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Title page

Long term resource consequences of a nationwide introduction of robotic surgery for women with early stage endometrial cancer

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Abstract

Objective: The majority of cost-studies related to robotic surgery has a short follow-up and primarily report the costs from the index surgery. The aim of this study was to evaluate the long-term resource consequences of introducing robotic surgery for early stage endometrial cancer in Denmark.

Methods: The study included all women with early stage endometrial cancer who underwent robotic, laparoscopic and open access surgery from January 2008 to June 2015. Data was linked from national databases to determine resource consumption and costs from hospital treatments, outpatient contacts, primary health care sector visits, labor market affiliation and prescription of medication. Each patient was observed in a period of 12 months before- and after surgery. The key exposure variable was women who were exposed to robotic surgery compared to those who were not.

Results: A total of 4133 women underwent surgery for early stage endometrial cancer. The study found additional costs of $7309 (95% confidence interval [CI] 2100-11620, P=0.001) per patient in the group exposed to robotic surgery including long-term costs post-surgery compared to the non-exposed group (non-robotic group). When controlling for time trends, the introduction of robotic surgery did not reduce the number of bed days (mean diff -0.42, 95% CI -3.03-2.19, P=0.752).

Conclusions: The introduction of robotic surgery for early stage endometrial cancer did not generate any long-term cost savings. The additional costs of robotic surgery were primarily driven by the index surgery. Any reduction in bed days could be explained by time trends.

1. Introduction

The robotic platform has been rapidly adopted for gynecological procedures in the US and Europe thereby reducing the use of Open Access Surgery (OAS) [1]. The establishment of robotic surgical availability is associated with high initial purchase costs of the platform and additional maintenance and surgical supply costs [2, 3]. In a recent review, we compared the methodological design in 32 cost studies within the gynecological field [2]. Most studies suffered from selection bias, as they were not able to control for data on tumor stage, comorbidities and/or unobservable patient characteristics [2, 4-8], nor did they control for prior levels of health care service use. The majority of these studies had a short follow-up reporting the costs from the index surgery without investigating the long-term resource implications of Robotic Minimally Invasive Surgery (RMIS) [2]. There is currently insufficient evidence as to whether the immediate costs of introducing RMIS are offset by long term savings due to e.g. reduced need for rehabilitation services, reduced utilization of primary care services, fewer outpatient visits and/or faster return to the labor market, compared to other surgical procedures. Previous studies comparing RMIS with OAS for women with endometrial cancer have shown shorter length of stay from the index surgery [9-11], fewer readmissions [9] and reduced risk of severe complications [12].

The present study aims to evaluate the long-term resource consequences of introducing RMIS for early stage endometrial cancer in Denmark. The evaluation strategy has three major strengths. Firstly, we took advantage of the fact that RMIS was introduced in the regions of Denmark at different points in time and at different paces between 2008 and 2013. This allowed assessment of exposed and non-exposed individuals simultaneously, and minimization of potential patient selection bias as exposure to RMIS depended on RMIS introduction patterns and not women's characteristics. Secondly, we applied an analytical approach where the patient acted as her own control. We controlled for use of health care resources one year prior to surgery, which allowed us to isolate the resource use associated with surgery. Thirdly, we operated with a follow-up period of one-year post-surgery, and used high quality registry data to monitor the long-term resource consequences of RMIS in the primary and secondary health care sector. We also measured production losses due to sickness leave or earlier exit from the labor market.

2. Materials and methods

Study design

RMIS was gradually introduced in Denmark over a five-year period from 2008 to 2013. We included all women in Denmark who underwent surgery for early stage endometrial cancer FIGO stage I-II from January 1st, 2008 to June 30th, 2015. Women operated before the date of the first RMIS performed in their region were allocated to the non-exposed group. The non-exposed group (non-robotic group) mainly underwent open access surgery and a minor proportion had conventional laparoscopy. Women in the exposed group were operated after the date of the first RMIS performed in their region and were considered as *exposed* to RMIS. The majority in the exposed group underwent robotic surgery and a minor proportion underwent laparoscopy and open access surgery.

