



Feasibility of laparoscopic ovarian tissue cryopreservation after open abdominopelvic tumor surgery



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ABSTRACT

Background: Laparoscopic oophorectomy with tissue cryopreservation (OTC) for fertility preservation is usually performed prior to therapy. When fertility preservation is considered after prior open abdominopelvic tumor surgery there may be a perceived barrier to laparoscopic OTC. This study evaluates the feasibility of OTC with a laparoscopic approach after open surgery.

Methods: This is a single institution retrospective study from 2011 to 2019.

Results: Planned laparoscopic OTC was performed after open surgery in 17 of 113 patients. Median age was 4.2 years. The most common diagnoses were Wilms Tumor (35%) and neuroblastoma (35%). The most common procedures were nephrectomy (41%) and exploratory laparotomy with biopsy (35%). The median amount of time between open surgery and OTC was 29 days. Sixteen (94%) had a laparoscopic OTC. Regardless of operative technique, patients resumed therapy a median of 3 days after OTC.

Conclusions: Prior abdominopelvic surgery should not be a barrier to OTC. Laparoscopic OTC is feasible after a variety of open oncologic operations, regardless of time-interval between the procedures and without incurring a significant delay in resuming oncologic therapy.

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Introduction

With the increased survival of childhood cancer, efforts to minimize late effects of therapy, including infertility, have gained increased importance. Although the aggregate 5-year survival of pediatric cancer is over 80%,¹ the majority of patients develop a chronic health condition, including endocrine and reproductive disorders, as adults.² The ability to have biological children is important to patients, and patients and families want to discuss fertility preservation options.^{3–7} Multiple societies recommend that every child who is undergoing cancer treatment should receive consultation with regard to the risk of infertility. Specifically, the American Society for Reproductive Medicine (ASRM), American Academy of Pediatrics and the American Society for Clinical Oncology (ASCO) all recommend discussions as early as possible to allow the patient to have the most flexibility regarding pretreatment options.^{5,8,9} The Children's Oncology Group supports the

recommendations of ASCO. Recently the National Comprehensive Cancer Network recommended that adolescents and young adults who are interested in pursuing fertility preservation be referred to a fertility clinic within 24 hours.¹⁰

For prepubertal girls, or for postpubertal girls in whom therapy must start quickly, ovarian tissue cryopreservation (OTC) is the only pretreatment fertility preservation option as ovarian stimulation with egg or embryo freezing is not possible. Although the 2019 practice committee report from the ASRM has defined OTC as an acceptable standard-of-care fertility preservation option, including for prepubertal patients, pediatric patients are still enrolled in an IRB-approved protocol to ensure proper tissue removal and processing for future fertility restoration.⁹ OTC requires surgical removal of ovarian tissue and has been shown to be safe with no delays in beginning or resuming cancer therapy.¹¹ In a recent systematic review, OTC cases were performed via oophorectomy (57%) or partial oophorectomy (43%), and further research to define optimal operative technique is ongoing.^{12,13}

When the timing of OTC follows abdominal or pelvic tumor surgery, surgeons may be concerned that OTC is no longer appropriate to offer or is not safe or feasible with a laparoscopic approach. To our knowledge, however, there are no studies

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addressing this concern. Additionally, previous studies have shown a lack of surgical standardization regarding technique for ovarian cortical tissue removal in children, including surgical procedure (oophorectomy vs. cortical biopsy) and approach (laparoscopic vs. open).¹² This work presents a series of OTC cases from a single institution that occurred after open abdominopelvic tumor surgery and evaluates the feasibility of a laparoscopic approach, which for this study is defined as the successful completion of a laparoscopic procedure with no perioperative complications.

Material and methods

A retrospective chart review was conducted to evaluate OTC patients in the Fertility & Hormone Preservation & Restoration program at Ann & Robert H. Lurie Children's Hospital of Chicago (IRB#2011–14420 L, IRB#2014–15534 L, IRB#2017–1149, IRB#2018–1509). Current IRB-approved protocols for pre- and postpubertal OTC were adopted from the Oncofertility Consortium's OTC protocols for adult women, where inclusion criteria specified a greater than 80% risk of premature ovarian insufficiency as a direct result of treatment (Table 1). Consent was obtained from parents for children younger than 18 years old and from patients older than 18 years. Assent was obtained from children greater than 12 years old.

From the OTC patient cohort, inclusion in this study consisted of patients who received a planned laparoscopic oophorectomy for OTC after a previous open abdominopelvic tumor surgery between April 2011 and December 2019. Prior abdominopelvic tumor surgery was defined to have occurred at any time and at any hospital prior to surgery for OTC. Patients who had concurrent abdominopelvic tumor surgery and OTC, and planned open OTC were excluded. All oophorectomies were performed by one of four pediatric surgeons.

