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Clinical Outcome of Isolated Serous Tubal Intraepithelial Carcinomas (STIC)

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Abstract

Objective—Risk-reducing salpingo-oophorectomy (RRSO) is recommended for women with *BRCA* mutation due to increased risk of pelvic serous carcinoma. Serous tubal intraepithelial carcinoma (STIC) is a pathologic finding of unknown clinical significance. This study evaluates the clinical outcome of patients with isolated STIC.

Materials/Methods—We retrospectively reviewed the medical records of consecutive patients with a germline *BRCA1/2* mutation or a high-risk personal or family history of ovarian cancer who underwent RRSO between January 2006 and June 2011. All patients had peritoneal washings collected. All surgical specimens were assessed using the sectioning and extensively examining the fimbria protocol, with immunohistochemistry when indicated. p53 signature lesions and secretory cell outgrowths were excluded.

Results—Of 593 patients who underwent RRSO, isolated STIC was diagnosed in 12 patients (2%). Five patients (42%)were *BRCA1* positive, 5 patients (42%)were *BRCA2* positive, and 2 patients (17%) had high-risk family history. Preoperatively, all patients with STIC had normal CA-125 levels and/or pelvic imaging results. Seven patients underwent hysterectomy and omentectomy, 6 patients (46%) had pelvic node dissections, and 5 patients (39%) had para-aortic node dissections. With the exception of positive peritoneal washings in 1 patient, no invasive or metastatic disease was identified. No patient received adjuvant chemotherapy. At median follow-up of 28 months (range, 16–44 months), no recurrences have been identified.

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Conclusions—Among the cases of isolated STIC after RRSO reported in the literature, the yield of surgical staging is low, and short-term clinical outcomes are favorable. Peritoneal washings are the most common site of disease spread. Individualized management is warranted until additional data become available.

Keywords

Serous tubal intraepithelial carcinoma; Prophylactic salpingo-oophorectomy; Ovarian carcinoma

As early as 1969, investigators postulated amultifocal origin of ovarian carcinoma, suggesting that the genesis of these tumors may occur outside the ovary and even potentially arise from the fallopian tube.[1–5] However, it was not until recently that the fallopian tube specifically came to be seen as a leading potential site of origin for pelvic serous carcinomas.[6,7] Some of the data supporting this include the identification of pathologic abnormalities in the fallopian tubes after risk-reducing salpingo-oophorectomy (RRSO) for germline *BRCA* mutation carriers, and the similarity of p53 mutations in concurrent serous tubal intraepithelial carcinoma (STIC) and invasive serous carcinoma.

Women with germline *BRCA* mutations are recommended to undergo RRSO to decrease their risk of pelvic serous carcinoma. It has been shown that occult fallopian tube carcinomas are more common in RRSO specimens than are occult ovarian carcinomas.[8] Immunohistochemical techniques (particularly p53 and Mib1) have allowed for closer examination of the fallopian tube from which distinct patterns of abnormalities have been identified. One such abnormality is STIC. Diagnosis of STIC is made with a combination of morphologic and immunohistochemical evaluation. Morphologic features include increased nuclear to cytoplasmic ratio, enlarged nuclei with prominent nucleoli, lack of ciliated cells, loss of polarity, and a complete lack of stromal invasion. Immunohistochemical stains supporting a diagnosis of STIC are p53 (overexpressed or null phenotype) and Ki-67. Serous tubal intraepithelial carcinomas have been defined by these histologic findings and can be distinguished from p53 signature and serous tubal intraepithelial (STIL) lesions, which carry some but not all of the unique histologic features of STIC.[9,10] In addition, fallopian tube abnormalities, including STIC, have been reported with greater frequency when the sectioning and extensively examining the fimbria (SEE-FIM) protocol, a more detailed sectioning of the tubal fimbriated end, is completed.[8,11–14] SEE-FIM, developed at Brigham and Women's Hospital, entails fixation of the entire tube and longitududinal sectioning of the distal 2 cm of the fibriated end of the fallopian tube into 4 pieces followed by serial sectioning every 2 to 3 mm of the entire length of the fallopian tube. SEE-FIM ensures a comprehensive evaluation of the fallopian tube; and in studies where it has been used, the detection rate for STIC is higher.[15]