The treatment of endometrial cancer in Denmark is conducted in accordance with national guidelines from the Danish gynecological cancer group [13] and revised every 3-4th year. The gold standard of surgery consists of total hysterectomy and bilateral salpingo-oophorectomy. Women with increased risk of metastatic disease undergo additional staging lymphadenectomy (pelvis +/- para-aortic) and omentectomy for certain histological subtypes [14]. To estimate the resource consequences of introducing RMIS we utilized the gradual phase-in of this new technology and constructed a quasi-experimental design comparing women who were exposed to robotic surgery with those who were not. We assume that the time and place at which a woman undergoes surgery for endometrial cancer is random and independent of patient characteristics such as age, BMI and comorbidity. Our key exposure variable is the fraction of women who had RMIS out of the total number of women receiving surgery for early stage endometrial cancer in a given region and at a specific time. Our primary outcomes are changes in resource use and costs, as well as labor market affiliation, in the first year after surgery compared to the year before surgery.

Data sources

The study population was extracted from the Danish Gynecological Cancer Database (DGCD) which covers clinical, surgical, and pathology data. Data are registered mandatory by gynecologists specialized in gynecological cancer surgery and pathologists [15]. The DGCD is a nationwide, clinical quality registry that covers 97% of women diagnosed with endometrial cancer [15]. From this database we extracted information on the surgical modality, date of surgery, location of the hospital, Body Mass Index (BMI), histological type, grade, FIGO stage, and information on whether lymphadenectomy was performed.

All Danish residents have a unique personal identification number (CPR-number) which enables accurate linkage between all national registers [16]. The study population was linked with individual-level register data from the Danish National Patient Register (NPR) [17], The Danish National Health Service Register [18], and The Danish Education register [19]. The NPR holds information on dates of all hospital admissions and discharges, hospital in-patient treatments, and operations including re-operations, outpatient contacts, and diagnoses [17]. The National Health Service Register holds data from the primary health care sector, accounting for health services [18]. Any production losses due to changes in job market affiliation were measured by comparing individual-level labor market data and sickness benefit data before and after surgery [20]. The DREAM database includes weekly information for all Danish citizens who have received social benefit or any other transfer benefit [21].

Costs of hospital admissions were estimated using unit costs derived from the Diagnosis Related Grouping system (DRG) for somatic in-patients [22], the Danish Ambulatory Grouping System (DAGS) for ambulatory patients [22], The National Health Service Register for primary health contacts [18], and The Danish National Prescription Registry. The Danish National Prescription Registry provide information on the costs for prescription medication handed out from pharmacies [23]. The national DRG-tariffs for surgery for endometrial cancer included activities from hospital admission to discharge. Outpatient visits and reoperations associated with the index hospitalization were reimbursed separately. DRG tariffs are based on annual detailed costing reporting´s from all public hospitals in Denmark, and reflect the national average operating costs within each DRG group [22]. The DRG tariffs thus represent reimbursement fees that do not reflect the precise cost of treating the individual patient. DRG-tariffs are adjusted each year and published by the Danish Health Authority [22]. All costs were adjusted to price index 2015 [24] and converted into USD ($).

Statistical methods

Each patient was observed in a pre-treatment period of 12 months before the date of the index surgery and a post-treatment period of 12 months after the date of the index surgery. To control for potential pre-surgery differences in health care service utilization, and to isolate the costs associated with surgery, we applied a

Difference-in-Difference (DiD) design. In the DiD design, the patient acts as her own control and the outcome variable is *change* in resource use post-surgery versus pre-surgery [25-27]. In the analyses, the focus is to estimate whether the introduction of RMIS, measured by level of exposure (proportion of patients being treated with RMIS out of the total number of patients in a given region and calendar year), was associated with changes in the primary outcome variables measuring resource use and costs as obtained from registers. Underlying the DiD design lies the common trends assumption to ensure internal validity of the approach. For ease of presentation the exposure variable was dichotomized (exposed; non-exposed) in the descriptive analyses but modelled as a continuous variable in the regression models. The common trends assumption requires the exposed and non-exposed group to have the same parallel trends in outcomes the year before index surgery. Time series in resource use were plotted graphically for outpatient visits, primary sector visits, employment status and sickness benefit and the pattern of costs were plotted for primary sector visits, outpatient visits, and prescription of drugs per woman to evaluate whether the common trends assumption was fulfilled in the one-year period prior to surgery (Figure 1).

