



# Unsolved Problems and Thoughts about End of Life Treatments in Cancer Patients

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## Abstract

The number of patients receiving chemotherapy/radiotherapy at the end of life (EOL) is increasing also as the number of cancer patient dying in acute care hospital. 20% of patients are receiving chemotherapy in the last 14 days of life. Older (>75 years) patients also receive chemo at EOL. Besides aggressive treatments and invasive procedures targeted therapy is also often administered in the EOL. Such approach is provoking exhausting side-effects, premature death and is producing more costs. In our Department 22.7% patients were admitted to receive palliative care, and 77.3% were admitted for planned chemo-and/or radiotherapy administration. More than 40% of patients received chemotherapy treatment. We have concern about the high percentage of patients who tried to provide oncology treatments in the three months before his death and about the percentage of patients dying in acute hospitals. We are conscious that death is inevitably for each of us, but we are still trying to avoid the talk about death and dying. Therefore care for oncology patients in EOL many times deviate in the field of dysthanasia.

**Keywords:** Palliative care; Chemotherapy; Radiotherapy; End of life; Dysthanasia

## Abbreviations

ICU: Intensive Care Unit; EOL: End of Life; OS: Overall Survival; QoL: Quality of Life; RT: Radiotherapy; PRT: Palliative Radiotherapy; CNS: Central Nervous System

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## Introduction

The number of patients undergoing aggressive chemotherapy at the end of life (EOL) is rapidly increasing. Furthermore, the number of cancer patient dying in acute care hospital is also increasing [1]. Up to 50% of cancer patients are dying in an acute care hospital and 2-3% of them had an ICU admission during the last 30 days of life. Up to 45% of patients with incurable cancer are treated with palliative chemotherapy in the last month of their lives and 20% of them are receiving chemotherapy in the last 14 days of life [2]. Frequency of chemotherapy use within 1 month before death is no less than 29% [3]. Older (>75 years) as well as younger patients dying with poor-prognosis cancer, experience high-intensity care in equal parts [4]. Patients with pancreatic, breast and ovarian cancer has higher rate of chemotherapy at the EOL and chemotherapy for gynecologic malignancies often includes aggressive treatments and invasive procedures [5,6]. Targeted therapy is also often administered in the EOL; more than half of patients who received systemic therapy within three months of death received targeted therapy (erlotinib, bevacizumab, rituximab, gemtuzumab, and temsirolimus) [7,8].

## Chemotherapy in EOL

Chemotherapy administered in EOL produces high rate of adverse effects such as febrile neutropenia, therefore precipitating hospitalizations in emergency departments and leading to use of expensive drugs like recombinant human erythropoietin and colony-stimulating factors. Moreover, such treatment is precluding entry into most hospices [9].

The largest contributors of increased costs are not costs of targeted drugs or supportive care drugs, but costs of acute inpatient care. It is unexpected, but about 20% of cancer patients is admitted to the ICU, 17% are intubated and 13% had cardiopulmonary resuscitative efforts in last 6 months of life [10].

What is the purpose of chemotherapy in metastatic disease? Improving overall survival (OS) and quality of life (QoL) of patients. Therefore, the real question is: what is the appropriateness of such a treatment for cancer patients with terminal disease, producing toxicity with no/or little benefit and producing excessive costs to society [11,12]? The leaders of American Society of Clinical Oncology (ASCO) decides that some benefit must be demonstrable but they could not decide on a minimal benefit for which chemotherapy is indicated, especially in the light of fact that receiving chemotherapy at EOL lead to shorter survival compared to best supportive care only [9,13]. However, there is an agreement that providing chemotherapy to cancer patients at the EOL can be option for patients of younger age and with chemo sensitive tumors [1]. Also, there are some evidences that palliative chemotherapy can increase OS and QoL in metastatic colorectal and prostate cancer [13].

A large proportion 30%-50% of patients die in the hospital, which is in about 25% of cases due to the harmful effects of chemotherapy which brings terminal cancer patients into such a state that they cannot be discharged from hospital. The next question is: why terminal cancer patients rather die in hospital than to be cured at home? The study reports suggest that no one of the medical team discussed the possibility of death with terminal cancer patients in 39% to 62% of cases [14]?!

### Radiotherapy in EOL

Not only chemotherapy but also RT is a commonly used in EOL. RT is modality for palliation of symptoms (pain, bleeding control, obstruction reduction, reduction of a tumor mass that causes symptoms) with doses and the number of fractions which are smaller compared to radical radiation therapy. RT seems to be less costly and more economic procedure; hospice care is associated with 32% decrease in total costs of care in the last month of life among patients receiving RT (if we take into account the palliative benefits for patients) [15]. Increased costs could be expected due to complications of cancer leading to hospitalizations and requiring RT rather than from RT itself [16]. The median OS after the first course of PRT is 5.2 months [17]. The most important prognostic factor is treated site. Breast cancer with 11.4 months and prostate cancer with 8.4 months of OS have more benefit from PRT than oesophageal/gastro-oesophageal junctional tumours (4.6 months,) and lung cancer (3.9 months). Also, clear benefit from PRT can be expected in metastatic bone cancer and brain [18,19]. About 10% of patients who will die in next 30 days receive PRT, but 50% of them do not complete it, mostly because of death [20,21]. As chemotherapy, PRT is also more delivered to younger patients [22].

