



Review

Futility: Clinical decisions at the end-of-life in women with ovarian cancer

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Abstract

Objective. The purpose of this article is to provide a review of the clinical meaning of futility, discuss current normative uses of futility assessments and propose guidelines for clinicians to use in dialogue regarding treatment decisions for patients with advanced ovarian cancers.

Methods. We performed a MEDLINE literature search of relevant clinical articles for this review that discussed futility and the application to women with ovarian cancer.

Results. Medical futility refers to treatments that serve no physiologic, quantitative or qualitative meaningful purpose. Despite the growth in options focused on symptom management rather than disease eradication, including hospice programs and the more recent development of palliative care programs, there is evidence that many patients continue to receive aggressive interventions, including chemotherapy, until days before their death. While the legal and moral acceptability of treatment limitation is well established, clarity in establishing goals of care, timing of the transition from cure to palliation and communication of specific decisions to withhold further aggressive interventions remain problematic for both patients and clinicians.

Conclusions. There continues to be a distinct need for both better understanding of the dynamics of patient choice and increased education of physicians in addressing end-of-life care planning. It is essential that we continue to test specific communication and supportive interventions that will improve our ability to help patients avoid the burden of futile therapy while maintaining hope.

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Introduction

“Futility” is a label that began to appear in medical literature in the late 1980s [1]. It was used to refer to treatments that clinicians believed served no meaningful purpose. The growing use of the term was prompted by several different concerns: the increasing incidence of requests from patients and families for treatments that the clinician viewed as ineffective, persistent ambivalence and uncertainty among clinicians about decisions to withhold or withdraw aggressive treatment, and concerns about the cost-effectiveness of aggressive and expensive treatments for dying patients [2]. Early analyses of the meaning and ethical implications of judgments of futility focused on cardiopulmonary resuscitation and use of critical care therapeutics, such as mechanical ventilation. Concerns about offers of or demands for ineffective interventions, however, are equally relevant in oncology.

Discussion of futility takes place within the context of norms establishing and limiting the obligation to provide or withhold medical treatment. In the latter half of the 20th century, societal, legal and medical norms gradually evolved to include recognition that there are moral and clinically appropriate reasons to limit the provision of available interventions. These include any situation in which a competent adult refuses initiation or continuation of treatment or in which an available treatment will be ineffective in promoting the patient’s goals [3,4]. With acceptance of this standard, attention shifted to focus more on the processes surrounding decision making about treatment limitations and barriers to providing quality care at the end-of-life [5].

The change in norms about treatment limitations was fueled by two developments. First was the increasing availability of very aggressive, burdensome and expensive technologies that delayed death for short periods of time but were unable to offer cure or reverse pathological processes. The second was the marked shift from a paternalistic decision mode to a consumer-driven, patient autonomy model. Passage of advance directive legislation in most states, establishing a legal mechanism to assure respect for decisions to limit the use of life-sustaining treatment in terminal states, reflects the widespread acceptance of these norms. The purpose of this article is to provide a review of the moral and clinical meaning of futility, discuss current normative uses of futility assessments and propose guidelines for clinicians to use in dialogue regarding treatment decisions for patients with advanced ovarian cancer.

Current futility standards

Lack of clarity in the meaning of the term “futile” has contributed to difficulty in analysis of the moral status of requests for ineffective interventions. “Physiologic futility” refers to the inability of the proposed intervention to achieve

the biologic result intended. For example, attempting dialysis in a patient who has refractory hypotension will not result in electrolyte correction or filtration. Similarly, administering a chemotherapeutic agent for a known chemoresistant tumor will not halt growth or promote shrinkage. A proposed treatment may also be futile in that, while it may produce some intended physiologic change, such as maintaining respiration or correcting electrolyte imbalance, it will not alter the duration of survival because it cannot affect the processes leading to death. Some have referred to this as “quantitative futility” [6]. Similarly, the term “qualitative futility” has been used to describe the inability of an intervention to achieve a desired quality of life goal, although the intervention might be successful in maintaining or even extending survival [7].

The meaning of the term futility has important moral implications. The ethical principles of autonomy, beneficence and nonmaleficence have long been accepted as providing a useful framework for analysis of moral problems in medicine [8–10]. Autonomy directs us to respect the choices, values and life plans of patients and generates the requirements for informed consent. Beneficence is particularly directive for health professionals in grounding our fundamental duties to promote the good or well-being of patients. Nonmaleficence, the duty to refrain from harm, reflected in the Hippocratic Oath, is thought to be the most stringent or exception less. Each of these will have different implications for futility cases depending on the sense of the term.

