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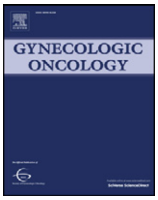

Incidence, risk factors and estimates of a woman's risk of developing secondary lower limb lymphedema and lymphedema-specific supportive care needs in women treated for endometrial cancer

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HIGHLIGHTS

- Lymphedema is experienced by 13% of women treated for endometrial cancer.
- The strongest risk factor for lymphedema is the number of nodes removed at surgery.
- Women with lymphedema have considerable unmet need for support for the condition.

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ABSTRACT

Objectives. Few studies have assessed the risk and impact of lymphedema among women treated for endometrial cancer. We aimed to quantify cumulative incidence of, and risk factors for developing lymphedema following treatment for endometrial cancer and estimate absolute risk for individuals. Further, we report unmet needs for help with lymphedema-specific issues.

Methods. Women treated for endometrial cancer ($n = 1243$) were followed-up 3–5 years after diagnosis; a subset of 643 completed a follow-up survey that asked about lymphedema and lymphedema-related support needs. We identified a diagnosis of secondary lymphedema from medical records or self-report. Multivariable logistic regression was used to evaluate risk factors and estimates.

Results. Overall, 13% of women developed lymphedema. Risk varied markedly with the number of lymph nodes removed and, to a lesser extent, receipt of adjuvant radiation or chemotherapy treatment, and use of non-steroidal anti-inflammatory drugs (pre-diagnosis). The absolute risk of developing lymphedema was >50% for women with 15+ nodes removed and 2–3 additional risk factors, 30–41% for those with 15+ nodes removed plus 0–1 risk factors or 6–14 nodes removed plus 3 risk factors, but ≤8% for women with no nodes removed or 1–5 nodes but no additional risk factors. Over half (55%) of those who developed lymphedema reported unmet need(s), particularly with lymphedema-related costs and pain.

Conclusion. Lymphedema is common; experienced by one in eight women following endometrial cancer. Women who have undergone lymphadenectomy have very high risks of lymphedema and should be informed how to self-monitor for symptoms. Affected women need greater levels of support.

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Introduction

Endometrial cancer is the most common malignancy of the female genital tract in developed countries [1]. Most women (80%) are diagnosed with early stage, low grade tumors, and have good prognosis (>90% survival at 5-years) [2]. There are currently no universally accepted guidelines for the management of women with endometrial cancer. While most women undergo a hysterectomy and bilateral salpingo-oophorectomy, both the surgical approach (abdominal, vaginal, laparoscopic, robotic) and extent of surgery vary substantially. Pelvic with or without para-aortic lymphadenectomy and omentectomy may be performed depending partly on the stage and grade of the cancer, but also on individual surgeon practice and patient factors. Patients at increased risk of recurrence might be offered post-operative radiotherapy in the form of vaginal vault brachytherapy or pelvic external-beam radiotherapy or, less commonly, chemotherapy [3]. Although often used, randomized trials have indicated no survival advantage with lymphadenectomy [4] or adjuvant radiotherapy [5] in women with early-stage disease at intermediate or high risk of recurrence. An increased rate of lymphedema (chronic lower-limb swelling) has been reported for women who received a pelvic lymphadenectomy [4].

Lymphedema is characterized by increases in extracellular fluid [6]. Secondary lymphedema presents as swelling of the limbs following cancer treatment [7]. Little is known about lower limb lymphedema following gynecological cancer treatment [8]. Incidence rates of lower limb lymphedema in women following endometrial cancer have been reported between 1 and 18%, but these figures are mostly based on retrospective chart audits [9–11] that are likely to under-report cases, case–control studies with selected patient groups who underwent particular surgical procedures [12,13], studies at a single site [7,9,11–14] and studies with modest numbers (n = 141–243) [7,15]. Studies assessing risk factors for lymphedema following endometrial cancer are subject to the same research shortcomings.

The impact of lower limb lymphedema can be significant including physical discomfort, pain, and reduction in mobility, body image issues, sexuality issues and distress [15,16]. The specific supportive care needs of women with lower limb lymphedema have only been looked at in one previous study of women with a mix of gynaecological cancer subtypes, of which only 20 women had lymphedema diagnosed following endometrial cancer [15].

