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Review Article

Development of Ismail's Guide Wheel on the Management of Epithelial Ovarian Cancer Including Fallopian Tube and Primary Peritoneal Cancer

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Abstract

We designed Ismail's Guidewheel on the Management of Epithelial Ovarian Cancer Including Fallopian Tube and Primary Peritoneal Cancer to help guide physicians through a standardized approach to the primary and adjuvant therapy for patients diagnosed with those conditions along with surveillance and the management of recurrent disease. We amalgamated recommendations from international health organizations on a wheel, which can easily be used during a consultation with a patient to provide a simplified yet comprehensive approach to their management. We included recommendations by the following organizations: the National Comprehensive Cancer Network (NCCN), the American College of Obstetricians and Gynecologists, the American Society of Clinical Oncology (ASCO), the Society of Gynecologic Oncology (SGO), the British Gynecological Cancer Society (BGCS), the National Institute of Care and Excellence (NICE), the Royal College of Obstetricians and Gynaecologists (RCOG), the Scottish Intercollegiate Guidelines Network (SIGN), the European Society of Gynaecological Oncology (ESGO), the European Society for Medical Oncology (ESMO), the Korean Society of Gynecologic Oncology (KSGO), the Spanish Society of Medical Oncology (SEOM), the Society of Obstetricians and Gynaecologists of Canada (SOGC) and the International Federation of Gynecology and Obstetrics (FIGO). This wheel is meant to be a quick and accessible resource for physicians but is not intended to replace alogorithms set by the aforementioned organizations.

Keywords: Chemotherapy; Epithelial ovarian cancer; Fallopian tube cancer; FIGO classification; Guidelines; Hereditary breast and ovarian syndrome; PARP inhibitors; Persistent or recurrent disease; Primary peritoneal cancer; Surgical staging; Surveillance; Systemic therapy; Therapy for relapse

Abbreviations: ACOG: American College of Obstetricians and Gynecologists; AJCC: American Joint Committee on Cancer; ASCO: American Society of Clinical Oncology; BGCS: British Gynaecological Cancer Society; BRCA1: breast cancer gene 1; BRCA2: breast cancer gene 2; CA-125: cancer antigen 125; CT: computed tomography; EOC: epithelial ovarian cancer; ESGO: European Society of Gynaecological Oncology; ESMO: European Society for Medical Oncology; FIGO: International Federation of Gynecology and Obstetrics; HE4: human epididymis protein 4 gene; HGSC: high-grade serous carcinoma; IHC: immunohistochemistry; KSGO: Korean Society of Gynecologic Oncology; LGSC: low-grade serous carcinoma; LN: lymph node; MRI: magnetic resonance imaging; NCCN: National Comprehensive Cancer Network; NICE: National Institute of Care and Excellence; OC: ovarian cancer; PARPi: poly-adenosine disphosphate-ribose polymerase inhibitor; PET: positron emission tomography; RCOG: Royal College of Obstetricians and Gynaecologists; RMI: Risk of Malignancy Index; ROMA: Risk of Ovarian Malignancy Algorithm; RRSO: risk-reducing salpingo-oophorectomy; SEOM: Spanish Society of Medical Oncology; SGO: Society of Gynecologic Oncology; SIGN: Scottish Intercollegiate Guidelines Network; SOGC: Society of Obstetricians and Gynaecologists of Canada; TNM: Tumors, Nodes, and Metastases

Introduction

Ovarian cancer (OC) is the second most common gynecologic cancer and is the most common cause of death due to gynecologic cancer accounting for more than 50% of deaths [1-11]. OC detected at stage I has a favorable prognosis [12]. However, due to the lack of effective screening for this disease, OC is diagnosed at an advanced stage in more than 75% of cases [4,9,12-16]. Risk factors for include advancing age, nulliparity, early menarche, late menopause, family history of OC or breast cancer, and endometriosis [4,6,8,10,14-19]. In fact, all women are subject to risk of developing OC [12]. 90% of OC are Epithelial Ovarian Cancers (EOC) [9,19]. According to the World Health Organization, there are five types of EOC including serous carcinoma, which is further classified as high-grade serous carcinoma (HGSC) or low-grade serous carcinoma (LGSC), clear-cell carcinoma, mucinous carcinoma and endometrioid carcinoma [8, 11, 20]. HGSC constitutes around 75% of all OC [15,20]. The mainstay of treating OC is surgery and chemotherapy [2,13,14,19]. Several international health organizations set recommendations on the management of patients with EOC, fallopian tube and primary peritoneal cancer. We compared guidelines by the National Comprehensive Cancer Network (NCCN), the American College of Obstetricians and Gynecologists, the American Society of Clinical Oncology (ASCO), the Society of Gynecologic Oncology (SGO), the British Gynaecological Cancer Society (BGCS), the National Institute of Care and Excellence (NICE), the Royal College of Obstetricians and Gynaecologists (RCOG), the Scottish Intercollegiate Guidelines Network (SIGN), the European Society of Gynaecological Oncology (ESGO), the European Society for Medical Oncology (ESMO), the Korean Society of Gynecologic Oncology (KSGO), the Spanish Society of Medical Oncology (SEOM), the Society of Obstetricians and Gynaecologists of Canada (SOGC) and the International Federation of Gynecology and Obstetrics (FIGO) [1,4-11,13,16-21]. In the interest of convenience, in this paper, OC collectively refers to EOC, fallopian tube and primary peritoneal cancer as they are managed in the same way. We designed a management guidewheel on the recommendations of treating patients with OC as per the aforementioned guidelines. This guidewheel aims to assist healthcare providers when counseling patients diagnosed with OC to provide them with a general insight on their expected course of treatment.

