Evolving trends in the surgical staging of endometrial cancer patients in Germany: Analysis of a nationwide registry with special emphasis on perioperative outcomes

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Abstract

Purpose

The present study compared the use and outcomes of open surgical staging, laparoscopic surgical staging and robotic-assisted surgical staging in all patients suffering from endometrial carcinoma undergoing surgery in Germany between 2007 and 2018.

Methods

All patients with the diagnosis of endometrial carcinoma undergoing open surgical staging, laparoscopic surgical staging and robotic-assisted surgical staging were identified by international classification of diseases (ICD) or specific operational codes (OPS) within the database of the German federal bureau of statistics.

Results

Between 2007 and 2018, a total of 85,204 patients underwent surgery for endometrial carcinoma. Since 2013 laparoscopy was the leading approach in the surgical staging. The use of robotic-assisted laparoscopy increased steadily since 2011 with a share of 3% in 2018. Open surgical staging was associated with a higher risk of in-hospital mortality than laparoscopic surgical staging (1.3% vs. 0.2%, p < 0.001), of prolonged mechanical ventilation (1.3% vs. 0.2%, p < 0.001), and of prolonged hospital stay (13.7 ± 10.2 vs. 7.2 ± 5.3, p < 0.001). 0.04% patients undergoing laparoscopy were converted to laparotomy. The perioperative outcomes of surgical staging by laparotomy compared with robotic-assisted were comparable. None of the robotic-assisted treated patients died or was converted into laparotomy. Costs were highest in the open laparotomy staging group, followed by robotic assisted. Conventional laparoscopic approach caused lowest costs (8286 ± 7533€ vs. 7083 ± 3893€ vs. 6047 ± 3509€).

Conclusion

The present analysis shows that conventional laparoscopy is the standard therapy of endometrial carcinoma with excellent in-hospital outcomes in clinical practice. Robotic-assisted laparoscopy is an emerging technology with convincing results similar to

Introduction

Endometrial cancer is the most common gynecological malignancy in Europe and continues to be a major cause of morbidity and mortality. The estimated number of new endometrial carcinoma cases in Europe in 2018 was 121 578 with 29 638 deaths. The incidence has been rising with an ageing
population and increased obesity. (Concin, Matias-Guiu et al. 2021) In 1988, the FIGO introduced the concept of surgical staging of endometrial cancer to provide reliable information about the pathological morphology of the primary tumour and lymph node status, as well as the resulting prognosis and possible indication for adjuvant therapy (Abu-Rustum, Zhou et al. 2011, Rungruang and Olawaiye 2012). Over the last decades, minimal invasive approaches came increasingly into use. Favorable complication rates, shorter hospital stay and comparable outcomes compared to open surgery observed in the LAP-2 trial turned the laparoscopic approach into standard treatment (Walker, Piedmonte et al. 2012, Capozzi, Sozzi et al. 2019).

A survey conducted by the German Gynecologic Laparoscopy Working Group highlighted the fact that more than 50% of the surgical staging procedures for endometrial cancer in Germany in 2012 were carried out by laparoscopy (Juhasz-Boss, Mallmann et al. 2013). Laparoscopic staging has been found to have similar outcomes to laparotomy for early stage (Palomba, Falbo et al. 2009, Walker, Piedmonte et al. 2012, He, Zeng et al. 2013, Asher, Obermair et al. 2018, Galaal, Donkers et al. 2018, Nasioudis, Frey et al. 2020) endometrial cancers in terms of disease-free survival and complications and has quickly supplanted open surgery as the most widely used approach.

In the last two decades robotic-assisted surgical techniques were developed, refined and introduced into clinical practice (Zanagnolo, Achilarre et al. 2018). The main advantages are thought to include three-dimensional vision, absence of tremor, camera stability, and shorter learning curves compared to the laparoscopic approach alone (Zanagnolo, Achilarre et al. 2018). In Germany, robotic-assisted surgical staging of endometrial cancer was introduced in 2011. Robotic assisted surgery may have advantages in several regards, but may also be more costly (Wright, Burke et al. 2012, Rabinovich 2015, Bogani, Multinu et al. 2016).

