# Treatment and prognosis of epithelial ovarian cancer. Five year multi-center study

**Article** *in* Saudi Medical Journal · January 2009

Source: PubMed

CITATIONS
3

READS
64

**5 authors**, including:

Seyed Hossein Yahyazadeh
Milad Hospital (Tehran)
**22** PUBLICATIONS **1,390** CITATIONS
SEE PROFILE

Mahmoodreza Gohari
Iran University of Medical Sciences
**60** PUBLICATIONS **1,034** CITATIONS
SEE PROFILE

Javad Shahidi
McGill University
**12** PUBLICATIONS **127** CITATIONS
SEE PROFILE

Ahmad Ameri
Shahid Beheshti University of Medical Sciences
**58** PUBLICATIONS **194** CITATIONS
SEE PROFILE

# Treatment and prognosis of epithelial ovarian cancer

## *Five year multi-center study*

***Reza Khodabakhshi,*** *MD,* ***Seyed H. Yahyazadeh-Jabbari,*** *MD,* ***Mahmod R. Gohari,*** *PhD,* ***Javad Shahidi,*** *MD,* ***Ahmad Ameri,*** *MD.*

## ABSTRACT

**الأهداف:** وصف مرضي وبائي مختصر، ومعدل الاستجابة لأساليب العلاج الكيميائي الشائع، وتحليل زيادة الناجيات من سرطان المبيض في طهران.

**الطريقة:** أدرج في هذه الدراسة الوصفية 98 امرأة تأكد إصابتهن بسرطان المبيض وأجريت لهن عملية جراحية، تلاها العلاج الكيميائي بثلاث مستشفيات (فايز بخش – شهداي تجريش – والإمام حسين) في طهران – إيران، خلال الفترة ما بين 1997م وحتى 2003م. تم الحصول على البيانات ذات الصلة بالعمر، المتغيرات المرضية، الإجراءات الجراحية، العلاج الكيميائي، معدل الاستجابة، وتقدم المرض. تم تقييم معدل الاستجابة لعدد 51 مريضة يعانين من سرطان ظهاري.

**النتائج:** من بين إجمالي عدد 98 مريضة، كان هنالك 81 (82.6%) حالة ظهارية، و12 (12.2%) خلية جرثومية تناسلية، و 4 (4.1%) ورم خلايا الغشاء المحبب، وحالة واحدة من الورم اللمفاوي. لدى حوالي 18 مريضة بقايا من الدرجة الثالثة، وكانت هي المرحلة الشائعة بنسبة (44.9%). تم رؤية استجابة جزئية أو كاملة لعدد (71.4%) من المريضات، بينما المريضات الأخريات ظهر عليهم استقرار أو تقدم المرض. كان أهم عامل إنذاري تكهني بداية العمر ($p$=0.034)، وامتداد الإجراءات الجراحية ($p$=0.045). بلغ متوسط النجاة الخالية من المرض 52.6 شهراً. وعلى الرغم من معدل الاستجابة العالية بواسطة عقار تاكسين المبني على العلاج المقارن لعلاج سيسبلاتين– سايكلوفوسفاميد (78.2% مقابل 71.4%)، ولكن لم يكن ملحوظاً إحصائياً ($p$=0.275). بلغ متوسط العمر لمرضانا (49.6 عاماً) لمريضاتنا وهو أقل من المتوقع. تمت إحالة النسبة الكبيرة من مريضاتنا إلى المراحل المتقدمة. حالياً لم يصنع العلاج الكيميائي معدل استجابة عالية ملحوظة.

**خاتمة:** حالياً لم يصنع العلاج الكيميائي الجديد معدل إستجابة عالية وملحوظة.

**Objectives:** To study the response rate for common chemotherapy regimens, and the progression free survival analysis in ovarian cancer in Tehran.

