Journal of Gynecology Obstetrics and Human Reproduction 48 (2019) 745–749

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Original Article

The effect of rural vs. urban setting on the management and outcomes of surgery for endometrial cancer

Dong Bach Nguyen[a], Nicholas Czuzoj-Shulman[b], Amani Alshaya[a], Walter H. Gotlieb[a,c], Haim A. Abenhaim[a,b,*]

[a] Department of Obstetrics and Gynecology, Jewish General Hospital, McGill University, Montreal, Quebec, Canada
[b] Centre for Clinical Epidemiology and Community Studies, Jewish General Hospital, Montreal, Quebec, Canada
[c] Division of Gynecologic Oncology, Segal Cancer Center, Jewish General Hospital, Montreal, Quebec, Canada

ARTICLE INFO

Article history:
Received 12 March 2019
Received in revised form 7 May 2019
Accepted 4 June 2019
Available online 5 June 2019

Keywords:
Endometrial cancer
Hysterectomy
Rural centers
Surgery
Urban centers

ABSTRACT

Introduction: To evaluate the proportion of endometrial cancers surgically managed in rural centers, and to compare the surgical management and perioperative morbidity of hysterectomies for endometrial cancer performed in rural settings with those performed in urban settings.
Materials and methods: We conducted a retrospective cohort study using the Nationwide Inpatient Sample (NIS) database from 2003 to 2010. We included all patients diagnosed with endometrial cancer who underwent a hysterectomy and compared surgical approaches, lymph node dissection rates, perioperative complication rates, and lengths of stay according to location of care provided (rural versus urban centers), using multivariate logistic regression models.
Results: Of the 52,299 women who underwent surgery for endometrial cancer, 6% were performed in rural centers—a proportion that trended down over the study period. A disparity in surgical management was noted between rural versus urban settings, with rural centers having lower rates of laparoscopy and robotics (6.9% vs. 18.5%; OR 0.35, CI 0.30–0.40), and lower rates of lymph node dissection both overall (39.4% vs. 67.0%; OR 0.32, CI 0.30–0.35) and for early (37.2% vs. 66.2%; OR 0.30, 95%CI 0.28–0.33) and advanced (57.7% vs. 71.7%; OR 0.56, 95% CI 0.44–0.70) stage disease. Perioperative morbidity was comparable in both settings, with lower rates of transfusion, sepsis, wound infection, ileus, and prolonged hospitalization in rural settings.
Conclusions: Although women obtaining care for endometrial cancer in rural centers receive differential surgical management than women cared for in urban centers, perioperative morbidity appears to be overall comparable.

Introduction

With a rising incidence estimated at over 61,000 new cases yearly for 2017 [1], endometrial cancer persists as the most common gynecological cancer in the United States, and the eighth most common cause of cancer-related deaths [2]. Given that most endometrial cancers (about 70%) are diagnosed early due to their early symptomatology, the management of FIGO stage I disease plays a pivotal role in overall disease outcome [3].

The surgery for clinical stage I endometrial cancer traditionally consisted of an extrafascial total abdominal hysterectomy. However, the initiation of concomitant pelvic lymphadenectomy in 1970 raised concerns of potential under staging when nodal sampling was not performed [4]. These findings prompted the FIGO Committee on Oncology to develop a more comprehensive "surgical" staging system in 1988, which remains essentially unchanged today, with only minor revisions in 2009 [5].

Since then, several studies, including a publication by the Society of Gynecologic Oncology (SGO), have advocated for the primary surgical management of endometrial cancer to be performed by gynecologic oncologists in tertiary care centers, given observed evidence that their involvement lead to improved lymph node dissection rate, staging, surgical outcomes, survival, and use of health care resources [6–9]. Nonetheless, referral and access to tertiary care centers may be inconvenient or difficult for patients living in remote areas. Accordingly, a proportion of surgeries for endometrial cancer are still performed in rural centers, where services by gynecologic oncologists are mostly unavailable.

