Factors influencing treatment decision and guideline conformity in high grade endometrial cancer patients—a population-based study

Sophia Scharl1, Tim Sprötge2, Michael Gerken2, Anton Scharf4, Atanas Iovatchinov, Elisabeth C. Inwald3, Olaf Ortmann3, Oliver Käbus5, Monika Klinkhammer-Schalke2, Thomas Papamichael4

1 Department of Radiation Oncology and Nuclear Medicine, Medizinisches Versorgungszentrum am Klinikum Rosenheim, Rosenheim, Germany, 2 Tumor Center, Institute for Quality Management and Health Services Research, University of Regensburg, Regensburg, Germany, 3 Department of Gynecology and Obstetrics, University Medical Center Regensburg, Regensburg, Germany, 4 Department of Gynecology and Obstetrics, Klinikum St. Marien Amberg, Amberg, Germany, 5 Department of Radiation Oncology, University Medical Center Regensburg, Regensburg, Germany

Purpose

National and international cancer guidelines have been established to aid physicians and patients in treatment decisions. Treatment according to guidelines has been demonstrated to improve survival in a number of different cancer entities. In a National Cancer Database study on 57,472 patients with non-endometrial endometrial cancer, the odds of survival were roughly 15% lower for patients not treated in accordance with NCCN guidelines. Nevertheless, only 43.8% received guideline-concordant therapy (GCT). Deviations from guidelines depend on several factors, including the patient’s preferences, age and comorbidities. The aim of this study was to assess the adherence to guideline recommendations concerning surgical and adjunct treatment in endometrial cancer. Furthermore, we sought to evaluate the reasons for non-adherence to guidelines by further examining the influence of comorbidities and age.

Methods

The influence of age, comorbidities, tumor stage and histological subtype on guideline adherence was evaluated by multivariable logistic regression in a cohort of 351 high grade endometrial cancer patients. High grade endometrial cancer was defined as carcinosarcoma, Type II (serous, clear cell, mixed cell carcinoma) and Type III histology.

As guideline recommendations were not very specific for FIGO stage IIB tumors, we carried out a second analysis including only stages IA/IIB (n=293).

Guideline conformity was measured according to the current German guideline at the time of diagnosis (DGGG Guideline available for 1998, 1999, 2004, 2006, 2008) and 52k guideline (published 2010).

Overall survival (OS) was calculated from the date of cancer diagnosis to the date of death from any cause. Risk-adjustment was performed in multivariable Cox regression analyses to adjust for confounding factors: age at diagnosis, year of diagnosis, comorbidity, obesity, LVE, lymph vessel invasion, blood vessel invasion, chemotherapy, radiotherapy and chemotherapy. Conformity was adjusted using Charlson Comorbidity Index (CCI) (Charlson et al. 1987). For multivariable binary logistic regression analysis, target variables were converted into a binary system (e.g. age ≥70/≤70; CCI≥1/+).

Results

Guideline adherence

FIGO stage I/IB (n=353)

The rate of GCT in the complete cohort was 34.3%. The extent in which patients were treated according to guideline recommendations significantly correlated positively with patients younger age (p<0.001) and higher tumour stage (p<0.001) (Table 3). While 42.3% of patients age <70 years received a guideline conform therapy, only 25.7% of patients ≥70 years were treated accordingly. The rate of patients treated in accordance with guideline recommendations was highest in the age group 50-59 years with 49.2% and lowest in the group of patients ≤80 years with only 13.3%. Comorbidities and CCI did not significantly influence guideline conformity (p=0.583 and p=0.543, respectively). The rate of patients treated according to guidelines in the group of CCI≥1 and CCI=0 was 37.5% and 33.1%, respectively. In a multivariable model, age (p<0.001) and tumour stage (p<0.001) remained significant.

FIGO stage I/IB (n=293)

The rate of GCT was 22.5%. GCT correlated positively with patients younger age (p<0.001), and higher tumour stage (p<0.020) (Table 4). Comorbidities and CCI did not significantly influence guideline conformity (p=0.877 and p=0.935, respectively). In a multivariable model, age (p<0.001) and tumour stage (p<0.021) remained significant.

Overall Survival

Kaplan-Meier analysis

CCI was associated with a significantly reduced OS (p<0.001), as was age 70 (p<0.001) (Figure 2). Other factors associated with worse OS were higher FIGO stage IIB, obesity, year of diagnosis (p<0.036), blood vessel invasion (p<0.016), lymph vessel invasion (p<0.001) and histological subtype (p<0.001). Surgery (p<0.001), systematic treatment (p<0.001) and radiotherapy (p<0.001) improved OS. When considering FIGO stages separately, CCI≥1 was only significant in FIGO stage I tumours (p<0.001) and unknown tumor stage (p<0.001). Age ≥70 years, on the other hand, was significant in stages I (p<0.001), II (p<0.030) and III (p<0.022). In stage IV tumours it trended towards significance (p=0.077). CCI≥1 was significantly associated with inferior OS in patients age 60-69 (p<0.001). In the other age groups, there was no statistically significant correlation between CCI≥1 and OS (p<0.001). Overall survival (OS) was remarkably lower in patients not treated according to guidelines (p=0.042) and in patients treated in conformity to guidelines (p=0.039).

Cox Regression Analysis

In a multivariable model, age (p<0.001), FIGO stage (p<0.001) and histological subtype (p<0.001), surgery (p<0.001), chemotherapy (p<0.001), obesity (p<0.011) and systematic treatment (p<0.001) significantly predicted OS. CCI≥1 (p=0.541), year of diagnosis (p=0.060), lymph vessel invasion (p=0.103), blood vessel invasion (p=0.322) and radiotherapy (p=0.155) were not significantly associated with OS.

Conclusions

Age seems to be the strongest independent factor leading to guideline deviation. Comorbidities were associated with less aggressive treatment, but not with deviations from guidelines.

References


Contact

Tumorzentrum Regensburg – Institut für Qualitätssicherung und Versorgungsforschung der Universität Regensburg
Am BioPark 9, 93053 Regensburg, zentrum.tumor@ur.de