



Variability in surgical management of benign ovarian neoplasms in children^{☆,☆☆}



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ABSTRACT

Background/purpose: Although most pediatric ovarian neoplasms are benign and may be treated with ovary-sparing surgery (OSS), consensus is lacking on the optimal surgical approach. We aimed to determine the proportion of pediatric benign ovarian neoplasms managed with OSS and to assess variability in management across hospitals and specialties.

Methods: Using the Pediatric Health Information System, we studied patients aged 6–21 years treated in 2006–2014 for a benign ovarian neoplasm with oophorectomy or OSS. Inter-hospital variability and predictors of the type of surgery were determined using logistic mixed effects models with random hospital effects.

Results: Of 1164 patients with benign ovarian neoplasms, 646 underwent oophorectomy, and 518 underwent OSS. Across hospitals, there was significant variability in the proportion of OSS (range: 21.7–76.6%). In multivariable analysis, patients managed by pediatric surgeons (vs. pediatric and adolescent gynecologists) (OR: 0.27, 95%CI: 0.17–0.43, $p < 0.001$), younger patients (OR: 0.94 per year, 95%CI: 0.90–0.98, $p = 0.007$), and those admitted through the emergency department (OR: 0.76, 95%CI: 0.58–0.99, $p = 0.04$) were less likely to undergo OSS. Inter-hospital variability remained significant after adjusting for relevant patient and hospital characteristics ($p < 0.001$).

Conclusions: Significant variability exists in management of benign ovarian neoplasms across hospitals and specialties. Collaborative efforts between treating specialists may improve implementation of evidence-based guidelines for OSS.

Type of study: retrospective study

Level of evidence: III.

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Although the true incidence of ovarian neoplasms in pediatric patients is unknown, it is estimated that they affect approximately 2.6 per 100,000 girls each year [1,2]. The majority of ovarian neoplasms in children and adolescents are benign in nature, with malignancy occurring in approximately 10% of cases [3,4]. Options for the surgical management of ovarian neoplasms include oophorectomy and ovary-sparing surgery (OSS). There are several reasons to attempt OSS for lesions with a high likelihood of benign pathology. Oophorectomy has been reported to place patients at increased risk for early menopause and premature ovarian failure [5,6]. Early menopause is associated

with a number of concerns both at the individual patient level and in the realm of public health; these concerns include impaired sexual health, decreased bone density, neurologic disease, and heart disease, a leading cause of death for American women. Although reports on fertility potential after unilateral oophorectomy are conflicting, studies have reported patients may have shorter reproductive lifespans and respond less well to ovarian stimulation for in vitro fertilization [7]. Additionally, affected patients are at increased risk for developing contralateral ovarian neoplasm and possibly torsion, which may result in surgical castration if oophorectomy on the remaining ovary, is required in the future [8–10].

Despite the potential benefits of OSS, others recommend oophorectomy for ovarian masses in children and adolescents owing to the potential for malignancy and to minimize the risk of upstaging tumors if inadvertent tumor rupture occurs intra-operatively. Although some reports suggest an increased risk of tumor upstaging and recurrence following intra-operative tumor rupture, these studies largely reflect

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adult patients with epithelial ovarian malignancies [11,12], which are exceedingly rare in children. The literature in children is limited, but a series of 53 children with 59 ovarian tumors concluded that intra-operative rupture did not increase the rate of recurrence or worsen the prognosis [13].

Due to the age range in which these neoplasms typically present, they are managed by either pediatric surgeons or pediatric and adolescent gynecologists (PAGs) depending on referral patterns and access to specialists. The objective of this study was to determine the proportion of pediatric and adolescent patients with benign ovarian neoplasms who are treated with ovary-sparing procedures across tertiary U.S. children's hospitals, and to assess whether variability in management exists across hospitals and physician specialties.

1. Methods

1.1. Data source and cohort development

We performed a multi-institutional retrospective cohort study of patients aged 6 to 21 years who underwent either OSS or oophorectomy for a benign ovarian neoplasm during 2006–2014. Data came from the Pediatric Health Information System (PHIS). The PHIS is a national administrative database that includes discharge data for inpatient, ambulatory surgery, emergency department, and observation unit visits at 47 tertiary children's hospitals affiliated with the Children's Hospital Association. We used the *International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM)* diagnosis code for benign ovarian neoplasm (220) to identify potential patients. We then used *ICD-9-CM* procedure codes to identify treated patients and to classify the surgical procedures as either OSS or oophorectomy (see Appendix A). Because we included procedures performed during either inpatient or observation status encounters, we included patients treated at one of 25 hospitals that continuously contributed data on both of these types of encounters during the entire study period of 2006–2014.

Because this study aimed to assess inter-hospital variability, patients seen at hospitals that treated fewer than 30 patients with benign ovarian neoplasms over the study time period were excluded. Only the first encounter of each patient that met inclusion criteria was included in the analyses. A single site chart review of patients treated at our institution was performed to estimate the misclassification rate of the diagnosis and procedure codes.

