"Invasive and Non-invasive Methods for the Diagnosis of Endometriosis" (2010), by Albert L. Hsu, Izabella Khachikyan, and Pamela Stratton

In 2010, Albert L. Hsu, Izebella Khchikyan, and Pamela Stratton published "Invasive and Noninvasive Methods for the Diagnosis of Endometriosis," henceforth "Methods for the Diagnosis of Endometriosis," in Clinical Obstetrics and Gynecology. In the article, the authors describe how specific types of endometriotic lesions appear in the body and evaluate five methods for diagnosing endometriosis. Endometriosis is the growth of endometrium, the tissue that normally lines the inside of the uterus, outside of the uterus. The authors state that although endometriosis impacts many women, the condition is difficult to identify. They identify laparoscopy, an invasive surgical procedure, as the most accurate diagnostic method. By analyzing the effectiveness of available diagnostic methods, the authors help physicians diagnose endometriosis and increase the quality of life for affected women.

When "Methods for the Diagnosis of Endometriosis" was published, Hsu, Khchikyan, and Stratton were all working at Eunice Kennedy Shriver National Institute of Child Health and Human Development in Bethesda, Maryland. Hsu was trained as a physician of obstetrics, the study of childbirth and the care for those giving birth, and gynecology, the study of the function and diseases specific to the reproductive systems of females. Hsu specialized in reproductive endocrinology, or the study of reproductive medicine as it relates to hormone function. Khchikyan, a medical doctor, has published many several on pelvic pain associated with endometriosis since 2010. As of 2019, Khchikyan is a medical officer at the US Food and Drug Administration, headquartered in Silver Spring, Maryland. Stratton was also working as a physician of obstetrics and gynecology. As of 2019, Stratton is a member of the World Endometriosis Society, headquartered in Vancouver, Canada, and has conducted studies on pelvic pain associated with endometriosis for thirty years.

Healthcare professionals classify endometriosis as a medical disorder of the uterus. Endometriosis is the growth of endometrium, the tissue that normally lines the inside of the uterus, outside of the uterus. The uterus is a muscular organ inside of the female pelvis, the area in the lower part of the trunk of the body, beneath the abdomen and above the thighs. The endometrium is where a fertilized egg cell will implant before developing into a fetus. When a patient has endometriosis, the endometrium will grow in abnormal places like the fallopian tubes or the ovaries. The ovaries are sac-like reproductive organs which hold eggs, and the fallopian tubes are a pair of tubes that connect the ovaries to the uterus. Common symptoms of endometriosis include chronic pelvic pain, painful menstruation called dysmenorrhea, painful intercourse called dyspareunia, infertility, and painful bowel movements or urination. As of 2019, there is no cure for endometriosis, but physicians can help patients with pain relief through medication and surgery.

In their introduction, Hsu, Khchikyan, and Stratton describe endometriosis and common types of diagnostic measures. Then, in a section called "Types and Locations of Endometriotic Lesions," the authors describe the three kinds of endometriosis and their associated disease symptoms. Next, they describe and compare five different methods for diagnosing endometriosis. In "Clinical Diagnosis," Hsu, Khchikyan, and Stratton outline the factors that may lead a physician to diagnose a patient with endometriosis during a physical examination. In the next section, "Laparoscopy," the authors discuss what a physician might see when viewing endometriotic lesions during an invasive surgical procedure. In the next section, "Imaging," the authors discuss the shortcomings of imaging techniques for diagnosing endometriosis. In Serum Markers, they describe the work that

has been done for developing serum markers, which are specific components in blood that physicians can measure to learn about the state of health in a patient, to diagnose endometriosis. In the next section, "Endometrial Nerve Fibers," the authors briefly mention endometrial biopsy, taking a small sample of tissue, from nerve fibers as a way to help diagnose endometriosis. In the final section, called "Conclusion," Hsu, Khchikyan, and Stratton make final recommendations about the best diagnostic tools for endometriosis.

