

# Early Epithelial Ovarian Carcinoma Treatment

Giorgio Maria Paul Graziano, Giovanni Castelli, Prof Antonino Graziano

**Abstract**— The 80-90% of ovarian cancer occurs in women aged between 20 and 65 years, and less than 5% in children. In the great majority of cases (80%) it comes to benign tumors: 60% of them is diagnosed in women aged less than 40 years. Numerous published studies regarding the treatment of initial states of ovarian cancer show that surgical treatment and chemotherapy have a close correlation in improved survival. . The purpose of this study is through an analytical review of reported cases to identify and remove the factors that influence the choice of surgical treatment so as to increase the survival and / or disease-free interval. **Materials and Methods:** From copies of medical records of patients have been incorporated all the necessary information for research, the following parameters: the FIGO staging The type of surgical treatment chemotherapy, the recovery of the disease, survival, with a cross-check with the 'pathological anatomy. In addition, the follow-up examinations blood chemistry markers tumor imaging studies (MRI tc) eco abdomen. **Results:** The complete treatment has affected n 118 cases (48%) in the treatment Fertile women only in cases of n 20/17%) in the remaining 44 cases (35%) The surgical treatment was incomplete. The grading in 75% of cases the tumor was poorly differentiated in the remaining 25% had serous type. **Discussion** In epithelial cancer signs and symptoms tend to delay their appearance or be absent. only during an occasional clinical monitoring is diagnosed that is when the swelling is palpable and has reached significant size with non-specific manifestations and the presence of ascites Surgical removal in fertile women with a family history of ovarian disease is the series that the response only in patients bearers gene mutation (BCRA1-2). **Conclusions** The diagnosis of early ovarian cancer is difficult to be implemented, but with a good chance of successful treatment. .The Results of a standardized management and accurate contributes in increasing the percentage of early diagnosis with an increase in disease-free interval and survival. The new concepts of ovarian carcinogenesis, while it makes it even more complex screening problems of this cancer, may change the preventive approach in women at risk hereditary-familial.

**Index Terms**— Early Epithelial Cancer Treatment .

## I. INTRODUCTION

The 80-90% of ovarian cancer occurs in women aged between 20 and 65 years, and less than 5% in children. In the great majority of cases (80%) it comes to benign tumors: 60% of them is diagnosed in women aged less than 40 years. 15-20% of ovarian tumors are malignant, and of these 90% are diagnosed in women over the age of 40. Finally, 5-10% of

ovarian cancers is defined in malignancy (1,2,3,4) intermediate (borderline). Unlike malignant tumors, which are observed mainly in old age, borderline tumors are more common in young women with peak incidence in the fourth and fifth decade. The incidence of malignant ovarian neoplasms varies in different geographical areas, with higher rates in Europe and North America [4,5,6,7]. In African countries and South-East Asia are observed within 2 new cases per year per 100,000 women, while in Europe and North America are registered 15 new cases per 100,000 women years The incidence of this disease in industrialized countries is increase, around 17 cases per 100,000 per year with a mortality rate of 12 / 100,000 per year; in 60-70% of cases begins at an advanced stage. (8,9,10,11) In recent decades, some epidemiological studies have led to develop three theories about the etiology of ovarian cancers: 1. (family genetic factors) A family history disease is a factor associated with an increased risk of cancer; 2. (endocrine factors) The incessant and gonadotropin stimulation ovulation can lead to cellular mutations and promote neoplastic transformation 3. (environmental factors) The ovary may be exposed to carcinogens through the vagina and the fallopian tubes. More recently, for high-grade serous tumors is assumed that the origins of cancer from a precancerous lesion (STIC) located in the tube. 4. (hypothesis of "incessant menstruation"). The tubal fimbria and 'exposed to oxidative stress induced by iron derived from the lysis of red blood cells during the retrograde menstruation The oxidation-reduction processes of iron (Fe<sup>3+</sup> + - Fe<sup>2+</sup>) generate reactive oxygen species (reactive oxygen species [ROS]), that cause lipid peroxidation breaks in DNA strands, activation and inhibition of oncogenes and tumor suppressor genes ([12,13,14,15). Even tumors clear cell and endometrioid seem related to the mechanism have not been indicated in the ovary morphological lesions that can represent the cancer precursors, and currently it is believed that tumors of both type I than type II originate from the junction cells extra-ovarian that are implanted secondarily on the gonad. [16,17,18,19] This injury may be the forerunner of high-grade serous cancer is in women with mutation of the BRCA1 or BRCA2 genes both in women without these mutations. The tubal fimbria and 'in close contact with the surface of the gonad at the time of ovulation, and is' therefore possible that tubal epithelial cells, come off the fimbria, is implanted in the' ovary. The STIC shows over-expression of p53 protein similar to high-grade serous carcinoma. The cell detachment from 'tubal epithelium may also explain the development of endosalpinx disease, a lesion frequently associated with low-grade serous tumors. Therefore it is believed that the present serous ovarian cancer is low that high grade does not derive from 'ovarian surface epithelium but by' tubal epithelium. Finally I mucinous tumors and Brenner tumors may arise through a process of metaplasia

