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Reassessing Hysterectomy

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Abstract

Hysterectomy is widely used for treating a variety of gynecologic conditions. Most hysterectomies are elective and are performed to treat benign indications for which there are other effective alternatives. Observational studies are increasingly highlighting the effects of hysterectomy and concomitant oophorectomy on a variety of long-term health outcomes including fracture risk, pelvic floor dysfunction, all-cause mortality, cardiovascular disease, and neurologic function. Individualizing therapy and discussing appropriate alternatives to hysterectomy is an important responsibility for all health care providers.

Attention became focused on the overuse of hysterectomy during the 1990s, when the Agency for Healthcare Research and Quality sponsored research and conferences on this topic. These forums highlighted the fact that there were clear differences in hysterectomy rates based on a variety of nonmedical factors including the geographic location of the patient, the race of the patient, and the sex of the gynecologist performing the surgery.[1] Both scientific and lay publications continue to discuss this important issue. Yet despite intensive assessment, the rate of hysterectomy continues to be high, with only a small decline happening in the last few years.[2]

During the past two decades, alternatives to hysterectomy have emerged. Treatment options for benign uterine diseases now include novel medical and surgical therapies.[3] Moreover, an increasing amount of data suggest there are long-term consequences of hysterectomy, with or without concomitant removal of the ovaries. Thus, it is puzzling why hysterectomy is still so commonly used for treating benign gynecologic disorders.

This article reviews the published data regarding hysterectomy and its sequelae, and discusses the growing number of alternatives to hysterectomy.

Prevalence and Indications

The lifetime risk of hysterectomy for a woman in the United States is 45%.[2] Hysterectomy remains the second most commonly performed surgical procedure for women of reproductive age, second only to cesarean section. [4] The rate of hysterectomy has undergone a slow decline, from 7.1 per 1,000 women in the 1980s to 5.0 per 1,000 in recent years.[2] However, it is done far more often than many other commonly performed surgeries. For

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example, according to National Hospital Discharge Summary data, 569,000 women underwent hysterectomy in 2006 compared with 168,000 men who underwent prostatectomy and 341,000 men and women who underwent appendectomy, including incidental appendectomy. [5]

Multiple studies indicate the use of hysterectomy varies widely by geographic region and provider characteristics. There are also racial disparities. Black women have a higher rate of hysterectomy and an increased risk of complications from hysterectomy than white women.[6] Based on the increasing racial diversity of the U.S. population, the rate of hysterectomy is expected to continue to climb through 2050.[7]

Most hysterectomies are elective. Uterine leiomyomas (uterine fibroids) are cited as the most common indication for hysterectomy, accounting for approximately one-third of all hysterectomies performed. [2] Abnormal uterine bleeding is the next most common indication, accounting for approximately 16% of hysterectomies, while gynecologic cancers account for less than 8% of all hysterectomies.[2] Fibroids and abnormal uterine bleeding thus account for five times as many hysterectomies as all gynecologic cancers combined. Interestingly, these are the two indications for which we have made the most progress in developing alternative treatments.

Outcomes of Gynecological Surgery

There has been remarkably little investigation into the long-term outcomes of hysterectomy, particularly given its widespread use. Studies limited to one year of follow-up consistently show that hysterectomy outcomes are good, with a low risk of complications and improved quality of life. However, findings from the few longitudinal studies that have been conducted suggest that there may be long-term consequences. Some studies report favorable symptom relief and quality of life improvement at five to eight years, whereas others raise concern about long-term risks related to dementia and cardiovascular disease.[8–11] Moreover, experts argue that many outcomes of hysterectomy require 20 to 30 years to manifest.[12]

Investigation into how hysterectomy might modify other disease processes has been conducted using Rochester Epidemiology Project (REP) data. These studies have linked hysterectomy to long-term health consequences including pelvic floor dysfunction and fracture risk, as well as dementia, depression, and Parkinson's disease. [13–17]

Most of the attention to long-term risk of morbidity and mortality after hysterectomy has centered on prophylactic bilateral salpingo-oophorectomy (BSO) at the time of hysterectomy. As recently as 2006, data showed that the rate of oophorectomy or salpingo-oophorectomy either alone or with hysterectomy was approximately 73% of the rate of hysterectomy (14.0/10,000 versus 19.1/10,000).[5]

