LAPAROSCOPIC TREATMENT OF ADNEXAL MASSES

At Desert Women's Care we have developed a treatment algorithm to assure appropriate referral of women with adnexal masses likely to represent ovarian cancer to Gynecologic Oncologists and treatment of adnexal masses felt to be benign using Minimally Invasive Surgical techniques while carefully observing standard principals of oncologic surgery.

Background

The prevalence of adnexal masses is relatively high in the general population. Ovarian cancer has non-specific symptoms and is usually silent in its early stages.[1] Presently we have no reliable screening test for ovarian cancer and we have a limited ability to detect it using current diagnostic strategies.[2-3]

Various studies have addressed the likelihood of malignancy within an ovarian mass. This likelihood ranges from 0.38% to 18.67%. (see Table 1) and is population dependent.[4-16]

Table 1. Likelihood of Malignancy in Adnexal Masses

Mage et al, 1990[4]	433	9	2.08%
Mecke et al, 1992[5]	773	11	1.42%
Nezhat et al, 1992[6]	1011	4	0.40%
Hulka et al, 1992[7]	13793	411	2.98%
Canis et al, 1994[8]	757	19	2.51%
Marzana et al, 1994[9]	527	2	0.38%
Wenzl et al, 1996[10]	16601	108	0.65%
Childers et al, 1996[11]	138	19	13.77%
Canis et al, 1997[12]	230	15	6.52%
Hidlebaugh et al, 1997[13]	405	8	1.98%
Malik et al, 1998[14]	292	11	3.77%
Mettler et al, 2001[15]	493	8	1.62%
Valentin et al, 2006[16]	1066	199	18.67%
Demir & Marchand 2012	257	15	5.84%
Total	36776	839	2.28%

The American College of Obstetricians & Gynecologists evaluated the various predictors of ovarian malignancy and published ACOG Committee Opinion 280 setting forth criteria to refer both premenopausal and postmenopausal women for care by Gynecologic Oncologists.[17] This has since been updated and is now embodied in ACOG Committee Opinion 477.[18]

These referral criteria are summarized in Table 2. Postmenopausal criteria include a lower CA 125 threshold or a nodular or fixed pelvic mass for referral. Importantly, only one referral criteria must be met for a patient to be referred to a Gynecologic Oncologist.

Table 2. ACOG Committee Opinion 280 and 477 Referral Criteria[17-18]

Premanopausal Women

CA 125 > 200 U/ml
Ascites
Evidence of abdominal or distant metastases
Family history 1st degree relative(s) with breast or ovarian cancer (deleted in CO 477)

Postmenopausal Women

Elevated CA 125
Ascites
Nodular or fixed pelvic mass
Evidence of abdominal or distant metastases
Family history 1st degree relative(s) with breast or ovarian cancer (deleted in CO 477)

Two prior studies have looked at the operational characteristics of ACOG Committee Opinion 280 and how it functions in actual practice. In 2005, Im, et al, demonstrated in a multi-center study using criteria in ACOG Committee Opinion 280 in a referral population to identify women at high risk for ovarian cancer yields a positive predictive value of 33.8% in premenopausal women and 59.5% in post menopausal women.[19] Data was not uniform from each of the seven centers and at some centers pelvic masses were only identified retrospectively. These investigators conceded their data did not address how ACOG Committee Opinion 280 would operate in a general population.

In a more elegant study, Dearking, et al, in 2007, demonstrated in a prospectively enrolled cohort using criteria set forth in ACOG Committee Opinion 280 in a non-referred population to identify women at elevated risk for ovarian cancer yields a positive predictive value of 13.6% in premenopausal women and 44.9% in postmenopausal women.[20] In their referral population applying the same selection criteria leads to a positive predictive value of 47.3% in premenopausal women and 90.5% in postmenopausal women. The referral population had a demonstrably higher prevalence of disease, positively influencing assessment of the selection criteria.

By whatever method, once located, the prognosis of an ovarian tumor is determined by surgical staging, histologic subtype and grade of tumor differentiation.[21]

How Have Women With Masses Suspected To Be Benign Been Treated In The Past?