**Giorgio Maria Paul Graziano**, University of Catania Medical School Italy.

**Giovanni Castelli**, MD University of Catania, Azienda, Policlinico.

**Prof Antonino Graziano**, Aggregate professor University of Catania, Medical School Italy Azienda, Policlinico , Dpt Sciences Medical Surgery and advanced technologies " G Ingrassia"

foci of transitional epithelial cells in the vicinity of the tube-peritoneal junction Numerous published studies and cited regarding the treatment of early ovarian cancer were shown as surgical treatment and chemotherapy have a close correlation in improved survival. early identification of the disease has become a priority in cancer policy is being frequently late diagnosis (80%) that the juvenile age association and the genetic risk. (20,21,22,23) The multifactorial etiology ago that each potential factor should be removed by considering both the intrinsic role that the overlap of its effect to that of the other causal factors in the absence of a unified theory of the origin of ovarian cancer .. the purpose of this study is through an analytical review of cases observed to identify and remove the factors that influence the choice of surgical treatment so as to increase the survival and / or disease-free interval.

II. MATERIALS AND METHODS

The study examined the database of patients related to maternal and child department and the specialist department of surgery II company Policlinico University of Catania studies from January 2000 to December 2014. From the copies of medical records of patients were transposed all information necessary for the research, the following parameters: the FIGO staging the type of chemotherapy surgery, the recovery of the disease, survival, with a cross-check with the pathological anatomy. In addition, the follow-up examinations blood chemistry markers tumor imaging studies (MRI tc) eco abdomen.(Ph. 2) In the biological characteristics of the tumor they are measured only malignant epithelial neoplasms or borderline. Were evaluated in addition The Prognostic factors in the early stages of the disease 1) Degree of differentiation: histological grade(Ph 1) is the most important prognostic factor in stage I; 2) Substage (with particular attention to breakage, especially preoperative, the cyst); 3) patient's age; 4) histological subtype (the undifferentiated: worse prognosis); 5) Growth extracapsular; 6) Ascites. Then for the purpose of research. E 'was crucial to run staging appropriate surgical procedure for a proper diagnosis, optimal treatment and an adequate definition prognostic signs and symptoms tend to delay their appearance or be absent in patients observed group, and . only during an occasional clinical control it was diagnosed with cancer that is when the swelling is palpable and has reached significant size with non-specific manifestations and the presence of ascites .In relation between histology and clinical signs (5) is confirmed in the study as this in mucinous tumors is abdominal distension, in endometrioid tumors abnormal vaginal bleeding, finally, in patients over 60 was found an absence or insignificant pain or distension regardless of histologic Therefore in this context were assessed for an effective improvement the survival of the standard treatment, the difference in treatment accorded to young women in premenopausal stage in cool G1-G2. And incomplete treatment, as shown in Table 1

Table 1: Surgical Treatment

Standard Treatment Complete	Hysterectomy+Omentectomy +Loin Aortic Lymphadenectomy And Paracavale +Random
Fertility Treatment	Oophorectomy Mono + Washig Peritoneal + Random
Treatment Incomplete	Hysterectomy Not Complete + Partial Omentectomy

In the adjuvant chemotherapy in accordance with the guidelines we have been chosen different drugs in relation to FIGO stage see table 1b.

