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Combined colonoscopy and endometrial biopsy cancer screening results in women with Lynch syndrome

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HIGHLIGHTS

- Fifty-five women with Lynch syndrome underwent endometrial and colonoscopic combined screening under sedation between 2002 and 2013.
- Combined screening was effective in the detection of (pre)cancerous endometrium and colonic polyps.
- We recommend changing to a 1-2 year endometrial screening interval, in parallel with the colonoscopy recommendations.

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ABSTRACT

Objective. Endometrial biopsy (EMBx) and colonoscopy performed under the same sedation is termed combined screening and has been shown to be feasible and to provide a less painful and more satisfactory experience for women with Lynch syndrome (LS). However, clinical results of these screening efforts have not been reported. The purpose of this study was to evaluate the long-term clinical outcomes and patient compliance with serial screenings over the last 10.5 years.

Methods. We retrospectively analyzed the data for 55 women with LS who underwent combined screening every 1–2 years between 2002 and 2013. Colonoscopy and endometrial biopsy were performed by a gastroenterologist and a gynecologist, with the patient under conscious sedation.

Results. Out of 111 screening visits in these 55 patients, endometrial biopsies detected one simple hyperplasia, three complex hyperplasia, and one endometrioid adenocarcinoma (FIGO Stage 1A). Seventy-one colorectal polyps were removed in 29 patients, of which 29 were tubular adenomas. EMBx in our study detected endometrial cancer in 0.9% (1/111) of surveillance visits, and premalignant hyperplasia in 3.6% (4/111) of screening visits. No interval endometrial or colorectal cancers were detected.

Conclusions. Combined screening under sedation is feasible and less painful than EMBx alone. Our endometrial pathology detection rates were comparable to yearly screening studies. Our results indicate that screening of asymptomatic LS women with EMBx every 1–2 years, rather than annually, is effective in the early detection of (pre)cancerous lesions, leading to their prompt definitive management, and potential reduction in endometrial cancer.

Introduction

Lynch syndrome (LS), or hereditary nonpolyposis colorectal cancer (HNPCC), is an autosomal dominant syndrome caused by a germ-line mutation in one of the DNA mismatch repair genes (*MLH1*, *MSH2*, *MSH6*, or *PMS2*) that increases the risk of cancer in these patients [1]. In a study of LS mutation positive patients in the United States, Stoffel [2] estimated lifetime risks for women of 43% for colorectal cancer (CRC) and 39% for endometrial cancer (EC). Similarly, Bonadona et al. [3] found a lifetime risk of 35% for endometrial cancer in French families with Lynch syndrome. Furthermore, women with LS have an estimated lifetime risk of 6.7–8% for ovarian cancer (OC) [1,3,4]. These cancers can occur at any age but typically occur at an earlier age of onset than the general population. Patients who develop an initial cancer are also at an elevated risk of developing second primary cancers [1,4–6].

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Due to these elevations in risk, screening recommendations have been implemented. In both women and men with LS, CRC screening with colonoscopy and performance of polypectomy has resulted in an 80% decreased incidence of CRC, and a reduction in both CRC-related and overall mortality [7–9]. National Comprehensive Cancer Network (NCCN) guidelines recommend colonoscopy starting at age 20–25 years or 2–5 years prior to the earliest colon cancer if it is diagnosed before age 25 and repeated every 1–2 years [8,10–12]. This contrasts with the general population in which CRC screening is usually recommended starting at age 50, and repeated at intervals of up to 10 years.

NCCN guidelines recommend prophylactic hysterectomy and bilateral salpingo-oophorectomy (BSO) as an endometrial cancer risk reducing option for women with LS who have completed childbearing [12–14]. Prior to or when risk reducing surgery is not performed, screening guidelines based on consensus opinion include annual endometrial biopsy starting at age 30–35 or 5–10 years prior to the earliest diagnosis of EC in the family [11]. Transvaginal ultrasound (TVUS) has also been used for endometrial cancer screening, but its efficacy is lacking. NCCN states that there is no clear evidence to support screening for endometrial or ovarian cancer for women with LS, and annual office endometrial sampling, transvaginal ultrasound and CA-125 measurement are described as optional [12]. Due to the elevated risk of endometrial cancer in these patients, and the lack of consensus with screening guidelines, many practitioners opt to screen these patients [11,15]. EC is not routinely screened for in the general population because it typically presents with warning symptoms, including post-menopausal or otherwise abnormal uterine bleeding. The endometrial cancer in women with LS however, is more likely to begin before menopause, with an average age of onset of 48, when abnormal uterine bleeding symptoms are less obvious.