Surgical treatment of adnexal masses suspected to be benign on pre-operative ultrasound has evolved over time. In each of these studies one anesthesia was used, usually with conversion to laparotomy , if frozen section diagnosed malignancy. Definitive staging was performed at the time of initial operation by Gynecologic Oncologists. This means that most women would undergo a mid-line laparotomy when most really did not need it.

What Is The Consequence of Rupturing The Mass During Surgery?

An important consideration in adnexal mass surgery is inadvertent opening of the ovarian capsule. Likelihood of cyst rupture either during laparotomic or laparoscopic removal ranges from 10.5 – 41.8% in published studies.[22-26]

In cases of ovarian malignancy where disease is confined to the ovary, rupture of the ovary increases the Stage to IC.

Vergote, et al, in 2001 reported on over 1500 patients with Stage I Epithelial Ovarian carcinoma and found intra-operative rupture worsened disease-free survival.[27] Various other retrospective multicenter studies support intra-operative cyst rupture as an independent predictor of disease free survival.[28-30]

Alternatively, another group of publications failed to demonstrate a difference in disease free survival based on intra-operative cyst rupture.[31-35] Limitations of both groups of older studies assessing long-term outcome of patients with inadvertent, intra-operative capsular rupture involve: inclusion of non-staged or incompletely staged cases, lack of consistent adjuvant treatments for women positive for malignancy and lack of separate analysis of Stage IC cases.

In perhaps the most definitive work on this topic, Bakkum-Gamez, et al, reported a retrospective study to specifically address outcomes related to intra-operative capsule rupture (stage IC) in treatment of stage I epithelial cancer between 1991 and 2007.[26] Of 161 cases meeting inclusion criteria, intra-operative capsule rupture occurred in 61 or 38%. All patients were treated in one anesthesia with definitive staging performed based on positive frozen section results. For patients whose only stage IC qualification was intra-operative capsular rupture there was found to be significantly higher recurrence and mortality rates.

In our practice we exercise great care to avoid opening adnexal masses during surgery.

What Is The Chance I Have Cancer If The Pre-Operative Testing Suggests The Mass Is Benign?

ACOG Committee Opinion 280 sets forth the Standard of Care for pre-operative discrimination of suspected malignant vs. suspected benign adnexal masses. But how successful is application of

Committee Opinion 280 in selecting a population of women at low-risk for ovarian malignancy and how should these women be optimally treated?

Im, et al, in 2005, showed that strict adherence to ACOG Committee Opinion 280 in a referral population yields a negative predictive value (NPV) of 92.0 % % for all cases of ovarian cancer in premenopausal women and an NPV of 91.1% in post menopausal women.[19]

Dearking, et al, in 2007, demonstrated that with strict adherence to ACOG Committee Opinion 280 in a non-referred population arising from their primary catchment area yields an NPV of 97.7% for all cases of ovarian cancer in premenopausal women and an NPV of 95.0% in post menopausal women.[20] In their referral population NPV was 91.0% in premenopausal and 90.5% in postmenopausal women, or essentially identical to the Im, et al, data.[19] Of the women not referred based on ACOG Committee Opinion 280 who were later found to have ovarian cancer, 8 of 10 premenopausal and 11 of 14 postmenopausal women were found to have Stage I or II disease at the time of definitive surgery. In other words, the majority of women predicted to have benign adnexal lesions who actually had malignant lesions, had early stage ovarian cancer the majority of the time.

What Happens If My Mass is Later Found To Be Malignant?

In this case a second surgery will be required.

Definitive staging of ovarian cancer includes: 1.) cytologic washings, total hysterectomy, bilateral salpingo-oophorectomy, peritoneal surface biopsies, total omentectomy and retroperitoneal lymphadenectomy from the pelvis and paraaortic regions to the left renal vessel.[36] Laparoscopy and laparotomy have equal efficacy in both early and advanced stage ovarian cancer.[37] The initial study on laparoscopic surgical staging in patients with early ovarian cancer was published in 1990.[38-39]

Because a final pathology report returning a diagnosis of invasive ovarian cancer is often a surprise, a subsequent procedure is required for definitive staging of disease. Frequency of upstaging in patients with EOC at initial examination is in the range of 10 – 35.7% (see Table 3).40-41, [72,73,79-87].