Table1 b: FIGO staging cancer and chemotherapy

FIGO STAGE IA G2 IIA	4-6 CILCI BASED PLATINUM,
FIGO STAGE IIB-IIC	Cbdca 6 Cycles
FIGO STAGE IA G1	NO

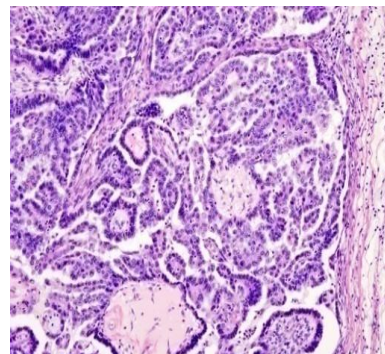


Fig 1: Histotype Epithelial Ovarian Ca

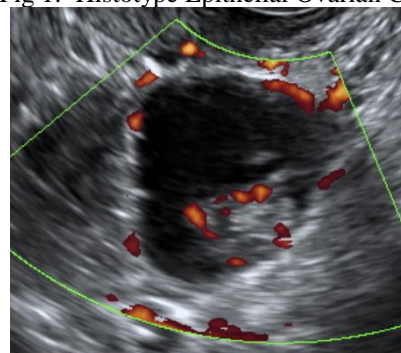


Fig 2: Echo Epithelial Ovarian Tumor



Fig 3: Cisty Ovarian

The specific patient variables that have influenced the surgical treatment such as age, FIGO stage, grading and histology that have been evaluated for statistical analysis. Factors associated with poor prognosis, such as: - The mucinous histology, in most cases the diagnosis is made at an early stage (stage Ia); But in cases of advanced disease often this histological type is associated with a reduced likelihood of response to the line platinum therapy ; - Residual disease after primary surgery (suboptimal debulking) ; - Serum levels of CA125. After radical surgical excision of the CA125 half-life is about six days. The persistence of higher levels the norm in the next 20 days is recognized as a negative prognostic factor. Significant clinical value also holds the normalization time in serum levels during chemotherapy

### III. RESULTS

The complete treatment has affected n 118 cases (48%), IL treatment in fertile women only No. 20 cases (17%) in the remaining 44 cases (35%) The surgical treatment was incomplete. The grading in 75% of cases the tumor was poorly differentiated in the remaining 25% had serous type.

Table 3: Illustrates The Histology

Histotype	N Cases	% of Incidence
Serous	45	-24%
Endometrial	45	-24%
Mucinous	14	-8%
Clearcell	14	-8%
Brenner	8	4%
Undifferentiated	8	4%
Mixed	4	2%
Borderlineserous	20	12%
Borderlinemucinous	20	12%
Bordelineendometrial	4	2%

The analysis of the comparison between surgical treatment and age shows how the latter influence the type of surgical procedure.(Ph 3) the analysis of survival at 5 years with a positive response of the follow-up of 89% of cases, has a 90% disease-free interval in the group of patients with standard treatment compared to 75% in the group of patients undergoing surgical procedure not standard. Achieving the standard procedure has been implemented in 31% of cases by a systematic staging, in 20% of cases with an initial diagnosis, 22% the tumor was confined to the pelvis with MTS lymph node, with histology confirmed. Factors such as histological grade surgical experience have influenced the choice of treatment in addition to the need of the young patients to

remain fertile .The limit to the standard treatment is represented in our retrospective analysis also by a specified procedure in hospitals not Related from consolidated oncology team. the results confirm that the serous tumors tend to be high grade with the event in late stage and diagnosed at an advanced stage. .the standard adjuvant chemotherapy has been formed by a regimen o platinum in combination with a second drug every 21 days for 6 cycles with good tolerability, and efficacy.