To ensure that potential differences in baseline characteristics did not drive differences in trends, a linear regression was performed. We adjusted for potential time trends by including fixed effects for calendar year, and for potential differences in resource use across regions by including fixed effects for each region.

This resulted in the fully adjusted model in which our exposure variable was defined as the proportion of patients being treated with RMIS out of the total number of patients receiving surgery for early stage endometrial cancer by calendar year and region:

$$\Delta C_i = C_{i1} - C_{i0} = c + \beta_1 p_{RMIS_i} + \sum_k \beta_k \times X_{ik} + \varepsilon_i$$

Here ΔC_i indicates the difference in costs per patient the year after surgery (C_{i1}) relative to the year prior to surgery (C_{i0}), c denotes the model intercept, β_1 is the key result denoting the association between the outcome variable ΔC_i and our exposure variable p_{RMIS_i}, X_{ik} represents covariates (age, BMI, Charlson comorbidity index, ASA score, histopathological risk groups, lymphadenectomy, education level, socioeconomic group) including region-of-surgery and year-of-surgery fixed effects, and ε_i denotes the residuals in the linear regression model. To investigate any possible over adjustment in time trends a sensitivity analysis was performed in which we analyzed data for a short time period only (2011-2012).

We performed a further sensitivity analysis excluding patients who underwent surgery in the region of Southern Denmark due to potentially confounding research projects related to the postoperative follow-up visits taking place in the region during the time of observation.

Results are reported as mean differences with 95% confidence intervals (CI) based on bootstrapping with 5000 replicates to take into account the skewed nature of cost and resource use data. The difference-in-difference mean estimates for resource use and costs one year post-operatively (contacts/costs per patient) are reported in three models, 1) an unadjusted model, 2) a model adjusted for patient characteristics and region of surgery and 3) a model that is further adjusted for surgical year. Resource use and costs are compared between 12 months before and 12 months after the index surgery. Resource use and costs of bed days were analyzed both including and excluding the index surgery stay to investigate if potential differences were driven by the index surgery stay. Resource use and costs are reported as year totals, while employment status and sickness benefit are reported as number of weeks per year.

A two-sided p-value below 0.05 was considered statistically significant. All analyses were performed using Stata version 15.1. Data was pseudo-anonymized and administered by Statistics Denmark.

Ethical consideration

The study was approved by the Data Protection Agency (18/43728).

3. Results

During the study period, 4133 women with early stage endometrial cancer underwent surgery in Denmark (Figure 2). Before RMIS was introduced 78% of women underwent open access surgery (Figure 2). During the 7.5 years of observation while robotic surgery was introduced nationwide, 72% of the women underwent minimally invasive surgery (laparoscopy and RMIS). In the present study these women are nominated “exposed” vs. “non-exposed” but modelled as proportions in the regression models. Figure 3 illustrates the introduction of RMIS nationwide and separately for each region. Conventional laparoscopy was used in 22% of the women in the exposed and the non-exposed group. As it appears, the use of conventional laparoscopy increased before the introduction of RMIS and decreased slightly during the RMIS period (Figure 3). Sociodemographic characteristics between the groups are given in Table 1.

Resource use

Patients assigned to the exposed group had almost four fewer bed days the year following surgery compared to the non-exposed group, when adjusting for patient characteristics only (Table 2). After further adjustment for surgical year no statistically significant difference was observed in bed days between the exposed and non-exposed group (Table 2). This was true for both index surgery and subsequent hospitalizations. Also, no statistically significant difference in resource use was observed for primary sector- or outpatient visits between the exposed and the non-exposed group (Table 2).