Requests for interventions that are physiologically futile are the most straightforward and there is relatively strong consensus about ethical implications. While autonomy establishes the right to pursue one’s goals without interference, it does not obligate others to provide whatever means of achieving those goals are desired. Thus, while autonomous individuals have an almost absolute right to refuse offered interventions, autonomy, in itself, does not establish any basis for claiming a right to be provided with a desired treatment. If a proposed intervention cannot produce the intended physiologic effect (e.g. prolongation of quantity or quality of life with chemotherapy) and is likely to inflict physiologic harm (e.g. neutropenic sepsis), the principle of nonmaleficence not only permits the physician to withhold the requested treatment, it may also obligate him/her to do so if the harms are certain and significant. This reasoning, most often applied to requests for resuscitation attempts, undermines position statements of professional societies and institutional policies developed to guide physicians in responding to such requests [11,12].

Unfortunately, there is far less clarity in the analysis of requests for therapy that the physician believes to be futile in either of the other two senses. An available therapy may be thought to be *quantitatively* futile when there is no evidence that it prolongs survival beyond a few days or weeks at most, and yet patients or families may insist on continuation of the therapy. A common example of this is

the use of mechanical ventilation or vasopressors in a patient dying of end-stage heart failure in the intensive care unit. The interventions are not physiologically futile in that they are maintaining oxygenation and circulation, although this effect is certain to be time-limited. Similarly, a clinician may argue that provision of artificial nutrition and hydration to the patient with terminal cancer is *qualitatively* futile. Total parenteral nutrition (TPN) cannot restore or alter the patient's experience or quality of life with end-stage ovarian cancer, yet it clearly achieves the intended physiologic effect of meeting hydration and nutritional needs. In end-stage cancer, TPN rarely extends survival and thus also is likely to be *quantitatively* futile.

Ethical analysis of requests for interventions that are not physiologically futile but possibly quantitatively or qualitatively futile is more difficult. Unlike judgments of physiologic futility, quantitative and qualitative futility judgments involve assessment of the benefit or worth of the effect. In the examples above, evaluating the justification for continuing use of mechanical ventilation and vasopressors entails an evaluation of the benefit of added days of life. Even a few more days of life may be of great value if they allow time for a distant relative to come and see the patient or prevents the death from occurring before an anniversary or family gathering. The meaning and importance of the added days can only be evaluated by the patient, her family and friends. For this reason, requests to continue therapy a few days are usually viewed as reasonable.

Particularly challenging are requests to provide therapy that is seen as both quantitatively and qualitatively futile and possibly in violation of duties of nonmaleficence. Some experts argue that physicians do not have a responsibility to provide futile care, and it may be considered unreasonable if the futile care is excessive and not generally agreed upon [13]. Treatments that impose significant burdens without physiologic benefit or increased survival, such as continued chemotherapy in progressive, chemotherapy refractory ovarian cancer, may represent this sense of futility and the implications of this should be considered before secondary surgical cytoreduction or platinum-resistant chemotherapy is offered. There is no longitudinal research that indicates prolonged platinum refractory chemotherapy with sequential regimens decreases symptoms or increases the quality of life. In addition, side effects of chemotherapy, such as neuropathy, may be acceptable with curative intent chemotherapy but are contrary to the goals of treatment during palliative care. Appreciation of the fact that patients need to maintain hope and often wish to avoid the perception of surrendering to the disease does not reduce the obligation of the clinician to avoid harm and to counsel patients and families about these choices.

Despite evidence that continued chemotherapy in some situations is both quantitatively and qualitatively futile, clinicians may perceive other reasons to offer such therapy. One justification specific to non-curative chemotherapy is the opportunity to participate in clinical research [14].

Patients with recurrent ovarian cancer may be offered the option of enrolling in a clinical trial. The chance of response in trials of experimental treatment often are quite low, especially in Phase I chemotherapeutic trials in which the goals of the trial are to examine safety, dose response and possibly pharmacokinetics. Phase II trials, designed to evaluate efficacy, may offer a more meaningful potential for benefit. Nevertheless, there are complex issues related to the participation of advanced cancer patients in trials, including patient vulnerability, likelihood of therapeutic misconception and ability to comprehend complicated protocols, that must be considered [15]. Even though predicted response rates in many trials are extremely low, patients may be motivated to participate in Phase I trials primarily for the chance of benefit to themselves despite clear disclosure in consent forms of Phase I trials of the absence of expected benefit to subjects [15,16].