The latest Cochrane review of robot-assisted surgery in gynecology (Lawrie, Liu et al. 2019) finds low-certainty evidence that there might be little or no difference in any complication rates between robotic-assisted and conventional laparoscopic hysterectomy, however these results combined studies with malignant and non-malignant underlying diseases.

Evidence suggests that robotic-assisted surgery may be advantageous in specific patient groups, such as obese patients, where traditional minimally-invasive surgery may be more difficult due to the increased abdominal wall and the amount of intraabdominal fat (Capozzi, Sozzi et al. 2019).

The main aim of this study was to analyze and describe the evolving trends in the surgical staging of endometrial cancer in Germany from 2007 and 2018.

**Methods**

Since 2005, data on all hospitalizations in Germany are available for scientific use via the Diagnosis Related Groups statistics collected by the Research Data Center of the Federal Bureau of Statistics (DESTATIS). These hospitalization data, including diagnoses and procedures, are a valuable source of
representative nationwide data on the in-hospital treatment of patients. This database represents a virtually complete collection of all hospitalizations in German hospitals that are reimbursed according to the Diagnosis Related Groups system. From this database, we extracted data on patients with endometrial carcinoma (ICD-10 (International classification of diseases, Version 10) C54*) that underwent surgery (Operation and Procedure Codes (OPS) 5-683.0, 5-683.1 or 5-683.2) with or without robotic assistance (OPS 5-987). Finally, three groups of patients were distinguished and compared:

1. open surgical staging by laparotomy
2. laparoscopic surgical staging
3. robotic-assisted surgical staging

Our study did not involve direct access by the investigators to data on individual patients but only access to summary results provided by the Research Data Center. Therefore, approval by an ethics committee and informed consent were determined not to be required, in accordance with German law. All summary results were anonymized by DESTATIS. In practice, this means that any information allowing the drawing of conclusions about a single patient or a specific hospital was censored by DESTATIS to guarantee data protection. Moreover, in order to prevent the possibility to draw conclusions to a single hospital, the data are verified and situational censored by DESTATIS in those cases.

The analysis focused on six different endpoints: in-hospital mortality, acute kidney injury, mechanical ventilation, discharge destination (home, other hospital of rehabilitation facility), length of hospital stay and reimbursement. Acute kidney was defined using ICD (N17*). In-hospital mortality, length of mechanical ventilation during operation and postoperative, discharge destination, length of hospital stay and reimbursement were part of DESTATIS’ main set of variables. The baseline characteristics were used to calculate the Charlson Comorbidity Index (CCI) in order to assess a general patient’s health status. (Charlson, Pompei et al. 1987)

No imputation for missing values could be conducted due to the absence of codes indicating that data were missing. If the patient’s electronic health record did not include information on a clinical characteristic, it was assumed that that characteristic was not present. Time trends were calculated using linear regression models. Between-group differences of patient characteristics and in-hospital outcomes were calculated using unpaired t-test and Fisher’s exact test without adjustment for multiple testing. Thus, p-values may not be interpreted as confirmatory but are descriptive in nature.

All analyses were performed with Stata 16 (StataCorp, College Station, Texas, USA).

Results

Trends of surgery techniques between 2007 and 2018

Between 2007 and 2018, a total of 85,204 patients underwent surgical staging for endometrial carcinoma (Fig. 1). While the overall number of surgeries increased from 6499 surgeries (2007) to 8032 (2018, p <
0.001), the annual number of laparotomies decreased from 5412 (2007) to 2497 (2018) (p < 0.001) while the number of minimal invasive surgeries increased from 1087 (2007) to 5364 (2018) (p < 0.001) (Fig. 1). Since 2011, the number of robotic-assisted laparoscopic surgery also increased steadily from 55 (2011) to 171 (2018), but still account to a very low share of all laparoscopic surgeries (3% in 2018, Fig. 1).

