Treatment Decision-making Processes in the Systemic Treatment of Ovarian Cancer: Review of the Scientific Evidence

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Abstract. *Background: The systemic treatment of epithelial ovarian cancer (OC) is one of the cornerstones in the multimodal management of advanced OC in both primary and recurrent stages of this disease. In most situations various treatment options are available but only few data exists about the treatment decision-making process. Therefore, we conducted a review of the current literature regarding the decision-making process concerning the systemic therapy in patients with advanced ovarian cancer. Materials and Methods: The electronic database MEDLINE (PubMed) was systematically reviewed for studies that evaluate the treatment decision-making processes in patients with advanced OC. Results: The PubMed database was searched in detail for all titles and abstracts of potentially relevant studies published between 1995 and 2011. An initial search identified 15 potentially relevant studies, but only seven met all inclusion criteria. Factors that influence treatment decisions in patients with OC include not only rational arguments and medical reasons, but also individual attitudes, fears, existential questions, various projections resulting from the physician patient relationship and the social environment. The physician's personal experience with OC treatment seems to be an important factor, followed by previous personal experience with medical issues, and the fear of side-effects and future metastases. Family and self-support organisations also seem to play a significant role in the treatment decision-making process. Conclusion: This review underlines the need for more research activities to explore the treatment decision-making process to enable the best individual support for patients in treatment decision-making. It is a challenge for*

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clinicians to determine the individual information needs of women with OC and to involve them during the decision-making process to the extent they wish.

Ovarian cancer is the fifth the most common type of cancer among women. The worldwide annual incidence rate varies considerably, ranging in 2008 from 9 per 100,000 in industrialized countries to 5 per 100,000 in developing countries. With a mortality rate of 3.8 per 100,000 women, the survival expectation of patients with ovarian cancer compared with other types of cancer of the female reproductive system is very low (1).

In most patients, primary cytoreduction followed by postoperative adjuvant chemotherapy with a platinum- and taxane-based regimen given for six cycles are the cornerstone in the clinical management of advanced ovarian cancer. In cases of advanced stage IIIb, IIIc and IV stage diseases recent randomized trials indicated a significantly better progression survival upon addition of maintenance therapy with bevacizumab for a period of 15 months. Despite improvements in radical surgery and systemic therapy, recurrences are frequent and most patients will die due to tumor progression. Based on the platinum-free interval, there are different treatment options for systemic chemotherapy for patients with recurrent ovarian cancer (2). The patient's preference should be considered in cases of relapsed ovarian cancer and is demanded by various guidelines, but surprisingly, only few data exists about the decision-making process in patients with cancer.

The increasingly advocated shared decision-making model can strengthen the physician-patient relationship and make the patient a part of the decision-making process. This process of treatment decision-making involves three stages (3): The first stage involves an information exchange regarding relevant disease and treatment options. The information exchange should also take into account the patient's attitudes and values, as well as their needs, emotions and preferences. The second stage is the deliberation- a process of identifying values which are

Table I. *Overview of the most relevant series regarding the decision-making process regarding therapy in ovarian cancer.*

