

Histopathological findings in ovarian vessels in comparison to the alterations in extraovarian, extrauterine and uterine vessels in the mare

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Summary

Angiopathies in the equine uterus have previously been described in detail, but until now histopathological investigations of the ovarian stromal vessels are missing. Through Doppler sonography distinct variations in ovarian blood flow and pressure during the mare's estrus cycle are indicated. Furthermore the ovarian perfusion is significantly lower in mares with uterine angiopathies compared with mares without pathological vascular findings. The objective of this study was to characterize the quality and quantity of ovarian and extraovarian angiopathies in the mare in comparison to the findings in uterine and extrauterine vessels. Specimens from both ovaries and the uterus as well as from extraovarian and extrauterine vessels of 60 mares of different breed and age (one day to 24 years) were stained with Hematoxylin-Eosin and with a modified Constantine's Picro-Sirius Red stain. The degenerative changes of the arteries were compared using the vascular degeneration index (VDI) as described by Ludwig et al. (2001). The results of the present study indicate that angioses in the genital system affect the uterus as well as the ovary. However, ovarian vessels are mainly affected by an age-related fibrosis. The extrauterine and extraovarian arteries show fibrosis corresponding to age and parity. The uterine vessels develop an elastosis predominantly increasing with the number of foalings. Furthermore, ovarian angiopathies are visible in a higher extent compared with uterine angioses. Based on these findings, it is possible to draw conclusions from the angiopathies in the endometrial biopsy to those in the ovaries, if the age of the mare is regarded. Ovarian angiopathies may cause disturbed follicular and luteal angiogenesis resulting in functional alterations.

Keywords: mare, reproduction, angiopathies, ovary, uterus, extraovarian and extrauterine vessels

Histopathologische Befunde an den Blutgefäßen der Ovarien im Vergleich zu den Alterationen der extraovariellen, extrauterinen und uterinen Gefäße bei der Stute

Während Angiopathien im Uterus der Stute detailliert beschrieben worden sind, fehlen histopathologische Untersuchungen zum Vorkommen von Angiosen im ovariellen Stroma bis heute vollständig. Dopplersonographische Untersuchungen haben gezeigt, dass es im Verlauf des Zyklus zu starken Schwankungen des ovariellen Blutflusses und Blutdruckes kommt, und dass die ovarielle Perfusion bei Stuten mit uterinen Angiopathien deutlich vermindert ist, im Vergleich zu Stuten mit unveränderten uterinen Blutgefäßen. Ziel der vorliegenden Studie ist daher die qualitative und semiquantitative Charakterisierung der ovariellen und extraovariellen Angiopathien der Stute in Korrelation zu den Befunden an den uterinen und extrauterinen Blutgefäßen. Es wurden Gewebeproben von beiden Ovarien, dem Uterus und den extraovariellen und extrauterinen Arterien und Venen von 60 Stuten verschiedener Rassen und unterschiedlichen Alters (1 Tag bis 24 Jahre alt) mittels Hämatoxylin-Eosin Färbung und Picro-Sirius Rot-Färbung untersucht. Die degenerativen Veränderungen der Arterien wurden unter Verwendung des von Ludwig et al. (2001) entwickelten Vaskulären-Schädigungs-Index (VDI) vergleichend betrachtet. Die Ergebnisse dieser Studie zeigen, dass Angiopathien im Genitalsystem nicht nur den Uterus, sondern auch die Ovarien betreffen. Während ovarielle Gefäße überwiegend altersassoziiert zunehmende Fibrosen aufweisen, treten Fibrosen in extraovariellen und extrauterinen Arterien in Abhängigkeit von der Zahl der Abfohlungen und dem Alter Stute auf. In den uterinen Gefäßen stehen hingegen graviditäts-assoziiert auftretende Elastosen im Vordergrund. Darüber hinaus kann festgestellt werden, dass die Angiopathien im Ovar in der Regel stärker ausgeprägt sind als im Uterus. Auf Grund dieser Studie sind nun, unter Berücksichtigung des Alters der Stute, auch an Hand endometrialer Biopsien Rückschlüsse auf die Gefäßalterationen im Ovar möglich. Die ovariellen Angiopathien führen möglicherweise zu einer Störung der folliculären und lutealen Angiogenese mit daraus resultierenden funktionellen Läsionen.