**Baseline characteristics**

In comparison to patients undergoing laparotomy, laparoscopic surgery patients were younger (p < 0.001) and were at lower risk of severe outcome and death according to the Charlson Comorbidity Index (CCI) (p < 0.001). Among the patients undergoing laparoscopic surgery, however, patients undergoing robotic-assisted laparoscopic surgery were again younger (p < 0.001) but were at higher risk of severe outcome and death according to the CCI (p < 0.001, Table 1). A detailed overview regarding age distribution of patients assigned to either surgical, laparoscopic, or robotic-assisted laparoscopic surgery are shown in Fig. 2 (Fig. 2). The peak age of patients undergoing open surgery (Mean age 68.29 ± 11.84), and laparoscopy (Mean age 66.24 ± 11.77) is between 73 and 74 years in contrast peak age is between 55 and 56 years in patients assigned for robotic assisted laparoscopy (Mean age 63.04 ± 11.40).

<table>
<thead>
<tr>
<th>Table 1: Baseline characteristics</th>
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<tbody>
<tr>
<td><strong>Laparotomy</strong></td>
</tr>
<tr>
<td>n = 45.639</td>
</tr>
<tr>
<td>Mean ± sd</td>
</tr>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td><strong>CCI</strong></td>
</tr>
</tbody>
</table>

* CCI Charlson Comorbidity Index

**In-hospital outcomes laparotomy vs. laparoscopic surgery**

Patients undergoing surgery by laparotomy were associated with a higher risk of in-hospital mortality than laparoscopic surgery patients (1.3% vs. 0.2%, p < 0.001). The share of post-operative prolonged mechanical ventilation was higher in the surgical group compared to the laparoscopic group (1.3% vs. 0.2%, p < 0.001). 0.04% patients undergoing laparoscopy surgery were converted to laparotomy. Moreover, open surgery patients had a longer hospital stay (13.7 ± 10.2 vs. 7.2 ± 5.3, p < 0.001) and were more likely to be discharged towards another hospital or rehabilitation facility (all p < 0.001). In summary, the open surgical approach causes significant higher reimbursement compared to the minimal invasive approach with laparoscopy (laparotomy: 8286 ± 7533€; conventional laparoscopy 6047 ± 3509€, p < 0.001) (Table 2).
### Table 2

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Laparotomy n = 45.639</th>
<th>Laparoscopy n = 38.793</th>
<th>Robotic assisted n = 772</th>
<th>p-value conv. vs. endo.</th>
<th>p-value endo. vs. robo.</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital mortality</td>
<td>1.3%</td>
<td>0.2%</td>
<td>0.00%</td>
<td>&lt; 0.001</td>
<td>0.64</td>
</tr>
<tr>
<td>Ventilation &gt; 48h</td>
<td>1.3%</td>
<td>0.2%</td>
<td>&lt; 0.4%*</td>
<td>&lt; 0.001</td>
<td>0.70</td>
</tr>
<tr>
<td>Conversion to open surgery</td>
<td>n/a</td>
<td>0.04%</td>
<td>0.00%</td>
<td>n/a</td>
<td>0.57</td>
</tr>
<tr>
<td>Length of stay (in days) ± SD</td>
<td>13.7 ± 10.2</td>
<td>7.2 ± 5.3</td>
<td>7.3 ± 5.9</td>
<td>&lt; 0.001</td>
<td>0.84</td>
</tr>
<tr>
<td>Discharge home</td>
<td>95.2%</td>
<td>98.6%</td>
<td>99.6%</td>
<td>&lt; 0.001</td>
<td>0.01</td>
</tr>
<tr>
<td>Discharge 2nd hospital</td>
<td>1.4%</td>
<td>0.5%</td>
<td>&lt; 0.4%*</td>
<td>&lt; 0.001</td>
<td>0.78</td>
</tr>
<tr>
<td>Discharge rehabilitation</td>
<td>0.8%</td>
<td>0.2%</td>
<td>&lt; 0.4%*</td>
<td>&lt; 0.001</td>
<td>0.66</td>
</tr>
<tr>
<td>Reimbursement ± SD in Euro</td>
<td>8286 ± 7533</td>
<td>6047 ± 3509</td>
<td>7083 ± 3893</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

* Due to privacy concerns a share of < 0.4% is blinded by the federal bureau of statistics