To date, the literature on STIC has focused on the incidence of the finding, not clinical follow-up. The prognostic significance of isolated STIC after RRSO and the next steps in management remain undefined. The open lumen of the fallopian tube into the peritoneal cavity raises a concern that cells could exfoliate from the fallopian tube, implant on a peritoneal surface, and develop into a pelvic serous carcinoma. A direct mechanism through which STIC leads to invasive serous carcinoma has yet to be defined. Pertinent questions

regarding need for surgical staging, frequency with which invasive lesions are identified from staging procedures, and whether there is benefit to adjuvant chemotherapy have not been answered. The purpose of the current study was to identify the rate of isolated STIC among patients with RRSO after the adoption of the SEE-FIM protocol at Memorial Sloan-Kettering Cancer Center in 2006, assess the clinical outcome of these cases, and review the literature reported to date. The data will help guide management of STIC lesions identified at RRSO.

MATERIALS AND METHODS

After obtaining approval from the Memorial Sloan-Kettering Cancer Center Institutional Review Board, clinical and pathologic databases were queried to identify all patients with a diagnosis of STIC between January 2006 and June 2011. All patients were planned for RRSO with or without hysterectomy, at the discretion of the surgeon and the patient. The procedures were performed with traditional laparoscopy, robotic-assisted laparoscopy and, rarely, via laparotomy. Patients with a concurrent diagnosis of pelvic serous carcinoma (endometrial, ovarian, fallopian tube, or primary peritoneal) were excluded. The medical, operative, and pathology records of the identified patients were reviewed. Data were collected including demographics, genetic testing results, preoperative assessment, pathology results, postoperative testing, follow-up recommendations, and recurrence details.

At the time of the pathologic review, all specimens were assessed using the SEE-FIM protocol. Serous tubal intraepithelial carcinoma was defined using a combination of morphologic evaluations to distinguish it from p53 signatures, STIL, and invasive carcinoma. Immunohistochemistry was performed only when nuclear atypia was present, and a diagnosis of STIC was considered based on review of sections stained by hematoxylin and eosin. Morphologic considerations included the following: nuclear/cytoplasmic ratio, nuclear pleomorphism, epithelial stratification with loss of polarity, irregular epithelial thickness, and exfoliation of cells into the tubal lumen. Immunohistochemical stains included p53 and Mib-1. Elevated Mib-1 (>15% nuclear cell staining) and abnormal p53 staining (null phenotype or >60% nuclear cell staining) were used as supportive evidence of the diagnosis. All histologic evaluations were performed by pathologists with advanced training in gynecologic pathology and reviewed at the gynecologic pathology division conference to determine a consensus diagnosis.

RESULTS

During the study period, 593 patients underwent RRSO for known *BRCA* mutation or high-risk personal or family history of ovarian carcinoma. Patients who underwent bilateral salpingo-oophorectomy exclusively for hormonal treatment of breast cancer or who had an abnormal imaging or CA-125 test result preoperatively were excluded. Of the 593 patients, 189 patients (31.9%) carried germline *BRCA1* mutations, 186 patients (31.4%) carried germline *BRCA2* mutations, 18 patients (3%) carried *BRCA* mutations of unknown significance, 104 patients (17.5%) were *BRCA* negative, and 94 patients (15.9%) had not undergone genetic testing. There were 2 patients (0.3%) with germline *BRCA* mutations documented in clinic notes, but there were no mutation details available. The SEE-FIM

protocol for RRSO was fully implemented by January 2006, and the first subsequent diagnosis of STIC was made in July 2006. Twelve patients with isolated STIC were identified (Table 1). The overall frequency of STIC in patients who underwent RRSO was 2%. When categorized according to BRCA status, 5 (2.65%) of 189 women with germline *BRCA1* mutations were found to have a STIC lesion, 5 (2.69%) of 186 *BRCA2* carriers and 0 (0%) of 104 patients negative for *BRCA* germline mutations. In the untested population (94 women), 2 women (2.13%) had a diagnosis of a STIC lesion.