Schlüsselwörter: Stute, Reproduktion, Angiopathien, Ovar, Uterus, extraovarielle und extrauterine Blutgefäße

Introduction

The vascular system of the female reproductive tract implements indispensable functions of metabolic and endocrine needs. Degenerative lesions of these vessels are mainly described in uterine and extrauterine arteries of various species caused by pregnancy and age sometimes leading to various complications as vascular ruptures (Ludwig et al. 2001, 2002) and malnutrition / malperfusion of the tissue (Schoon et al. 1999). In 80% of the routinely investigated endometrial biopsies of the mare degenerative angiopathies are dia-

gnosed. These angioses are described in detail by Schoon et al. (1997, 1999). The degree of angiosis increases with the age and number of foalings (Grüninger et al. 1998). Endocrine and hemodynamic influences are possible causes for vascular remodelling processes (Grüninger et al. 1998, Schoon et al. 1999).

Endometrial and myometrial arteries and veins of adult non-pregnant mares show mild to moderate panfibroelastosis and panelastofibrosis, whereas alterations of extrauterine vessels are mainly classified as fibrosis or fibroelastosis. The degree

of angiogenesis increases from the endometrium to the myometrium to the extrauterine vessels (Ludwig et al. 2001).

Histopathological and Doppler ultrasonographic studies of the A. uterina demonstrate that an increasing degree of fibrosis is accompanied by an elevated vascular resistivity possibly leading to a reduced uterine perfusion (Blaich et al. 1999). Furthermore, endometrial angiosclerosis may result in reduced endometrial drainage and perfusion. Additionally, synergistic effects on the development of endometriosis are discussed (Schoon et al. 1999).

Few studies on equine ovarian vessels are available. Exclusively the vascularization of follicles and corpora lutea are investigated histologically (Watson and Al-zia'bi 2002, Ferreira-Dias and Mateus 2003). Doppler sonography reveals that ovarian vascular development and regression during the mare's estrus cycle are accompanied by dramatical changes in ovarian blood flow and pressure (Bollwein et al. 2000, Wein 2003). Wein et al. (2002) report that the ovarian perfusion is significantly lower in mares with uterine angiopathies compared to mares without pathological findings.

Ovarian angiopathies may lead to an impaired perfusion, resulting in disturbed follicular and luteal development as well as endocrine insufficiency causing embryonic death in the mare (Allen 2001). The purpose of this study was to characterize the quality and quantity of ovarian and extraovarian angiopathies in the mare in correlation to the findings in uterine and extrauterine vessels.

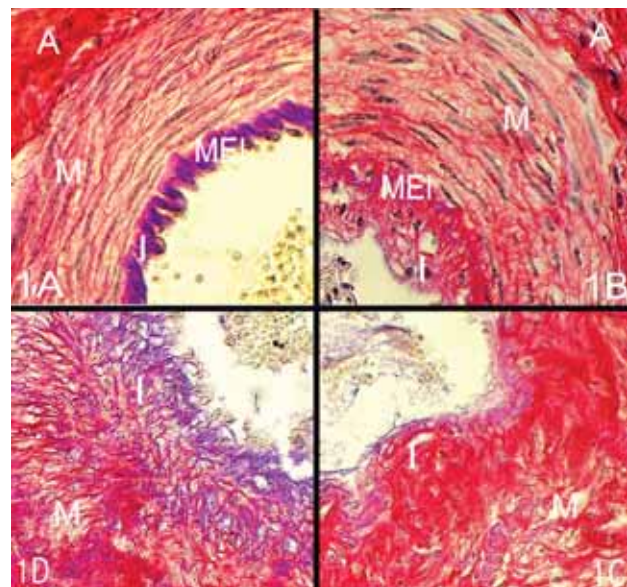
Material and methods

Tissue from 60 mares of different breed and age (one day to 24 years), was collected at the Institut für Veterinär-Pathologie, Universität Leipzig, during routine necropsies. The mares were grouped according to their age and stage of reproduction (Tab. 1). The classification of parity (nulliparous, primiparous, multiparous) was estimated by the investigation of the endometrial vessels as reported by Schoon et al. (1999).