### IV. DISCUSSION

Epithelial carcinoma accounts for 60% of ovarian cancers, and affects both women of reproductive age and those of advanced age. Classification is carried out according to both the cell type (serous, mucinous, endometrioid, clear cell, transitional), and subclassified (borderline, medium-high and low-grade malignancy) that according to the architectural design, the nuclear characteristics and the presence or absence of stromal invasion. this aspect of paramount clinical importance because it correlates with the prognosis, and then with the therapeutic approach. Regardless of age at diagnosis and the presence of family history for cancer genetic syndromes identified in 10% of cases were: - The Breast-ovarian cancer syndrome (linked to a mutation of the BRCA1 / BRCA2 genes); - The site-specific ovarian cancer syndrome (linked to a mutation of the BRCA1 / BRCA2 genes); - Syndrome Lynch 2 (HNPCC) which includes colon cancer nonpolyposis, endometrial carcinoma, breast, ovarian and other less frequently; (24,25,26) Endocrine factors such as the multiparity, breastfeeding and prolonged use of oral contraceptives that reduce the risk of ovarian cancer were present in 40% of cases, the environmental factors with asbestos exposure (biancavilla) and talc, alcohol abuse, obesity and a diet fat was present in 10% of cases. It is considered necessary, therefore, an awareness campaign and screening aimed to pay attention to the disease for the purpose of diagnosing ovarian cancer at an early stage. It still remains to define what are the clinical or laboratory examinations that meet the requirements for sensitivity and specificity for screening of early diagnosis. At the moment the echo trans vaginal and color doppler flowmeter with AC-125> 35 U / MI associated to 4 symptoms: bloating, pelvic pain, loss of appetite, and urination frequently are sufficient and always encountered in clinical analysis of treated cases. The most extensive CT MRI, PET examinations confirmed the diagnosis with quality images, by detecting the local spread and distant tumor. Surgical removal in fertile women with a family history of ovarian disease is in such cases the response only in patients carriers of gene mutation (BCRA1-2) .While no surgical removal was performed in postmenopausal women with ovarian abnormalities. The only unilateral oophorectomy has been proposed in those cases where it is positive familiarity for ovarian cancer in the presence of ovarian alterations. (27,28,) The initial surgical approach plays a key role in the event of a suspected ovarian neoplasm is for diagnostic purposes, allowing the histopathological assessment of the nature of the ground, both for therapeutic purposes, allowing its removal and accurate assessment anatomic extent of the disease .. the ovarian cancer surgery is essentially a laparotomy surgery; the laparoscopic technique is a recent application, in experienced hands and in selected centers, the surgical restaging of incidental diagnosis of