Costs

The total costs one-year post-surgery from hospitalization, primary sector visits, outpatient visits and prescription drugs were $7309 higher per patient in the exposed group compared to the non-exposed group (p=0.001) (Table 3). The costs related to the hospitalization including the index surgery and subsequent hospitalizations were $7434 higher per person in the exposed group vs. non-exposed group (p=0.001) (Table 3). No statistically significant cost difference was found between the exposed and the non-exposed group for the other cost categories (Table 3).

A sensitivity analysis, which included a smaller sample based on a shorter time period showed results consistent with the main analysis, indicating no signs of over-adjustment for time trend. The sensitivity analysis excluding patients from the Region of Southern Denmark did not change any results significantly.

4. Discussion

This study included all women with early stage endometrial cancer who underwent surgery at Danish hospitals over a period of 7.5 years. Long-term resource use and costs related to their index surgery and the year following surgery were evaluated. The introduction of robotic surgery did not generate any long-term cost savings related to primary sector, outpatient visits, or prescription of medicine in this population of gynecological cancer patients. The introduction of robotic surgery was associated with additional costs of

$7309 per patient in the exposed group compared to non-exposed and the extra costs were mainly attributable to the index surgery. Our findings are in line with other cost studies reporting RMIS to be more costly than open and conventional laparoscopic surgery in women with endometrial cancer [4, 7, 28-31]. Smith et al. reported that the overall hospital charge was 40% higher with RMIS compared to laparoscopy and open access surgery [31]. In contrast to our findings, Laursen et al. found that RMIS generated cost savings of $3861 per women when compared with open access surgery and increased costs of €$3749 when compared with laparoscopy in Danish cancer patients [32]. Important differences between the study of Laursen and the present study concern the selection of the patient population and the data source. Further, our study applied an intention to treat approach thus minimizing the risk of selection bias due to non-random allocation to treatment modalities. Importantly, our findings relate to the particular patient group of women with early stage endometrial cancer who are comparatively unaffected by their cancer when diagnosed. Hence, our results cannot be used to generalize about resource use and costs related to robotic surgery in other patient groups with e.g. a greater need of longer rehabilitation or sick leave. However, the evaluation method used in the present study can be applied to other patient groups for a valid non-biased evaluation of resource use and costs related to the introduction of a new technology.

In a recent study, we showed that a Danish nationwide introduction of robotic surgery for early stage endometrial cancer is associated with reduced risk of severe complications and improved survival independent of histopathological risk group [12, 33]. However, taking time trends as well as patient characteristics into account, the present study was unable to demonstrate that the introduction of RMIS was associated with a significant reduction in bed days as would be expected in case of fewer re-admissions due to severe complications after minimally invasive surgery. Scrutinizing the graphical presentation of the RMIS introduction in the different regions in Denmark reveals different trends of robotic introduction in two regions (the region of central Jutland and the Zealand region). These regions had a very slow introduction of RMIS compared to the other regions while the proportion of women undergoing conventional laparoscopy increased dramatically. This led to an increased use of conventional laparoscopy already before the introduction of RMIS in these regions and contributed to the decrease in bed days in the non-exposed group. Further, during the time period with robotic introduction another time trend arose; even women who underwent open surgery had fewer bed days compared to earlier time periods. This was likely due to emerging evidence regarding the importance of early mobilization and faster recovery at home. It may be looked at as a paradigm shift and is likely to influence on the results when including a comparatively large time period in the analyses. This emphasizes the importance of adjusting for potential time trends when including patients over several years. In the present study, length of stay was driven by time trends rather than surgical modality.