About this Guide Wheel

Ismail's Guide wheel on the Management of Epithelial Ovarian Cancer Including Fallopian Tube and Primary Peritoneal Cancer integrates the recommendations of various organizations regarding the management of epithelial ovarian cancer and fallopian tube and primary peritoneal cancer. The inner wheel (Figure 1) can be rotated along the base of the guide wheel (Figure 2) to match the treatment modalities to the type of ovarian cancer, stated on the outer rim of the guide wheel, and displays the recommended steps in chronological order (Figure 3).

The types of ovarian cancer displayed on the outer rim of the guidewheel are broadly categorized as follows:

- Primary Treatment of All Ovarian Cancer, Fallopian Tube (FT) and Primary Peritoneal Cancer
- Diagnosis by Previous Surgery
- Chemotherapy for Grades 2 and 3 Endometrioid and Serous Carcinoma
- Adjuvant Therapy for Grade 1 Endometrioid Carcinoma and LGSC
- Maintenance Therapy for Stages II, III and IV After Primary Therapy
- Therapy for Persistent or Recurrent Disease
- Adjuvant Therapy of Ovarian Borderline Epithelial Tumors (Low Malignant Potential)
- The inner wheel (Figure 1) displays the different treatment modalities as follows:

- Primary Treatment: a. Surgery; b. Neoadjuvant Therapy
- Surgical Therapy: a. Surgical Staging; b. Hysterectomy; c. Fertility-Sparing Surgery; d. Unilateral Salpingo-oophorectomy (USO); e. Bilateral Salpingo-oophorectomy (BSO); f. Debulking; g. Cytoreduction; h. Resection; i. Completion
- Work-Up: a. Pathology (A. Histology, B. Immunohistochemistry (IHC)); b. Genetic; c. Molecular; d. T-Markers; e. Imaging
- Adjuvant Therapy: a. Chemotherapy; b. Hormonal; c. Observation; d. Systemic Therapy
- Neo-Adjuvant Therapy: a. Chemotherapy; b. Immunotherapy; c. Biological (targeted)
- Systemic Therapy
- Maintenance Therapy: a. Immunotherapy; b. Biological (targeted); c. Hormonal; d. Observation
- Therapy for Persistent/Recurrent Disease: a. Clinical Trial
- Observation
- Monitoring / Follow-Up
- Care

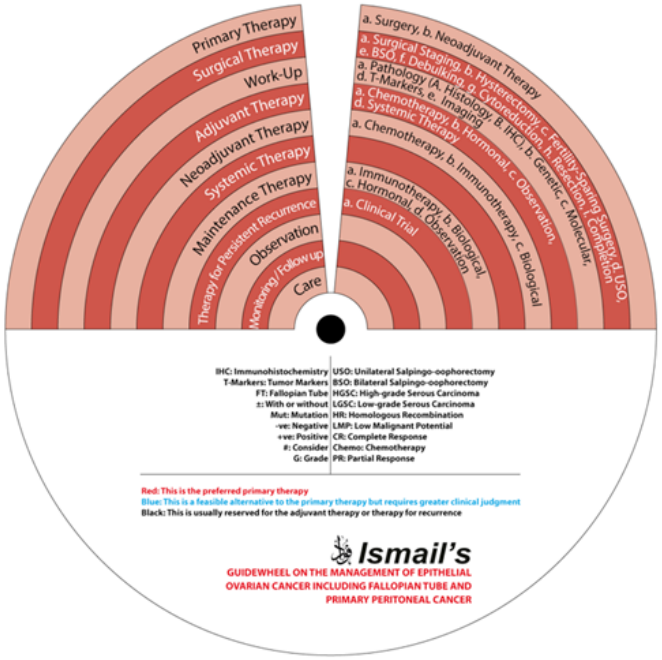

Figure 1: The inner wheel of the guidewheel demonstrating the different treatment modalities and the options for each.

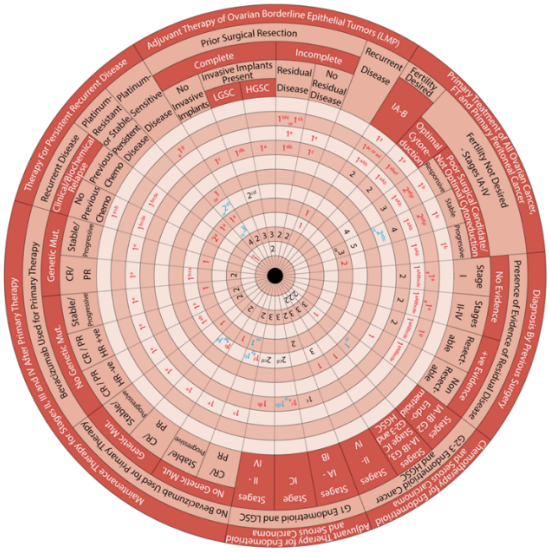

Figure 2: The base of the guidewheel displaying the color-coded steps the correspond to the types and stages of ovarian cancer.