**Methods:** Ninety-eight women with confirmed ovarian cancer who had surgery, followed by chemotherapy at the 3 hospitals in (Fayazbakhsh, Shohadayee Tajrish, and Imam-Hossein), Tehran, Iran, between 1997 and 2003 were enrolled in this retrospective descriptive study. Data regarding age, pathologic variations, surgical procedures, chemotherapy regimens, response rates, and time to progression of the disease were collected. Response rate was evaluated for 51 patients with epithelial cancer.

**Results:** From a total of 98 patients, there were 81 (82.6%) epithelial, 12 (12.2%) germ cell, 4 (4.1%) granulosa cell tumors, and one case of lymphoma. Staging with optimal residue was performed for 18 patients. Stage III was the most common stage (44.9%). In 71.4% of patients, complete or partial response was seen, while the other patients showed stable, or progressive disease. The most important prognostic factors were the initial stage ($p$=0.034), and the extent of surgical procedure ($p$=0.045). Median disease-free survival was 52.6 months. Although, higher response rate was produced by taxane-based regimen in comparison with cisplatin-cyclophosphamide regimen (78.2 % versus 71.4%), but it was not statistically significant ($p$=0.275). Median age (49.6 years) of our patients is lower than expected. Besides, a large proportion of the patients are referred in advanced stages.

**Conclusion:** New chemotherapy practically has made no significant higher response rate.

***Saudi Med J 2008; Vol. 29 (12): 1735-1738***

*From the Department of Radiation Oncology (Khodabakhshi, Jabbari), Fayazbakhsh Hospital, Social Security Organization of Iran, Department of Statistics (Gohari), Iran University of Medical Sciences, Department of Radiation Oncology (Ameri), Imam Hossein Hospital, Tehran, Iran, and the Division of Experimental Medicine (Shahidi), Faculty of Medicine, McGill University, Montreal, Quebec, Canada.*

*Received 21st July 2008. Accepted 10th November 2008.*

*Address correspondence and reprint request to: Dr. Reza Khodabakhshi, Department of Radiation Oncology, Fayazbakhsh Hospital, Khalij Street, 7th km. Old Karaj Road, Tehran, Iran. Tel. +98 (21) 66250645-50. Fax: +98 (21) 66263351. Email: Rokh17@yahoo.com*

Ovarian cancer is the most common leading cause of death among gynecologic cancers in the United States and Europe, and it has often been described as a 'silent killer'.[1] Among women in the United States, ovarian cancer is the eighth most common malignancy, and the fifth most common cause of cancer-related death. An incidence of 21,650 cases, and 15,520 deaths attributable to this disease are estimated in 2008.[1] Unfortunately, 75% of ovarian cancers are diagnosed as stage III or IV.[2] Surgery has always played a major role in the treatment of ovarian cancer, but the majority of patients present in advanced stages of disease, that makes optimal surgical debulking of tumor almost impossible.[3] Despite surgical advances and new chemotherapeutic regimens, the overall 5-year survival of patients with advanced stages of disease has remained relatively unchanged over the last decades, however in several large population-based studies, there have been some improvements in the overall survival of women with ovarian cancers.[4,5] Although surgery is becoming more radical in many institutions, the efficacy and variety of different chemotherapeutic agents have also increased. Platinum agents combined with taxane are now the standard of care.[4-7] Most patients with advanced ovarian cancer respond to initial therapy, however, the relapse rate is high, and more than 50% of the patients will experience relapse.[4,5] Adjuvant chemotherapy has been demonstrated as an effective treatment especially in the early stages of the disease.[2] Median survival time for women with optimally debulking adenocarcinoma of ovary, treated with intravenous chemotherapy was 41-52 months, and the 2-year survival rate was 65-70%.[8,9] Recent studies suggest that the size of residual tumor after first surgery, is the most important variable in predicting the response to therapy, which makes optimal surgery a crucial step in the ovarian cancer treatment.[9]

The primary objective of this retrospective study is to provide a general description of ovarian cancer and its pathologic distribution in the 3 referral hospitals at Tehran, Iran and the secondary objective is to define the response rate for common chemotherapy regimen that were used in our patients. We have a few specialized gynecologic cancer centers, and furthermore, we are developing a comprehensive cancer registry, and this study will draw a perspective on our current practical situation.