**Outcomes of conventional laparoscopic and robotic assisted laparoscopic approach**

We sought to compare the outcomes of both approaches. Of patients staged by robotic assisted surgery no patients died since its introduction in 2011. However, the difference to conventional laparoscopic surgery regarding in-hospital mortality did not reach significance (0.2% vs. 0.0%, p = 0.64). The share of prolonged ventilation was similar in both treatment groups (0.2% vs. <0.4% (p = 0.70). No patient treated with robotic assisted laparoscopy had to undergo conversion to open surgery. The use of robotic assisted surgery did not alter length of hospital stay (7.2 ± 5.3 7.3 ± 5.9, p = 0.84), but patients undergoing robotic assisted laparoscopy were more likely to be discharged home (instead of transfer to another hospital or rehabilitation facility, p = 0.01). At the same time, robotic-assistance is associated with a higher reimbursement in comparison to laparoscopic surgery without robotic assistance (robotic assisted: 7083 ± 3893€; conventional laparoscopy: 6047 ± 3509€, p < 0.001) (Table 2).

**Discussion**

The present study analyzed the use and in-hospital outcomes of patients undergoing surgery for endometrial cancer. We demonstrated with a nationwide dataset including all cases performed in Germany between 2007 and 2018 that minimal-invasive surgery has increasingly become the standard staging procedure for patients with endometrial cancer with superior in-hospital outcomes in clinical...
practice compared to surgery by laparotomy. Moreover, the use of robotic assisted laparoscopy is emerging with comparable in-hospital safety profile as conventional laparoscopic surgery. This is in line with studies from other countries (Jorgensen, Mogensen et al. 2019).

Endometrial carcinoma is a major cause of morbidity and mortality since it is a common cancer in women with rising incidence and mortality (Henley, Ward et al. 2020, Lu and Broaddus 2020). Accordingly, we found increasing operation procedures during the observed period between 2007 and 2018 in Germany indicating an increasing incidence. Since 2013 patients suffering from endometrial carcinoma were more often treated with laparoscopy than open surgery in Germany.

Although we found increasing use of robotic assisted laparoscopy from 2011 until 2018, the share of robotic-assisted treatment in all patients suffering from endometrial carcinoma was around 2%. Compared to other countries, in Germany there is a long lasting tradition in minimal-invasive techniques in gynecological surgery (Lehmann-Willenbrock, Riedel et al. 1992). This might be a reason for the relatively slow increase in robotic assisted surgeries for the surgical staging in endometrial cancer. Patients assigned to robotic-assisted laparoscopy were younger but had a higher risk as assessed by CCI compared to conventional laparoscopic treated patients.

Two randomized trials showed the superiority of laparoscopic surgery in respect to in-hospital complications and quality of life compared to open surgical staging. (Walker, Piedmonte et al. 2009, Janda, Gebski et al. 2010) The present study confirms these findings in clinical practice. Laparoscopic treated patients had lower in-hospital mortality and were less frequently prolonged ventilated after surgery. A conversion to open surgery was a rare event and occurred in only 0.04% of all laparoscopic treated patients. Moreover, the length of hospital stay was almost halved after minimal invasive approach.

Although robotic assisted laparoscopy was less frequently used in the current study, in-hospital outcomes are comparable with conventional laparoscopic surgery. Until 2018 no reported death among patients undergoing robotic assisted surgery was recorded. Furthermore, no conversion to open surgery was necessary. This is in line with the result from randomized controlled trial (Maenpaa, Nieminen et al. 2016).

Additionally, the national introduction of robotic surgery in Denmark changed the surgical approach for early-stage endometrial cancer from open surgery to minimally invasive surgery. This change in surgical approach was associated with a significantly reduced risk of severe complications (Jorgensen, Mogensen et al. 2019). In the current study, robotic-assisted treated patients were even more often discharged home. However, the total number of robotic-assisted procedures reported in the present analysis was very low and may account for the beneficial effects. Nevertheless, the advantages of robotic assisted laparoscopy may increase with increasing experience and further refinement of the technology (Bahra and Pratschke 2020).
Current evidence from the Danish Gynecological Database showed that national introduction of robotic surgery for early-stage endometrial cancer was associated with improved survival compared to open surgery. This intriguing observation must finally be proven in randomized clinical trials.