ovarian cancer in the absence of frank peritoneal impairment and intraoperative assessment of advanced disease in order to assess the possibility of an optimal cytological reduction, with a minimally invasive approach that in the event of inoperability of the patient, enabling an early start of chemotherapy treatment. In cases in which it has not been possible to obtain optimal cytoreduction at the first operation, the surgical therapy can be used at a later time and subsequently the beginning of the chemotherapeutic treatment. This has as main objective to reduce the tumor burden in advanced tumors to decrease the risk of perioperative complications for the same therapeutic results. Today it is agreed to discourage the "second look" procedure, i.e. for surgical evaluation after chemotherapy, in patients who have undergone a non-radical surgery, in order to assess the persistence of residual disease, where clinical and instrumental exams are negative. In recurrent disease (29,30,31) the three main indications for surgery may include alleviation of intestinal obstruction in selected cases, the debulking of the tumor in patients with platinum-sensitive relapse, and removal of the individual sites of disease who are symptomatic or slow growth. Borderline tumors representing in this series 26% of epithelial ovarian cancers and unlike invasive forms tend to occur at an earlier stage and at a younger age. Clearly better compared to invasive forms is surely the prognosis, with a 5-year survival in stage I (which includes 75-85% of these tumors) greater than 95%. (32,33) The borderline tumors were bilateral in 10% of cases, and in 80% of cases were limited at the time of diagnosis, the ovaries (stage I); However, it can not predict with certainty the histological appearance on the basis of simple macroscopic evaluation, but it was necessary to make an adequate sampling of the ovarian mass in order to allow a correct differential diagnosis between borderline forms and invasive cancer on histology. Recent studies on the histogenesis of invasive serous carcinomas high degree of malignancy refer to a scratch origin of coelomic epithelium surface epithelium or the epithelial inclusion cysts from coelomic epithelium itself. Histopathological features are supported by data that come from genetic studies that observe mutations of the p53 protein in the majority of carcinomas invasive serous high-grade malignancy, and mutations of K-ras in most carcinomas invasive serous low-grade malignancy. [34] The category of serous borderline tumors, despite having been defined for over 30 years, still continues to create controversy about the prognostic significance of peculiar histological. The aspects of greatest controversy are: the serous borderline tumors with or without papillary architecture, serous borderline tumors with stromal small invasion, involvement by a serous borderline tumor of the ovary surface, the epithelial proliferations architecturally complex peritoneal, associated with serous borderline ovarian tumor, which are defined as "facilities", and these findings are present in approximately 20-30% of serous borderline tumors at the time of their diagnosis. Another issue discussed concerns small invasion. Although ovarian serous borderline tumors are distinguished from low-grade invasive serous carcinomas based on their invasion of the stroma, in 10-15% of serous ovarian borderline tumors can be observed micro-foci of stromal invasion. This finding, however, because it is associated with a good prognosis must not change the classification of the tumor. As it is clear from

almost all of the literature, in the initial stages of the disease (I-II), when it is desirable to maintain the reproductive capacity, is considered appropriate a conservative surgical treatment. [35] In other cases, the recommended primary surgery is the same invasive forms. In patients with advanced disease (stage III) it has recommended a radical surgery, although, in selected cases, also be possible in this condition consider a conservative surgery. Both for the initial stages and for those with residual disease there is little evidence that chemotherapy and / or radiation therapy, given after surgery, can improve the prognosis, already good, independent adverse prognostic factors are still considered the advanced stage (stage II and III), the need to perform the bladder removal during the excision of the tumor and pre-elevated CA 125 levels operators (36,37)

## V. CONCLUSIONS

The diagnosis of early ovarian cancer is difficult to be implemented, but with a good chance of successful treatment. Survival in patients who underwent complete surgical treatment improves, but running a staging is altered by factors that depend on both the disease: the age of the patient, the stadium, the grade, the histological type, which the hospital that detects the patient with the tumor. All these variables affect the adoption of comprehensive surgical treatment. The management of the neoplasm by consolidated oncological team associated with a correct and accurate staging increases the survival rate with the adoption of standardized treatments and coordinated. Complete surgical removal of the neoplasm therapy to obtain the absence of residual tumor has increased the difference in the median survival of 6-15% of cases, compared to the incomplete treatment. In young patients and fertile stage I G1-2 surgical treatment proposed was content but complete for staging and procedures. The results of a standardized management and accurate contributes in increasing the percentage of early detection with a range increase disease free. The new concepts of ovarian carcinogenesis, while it makes it even more complex screening problems of this cancer, may change the preventive approach in women at risk hereditary-family. If the tubal epithelium and 'the source of origin of serous ovarian tumors that represent the most' frequent, prophylactic surgery in women at risk could be limited to bilateral fallopian tube removal with preservation of gonads and then with both preservation of endocrine function is fertility, albeit with the aid of techniques of assisted procreation. However, that the bilateral fallopian tube ovary removal -before age 40, and 'can also reduce the incidence of breast cancer is widely in the literature. Some authors consider the possibility of a fallopian tube removal prophylactic around 35-40 years with the 'intention to spread the' ovary removal in age 'more' advanced in women with BRCA mutations. [38] Nevertheless Prophylactic treatment does not find unanimous consent for which clinical studies are needed to verify the validity of the fallopian tube removal prophylaxis in reducing the 'incidence of ovarian cancer. [39, 40,41].