**Methods.** All referred patients to the 3 hospitals of Tehran (Fayazbakhsh, Shohadayee Tajrish, and Imam-Hossein) Iran with confirmed diagnosis of ovarian cancer from 1998 to 2003, were entered in the study in a retrospective approach. Patients without any approved documents for ovarian cancer were excluded, such as peritoneal carcinomatosis with unknown primary origin. Required data were gathered using patients' medical documents, and the International Federation of Gynecology and Obstetrics (FIGO) staging system was applied to all of them. Patients were categorized into 3 groups according to the type of surgery: 1) complete surgery with optimal residual and staging, 2) partial surgery, and 3) biopsy only. In addition, 2 groups of patients were defined according to the residual tumor after surgery: 1) less than 2 cm residual tumor, and 2) more than 2 cm residual tumor. Chemotherapeutic regimens were classified into 4 classes: 1) cisplatin/cyclophosphamide 2) taxane-based regimens (Paclitaxel or Docetaxel), 3) other treatments, and 4) no chemotherapy. Patients were classified into 4 groups based on clinical, radiological, and biochemical response. Response evaluation criteria in solid tumors was used to classify tumor response in complete response (CR), partial response (PR), stable disease, and progressive disease.[10] We have compared response rate (CR+PR) in 2 chemotherapeutic regimens as taxane-based regimen, and cisplatin-cyclophosphamide (CP). According to the last known disease status, 4 groups were defined: 1) no evidence of disease, 2) recurrence or metastasis, 3) death, and 4) unknown. The local ethic committee has approved the research program (No: 1387-564). This is a non-randomized descriptive retrospective study.

The software used for data entering and analysis was Statistical Package for the Social Science version 12.0, and Statistical Analysis System version 8.2. Chi-square test, Fisher-exact test, student t-test, and Kaplan-Meier test were applied for data analysis. *P*-values of less than 0.05 were considered statistically significant.

**Results.** From a total of 98 referred ovarian cancer patients during the study period, 81 (82.6%) had the diagnosis of epithelial ovarian cancer. Pathologic classification of tumors is shown in **Table 1**. The overall mean age was 46.7 years, the mean age for all epithelial cancer patients was 49.6 years, and non-epithelial cancer patients was 34.3 years. The age range for epithelial

**Table 1 -** Characteristics of pathologic distribution of ovarian cancer.

| Histology | n (%) |
|---|---|
| Epithelial carcinoma | 81 (82.6) |
| Germ cell tumor | 12 (12.2) |
| Granulosa cell tumor | 4 (4.1) |
| Lymphoma | 1 (1.1) |
| **Total** | **98 (100)** |

**Table 2 -** Response rate in correlation of chemotherapy regimens in 51 patients with epithelial ovarian carcinoma.

| Chemotherapy | CR | PR | SD | PD |
|---|---|---|---|---|
| | | n (%) | | |
| CP (n=28) | 18 (64.5) | 2 (7.1) | 6 (21.4) | 2 (7.1) |
| Taxen-based (n=23) | 15 (65.2) | 3 (13) | 3 (13) | 2 (8.8) |
| **Total (n=51)** | **33** | **5** | **9** | **4** |

CP - cisplatin-cyclophosphamide, SD - stable disease,
PD - progressive disease, PR - partial response, CR - complete response

carcinoma was 23-72. Median disease-free survival was 52.6 months in all cases with epithelial carcinoma. Among epithelial malignancies, the most common pathology was papillary serous cystadenocarcinoma (54 patients, 66.7%). Forty-four patients (44.9%) were first referred in stage III, according to the FIGO staging system. At the time of first referral, 15.7% of patients were in stage I, 23.1% in stage II, and 16.3% in stage IV. Complete surgical resection of tumor was performed in 22.5% of the cases, while 56.9% of patients underwent incomplete surgery, and 20.6% underwent only biopsy. **Table 2** shows response rates in 51 patients receiving CP, or taxane-based regimens that we were able to assess treatment response. It can be inferred that the overall response including complete or partial, in the CP group was 78.2%, and in the taxane-based group was 71.4%. As shown in **Table 2**, we obtain approximately the same CR rate (64.5% versus 65.2%), and the difference has produced in PR rate (7.1% versus 13%). The most important prognostic factors were the initial stage ($p$=0.034), and extent of surgical procedure ($p$=0.045).

