An immunohistochemical analysis of fibroid vasculature

R. Casey, P.A.W. Rogers and B.J. Vollenhoven

Department of Obstetrics & Gynaecology, Monash University, Melbourne, Victoria 3168, Australia

1To whom correspondence should be addressed at: Department of Obstetrics & Gynaecology, Monash University, Melbourne, Victoria 3168, Australia.

E-mail: beverley.vollenhoven@med.monash.edu.au

This study aimed to compare vascular parameters between fibroid and myometrium. From 10 uteri, specimens were taken from small fibroids (<0.5 cm), from the inner and outer parts of large fibroids (>3 cm), and from myometrium. Antibodies to endothelial cell markers CD31, CD34, factor VIII-related antigen (FVIII), and Ulex europaeus lectin were used in routine immuno- and lectin chemistry protocols. Parameters calculated were vascular area (VA), microvascular density (MD) and vascular luminal diameter. VA measures showed that myometrium had a greater area stained than small fibroids (P = 0.03) using CD31 and both inner (P = 0.04) and outer (P = 0.01) regions of large fibroids using FVIII, and than all groups (small, P = 0.02; inner, P = 0.02; outer, P = 0.006) using the lectin U. europaeus. MD was higher in myometrium than all uterine fibroid groups, small, P = 0.009; inner, P = 0.01; outer, P = 0.01) using U. europaeus lectin, than both regions of large (inner, P = 0.04; outer, P = 0.02) fibroids using FVIII, and than outer regions of large fibroids using CD31 (P < 0.05). There were significantly larger diameter vessels in myometrium and large fibroids compared with small fibroids using CD34, FVIII and the lectin U. europaeus (P ≤ 0.04). These differences in vasculature may represent differences in angiogenesis and vascular remodelling.

Key words: fibroids/immunohistochemistry/leiomyoma/myometrium/vasculature

Introduction

Uterine fibroids or leiomyomata are the most common solid tumours in women, affecting at least 50% over 30 years of age (Wallach, 1992). Traditionally, fibroids have been treated surgically. Therefore, as a public health issue, these tumours represent a major problem with 21.7% of all hysterectomies performed in Australia being due to fibroids. The prevalence of hysterectomy in Australia is 3.97 per 1000 women, making hysterectomy one of the most common surgical procedures performed (Renwick and Sadhowsky, 1991).

For a tumour that is so common and so costly, very little is known of the aetiology of uterine leiomyomas. It is known that there are a number of risk and protective factors for and against fibroid growth related to oestrogen (reviewed by Vollenhoven, 1998) and that there are increased numbers of sex steroid receptors in fibroids compared with myometrium (Tamaya et al., 1985; Wilson et al., 1987; Vollenhoven et al., 1994; reviewed by Anderson, 1998). Other factors that may be associated with fibroid aetiology include peptide growth factors such as the insulin-like growth factor (IGF) family and epidermal growth factor (EGF) as well as possible chromosomal and subsequent gene changes within these tumours (Vollenhoven et al., 1993, 1995, reviewed by Anderson, 1998).

The vasculature of fibroids has not been studied in detail or in a quantitative manner. To date, research has focused on describing structural arrangements within these tumours as well as blood flow studies. Earlier structural studies (Sampson, 1912; Farrer-Brown et al., 1970a,b) using similar methods of pigment or radio-opaque dye injection demonstrated that the arterial vessels of uterine leiomyoma were typically increased in size, especially in larger tumours, whereas the degree of arterial vascularity was variable. It was also observed that small uterine leiomyomas were usually, but not always, less vascular than the surrounding myometrium, while larger leiomyomas were usually more vascular than the myometrium. Farrer-Brown et al. (1970b) also demonstrated that there was no intrinsic vascular pattern in uterine fibroids but rather the arrangement appeared to represent a localized expansion of the myometrial vasculature with the vessels within these tumours orientated in the direction of the muscle cell bundles. They also showed there were changes in vasculature distant to the tumour, with dilation and congestion of vessels contralateral to the site of the uterine leiomyoma.