In the "Introduction" section, Hsu, Khchikyan, and Stratton define endometriosis, common symptoms, treatments, and diagnostic tools. The authors describe endometriosis as a common disease caused by the growth of endometrial tissue, which usually lines the inside of the uterus in females outside of the uterus. The authors establish that healthcare professionals typically diagnose endometriosis with laparoscopy, which is an invasive surgical procedure where a physician makes small incisions in the body to insert a small camera to view the inside of the body. To supplement laparoscopy, physicians commonly use histological confirmation, which requires viewing tissue sampled from an area of interest under a microscope, or a biopsy, doing tests on a small sample of tissue from an area of interested. According to the authors, physicians often suspect that patients with painful and heavy menstrual cycles have endometriosis. However, the correlation between endometriosis and pain is weak, because the stage of endometriosis is not directly related to the severity of pain. Hsu, Khchikyan, and Stratton state that it is difficult for physicians to diagnosis endometriosis because it is difficult to discern the correlation between symptoms of endometriosis and severity of pain. For example, a woman with severe, stage IV endometriosis may be asymptomatic. Also, twenty percent of women with endometriosis have concurrent chronic pain conditions, which further adds to the difficulty of diagnosing endometriosis.

In the next section, "Types and Locations of Endometriotic Lesions," the authors describe the three primary types and locations of endometriotic lesions: superficial peritoneal endometriosis, cystic ovarian endometriosis, and deep infiltrating endometriosis. Endometriotic lesions typically appear on the pelvis in areas such as the ovaries, uterus, fallopian tubes, or uterosacral ligaments. The lesions are a result of the endometrial tissue growing outside the endometrium, which lead to pain in affected patients. The authors state that each type of lesion is associated with chronic pelvic pain, but not necessarily the severity of that pain. In other words, an endometriotic lesion in one area of the body does not necessarily cause more pain than a lesion in another area in the body. Hsu, Khachikyan, and Stratton first describe superficial peritoneal lesions, which occur on the pelvic organs or the membrane that lines the pelvis. According to the authors, superficial peritoneal lesions may appear to be blue or blue-black during laparoscopy, but in rare instances, lesions may appear to be clear, red, or white.

As their description of different lesions continues, the authors detail ovarian endometriomas, which are endometriotic lesions that look like cysts and occur within the outermost layer of the ovary, called the ovarian cortex, and attach to nearby pelvic structures. That kind of endometriotic lesion appears to be dense and brown during laparoscopy. The authors refer to the third type of endometriotic lesion as deep infiltrating endometriosis. Those lesions usually appear on ligaments of the uterus or rectovaginal fascia, which is tissue that separates the vagina and rectum. According to Hsu, Khchikyan, and Stratton, women with deep infiltrating endometriosis lesions may experience bowel symptoms such as diarrhea. Other unusual locations of lesions may cause cyclic hematochzia, or blood in the stool. After their descriptions of the three lesion types, the authors describe five specific ways to diagnosis endometriosis.

First, they outline how physicians diagnose endometriosis in the section titled "Clinical Diagnosis." Generally, a physician will diagnose endometriosis in a clinical setting by taking a complete history of the patient's symptoms and by conducting a physical examination of the patient. Physicians often look for or ask patients about pelvic pain specifically. A patient may express that pain occurs at various points during the menstrual cycle, such as ovulation, when a mature egg is released from the ovary, which can be connected to endometriosis. The authors also note that different types of endometriotic lesions may be correlated to specific symptoms. For example, a patient with gastrointestinal symptoms may have deep infiltrating endometriosis lesions. According to the authors, such symptoms are helpful in clinical diagnoses for planning further treatment. However, they emphasize that clinical diagnosis may not adequately diagnosis endometriosis.

pain is not always a symptom of endometriosis, and a woman with pain may suffer from a different health issue. Also, the authors point out that healthcare professionals cannot identify abnormalities due to endometriosis, such as endometriotic lesions, during a physical examination. Thus, the authors claim that clinical diagnosis has poor specificity or predicative value in the diagnosis of endometriosis.