**Discussion.** Several studies have shown that the most important prognostic factors were residual tumor after surgery (extent of surgery), stage of the disease, tumor grade, residual disease, and patient age.[10,11] The value of debulking surgery in the management of advanced ovarian cancer was demonstrated by a randomized European Organization for Research and Treatment of Cancer study, which showed a benefit in both progression-free and overall survival with debulking surgery.[12] Unfortunately, in our series 22.5% patients underwent standard surgery, whereas while reviewing the literature, the rates of optimal or complete cytoreduction range was from 20-90%, with higher rates occurring more often, when patients are managed by specialists trained.[12] Precious staging is essential for further management of patient's with ovarian cancer, since the decision making is based on this, and the large percentage of the patients can be optimally cytoreduced with increased survival.[11,12] We observed that, without an appropriate surgery, we cannot reach an optimal result even with the new chemotherapeutic agents.

The National Cancer data base in the US (1994) has demonstrated 33% in stage III, and 23% in stage IV; and the Southwest of England data revealed 53% in stage III, and 8% in stage IV,[13,14] whereas our data have shown 44.9% in stage III, and 16.3% in stage IV. Taxane-based regimen in comparison to CP has produced higher response rate (60% versus 73%), and higher disease-free survival in previous studies.[5,14] Although higher response rate has been produced by taxane-based regimen in comparison of traditional chemotherapy in the current study, the difference was not significant ($p$=0.275). However, many factors could influence our result, and we think that this survey could give us a perspective of our situation, and we need further, precious randomized study to define our deficiency.

The limitations of this study were: small study population, retrospective method of study, inappropriate non-uniform use of chemotherapeutic agents, and the absence of optimal cytoreduction therapy in vast majority of our cases.

In addition, there are evidences that despite published guidelines, some women did not receive optimum treatments even in developed countries.[15] It is essential to start organizing more subspecialty oncology centers such as gynecologic cancer centers with surgeons and oncologists, who work specifically on these tumors, and several specialized active programs is required to ensure optimal managements. For a complete view of cancer care in our region and investment in this clinically important area, it is essential to evaluate the impact of new strategy on future care. Furthermore, it should be considered that the use of new agents are expensive, and several new and more expensive drugs, such as targeted therapy are developing,[16,17] so it is reasonable to evaluate the cost effectiveness of our management.

**Acknowledgment.** *The authors are very grateful to Dr. B. Sadrolhefazi, Dr. A. Mosavizadeh, Dr. H. Madani, F. Bahor, B. Sharifi for their kind assistance in preparing the data.*

## References

1. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, et al. Cancer statistics, 2008. ***CA Cancer J Clin*** 2008; 58: 71-96.
2. Ozols RF, Rubin SC, Thomas GM, Robboy SJ. Epithelial ovarian cancer. In: Hoskins WJ, Perez CA, Young RC, Barakat RR, Markman M, Randall ME, editors. Principles and Practice of Gynecologic Oncology. 4th ed. Philadelphia (PA): Lippincott Williams & Wilkins; 2005. p. 916.
3. Thigpen T. The if and when of surgical debulking for ovarian carcinoma. ***N Engl J Med*** 2004; 351: 2544-2546.