Specimens were obtained from both ovaries, uterus (both cornua and corpus uteri) and bilateral extraovarian and extrauterine vessels (Arteriae and Venae uterinae and ovaricae). The specimens were fixated in 4% formalin and routinely embedded in paraplast. The sections were stained with Hematoxylin-Eosin and a modified Constantine's Picro-Sirius Red stain (Grüniger 1996). The quality of the vascular lesions was classified (hyperplasia of the intima, elastosis, fibrosis, elastofibrosis, fibroelastosis, alterations of the membrana elastica interna, inflammatory lesions) and graded

semiquantitatively according to Grüniger (1996) and Ludwig et al. (2001). Vascular changes of the arteries were compared using the vascular degeneration index (VDI) as described by Ludwig et al. (2001).

Fig 1 A. Normal ovarian artery with normal intima (I), a continuous membrana elastica interna (MEI), circularly arranged myocytes in the media (M) and numerous densely packed layers of collagenous fibres (red stained) in the adventitia (A) in a 1-year-old juvenile mare. B. Mildly hyperplastic and vacuolized intima and moderate intima and mild media fibrosis in the ovarian artery of a 5-year-old, nulliparous mare. C. Severe fibrosis of the intima and media, the membrana elastica interna is completely destroyed in the ovarian artery of a 19-year-old, nulliparous mare. D. Severe deposits of elastic fibres (violet stained) in the intima, severe destructive mediafibrosis in the ovarian artery of a 22-year-old, multiparous mare. (Picro-Sirius Red stain, magnification 62.5x)



A. Unveränderte Ovararterie mit normaler Intima (I), kontinuierlicher Membrana elastica interna (MEI), zirkulär angeordneten Myozyten in der Media (M) und mehreren kompakten Lagen kollagener Fasern (rot angefärbt) in der Adventitia bei einer einjährigen nulliparen Stute. B. Geringgradige Vakuolisierung und Hyperplasie der Intima, mittelgradige Intima- und geringgradige Mediafibrose in der Ovararterie einer fünfjährigen nulliparen Stute. C. Hochgradige destruiierende Fibrose der Intima und Media, mit vollständiger Destruktion der Membrana elastica interna in der Ovararterie einer 19-jährigen nulliparen Stute. D. Hochgradige Zubildung elastischer Fasern (violett angefärbt) in der Intima und hochgradige destruiierende Mediafibrose in der Ovararterie einer 22-jährigen multiparen Stute. (Pikro-Sirius Rot-Färbung, Gerätevergrößerung 62,5x)

Group	Identification	Number (n = 60)	Age	Average age	Stage of reproduction		
					nulliparous	primiparous	multiparous
1	juvenile, prepubertal	n = 9	1d – 365 d	123.6 d	n = 9	-	-
2 a-f*	adult, cyclic	n = 41	2 a – 24 a	9.4 a	n = 13	n = 16	n = 12
3 a-d*	adult, pregnant	n = 7	7 a – 15 a	9.8 a	n = 0	n = 5	n = 2
4 a-b*	adult, post partum	n = 3	10 a – 15 a	13.3 a	n = 0	n = 1	n = 2

Tab 1 Age, parity and number of mares investigated. legend: a = year; d = day; * s. legend of tab. 2-4

Alter, Parität und Anzahl der untersuchten Stuten

Results

In this study exclusively the stromal vessels of the ovary are investigated. The alterations appear to be independent of the neighbourhood of present follicles or corpora lutea. Variations associated to the actual stage of the ovarian cycle have not been observed.

The findings in extrauterine and extraovarian vessels are summarized since the quality of angiosis is similar. However, the lesions were visible in a slightly higher degree in the extraovarian vessels.

Group 1 (juvenile mares, n=9)

In juvenile mares the arteriolae were composed of endothelium, a very thin stratum subendotheliale and some layers of media-myocytes. A distinct membrana elastica interna (MEI) is missing.

In small ovarian arteries the intima consisted of a stratum subendotheliale containing few collagenous fibres, mesenchymal spindle cells and a regular continuous membrana elastica interna (MEI). The media was formed by two or three layers of circularly arranged myocytes and single collagenous fibres. The adventitia consisted of a few layers of collagenous fibres.

In medium-sized and large ovarian arteries the intima was similar to those in small ovarian arteries. The MEI was regular and continuous. The media was formed by numerous myocytes and some collagenous fibres. The adventitia consisted

of conspicuously densely packed layers of collagenous fibres (Fig. 1A)

In the ovarian veins - as normal - the stratum subendotheliale could not be distinguished from the media and a MEI was missing. Media and adventitia were composed of fine collagenous and some elastic fibres with some myocytes lying between them.