Blood flow studies have been performed in leiomyomas. The vasculature of uterine leiomyoma was investigated using colour Doppler ultrasound (Kurjak et al., 1992). Their results concurred with the earlier work of Sampson (1912) showing that the vascularity of these tumours was largely dependent on the tumour size, position and the extent of secondary degenerative changes. Other studies by (Forssman, 1976a,b) employing local and intra-arterial injection of 133Xe demonstrated statistically significantly lower blood flow in uterine fibroids compared to surrounding myometrium. This author cited the lowered blood flow as a possible contributing factor to degenerative changes frequently seen within these tumours. However, more recent studies using transvaginal Doppler ultrasound have produced differing results to those of Forssman (1976a,b). These studies reported a lower resistance index (RI) and pulsatility index (PI) in uterine and fibroid arteries in patients with these tumours compared to the uterine arteries.
in women without fibroids (Kurjak et al., 1992; Alatas et al., 1997). Huang et al., performing similar studies, demonstrated a statistically significant negative correlation between uterine leiomyoma size and PI values and leiomyoma volume and PI values (Huang et al., 1996). This correlation between blood flow and uterine leiomyoma size reported by Huang et al. (1996) is also supported by others (Sosic et al., 1996; Alatas et al., 1997). It has also been recognized that differing regions exist within these tumours in terms of blood flow and tissue perfusion (Forssman 1976a; Kurjak et al., 1992). It is perhaps this difference that may explain the variability in reported results.

Therefore, the aim of this study was to examine the vascular arrangements of uterine leiomyomata compared with myometrium using immunohistochemical techniques. In particular, we aimed to quantitatively examine the vasculature of uterine leiomyomata and myometrium with respect to structure and vascular density. Knowledge of vascular differences may provide information on basic biology, aid understanding of the variability of symptoms reported by women with fibroids, better define the mode of action of some of the current medical managements [gonadotrophin releasing hormone agonists (GnRHa) and RU 486] and lastly provide knowledge of the future utility of angiogenesis inhibitors for treatment.

Materials and methods

Patients

A total of 10 women having hysterectomies for symptomatic multiple fibroids was recruited. All were pre-menopausal, menstruating regularly, had not been on any hormonal medication for at least 1 month prior to surgery and the only gynaecological pathology was their fibroids. All women were Caucasian. After specimens were obtained, the uterus was examined histologically and the endometrium density selected. Previous studies have shown that this method reliably obtained, the uterus was examined histologically and the endometrium density selected. Previous studies have shown that this method reliably

Microvascular density quantification

Computer images were used to perform manual counts of stained microvessels with each vessel marked after being counted to prevent duplicate counting of vessels. Vessel counts per field were converted to vessels per mm².

Vascular luminal diameter quantification

Computer images were used to perform manual measurements of the maximum luminal diameter of stained microvessels for which a vessel
Immunohistochemistry of fibroid vasculature

Figure 1. Photomicrographs of human myometrium and fibroid stained with different vascular markers. (a) Myometrium histochemically stained with Ulex europaeus lectin. Scale bar = 50 µm. (b) Large fibroid stained with U. europaeus lectin. Scale bar = 50 µm. (c) Myometrium immunostained with CD31. Scale bar = 50 µm. (d) Large fibroid immunostained with CD34. Scale bar = 50 µm. (e) Myometrium stained with U. europaeus lectin. Scale bar = 25 µm. (f) Myometrium immunostained with CD34. Note high level of non-endothelial background immunostaining. Scale bar = 25 µm. (g) Small fibroid (F) with adjacent myometrium (M) stained for FVIII. Note reduced vascular density in fibroid compared to myometrium. Scale bar = 100 µm.

lumen was clearly present. Each vessel was marked after luminal diameter measurement to prevent duplicate measurement of vessels.

Statistical analysis
Data are presented as mean ± SD. Statistical analysis was undertaken using the non-parametric Mann–Whitney test. All data collected were collated and statistics performed using Minitab Release 10.2 with the criterion of statistical significance being $P < 0.05$.

Results
Vascular area quantification
Examples of immunostaining with each vascular marker are shown in Figure 1. All negative controls were completely blank with no immunostaining. For this reason images of the negative controls have not been included in Figure 1.

Comparison of proportional areas stained between regions using CD31 showed that myometrium had a significantly greater area stained for blood vessels than small fibroids ($P = 0.03$). Data for CD34 were limited by problems with elevated background staining of myometrial sections (see Materials and methods). There were no significant differences between the other regions studied. Comparison of proportional area stained between regions using FVIII revealed that myometrium had a significantly greater area stained for blood vessels than both inner ($P = 0.04$) and outer regions of large fibroids ($P = 0.01$). Comparison of proportional area stained
between groups using *U. europaeus* lectin revealed that myometrium had a significantly greater area stained for blood vessels than small fibroids (*P* = 0.02) and more than both inner (*P* = 0.02) and outer regions of large fibroids (*P* = 0.006) (Table I).

