Cytoreductive surgery for advanced or recurrent endometrial cancer: a meta-analysis

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CRD summary
This review assessed the effect of multiple prognostic variables on overall survival in patients with advanced or recurrent endometrial cancer undergoing cytoreductive surgery. The authors concluded that complete cytoreduction to no gross residual disease significantly improved overall survival. Given the limited, varied evidence base, and the potential for bias in the review, the authors' conclusions should be interpreted with caution.

Authors' objectives
To determine the effect of multiple prognostic variables on overall survival in patients with advanced or recurrent endometrial cancer undergoing cytoreductive surgery.

Searching
PubMed was searched for English language articles. Search terms were reported, but search dates were not. Reference lists of retrieved articles were manually searched. It appeared that the review was restricted to published studies, although this was not explicitly stated.

Study selection
Studies that assessed the effects of cytoreductive surgery on overall survival in at least one cohort of patients with advanced or recurrent endometrial cancer were eligible for inclusion. Studies were only eligible if they compared the effects of cytoreductive surgery in patients with optimal versus suboptimal postoperative disease status.

Included studies were published between 1997 and 2009. The median age of included women ranged between 62 and 70 years (where reported). Most included studies were of patients with advanced primary endometrial cancer, but some were of patients with recurrent endometrial cancer. Studies assessed patients with uterine papillary serous histology and/or clear cell histology. Where applicable, 30 to 100% of patients had Grade 3 tumours; 10 to 100% had Federation of Gynaecology and Obstetrics (FIGO) stage IV disease.

In included studies, the proportion of patients undergoing optimal surgical cytoreduction (defined as ≤1, ≤2, or no gross evidence of disease) ranged from 52 to 75%; those undergoing complete surgical cytoreduction ranged from 18 to 75% (where applicable). Most studies included adjuvant therapy; 16 to 87% of patients received adjuvant chemotherapy, 11 to 71% received platinum-based chemotherapy, and 3 to 73% received adjuvant radiation therapy (it was unclear whether patients received chemotherapy and radiation alone or in combination).

The authors did not state how many reviewers screened studies for inclusion.

Assessment of study quality
The authors did not state that they assessed study quality.

Data extraction
The number of patients with optimal or complete overall survival, and numbers for total overall survival were extracted. Data on the prognostic variables were extracted including median age and the proportion of patients with or undergoing the following: advanced primary versus recurrent endometrial cancer, uterine papillary serous histology, clear cell histology, grade 3 tumours, FIGO stage IV disease, optimal surgical cytoreduction, complete surgical cytoreduction, adjuvant chemotherapy, platinum-based chemotherapy, or adjuvant radiation therapy. Authors were contacted for further details where necessary.

The authors did not state how many reviewers extracted the data.

Methods of synthesis
Studies were pooled to calculate the change in median overall survival time (months), along with their 95% confidence intervals (CIs) for each of the above mentioned variables. Each 10% increase in each variable was quantified to correlate with an associated positive or negative change in median overall survival time. Multivariate analysis was not undertaken due to the limited number of studies.

It was unclear whether statistical heterogeneity was assessed.

**Results of the review**
Fourteen retrospective studies were included in the review (n=672 women; range 20 to 75).

A statistically significant positive association was found between median overall survival time and an increasing proportion of patients undergoing complete surgical cytoreduction (each 10% increase improved survival by 9.3 months, 95% CI 0.1 to 18.5) and an increasing proportion of patients receiving post-operative radiation therapy (each 10% increase improved survival by 11.0 months, 95% CI 4.3 to 17.6). A negative association was reported for an increasing proportion of patients receiving chemotherapy (each 10% increase decreased survival by 10.4 months, 95% CI -17.3 to -3.4).

None of the other variables investigated showed a statistically significant association with survival.

**Authors' conclusions**
In patients with advanced or recurrent endometrial cancer, complete cytoreduction to no gross residual disease was associated with significant improvement in median overall survival. The correlation between treatment modality and survival may be a surrogate marker for more precise factors such as location of disease, which may have influenced the decision to administer adjuvant radiation versus chemotherapy and were not able to be controlled for due to the limitations of the data in the included studies.

**CRD commentary**
The review question was clearly stated and was supported by appropriate inclusion criteria. The search of the literature was restricted to one database and included only English language articles, so language bias may have been introduced. It appeared that only published articles were sought, which meant that potentially relevant studies may have been missed. The authors did not state how each stage of the review process was undertaken, so reviewer error and bias could not be ruled out.

Study quality was not formally assessed; given that all the included studies were retrospective, the limitations inherent with this type of study design must be taken into consideration. The authors acknowledged certain limitations with the included studies, such as the small sample sizes, the small number of studies which prevented multivariate analysis, clinical heterogeneity, and selection bias. The methods for combining the studies were not explicitly stated and statistical heterogeneity was not formally assessed, so it was unclear whether pooling of the studies was appropriate.

Given the limited and heterogeneous evidence base, and the potential for missed studies and bias in the review, the authors' conclusions should be interpreted with caution.

**Implications of the review for practice and research**
**Practice:** The authors stated that, in the absence of contradictory evidence, it appears that surgical resection of all visible disease should be the goal for patients with advanced or recurrent endometrial cancer undergoing operative intervention.

**Research:** The authors stated that further research is needed to identify appropriate candidates for surgical cytoreduction.

**Funding**
Not stated.
Bibliographic details
Barlin JN, Puri I, Bristow RE. Cytoreductive surgery for advanced or recurrent endometrial cancer: a meta-analysis.
Gynecologic Oncology 2010; 118(1): 14-18

PubMedID
20434198

DOI
10.1016/j.ygyno.2010.04.005

Original Paper URL
http://dx.doi.org/10.1016/j.ygyno.2010.04.005

Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Cohort Studies; Endometrial Neoplasms /surgery; Female; Humans; Middle Aged; Neoplasm Recurrence, Local /surgery; Prognosis; Retrospective Studies; Survival Rate; Treatment Outcome

AccessionNumber
12010004566

Date bibliographic record published
29/09/2010

Date abstract record published
01/06/2011

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.