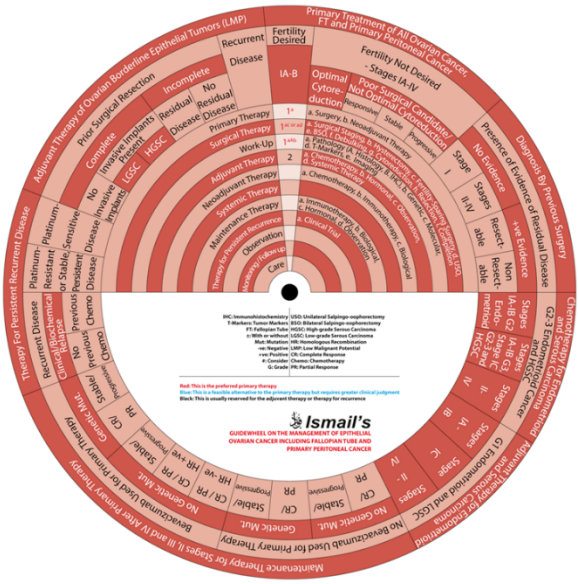

Figure 3: Ismail's Guidewheel on the Management of Epithelial Ovarian Cancer Including Fallopian Tube and Primary Peritoneal Cancer fully assembled showing the management of a patient with stage IA-IB while preserving fertility.

How to Use the Guide Wheel

The back of the guidewheel (Figure 4) explains how to use Ismail's Guidewheel on the Management of Epithelial Ovarian

Cancer Including Fallopian Tube and Primary Peritoneal Cancer. The inner wheel is rotated along the base of the guidewheel and the management of a particular ovarian cacner type is displayed in the viewing slot. The steps are in chronological order and color-coded as follows:

- Red: This is the preferred primary therapy.
- Blue: This is a feasible alternative to the primary therapy but requires greater clinical judgment.
- Black: This is usually reserved for the adjuvant therapy or therapy for recurrence.

Abbreviations used on the wheel include the following:

±	With or without	USO	Unilateral salpingo-oophorectomy
#	Consider	BSO	Bilateral salpingo-oophorectomy
+ve	Positive	Chemo	Chemotherapy
-ve	Negative	LGSC	Low-grade Serous Carcinoma
IHC	Immunohistochemistry	HGSC	High-grade Serous Carcinoma
FT	Fallopian tube	HR	Homologous Recombination
G	Grade	CR	Complete Response
T-Markers	Tumor markers	PR	Partial Response
Mut	Mutation	LMP	Low Malignant Potential

The FIGO 2017 classification of ovarian, fallopian tube and primary peritoneal cancer, along with the corresponding Tumors, Nodes and Metastasis system developed by the American Joint Committee on Cancer (AJCC), is displayed on the back of the wheel (Figure 4) and is listed as follows [16]:

Stages and Descriptions	
FIGO Stage I (TNM T1): The tumor is confined to the ovaries or fallopian tube(s).	
FIGO IA (TNM T1a)	Tumor limited to 1 ovary (capsule intact) or fallopian tube; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings
FIGO IB (TNM T1b)	Tumor limited to both ovaries (capsules intact) or fallopian tubes; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings
FIGO IC (TNM T1c)	Tumor limited to 1 or both ovaries or fallopian tubes, with any of:
FIGO IC1 (TNM T1c1)	Surgical spill
FIGO IC2 (TNM T1c2)	Capsule ruptured before surgery or tumor on ovarian or fallopian tube surface
FIGO IC3 (TNM T1c3)	Malignant cells in the ascites or peritoneal washings
FIGO Stage II (TNM T2): The tumor involves 1 or both ovaries or fallopian tubes with pelvic extension (below pelvic brim) or peritoneal cancer.	
FIGO IIA (TNM T2a)	Extension and/or implants on uterus and/or fallopian tubes and/or ovaries
FIGO IIB (TNM T2b)	Extension to other pelvic intraperitoneal tissues
FIGO Stage III (TNM T3): The tumor involves 1 or both ovaries or fallopian tubes, or peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes.	
FIGO IIIA1 (TNM T3a1 N0/1)	Positive retroperitoneal lymph nodes only (cytologically or histologically proven)
FIGO IIIA1(i)	Metastasis up to 10mm in greatest dimension
FIGO IIIA1(ii)	Metastasis more than 10mm in greatest dimension
FIGO IIIA2 (TNM T3a2 N0/1)	Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes
FIGO IIIB (TNM T3b N0/1)	Macroscopic peritoneal metastasis beyond the pelvis up to 2cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes
FIGO IIIC (TNM T3c N0/1)	Macroscopic peritoneal metastasis beyond the pelvis more than 2cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes (includes extension of tumor to capsule of liver and spleen without parenchymal involvement of either organ)