Comparing proportional area stained between vascular markers within each individual tissue revealed significantly reduced staining for CD31 in myometrium compared with staining for FVIII (*P* = 0.04) and *U. europaeus* lectin (*P* = 0.02). There was also reduced staining for CD31 in small fibroids compared with staining for CD34 (*P* = 0.01) and FVIII (*P* = 0.03). There were no other differences seen.

**Microvascular density quantification**

Comparison of average microvascular density using CD31 between groups revealed that there were significantly more blood vessels in myometrium than outer regions of large fibroids (*P* = 0.05). There was also a trend for more blood vessels in myometrium than in small fibroids but this did not reach statistical significance. With no data from myometrial sections, comparison of average microvascular density for CD34 between the remaining groups revealed no significant differences. Comparison of average microvascular density for FVIII between groups revealed that there were significantly more blood vessels in myometrium than both outer (*P* = 0.02) and inner regions of large fibroids (*P* = 0.04). Comparison of average microvascular density for *U. europaeus* lectin between groups revealed that there were significantly more vessels in myometrium than small fibroids (*P* = 0.009) and more than in both outer (*P* = 0.01) and inner (*P* = 0.01) regions of large fibroids (Table II).

Comparing microvascular density between vascular markers within each individual tissue revealed no significant differences, but there was a trend for reduced numbers of blood vessels in small fibroids stained for CD34 compared with staining for CD34.

**Vascular luminal diameter quantification**

Comparison of average vascular luminal diameter for CD31 between groups revealed no significant differences. With no data from myometrial sections, comparison of average microvascular density for CD34 for inner regions of large fibroids revealed larger vessels in this tissue compared to small fibroids (*P* = 0.004). Comparison of average vascular luminal diameter for FVIII between groups revealed larger blood vessels in myometrium than small fibroids (*P* = 0.004) and smaller vessels in small fibroids compared with both inner (*P* = 0.005) and outer regions of large fibroids (*P* = 0.02). Comparison of average vascular luminal diameter for *U. europaeus* between groups revealed larger blood vessels in myometrium than small fibroids (*P* = 0.04) and smaller vessels in small fibroids compared with inner (*P* = 0.02) regions of large fibroids. There was a trend for smaller blood vessels in small fibroids compared with outer regions of large fibroids but this did not reach statistical significance (Table III).

Comparing vascular luminal diameter between vascular markers within each individual tissue revealed smaller luminal diameter in inner regions of large fibroids stained for CD34 compared with FVIII (*P* = 0.03) and *U. europaeus* lectin (*P* = 0.04). There was greater luminal diameter staining in outer regions of large fibroids for CD31 compared with CD34 (*P* = 0.04). For small fibroids there were greater

---

**Table I. Proportional vascular area quantification for all markers (mean ± SD)**

<table>
<thead>
<tr>
<th></th>
<th>Myometrium (n = 10)</th>
<th>Inner large fibroid (n = 9)</th>
<th>Outer large fibroid (n = 9)</th>
<th>Small fibroid (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD31</td>
<td>1.9 ± 1.1</td>
<td>1.2 ± 0.8</td>
<td>1.2 ± 1.3</td>
<td>0.5 ± 0.3</td>
</tr>
<tr>
<td>CD34</td>
<td>ND</td>
<td>1.8 ± 1.2</td>
<td>1.9 ± 1.1</td>
<td>1.5 ± 0.3</td>
</tr>
<tr>
<td>FVIII</td>
<td>3.6 ± 1.8</td>
<td>1.9 ± 1.0&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.5 ± 1.2&lt;sup&gt;c&lt;/sup&gt;</td>
<td>2.0 ± 1.0</td>
</tr>
<tr>
<td>Ulex</td>
<td>4.1 ± 2.1</td>
<td>1.9 ± 1.2&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.6 ± 1.0&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1.4 ± 1.2&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>*P* = 0.03 myometrium compared with small fibroids.  
<sup>b</sup>*P* = 0.04 myometrium compared with inner regions of large fibroids.  
<sup>c</sup>*P* = 0.01 myometrium compared with outer regions of large fibroids.  
<sup>d</sup>*P* = 0.02 myometrium compared with inner regions of large fibroids.  
<sup>e</sup>*P* = 0.006 myometrium compared with outer region of large fibroids.  
<sup>f</sup>*P* = 0.02 myometrium compared with small fibroids.  
ND = no data included in study (see Materials and methods); FVIII = factor VIII-related antigen; Ulex = *Ulex europaeus* lectin.