The findings in the small ovarian arteries, arteriolae and veins were defined as being „normal“ (Tab. 2). These extrauterine/extraovarian and uterine vessels showed a normal structure (Tab. 3).

Group 2 (adult and cyclic mares; n=41)

The small, medium, and large-sized ovarian arteries of young nulliparous (n=11) and primiparous (n=7) mares (two to nine years old) showed mild intimal hyperplasia, mild accumulations of mucopolysaccharides, and a few deposits of collagenous fibres in the intima (intimafibrosis) (Fig. 1B). A distinct fragmentation and irregularity of the MEI often appeared. In some large arteries a mild deposition of collagenous fibres in the media (mediafibrosis, n=9) and of the whole wall of small arteries (panfibrosis, n=6) was discovered. The collagenous fibres of the adventitia were loosely arranged. In five mares the ovarian arteriolae showed some elastic fibres spread through the vessels wall (mild panelastosis). Mild to moderate perielastosis (deposition of elastic fibres in the adventitia) in ovarian veins was found in six mares. In contrast to the ovarian vessels (Tab. 2), differences between young

Tab 2 Histopathological findings in ovarian vessels in juvenile and adult mares

periE: perielastosis
panE: panelastosis
panF: panfibrosis
IEF: intimaelastofibrosis
MF: mediafibrosis
IF: intimafibrosis

+: mild
++: moderate
+++: severe
destr.: destructive

Histopathologische Befunde an den ovariellen Blutgefäßen bei juvenilen und adulten Stuten

group		ovarian vessels			
		large and medium-sized arteries	small arteries	arteriolae	veins
juvenile mares	n = 9	densely packed collagenous fibres in the adventitia	normal	normal	normal
young nulliparous mares	n=11	+ IF (n=11) and + MF (n=5)	+ IF (n=9) + panF (n=2)	normal (n=8) + panE (n=3)	normal (n=7) + periE (n=4)
young primiparous mares	n=7	+ IF (n=7) + MF (n=4)	+ IF (n=3) and + panF (n=4)	normal (n=5) ++ panE (n=2)	normal (n=5) + periE (n=2)
old nulliparous mares	n=2	++ IF (n=2) ++ MF (n=2)	++ panF (n=2)	+ panE (n=2)	+ / + + periE (n=2)
old primiparous mares	n=9	+ / + + IF (n=9) and ++ MF (n=7)	++ panF (n=9)	++ panE (n=5) normal (n=4)	+ / + + periE (n=8) normal (n=1)
young multiparous mares	n=5	+ / + + + destr. IEF and + / + + MF (n=5)	+ / + + + destr. panF (n=5)	++ panE (n=5)	+ / + + periE (n=5)
old multiparous mares	n=7	+ / + + + destr. IEF (n=7) + + MF (n=7)	+ / + + + destr. panF (n=7)	+ / + + + panE (n=6) normal (n=1)	+ / + + periE (n=6) normal (n=1)
pregnant mares 9 th -10 th month of pregnancy	n=3	+ / + + IEF (n=3) and + + elastolysis/collagenolysis (n=2)	+ / + + IEF (n=3) and + + elastolysis/collagenolysis (n=2)	normal (n=2) + / + + + PanE	+ / + + periE (n=2) normal (n=1)
mares 1-11 days post partum	n=2	+ / + + IEF (n=2) + + elastolysis/collagenolysis (n=2)	+ / + + IEF (n=2) + + elastolysis/collagenolysis (n=2)	++ panE (n=1) normal (n=1)	+ periE (n=2)
multiparous mare 28 days post partum	n=1	+ / + + IF + + MF	+ / + + IF + MF	normal	+ periE

nulliparous and primiparous mares was detected in the extra-ovarian/extrauterine and uterine vessels: In primiparous mares mild alterations (e.g. panfibroelastosis or panelastosis) appeared in numerous vessels, whereas they were normal in nulliparous mares (Tab. 3). In old nulliparous (n=2) and primiparous (n=9) mares aged between 15 and 24 years of age, the large and medium-sized ovarian arteries were characterized by a moderate intima- and mediafibrosis (Fig. 1C), whereas the small arteries showed a moderate panfibrosis. Arteriolae in the ovary of old nulliparous mares revealed a mild panelastosis and in five old primiparae a moderate panelastosis was seen. The ovarian veins developed a mild to moderate perielastosis (Tab. 2). Lesions of the extraovarian/extrauterine and uterine vessels showed similar characteristics but were more accentuated than that of young primiparous mares (Tab. 3).