FIGO Stage IV (TNM M1): Distant metastasis excluding peritoneal metastases	
FIGO IVA (TNM M1a)	Pleural effusion with positive cytology
FIGO IVB (TNM M1b)	Parenchymal metastases and metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)

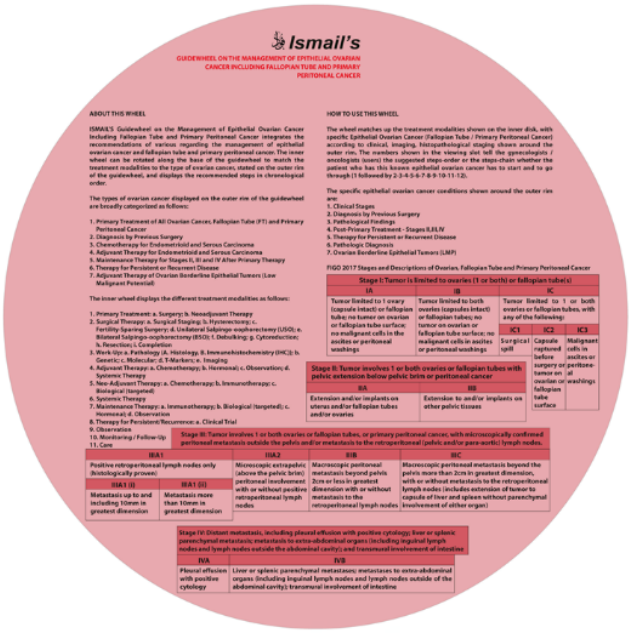

Figure 4: The back of the guidewheel displays the FIGO staging system of ovarian cancer [16] and how to use the guide wheel.

Recommendations on Managing Patients with Epithelial Ovarian, Fallopian Tube and Primary Peritoneal Cancer Using the Guidewheel

Sector 1. Primary Treatment of All Ovarian Cancer, Fallopian Tube (FT) and Primary Peritoneal Cancer (Figure 5)

For patients with ovarian, FT or primary peritoneal cancer stages IA and IB who desire to preserve their fertility, primary treatment (1) is surgical (a) with surgical staging and USO (ad) for stage IA disease or surgical staging and BSO (ae) for stage IB disease. This is followed by further workup (1a) with pathologic staging (A) and genetic testing (b) if not done before. The next step (2) is adjuvant therapy.

Patients who do not desire to preserve their fertility must be further managed depending on the probability of optimal cytoreduction. Patients with disease stages IA-IV with optimal cytoreduction are managed with primary treatment (1) being surgical (a). The first step (1) is surgical treatment with surgical staging (a), hysterectomy (b), BSO (e), and debulking (f). This is then followed by further workup (a) with pathologic staging (A) and genetic testing (b) if not done before. The next step (2) is adjuvant therapy.

On the other hand, patients who do not desire to preserve their fertility but are poor surgical candidates or have a low likelihood of undergoing optimal cytoreduction, management starts with neoadjuvant therapy and further steps depend on their response to the therapy. Patients demonstrating response to therapy are managed primarily (1) with neoadjuvant therapy (b). This is followed by further workup (1a) with pathologic staging (A) and genetic testing (b) if not done before. The second step (2) is surgical treatment with BSO (e), debulking (f), cytoreduction (g), and completion hysterectomy (i). The next step (3) is adjuvant therapy. The next step (4) can involve maintenance therapy.

Patients who have stable disease following neoadjuvant therapy (1b) undergo further workup (a) with pathologic staging (A) and genetic testing (b) if not done before. The second step (2) is surgical treatment with BSO (e), debulking (f), cytoreduction (g), and completion hysterectomy (i). An alternative (or) for the second step (2) is to continue neoadjuvant therapy for at least 6 cycles in total with chemotherapy (a), immunotherapy (b) or biological therapy (c). Another alternative (or) is therapy for recurrent disease (3). The next step (4) is adjuvant therapy. The next step (5) can involve maintenance therapy.

Patients with progressive disease are managed in the form of primary treatment (1) with neoadjuvant therapy (b). This is followed by further workup (a) with pathologic staging (A) and genetic testing (b) if not done before. The second step (2) is therapy for recurrent disease.

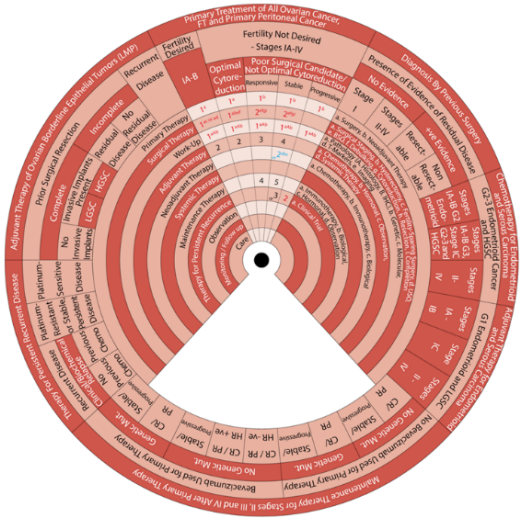

Figure 5: Primary Treatment of All Ovarian Cancer, Fallopian Tube (FT) and Primary Peritoneal Cancer.

