Ovarian cancer – where are we today?

Irina BALESCU[1], Nicoale BACALBASA[2], Iulian BREZEAN[2,3], Claudia STOICA[4,5],
Cezar Laurentiu TOMESCU[6,7], Cristina MARTAC[8], Andrei VOICHITOIU[9,10], Bogdan GASPAR[2,11]

[1]Doctoral School, ”Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania
[2]Department of Surgery, ”Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania
[3]Department of Surgery, ”Ion Cantacuzino” Clinical Hospital, Bucharest, Romania
[4]Department of Anatomy, ”Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania
[5]Department of Surgery, ”Ilfov” County Emergency Hospital, Bucharest, Romania
[6]Department of Obstetrics and Gynecology, County Hospital Constanta, Romania
[7]”Ovidius” University of Medicine and Pharmacy, Constanta, Romania
[8]Department of Anesthesiology, Fundeni Clinical Institute, Bucharest, Romania
[9]Department of Obstetrics and Gynecology, ”Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania
[10]Department of Obstetrics and Gynecology, ”Alessandrescu-Rusescu” National Institute of Mother and Child Care, Bucharest, Romania
[11]Department of Visceral Surgery, Floreasca Clinical Emergency Hospital, Bucharest, Romania

ABSTRACT

Despite progress reported in terms of paraclinical tests and imagistic studies, ovarian cancer represents one of the most lethal malignancies affecting women worldwide. Therefore attention was focused on identifying new prognostic markers in order to better identify candidates for primary cytoreductive surgery versus interval debulking surgery. Moreover, the wide introduction of the concept of personalized medicine gave the opportunity to benefit from more targeted treatments according to each patient needs and particularities. This is a literature review of the current status of ovarian cancer worldwide.

INTRODUCTION

Genital malignant disease represents one of the most lethal cancers affecting women worldwide, especially due to the diagnostic in late stages of the disease [1-3]. Among these cases, ovarian cancer remains maybe the most dangerous one, especially due to the late diagnostic, in advanced stages of the disease, when disseminated lesions via multiple pathways (lymphatic, hematogenous, peritoneal route) are already present [4-6].

Diagnostic means at the time being

The diagnostic and extent of the disease nowadays can be evaluated by using imagistic methods such as computed tomography, magnetic resonance imaging or even surgical procedures such as exploratory laparoscopy. However the final diagnostic is established after performing radical surgical procedures which will give important information regarding the local extent of the tumor, the lymph node status and the presence or absence of distant hematogenous, peritoneal and lym-

phatic metastases. All these information offers a correct staging under the aspect of TNM classification at the time being, giving in this way the possibility to provide a better personalized therapy for each patient [7-9].

Evaluation of the aggressiveness of the tumor and of the overall prognostic

Until the time of speaking, when discussing the overall prognostic, the main issue which has been taken into consideration was represented by the tumoral stage, little attention being paid to the biology of the tumor. Although the impact of the type of the tumor was considered to be given only by the histopathological subtype, it has been proven that among the same histopathological subtype very different types of evolution could be observed; therefore, it has been thought that other biological particularities exist, which are further responsible for the different courses of the disease.in this respect, the concept of personalized medicine gained more consideration [10,11].

The correlation ship between tumoral extension and homeostasis

Data achieved in the last decade came to demonstrate that the extension of the tumoral process is strongly influenced by the organisms' homeostasis. Moreover, it has been widely demonstrated the fact that the presence of tumoral processes is strongly corelated with the presence of a proinflammatory and procoagulant status at the level of the host.

According to recently published studies, chronic inflammation not only favorites local extension of the disease but also increases the capacity of apparition of distant metastases; interestingly, the capacity of metastasizing might be also expressed by benign tumors and might lead to the apparition of distant lesions [12,13]. Therefore, attention was focused on identifying other potential prognostic markers regarding the tumoral biology and aggressiveness, a particular interest being given to the number of circulating platelets, lymphocytes and monocytes, as well as to the serum levels of fibrinogen and D dimers [14-17]. Once these correlations have been widely demonstrated, the implication

of homeostatic status of the patient (defined by the coagulant and inflammatory response) is clearly demonstrated. Moreover, these parameters can be easily accessed by studying ovarian cancer patient's hemograms, a basic blood test which is retrieved preoperatively as well as during chemotherapy. Meanwhile, it is a cost-effective analysis which can be obtained in any medical center, increasing in this way the availability of the method.