Although colonoscopy is typically performed under sedation, EMBx is usually performed in an office setting without anesthesia. Patients often experience moderate discomfort and cramps. Combined screening, with EMBx at the time of colonoscopy to take advantage of the intravenous sedation, has been shown to be feasible and acceptable to patients at our institution [16]. Following our proof of principal demonstration, combined screening is now being routinely performed. While we know that this combined screening approach is very well liked by our patients, we do not know how combining these two screening procedures will affect clinical outcomes and patient compliance.

The primary purpose of our study was to analyze pathologic outcomes of EMBx, with attention to the diagnosis of hyperplasia and cancer, as well as resultant treatments following diagnosis. We also analyzed the pathologic profiles of colorectal polyps removed by colonoscopy and patient adherence with this combined screening program over a 10.5 year time period. Toward these ends, we performed a retrospective chart review of 55 women from our LS database who underwent EMBx and colonoscopy as a combined procedure.

Methods

Patient selection

LS patients were identified following referral for high-risk gynecologic management, and then scheduled for combined screening in coordination with their upcoming endoscopy. All routine EMBxs for LS patients are offered as joint procedures with colonoscopy. A total of 62 women had undergone combined screening from July 1, 2002, to March 1, 2013, at The University of Texas MD Anderson Cancer Center. Women were identified if they had undergone one or more combined screening visits for elevated risk of EC. For the current study, patients were included only if they either met Amsterdam II criteria, or had a genetic mutation for LS. Seven patients were excluded based on these criteria, leaving 55 women who were included in our study. Of these, 32 (58%) patients had MMR mutations: *MSH2* in 17 (53%) patients, *MLH1* in 8 (25%) patients, *MSH6* in 4 (13%), and *PMS2* in 3 (9%). The remaining 23 (42%) patients met Amsterdam II criteria.

Data collected

For our analysis of all study-eligible patients, we collected and retrospectively evaluated data from the patients' medical record for each patient's age, height, weight, diagnostic criteria for LS, CA125 levels and pelvic ultrasonography (including endometrial stripe thickness), pathology results from EMBx and colonoscopy, intervals between combined screenings, gravidity, parity, race/ethnicity, menopausal status, all cancer diagnoses preceding and during the study period, cervical stenosis, and surgeries performed owing to combined screening results. This study received approval from The University of Texas MD Anderson Cancer Center institutional review board.

Clinical examination

The annual clinic visit included a physical examination, Pap smear, pelvic examination, CA125 measurement, TVUS, and genetic counseling as needed starting at age 30. A review of clinical symptoms included whether the patient had experienced early satiety, abdominal bloating, pelvic pain or pressure, abnormal uterine bleeding, or postmenopausal bleeding. These patients had also been seen by the gastroenterologist prior to colonoscopy, and by a genetic counselor.

TVUS

TVUS was ordered for ovarian cancer screening on all patients starting at age 30 on a yearly basis. Interpretation by the radiologist included measurement of uterine size, uterine anatomy, endometrial stripe thickness, and ovarian morphology. If abnormal ovarian findings were reported, follow-up imaging was repeated after a shortened interval. Endometrial stripe thickness on TVUS was documented, but only used for retrospective analysis, as routine EMBx was performed during the study. Endometrial stripe thickness was deemed abnormal (during the retrospective analysis) when >12 mm in premenopausal women, or >5 mm in postmenopausal women [17,18].

Combined screening/EMBx

At the time patients were originally seen, combined screening consisted of a colonoscopy performed by a gastroenterologist followed by an EMBx performed by a gynecologist, both while the patient was under intravenous sedation in the endoscopy suite. The endometrial biopsy portion of the combined screen was started at age 30. Negative results from a urine pregnancy test were required before EMBx could be carried out. As time progressed the order of the procedures was changed and the gynecologist went first followed by the gastroenterologist. This modification allowed the gynecologist to finish quickly and return to their clinic, and not have to wait for the colonoscopy to be completed.

Combined screenings were performed in the endoscopy suite under intravenous sedation using versed, fentanyl and on occasion propofol. The patient was placed on a stirrup-equipped stretcher. For the EMBx, the patient's feet were moved into the stirrups and the patient placed in the dorsal lithotomy position. The EMBx was performed using a 3- or 4-mm pipelle (Cooper Surgical, Trumbull, CT) with or without a tenaculum. A bimanual examination of the uterus and ovaries was performed upon completion of the EMBx. Gynecologic supplies for the EMB were brought to the endoscopy suite by the clinical nurse. If cervical stenosis or insufficient endometrial tissue was encountered, hysteroscopy and dilation and curettage were scheduled.