Sector 2. Diagnosis by Previous Surgery (Figure 6)

Patients who are referred with a diagnosis of OC after a surgical procedure should be further evaluated by a gynecologic oncologist and further management depends on the presence of residual disease on further workup. If patients diagnosed with stage I-IV disease and no residual disease, the first step (1) is to consider (#) surgical staging (a). This is followed by further workup (a) with pathologic staging (A) and IHC (B), genetic testing (b) if not done before, molecular testing (c), tumor markers (d), and imaging (e) as clinically indicated. The next step (2) is adjuvant therapy.

However, the management of patients who have residual disease on further workup depends on the resectability of the residual disease. If it is resectable, then primary treatment (1) is cytoreduction (g). This is followed by further workup (a) with pathologic staging (A) and IHC (B), genetic testing (b) if not done before, molecular testing (c), tumor markers (d), and imaging (e) as clinically indicated. The next step (2) is adjuvant therapy.

If the residual disease is non-resectable, then primary treatment is neoadjuvant therapy (1). This is followed by further workup (a) with pathologic staging (A) and IHC (B), genetic testing (b) if not done before, molecular testing (c), tumor markers (d), and imaging (e) as clinically indicated.

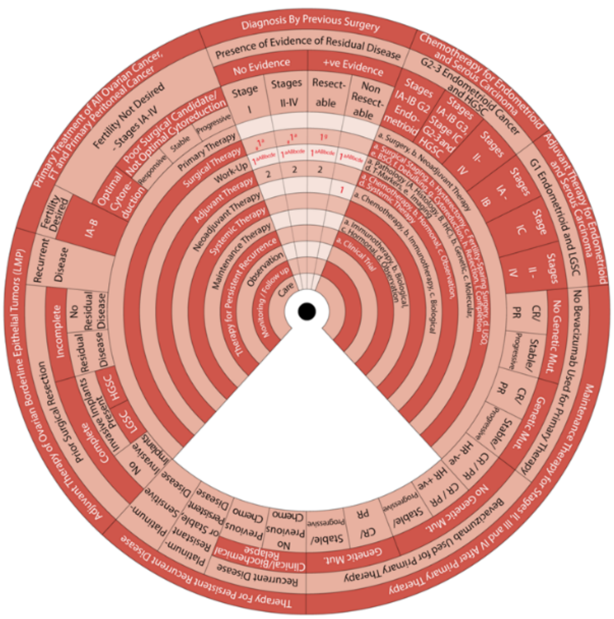

Figure 6: Diagnosis by Previous Surgery.

Sector 3. Chemotherapy for Grades 2 and 3 Endometrioid and Serous Carcinoma (Figure 7)

Patients with stage IA or IB grade 2 endometrioid cancer are first managed with observation (1). An alternative (or) is systemic therapy (1). The next step (2) is best supportive care. Then, monitoring (3) is indicated. Patients with stage 1A or IB grade 3 endometrioid cancer or HGSC and those with stage IC HGSC or endometrioid cancer grades 2 or 3 are first managed with systemic therapy (1). The next step (2) is best supportive care. Then, monitoring (3) is indicated. Patients with stages II-IV are also first managed with systemic therapy (1). The next step (2) is best supportive care. Then, monitoring (3) and maintenance therapy (3) are indicated.

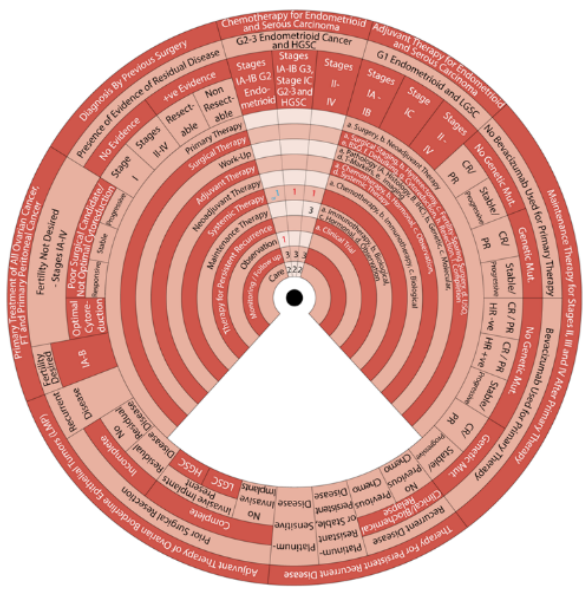

Figure 7: Chemotherapy for Grades 2 and 3 Endometrioid and Serous Carcinoma.

Sector 4. Adjuvant Therapy for Grade 1 Endometrioid Carcinoma and LGSC (Figure 8)

Adjuvant therapy for patients with grade 1 endometrioid cancer or LGSC stages IA and IB is observation (1c). The next step (2) is monitoring/follow-up. In addition to monitoring is therapy for recurrent disease (2). The preferred adjuvant therapy (1) for patients with disease stage IC is observation (c). An alternative (or 1) is systemic therapy (d) or hormonal therapy (b). The second step (2) is maintenance therapy with observation (d) or hormonal therapy (c) with letrozole, for instance. The third step (3) is monitoring and follow-up.