There has been little research investigating the reasoning of oncologists in decision-making regarding continued provision of high-burden treatment, such as chemotherapy, in the face of no meaningful probability of physiologic benefit. There have been, however, a number of investigations of factors associated with physician decisions about life-sustaining treatment, such as antibiotics, artificial nutrition and hydration and mechanical ventilation. For example, Hinkka et al. found that physicians' decisions to forgo life-sustaining treatments in a terminal cancer scenario were influenced by personal and background factors, such as gender, experience and postgraduate education [17]. Mebane et al. found race to be strongly associated with decisions, as African-American physicians were six times more likely to prescribe aggressive treatments than Caucasian physicians [18]. Christakis and Asch reported that physicians who were young and spent more time in clinical practice were more willing to withdraw therapy [19]. There are other personality factors of physicians that guide decision making at the end-of-life that are not as readily measurable. For example, physicians who deny medical futility may be influenced by religion, the practice of legal defensiveness, aggressive practice style and emotional detachment [20]. Patient-related factors, such as recent treatment initiation, age of the patient and diagnosis, also influence decisions independently of actual prognosis [21–24]. Thus, it is clear that the subjective judgments of futility are not solely a function of assessment of benefit and burden, but are also influenced by personal characteristics of both physicians and patients.

Despite the growth in options focused on symptom management rather than disease eradication, including inpatient and out-patient hospice programs and the more recent development of palliative care programs, there is ample evidence from the United States and other countries that many patients continue to receive aggressive interventions, including chemotherapy, until days before their death [25–27]. In late stage cancer participants from the Study to Understand Prognoses and Preferences for Risks of Treat-

ments (SUPPORT), there was no association between aggressiveness of care and overall survival [28]. Oncologists' may feel a reluctance to disclose prognosis and the need to preserve patient hope [29]. Baile et al. surveyed oncologists at the American Society of Clinical Oncology in 1999 pertaining to attitudes and practices in disclosure of unfavorable medical information to cancer patients [30]. The most difficult conversations were those that dealt with the lack of additional treatment options and 24% said that they occasionally administered treatment that was not likely to work in order to maintain patient hope [30].

Despite promising advances in cancer therapeutics, gynecologic oncologists will continue to face frequent challenges in shifting goals of care from cure to maintenance of hope and promotion of quality of life. As illustrated in Fig. 1, patients with advanced disease look to the oncologist for treatment that offers them the promise of survival and the assurance of the best possible care. The oncologist, in turn, is faced with the dilemma of designing a plan of care that supports patient hope, avoids harm and meets expectations for quality care. This challenge may be further complicated by concerns about the perception of abandonment if no further chemotherapy or surgery is offered or the perception among colleagues that the surgeon is not sufficiently aggressive. Responding to these challenges requires both professional and personal resources.

Futility in gynecologic oncology

In 2004, it is anticipated that there will be 16,090 deaths from ovarian cancer, 7090 from endometrial cancer, 3900 from cervical cancer, 850 from vulvar cancer and 790 from vaginal and other genital cancers [31]. Therefore, gynecologic oncologists will deal with end-of-life care and the potential issue of futility more than 28,000 times this year.

Ramondetta et al. surveyed members of the Society of Gynecologic Oncologists in 2000 on end-of life issues [32]. Although the return rate of the survey was only 35%, they found that 44% of respondents believed that gynecologic oncologists paternalistically influence end-of-life discussions [32].

End-of-life discussions should be considered long before the onset of imminent death. Since the majority of women with ovarian cancer present with advanced disease, and the majority recur and die, the gynecologic oncologist must decide when to initiate a discussion of revising goals of care. Some will begin discussions when the cancer recurs, while others wait until platinum resistance is established, and sometimes this discussion is postponed until the patient is frankly terminal. When gynecologic oncology patients were surveyed on end-of-life decisions, 96% emphasized "straight talk" and 64% expected compassion [33]. In order to develop useful guidelines for these discussions, reliable data about the pattern of ovarian cancer, prognostic indicators and an understanding of psychological factors in patient preferences and decisions are needed.

The ability of clinicians to estimate survival time tends to be inaccurate and optimistic [34,35]. In addition, patients typically overestimate prognosis, positively reinterpret their prognosis and confuse "response" with "cure" [36–39]. General and specific tumor site guidelines may be helpful in guiding practitioners in the choice of reasonable treatment or withdrawal of therapy [40–43]. Integrating measurable objective variables may avoid medical futility and provide a foundation for end-of-life decisions [44].