The rationale for elective BSO at the time of hysterectomy has been twofold: BSO would decrease the risk of ovarian cancer, and once a woman reached menopause, her ovaries were no longer hormonally active and, thus, no longer useful. Both suppositions are flawed. First, research has shown that hysterectomy with BSO puts women at greater risk for mortality from conditions and diseases far more common than ovarian cancer. Although ovarian cancer can be difficult to diagnose, it is a relatively rare disease. When considering mortality risk for more common diseases including coronary artery disease and hip fracture, a decision analysis model favored retention of the ovaries until at least age 65 for women with an average risk for ovarian cancer.[18] Similarly, in a large nationwide cohort study, hysterectomy alone performed in women younger than 50 years of age increased the risk of cardiovascular disease later in life, and there was additional risk among those who undergo oophorectomy.[11] Second, the notion that the ovaries are no longer useful after menopause

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has been shown to be flawed as well. Although ovarian estrogen production plummets after menopause, the ovaries continue to make substantial amounts of androgens.[12] These ovarian androgens undergo peripheral conversion to estrogens and may have direct beneficial effects on mood and libido.[12] Recent REP studies have focused attention on the long-term risks of removal of the ovaries with or without hysterectomy.[15,16,19,20]

Even hysterectomy with ovarian conservation has been shown to have significant effects on ovarian function, resulting in earlier menopause.[21–23] Moreover, losing one ovary early in life appears to be associated with a significant increase in risk for dementia late in life.[24] This challenges conventional gynecologic thought that the loss of one ovary would not have serious medical consequences. In fact, it appears there may be a stepwise increase in dementia risk for women who have undergone hysterectomy alone, hysterectomy with unilateral oophorectomy, and hysterectomy with BSO.[9,15,24] In summary, the removal of either ovary or of the uterus may have far-reaching health consequences. Therefore, the surgical removal of female reproductive organs should be considered carefully.

Alternative Treatments for Uterine Fibroids and Abnormal Menstrual Bleeding

Because of the accumulating data regarding the long-term effects of hysterectomy, it seems prudent to use alternatives when possible. Abnormal uterine bleeding and uterine fibroids are two indications for which more alternatives to hysterectomy exist than ever before. For women with uterine fibroids, an assessment of their symptoms (heavy or prolonged menses, bulk-related symptoms secondary to uterine enlargement or both) is the first step in determining the appropriate alternative to hysterectomy.[3,25] Additionally, determining the size, number, and location of fibroids as well as the woman's plans for future pregnancies is important in selecting a therapy.[3,25] Finally, since menstruation ceases at menopause and fibroids also shrink, a woman's age and distance from menopause is also a consideration in choosing a therapy. For women with heavy or prolonged menses, whether or not they have fibroids, the treatment options are similar.

Treatments for Heavy Menstrual Bleeding

Treatment should be considered for women who experience seven or more days of menstrual bleeding or for women who have a normal cycle length but heavy menstrual bleeding. Heavy menstrual bleeding is bleeding that is sufficient to cause frequent use of double sanitary products or the need to change pads or tampons hourly, the need for adult diapers, or frequent staining of clothing or bedding. Women with such bleeding may develop iron-deficiency anemia from chronic blood loss.

The first treatment option involves the use of contraceptive steroids (birth control pills, patches, or vaginal rings), long-acting progestational agents (Depo-Provera or Implanon), or medicated intrauterine devices (Mirena). All of these are relatively simple to use and have the advantage of being reversible if a woman desires future pregnancy. There is even some data to suggest that long-acting progestins are associated with a decreased risk of uterine fibroids.[26,27] Although the use of contraceptive pills for heavy menstrual bleeding has been extensively studied, little research is available on the relative advantages or disadvantages of transdermal or transvaginal therapy for fibroids or heavy bleeding.

Antifibrinolytic medicines are a new option for women in the United States. Tranexamic acid (Lysteda) has been used outside this country for decades but was only recently approved for use in the United States by the Food and Drug Administration (FDA).[28] Tranexamic acid is an oral agent that can slow menstrual bleeding. It only needs to be taken during menses and is not contraindicated in women who wish to maintain fertility. Although

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prescribing information indicates that the drug is associated with an increased risk of thrombosis, clinical studies have not convincingly demonstrated this side effect.

Another option is minimally invasive surgery. Hysteroscopic myomectomy is performed when fibroids are located within the endometrial cavity or extend less than 50% into the myometrium. This procedure is safe for women who want future pregnancies and is sometimes employed when infertility or recurrent miscarriage is the primary or sole fibroid symptom.