Author	Stewart *et al.* (4)	Kitamura *et al.* (5)	Elit *et al.* (6)	Jolicouer *et al.* (7)
Year	2000	2010	2003	2009
Country	Canada	Japan	Canada	
Type	6 Different self-report questionnaires were used to refer patients preferences (concerning type and amount of information they wanted, decision-making preferences), sociodemographic information, disease-related, and psychological factors	Questionnaire with paired priority scale containing the patients basic characteristics, *e.g.* operation year, treatment and 15 items related to the analytical hierarchical process	Semistructured personal interview	Personal interview
Physician	Physician in ambulatory tertiary care, clinicians at a Canadian university general hospital and comprehensive cancer center		Five gynecological oncologists and three medical oncologists	
Study population	139 Women with OC, 105 (75.5%) completed the questionnaire, 61% of the 105 women were in follow-up after treatment, 39% were in active treatment	31 Women with OC and endometrial cancer out of 33 responded to the questionnaire	21 Women with advanced epithelial OC who had just undergone surgery and were receiving first-line chemotherapy	21 Women with ROC
Main results	Which information is necessary for treatment decision making, role of women in decision-making, influencing factors	An analytic hierarchical process is used to study criteria and priorities of patients in treatment decision-making	Extent on the understanding of women regarding the treatment benefits and risks on survival and life quality, the risk of chemotherapy. Their role in treatment decision-making, factors overwhelming them (*e.g.* severity of illness, diagnosis of cancer). The possibility of treatment choice and how the women experience it (is there a choice of treatment or not?). The physician-patient relationship (satisfaction with the physician, his treatment and work). Social support during decision-making (individual persons, past experience with cancer, faith)	Describes the decision-making needs of women with ROC, shows that making a treatment decision for patients is not choosing between options or treatment possibilities, but rather accepting the physicians treatment recommendation
Factors influencing treatment decision making	Higher educational level was related to need for more detailed information ($p<0.05$) and age of patient, more questions related to the physical aspect of their health were asked the older the patient was ($p<0.05$), disease progression During diagnosis, treatment and after treatment, 82 to 90% of the women wanted detailed information	Fear of recurrence and metastases, recommendations from medical staff	People who supported them (family, friends), faith and already existing experience with cancer (own or of relatives), treatment recommendation	Personal experience with medical topics, information about the disease incurability, physicians treatment recommendations

Table I. *continued*

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Author	Stewart *et al*. (4)	Kitamura *et al*. (5)	Elit *et al*. (6)	Jolicouer *et al*. (7)
Decision-making	105 Women with OC completed the questionnaire. 60% of them had metastatic diseases, >80% wanted detailed information about OC during diagnosis and treatment and post treatment stages of the disease. Most women wanted the decision to be shared with the physician, only a small number of patients wanted to decide alone about treatment or leave the decision to the physician alone Most-wanted information concerning treatment: seeding of the tumor (metastasis), treatment concerns (treatment options and their outcome), possible self-care options to improve outcome 62.9% Women at diagnosis, 59.6% women at treatment and 61.9% women after treatment wanted shared decision-making with their physician, 14.3% of women with diagnosis, 17.3% at treatment and 15.2 after treatment wanted to decide alone after considering doctors recommendation 22.9% at diagnosis, 23.1% at treatment and 21.9% after treatment wanted the doctor to make the treatment decision Women with progressive disease (*e.g.* metastasis) preferred shared decision making beyond deciding alone or dedicating it to the physician (*p*=0.001)	The analytic hierarchy process helps the patient in decision making by pointing out the main criteria that seem important to the patient. Participants were 8 patients with OC and 9 with endometrial cancer. The consistency index (CI) showed patients participating intensity in the answer: 8 patients had CI <0.15, 17 patients had a CI ≤0.03 and 13 had a CI of ≥0.03. 31 Patients who answered the questionnaire were satisfied with the logical consistency of the model	Patients articulated more the risk information concerning treatment than the benefit information. All the women felt overwhelmed with the treatment decision. They did not recognize that they could select between therapies and decide by themselves. 4 Women recognised treatment *versus* no treatment as an option. 4 Women did not want chemotherapy 1 Women perceived a choice between one drug *versus* two drugs 12 Women stated that they made the decision. 5 Women stated that the physician made the decision 1 Woman reported a shared decision-making process Treatment choice was influenced by the physicians' treatment recommendation	11 Women had no problem with treatment decision. 13 women reported the decision-making process was shared. 5 Perceived there was a treatment option. 7 Women stated that they had a passive role in decision-making. No treatment was also an option

OC: Ovarian cancer. ROC: Recurrent ovarian cancer.

important for the patient/physician interaction and details about treatment preferences. The last stage is the actual decision-making stage, where the treatment is determined by a consensus. This last stage is mainly influenced by the patients perception of the disease, as well as the balance between treatment advantages and toxicity and the goal of therapy. Study by Stewart *et al*., 105 women with ovarian cancer were asked who should ideally make the final treatment decision. Almost 20% of the patients expected their physician to make the decision about the treatment, 15% of the women wanted to make the final decision themselves, and 60% wished to have a shared decision-making process with their treating physician. However, all women required detailed and broad information about their disease and the various treatment options (4).