Table 3. Frequency of Upstaging at Definitive Procedure

Pomel et al [79] 1995	10	1	10.00%
Childers et al [80] 1995	14	5	35.70%
Stier et al [81] 1996	45	7	15.56%
Tozzi et al [83] 2004	24	5	20.80%
Leblanc et al [84] 2004	44	8	18.20%
Spirtos et l [85] 2005	58	6	11.00%

Chi et al [86] 2005	20	2	10.00%
Ghezzi et al [87] 2007	15	4	26.70%
Colomer et al [72] 2008	20	4	20.00%
Nezhat et al [73] 2009	36	7	19.44%
Demir & Marchand 2012	9	4	44.44%
Total	295	53	17.96%

Results of Desert Women's Care Study

Of 257 consecutive cases with stated inclusion criteria, six were found to have disseminated ovarian malignancy at the time of laparoscopy (see Table 4). Eleven cases were judged not to be candidates for inclusion in this study at the time of laparoscopy (see Table 5). A total of 240 patients successfully completed intended treatment (93.38%). Of patients successfully completing treatment 234 did not require admission (97.5%). One patient had an inadvertent bowel injury secondary to adhesiolysis requiring re-operation during the admission. One patient developed deep vein thrombosis well after discharge. Nine patients (3.75%) required re-operation by Gynecologic Oncologists after final pathology was available.

Table 4: Outcome Data

Total Patients in study period	257	
–surgery ends with laparoscopy	6	2.33%
–failed inclusion at laparoscopy	11	4.28%
total patients successfully completing	240	93.38%
--out-patient only	234	97.50%
--one hospital day	5	2.08%
--two or more hospital days	2	0.84%
–inadvertent rupture of mass	3	1.25%
--Cuff Cellulitis	0	0.00%
--febrile morbidity	9	3.75%
--injury to bowel	1	0.42%
--injury to bladder	0	0.00%
--injury to ureter	0	0.00%
--injury to major vessels	0	0.00%
--deep vein thrombosis	1	0.42%
--pulmonary embolism	0	0.00%
--port site hernia	0	0.00%
--re-operation this admission	1	0.42%
--death	0	0.00%
Washings Positive for malignancy	6	2.50%
Re-operated later by GYN Oncology	9	3.75%

Laparoscopic surgery combined with posterior colpotomy has a low incidence of significant complications. Outcome data shows that by observing the principals of Minimally Invasive Surgery, 97.50% of women were successfully treated as out-patients and enjoy the benefits associated with this surgical route as compared with those of laparotomy.

Table 5. Patients Not Meeting Inclusion Criteria (eleven patients)

--Adhesions prevent laparoscopic visualization	3	27.27%
--Frozen pelvis	2	18.18%
--Fallopian Tube Cyst / Hydrosalpinx	3	27.27%
--Fallopian Tube Cancer	1	9.09%
--Fibroid Uterus / Pedunculated Myomas	1	9.09%
--GI Malignancy	1	9.09%

Intra-operative rupture of the ovarian capsule was extremely uncommon in our series. Capsular rupture was noted in just 1.25% of cases.

Distribution of pathologic results is not surprising (see Table 6). The most common lesions were cystadenomas, endometriomas, cysts and mature teratomas accounting for 85% of all cases. Borderline tumors accounted for 5% of lesions while invasive ovarian malignancy represented 3.75% of the specimens.

Table 6. Pathology Results

--Ovarian Cystadenoma	64	26.67%
--Functional Cyst	47	19.58%
--Endometrioma	34	14.17%
--Simple Cyst	32	13.33%
--Mature Teratoma	27	11.25%
--Ovarian Fibroma	5	2.08%
--Other Benign Ovarian Lesions	10	4.17%
--Borderline Ovarian Tumor	12	5.00%
--Invasive Ovarian Cancer	9	3.75%

Laparoscopies abandoned based on presumption of disseminated disease had significant findings at the time of definitive staging by Gynecologic Oncologists: Stage I- 0%, Stage II – 16.67%, Stage III – 50% and Stage IV – 33.33% (see Table 7). In the nine cases we treated that later returned invasive carcinoma on final pathology, all were believed to be Stage I disease at the time of referral to GYN Oncology. No capsules had excresences, no disease was noted elsewhere in the abdomen and pelvis, but six had positive washings. Definitive staging upstaged four of the nine lesions or 44.44% (see Table 7).