* Corresponding author at: Jewish General Hospital, Obstetrics & Gynecology, McGill University, Pav H, Room 325, 5790 Cote-Des-Neiges Road, Montreal, Quebec, H3S 1Y9, Canada.
E-mail address: haim.abenhaim@gmail.com (H.A. Abenhaim).

http://dx.doi.org/10.1016/j.jogoh.2019.06.001
2468-7847/

Studies have shown that in general there are disparities in health between rural and urban dwellers, which have been attributed to receiving suboptimal medical treatment in rural areas, leading to poorer health outcomes [10]. The aim of our study is to evaluate the prevalence, surgical modalities, and perioperative outcomes of hysterectomies for endometrial cancer performed in rural settings as compared with urban settings.

Materials and methods

Sponsored by the Agency for Healthcare Research and Quality, the Healthcare Cost and Utilization Project Nationwide Inpatient Sample (HCUP-NIS) database is a nationwide database of hospital inpatient stays and discharges that samples 4500 hospitals across 46 states and covers 97% of the U.S. population. The HCUP-NIS contains data to allow researchers to better comprehend health-services related outcomes. With a self-weighted design, the HCUP-NIS sampling ensures to be representative of the population on critical factors, notably for "urban-rural location" [11].

We conducted a retrospective population-based cohort study using the HCUP-NIS database between 2003 and 2010. Using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), we identified all women with endometrial cancer (ICD-9 diagnostic code 182, GYN22) who underwent a hysterectomy (ICD-9 procedural codes 684-689). We then separated the subjects into two groups according to location of care (rural center versus urban center). The HCUP-NIS defines urban areas as cities and suburbs with a population of 50,000 or more, whereas rural counties encompass areas with a population of 49,999 or less [11].

First, we examined the temporal trends in the proportion of endometrial cancer cases treated in rural centers over the study period, which we stratified by cancer clinical stage using the ICD-9 codes STAGE 0.00-3.05. Our early stage group encompassed patients found to have FIGO clinical stage I on preoperative evaluations, and we clustered those found to have stages II to IV preoperatively into the advanced stage group. We then compared the two groups' baseline demographics and clinical characteristics, including comorbidities. Comorbidities of interest included obesity (ICD-9 codes 278.00, 278.01), hypertension (ICD-9 code 401), cardiovascular disease (ICD-9 codes 393-398), diabetes mellitus (ICD-9 code 249), pulmonary disease (ICD-9 code 490), and renal disease (ICD-9 code 403). We then used multivariate logistic regression to compare the surgical approaches, lymph node dissection rates (ICD-9 codes 400-409) and perioperative complications between rural centers and urban centers, while controlling for baseline demographics, for clinical characteristics (age, race, comorbidities, income quartiles, payment source), as well as for surgical approach and lymph node dissection rates.

All analyses were performed using the statistical software SAS V9.2 (SAS Institute, Cary, North Carolina, USA). P-values less than 0.05 were considered statistically significant. As this study used publicly available data, the Jewish General Hospital Medical/Biomedical Research Ethics Committee has deemed this study to be exempt from approval in accordance with the 2010 Tri-Council Policy statement.

Results

In our cohort, a total of 52,299 women underwent a primary surgery for endometrial cancer between 2003 and 2010. Of these, most (94%) were performed in an urban setting, compared with only 6% in a rural setting. Overall, 85.7% of cancers were found to be early stage and 14.3% were advanced stage. As shown in Fig. 1, there was a decreasing trend in the proportion of endometrial cancers, both low and high stage, treated rurally. This reflects a progressive transition of care from rural to urban centers.

As shown in Table 1, baseline patient characteristics were similar between the groups, with minor exceptions. Urban patients were more commonly morbidly obese and had a slight tendency towards hypertension and pulmonary disease. A greater proportion of rural patients had lower incomes and received Medicaid, in contrast to urban patients, who had higher incomes and were more often privately insured. Finally, women treated rurally had lower staged disease clinically (89.0% in rural settings were stage I, compared to 85.5% in urban settings).

Table 2 lists the surgical approaches and complications in each group. Hysterectomies in rural centers, compared with urban centers, were more likely to be abdominal (OR 1.69, 95% CI 1.51–1.88) or vaginal (OR 2.13, 95% CI 1.74–2.61), and less likely to be laparoscopic or robot-assisted (OR 0.35, 95% CI 0.30–0.40). The rate of lymph node dissection was lower in rural settings for both early (OR 0.30, 95% CI 0.28–0.33) and advanced (OR 0.56, 95% CI 0.44–0.70) clinical stage disease.