The raw materials and supplies of conventional and robotic-assisted laparoscopy are higher than those of conventional open surgery. We found that the increased reimbursement were outreached by higher resource utilization after open surgical approach. The reimbursement was 2000€ lower in laparoscopic group compared to open surgery. Robotic assisted laparoscopy was more expensive than conventional laparoscopy but caused still less costs than open surgery. However, robotic systems are still more costly but costs for robotic surgery will decline in the next years due to its increased use. Thus the cost effectiveness of robotic surgery is controversial and varies greatly in different fields (Ramsay, Pickard et al. 2012). Our study suggests that robotic assisted laparoscopy in treatment of endometrial cancer is cost-effective compared to open surgery; however, a benefit in comparison to conventional laparoscopy has to be proven.(Knight and Escobar 2014)

**Strengths and limitations**

The strengths of this study include a large nationwide dataset of patients with endometrial cancer. The dataset is well controlled by independent supervision. Therefore, it is reliable in respect to clinical characteristics and outcome risk analyses according to the three treatment groups. Several limitations need to be considered. Analyses were performed in a registry study setting from a national database according to ICD and OPS codes. Important clinical factors of patients such as a decision to palliative care might therefore not have been considered. Furthermore, there was no follow-up to evaluate long-term oncological outcomes of the three treatment groups.

**Conclusion**

The present analysis shows that minimal-invasive surgical staging is the standard therapy of endometrial carcinoma in Germany with excellent in-hospital outcomes in clinical practice. Robotic-assisted laparoscopy is an emerging technology with convincing results, which are comparable to conventional laparoscopy.

**Declarations**

**Funding**

The study was supported by internal funding of the University Hospital Freiburg

**Conflicts of interest/Competing interests**

All authors declare no conflicts of interest.

**Availability of data and material**
Data is available from the German Federal Bureau of Statistics

**Code availability (software application or custom code)**

Not applicable

**Authors’ contributions**

Katrin Roth: Conception, design of the work. Acquisition, analysis, and interpretation of data for the work; writing manuscript, drafting the work and final approval

Klaus Kaier: Statistical analysis and interpretation of the data, writing manuscript, final approval.

Peter Stachon: Conception, design of the work. Acquisition, analysis, and interpretation of data for the work; drafting the work and final approval

Constantin von zur Mühlen: Acquisition, analysis, and interpretation of data for the work, final approval.

Florin-Andrei Taran: Acquisition, analysis, and interpretation, critical revision, and final approval Daniel Duerschmied: Acquisition, analysis, and interpretation, critical revision, and final approval

Maximilian Klar: Supervision, interpretation, critical revision, and final approval

Ingolf Juhasz-Böss: Supervision, conception, design of the work. Acquisition, analysis, and interpretation of data for the work, critical revision, and final approval

**Ethics approval**

Our study did not involve direct access by the investigators to data on individual patients but only access to summary results provided by the Research Data Center. Therefore, approval by an ethics committee and informed consent were determined not to be required, in accordance with German law.

**Consent to participate (include appropriate statements)**

Our study did not involve direct access by the investigators to data on individual patients but only access to summary results provided by the Research Data Center. Therefore, approval by an ethics committee and informed consent were determined not to be required, in accordance with German law.

**Consent for publication**

All authors gave their consent for publication.

**References**


**Figures**

![Graph showing the number of procedures per year for laparotomy, laparoscopy, and robotic-assisted laparoscopy.](image)

**Figure 1**

Number of procedures All procedures in patients with endometrial carcinoma were identified by ICD codes and operational procedures codes. The blue line shows conventional surgery per year, red line is laparoscopy, and the green line robotic-assisted laparoscopy.
Figure 2

Age distribution of patients. All procedures between 2007 and 2018 and age distribution was determined for conventional surgery (above), laparoscopy (middle), and robotic-assisted laparoscopy (below).