The 12 patients with isolated STIC at the time of RRSO had a mean age of 54 years (range, 39–77 years). Five women were carriers of a *BRCA1* mutation; 4 women had a *BRCA2* mutation; 1 woman had a *BRCA2* rearrangement; and for 2 patients, the *BRCA* status was unknown. The 2 women of unknown *BRCA* status both had high-risk personal and family histories for ovarian carcinoma. Both had a personal history of bilateral breast cancer and a family history of breast and ovarian cancer. Ten (83%) of the 12 women with STIC identified at RRSO had preoperative CA-125 testing. All values were normal for the reference laboratory, ranging from5 to 29U/mL; 6 patients (50%) had a CA-125 level of less than 10 U/mL. Both of the women who did not have preoperative CA-125 testing had CA-125 assayed after the time of RRSO; in both cases, the results were less than 10 U/mL. Ten (83%) of the patients with STIC identified at RRSO had preoperative ultrasound, and all results were normal. All patients with STIC at the time of RRSO had either a normal CA-125 level or imaging preoperatively.

Risk-reducing salpingo-oophorectomy was performed laparoscopically in 10 (83%) of the 12 patients, and robotically in 2 patients (17%). Serous tubal intraepithelial carcinoma was identified bilaterally in 2 patients (17%) and unilaterally in 10 patients (83%). Additionally, the STICs were characterized as multifocal in 3 women (25%) and unifocal in 9 women (75%). One woman had a concurrent serous adenofibroma, and 1 woman had evidence of endosalpingiosis. No endometriosis was seen. Washings were performed in all 12 patients and were negative in 11 (92%) cases. Ten patients (83%) underwent dilation and curettage, and all specimens were benign. No other procedures were performed at the time of RRSO. Four patients had additional postoperative imaging, and none showed evidence of metastatic disease. The 2 women who did not have preoperative imaging are among those who had postoperative imaging.

With the exception of 1 patient whose condition was diagnosed early during the study period, all patients were recommended to undergo a staging procedure. Three women declined surgical staging, and 1 woman elected to have her staging procedure with a local provider. The remaining 7 women underwent staging at Memorial Sloan-Kettering Cancer Center. Three procedures were performed with standard laparoscopy, and 4 procedures were performed with robotic assistance. All 7 women underwent hysterectomy, omentectomy, and peritoneal washings. Of the 7 staging procedures, pelvic and para-aortic nodal dissection was performed in 5 cases and pelvic node dissection alone was performed in 1 case (14%). A mean of 17 (range, 4–34) pelvic nodes and 10 (range, 7–19) paraaortic nodes were removed. Peritoneal biopsies were taken in 6 patients (86%) and diaphragm biopsies in 3 patients (43%). All surgical staging results were benign, with the exception of 1 patient with

peritoneal washing suspicious for carcinoma; this finding was consistent with the cytology read from the washings performed at the time of RRSO.

No recommendation for adjuvant chemotherapy was made to any of the patients. Follow-up recommendations were based on discussion with individual patients and included combinations of CA-125 testing, imaging, and office visits. Eleven patients have available follow-up data. After a median follow-up of 28 months (range, 16–44 months), there have been no recurrences noted. One patient had a diagnosis of pancreatic carcinoma 32 months after RRSO and died of her disease 2 months later.

