



Surgical management of ovarian tumors without the support of intraoperative pathology readings in Bhaktapur Cancer Hospital

Michelle Marinone^{a,*}, Eliza Shrestha^{b,1}, Anita Thapa^b, Ruhee Tuladar^b, Dorothy B. Wakefield^c, Linus Chuang^a

^a Department of Obstetrics, Gynecology and Reproductive Biology, Danbury Hospital, Western Connecticut Health Network, CT, USA

^b Department of Gynecologic Oncology, Bhaktapur Cancer Hospital, Bhaktapur, Nepal

^c Danbury Hospital, USA



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ABSTRACT

Intraoperative frozen section plays an important role in surgical management of ovarian masses. Many hospitals in low- and middle-income countries lack this intraoperative pathologic guidance. In this retrospective analysis, we assessed the management of 62 patients who underwent surgical treatment for ovarian masses at Bhaktapur Cancer Hospital in Nepal in light of the final histopathology results. Final histopathology found that 64.5% of the ovarian masses were malignant, 1.0% were borderline, and 30.6% were benign. 55 of the 62 total cases were considered “clinically suspicious” and 52 of the 62 cases underwent hysterectomy and staging procedures in addition to oophorectomy. There was no significant difference in the surgical management or in the post-operative complications when comparing benign, borderline, and malignant masses. Without the support of intraoperative frozen section, benign and malignant masses were treated the same way. The majority of benign cases were overtreated and were exposed to additional risks of postoperative complications. Several malignant cases were undertreated and required additional surgery to appropriately treat and stage malignant ovarian masses. Improved pathology support in Bhaktapur Cancer Hospital would result in better patient outcomes, fewer complications, and avoidance of additional staging surgeries.

1. Introduction

Bhaktapur Cancer Hospital is a 110-bed hospital, which sees more than 5,000 patients each year. It is located in Bhaktapur, Nepal, approximately 20 km east of the capital city, Kathmandu. Similar to many hospitals in low-resource areas, Bhaktapur Cancer Hospital does not have a cryostat machine, the technology required for intraoperative frozen section (IOFS). IOFS allows the tissue to be quickly frozen using a cryostat machine, then thinly sliced and made into a slide. This allows the tissue to be examined by a pathologist, providing intraoperative guidance for surgical management. When managing ovarian masses in gynecology, the ovarian mass is removed and immediately sent to pathology to be transformed into a frozen section. The pathologist's report then dictates the remainder of the surgery. A gynecologic oncologist may consult intraoperatively to continue with lymph node biopsy and other staging procedures if the report is malignant or end the case if the report is benign.

Multiple studies have found IOFS to be highly accurate in

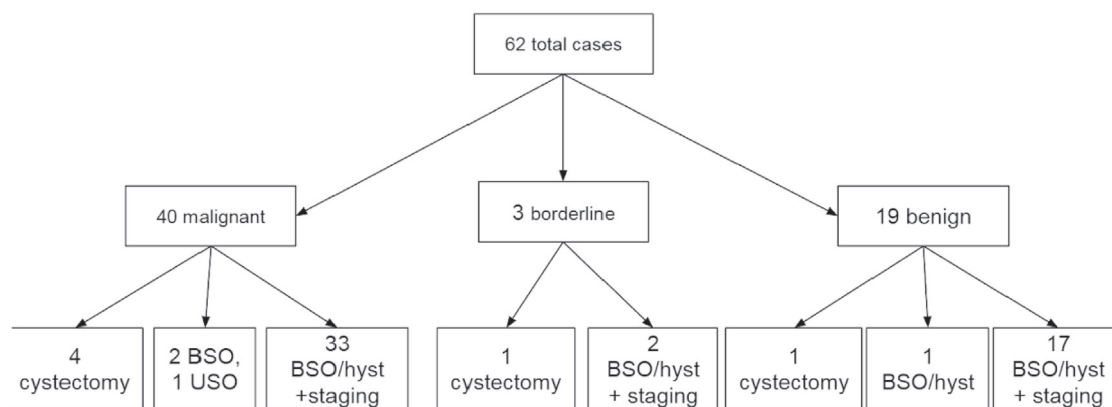
diagnosing ovarian masses when compared to the final pathology reading. Basaran, et al. found an overall 96.8% agreement between final pathology and IOFS results of ovarian masses (Basaran et al., 2015). Pinto et al. looked at the accuracy of IOFS depending on the type of ovarian mass. For malignant, borderline, and ovarian masses, the accuracy rates were 98.5%, 76.9% and 94%, respectively (Pinto et al., 2001).

Despite the utility of IOFS for surgical guidance, IOFS equipment is expensive and many hospitals in low- and middle-income countries do not have the financial means to obtain cryostat machines. In these settings without IOFS technology, gynecologic surgeons must rely on clinical suspicion and laboratory results when choosing the appropriate surgical procedure. The purpose of our study is to evaluate the effect on the surgical management of ovarian masses in Bhaktapur Cancer Hospital where IOFS is not available.