The aims of the most recent studies conducted on the theme of prognostic factors in ovarian cancer were represented on identifying unusual correlation ships between hemograms or coagulograms and the perioperative, postoperative and long-term outcomes of ovarian cancer, a special interest being shown for peritoneal carcinomatosis originating from ovarian cancer [18-20]. According to these newly published studies, personalized therapies including monoclonal antibodies, targeted anti-interleukine therapies, antiaggregant and anticoagulant therapies have been proposed in association with standard chemotherapy or immunotherapy with promising results. However, larger studies are still needed in order to modify the current state of art in ovarian cancer treatment. Once other prognostic factors will be discovered, it is expected that the standard current staging of ovarian cancer patients will change. The exchange of the current paradigm is expected to improve the outcomes of advanced stage ovarian cancer patients and to create new premises for personalized medicine [20-24].

CONCLUSIONS

Nowadays, the standard diagnostic tools, prognostic factors as well as the standard therapeutic strategies have been submitted to permanent changes especially in the field of advanced stage ovarian cancer. Once the implications of homeostasis related factors have been widely demonstrated, a more precise tumoral classification according to the biological features is to be expected; moreover, newer therapeutic strategies will be successfully identified and associated to the current standard options of treatment, improving in this way the basis of personalized medicine.

REFERENCES

1. Huang Z, Zheng Y, Wen W, Wu C, Bao P, Wang C et al. Incidence and mortality of gynaecological cancers: Secular trends in urban Shanghai, China over 40 years. *Eur J Cancer*. 2016 Aug;63:1-10.
2. Wang Z, Guo E, Yang B, Xiao R, Lu F, You L, Chen G. Trends and age-period-cohort effects on mortality of the three major gynecologic cancers in China from 1990 to 2019: Cervical, ovarian and uterine cancer. *Gynecol Oncol*. 2021 Nov;163(2):358-63.
3. Kaur A, Wang S, Steinberg L, Kumar A. Impact of racial disparities on potential years of life lost due to gynecologic cancer in the United States: trends from 1975 to 2017 based on SEER database. *Gynecol Oncol*. 2021;162(1):181-2.
4. Akhtar-Danesh N, Lytwyn A, Elit L. Five-year trends in mortality indices among gynecological cancer patients in Canada. *Gynecol Oncol*. 2012 Dec;127(3):620-4
5. Hicks-Courant K, Melamed A, Worley MJ Jr, Kim YB, Schorge JO, Rauh-Hain JA. Trends in Place of Death Among Patients With Gynecologic Cancer in the United States. *Obstet Gynecol*. 2018 Jun;131(6):1111-20
6. Kaushik S, Hounsome L, Verne J. National trends in the place of death and the impact of unscheduled admissions in patients with gynecological cancer in England. *Gynecol Oncol*. 2014;133(1):201.
7. Gao Y, Zeng S, Xu X, Li H, Yao S, Song K, Li X et al. Deep learning-enabled pelvic ultrasound images for accurate diagnosis of ovarian cancer in China: a retrospective, multicentre, diagnostic study. *Lancet Digit Health*. 2022 Mar;4(3):e179-e187
8. Bristow RE, Duska LR, Lambrou NC, Fishman EK, O'Neill MJ, Trimble EL, Montz FJ. A model for predicting surgical outcome in patients with advanced ovarian carcinoma using computed tomography. *Cancer*. 2000 Oct 1;89(7):1532-40.