The perioperative complication rates and lengths of stay by center are displayed in Table 3. The rate of intraoperative complications was equivalent in both settings, for hemorrhage, vascular injury, bowel injury, ureteral injury, bladder injury, and

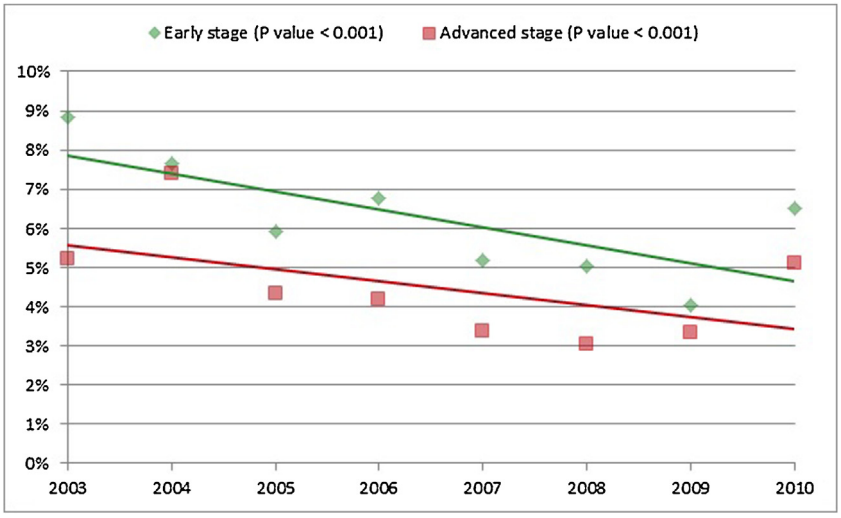

Fig. 1. Trend in the proportion of care in rural centers for endometrial cancer in the U.S., stratified by stage.

Table 1
Comparison of baseline characteristics of subjects undergoing a hysterectomy for endometrial cancer in rural vs urban centers.

	Rural centers (N = 3107), %	Urban centers (N = 49,192), %
Age (years)		
<40	2.7	3.1
40–49	9.7	9.8
50–59	25.8	28.7
60–69	28.7	30.4
70–79	20.6	18.8
≥80	12.5	9.2
Race		
White	67.9	60.3
African-American	1.7	6.4
Hispanic	1.3	5.8
Other	1.7	5.1
Comorbidities		
Obesity	11.6	11.5
Morbid obesity	8.1	12.0
Hypertension	49.6	53.2
Cardiovascular disease	3.7	3.8
Diabetes mellitus	21.2	21.8
Renal disease	2.9	3.9
Pulmonary disease	9.0	11.5
Income Quartiles		
Q1	38.3	20.2
Q2	43.2	23.0
Q3	15.4	26.2
Q4	3.1	30.6
Payment source		
Medicaid	48.2	40.8
Medicare	5.4	4.9
Private	39.4	48.7
Other	6.9	5.6
Endometrial cancer FIGO staging		
Early stage (I)	89.0	85.5
Advanced stage (II–IV)	10.9	14.5

laceration. Postoperative complications were comparable in both settings, although care in a rural center led to a lower risk of transfusion (OR 0.50, 95% CI 0.41–0.61), sepsis (OR 0.31, 95% CI 0.10-0.99), wound infection (OR 0.60, 95% CI 0.39–0.92), and ileus (OR 0.71, 95% CI 0.60–0.83). However, the overall incidence of complications was low. Women receiving hysterectomies in a rural center also had shorter lengths of stay in hospital than those receiving surgery in urban centers (>3 days OR 0.80, 95% CI 0.74–0.86).

Discussion

Although only 6% of hysterectomies for endometrial cancer are still performed rurally, this number is significant considering the estimated incidence of over 61,000 new cases per year for 2017 [1]. However, our data shows that this percentage is decreasing, which reflects a continued transition of care from rural to urban centers. Nevertheless, the proportion of advanced stage disease treated rurally (10.9%) remains comparable to that performed in urban centers (14.5%), which raises the concern as to whether patients are receiving the optimal care, in terms of surgical staging and appropriate initial management in rural centers. Of specific interest are the observed lower rate of lymph node dissection and the less frequent use of minimally invasive surgery in rural settings as compared with urban settings.