Prognostic indicators such as performance status, clinical symptoms and laboratory values have been explored in cancer patients [34,35]. Bowel obstruction, ascites, pleural effusions, DVT and metastases have been shown to be indicators of poor prognosis in ovarian cancer [45–49] but do not precisely indicate duration of survival.

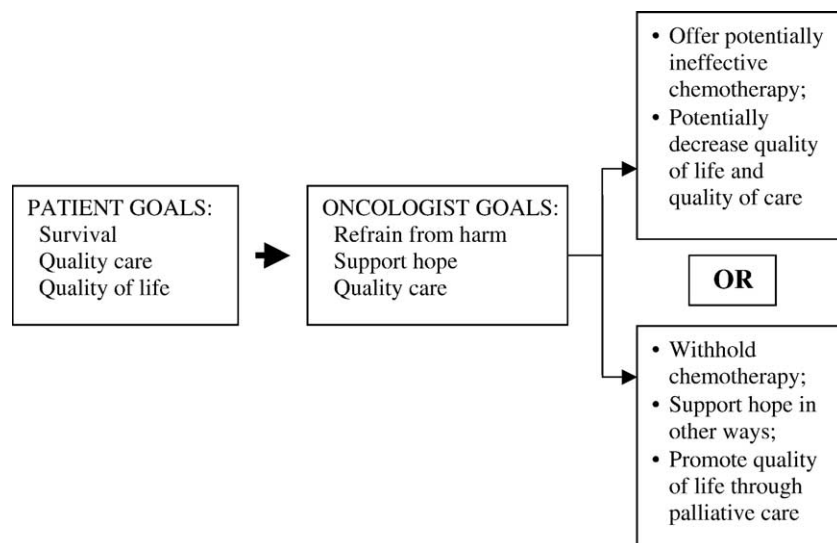


Fig. 1. Goals and choices at the end-of-life.

In a retrospective study of deceased ovarian cancer patients, bowel obstruction and procedures such as thoracentesis and paracentesis rarely occurred during the 7 to 12 months preceding death but increased during the last 6 months of life [26].

It is well known that, for some individuals, continuing “the fight,” regardless of effectiveness, has great meaning and adds value to existence. For example, Brown et al. reported that only 5% of his sample of 108 women with gynecologic malignancies predicted that they would “give up the fight” if the time came that their treatment was no longer working [50]. Donovan’s study examining treatment preferences using a decision board found that 25% of recently diagnosed ovarian cancer patients indicated that they would never switch to palliative care but would choose salvage therapy even if the anticipated median survival time was less than 1 week [51].

End-of-life discussions are often difficult and require careful planning. Clinical presentations and complications secondary to cancer are valuable prognostic indicators and can guide the physician in addressing the appropriateness of stopping chemotherapy. Understanding the ambivalence patients feel in changing goals of care, as well as the importance of maintaining hope [52] while avoiding the unintended imposition of burdens associated with futile therapy, has important implications for how physicians counsel patients or families requesting interventions that the medical team views as non-beneficial.

Guidelines for patient, family and treatment team communication

Communication and understanding between the physician, patient and family is pivotal to avoid futile care in cancer. Most patients are well informed about cancer treatment but disparities remain among physicians in discussion of prognosis and alternatives to anticancer treatments [53]. The majority of cancer patients report a preference for detailed information about their disease [54], although some prefer to negotiate the extent and timing of the information they receive from oncologists [54].

Few physicians have received training in the adequate communication skills necessary to discuss palliative care and end-of-life [39]. It is imperative that physicians start by choosing the appropriate setting to hold these conversations. A private area should be chosen and all those involved should be sitting. Invite a support network for the patient to the appointment, such as family or friends. Physicians do not need to hold these conversations alone; often it is supportive to both patient and physician to have the patient’s primary chemotherapy nurse or social worker in the room. These providers can be helpful in reframing or restating terminology for the patient and her family. Physicians need to be aware of the time commitment of such discussions and schedule sufficient time in the clinic or on hospital rounds.

Options for beginning the conversation include starting with a warning phrase, “I’m afraid I have bad news”, or with some form of a question, “Do you feel well enough to talk for a bit” [39,55]. Periods of silence can also be used to help the patient communicate preference on how they want to receive the “bad news” [55,56]. More than one session may be needed, and it can be an ongoing conversation from clinic visit to clinic visit. The following aspects and techniques have been identified as helpful in these difficult discussions:

- Talk with patients in an honest, sensitive and straightforward way.
- Be willing to talk about dying and to use the words “death” and “dying.”
- Listen to the patient without interrupting.
- Encourage questions.
- Do not discourage hope; focus as appropriate on what can be done to maintain the quality of life, however long that is [39,56,57].