**Table II. Microvascular density quantification (vessels/mm²) for all markers (mean ± SD)**

<table>
<thead>
<tr>
<th></th>
<th>Myometrium (n = 10)</th>
<th>Inner large fibroid (n = 9)</th>
<th>Outer large fibroid (n = 9)</th>
<th>Small fibroid (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD31</td>
<td>317.5 ± 137.7</td>
<td>261.3 ± 138</td>
<td>212.1 ± 89.7&lt;sup&gt;g&lt;/sup&gt;</td>
<td>191.3 ± 86.2</td>
</tr>
<tr>
<td>CD34</td>
<td>ND</td>
<td>301.5 ± 132.3</td>
<td>265 ± 111.1</td>
<td>294.2 ± 63.7</td>
</tr>
<tr>
<td>FVIII</td>
<td>395.6 ± 157.7</td>
<td>255.6 ± 97.6&lt;sup&gt;h&lt;/sup&gt;</td>
<td>210.4 ± 91.7&lt;sup&gt;i&lt;/sup&gt;</td>
<td>252.9 ± 84.1</td>
</tr>
<tr>
<td>Ulex</td>
<td>394.6 ± 135.5</td>
<td>245.4 ± 78.7&lt;sup&gt;j&lt;/sup&gt;</td>
<td>232.5 ± 142.1&lt;sup&gt;k&lt;/sup&gt;</td>
<td>197.1 ± 84.5</td>
</tr>
</tbody>
</table>

<sup>a</sup>*P* < 0.05 myometrium compared with outer regions of large fibroids.  
<sup>b</sup>*P* = 0.04 myometrium compared with inner regions of large fibroids.  
<sup>c</sup>*P* = 0.02 myometrium compared with outer regions of large fibroids.  
<sup>d</sup>*P* = 0.01 myometrium compared with inner regions of large fibroids.  
<sup>e</sup>*P* = 0.01 myometrium compared with outer region of large fibroids.  
<sup>f</sup>*P* = 0.009 myometrium compared with small fibroids.  
ND = no data included in study (see Materials and methods); FVIII = factor VIII-related antigen; Ulex = *Ulex europaeus* lectin.

**Table III. Vascular luminal diameter quantification (µm) for all markers (mean ± SD)**

<table>
<thead>
<tr>
<th></th>
<th>Myometrium (n = 10)</th>
<th>Inner large fibroid (n = 9)</th>
<th>Outer large fibroid (n = 9)</th>
<th>Small fibroid (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD31</td>
<td>29.8 ± 11.9</td>
<td>42.3 ± 44.1</td>
<td>28.8 ± 8.5</td>
<td>26.4 ± 9.7</td>
</tr>
<tr>
<td>CD34</td>
<td>ND</td>
<td>19.0 ± 4.9</td>
<td>20.2 ± 7.0</td>
<td>13.2 ± 2.3&lt;sup&gt;i&lt;/sup&gt;</td>
</tr>
<tr>
<td>FVIII</td>
<td>21.8 ± 5.0</td>
<td>27.1 ± 10.3</td>
<td>26.3 ± 9.9</td>
<td>12.7 ± 3.1&lt;sup&gt;l&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ulex</td>
<td>22.5 ± 4.7</td>
<td>28.5 ± 13.0</td>
<td>24.5 ± 7.2</td>
<td>16.4 ± 5.7&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>*P* = 0.04 inner regions of large fibroids compared with small fibroids.  
<sup>b</sup>*P* = 0.004 myometrium compared with small fibroids.  
<sup>c</sup>*P* = 0.005 inner regions of large fibroids compared with small fibroids.  
<sup>d</sup>*P* = 0.02 outer regions of large fibroids compared with small fibroids.  
<sup>e</sup>*P* = 0.04 myometrium compared with small fibroids.  
<sup>f</sup>*P* = 0.02 inner regions of large fibroids compared with small fibroids.  
ND = no data included in study (see Materials and methods); FVIII = factor VIII-related antigen; Ulex = *Ulex europaeus* lectin.
diameter vessels stained for CD31 compared with FVIII \((P = 0.04)\) and a similar trend for CD34 and \(U. \text{ europaeus}\) which did not reach statistical significance.