Patient information including demographics, diagnosis, surgical history and cancer therapy timing was collected. The primary outcome was the feasibility of completing a laparoscopic oophorectomy. Oophorectomies that were laparoscopic and then converted to an open procedure, were considered an open procedure. Secondary outcomes included delay in starting therapy and postoperative complications.

Patient demographics are reported as proportions for categorical variables and medians with interquartile ranges for continuous variables. This study was not powered to compare factors between patients undergoing laparoscopic and open OTC.

Results

A total of 113 patients underwent oophorectomy for OTC during the study period. Nineteen patients underwent OTC after abdominopelvic tumor surgery, including 17 patients (17/113, 15%) who had a planned laparoscopic OTC and 2 patients who had a planned open OTC because of concurrent additional tumor surgery. Patients were pre- and postpubertal (median age 4.2 years, IQR 2.7–10.4 years). Most patients were Tanner Stage 1 (82.4%). The most common diagnoses included Wilms tumor (35.3%) and neuroblastoma (35.3%). For the majority of patients this was their initial diagnosis (70.6%) and they had metastatic disease (82.4%), most commonly to an abdominal solid organ (17.6%) (Table 2).

The most common prior open abdominopelvic tumor surgeries were nephrectomy (41.2%) and exploratory laparotomy with incisional biopsy (35.3%) (Fig. 1). For all patients, surgeries were performed with a transperitoneal approach, whether the resection occurred in the intraabdominal or retroperitoneal space. The median time between last open surgery and OTC was 29 days (range 11–331 days, IQR 15–52). There were two patients with a difference of greater than 100 days, but these patients did not initially

Table 1

Inclusion criteria for pre- and postpubertal ovarian tissue cryopreservation IRB-approved studies.

General Criteria	
• Any health condition that requires removal of both ovaries	
• Less than 30 years old	
Alkylating-Intensive Chemotherapy	
• Cyclophosphamide equivalent dose ≥ 4000 mg/m ² ^a	
• Busulfan cumulative dose >600 mg/m ²	
• Any treatment containing procarbazine	
• Conditioning regimen prior to stem cell transplant	
Radiation Therapy	
• Whole abdomen or pelvic external beam radiation ≥ 15 Gy (prepubertal) or ≥ 10 Gy (postpubertal)	
• Total body external beam radiation	
• Cranial external beam radiation ≥ 30 Gy	

^a Cyclophosphamide equivalent dose is a risk-stratification calculation using dosages of alkylating agents. (<https://fertilitypreservationpittsburgh.org/fertility-resources/fertility-risk-calculator/>).

qualify for OTC and became eligible upon relapse. The majority of patients received chemotherapy alone (8/17, 47.1%) or had no treatment between their open surgery and OTC (6/17, 35.3%). Three patients (3/17, 17.6%) received both chemotherapy and radiation therapy. For those who received chemotherapy (n = 11), the majority received only one cycle (7/11, 63.6%), one patient received two cycles (1/11, 9.1%) and three patients received greater than three cycles (3/11, 27.3%). For the patients who had radiation therapy (n = 3), two (2/3, 66.7%) received flank radiation alone, and one (1/3, 33.3%) received whole abdominal radiation.

Sixteen patients (16/17, 94.1%) had a successfully completed laparoscopic oophorectomy. There were no intraoperative complications. For the one patient who had an open OTC, the laparoscopic procedure was converted to an open Pfannenstiel approach. This patient had rhabdomyosarcoma with carcinomatosis and although it was 29 days since her exploratory laparotomy with biopsy and omentectomy, she had dense adhesions that precluded a safe laparoscopic procedure. Whether laparoscopic or open OTC was performed, all oophorectomies were successfully completed, and

Table 2

Patient and tumor characteristics of 17 patients who underwent planned laparoscopic oophorectomy for ovarian tissue cryopreservation after open tumor surgery.

	Number (n)	Percentage (%)
<i>Age</i>		
Prepubertal	15	88.2
Postpubertal	2	11.8
<i>Tanner Stage</i>		
1	14	82.4
2	1	5.9
5	2	11.8
<i>Diagnosis</i>		
Wilms Tumor	6	35.3
Neuroblastoma	6	35.3
Other Sarcoma	3	17.6
Rhabdomyosarcoma	2	11.8
<i>Relapse</i>		
No	12	70.6
Yes	5	29.4
<i>Metastatic Disease</i>		
No	3	17.6
Yes – abdominal solid organ	3	17.6
Yes – retroperitoneum	2	11.8
Yes – carcinomatosis	2	11.8
Yes – lymph nodes	2	11.8
Yes – bone marrow	2	11.8
Yes – brain	1	5.9
Yes – lungs	1	5.9
Yes – bones	1	5.9