During the conversation, validate that the message is being received. For example, periodically stop to ask “Do you understand?”, “Do you have any questions?”, or “Am I being clear?” Reinforce and clarify the information frequently. Have the patient or family member repeat what you have been saying. Conversations with the patient and family should include truthful disclosure of medical facts with an assessment of response to chemotherapy, duration of response and clarification that “response” is not a “cure” [58,59]. The clinician should clearly explain that, at some point in the patient’s disease course, treatment may not be aimed at altering the course of the disease but at relieving symptoms [59].

In advanced disease stages, the frame of reference of hope will change. For example, the hope of prolongation of life will change to the hope of a good quality of life at the end-of-life, minimization of symptoms and opportunity to accomplish whatever activities or goals are important to the patient. If these discussions are not held, patients may seek others who offer false hope in alternative therapies [60]. If gynecologic oncologists are not comfortable in a primary communicative role, then referral to a palliative care specialist is appropriate [20,59]. If the patient’s desire for continued futile therapy persists, nonjudgmental exploration of underlying feelings and sharing of responsibility should be discussed at ongoing appointments [61].

Resources, guidelines and education of physicians in end-of-life in care

The American College of Surgeon’s website provides references for physicians in regards to ethics and futility through an onsite search engine [<http://www.facs.org>]. The American College of Obstetricians and Gynecologists

(ACOG) has a site on their website dedicated to ethics in Obstetrics and Gynecology; this includes sections on medical futility and end-of-life decision-making [<http://www.acog.org>]. ACOG proposes a definition of medical futility as, “a lethal diagnosis or prognosis of imminent death; therapy is unable to achieve its physiologic goal; therapy cannot achieve the patient’s or family’s goals; therapy that will not extend the patient’s life span; or, therapy that cannot enhance the patient’s quality of life”. In designing a medical futility policy, ACOG refers to the American Medical Association (AMA) Council on Ethical and Judicial Affairs report [<http://www.ama-asa.org>]. This report recognizes the necessary value judgments involved that must be given consideration. Also included is a recommendation for the development of organizational policies for guidance when conflicts between physician, provider, family or patient exist.

The American Society of Clinical Oncology (ASCO) has published an executive summary on cancer care during the last phase of life [40]. This report stresses that the role of the oncologist is not simply to treat cancer, but to provide comprehensive palliative and anticancer therapy throughout the course of an illness. In addition, the society urges that oncologists learn to recognize and respond to the transition point in a patient’s care when disease-oriented anticancer therapy must give way to symptom-oriented palliative therapy. Educational initiatives must include formal training in pain/symptom management, recognition when anticancer therapy will not help, palliative care, communication, ethics and psychosocial support. The learning guide in gynecologic oncology, under The American Board of Obstetric and Gynecology (ABOG), largely focuses on diagnosis, pathology, physiology, carcinogenesis, genetics, statistics, immunology, chemotherapy, pharmacology, radiation therapy and surgical procedures [<http://www.abog.org>]. Under miscellaneous “enabling” objectives, they do state that the gynecologic oncology fellow should understand the principles of medical ethics, advanced directives, palliative care, hospice care and death and dying. However, when gynecologic oncologists were surveyed, 77% responded that more training, in the form of educational workshops, teaching emphasis and/or taped practice sessions during fellowship would help them better prepare to deal with patients at the end-of-life [32]. Clearly, this suggests that oncologists responsible for the design of training programs must include formal, explicit educational sessions addressing these topics.

Summary

Medical futility refers to treatments that physicians believe serve no meaningful purpose. Establishing futility is not solely a function of assessment of physiologic benefit and burden, but is also influenced by personal characteristics of both physicians and patients. The concept of futility in the treatment of women with advanced ovarian

cancer should be considered before secondary surgical cytoreduction, continued platinum-resistant chemotherapy, phase I clinical trials and the use of TPN. When physicians are communicating with terminal patients and family, it is essential to deliver a straightforward prognosis with an honest, sensitive and hopeful approach. Hope is a dynamic concept with a changing point of reference in the course of the patient’s disease. While research in palliative care at the end-of-life in women with ovarian cancer is mounting, it is imperative that clinical trials aid clinicians in providing improved quality of care at the end-of-life. In addition, requirements for formal training of gynecologic cancer care during the last phase of life should be implemented.

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