In multiparous mares (n=12), aged 7 to 24 years, vascular alterations in the ovary were characterized by an intimaelastosis increasing with the number of foalings and an intima- and mediafibrosis advancing with the mare's age (Tab. 2). An outstanding fact is that not all vessels in one ovary were altered in the same degree: Mildly affected vessels were found beside severely altered ones. Depending on the age and parity, two different patterns of degenerative lesions in medium-sized and large ovarian arteries can be subdivided (Tab. 2).

In young to middle-aged mares (7 - 15 years) with few foalings intense intimal alterations of the ovarian arteries occurred. They were characterized by mild to moderate intimal hyperplasia and vacuolization as well as moderate to severe amounts of elastic and numerous collagenous fibres in the intima and a slight mediafibrosis. Duplication, fragmentation and destruction of the membrana elastica interna were found, whereas the adventitia is not affected.

In older (17-24 years old) mares with numerous foalings the

ovarian arteries typically showed intense intimal alterations as described in the younger mares. Whereas in addition, a destructive mediafibrosis and in advanced stages a severe destructive panfibrosis occurred (Fig. 1D). The arteriolae frequently showed a moderate to severe panelastosis, increasing with age and parity. The ovarian veins were mostly affected by a mild to moderate perielastosis (Tab. 2). The findings in the extraovarian/extrauterine and uterine vessels are summarized in Table 3.

In seven of the multiparous mares (n=13) the vessels of both ovaries were affected with similar intensity. But in some mares the vascular lesions seemed to be more accentuated in the right (n=4) or the left (n=2) ovary.

Further histopathological findings, which occurred sporadically in the ovarian vessels (small and medium-sized arteries) were eosinophilic degeneration of the vascular wall (n=8), subendothelial asteroid mineralization (n=6), and mild lymphocytic (peri)-vasculitis (n=1). In these vessels there was no obvious correlation to the degree of the elastosis/fibrosis or the parity.

Group 3 (pregnant mares, n=7)

In two 7 and 10 years old mares (1st and 2nd month of pregnancy) the ovarian arteries exhibited a mild intimal hyperplasia and fibrosis as well as little subendothelial deposits of acid mucopolysaccharides. The ovarian veins and arteriolae appear to be normal.

In one 5 year old mare (3rd month of pregnancy), the ovarian arteries showed a fragmented and discontinuous MEI. In single vessels a mildly edematous adventitia could be observed. The ovarian veins and arteriolae also appeared to be normal.

The histological findings of ovarian arteries of a 12 year old multiparous mare (3rd month of pregnancy) were similar to

Tab 3 Histopathological findings in the extraovarian/extrauterine, myometrial and endometrial vessels in juvenile and adult non pregnant mares. *Histopathologische Befunde der extraovariellen/extrauterinen, myometrialen und endometrialen Blutgefäße bei juvenilen und adulten nicht graviden Stuten*

Group 1: juvenile mares, group 2a: young adult nulliparous mares, group 2b: young adult primiparous mares, group 2c: old adult nulliparous mares, group 2d: old adult primiparous mares, group 2e: young adult multiparous mares, group 2f: old adult multiparous mares

group		extraovarian / extrauterine vessels		myometrial vessels		endometrial vessels	
		arterial	venous	arterial	venous	arterial	venous
1	n=9	normal	normal	normal	normal	normal	normal
2a	n=11	normal	normal	normal	normal	normal	normal
2b	n=7	+ / + + panFE (n=7)	normal (n=6) n.i. (n=1)	+ IFE (n=3), + periE (n=4)	+ / + + panFE (n=7)	normal (n=6) + panE (n=1)	normal (n=4) + panE (n=3),
2c	n=2	+ MF (n=2)	n.i. (n=2)	normal (n=2)	+ panE (n=1) normal (n=1)	+ panE (n=1) normal (n=1)	normal (n=2)
2d	n=9	+ / + + panF (n=9)	+ panF (n=8) n.i. (n=1)	+ / + + panFE (n=6) normal (n=3)	+ / + + panE (n=6) normal (n=3)	normal (n=6) + panE (n=3)	normal (n=6) + panFE (n=3)
2e	n=5	+ panFE (n=5)	+ panFE (n=1) n.i. (n=4)	+ / + + panFE (n=4) n.i. (n=1)	+ / + + panFE (n=5)	+ / + + panE (n=5)	+ / + + panFE (n=4) normal (n=1)
2f	n=7	+ + / + + + destr. panFE (n=7)	+ panE (n=3) + + destr. panF (n=4)	+ + / + + + panE (n=7)	+ + / + + + panE (n=6) n.i. (n=1)	+ + + panE (n=7)	+ + + panE (n=6) n.i. (n=1)