4. Piccart M, Bertelsen K, Stuart G, Cassidy J, Mangioni C, Simonsen E, et al. Long-term follow-up confirms a survival advantage of the paclitaxel-cisplatin (TP) regimen over the cyclophosphamide-cisplatin combination in advanced ovarian cancer. ***Int J Gynecol Cancer*** 2003; 13 (Suppl 2): 144-148.
5. McGuire WP, Hoskins WJ, Brady MF, Kucera PR, Partridge EE, Look KY, et al. Cyclophosphamide and cisplatin compared with paclitaxel and cisplatin in patients with stage III and stage IV ovarian cancer. ***N Engl J Med*** 1996; 334: 1-6.
6. Armstrong DK, Bundy B, Wenzel L, Huang HQ, Baergen R, Lele S, et al. Intraperitoneal cisplatin and paclitaxel in ovarian cancer. ***N Engl J Med*** 2006; 354: 34-43.
7. Ozols RF, Bundy BN, Greer BE, Fowler JM, Clarke-Pearson D, Burger RA, et al. Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected stage III ovarian cancer: a Gynecologic Oncology Group study. ***J Clin Oncol*** 2003; 21: 3194-3200.
8. Chan JK, Cheung MK, Husain A, Teng NN, West D, Whittemore AS, et al. Patterns and progress in ovarian cancer over 14 years. ***Obstet Gynecol*** 2006; 108: 521-528.
9. Krag KJ, Canellos GP, Griffiths CT, Knapp RC, Parker LM, Welch WR, et al. Predictive factors for long term survival in patients with advanced ovarian cancer. ***Gynecol Oncol*** 1989; 34: 88-93.
10. Van der Burg ME, Van Lent M, Buyse M, Kobierska A, Colombo N, Favalli G, et al. The effect of debulking surgery after induction chemotherapy on the prognosis in advanced epithelial ovarian cancer. ***N Engl J Med*** 1995; 332: 629-634.
11. Therasse P, Arbuck SG, Eisenhauer EA, Wanders J, Kaplan RS, Rubinstein L, et al. New guidelines to evaluate the response to treatment in solid tumors. European Organization for Research and Treatment of Cancer, National Cancer Institute of the United States, National Cancer Institute of Canada. ***J Natl Cancer Inst*** 2000; 92: 205-216.
12. Wakabayashi MT, Lin PS, Hakim AA. The role of cytoreductive /debulking surgery in ovarian cancer. ***J Natl Compr Canc Netw*** 2008; 6: 803-811.
13. Olaitan A, Weeks J, Mocroft A, Smith J, Howe K, Murdoch J. The surgical management of women with ovarian cancer in the south west of England. ***Br J Cancer*** 2001; 85: 1824-1830.
14. Piccart MJ, Bertelsen K, James K, Cassidy J, Mangioni C, Simonsen E, et al. Randomized intergroup trial of cisplatin-paclitaxel versus cisplatin-cyclophosphamide in women with advanced epithelial ovarian cancer: three-year results. ***J Natl Cancer Inst*** 2000; 92: 699-708.
15. Cress RD, O'Malley CD, Leiserowitz GS, Campleman SL. Patterns of chemotherapy use for women with ovarian cancer:a population-based study. ***J Clin Oncol*** 2003; 21: 1530-1535.
16. Han ES, Monk BJ. Bevacizumab in the treatment of ovarian cancer. ***Expert Rev Anticancer Ther*** 2007; 7: 1339-1345.
17. Burger RA, Sill MW, Monk BJ, Greer BE, Sorosky JI. Phase II trial of bevacizumab in persistent or recurrent epithelial ovarian cancer or primary peritoneal cancer: a Gynecologic Oncology Group Study. ***J Clin Oncol*** 2007; 25: 5165-5171.

## Related topics

Anfinan NM, Sait KH, Al-Maghrabi JA. Primitive neuroectodermal tumor of the ovary. ***Saudi Med J*** 2008; 29: 444-446.

He X, Lin B, Kong L, Zhang J. The potential mechanism of chemosensitive difference between 2 types of ovarian cancer. ***Saudi Med J*** 2007; 28: 1044-1049.

Aktas S, Yigit S, Diniz G, Pehlivan FS, Ortac R. Comparison of underlying lesions in pediatric and adult ovarian torsion. ***Saudi Med J*** 2006; 27: 1183-1186.