## CONFLICT OF INTEREST

I declare absence of economic conflicts for me and my co-workers.

REFERENCES

- [1] Trovassoli FA et al Pathology and genetics in tumors of the breast and female genital organs WHO classification of tumor geneva WHO 2003 p12.
- [2] Bray f et al La VC Ovarian cancer in Europe cross sectional trends in incidence and mortality in 28 countries 1953-2000 Int j Cancer 2005 113(6) 977-90.
- [3] Ferla Y J et al Estimates of cancer incidence and mortality in Europe in 2008 Eur J cancer 2010 46(4) 765-81.
- [4] Toriola at surcel hm agborsangaya c grankvist k tuohimaa p tniolo p lukanova a pukkala e lehtinen m serum 25 hydroxyvitamin d and the risk of ovarian cancer Eur J Cancer 2010 Jan 46(2) 364-9.
- [5] Lurie G Wilkens Ir Thompson pj matsuno rk carney me goodman Mt Symptom presentation in invasive ovarian carcinoma by tumor histological type and grade in a multiethnic population a case analys Gynecol Oncol 2010 Nov 119(8) 278-84
- [6] Bhoola s et al diagnosis and management of epithelial ovarian cancer Obstet gynecol 2006 Jun 107(6)1399-410-
- [7] Purdie DM, et al ovulation and risk of epithelial ovarian cancer Int J of Cancer 2003 104 228-232.
- [8] Munksgaard, P.S. et al , The association between endometriosis and ovarian cancer: a review of histological, genetic and molecular alterations. Gynecol Oncol, 2012. 124(1): p. 164-9.
- [9] Heidemann, L.N., et al., The relation between endometriosis and ovarian cancer - a review. Acta Obstet Gynecol Scand, 2014. 93(1): p. 20-31.
- [10] Maeda, D. and M. Shih Ie, Pathogenesis and the role of ARID1A mutation in endometriosis-related ovarian neoplasms. Adv Anat Pathol, 2013. 20(1): p. 45-52.
- [11] Gadducci, A., Novel insights on the malignant transformation of endometriosis into ovarian carcinoma. Gynecol Endocrinol, 2014. 30(9): p. 612-7.
- [12] Toyokuni, S., Role of iron in carcinogenesis: cancer as a ferrototoxic disease. Cancer Sci, 2009. 100(1): p. 9-16.
- [13] Vercellini, P., et al., The 'incessant menstruation' hypothesis: a mechanistic ovarian cancer model with implications for prevention. Hum Reprod, 2011. 26(9): p. 2262-73.
- [14] Alsop, K., et al., BRCA mutation frequency and patterns of treatment response in BRCA mutation-positive women with ovarian cancer: a report from the Australian Ovarian Cancer Study Group. J Clin Oncol, 2012. 30(21): p. 2654-63.
- [15] Risch, H.A., et al., Prevalence and penetrance of germline BRCA1 and BRCA2 mutations in a population series of 649 women with ovarian cancer. Am J Hum Genet, 2001. 68(3): p. 700-10.
- [16] Schrader, K.A., et al., Germline BRCA1 and BRCA2 mutations in ovarian cancer: utility of a histology-based referral strategy. Obstet Gynecol, 2012. 120(2 Pt 1): p. 235-40.
- [17] Soegaard, M., et al., BRCA1 and BRCA2 mutation prevalence and clinical characteristics of a population-based series of ovarian cancer cases from Denmark. Clin Cancer Res, 2008. 14(12): p. 3761-7.
- [18] Risch, H.A., et al., Population BRCA1 and BRCA2 mutation frequencies and cancer penetrances: a kin-cohort study in Ontario, Canada. J Natl Cancer Inst, 2006. 98(23): p. 1694-706.
- [19] Malander, S., et al., One in 10 ovarian cancer patients carry germ line BRCA1 or BRCA2 mutations: results of a prospective study in Southern Sweden. Eur J Cancer, 2004. 40(3): p. 422-8.
- [20] Song, H., et al., The contribution of deleterious germline mutations in BRCA1, BRCA2 and the mismatch repair genes to ovarian cancer in the population. Hum Mol Genet, 2014. 23(17): p. 47-039.