The paths followed, by both physicians and patients that lead them to their final decision regarding treatment are difficult and complex, as is the identification of the actual criteria and factors that influence this decision. Potential influential factors on the patients side are fear of reccurence or metastasis and toxicity, while the advice of family and medial staff also play a relevant role (5). Physicians are supposed to support their patients throughout the entire process, even though it is very complex to find a consistent method that supports the patient in decision-making. There are very few data about this relevant topic regarding patients with ovarian cancer. Therefore, we conducted this review to analyze the current literature to identify the potential factors influencing treatment decision-making in patients with ovarian cancer.

Materials and Methods

Inclusion and exclusion criteria. Medical literature was systematically reviewed for studies evaluating processes regarding decision-making in ovarian cancer. PubMed was searched by using the following key words "ovarian cancer, gynecological cancer and treatment decision-making". The evaluated period covered 16 years, namely 1995 to 2011.

All full papers of the individual studies dealing with treatment decision-making in patients with ovarian cancer were retrieved. All studies with ovarian cancer patients, regardless of study type, size of study population, geographic region and cancer progress during treatment decision (first-line therapy, recurrence) were included. Studies dealing with the decision-making process in patients with gynecological cancer where ovarian cancer was included were also considered. Studies were excluded if their abstract did not contain the sought key words. They were also excluded if their contents did not cover the researched topics although their title contained the relevant key words.

Results

Search results. The MEDLINE (PubMed) search identified 15 relevant studies regarding the decision-making process in gynecological cancer (4-18). Seven studies focused on decision-making process in patients with ovarial cancer (4-10).

Only one study was identified that evaluated the decision-making process of patients with gynecological cancer in general, but patients with ovarian cancer were analyzed separately as a subgroup (5).

Eight studies out of the 15 identified were excluded because their contents did not cover the researched topics although their title contained the relevant key words (11-18). Two of these excluded studies deal with the decision-making process regarding risk reduction for patients with hereditary breast or ovarian cancer; another study analyzed the impact of [^{18}F]-fluorodeoxyglucose positron emission tomography and computed tomography (FDG-PET/CT) in the decision-making of a suspected ovarian cancer recurrence (11-13).

Study overview. The main methodological characteristics and influencing factors of the relevant articles are summarized in Table I.

Discussion

The present analysis is an attempt to give an overview of the factors influencing the decision-making process in patients with primary or relapsed ovarian cancer who are scheduled to undergo a systemic treatment. The overall knowledge and sensitive regarding this important issue is very scarce and only a few studies exist that have systematically evaluated treatment decision-making in patients with ovarian cancer. A better insight into the involved processes will not only

contribute to a better understanding of the interaction between patients and physicians, but will also improve patient's compliance.

In the two studies of Elit and colleagues from the 2003 (patients with primary OC) and 2010 (patients with ROC) the expectations and behavior of patients on their way to treatment decision did not follow the shared decision-making model (1) like that described by Charles *et al.* (3). Elit *et al.* showed that patients with ovarian cancer usually follow the physician's recommendation without restrictions, are not expecting to know exact details about treatment toxicity or the names of the applied substances. Furthermore, the authors showed that most patients wished to be treated by the same physician who treated them at the initial manifestation of the disease, so that there would be no need to elucidate their beliefs and perspectives in the treatment decision-making again. This continuity facilitates the communication process.

Both studies of Elit *et al.* share the same background in terms of the patients' attitudes. The difference between these two studies is that patients with recurrent ovarian cancer had different goals compared with patients with primary diagnosis. The primary objective in the primary situation is cure, whereas symptom control and quality of life aspects are generally the aims for recurrent disease.

As expected, the data show that the patients with recurrent disease from the year 2010 appear to be more involved in the treatment decision process than at the time of first diagnosis. However, in both studies, the authors showed that patients feel overwhelmed by the entire decision-making process regardless of their disease stage or status of disease (*i.e.* primary *vs.* relapse). The most important influential factors in both studies were the family and friends, as well as other patients with ovarian cancer (6, 9). In almost all studies the physician's treatment recommendation played a decisive role in the patient's treatment decision-making. Moreovers the personal experience of the patient herself seems to play a crucial role in the attitude which is developed towards the disease.