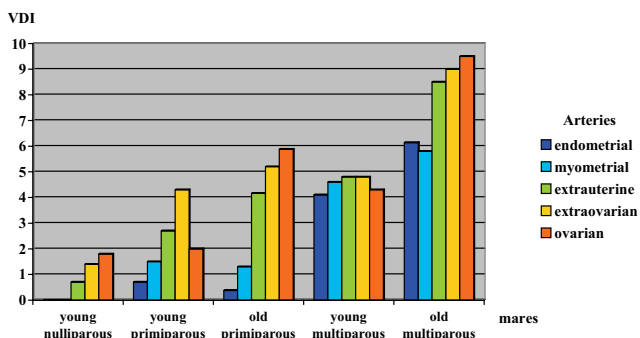
+ : mild
+ + : moderate
+ + + : severe
destr.: destructive
n.i.: not investigated

panFE: panfibroelastosis
panF: panfibrosis
MF: mediafibrosis
panE: panelastosis
IFE: intima-fibroelastosis
periE: perielastosis

those described above. But moderate deposits of intimal mucopolysaccharides were seen. The ovarian veins and arteriolae were normal. The findings in the extraovarian/extrauterine and uterine vessels (Tab. 4) were mostly in accordance with those recognized in non pregnant multiparous mares.

In three 8, 12, and 15 years old mares (9th month (n=1) and 10th month (n=2) of pregnancy) the ovarian arteries showed

Fig 2 Comparison of the vascular degeneration index (VDI) of endometrial, myometrial, extrauterine, extraovarian and ovarian arteries in mares of different age and parity



Vergleich des Gefäßschädigungsindex (VDI) von endometrialen, myometrialen, extrauterinen, extraovariellen und ovariellen Arterien bei Stuten unterschiedlichen Alters und verschiedener Parität

a moderate intimal elastofibrosis, vacuolization and moderate deposits of acid mucopolysaccharides as well as a discontinuous MEI. The media was characterized by the loss and dearrangement of elastic and collagenous fibres (elastolysis/collagenolysis). The adventitia showed a mild to moderate edema. The arteriolae appeared to be normal in two cases and showed a moderate panelastosis in the 15 year old mare. The ovarian veins revealed a mild to moderate perielastosis.

Group 4 (1– 28 days post partum, n=3):

One to eleven days post partum the findings in the ovarian vessels of one 10 year old mare with few previous foalings and one 15 years old multiparous mare corresponded to the

alterations observed in the 9th /10th month of pregnancy. These findings were not detectable any more 28 days-post partum in a multiparous 15 year old mare (Tab. 2). The ovarian arteries showed a mild intimafibrosis and a moderate mediafibrosis. An intimaelastosis was not yet rebuilt. The findings in the extraovarian/extrauterine and uterine vessels are summarized in Table 4.

Short comparison of the findings in ovarian, extraovarian, extrauterine, myometrial and endometrial arteries in adult non-pregnant mares.

The most striking finding in this study was the intense ovarian angiosis, which increases in relation to the age of the animal. Additionally, numerous foalings lead to further and extended alterations of the ovarian arteries (Fig. 2).

Extrauterine and extraovarian arteries showed a similar quality of angiosis. However, extrauterine arteries were usually less affected than extraovarian vessels. The degree of alterations corresponded to age and parity.

Myometrial arteries showed similar or more intense lesions than endometrial vessels do, but they were less affected than the extrauterine/extraovarian vessels. The endometrial and myometrial arterial alterations were predominantly related to the number of foalings, and to a lesser extent to the age (Fig. 2). Whereas ovarian, extrauterine and extraovarian vessels were mainly affected by fibrosis, the uterine vessels mainly developed elastosis.