Using the Danish DRG-tariffs, all gynecological procedures were listed as more expensive when involving robotic surgery i.e. a simple hysterectomy with bilateral salpingo-oophorectomy without lymph node dissection is valued at $11259 using robotic surgery versus $7722 without the robotic assistance for the same procedure. The in-hospital costs of RMIS is likely to decrease in the years to come due to increased surgeon experience and hence reduction in procedure- and operating room time. This prediction is supported by Avondstondt et al. who found a reduction in total costs attributable to a decrease in the operating room costs and costs of anesthesia after five years of experience with RMIS [34]. In addition, present patents related to the robotic platform will expire in the near future. The lack of market competition is highly related to the high costs of robotic instrument supplies. Same-day discharge may be another cost-saving procedure for RMIS. Several studies have found this safe and feasible for the majority of women undergoing minimally invasive surgery [35-38]. According to the literature, Enhanced Recovery After Surgery (ERAS) protocols decreased length of stay by 30% to 50% thereby lowering hospital costs [39]. ERAS, a comprehensive program with multimodal approaches of perioperative pathways, has resulted in early recovery after surgery and has shown to improve outcomes in almost all major surgical specialties [39-41]. A recent study reported that ERAS was feasible and safe in older patients undergoing gynecologic oncological surgery as in younger patients [42]. ERAS protocols have not been implemented systematically in this population. However, Fast-Track principle has been used to optimizing patient outcomes in Denmark outlined in the national guidelines from the Danish gynecological cancer group. This is likely to influence on the observed effect of time-trend adjustment.

To our knowledge, this is the first detailed investigation of job market affiliation related to treatment of endometrial cancer. No statistically significant effect was observed regarding women’s return to the labor market and their use of sickness benefits. A plausible explanation for this is that we included a population with a median age of 67 years at the time of surgery which meant that the majority of the women received pension both before and after the index surgery. Only 40.2% of the women were working at least one week the year before surgery. Further, endometrial cancer is often diagnosed in an early stage and the operation therefore often leads to a rather short sick leave. Since only periods of leave longer than 14 days are observable in the Danish registries, our estimate of total days of leave may be underestimated.

An important strength of our study is the use of the gradual implementation of RMIS as the basis of a quasi-experimental design, thus minimizing patient selection bias. We also controlled for differences in baseline characteristics, time trends and differences in resource consumption across regions. Another strength of this study relates to the large population and the DiD design evaluating differences in resource use and cost patterns one-year pre- versus one-year post-surgery. A further advantage is the use of high-quality national databases, thereby allowing for systematic and objective measurement of resource use at an individual patient level.

An inherent limitation in the study design is the use of retrospective data and a comparatively long time period. Using registry data some clinical details are not routinely recorded e.g. surgeon experience and we cannot completely preclude some institutional selection bias. A further limitation is the use of DRG-tariffs as an approximation of the costs of hospital admissions. The Danish DRG-tariffs do not include the purchase or the maintenance cost of the robot. Another Danish study reported costs for instruments and disposals to be $2500 for each procedure and the purchase cost of the robotic platform was estimated to cost $2.4 million which amounts to $800 per operation with an amortization over 10 years [10].

5. Conclusion

The introduction of robotic surgery in Denmark did not generate any long-term cost savings in women with early stage endometrial cancer. The additional costs of robotic surgery are primarily driven by the index surgery. The introduction of robotic surgery decreased the number of bed days but adjusting for time trends outweighed any difference between the group exposed to robotic surgery and those who were not.

Conflict of interest

The authors have no conflicts of interest to disclose.

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Author contribution

MK, DGH, SM, PTJ: Contributed to the conception and design, processing of data, statistical analysis and interpretation of data; drafting the article, revising it critically for important intellectual content and final approval of the version to be published.

OM, SLJ, LS: Contributed to the conception and design, processing of data, interpretation of data; drafting the article, revising it critically for important intellectual content and final approval of the version to be published.

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Legends of included figures and tables

Figure 1: Resource use and costs one year before and after the index hospitalization

Figure 2: Flowchart of included patients

Figure 3: The introduction to robotic surgery in DK and each region Jan. 2008- July 2015

Legends of included figures and tables

Table 1: Demographic characteristics of included women

Table 2: Resource use associated with the introduction of robotic minimally invasive surgery for women with early stage endometrial cancer

Table 3: Costs associated with the introduction of robotic minimally invasive surgery for women with early stage endometrial cancer