If the fibroid is intramural, or if the uterus is structurally normal, an endometrial ablation may help control bleeding. With this technique, the endometrium is destroyed using an instrument placed inside the uterus. Endometrial ablation should not be done for women who want future pregnancies and may not be optimal for women at high risk for endometrial cancer, since 100% destruction of the endometrium is not guaranteed. Although this procedure originally required advanced surgical skills, newer devices allow general gynecologists to perform it.

Treatments for Bulk Symptoms With and Without Heavy Menses

Many women with fibroids also have symptoms caused by the size of the fibroids. Fibroids are often the size of a tennis ball or grapefruit, and a few may grow as large as a basketball. Thus, large fibroids may press on the bladder causing urinary symptoms, on the bowel causing constipation, or on the spine causing back pain.[3, 25] For women with bulky fibroids, shrinking, softening, or removing them is needed for symptom relief.

Gonadotropin-releasing hormone (GnRH) agonists are effective therapy for women with fibroids who experience both bulk and bleeding symptoms because these drugs induce amenorrhea and cause volume reduction. However, they cause severe hypoestrogenic symptoms, lead to bone loss, and can result in the fibroid returning to pretreatment size when discontinued. [3] Thus, GnRH agonists should be used primarily short-term for preoperative therapy, for women late in the perimenopausal transition, or for women who require short-term treatment while undergoing care for other medical conditions (eg, chemotherapy for cancer).

For women with fibroids on the outer surface of the uterus, laparoscopic or robotic myomectomy is a minimally invasive option. Laparoscopic and robotic technology allow for increased mobility of the surgical instrument and better approximation of suturing techniques than in open surgeries. Although abdominal myomectomy is still sometimes performed, particularly when a woman is trying to become pregnant, most women choose less-invasive surgical options.

Two FDA-approved procedures are now available for treating larger or more complicated fibroids in a minimally or noninvasive manner. The first, uterine artery embolization (UAE), also called uterine fibroid embolization, is widely used for controlling fibroid symptoms. A small incision is made in the groin, and, using fluoroscopic guidance, both the right and left uterine arteries are catheterized.[3] Embolic agents are then infused to block the blood flow to the uterus. Because fibroids have a richer blood supply than normal uterine tissue, they typically are devascularized and regress following embolization while the myometrium is usually spared.

Randomized clinical trials comparing UAE to surgery have been conducted in Europe and showed similar short-term outcomes and complication rates.[29] Uterine artery embolization is associated with less blood loss, a quicker return to work, and less pain than surgery; but a subset of women undergoing the procedure will at a later date require hysterectomy.[29] And

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there are data to suggest that UAE can detrimentally affect ovarian reserve. Earlier studies suggested that a subset of women would develop amenorrhea in response to therapy, and more recent studies examining serum markers of ovarian reserve suggest that UAE causes changes in ovarian function similar to hysterectomy.[30] Thus, tracking long-term outcomes for UAE will be as important as it is for hysterectomy and oophorectomy.

The newest fibroid therapy is magnetic resonance-guided focused ultrasound surgery (MRgFUS or FUS). Treatment takes place with the woman lying prone in an MRI machine. While the MR provides real-time image guidance, highintensity ultrasound waves are transmitted through the abdominal wall, where they converge and cause coagulative necrosis to destroy the fibroid.[31,32] Each individual fibroid can be treated separately with this procedure without injuring the myometrium. Focused ultrasound surgery allows for outpatient treatment with light sedation; women can usually return to work after one or two days. This fibroid-specific approach may hold advantages both for women who want future pregnancies and for long-term preservation of ovarian function. Thus, early series of pregnancy outcomes appear good, and the transient amenorrhea seen following UAE has not been reported following FUS.

Research into the development of alternatives to hysterectomy is ongoing. New pharmacologic agents including aromatase inhibitors and progesterone receptor modulators are being studied, and now some comparative effectiveness research of alternatives to hysterectomy is being carried out in the United States. In fact, Minnesota women are able to participate in a National Institutes of Health-funded randomized clinical trial comparing UAE and MRgFUS (NCT00995878, clinical-trials. gov).

Conclusion

Hysterectomy remains a one-size-fits-all remedy for gynecologic conditions, despite its clear limitations. It is critical to continue to develop better alternatives to hysterectomy and to investigate its longterm consequences as well as those of its alternatives. In the meantime, providing women with information to determine the most appropriate treatment options for their particular gynecologic concern is a key responsibility for primary care providers, gynecologists, and other health care professionals.

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Educational objectives

To educate primary care providers about

- the long-term health consequences of hysterectomy
- alternative treatments for uterine fibroids and abnormal uterine bleeding

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