Patients with disease stages II-IV should receive adjuvant therapy (1) in the form of systemic therapy (d) or hormonal therapy (b). The second step (2) is maintenance therapy with observation (d) or hormonal therapy (c) with letrozole, for instance. The third step (3) is monitoring and follow-up.

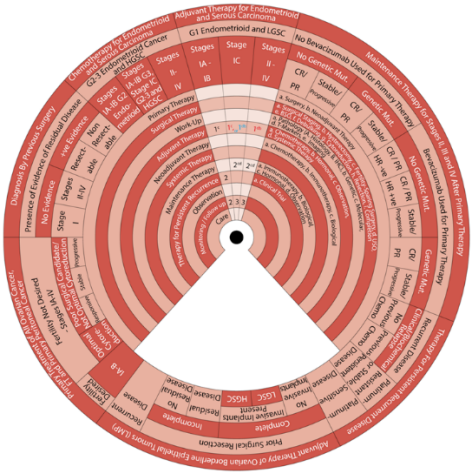

Figure 8: Adjuvant Therapy for Grade 1 Endometrioid Carcinoma and LGSC.

Sector 5. Maintenance Therapy for Stages II, III and IV After Primary Therapy (Figure 9)

Following primary treatment of patients with stage II, III, and IV, maintenance therapy depends on whether or not bevacizumab was used during primary treatment and the presence or absence of a genetic mutation in breast cancer gene 1 (BRCA1) or 2. It also depends on the response to primary treatment. The first step (1) is further workup with imaging (e), such as CT, MRI, or PET/CT of the chest, abdomen, and pelvis. If no bevacizumab was used, there is no mutation in BRCA1/2 and the disease demonstrates complete or partial response to primary treatment, maintenance therapy (1) is observation (d) in the case of complete response. An alternative (or) to the first step (1) is biological treatment (b) with PARPi niraparib. Another alternative (or 1) is therapy for recurrent disease. The next step (2) is monitoring and follow-up.

If no bevacizumab was used, there is a mutation in BRCA1/2 and the disease demonstrates complete or partial response to primary treatment, maintenance therapy (1) is biological therapy (b) with PARPi, such as olaparib or niraparib. An alternative (or) to the first step (1) is to consider (#) observation (d) for stage II disease only. The next step (2) is monitoring and follow-up.

If there is stable or progressive disease regardless of the use of bevacizumab during primary treatment or the presence of BRCA1/2 mutation, the first step (1) of maintenance therapy is therapy for recurrent disease.

If bevacizumab was used during primary treatment, the first step (1) is further workup with imaging (e). Further management depends on the response to the primary treatment and the presence or absence of BRCA1/2 mutation. Patients with no genetic mutation and demonstrating complete or partial response to primary therapy should be assessed whether they are homologous recombination (HR) proficient or deficient. Those who are HR deficient should be managed with maintenance therapy (1) with immunotherapy (a) with bevacizumab and biological therapy (b) with olaparib. On the other hand, those who are HR proficient should receive maintenance therapy (1) with immunotherapy (a) in the form of bevacizumab. The next step (2) is monitoring regardless of the HR status.

Patients with a BRCA1/2 mutation demonstrating complete or partial response to primary thearpy should be treated with maintenance therapy (1) with biological therapy (b) with or without (±) immunotherapy (a) with bevacizumab. This is followed up by monitoring and follow-up (2).

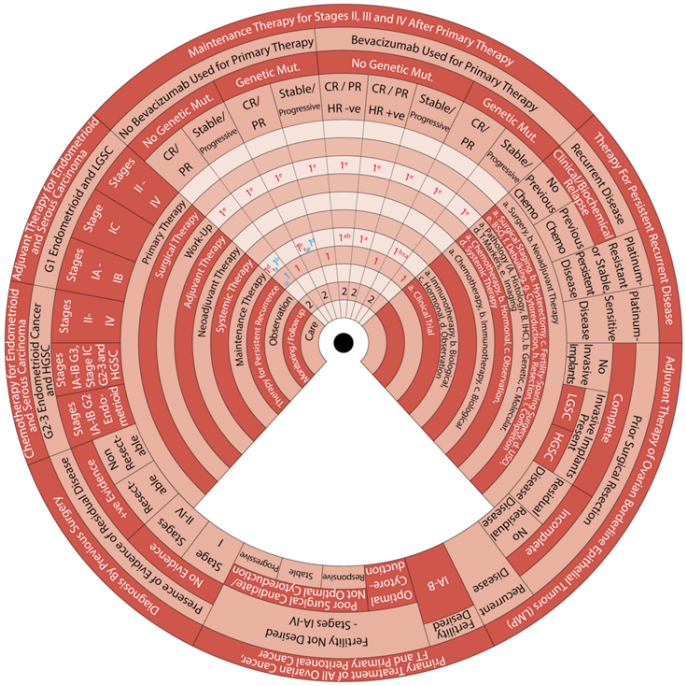

Figure 9: Maintenance Therapy for Stages II, III and IV After Primary Therapy.