9. Lof P, Retèl VP, Algera MD, van Gent MDJM, Gaarenstroom KN, van Driel WJ. Clinical implementation of routine diagnostic laparoscopy to guide initial treatment in patients with advanced-stage epithelial ovarian cancer in Dutch clinical practice: Evaluation of support and a budget impact analysis. *Gynecol Oncol*. 2022 Jun;165(3):459-65.
10. Gaitskell K, Hermon C, Barnes I, Pirie K, Floud S, Green J et al. Million Women Study Collaborators. Ovarian cancer survival by stage, histotype, and pre-diagnostic lifestyle factors, in the prospective UK Million Women Study. Cancer *Epidemiol*. 2022 Feb;76:102074
11. Wen ZY, Liu C, Liu FH, Wei YF, Xu HL, Wang R et al. Association between pre-diagnostic dietary pattern and survival of ovarian cancer: Evidence from a prospective cohort study. *Clin Nutr*. 2022 Feb;41(2):452-9
12. Steiner P. Metastasizing fibroleiomyoma of the uterus: a report of a case and review of the literature. *Am J Pathol*. 1939;15:89–109
13. Joseph V, Chacko G, Raghuram L, Rajshekhar V. Benign metastasizing leiomyoma causing spinal cord compression. *Surg Neurol*. 2003 Dec;60(6):575-7.
14. Yun TH, Jeong YY, Lee SJ, Choi YS, Ryu JM. Neutrophil-Lymphocyte and Platelet-Lymphocyte Ratios in Preoperative Differential Diagnosis of Benign, Borderline, and Malignant Ovarian Tumors. *J Clin Med*. 2022 Mar 1;11(5):1355
15. Giannakeas V, Kotsopoulos J, Cheung MC, Rosella L, Brooks JD, Lipscombe L, et al. Analysis of Platelet Count and New Cancer Diagnosis Over a 10-Year Period. *JAMA Netw Open*. 2022 Jan 4;5(1):e2141633
16. Amroun K, Scholer V, Djerada Z, Renard Y, Bouche O, Rhaiem R, Kianmanesh R. Inflammatory biomarkers to predict postoperative infectious complications after cytoreductive surgery and HIPEC for peritoneal carcinomatosis. *Eur J Surg Oncol*. 2022 Feb;48(2):455-61
17. Psomiadou V, Prodromidou A, Galati E, Kostakis ID, Maliaros A, Mamais I, Blontzos N, Lefkopoulos F, Iavazzo C, Vorgias G. The role of inflammation biomarkers in differential diagnosis of pelvic tumours of ovarian origin: a single-centre observational study. *Contemp Oncol (Pozn)*. 2021;25(1):7-11.
18. Zhang L, Guan Z, Yin Y, Ou C, Qian H, Tang M, Shen A. Predictive value of indicator of CA125 combined with D-dimer (ICD) for lymph node metastasis in patients with ovarian cancer: A two center cohort study. *J Cancer*. 2022 May 1;13(8):2447-56
19. Li H, Sun L, Chen L, Kang Z, Hao G, Bai F. Effects of adiponectin, plasma D-dimer, inflammation and tumor markers on clinical characteristics and prognosis of patients with ovarian cancer. *J Med Biochem*. 2022 Feb 2;41(1):71-8
20. Chen W, Shan B, Zhou S, Yang H, Ye S. Fibrinogen/albumin ratio as a promising predictor of platinum response and survival in ovarian clear cell carcinoma. *BMC Cancer*. 2022 Jan 21;22(1):92
21. Tamura R, Yoshihara K, Enomoto T. Therapeutic Strategies Focused on Cancer-Associated Hypercoagulation for Ovarian Clear Cell Carcinoma. *Cancers (Basel)*. 2022 Apr 24;14(9):2125
22. Stevenson JL, Varki A, Borsig L. Heparin attenuates metastasis mainly due to inhibition of P- and L-selectin, but non-anticoagulant heparins can have additional effects. *Thromb Res*. 2007; 120(Suppl 2): S107-S111.
23. Rothwell PM, Wilson M, Price JF, Belch JF, Meade TW, Mehta Z. Effect of daily aspirin on risk of cancer metastasis: a study of incident cancers during randomised controlled trials. *Lancet*. 2012; 379(9826):1591-601.
24. Guo Y, Xu F, Lu T, Duan Z, Zhang Z. Interleukin-6 signaling pathway in targeted therapy for cancer. *Cancer Treat Rev*. 2012;38(7):904-10.