**Discussion**

Our studies measuring proportional area stained as an indicator of vascular density have shown that myometrium has a significantly greater microvascular density than small fibroids using CD31 and both inner and outer regions of large fibroids using FVIII, and than small fibroids and both regions of large fibroids using the lectin \(U. \text{ europaeus}\).

Microvascular density, measured by discrete microvessel count, was significantly higher in myometrium than all uterine fibroid groups using \(U. \text{ europaeus}\) lectin, and than both regions of large fibroids using FVIII, and than outer regions of large fibroids using CD31.

Our quantitative microvascular density data agree in part with the qualitative results of Sampson (1912) who reported that small uterine fibroids are usually less vascular than the surrounding myometrium. However, Sampson (1912) also reported that the vascularity of large fibroids was typically greater than that of myometrium, an observation supported by others (Kurjak et al., 1992) in assessing tumour vascularization using transvaginal colour Doppler ultrasound. In contrast to these studies, our quantitative data show that the vascular density of myometrium is in general greater than that of large uterine fibroids.

It is thought that the growth of a tumour is limited by its blood supply, with tumours dependent upon the ingrowth of capillary sprouts from surrounding tissues for growth beyond a diameter of a few millimetres (Alberts et al., 1994). The differences in vascular density between myometrium and uterine fibroids may represent a difference in angiogenesis and vascular remodelling in these vascular beds. These differences in angiogenesis may be the result of changes in the balance between angiogenic promoters and inhibitors. Such factors regulate the growth of blood vessels through a complex combination of signals. Angiogenic promoters, such as vascular endothelial growth factor (VEGF) and members of the fibroblast growth factor (FGF) family of proteins, are often up-regulated by stimuli such as hypoxia, tissue damage or new tissue growth (Stewart and Nowak, 1996). VEGF mRNA expression has been reported present in uterine leiomyoma and myometrium with no difference in expression between the tissues (Harrison-Woolrych et al., 1995). In addition, a cyclic variation in VEGF mRNA expression was found in myometrium, but not in fibroids (Harrison-Woolrych et al., 1995). Of particular interest is a report (Brown et al., 1997) which demonstrated the presence of VEGF receptors, Flt-1 and KDR, typically found only on vascular endothelial cells and on myometrial smooth muscle cells. They also demonstrated that the proliferative effect of VEGF on these cells is of the same magnitude as that on endothelial cells, although the role and regulation of this mitogen in myometrial biology is unclear.

Genetic aberrations in fibroids may lead to a greater tolerance for angiogenic stimuli or a reduced capability to produce or respond to angiogenic promoters as the fibroid increases in size. One such genetic aberration described in other tumour tissues is the disruption of expression of hypoxia inducible factor (HIF)-1\(\alpha\), the reduced expression of which prevents formation of large vessels and impairs vascular function, resulting in hypoxic microenvironments within the tumour mass (Carmeliet et al., 1998). Similarly, genetic aberrations leading to differences in tissue production or response to angiogenic inhibitors such as angiostatin (O’Reilly et al., 1994) may also account for differences between myometrium and fibroid microvascular density. Reduced microvascular density in fibroids as a result of differences in tissue production and response to angiogenic promoters and inhibitors may also account for the clinical picture of degeneration within some of these tumours.

An alternate hypothesis to explain the differences in microvascular density between myometrium and fibroids is that changes induced in the vasculature of the myometrium result in an increase in vascular density of this vascular bed relative to that of fibroids. While research by Farrer-Brown et al. described the vasculature of fibroids as a localized expansion of the host myometrium, they also observed that the presence of these tumours induced changes in the vasculature of the myometrium within the myomatous uterus (Farrer-Brown et al., 1970b). Increased microvascular density in myometrium may be the result of the action of angiogenic factors induced by small uterine fibroids. These tumours, small in size with minimal intrinsic blood supply, may release angiogenic promoters which lead to an increase in the vascular density of the surrounding myometrium. This increase in vascular density of the myometrium surrounding these fibroids may in turn give rise to capillary sprouts that vascularize the small fibroid, promoting its growth and enlargement. This increase in vascular density of myometrium may account for the symptoms of menorrhagia observed in women with fibroids and the problems with bleeding often present during myomectomy. Alternatively, fibroids may have reduced angiogenic response or increased angiogenesis inhibitors such that the myometrium responds by increasing peri-fibroid vascular growth and blood flow in an attempt to compensate. This may result in the peri-fibroid vascular plexus that can be a major source of bleeding at myomectomy.