Given the variation of STIC lesions identified, 2 patients warranted additional clarification of clinical outcome due to the extent of their histologic findings (Table 2). One of these, patient 32, is a 44-year-old woman with a personal and family history of breast cancer who had a diagnosis of a *BRCA1* 185delAG mutation 3 months before her RRSO. Before surgery, she had a CA-125 level of 29 U/mL and had not had any imaging. She was found to have bilateral STIC with multiple foci in each tube. Her staging procedure included hysterectomy, omentectomy, and bilateral pelvic lymph node dissection, as well as biopsies of the pelvic and diaphragm peritoneum. All specimens were benign. She is now 19 months from diagnosis, and her CA-125 level has declined to 6 U/mL. She remains without evidence of disease and is under observation with semiannual physician visits. The patient with positive peritoneal washings (patient 30) is a 77-year-old woman with a personal history of breast cancer who had a *BRCA2* 6174delT mutation identified before RRSO. Pathologic findings revealed STIC in multiple foci on a single fallopian tube and positive washings. Her CA-125 level was 15 U/mL. She returned to the operating room for staging, at which time she had washings, hysterectomy, omentectomy, pelvic peritoneal biopsies, and resection of an umbilical nodule. All pathologic specimens were benign, but the washings were suspicious, not diagnostic, for adenocarcinoma. After counseling regarding her options, the patient elected to proceed with observation consisting of office visits and CA-125 assays every 3 months, with extension of the visit interval anticipated. At her most recent evaluation, 16 months after RRSO, her CA-125 level was 20 U/mL, her CT scan demonstrated severe diverticulosis, and her PET scan was negative for metastatic disease.

DISCUSSION

The data presented here support overall favorable short-term clinical outcomes for patients with STIC: no recurrences and no evidence of distant disease at the time of subsequent surgical staging. Until now, most information regarding the clinical course of patients with STIC has been embedded in articles regarding the frequency of occult malignancy at the time of RRSO, with limited clinical outcomes data. Nine main series, in some cases presented in more than one publication to allow for updates, provide clinical information about the 37 previously published cases of STIC (Table 2).[8,12,14,16–23] There are additional publications on frequency of STIC, which do not provide follow-up information and are not included in this discussion.

In the current report, the incidence of STIC lesions identified at the time of RRSO was found to be 2%; this is consistent with prior reports in the literature, in which the incidence

ranges from 0.6% to 7%. The differences seen among these reports could be easily attributed to statistical variation of small sample sizes and a rare event. However, more concrete components of study design and patient population are likely contributory. For example, *BRCA* mutation was an inclusion criteria for most but not all of the prior reports; for some, high-risk personal and family history was sufficient for inclusion.[11,16,17,19,20,24] As demonstrated by Manchanda et al, the risk of an occult lesion is lower among patients without documented *BRCA* mutation. In this series, no patients known to be *BRCA* negative were found to have a STIC lesion. Similarly, none of the previously published 37 cases of isolated STIC were patients known to be *BRCA* negative. In one case, a 56-year-old woman with a personal history of breast cancer at the age of 28 had a BRCA2 mutation of unknown significance (ALA2306Pro). Age is a risk factor for the development of malignancy in patients with *BRCA* mutations; hence, the guiding recommendation is that patients with *BRCA1* and *BRCA2* mutations undergo RRSO between the ages of 35 and 40 after completion of childbearing. Patients who undergo risk-reducing surgery at a later age have a higher incidence of STIC on final pathology.[16] Powell et al recently compared the age at diagnosis of STIC to the age at diagnosis of an occult carcinoma and found that patients with STIC were in fact older than those with an invasive carcinoma. In each of the reported studies, the mean or median age was between 46 and 51 years, with patients completing RRSO anywhere from age 30 to 76 years. In addition, the extent to which the fallopian tube is examined can affect the frequency of finding occult histologic changes. Our current report reflects the rate of STIC in which all RRSO specimens were examined with the SEE-FIM protocol, in contrast to the other publications included in Table 3.[15,25]

