.55)	7.95 (2.82)
Heritability	0.39	0.34

¹ The average area of the right pampiniform plexus vessels (AAR).

² The average area of the left pampiniform plexus vessels (AAL).

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