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Minimally invasive methods with no fibroid surgical removal to treat uterine fibroids: utility or advertising?

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The most prevalent benign uterine tumours, known as fibroids or myomas, are a type of monoclonal tumour that develops from the growth of smooth muscle cells with a significant amount of extracellular matrix, affecting about 70% of middle-aged women. While many fibroids are asymptomatic, 25%–50% of them can result in pelvic pain and pressure, abnormal uterine bleeding, intestinal and/or urine symptoms and/or issues with infertility.[1] Women with fibroids should have customised treatment, which is typically determined by the patient's age and desire for future pregnancy, the size, quantity and location of the fibroid, the clinical symptoms, and the availability of various therapeutic alternatives.

Traditional minimally invasive surgical treatment options include myomectomy for patients with unsatisfied reproductive desires and hysterectomy as a last procedure for women who do not wish to preserve future fertility.[2] Some literature has proposed some alternative minimally invasive non-removal surgical methods for fibroid therapy, which aim to present themselves as an alternative to traditional surgical therapy with fibroid removal from the uterus.

To mitigate some of the hazards associated with traditional surgery, minimally invasive procedures using heat-producing devices, such as radiofrequency (RF), have been developed. The focused tissue undergoes irreversible degeneration, coagulation and necrosis as a result of the RF treatment, which uses an alternating current operating at a frequency of 300–500 kHz. This energy is then transformed into heat. It also requires the least amount of time to recuperate and leaves no scars behind.[3] The RF is a technique that works blindly on an intrauterine mass that could theoretically be neoplastic (given what has happened with the Food and Drug Administration (FDA) since 2014 in the USA with the morcellation problem). Furthermore, the anatomical-functional changes that occur to the treated mass that is left in place in the myometrium are unknown. Because of the unknowns surrounding the biology of the myometrium, no reproductive society actually advises RF therapy of fibroids for procreative purposes. Lastly, it is unknown how heat from RF would affect the pseudocapsule, the basic biological framework enclosing the fibroid.

Under the guidance of ultrasound or magnetic resonance, high-intensity focused ultrasound (HIFU) concentrates low-intensity ultrasound in vitro on the target area in vivo. This creates a high-energy density focus, which causes the surrounding tissue to heat up quickly. The thermal effect of the ultrasound is then used to cause local coagulation, necrosis of solid tumours or ablation. Clinical trials validated the safety and effectiveness of HIFU for fibroids health technology, which was approved by the US FDA in 2004.[4] The same criticisms expressed for RF are equally expressed for HIFU, given that the thermal damage to the fibroid and uterus produced by this technique is similar.

One type of vascular interventional therapy is uterine artery embolisation (UAE). The UAE stops the flow of blood to the uterus by using non-spherical polyvinyl alcohol or trisacryl gelatin microspheres, which results in ischaemic necrosis of the fibroids. The main goal of the UAE treatment for fibroids is to stop the growth of the lesions by generating ischaemia necrosis. After that, the lesions can dissolve, absorb, shrink or even go away, which would relieve the patient's discomfort. The problem is that this procedure treats the whole uterus rather than the fibroids specifically and has the potential to permanently impair uterine and ovarian function.[5]

The UAEs are also questionable in the minimally invasive treatment of fibroids, for the same issues expressed for RF and HIFU. Any intrauterine formation or mass that is treated without

enucleation can potentially be an invasive neoplasm. The biological alteration brought about by UAE then establishes a biological influence on the myometrium's functionality that cannot be fully measured, which is why it is not recommended for younger patients who wish to become pregnant.

It is yet uncertain how the uterus will react biologically to all of these minimally invasive non-removal surgical procedures for treating fibroids in terms of future fertility and potential gynecologic cancer of these 'supposed fibroids'. The myometrium's biology, which is highly complex given that it is a dynamic reproductive viscera that can weigh anywhere from 50 g to 1.5 kg at term of pregnancy, is the major issue regarding the potential impact of these procedures on conception. The thin structure of the myometrium facing the fibroid, the pseudocapsule, dividing it from the myometrium, must now be discussed. The fibroid pseudocapsule is a neurofibrovascular network that completely envelops the fibroid and supplies it with blood and hormones.[6] Through its own circulatory network, the pseudocapsule itself supplies vascular supplementation of fibroids. Furthermore, the nerve fibres of the pseudocapsule are rich in neurotransmitters for myometrial biological function and postmyomectomy physiological myometrial healing as a neurofibrovascular bundle.[7]

There has never been an assessment of how any of these techniques (RF, HIFU and UAE) affect the pseudocapsule. Since the pseudocapsule measures only 1–3 mm, the injury to this thin and delicate neurofibrovascular structure is a plausible hypothesis. During a myomectomy, in fact, the myometrium must never be touched because damaging the muscle will render it useless. The fibroid pseudocapsule is an integral component of the muscle and should never be damaged or in a necrotic state. If not, the muscle in that region will fibrose and become useless for the myometrium's physiology.[8] Furthermore, the transient hypoxia produced by UAE impacts muscle and endometrial biology. What type of impact this has, whether negative or not, we do not know, nor can we know, as we haven't yet published in vivo studies on the biological effects of transient hypoxia on the myometrium and endometrium.

Finally, one crucial factor to take into account when treating fibroids is the potential for an underlying, concealed cancer to be discovered. Because the symptoms of benign fibroid illness and cancer, particularly leiomyosarcoma (LMS), are similar, it can be challenging to differentiate between the two on a clinical basis. Currently, there is no conclusive laboratory or imaging test that can accurately distinguish between these entities. When myomectomy or hysterectomy is performed for symptomatic assumed benign fibroid illness, the frequency and prognosis of concealed LMS are unknown. Between 1 in 350 and 1 in 8000 cases are included in these incidence estimates.[9] A group of authors studied 491 patients following HIFU or UAE to determine the future detection of malignancy in women who have non-surgical therapy for uterine fibroid disease using HIFU and UAE techniques. A total of 106 people had their fibroids surgically treated after that. Four individuals (1.2%) out of the 346 patients who had follow-up had a diagnosis of LMS following their interventional treatment for fibroids. Two more cases of endometrial adenocarcinoma and one case of an endometrial premalignant lesion were reported.[10]

What we have illustrated and discussed must make us reflect on the indiscriminate diffusion of these alternative non-removal surgical methods, thinking critically either about their actual usefulness and effectiveness or about the cost-effectiveness and possible side effects of the procedures, to respond in a scientifically adequate manner to patients with doubts about what to choose to surgically treat a fibroid.

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