- [21] Collaborative Group on Epidemiological Studies of Ovarian, C., et al., Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23,257 women with ovarian cancer and 87,303 controls. Lancet, 2008. 371(9609): p. 303-14.
- [22] Cibula, D., et al., Oral contraceptives and risk of ovarian and breast cancers in BRCA mutation carriers: a meta-analysis. Expert Rev Anticancer Ther, 2011. 11(8): p. 1197-207.
- [23] Moorman, P.G., et al., Oral contraceptives and risk of ovarian cancer and breast cancer among high-risk women: a systematic review and meta-analysis. J Clin Oncol, 2013. 31(33): p. 4188-98.
- [24] Gambacciani, M., et al., Hormone replacement therapy and endometrial, ovarian and colorectal cancer. Best Pract Res Clin Endocrinol Metab, 2003. 17(1): p. 139-47.
- [25] Beral, V., et al., Ovarian cancer and hormone replacement therapy in the Million Women Study. Lancet, 2007. 369(9574): p. 1703-10.
- [26] Lacey, J.V., Jr., et al., Menopausal hormone therapy and ovarian cancer risk in the National Institutes of Health-AARP Diet and Health Study Cohort. J Natl Cancer Inst, 2006. 98(19): p. 1397-405.
- [27] Morch, L.S., et al., Hormone therapy and ovarian cancer. JAMA, 2009. 302(3): p. 298-305.
- [28] Danforth, K.N., et al., A prospective study of postmenopausal hormone use and ovarian cancer risk. Br J Cancer, 2007. 96(1): p. 151-6.
- [29] Hildebrand, J.S., et al., Postmenopausal hormone use and incident ovarian cancer: Associations differ by regimen. Int J Cancer, 2010. 127(12): p. 2928-35.
- [30] Ursic-Vrscaj, M., S. Bebar, and M.P. Zakelj, Hormone replacement therapy after invasive ovarian serous cystadenocarcinoma treatment: the effect on survival. Menopause, 2001. 8(1): p. 705.
- [31] Biglia, N., et al., Hormone replacement therapy in cancer survivors. Maturitas, 2004. 48(4): p. 333-46.
- [32] Mascarenhas, C., et al., Use of hormone replacement therapy before and after ovarian cancer diagnosis and ovarian cancer survival. Int J Cancer, 2006. 119(12): p. 2907-15.
- [33] Finch, A., G. Evans, and S.A. Narod, BRCA carriers, prophylactic salpingo-oophorectomy and menopause: clinical management considerations and recommendations. Womens Health (Lond Engl), 2012. 8(5): p. 543-55.
- [34] Marchetti, C., et al., Hormone therapy in oophorectomized BRCA1/2 mutation carriers. Menopause, 2014. 21(7): p. 763-8.
- [35] Whittemore, A.S., R. Harris, and J. Itnyre, Characteristics relating to ovarian cancer risk: collaborative analysis of 12 US case-control studies. II. Invasive epithelial ovarian cancers in white women. Collaborative Ovarian Cancer Group. Am J Epidemiol, 1992. 136(10): p. 1184-203.
- [36] Sanner, K., et al., Ovarian epithelial neoplasia after hormonal infertility treatment: long-term follow-up of a historical cohort in Sweden. Fertil Steril, 2009. 91(4): p. 1152-8.
- [37] Kallen, B., et al., Malignancies among women who gave birth after in vitro fertilization. Hum Reprod, 2011. 26(1): p. 253-8.
- [38] Van Leeuwen, F.E., et al., Risk of borderline and invasive ovarian tumours after ovarian stimulation for in vitro fertilization in a large Dutch cohort. Hum Reprod, 2011. 26(12): p. 3456.65.
- [39] Gadducci, A., Fertility drug use and risk of ovarian tumors: a debated clinical challenge. Gynecol Endocrinol, 2013. 29(1): p. 30-5.