Sector 6. Therapy for Persistent or Recurrent Disease (Figure 10)

Patients who undergo recurrence both clinically or biochemically, with rising CA125 levels, are managed depending on the use of chemotherapy during their primary treatment. Either way, further workup (1) is indicated with molecular testing (c), and imaging (e) as clinically indicated. If no chemotherapy was used, primary therapy (1) is surgery (a) with or without (±) neoadjuvant therapy (b). Otherwise, if chemotherapy was used, the next step (2) is therapy for recurrent disease with an option of clinical trial (a).

Regarding the response of the disease to platinum-based chemotherapy, it can either be platinum-resistant or platinum-

sensitive. Patients who progress on primary, maintenance or recurrence therapy, have stable, persistent disease or develop complete remission then relapse less than 6 months after completing chemotherapy are identified as platinum-resistant and are advised to undergo treatment for recurrent therapy (1) with clinicial trial (a). An alternative (or) is best supportive care (1). If a patient is platinum-sensitive, meaning they developed complete remission and relapsed 6 months or more after completing treatment, primary treatment (1) is therapy for recurrence with clinical trial (a). If there is evidence of relapse clinically or radiographically, secondary cytoreductive surgery (g) can be considered (#). An alternative (or) is systemic therapy (1). An alternative (or) second step (2) is maintenance therapy with immunotherapy (a) with bevacizumab and biological therapy (b) with PARPi, if not used before. An alternative (or) third step is observation (3). Finally, monitoring is indicated (4).

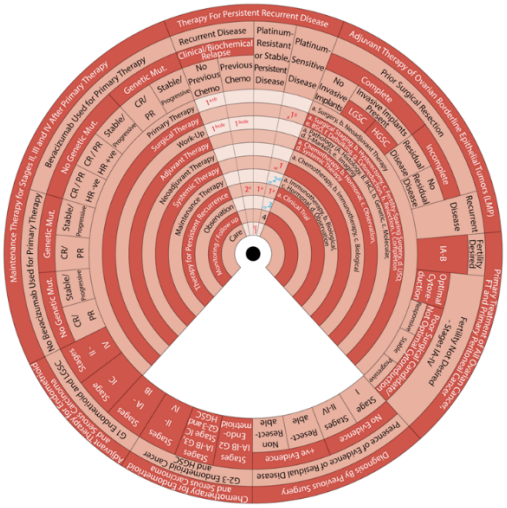

Figure 10: Therapy for Persistent or Recurrent Disease.

Sector 7. Adjuvant Therapy of Ovarian Borderline Epithelial Tumors (Low Malignant Potential) (Figure 11)

Patients with ovarian borderline epithelial tumors are managed according to the state of the surgical resection, whether it was complete or incomplete. Those who underwent complete resection and have no invasive implants can be observed (1c). The next step (2) is monitoring. Those who had a complete resection and diagnosed as LGSC are treated adjuvantly (1) with systemic therapy (d) or hormonal therapy (b). Maintenance therapy (2) with hormonal therapy (c) or observation (d). The next step (3) is monitoring. Patients diagnosed with HGSC and no residual disease, the first step (1) is adjuvant therapy with chemotherapy (a). The next step is best supportive care (2) and this is followed by monitoring (3).

Patients who underwent incomplete surgical resection of the disease are advised to undergo further workup (1) with imaging (e). If there is residual disease on imaging, then primary therapy (1) involves hysterectomy (b), resection (h) of residual disease, and completion (i) surgery or fertility-sparing surgery (c) and resection (h) of residual disease. Adjuvant therapy (1) involves systemic therapy (d) or hormonal therapy (b). The next step (2) is monitoring. If there is no residual disease on imaging, then adjuvant therapy (1) with observation (c) is warranted. The next step (2) is monitoring.

In the case of recurrent ovarian borderline epithelial tumors, observation (1) is warranted in the case of non-invasive disease while therapy for recurrent disease (1) is indicated for invasive implants or invasive carcinoma.

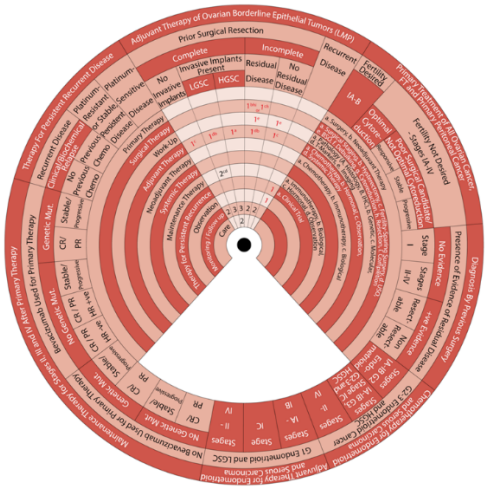

Figure 11: Adjuvant Therapy of Ovarian Borderline Epithelial Tumors (Low Malignant Potential).