A few studies have questioned the role of rural centers in the initial management of endometrial cancer. For instance, a study based on the Kentucky Cancer Registry showed that rural women more often underwent less comprehensive surgical evaluation, and had less multimodality treatment [12]. Likewise, in the South and West regions of England, a prospective regional audit of the surgical management of endometrial cancer revealed that management was often inadequate in the audited region, with only one-third of patients having basic staging procedures performed fully [8]. Also, while gynecologic oncologic service is mostly unavailable in rural centers, a patient care evaluation study in 1996 spanning 713 hospitals in the U.S. revealed that only 33% of patients had a gynecologic oncologist as their primary surgeon, despite the three-fold likelihood of having lymph node sampling when a gynecologic oncologist was involved [13]. Similarly, studies have found the initial management by a gynecologic oncologist to be associated with more comprehensive staging, more efficient use of health care resources, and lessened need for radiation therapy and its associated morbidity [6,7].

Although the aforementioned studies have shown less comprehensive staging in rural areas, the actual survival benefit of lymph node sampling in stage I disease remains unproven by randomized control trials. The first documented series of lymphadenectomy in 1970 may have suggested lymph node involvement in 11.2% of apparent stage I disease [4], a number that could be as high as 22% according to a series later published by the Gynecologic Oncology Group Study in 1987 [14]. However, two randomized controlled trials, the 2009 MRC ASTEC trial and the 2008 trial by Panici et al, have compared the survival outcomes of women with stage I endometrial cancer undergoing a TAH-BSO with either routine lymphadenectomy or selected lymphadenectomy [15,16]. Although these trials have been the object of extensive criticism [17], both seem to suggest that systematic lymph node sampling does not have a large impact on overall survival. While one can argue that lymphadenectomy may help to triage those early stage patients who could avoid adjuvant radiation therapy [15], lymphadenectomies hold their own morbidity, which should be weighed against that of radiation therapy [17]. Hence, until further research can clearly outline the benefits of selective or systematic lymph node sampling, one cannot recommend against surgical treatment in rural centers for early stage disease based solely on nodal count.

In terms of surgical approach, care in rural settings resulted in higher rates of laparotomy and lower rates of laparoscopy and robotics. This bears significance knowing that the LAP-2 trial, the

Table 2
Comparison of surgical approaches and lymph node dissection rates between rural and urban centers.

	Rural % (N = 3107)	Urban % (N = 49,192)	Adjusted OR (95% CI)[†]	P value
Surgical approach				
Abdominal / Converted	88.7	79.4	1.69 (1.51–1.88)	<0.001
Vaginal	4.4	2.1	2.13 (1.74–2.61)	<0.001
Laparoscopy / Robotic	6.9	18.5	0.35 (0.30–0.40)	<0.001
Lymph node dissection rates				
All patients	39.4	67.0	0.32 (0.30–0.35)	<0.001
Early stage	37.2	66.2	0.30 (0.28–0.33)	<0.001
Advanced stage	57.7	71.7	0.56 (0.44–0.70)	NS

Abbreviation: NS, non-significant: Adjusted for subject age, race, comorbidities, income quartiles, and payment source.
[†] Adjusted for subject age, race, comorbidities, income quartiles, and payment source.

Table 3
Comparison of perioperative complication rates and lengths of stay between rural and urban centers.

	Rural % (N = 3107)	Urban % (N = 49,192)	Adjusted OR (95% CI)[†]	P value
Intra-op complications				
Hemorrhage	1.1	1.2	0.85 (0.58–1.24)	NS
Vascular Injury	<1	<1	0.85 (0.11–6.54)	NS
Bowel Injury	<1	<1	1.22 (0.42–3.54)	NS
Ureteral Injury	<1	<1	–	–
Bladder Injury	<1	<1	1.45 (0.48–4.45)	NS
Lacerations	2.2	2.3	1.01 (0.78–1.32)	NS
Post-op complications				
Transfusion	4.0	7.9	0.50 (0.41–0.61)	<0.001
Hematoma	<1	<1	0.91 (0.54–1.54)	NS
Seroma	<1	<1	0.85 (0.39–1.85)	NS
Venous thromboembolism	1.1	1.4	0.78 (0.54–1.12)	NS
DIC	<1	<1	0.76 (0.10–5.80)	NS
Sepsis	<1	<1	0.31 (0.10–0.99)	<0.05
Wound infection	<1	1.2	0.60 (0.39–0.92)	<0.05
Pneumonia	1.1	1.4	0.83 (0.58–1.18)	NS
Myocardial infarction	<1	<1	0.87 (0.47–1.59)	NS
Renal failure	1.3	2.0	0.82 (0.52–1.29)	NS
Acute kidney injury	<1	1.1	0.66 (0.41–1.04)	NS
Urinary retention	1.4	1.6	0.80 (0.57–1.11)	NS
Ileus	6.0	8.0	0.71 (0.60–0.83)	< 0.001
C. difficile colitis	<1	<1	0.49 (0.18–1.34)	NS
Bowel obstruction	<1	<1	0.58 (0.25–1.34)	NS
Death	<1	<1	1.24 (0.69–2.24)	NS
Length of stay				
>3 days	63.9	68.9	0.80 (0.74–0.86)	<0.001
≥8 days	5.34	7.64	0.64 (0.53–0.76)	<0.001