* Corresponding author at: Western Connecticut Health Network, 24 Hospital Ave, Danbury, CT 06810, USA.

E-mail address: Michelle.Marinone@wchn.org (M. Marinone).

¹ These authors share first authorship and contributed equally to the manuscript.



BSO bilateral salpingo-oophorectomy; USO unilateral salpingo-oophorectomy; Hyst hysterectomy

Fig. 1. Flowchart of case composition and surgical management. BSO bilateral salpingo-oophorectomy; USO unilateral salpingo-oophorectomy; Hyst hysterectomy.

Table 1

Types of masses found on final pathology.

	N (%)
Serous	47 (75.8%)
Endometrioid	1 (1.6)
Mucinous	8 (12.9%)
Unspecified	6 (9.7%)
Total	62

Table 2

Cancer staging.

	N (%)
Benign	16 (26%)
Borderline	4 (6%)
Stage I	25 (40%)
Stage II	2 (3%)
Stage III	15 (24%)
Total	62

Table 3

Features of the masses.

	Benign (n = 19)	Borderline (n = 3)	Malignant (n = 40)	P-value
Clinically suspicious	16 (84.2%)	3 (100.0%)	36 (90.0%)	0.62
Elevated CA 125 (> 35 U/mL)	14 (73.7%)	1 (33.3%)	29 (72.5%)	0.35
Lymph node biopsy	17 (89.5%)	1 (33.3%)	33 (82.5%)	0.32
Postoperative complications	4 (21.1%)	1 (33.3%)	7 (17.5%)	0.78

2. Materials and methods

We performed a retrospective analysis of all patients who underwent surgical treatment for ovarian masses at Bhaktapur Cancer Hospital in Nepal between May 1, 2015, through October 30, 2017. The study received approval from the institutional review board. Preoperatively, records were kept of the patients' ages and laterality of the ovarian masses. Pelvic ultrasounds were obtained for all patients who underwent surgeries at Bhaktapur Cancer Hospital. CT scans were performed in symptomatic patients or patients who were suspicious for metastatic disease. The surgeons made note of which masses were suspicious for malignancy based on imaging, intraoperative evaluation and tumor markers. Additional data included: the type of surgery performed, intraoperative and postoperative complications, and final

histopathology reports. Data were analyzed using Fisher's exact test and chi-square test to assess categorical variables and Wilcoxon signed-rank test to assess continuous variables.

3. Results

A total of 62 cases were included in the study (Fig. 1). The patient's ages ranging from 19 to 78, with a median age of 50. There was no significant difference in the patients' ages between the benign and borderline/malignant cases (p = 0.47). There were 36 unilateral ovarian masses (58%) and 26 bilateral ovarian masses (42%), and there was no significant difference between the benign and borderline/malignant groups in regards to laterality (p = 0.59). Of the 62 total cases, final pathology found that 40 patients had malignant ovarian masses (64.5%), 3 had borderline ovarian masses (1.04%), and 19 patients had benign ovarian masses (30.6%). Of the malignant and borderline masses, final histopathology demonstrated that the majority were serous carcinomas (n = 29, 67.4%); the remaining were endometrioid (n = 1, 2.3%), mucinous (n = 8, 18.6%), and "other" (n = 5, 11.6%). The majority (n = 45, 72.6%) of ovarian masses were confined to the ovary with no extraovarian spread. The histopathologic classifications of the masses are demonstrated in Tables 1 and 2.

Pelvic washings were obtained in all cases for cytology. The majority of patients underwent a hysterectomy, bilateral salpingo-oophorectomy, and staging by pelvic and para-aortic lymph node biopsy and/or omentectomy (n = 52, 83.9%). Of the 40 malignant cases, 4 patients underwent ovarian cystectomy (10%), 2 underwent bilateral salpingo-oophorectomy (5%), 1 underwent unilateral salpingo-oophorectomy (2.5%), and 33 underwent hysterectomy, bilateral salpingo-oophorectomy, and staging (82.5%). Of the 3 borderline tumors, 1 patient had an ovarian cystectomy (33.3%) and 2 underwent a hysterectomy, bilateral salpingo-oophorectomy, and staging (66.7%). Of the 19 benign cases, 1 had an ovarian cystectomy (5.3%), 1 had a hysterectomy and bilateral salpingo-oophorectomy without staging (5.3%), and the remaining 17 underwent a hysterectomy, bilateral salpingo-oophorectomy with staging (89.4%).

The surgeons took note of which masses were "clinically suspicious," which was defined as CA 125 level greater than 35 U/mL, imaging findings of cystic and solid tumor with surface excrescences, gross ascites, or abnormal intra-abdominal findings. 16 of the 19 benign cases, all 3 of the borderline cases, and 36 out of 40 malignant cases were deemed "clinically suspicious" (p = 0.62). In these cases, deeming a mass "clinically suspicious" did not predict the final pathology. When evaluating cases with elevated CA 125 level (> 35 U/mL), 14 of the 19 benign cases, 1 of the 3 borderline cases, and 29 of the 40 malignant cases had CA 125 greater than 35 U/mL (p-value as 0.34) (Table 3).