Cataloging the clinical course of these patients to increase understanding and inform future clinical recommendations is critical. Combining this series of 12 patients and the 37 previously published cases, there is clinical information regarding 49 patients in the published literature. Two patients reported in the literature have developed a primary peritoneal carcinoma (PPC). The first case has not been formally published in a series on RRSO but was described in an editorial on the topic. She had a germline BRCA1 mutation and developed PPC 6 years after RRSO. At the time of RRSO, she had no peritoneal washing assessment and the pathologic examination of the fallopian tubes was not done with SEE-FIM. After her diagnosis of PPC, the RRSO specimen was retrospectively examined with a more detailed sectioning and revealed a single focus of STIC.[20] The second patient is the only person who has developed PPC after diagnosis of an isolated STIC at the time of RRSO. She was 49 at the time of RRSO. She had a BRCA1 mutation and developed PPC43 months after the RRSO after an elevation in CA-125 level was noted. She was treated with primary debulking surgery and chemotherapy and is currently alive without evidence of disease 16 months later. The numbers here are too small to draw conclusions; however, this rate of PPC, 2% (1 of the 48 women reported in a case series), is in line with published literature reporting 1% to 4% risk of developing primary peritoneal cancer after RRSO.[8,26]

A variety of clinical approaches to the care of patients after RRSO have been described. As is the case for previous reports, this series is limited by a small cohort and individualized treatment plans. Although a median follow-up of 28 months might be considered short, the literature on PPC after RRSO suggests that a high-risk time period is in the first 2 years.[21,27–29] A challenge lies in developing recommendations for appropriate next steps

once the diagnosis of STIC has been made, in particular, the role of surgical staging, chemotherapy, and surveillance.

Of the 49 patients reported in the literature (including the current series), 47 patients (96%) had washings obtained, and 26 patients (53%) underwent hysterectomy. Twenty-two patients (45%) underwent omental biopsy or omentectomy, with no invasive disease identified in the omental specimen. For the 34 women whose information regarding lymph node sampling was available, 8 women (24%) had lymph nodes removed and none were positive. Complete information on the extent of surgical staging is available for 27 patients (Fig. 1). Some publications indicate patients underwent “staging,” but the authors do not provide the details regarding what was included as part of the staging procedure, specifically regarding peritoneal biopsies, omentectomy, and lymph node dissection. Washings are the one component of the evaluation, along with complete removal of both tubes and ovaries, which was consistently performed. The importance of washings is supported by the aggregate data; 15% of the patients were found to have positive washings at the time of RRSO. Thus, we support peritoneal washings as a component of all RRSO procedures. Some series include hysterectomy as part of risk-reducing surgery to ensure that all tubal tissue is excised. As data increasingly demonstrate, the distal tube, and not the interstitial component, is the primary site of both STIC and occult invasive carcinomas. Thus, hysterectomy may not be required at the time of RRSO for pelvic serous carcinoma prevention. However, it may be prudent to consider hysterectomy at the time of RRSO for other issues pertinent to the gynecologic history. Owing to the small number of cases in the literature and the significant institutional variation, there is limited room for broad conclusions to be made regarding the necessity for, and the most appropriate extent of, surgical staging after the diagnosis of STIC at the time of RRSO. Individualized patient decisions should include the extent of peritoneal cavity assessment at the time of RRSO, results of washings, and whether or not the outcome of a staging procedure would change recommendations for adjuvant therapy.

Treatment recommendations for patients with STIC, positive washings, and no other evidence of invasive malignancy at time of RRSO are important. As stated, 7 reported cases (15%) had positive washings, with the remainder of the surgical pathology without evidence of metastatic disease. Among these patients, 2 patients received chemotherapy and 4 patients did not. Of the 2 patients who received chemotherapy, only 1 patient had a surgical staging procedure. The parameters of the staging procedure are not clearly defined. Follow-up on the 7 patients with positive washings and no other evidence of disease ranges from 16 to 150 months, and there have been no recurrences. Of note, there were 4 patients with STIC and negative washings who received adjuvant chemotherapy. At a median follow-up of 58 months, no documented recurrences have been reported (Table 2). Chemotherapy was given by 1 institution to all patients in their cohort regardless of washings. The presence of positive washings implies circulating malignant cells in the peritoneal cavity, prompting some institutions to offer adjuvant chemotherapy. However, in the absence of invasive disease, particularly if there has been a negative staging procedure, observation remains a reasonable option and obviates the potential for chemotherapy-induced adverse effects.