It may also be that the vascular density in myometrium and fibroids is the same if calculated per smooth muscle cell, as a greater percentage of fibroid tissue is composed of extracellular matrix compared to myometrium. Also, the myometrium may be more vascular simply to meet its functional demands such as growth during pregnancy or contraction during menstruation.

We found a number of differences in vascular diameter between tissues. In general there were larger vessels in myometrium and large fibroids compared with small fibroids using CD34, FVIII and the \(U. \text{ europaeus}\) lectin. Farrer-Brown et al. (1970b) observed greater average vascular diameter in myometrium. They observed displacement and distortion of the surrounding arcuate and radial arteries and compression and distention of arcuate venous plexi of the myometrium. In addition to these direct compression effects of the uterine fibroids on the vasculature, dilation and congestion of the
vasculature of myometrium was observed distant to the site of the uterine fibroid.

Differences in immunostaining for each vascular marker may reflect the function of these markers and changes in the normal vascular physiology. CD31 glycoprotein, also known as platelet/endothelial cell adhesion molecule-1 (PECAM-1), is concentrated at the junctions between endothelial cells and is expressed on continuous endothelia in all tissues (Berman et al., 1996). Differences in the expression of this glycoprotein may represent a difference in either endothelial cell junctions or vascular permeability within blood vessels. CD31, in general, stains a smaller vascular area though this is only significantly different in small fibroids and in myometrium compared with the other markers. However, CD31 also stains vessels with a larger luminal diameter in outer regions of large fibroids and small fibroids compared with the other markers. Therefore, CD31 may be selectively staining larger vessels and not the smaller ones. It has been reported previously that CD31 and CD34 may stain different groups of microvessels, or selectively stain some endothelial cells and not others (Rosamilia et al., 1999).

CD34 is a surface glycoprotein of unknown function and is a haemopoietic stem cell marker also expressed on vascular endothelial cells (Krause et al., 1996). Results in inner regions of large fibroids showed a smaller luminal diameter compared with the other stains. This factor may not only be staining endothelial cells but also, for example, lymphoid cells involved in fibroid degeneration. CD34 may also be identifying other cell types or endothelial progenitors (Asahara et al., 1997). All myometrial slides stained for CD34 showed increased background staining, indicating that in myometrium CD34 is located on other cell types.

FVIII forms part of the von Willebrand factor complex, plays a part in the coagulation cascade and its expression is reduced in smaller, less mature blood vessels (Fay, 1993). The vascular staining for this factor was no different to the other markers. The U. europaeus lectin binds to carbohydrate but its role in vascular tissues is unknown. Likewise vascular staining for this factor was no different to the other markers.

One limitation of this study is the lack of comparison of measurements between myomatous myometrium and normal myometrium. Such comparisons between study groups would allow for expansion upon the work of Sampson (1912) and Farrer-Brown et al. (1970b) which described changes in the vasculature of myomatous myometrium compared to that of normal myometrium. In the present study this comparison was not possible due to the lack of availability of normal myometrium samples. Women who have hysterectomies do so for a reason, and we found it difficult to identify uteri that did not either have fibroids or adenomyosis. Indeed, it was reported (Cramer and Patel, 1990) that fibroids were present in over 70% of hysterectomy specimens, whether the woman was undergoing the procedure for fibroids or not.

In conclusion, our results show that quantitative differences in the vasculature exist between fibroids and myometrium. We have reported that in general the myometrium is more vascular than fibroids of differing sizes. Further research in the area of vascular biology of these tumours will not only explain different symptoms, especially menorrhagia, in different patients with fibroids but may also lead to novel treatments for these common tumours.

Acknowledgements

We gratefully acknowledge the assistance of Sister Nancy Taylor for the collection of specimens as well as the gynaecologists of the Monash Medical Centre who provided the patients for this study. We also thank Ms Fiona Lederman for teaching immunohistochemistry techniques to R.C. P.R.’s salary is paid by National Health and Medical Research Council Grant Number 960041.

References


Received on November 29, 1999; accepted on March 29, 2000