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SCIENCE DIRECT
Gynecologic Oncology 101 (2006) 520–529
Gynecologic Oncology
www.elsevier.com/locate/ygyno

Review

Follow-up after primary therapy for endometrial cancer: A systematic review

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On behalf of the Cancer Care Ontario Program in Evidence-based Care Gynecology Cancer Disease Site Group

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Received 22 November 2005
Available online 23 March 2006

Abstract

Objective. To determine the optimum follow-up of women who are clinically disease-free following potentially curative treatment for endometrial cancer.

Methods. A systematic search of MEDLINE, EMBASE and the Cochrane Library databases (1980 to October 2005) was conducted. Data were pooled across trials to determine overall estimates of recurrence patterns.

Results. Sixteen non-comparative retrospective studies were identified. The overall risk of recurrence was 13% for all patients and 3% or less for patients at low risk. Approximately 70% of all recurrences were symptomatic, and 68% to 100% of recurrences occurred within approximately the first 3 years of follow-up. No reliable differences in survival were detected between patients with symptomatic or asymptomatic recurrences nor were differences in patient outcomes reported by type of follow-up strategy employed. Detection of asymptomatic recurrences ranged from 5% to 33% of patients with physical examination, 0% to 4% with vaginal vault cytology, 0% to 14% with chest X-ray, 4% to 13% with abdominal ultrasound, 5% to 21% with abdominal/pelvic CT scan, and 15% in selected patients with CA 125.

Conclusions. There is limited evidence to inform whether intensive follow-up schedules with multiple routine diagnostic interventions result in survival benefits any more or less than non-intensive follow-up schedules without multiple routine diagnostic interventions. Routine testing seems to be of limited benefit for patients at low risk of disease. Most recurrences tend to occur in high risk patients within 3 years, and most recurrences involve symptoms. The most appropriate follow-up strategy is likely one based upon the risk of recurrence and the natural history of the disease. Counseling on the potential symptoms of recurrence is extremely important because the majority of patients with recurrences were symptomatic. A proposed routine follow-up schedule is offered.

Keywords: Follow-up; Endometrial; Cancer; Surveillance; Systematic; Review

Contents

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doi:10.1016/j.ygyno.2006.02.011

Introduction

What is the most appropriate strategy for the follow-up of patients with endometrial cancer who are clinically disease-free after receiving potentially curative primary treatment? Specifically, do differences in follow-up intervals, diagnostic interventions, clinical setting or specialty, influence patient outcomes related to local or distant recurrence, survival, or quality of life?

Endometrial cancer, the most common gynecologic malignancy, accounts for 3700 new cases a year in Canada, with 1450 occurring in Ontario [1]. The disease presentation is such that the majority of cases are clinically stage I or II with a case fatality ratio of approximately 0.19 or 19% of patients [1]. Treatment for stage I or II endometrial cancer generally includes a total abdominal hysterectomy and bilateral salpingo-oophorectomy with or without pelvic and/or para-aortic lymphadenectomy. Surgical pathologic factors that predict survival and disease recurrence include tumor grade, histology, depth of myometrial invasion, presence of lymph node metastasis, and the presence of extrauterine disease [2]. Patients who are deemed to be at a higher risk for recurrence (i.e., stage IA or IB, grade 3, or stage IC or advanced stage) may receive postoperative adjuvant radiation therapy in the form of vaginal vault brachytherapy, pelvic external-beam radiation therapy, or other modalities. Randomized trials have shown that in early stage endometrial cancer adjuvant pelvic radiotherapy improves local–regional control but does not improve overall survival [3,4].

The anatomic locations of recurrences are roughly equivalent between local (pelvic) and distant (abdominal and chest) [3–6], with the most common sites being the vaginal vault, pelvis, intra-abdominal region, and lungs [7]. There is some controversy surrounding the salvage rate among patients who recur. Published salvage rates range from 10% to 38% [7,8]. Radiation also seems to affect the pattern of recurrence—women who receive radiation therapy seem to have fewer local recurrences but not fewer distant recurrences than women (in similar risk categories) who do not receive radiation therapy [3–6].

The concept of long-term surveillance of patients treated with curative intent is based on the premise that early detection will result in decreased morbidity and mortality. At present, follow-up protocols to date that have been used in this population have been highly variable, utilizing a number of tests at a variety of intervals [7]. There are no formal recommendations regarding the optimal program for monitoring patients. The primary aim of this series is to outline, if possible, an optimal program for following patients based on previously published evidence. Specific components of such a program to be addressed would include optimal intervals for follow-up; optimal location for follow-up (cancer centers, local gynecologist, etc.); accuracy of the surveillance tests presently being done; and modification of the follow-up program based on an individual patient's risk of recurrence.

Methods

This systematic review was developed by Cancer Care Ontario's Program in Evidence-based Care (PEBC). Evidence was selected and reviewed by members of the PEBC Provincial Gynecology Cancer Disease Site Group and methodologists.

This systematic review is a convenient and up-to-date source of the best available evidence on the follow-up of patients after potentially curative primary therapy for endometrial cancer. The body of evidence in this review is comprised of retrospective data. That evidence, combined with expert consensus, forms the basis of a clinical practice guideline developed by the Provincial Gynecology Cancer Disease Site Group (www.cancercare.on.ca). The systematic review and companion practice guideline are intended to promote evidence-based practice in Ontario, Canada. The PEBC is editorially independent of Cancer Care Ontario and the Ontario Ministry of Health and Long-term Care.

Literature search strategy

The literature was searched using MEDLINE (OVID: 1980 through October 2005), EMBASE (OVID: 1980 through October 2005), the Cochrane Library (OVID: Issue 3, 2005), the Canadian Medical Association Infobase, and the National Guideline Clearinghouse. In addition, the proceedings of the meetings of the American Society of Clinical Oncology (1999–2005) and the American Society for Therapeutic Radiology and Oncology (1999–2003) were searched