



Original Research

# Less-favourable prognosis for low-risk endometrial cancer patients with a discordant pre- versus post-operative risk stratification



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## KEYWORDS

Endometrial cancer;  
Risk stratification;

**Abstract Background:** Pre-operative risk stratification based on endometrial sampling determines the extent of surgery for endometrial cancer (EC). We investigated the concordance of pre- and post-operative risk stratifications and the impact of discordance on survival.

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Histology;  
Clinical decision-  
making;  
Overall survival

**Methods:** Patients diagnosed with EC within the first 6 months of the years 2005–2014 were selected from the Netherlands Cancer Registry (N = 7875). Pre- and post-operative risk stratifications were determined based on grade and/or histological subtype for 3784 eligible patients.

**Results:** A discordant risk stratification was found in 10% of patients: 4% (N = 155) had high pre- and low post-operative risk and 6% (N = 215) had low pre- and high post-operative risk. Overall survival of patients with high pre- and low post-operative risk was less favourable compared to those with a concordant low risk (80% versus 89%,  $p = 0.002$ ). This difference remained significant when correcting for age, stage, surgical staging and adjuvant therapy (hazard ratio 1.80, 95% confidence interval 1.28–2.53,  $p = 0.001$ ). Survival of patients with low pre- and high post-operative risk did not differ from those with a concordant high risk (64% versus 62%,  $p = 0.295$ ).

**Conclusion:** Patients with high pre- and low post-operative risk have a less favourable prognosis compared to patients with a concordant low risk. Pre-operative risk stratifications contain independent prognostic information and should be incorporated into clinical decision-making.

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## 1. Introduction

Endometrial cancer (EC) is the most common gynaecologic malignancy in developed countries, affecting approximately 1 in 37 women [1]. Standard treatment for patients with low-risk EC typically consists of hysterectomy and bilateral salpingo-oophorectomy. In patients with high-risk disease, lymphadenectomy or complete surgical staging and adjuvant therapy is recommended. Adjuvant therapy usually involves vaginal brachytherapy (VBT) or external beam radiotherapy (EBRT), sometimes with chemotherapy. Factors that are used to stratify patients into risk groups are histological subtype, grade, stage and lymphovascular space invasion (LVSI) [2–7].

To guide the choice of surgical treatment and extent of surgical staging, accurate pre-operative stratification of patients into low- and high-risk groups is essential. In case of clinical early-stage disease, pre-operative risk stratification is based on pre-operative endometrial samples, obtained by micro-curettage or curettage. The post-operative risk stratification is used to guide adjuvant therapy, and is based on the histological examination of tissue removed during surgery. Importantly, the post-operative risk stratification is currently viewed as the gold standard.

Discordance between pre- and post-operative risk stratifications may result in over- or under-treatment and may ultimately affect survival. In a high-risk EC cohort studied by Di Cello *et al.* [8], failure to recognise high-risk disease pre-operatively resulted in less-favourable survival outcomes compared to patients who were adequately stratified. On the other hand, the prospective MoMaTEC trial demonstrated that patients with discordant risk stratification had an intermediate prognosis compared to patients with concordant low- or

high-risk stratifications [9]. Studies based on larger patient cohorts are needed to clarify the effect of discordant risk stratification on survival of EC patients.

We aimed to investigate the concordance of pre- and post-operative risk stratifications in a large, unselected, population-based cohort, and to evaluate whether discordant risk stratification influences prognosis.

## 2. Methods

### 2.1. Data collection

Data from all consecutive patients diagnosed with EC between 1st January and 1st July of every year within the period 2005–2014 were retrospectively retrieved from the Netherlands Cancer Registry (NCR). The NCR contains data from all patients diagnosed with cancer in the Netherlands from 1989 onwards. The data of newly diagnosed patients are entered into the NCR after automated notifications from the Dutch Pathology Network (PALGA). The PALGA database contains the pathology assessments from all national pathology departments. It was established in 1971, and plays an important role in facilitating epidemiological research in the Netherlands. Within the NCR, information on vital status is obtained by annual linkage to the Municipal Personal Records Database and was available up to 1st February 2016.

Patients who were selected from the NCR were matched with pathology assessments in the PALGA database. All pathology assessments that were available within 6 months before and 6 months after surgery were retrieved. Pathology assessments from tissue specimens taken outside of that period were considered irrelevant for this study.

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