1.2. Predictors of treatment

Patient demographic characteristics (age, race, ethnicity, insurance status), whether or not the patient was admitted through the emergency department (ED), specialty of the physician performing the ovarian procedure, year of treatment, and several hospital-level characteristics were examined as predictors of the outcome of interest (treatment with OSS or oophorectomy). Physician specialty was categorized as pediatric surgeon, PAG, other (e.g. pediatrician, adolescent medicine, etc.), or unknown. The following hospital-level characteristics during the study period were examined: presence of a PAG fellowship program, volume of patients with a benign ovarian neoplasm diagnosis, volume of patients with a benign ovarian neoplasm diagnosis and an ovarian procedure, volume of procedures of any type performed by a PAG, and proportion of all included ovarian procedures that were performed by a PAG. Based on the volume of procedures of any type performed by a PAG, a high volume PAG hospital was defined as a hospital at which the number of procedures performed by a PAG was greater than the median across all included hospitals.

1.3. Statistical analyses

Patient demographic and clinical characteristics were reported as frequencies and percentages for categorical variables and as medians

and interquartile ranges for continuous variables. These were compared between treatment groups using logistic mixed effects models with hospital-level random intercepts. Hospital characteristics were reported as frequencies and percentages for categorical variables and as medians and interquartile ranges for continuous variables. Inter-hospital variability was examined before and after adjustment for all evaluated patient, physician, and hospital-level characteristics. To display the magnitude of inter-hospital variability, empirical Bayes estimates and confidence intervals of the random hospital-specific intercepts from these logistic mixed effects models were plotted after inverse logit transformation. The model that included all examined patient, physician, and hospital-level characteristics was also used to identify the significant independent predictors of treatment. Finally, interactions between physician specialty and year and between physician specialty and admission through the ED were tested in the multivariable models in order to determine whether trends in treatment practice over time varied by specialty and whether the relative odds of receiving OSS among emergent vs. non-emergent cases varied by specialty. All statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC). Statistical significance was defined as $p < 0.05$. This study was approved by Nationwide Children's Hospital Institutional Review Board.

2. Results

From 2006 through 2014, there were 1339 patients between the ages of 6 and 21 who were treated for a benign ovarian neoplasm at one of the 25 included hospitals. Of those patients, 1260 also underwent operative intervention for the ovarian mass. Our final analyses included 1164 patients who were managed at 20 hospitals that treated at least 30 cases (Fig. 1). At our institution, 53 patients were surgically managed for benign ovarian neoplasms during the study period. The *ICD-9-CM* diagnosis code for benign ovarian neoplasm was accurate in 91% of cases, and the *ICD-9-CM* procedure codes were accurate in 98% of cases.

Table 1 shows the characteristics of patients who were surgically treated for a benign ovarian neoplasm as well as the characteristics of the treating physicians and hospitals. A total of 646 (55.5%) patients were managed with oophorectomy and 518 (44.5%) were managed with OSS. The median age of the cohort was 13 years, though OSS patients were an average of two years older than oophorectomy patients. Patient race, ethnicity, and primary payer were not different between groups. Patients admitted through the ED were more likely to be managed by oophorectomy (58.6% vs. 53.1%, $p = 0.02$). Patients managed by pediatric surgeons were more likely to undergo oophorectomy (63.9% vs. 36.1%, $p < 0.001$), while those managed by PAGs were more likely to undergo OSS (68.5% vs. 31.5%, $p < 0.001$). At hospitals with a high volume of procedures of any type performed by PAGs, patients were more likely to undergo OSS (51.6% vs. 36.6%, $p = 0.02$). The presence of a PAG fellowship program at a hospital did not influence the rate of OSS.

Odds ratios for undergoing OSS, associated with each predictor in the multivariable regression model, are shown in Table 2. Older patients were more likely to undergo OSS (odds ratio (OR) per year of age: 1.06, 95% confidence interval (CI): 1.02–1.11, $p = 0.007$), whereas patients admitted through the ED were less likely to undergo OSS (OR: 0.76, 95% CI: 0.58–0.99, $p = 0.04$). Patients whose procedures were performed at hospitals at which a high volume of procedures (more than 127 procedures of any type) were performed by PAGs were more likely to be managed with OSS (OR: 2.71, 95% CI: 1.42–5.16, $p = 0.003$). As compared to patients managed by PAGs, patients managed by pediatric surgeons (OR: 0.27, 95% CI: 0.17–0.43, $p < 0.001$) and physicians whose listed specialty was something other than pediatric surgery or gynecology (OR: 0.23, 0.12–0.43, $p < 0.001$), were less likely to undergo OSS. The effect of specialty on the likelihood of undergoing OSS remained significant when PAG was compared to all other specialties (OR: 3.80 (95% CI: 2.43–5.96, $p < 0.001$) and when pediatric surgeons were compared to all other specialties (OR: 0.42, 95% CI: 0.29–0.61, $p < 0.001$). When

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