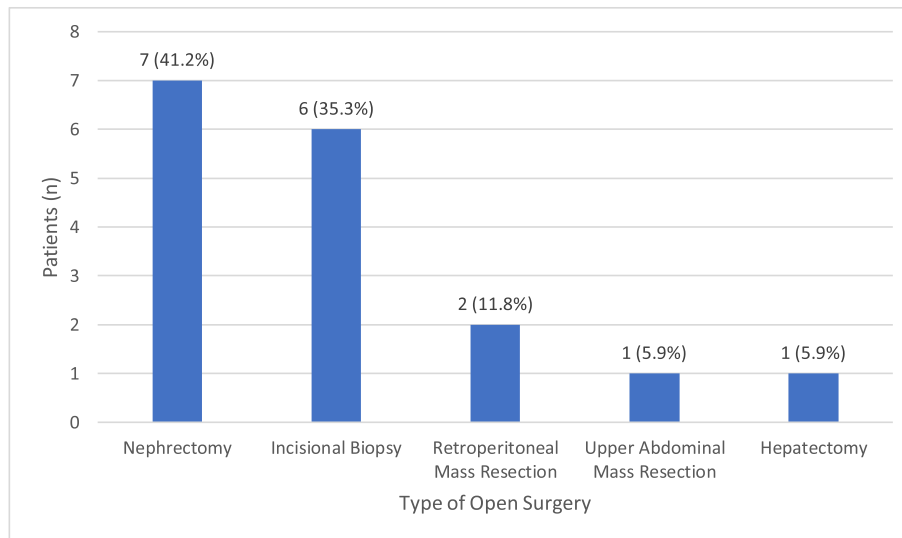


Fig. 1. Prior open abdominopelvic tumor surgeries.

tissue was cryopreserved and sent to long-term storage.

Regardless of laparoscopic or open surgical approach for oophorectomy, patients were able to resume chemotherapy or radiation therapy a median of 3 days after OTC (range 1–8 days, IQR 1–6). The majority of patients had no post-operative complications (16/17, 94.1%). There was one patient who had a post-operative fever of unknown etiology, which resulted in a two-day delay in restarting therapy (from post-operative day 3–5). This patient had received four cycles of chemotherapy prior to OTC.

Discussion

Fertility preservation is an important long-term quality of life consideration for pediatric patients and their families.^{3,4} The timing of diagnosis and treatment, including surgery for abdominopelvic tumors, are factors that can affect which fertility preservation options are available. In patients who qualify, OTC should be done in a way that does not delay therapy and allows for adequate tissue cryopreservation, which is why a laparoscopic approach is preferred. Laparoscopic oophorectomy, especially in infants and small children, results in a magnified view of the ovary and pelvis, which allows for successful use of the “no touch” technique whereby manipulation of the ovarian capsule is minimized, and adequate ovarian cortex is cryopreserved.¹¹ Additionally, laparoscopy for OTC is most often scheduled as outpatient surgery, with short postoperative recovery, including early feeding, decreased pain and better cosmesis with smaller incisions,^{14,15} all of which allow patients to quickly resume their medical therapy.

Although OTC is ideally performed before the initiation of therapy, our study demonstrates that oophorectomy for OTC with a laparoscopic approach is feasible after open abdominopelvic surgery regardless of the type of surgery or duration since the procedure. However due to the potential for adhesions from the original abdominopelvic surgery, patients and families are counseled about the risk of conversion to an open incision during the consent process. After oophorectomy our patients were able to start or resume their cancer therapy as planned, indicating that surgery for fertility preservation can be accomplished without disrupting the patient’s cancer therapy and should not be a barrier to consideration of ovarian cryopreservation.

Despite the increased awareness of fertility preservation, and the known importance to patients, fertility discussions and

referrals, from both medical and surgical providers, still remain low.^{16–18} Not all hospitals have the infrastructure to create OTC programs, but several excellent articles exist to help establish protocols.^{9,19,20} For surgeons, instructional videos are available that delineate specific techniques to use when performing a laparoscopic oophorectomy for OTC.²⁰ Given that surgeons are an integral part of the comprehensive cancer care for many patients, and that pediatric surgical subspecialists are trained in delicate tissue handling and advanced laparoscopic skills for infants, children and adolescents, surgeons should be involved in fertility preservation programs.²¹ Surgeons can also advocate for the feasibility of these procedures when indicated, even when perceived barriers may exist, such as after abdominopelvic surgery.

We recognize that there are several limitations to the generalizability of our study including that this patient population came from a single institution and that the pediatric surgeons who performed the oophorectomy for OTC were specialists in surgical fertility preservation procedures. The majority of our patients had abdominal surgery, and more data in cases of OTC following pelvic surgery could reveal a higher conversion rate to open surgery in those patients. Despite these limitations, our study represents the removal of another barrier to performing laparoscopic oophorectomy for OTC in pediatric patients.

Conclusions

Laparoscopic oophorectomy for OTC is feasible after open abdominopelvic surgery without delay in resuming cancer therapy. A laparoscopic approach for OTC in children can be considered regardless of the type of initial surgery, or duration since that procedure.

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