Table 7. Cancer Staging From GYN Oncology

INVASIVE OVARIAN CANCER ON INSPECTION—LAPAROSCOPY TERMINATED: six patients		
--Stage I	0	0.00%
--Stage II	1	16.67%
--Stage III	3	50.00%
--Stage IV	2	33.33%
INVASIVE OVARIAN CANCER—OVARY REMOVED AND LATER DIRECTED TO GYN ONCOLOGY: nine patients		
--Stage I	5	55.56%
--Stage II	3	33.33%
--Stage III	1	11.11%
--Stage IV	0	0.00%

Finally, we examined the relationship of menopausal status and cancer Stage of all fifteen patients found to have invasive ovarian malignancy (see Table 8). Being postmenopausal conferred a greater likelihood of having any ovarian malignancy (8 / 88 or 9.09%) compared with pre-menopausal women (7 / 158 or 4.43%).

Table 8. Cancer Stage Based On Menopausal Status

ALL CASES OF INVASIVE OVARIAN CANCER (6 Initially excluded and 9 positive on final pathology)

	PREMENOPAUSAL	POSTMENOPAUSAL
Stage I	3	2
Stage II	2	2
Stage III	1	3

Stage IV	1	1
Total Patients	7 / 158 (4.43%)	8 / 88 (9.09%)
NPV ACOG 280	151 / 158 (95.57%)	80 / 88 (90.91%)

The Negative Predictive Value of ACOG Committee Opinions 280 and 477 as a de-selector for having invasive ovarian malignancy in our population was 95.57% for premenopausal and 90.91% for postmenopausal women.

Table 9. Negative Predictive Value of ACOG Committee Opinion 280

	Premenopausal	Postmenopausal
Im et al [45] 2005	92.00	91.10
Dearking et al [46] 2007		
--overall	93.10	91.70
--referral population	91.00	90.50
--general population	97.70	95.00
Demir & Marchand 2012	95.57	90.91