Finally, our study examined the use of disease surveillance schedules. The data from the publication of Powell et al and this series seem to be the only 2 reports with details as to the

follow-up recommendations made to patients.[14,18,23,25] The options for follow-up include annual visit with review of systems and examination, tumor marker assays (CA-125 and/or HE4), and imaging (ultrasound, computed tomographic scan, and magnetic resonance imaging). We agree with Powell et al that although no screening system has been found that successfully identifies patients with primary peritoneal cancer before diffuse spread of disease, patients with STIC identified at the time of RRSO fall into a risk category that necessitates continued surveillance, which should be determined at the discretion of the patient and oncologist but could include a combination of review of systems, physical examination, and CA-125 testing.

In the coming decade, the number of women who have undergone RRSO with SEE-FIM will likely increase and additional cases of STIC with clinical follow-up will be reported. In parallel, molecular characterization of STIC, and investigation into its relevance to the pathogenesis of pelvic serous carcinomas will contribute additional pertinent and potentially prognostic information. In the meantime, the body of data currently available is presented here and emphasizes the association of isolated STIC at the time of RRSO with germline BRCA mutation, the importance of obtaining peritoneal washings (as they are positive in 15% of the cases), and the overall favorable short-term outcomes for patients with isolated STIC at the time of RRSO.

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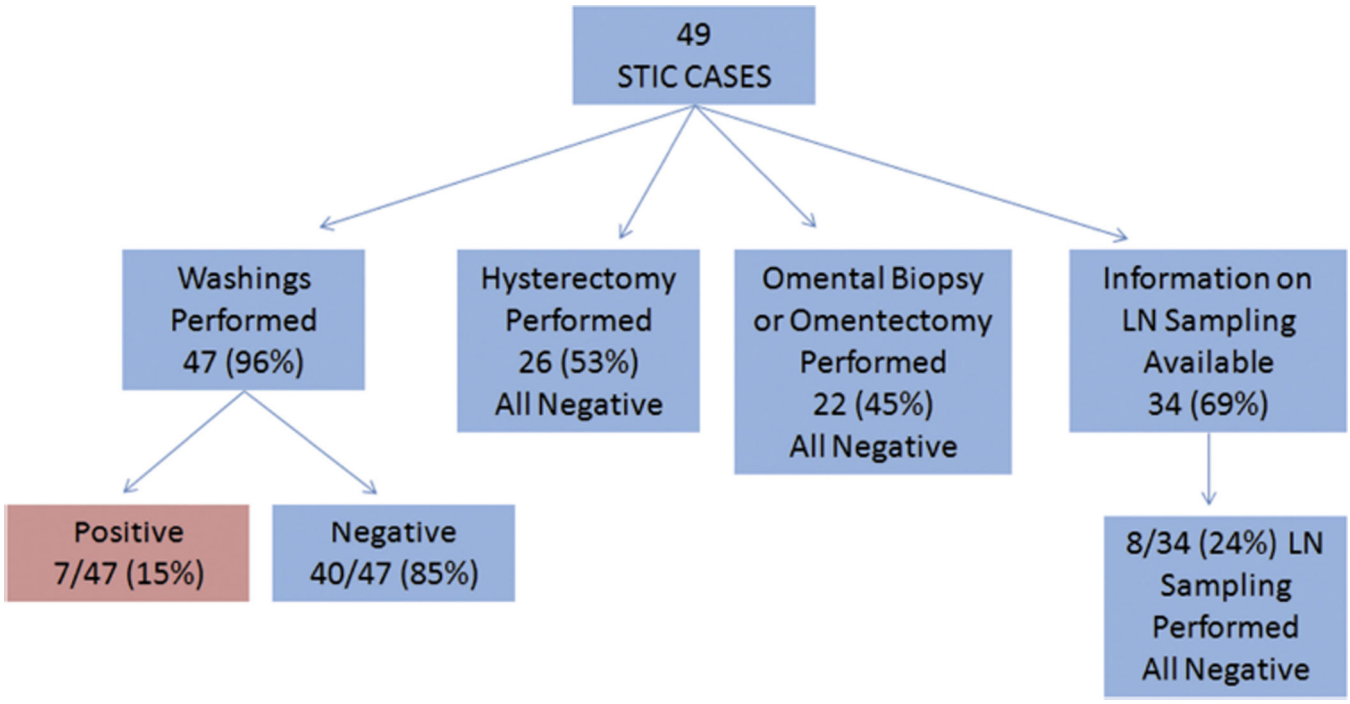