Discussion

Alterations of the equine ovarian vessels have not been described histopathologically in detail until now. In the present study, the stromal ovarian vessels show different signs of angioses depending on the age and parity of the mares. While juvenile mares show normal vessels, in young adult nulliparous mares a moderate intimafibrosis develops and in older nulliparous mares a moderate fibrosis spreads through the media of the arteries.

Tab 4 Histopathological findings in the extraovarian/extrauterine, myometrial and endometrial vessels in pregnant and post partum mares
Histopathologische Befunde der extraovariellen/extrauterinen, myometrialen und endometrialen Blutgefäße bei graviden und postpartalen Stuten

Group 3a: primiparous mares 1st – 3rd month of pregnancy, group 3b: multiparous mare 3rd month of pregnancy, group 3c: primiparous mares 9th and 10th month of pregnancy, group 4a: primiparous and multiparous mares 1-11 days post partum group 4b: multiparous mare 28 days post partum

group	n	extraovarian / extrauterine vessels		myometrial vessels		endometrial vessels	
		arterial	venous	arterial	venous	arterial	venous
3a	n=3	normal	normal	normal	normal	normal	normal
3b	n=1	+ / ++ panF	+ panF	+ panF	+ / ++ panEF	+ panE	+ panE
3c	n=3	+ IFE and ++ elastolysis / collagenolysis (n=2) n.i. (n=1)	+ panF (n=1) n.i. (n=2)	normal (n=2) + periE (n=1)	+ panEF (n=2), normal (n=1)	normal (n=3)	normal (n=3)
4a	n=2	+ IFE, ++ elastolysis / collagenolysis (n=1), n.i. (n=1)	n.i. (n=2)	+ periE (n=1) normal (n=1)	+ periE ++ elastolysis (n=2)	+ periE (n=1), normal (n=1)	+ periE (n=1), normal (n=1)
4b	n=1	+ panEF	n.i.	+ panEF	+ panE	+ periE	+ panE

+: mild
++: moderate
+++: severe
destr.: destructive
n.i.: not investigated

panEF: panelastofibrosis
panF: panfibrosis
panE: panelastosis
periE: perielastosis
IFE: intimafibroelastosis

By the use of Doppler sonography, distinct variations of the ovarian bloodflow during the estrus cycle of the mare have been reported (Bollwein et al. 2000, Wein 2003). This variability and the permanent remodelling of the ovarian structures due to the building and regression of follicles and corpora lutea may be associated with an intense paracrine and enzymatic activity, which also affects the ovarian stromal vessels. During pregnancy and puerperium alterations and remodelling of the uterine (Schoon et al. 1999, Wrede 1999) and extrauterine (Ludwig et al. 2001) vessels were observed. It is suggested, that functional and endocrine demands are responsible for these processes leading to a persisting „pregnancy-sclerosis“ (Grüninger et al. 1998, Wrede 1999). Similar effects can be observed in the ovarian vessels: young multiparous mares show a moderate intimaelastosis and mediafibrosis, whereas older multiparous mares develop moderate to severe destructive intimaelastosis and mediafibrosis in the ovarian arteries. As described for endometrial vessels during pregnancy (Grüninger et al. 1998, Ludwig et al. 2001), the ovarian veins and arterioles are altered by an increasing elastosis, as well. Woschee (1999) reported that the vascular resistance of the A. ovarica declines during pregnancy and increases during puerperium.

This study indicates that the ovarian arteriosclerosis is predominantly caused by age-related remodelling processes. Additionally, lesions caused by pregnancy correspond to those of the endometrial vessels, which are functionally confirmed by the findings of Doppler-sonography (Wein 2003).

It has been reported that endometrial angiosis is one factor leading to sub- or infertility in the mare (Schoon et al. 1997, 1999). The results of the present study indicate that angioses of the genital system do not exclusively affect the uterus, but the ovaries also. Angiosis in the ovarian vessels might possibly cause a disturbed follicular and luteal angiogenesis and perfusion resulting in endocrine disturbances as assumed in humans (Glock and Brumsted 1995, Klogirou et al. 1997). The endometrial biopsy is a potential tool for the diagnosis of uterine and extrauterine angioses (Ludwig et al. 2001). Evidently this study concludes that additional information can be concluded from a biopsy regarding histopathological alterations of extraovarian and ovarian vessels. These findings are in accordance to the results of Doppler-sonography (Wein et al. 2002).

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