Table 4
Postoperative complications.

Age	Complication	Surgery	Final pathology	Histology and staging
50	DVT	Hysterectomy, BSO, lymph node dissection	Benign	n/a
46	Wound infection	Hysterectomy, BSO, omentectomy, lymph node dissection	Benign	n/a
74	Wound infection	Hysterectomy, BSO, omentectomy, lymph node dissection	Benign	n/a
34	Wound infection	Hysterectomy, BSO, omentectomy, lymph node dissection	Benign	n/a
55	Wound dehiscence	Hysterectomy, BSO, omentectomy	Borderline	Mucinous, Stage 1a
68	Wound infection	Hysterectomy, BSO, omentectomy, lymph node dissection	Malignant	Serous, Stage 1a
65	Wound dehiscence	Hysterectomy, BSO, omentectomy, lymph node dissection	Malignant	Serous, stage 3c
66	Wound dehiscence	Hysterectomy, BSO, omentectomy, lymph node dissection	Malignant	Serous, stage 3c
78	Wound infection	Hysterectomy, BSO, omentectomy, lymph node dissection	Malignant	Mucinous, stage 3c
30	Wound infection	BSO, omentectomy, lymph node dissection	Malignant	Mucinous, stage 5
69	Wound dehiscence	Hysterectomy, BSO, omentectomy, lymph node dissection	Malignant	Serous, stage 3c
72	Wound dehiscence	Hysterectomy, BSO, omentectomy, lymph node dissection	Malignant	“Other”, stage 1

Regarding the surgical management of these cases, 17 of 19 benign cases and 1 of the 3 borderline cases, and 33 out of 40 malignant cases had lymph node biopsies performed. When compared, the p-value is 0.32, indicating that benign, borderline, and malignant cases were essentially managed in the same way. Without intraoperative guidance from pathology, 89.5% of benign cases underwent unnecessary staging. In addition, postoperative complications experienced by patients were similar across the groups (4/19 benign cases, 1/3 borderline cases, and 7/40 malignant cases, $p = 0.78$) (Tables 3 and 4).

4. Discussion

In our study, clinical suspicion and CA 125 levels were poor predictors of final pathology. Without the support of the intraoperative frozen section, malignant and benign masses were treated similarly. Patients with benign masses underwent unnecessary staging, causing postoperative complications that may have been avoided if the additional staging procedures were not performed. Several patients with malignant masses were also undertreated and required additional staging surgery when the final pathology was obtained. Low-resource centers like Bhaktapur Cancer Hospital would benefit from intraoperative pathology support during surgical management of ovarian masses. Improved pathology infrastructure in low- and middle-income countries would result in better patient outcomes, fewer complications, and avoidance of additional staging surgeries.

The high complication rate, although mostly minor complications, in our study can be attributed to the lack of resources. Bhaktapur Cancer Hospital does not carry many standard perioperative supplies, such as antithrombotic stockings, and has a limited supply of antibiotics.

Limitations of the study include a small study size and the retrospective nature of the data. In addition, the data set was subject to a degree of selection bias as Bhaktapur Cancer Hospital is a tertiary referral center and therefore an increased level of clinical suspicion was likely present before each operation.

One possible method and area for future research is the use of intraoperative cytology using scrape smears, where a slide is used to scrape cells from the mass which are then smeared onto a slide and examined by the pathologist. Two small studies in India have found this to have comparable accuracy compared to the frozen section for ovarian masses (Bohara et al., 2018; Shahid et al., 2012). One such

study looked at 48 cases of ovarian masses that were examined with intraoperative cytology, intraoperative frozen section, and final histopathology. The researchers found an accuracy of 92.3% with intraoperative cytology, which was comparable to IOFS (Bohara et al., 2018). Another study found that intraoperative cytology had an accuracy of 95.6% when compared with final pathology (Shahid et al., 2012). This method requires no expensive equipment and can be performed rapidly, which would presumably be a better method for low resource settings than having no intraoperative pathology guidance at all. Management of ovarian masses at Bhaktapur Cancer Hospital was also limited by a lack of in-house pathologists. Scrape smears combined with telemedicine technology would allow the surgeons to have an inexpensive method to create slides for outside pathologists to review.

Author contributions

Eliza Shrestha, Anita Thapa, and Ruhee Tuladar conceived of the study idea, designed the study, and collected the data. Michelle Marinone and Dorothy Wakefield interpreted the data and provided statistical analysis. Michelle Marinone wrote the manuscript in consultation with Linus Chuang, Eliza Shrestha, Anita Thapa, and Ruhee Tuladar. Linus Chuang supervised the project.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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