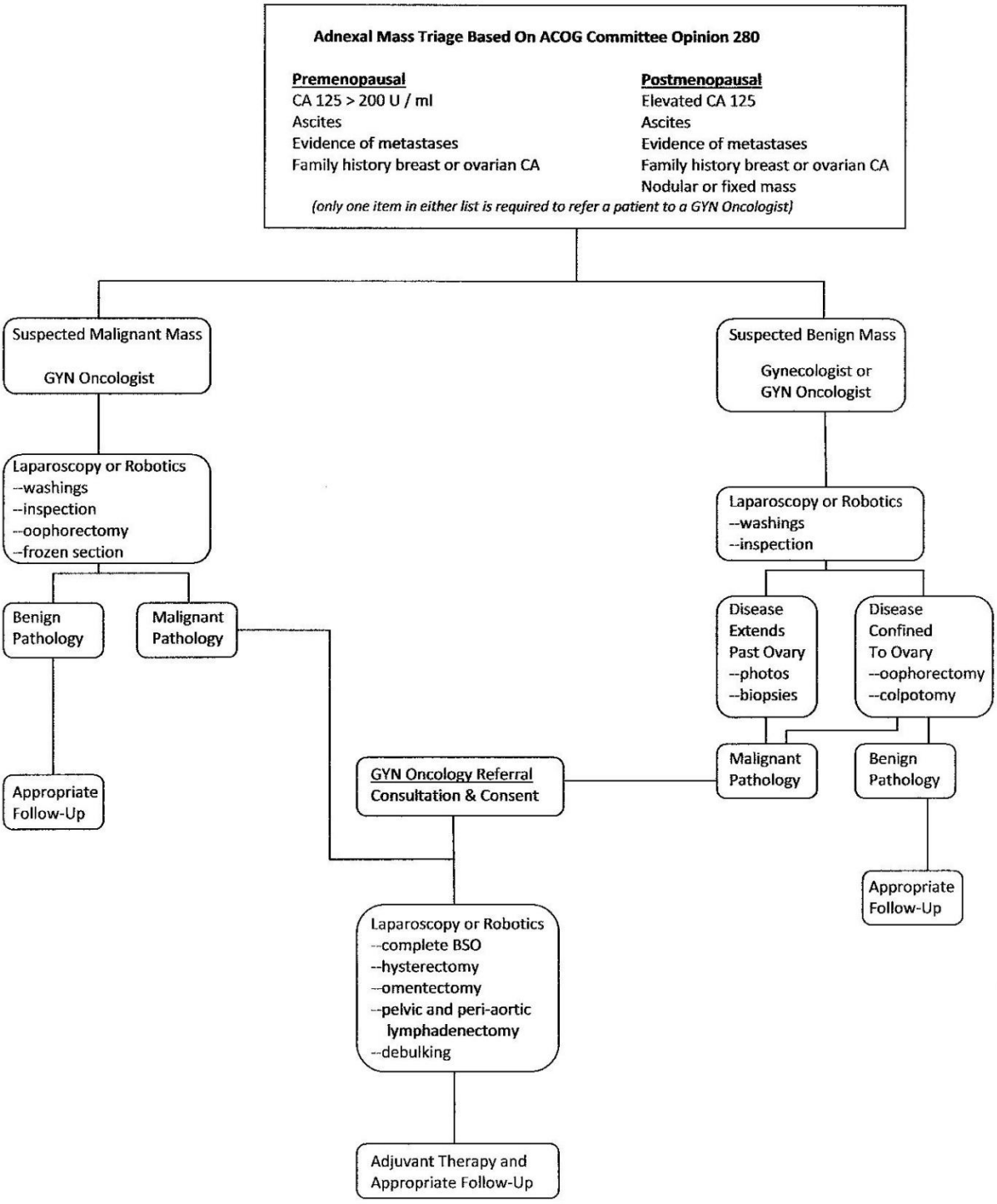
What This Means To You

Laparoscopic adnexectomy, bagging and colpotomy is a desirable goal for patients with adnexal masses meeting selection criteria for suspected benign lesions outlined in ACOG Committee Opinions 280 and 477 affording a minimally invasive approach with attendant benefits including out-patient treatment, decreased incidence of capsular rupture, few complications and low necessity for re-operation after final pathology is evaluated (see Figure 1).

The negative predictive value of ACOG Committee Opinions 280 and 477 selection criteria for encountering malignancy in suspected benign cases are set forth in Table 9. Data from the present study is consistent with other reports in the literature. Although re-operation is required 6.09% of the time (15 out of 246 patients) in our algorithm for women with suspected benign lesions, this risk is substantially outweighed by saving laparotomy in 93.91% of patients successfully operated found to have benign disease and in reducing 234 of 240 patients' treatment to a single out-patient encounter with decreased pain, less morbidity, enhanced satisfaction and lower cost through judicious application of principals of Minimally Invasive Surgery.

Another benefit of operation by experienced Minimally Invasive Surgeons is the lower observed incidence of capsular rupture of 1.25% compared to reported rates ranging from 10.5 – 41.8% during both laparotomic and laparoscopic surgeries reported in the literature [55,56,59-61].

No laboratory or imaging modality can guarantee the results of the final pathology report. It is therefore inevitable that some women believed to have benign adnexal masses pre-operatively will be told they have cancer. Correspondingly, some women operated in believing they have cancer will be told their mass is benign on final pathology.



We believe our treatment algorithm leads to fewer laparotomies, fewer women unnecessarily upstaged as a consequence of inadvertent capsular rupture and heightened ability to offer out-patient treatment for women with presumed benign adnexal masses.

Irrespective of which arm a patient is assigned to based on ACOG Committee Opinions 280 and 477, there will be inaccuracies until the final pathology report is received. If a woman is referred to GYN Oncologists based on this algorithm, there is a 13.6% Positive Predictive Value (PPV) for cancer in premenopausal women and a 44.9% PPV in postmenopausal women. This means the majority of women will not have cancer who were referred to Gynecologic Oncologists.

Women suspected to have a benign mass based on ACOG Committee Opinions 280 and 477, a small possibility exists the tumor may be malignant on final pathology (see Table 9). The Negative Predictive Value is 2.3 % for premenopausal women and 5.0% for postmenopausal women according to the Dearking study [46]. In our data the NPV is 4.43% for premenopausal and 8.19% for postmenopausal women. We believe our treatment algorithm minimizes the likelihood a woman will need her abdomen opened (laparotomy) while containerizing the ovarian mass and removing it intact so that if it is ultimately shown to be cancerous, disease is not spread during removal.

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