- [40] Piek, J.M., et al., Dysplastic changes in prophylactically removed Fallopian tubes of women predisposed to developing ovarian cancer. J Pathol, 2001. 195(4): p. 451-6.
- [41] Kurman, R.J. and M. Shih Ie, The origin and pathogenesis of epithelial ovarian cancer: a proposed unifying theory. Am J Surg Pathol, 2010. 34(3): p. 433-43.
- [42] Kindelberger, D.W., et al., Intraepithelial carcinoma of the fimbria and pelvic serous carcinoma: Evidence for a causal relationship. Am J Surg Pathol, 2007. 31(2): p. 161-9.
- [43] Holman, L.L., et al., Acceptability of prophylactic salpingectomy with delayed oophorectomy as risk-reducing surgery among BRCA mutation carriers. Gynecol Oncol, 2014. 133(2): p. 283-6.
- [44] Committee on Gynecologic, P., Committee opinion no. 620: Salpingectomy for ovarian cancer prevention. Obstet Gynecol, 2015. 125(1): p. 279-81.
- [45] Heintz, A.P., et al., Carcinoma of the ovary. J Epidemiol Biostat, 2001. 6(1): p. 107-38.
- [46] Vergote, I., et al., Prognostic importance of degree of differentiation and cyst rupture in stage I invasive epithelial ovarian carcinoma. Lancet, 2001. 357(9251): p. 176-82.
- [47] Kang, W.D., et al, Value of serum CA125 levels in patients with high-risk, early stage epithelial ovarian cancer. Gynecol Oncol, 2010. 116(1): p. 57-60.
- [48] Marchini, S., et al., Association between miR-200c and the survival of patients with stage I epithelial ovarian cancer: a retrospective study of two independent tumour tissue collections. Lancet Oncol, 2011. 12(3): p. 273-85.
- [49] Pisano, C., et al., Activity of chemotherapy in mucinous epithelial ovarian cancer: a retrospective study. Anticancer Res, 2005. 25(5): p. 3501-5.
- [50] Bristow, R.E., et al., Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. J Clin Oncol, 2002. 20(5): p. 1248-59.
- [51] Gadducci, A., et al., Serum half-life of CA 125 during early chemotherapy as an independent prognostic variable for patients with advanced epithelial ovarian cancer: results of a multicentric Italian study. Gynecol Oncol, 1995. 58(1): p. 42-7.
- [52] Linee guida tumori dell'ovaio AIOM Edizione 2015
- [53] Crawford, S.M. et al, Does the nadir CA125 concentration predict a long-term outcome after chemotherapy for carcinoma of the ovary? Ann Oncol, 2005. 16(1): p. 47-50.
- [54] Kim, S., T.A. et al, Racial differences in stage at diagnosis and survival from epithelial ovarian cancer: a fundamental cause of disease approach. Soc Sci Med, 2010. 71(2): p. 274-81.

- [55] Konstantinopoulos, P.A., et al., Gene expression profile of BRCAness that correlates with responsiveness to chemotherapy and with outcome in patients with epithelial ovarian cancer. *J Clin Oncol*, 2010. 28(22): p. 3555-61

### COMMENT

The original and innovative study examines the variables that affect the adoption of comprehensive surgical treatment of early ovarian cancer, through the management of the cancer by consolidated oncology team that increases the survival rate with the adoption of standardized treatments and coordinated. It also highlights how accurate removal of the tumor until the absence of residual tumor increased the difference of the 6-15% median survival of cases, compared to incomplete. the study it is creative for treatment is then the preventive approach in women a hereditary-familare risk of ovarian cancer with new concepts of ovarian carcinogenesis. worthy Prof Vincenzo Cavallaro full Prof of Surgery Before Dpt Medical sciences of surgery and transplanted.