The authors then move on to a second type of diagnostic method for endometriosis, laparoscopy, in the section "Laparoscopy." According to the authors, laparoscopy is useful in the diagnosis of endometriosis because the surgical procedure allows physicians to view lesions of the pelvis that may be indicative of endometriosis. As the authors detail, diagnosis of endometriosis via laparoscopy requires that a physician finds endometrial tissue located outside of the endometrium. The physician usually takes a small sample of the tissue, also called a biopsy, to test histologically, or by viewing the tissue under a microscope. According to the authors, approximately half of endometriotic lesions require histological confirmation because lesions can indicate other health issues like inflammatory changes in the pelvis.

Third, in the section called "Imaging," the authors describe imaging techniques that have been used in attempts to diagnose endometriosis. They assert that there is a limited number of useful imaging techniques for the diagnosis of endometriosis. Specifically, the authors outline three imaging techniques that are used to diagnose endometriosis: ultrasound, magnetic resonance imaging, or MRI, and computed tomography, or CT, scan of the pelvis. In their discussion of ultrasound, which is an imaging method that uses sound waves in order to view organs inside of the body, the authors note that ultrasound is useful in identifying deep infiltrating endometriosis lesions. Ultrasound is also easily accessible and affordable, which may be beneficial for women with endometriosis who face economic barriers to treatment. According to Hsu, Khchikyan, and Stratton, an MRI, while expensive, is more accurate in detecting endometriosis than an ultrasound. Specifically, using MRI, healthcare professionals can diagnose deep infiltrating endometriosis lesions in unusual sites such as the uterosacral ligaments, which are structural tissues that connect the bottom of the spine to the cervix, or rectovaginal fascia, which is the tissue that separates the vagina and rectum. The authors discuss a CT scan of the pelvis as a way to diagnose endometriosis. However, they note that a CT scan of the pelvis does not adequately visualize pelvic organs.

In the section "Serum Markers," the authors describe a fourth type of diagnosis method for endometriosis. Serum markers are specific components in the blood that physicians can measure to learn about the state of health in a patient. Ideally, serum markers would allow physicians to measure disease activity and monitor improvement in patients with endometriosis. However, researchers have not yet found a serum marker to specifically identify endometriosis. The authors indicate that more research on serum markers is crucial to fully understanding how that particular diagnostic method can impact the treatment of endometriosis.

Finally, in the section "Endometrial Nerve Fibers," the authors describe the potential for biopsy of endometrial nerve fibers to work as a diagnostic tool for endometriosis. Nerve fibers usually transmit information to different areas of the body. Hsu, Khchikyan, and Stratton state that studies have demonstrated that women with endometriosis have an increased number of nerve fibers in their endometrium. However, according to the authors, the amount of nerve fibers present in the endometrium has not been found to be an adequate type of diagnosis of endometriosis, and researchers are still exploring that topic as of 2019.

In the "Conclusion" section, the authors reiterate that although many cases of endometriosis are predicted in a clinical setting, healthcare professionals often diagnose endometriosis with laparoscopy and histological confirmation. According to Hsu, Khchikyan, and Stratton, non-invasive methods to diagnose endometriosis, such as imaging, may help guide surgical approaches, especially in women with deeply infiltrating endometriosis lesions. They also note, however, that imaging is not as accurate of a diagnosis of endometriosis as laparoscopy. Finally, the authors indicate that researchers must conduct more studies to determine the benefit of serum markers and endometrial nerve fibers as reliable methods for diagnosing endometriosis.

"Methods for the Diagnosis of Endometriosis" has been cited more than one hundred times in later studies about the diagnosis of endometriosis as of 2019. Many of those studies are concerned with

the development of new diagnostic tools, including imaging and serum markers, for the diagnosis of endometriosis. As of 2019, there is still no definitive method for diagnosing endometriosis.

Sources

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