FIGURE 1.
Cumulative staging information for STIC cases identified with RRSO.

TABLE 1

Patients' characteristics

Patients with STIC	**12**
Age, mean (SD), yrs	54 (39–76)
Germline BRCA mutation, n (%)	
BRCA1	5 (42)
BRCA2	5 (42)
BRCA unknown	2 (17)
Preoperative assessment, n (%)	
CA125	9 (75)
Pelvic imaging	10 (83)
STIC location, n (%)	
unilateral	10 (83)
bilateral	2 (17)
single focus	9 (75)
multifocal	3 (25)
Peritoneal washings positive, n (%)	
Yes	1 (8)
No	11 (92)
Follow-up, median (range), mos	28 (16–44)

TABLE 2

Reported cases of patients with a diagnosis of STIC at RRSO

Patient Number	Institution	Age	BRCA Status	Procedures	Nodal Sampling	Washings	Adjuvant Treatment (No. cycles)	Follow-Up
1	A[8]	64	BRCA1	TAH, BSO, omentectomy	None	Negative	Unknown	Unknown
2	B[12]	61	BRCA1	BSO	None	Negative	None	38 m ned
3	B	48	BRCA1	BSO	None	Negative	None	7 m ned
4	B	49	BRCA1	TAH, USO	None	None	None	87 m ned
5	C[14]	44	BRCA1	TAH, BSO	None	Negative	Carboplatin/ paclitaxel	Median PFS, 36 months
6	C	44	BRCA2	TAH, BSO, “staging”	Unknown	Positive	Carboplatin/ paclitaxel	
7	C	66	BRCA2	TAH, BSO, staging	Unknown	Negative	Carboplatin/ Paclitaxel	
8	D[16–18]	52	BRCA1	BSO	Unknown	Negative	None	Ned at surgery
9	D	46	BRCA1	BSO	Unknown	Negative	None	ned at surgery
10	D	53	BRCA1	BSO	None	Negative	None	99 m ned
11	D	45	BRCA1	BSO	None	Negative	None	80 m ned
12	D	47	BRCA1	LAVH, BSO	None	Positive	Carboplatin/ paclitaxel (6)	150 m ned
13	D	46	BRCA2	BSO	None	Negative	Carboplatin/ Paclitaxel (3)	58 m ned
14	D	65	BRCA2	LAVH, BSO	None	Negative	Carboplatin/ paclitaxel (3)	138 m ned
15	E[19,20]	48	BRCA1	BSO	None	Negative	None	Ned at surgery
16	E	40	BRCA1	BSO	None	Negative	None	Ned at surgery
17	E	67	BRCA1	BSO	None	Negative	None	Ned at surgery
18	E	43	BRCA1	TLH, BSO, omentectomy	None	Positive	None	40 m ned
19	E	60	BRCA2	BSO	None	Suspicious	None	24 m ned
20	E	60	BRCA2	BSO	None	Negative	None	12 m ned
21	E	60	unknown high risk family history	BSO	None	Negative	None	48 m ned
22	E	44	unknown high risk family history	BSO	None	Negative	None	Ned at surgery
23	E	55	unknown high risk family history	TLH, BSO, omx	None	Positive	None	28 m ned