Abbreviations: DIC, disseminated intravascular coagulation; NS, non-significant.
[†] Adjusted for age, race, comorbidities, income quartiles, payment source, and stage of disease.

largest randomized controlled trial to date comparing laparoscopic to abdominal hysterectomy for endometrial cancer, has shown that a laparoscopic approach resulted in reduced postoperative adverse events, shorter hospitalizations and improved quality-of-life at 6 weeks, despite significantly longer operating times and similar intraoperative complications [18]. Furthermore, quality-of-life at 6 months and 5-year overall survival rate were equivalent between laparoscopic and abdominal approaches [19]. Hence, since the first reported series of successful uterine cancer staging and para-aortic lymph node dissection by laparoscopy in the U.S. in 1994 [20], the use of minimally invasive surgery has slowly taken breadth according to a survey to members of the SGO [21]. Laparoscopy remains underused though, with only half of SGO members practicing laparoscopic assisted staging in 2005 [21,22]. Our data suggests that, as an average between 2003 and 2011, 18% of primary surgeries for endometrial cancer were performed by a minimally invasive approach, a number that trended up throughout the study period. This trend is consistent with recently published analyses of laparoscopic use in the U.S. [23], as well as in *Canada*, where the percentage has increased from 7% in 2002 to 30% in 2011, for an average of 17.5% [24].

Despite a lower use of minimally invasive approach in rural settings, our data shows similar intraoperative complication rates, comparable postoperative complication rates and a shortened length of hospitalization for women operated rurally. While the rate of postoperative sepsis and wound infection appeared lower in the rural group, even after adjusting for the variation in obesity in both groups, the absolute numbers are very small and are unlikely to bear clinical significance. The rate of postoperative ileus was also lower in rural settings; however, the difference in rate likely reflects the inconsistent definition of ileus rather than actually improved outcomes. Therefore, all in all, surgical complications were clinically comparable in both settings. Our findings parallel that of a population-based study that found similar surgical outcomes for primary surgeries for endometrial cancer between university hospitals and community hospitals [25].

Limitations inherent to the NIS database must be recognized as part of this study. The most important limitation is the absence of data on survival and recurrence outcomes, on the subsequent requirement of adjuvant therapy, on details of cancer pathology, on patients' prior surgical history, on use of pre-operative imaging, on hospital volume, and on the proportion of surgeries in urban centers attended by a gynecologic oncologist. Furthermore, data from the NIS did not allow us to evaluate the potential impact of geographic access and delayed referrals on patient outcomes.

Despite these limitations, our study does have important strengths. Few if any studies have sought to specifically evaluate the outcomes of patients with endometrial cancer depending on whether they were initially managed in a rural or an urban setting. Furthermore, our study gives insight into this matter on a nationwide scale, by virtue of our comprehensive population-based cohort that encompassed 46 states. A further strength of our study lies in our large sample size, which assures statistical power and accuracy to our comparative findings.

In conclusion, although women obtaining care for endometrial cancer in rural centers receive differential surgical management than women cared for in urban centers, perioperative morbidity appears to be overall comparable. When the primary surgical management of clinical stage I endometrial cancer cannot be deferred to urban centers, our results suggest that care in rural centers remains a safe alternative. However, further research is needed to evaluate long-term outcomes, such as survival, recurrence and subsequent need for adjuvant therapy.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

The authors have no conflicts of interest to disclose.

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