We therefore undertook a large population-based study to assess lymphedema incidence and key personal, behavioral and clinical risk factors of post-treatment lymphedema among women with endometrial cancer and to estimate absolute risk for individuals. Further, we report the proportion of women with unmet needs for help with lymphedema-specific issues.

Methods

Participants and procedures

The study was approved by the Ethics Committee of QIMR Berghofer Medical Research Institute and all participating hospitals. Participants provided informed consent for each round of data collection.

Women newly diagnosed with primary endometrial cancer between May 2005 and December 2007 were recruited for the Australian National Endometrial Cancer Study (ANECS), an Australia-wide, population-based case–control study. Full details of the study design and participant recruitment have been reported previously [17,18]. In brief, eligible women were aged 18–79 years and of the 2192 eligible women who were invited to participate, 1399 (64%) completed a telephone interview and form the ANECS cohort.

During 2009–2011, which coincided with a minimum of 3 years and up to 5 years after the participants' original diagnosis, information about treatment and outcomes, including a diagnosis of lymphedema (if recorded), was abstracted from the medical records of the full ANECS cohort (n = 1399). ANECS women were also recontacted and asked to complete a self-administered questionnaire regarding their current lifestyle and quality of life, as well as lower limb lymphedema symptoms and diagnosis, and lymphedema-specific supportive care needs. Of the 1399 ANECS participants, 116 had died, 258 chose not to participate in the follow-up questionnaire; 356 could not be contacted by phone or mail; and 26 women (or a family member) stated that they were too sick. The remaining 643 women (50%) responded to the follow-up questionnaire.

We combined medical record data (n = 1140 with recorded lymphedema status) and self-report data (n = 643) of a diagnosis for lymphedema for our risk factor analysis. Together this provided information about lymphedema status on 1243 women or 89% of the cohort; the remaining 156 women were excluded as they did not complete the ANECS follow-up questionnaire and information about their lymphedema status was not recorded within their medical record (n = 152), or they had been diagnosed with primary lymphedema before undergoing surgery for endometrial cancer (n = 4).

Measures

Outcome measures

Lymphedema status. Within the ANECS follow-up questionnaire, we used previously developed questions that asked ‘since being treated for endometrial cancer have you (a) experienced swelling in your legs, feet or groin? and (b) been told by a doctor or other health professional that you have lymphedema?’ and, if yes, ‘When were you diagnosed?’ [15]. Trained research nurses also accessed women's medical records a minimum of 3 years after diagnosis to abstract detailed information regarding treatment and all follow-up visits including the reason for the visit and any symptoms present. Women who self-reported lymphedema on the follow-up questionnaire or who had a report of lymphedema in their medical record were classified as having lymphedema.

Lymphedema-specific supportive care needs. Women who completed the ANECS follow-up questionnaire and self-reported having lymphedema were asked a further set of eight lymphedema-specific supportive care need items. These items [15] asked participants to indicate their level of need for help with each item on a 5-point scale where 1 = not applicable (no need), 2 = satisfied (need was met), 3 = low unmet need, 4 = moderate unmet need and 5 = high unmet need.

Potential lymphedema risk factor variables measured

Information about personal and behavioral factors. Relating to the one year period prior to endometrial cancer diagnosis was collected via interview at recruitment to ANECS. Information included: age, marital status, education, income, employment status, smoking status (current, ex, never), number of full-term pregnancies, age at menopause, history of common comorbidities (including type 1 and 2 diabetes, hypertension and breast cancer) and use of common medications (average use over the last five years of aspirin, acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs)). Physical activity was assessed by two items asking about how many times per week participants did (a) strenuous and (b) moderate physical activity for at least 20 min in their leisure time. This was then coded based on previously established classification [19,20] into a three-level physical activity index. We also used women's postcode at diagnosis to classify the area they lived according to the Accessibility/Remoteness Index of Australia (ARIA) [21] and Socio-Economic Indexes for Areas (SEIFA) [22]. Body mass index (BMI, kg/m^2) was derived from self-reported weight one year before cancer diagnosis and height at diagnosis, and grouped into underweight (<18.5), normal weight (18.5–24.9), overweight (25.0–29.9), moderately obese (30.0–34.9), severely obese (35.0–39.9) and very severely obese (≥40.0).