In contrast to the 2003 study, 2010 study of Elit *et al.* examine the perceptions of patients in the treatment decision process very closely. However, the study does not verify exactly how the patient's perception influences the physician's behavior and communication style (9).

Other studies, like that from Stewart *et al.* showed that most patients demand shared decision-making processes at every stage of their illness, especially if the disease is progressive.

In another study by Kitamura, the pair-wise comparisons by the analytic hierarchy process (AHP) offers a possibility to understand the patient's choice and it also demonstrates the need to question the importance of various criteria, *e.g.* social demographic and psychological factors, because they have an effect on the investigation.

Table II. *Overview of the most relevant series regarding decision-making process in ovarian cancer.*

Author	Fitch *et al*. (8)	Elit *et al*. (9)	Ziebland *et al*. (10)
Year	2003	2010	2006
Country		Canada	UK
Type	Phone interview	Personal interview	Interview
Physician		Oncologist	GP, hospital consultants and specialist nurses
Study population	18 Women with newly diagnosed primary OC	26 Women with first ROC	43 Women with OC
Main results	Point out women's perceptions of living with OC and their experiences with therapy and treatment decision-making	Experience with treatment decision-making in women with ROC. Shared decision-making needs bilateral contribution of the patient and physician. Physicians continuity in treatment was very important.	Inclusion of women in treatment decision-making
Factors influencing treatment decision-making	Information about the side-effects of treatment, symptom treatment	Patients personal experience with the disease, the doctor's communication style and his recommendations	Physician's recommendations, patient's uncertainty
Decision-making	Treatment decision was made by the physician, majority of the women did not feel involved and sufficiently informed about the disease	Patients themselves decide on the treatment and/or influenced the time point for chemotherapy, participation in decision-making was more active. 16 Patients said that it was an advantage to have the same oncologist at ROC as at their first diagnosis. 14 Patients felt overwhelmed with statistics and progression of information. 24 Patients saw treatment benefit in prolonging life, not curing, 15 women saw treatment as controlling cancer, 4 as controlling symptoms, and 5 as extending life. 21 Women felt ROC equalled with limited life. 13 Women did not believe in complete cure. 7 Women said there was no treatment option, 6 felt there was	Most women felt overwhelmed to make a treatment choice and expected the doctor to decide alone because he was the "expert". Many women participated in the treatment decision-making and went along with the doctors opinion. Some women made more autonomous decisions concerning treatment.

OC: Ovarial cancer. ROC: Recurrent ovarian cancer. GP: General practitioner.

Such a model supports the treatment decision process of patients in order to quantitatively represent the patient's situations and help the patient to ask specific questions regarding treatment options (5). Recently, the North-Eastern German Society of Gynecological Oncology (NOGGO) finished enrolment of a study in elderly patients with relapsed ovarian cancer (preference trial). Patients had a free choice of the alkylating agent treosulfan given intravenously (*i.v.*) or as tablets. Interestingly, most patients preferred the *i.v.* application because most had already been taking many other tablets for their co-morbidities (19).

An international survey on patients' preferences and attitudes regarding physician-patient relationship and cancer management is ongoing (20). A recent interim analysis showed that most patients demand more explanations about side-effects to be able to make a choice of a specific cancer treatment (21). The final analyses of this study, with more than 1500 participants, will be awaited in 2013 and will also try to identify cultural-based differences in the patients' expectations.

Conclusion

The currently available literature does not provide enough evidence to identify the relevant and reproducible factors of a treatment decision-making for patients with relapsed ovarian cancer. The patient physician interaction seems to be mainly based on random events without any systematic basis, while efforts towards an improvement of this process are not sufficient, with a global lack of overall attention to this highly important issue. As novel treatments and therapeutic options are continuously emerging, patients are now more than ever called to make critical decisions without any systematic or professional psychosocial support. Therefore, there is an urgent need to understand better the factors that underpin the treatment decision-making process. This would undoubtedly lead to an increase in patients' compliance and satisfaction.

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