Discussion

OC is staged using the International Federation of Gynecology and Obstetrics (FIGO) [2,15,16,21]. Patients are either asymptomatic or can present with abdominal or pelvic pain, urinary symptoms or early satiety [3-5,11,16,21]. Several biomarkers are associated with OC, such as cancer antigen 125 (CA-125) and human epididymis protein 4 gene (HE4). CA-125 is not only high in OC but can also be elevated in cases of endometriosis and pregnancy [4,14,17]. Recent studies proved that HE4 is more effective at differentiating between benign and malignant ovarian masses than CA-125 [4,9,17,20]. Various prediction models were designed to assess the risk of malignancy in ovarian masses. The Risk of Malignancy Index (RMI) only takes into consideration the CA-125 level while the Risk of Ovarian Malignancy Algorithm (ROMA) considers both CA-125

and HE4 making the latter model more sensitive [3,8,10,17,19,20]. Genetic counseling is recommended for all women with ovarian, fallopian tube or primary peritoneal cancer [16,18]. Numerous genetic mutations associated with an increased risk of OC include breast cancer gene 1 or 2 (BRCA1/2), RAD51C/D, ARID1A, BRIP1 and PALB2, among others [6,9,15,18,19]. Genetic testing for the presence of the BRCA1/2 is recommended for all women diagnosed with high-grade EOC regardless of the age at diagnosis or family history [4,9,16,18-20]. Knowing the BRCA1/2 status in a woman can help determine the response to the tumor to platinum-based chemotherapy, maintenance therapy with PARPi, and the likely prognosis [2,4,9,14,18,20]. Patients with a known mutation in BRCA1/2, RAD51C/D and BRIP1 might benefit from a risk-reducing salpingo-oophorectomy (RRSO) to reduce their risk of developing both OC and breast cancer [4,6,10,14-16,18,19]. Generally, pelvic ultrasound is an initial imaging modality to help diagnose OC and if malignant disease is suspected, patients are referred for computed tomography (CT) of the chest, abdomen, and pelvis [3-5,13,14,19,21].

When a patient is diagnosed with OC, they are required to undergo complete surgical staging involving the resection of the ovaries, uterus, fallopian tubes, infracolic omentum, and bulky lymph nodes and the inspection of bowel serosa and peritoneal surfaces [3,4,7, 8,11,12,15,16,19,21]. For patients with apparent early-stage OC, a fertility-sparing procedure can be considered with comprehensive staging rather than complete surgical staging [7-9,11,12,14,15,19]. It is important to note that endometrioid carcinoma and serous tumors are associated with a high likelihood of bilateral involvement [14]. Patients are classified as having either a high or low likelihood of achieving optimal cytoreduction [13]. If optimal cytoreduction can be achieved, primary treatment can proceed with surgery, otherwise, neoadjuvant chemotherapy is recommended followed by interval cytoreductive surgery [2,4, 7,10,13,15,16,19,21]. The aim of surgical staging is to accurately stage the disease to help plan treatment and determine likely prognosis since the risk of relpase increases in patients who are incompletely staged [4,9,12]. Since EOC is highly chemosensitive, chemotherapy constitutes a major aspect of treatment [2]. First-line chemotherapy typically includes a combination of carboplatin and paclitaxel [21]. Adjuvant chemotherapy is recommended for patients with high grade early-stage disease due to the higher risk of recurrence [2,8,9,19]. It is not necessary for patients with low-grade early-stage OC because they generally have a better prognosis [16]. Patients with a known BRCA1/2 mutation are advised to undergo maintenance therapy with PARPi after responding to chemotherapy [9,11,14, 16,18,21]. Participation in clinical trials for women with OC is highly recommended [2,10,19,21].

The aim of surveillance of patients with OC is to monitor improvement in symptoms related to the disease and detect any recurrences that might require additional treatment [1,21]. Patients also need to be educated regarding the importance of close follow-up, symptoms of recurrence and the possible complications of treatment [5,9]. Recurrence occurs in 70-75% of women with EOC [14,19]. Factors associated with a higher risk of recurrence include residual macroscopic disease following resection, age of 65 years or more, and having advanced stage at diagnosis [1]. When recurrent disease is suspected, imaging with CT is advised along with measuring tumor markers, including CA-125 [1,4,15]. Those with recurrent OC might benefit from a secondary cytoreductive surgery or further chemotherapy with or without bevacizumab in addition to palliative care [4,9,12,14,16].

A management guidewheel is aimed to provide a quick and accessible resource for the treatment of patients with OC. This is similar to guidewheels we designed for abnormal pap smears, uterine, cervical and vulvar cancer [22-25]. We also designed another guidewheel to describe the management of less common OC called Ismail's Guidewheel on the Management of Less Common Ovarian Cancers which is covered in another manuscript. We wrote several chapters on the management of cervical cancer and abnormal pap smear results [26-29]. In general, these guidewheels reflect the recommendations on managing patients in an ideal situation with all resources available. They do not provide any modifications to managing patients during the COVID-19 pandemic. Since the NCCN guidelines are continuously updated, the recommendations on this guidewheel mainly reflect the most recent guidelines.

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