Patient Number	Institution	Age	BRCA Status	Procedures	Nodal Sampling	Washings	Adjuvant Treatment (No. cycles)	Follow-Up
24	F[20]	44	BRCA1	BSO	None	None	None	Primary peritoneal carcinoma, 72 m
25	G[21]	57	BRCA2	Unknown	Unknown	Negative		26 m ned
26	G	50	BRCA2	Unknown	Unknown	Negative		8 m ned
27	G	56	BRCA2, variant of unknown significance	Unknown	Unknown	Negative		2 m ned
28	H[18,22,23]	51	BRCA1	BSO, omental biopsies	None	Negative	None	88 m ned
29	H	52	BRCA1	BSO, omental biopsies	None	Positive	None	101 m ned
30	H	50	BRCA1	BSO, omental biopsies	None	Negative	None	64 m ned
31	H	43	BRCA2	BSO, omental biopsies	None	Negative	None	47 m ned
32	I[18]	73	BRCA1	no staging	None	Negative	None	133 m ned
33	I	54	BRCA1	no staging	None	Negative	None	40 m ned
34	I	49	BRCA1	no staging	None	Negative	None	Primary peritoneal carcinoma, 43 m
35	I	61	BRCA1	staging with nodes	Yes	Negative	None	99 m ned
36	I	58	BRCA1	staging with nodes	Yes	Negative	None	78 m ned
37	I	76	BRCA2	staging without nodes	None	Negative	None	75 m ned
38	J	44	BRCA1	TAH, omentectomy, PLND, biopsies	Yes	Negative	None	19 m ned
39	J	39	BRCA1	TAH, omentectomy, PPALND	Yes	Negative	None	20 m ned
40	J	65	BRCA1	TAH, omentectomy, PPALND, biopsies	Yes	Negative	None	29 m ned
41	J	44	BRCA1	TAH, omentectomy, PPALND, biopsies	Yes	Negative	None	30 m ned
42	J	45	BRCA1	TAH, omentectomy, PPALND, biopsies	Yes	Negative	None	26 m ned
43	J	67	BRCA2	BSO	None	Negative	None	33 m ned
44	J	50	BRCA2	Offered, declined	None	Negative	None	34 m ned
45	J	46	BRCA2	Offered, declined	None	Negative	None	20 m ned
46	J	68	BRCA2	Performed at outside hospital	None	Negative	None	41 m ned
47	J	77	BRCA2	TAH, omentectomy, biopsies	None	Positive	None	16 m ned
48	J	60	unknown high risk family history	offered, declined	None	Negative	None	23 m ned
49	J	47	unknown high risk family history	TAH, omentectomy, PPALND, biopsies	Yes	Negative	None	44 m ned

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TABLE 3

Clinical reports on STIC at RRSO

Author	No. RRSO Cases	No. STIC Cases	Age Range (Years)	Inclusion Criteria	Pathology Protocol
Lamb *[16]	113	4 (3.5%)	47–65	BRCA mutation carrier or high-risk personal/family history	2–3 mm sectioning for 23/30 patients
Carcangiu[12]	50	3 (6%)	48–61	BRCA mutation carrier	2–12 slides reviewed per tube or ovary, for 20 patients the tubes and ovaries were submitted in their entirety
Powell[23]	111	4 (3.6%)	43–52	BRCA mutation carrier	Rigorous pathology protocol
Callahan[14]	122	3 (2.5%)	44–66	BRCA mutation carrier	2–3 mm sectioning for patients before 2/2005, SEE-FIM 2/2005 and after
Finch[8]	159	1 (0.6%)	64	BRCA mutation carrier	2 mm sectioning for 91/159 patients
Manchanda[19,20]	308	9 (3%)	40–67	BRCA mutation carrier or high risk personal/family history	2–3 mm sectioning for all patients
Wethington (current study)	593	12 (2%)	39–77	BRCA mutation carrier or high-risk personal/family history	SEE-FIM
Total	1456	36 (2%)	39–77		

*Some patients'details are provided in prior publications by Leeper et al,[17] Paley et al,[24] and Agoff et al.[9]

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