Results from our previously published study showed that the most common primary sites of cancer in patients who died in our Department were the lungs (40.1% of all patients), and then the breast [23]. Only 22.7% of patients were admitted to receive palliative care, and to others was planned to conduct chemo-and/or radiotherapy. Furthermore, 40.9% of patients underwent chemotherapy treatment within three months before death. In opposite to other study data, these patients were not found to be either of younger age, or that there were any difference by sex. To 34.1% of patients planned palliative RT was either initiated or completed. Palliation for dyspnea in lung cancer and PRT over the CNS region for patients with confirmed brain metastases with or without accompanying neurologic symptoms were the most common reasons for PRT use. These results are compatible with other study data [23].

## Discussion

Spotlight of every society is care for beginning of life as well as dying and death. We have about 14 millions of new cancer cases and 8 million of cancer deaths yearly worldwide [24]. Of modern oncology we expect prolonging a life OS, improving QoL also in the EOL, and dignified dying. What is appropriate role of chemotherapy near the EOL? This is a complex issue with inconclusive answers [1]. Patients with poor prognosis, with poor performance status who already failed on previous chemotherapy regimens, will not have any benefit from chemotherapy in the EOL. Such type of chemotherapy is producing toxicity, worsen QoL and can cause death even faster than expected. Moreover, such behavior is producing useless costs to Health Systems [25]. Today, there are evidences that OS is significantly longer for hospice patients receiving best supportive care only comparing with those who received chemotherapy and were not admitted to hospice [9]. These discoveries caused slight decrease (5%-6%) in the percentage of patients receiving chemotherapy in EOL [11].

Not only with excessive chemo/radiotherapy use are we also facing with increasing daily use of different technologies for the patients at the EOL leading us to a field of dysthanasia [26]. The small number of patients in our study who were admitted to receive palliative care could be a reflection of good outpatient palliative care but large percentage of patients for whom cancer therapy was provided in the last three months before death is a point for concern. Patients who died in our Department suffered from classical symptoms of end stage cancer disease (pain, immobility, anemia, fever, nutritional deficiency) and therefore we are not sure that it was reasonable to provide active antitumor therapy to them [23]. Despite the lack of sufficient data regarding the use of chemotherapy in elderly patients (70-75 years of age) we planned to administered it in our group of patients where 75% were elderly [23].

Seem that in clinical practice we are still guided by the principles of treatment 'to the end' in this way prolonging patient's agony and suffering. There is no (or is very small) benefit but anticipatory death is more common [27]. Oncologist's duty is not only prolonging OS and maintain QoL of patients but must be capable to estimate when a patient is near the "end stage of the disease" and must stop to conduct useless active antitumor treatments replacing it with best supportive care with purpose of preserveing QoL for the patient and the family [28,29].

Informed patients prefer to die at home rather than in hospital if we can provide to them good palliative care. Family members play a huge role in decisions making process to withhold active treatment sometimes with disagreements with the oncologists. Patients and their families often believe that any treatment at the end-stage disease is better than receiving none and simply "waiting for death". Many times, chemotherapy is misusing as source for giving the false hope. We need better, open and honest conversation about EOL issues between doctors, patients and families. Although hospice referral and discussions about end-of-life care have become recognized as critical needs for patients with cancer, from the study data we can notice that large proportion of patients and families are not clearly meet with patient's condition! Our intention has to be reducing mental and physical suffering of the patient, and the family to a minimum possible [30]. We have to be able to resist to any pressure for implementation of procedures which can lead our patient to dysthanasia [31].

The public opinion (but also and scientific ones!) is that

oncologist's have to provide both culturally and religiously sensitive communication with patients and their families that provides an explanation of practices for withdrawal of life support. In general, we can say that this is not always possible. Oncologist cannot be a psychologist, psychiatrist and religious practitioner in one person, always able to adequately fulfill requirements of patient and family/caregivers. Because the expectations of oncologists are too high, as rebound phenomena we have significant proportion of uninformed patients/families about procedures in EOL (with 39%-62% of patients in EOL nobody was discussed possibility of death!). Although we are conscious that death is inevitably for each of us, the public opinion is still avoiding to talk about death and preparation for death. Therefore, no education about death and dying is either not included in the medical school curriculums. Death and dying in modern medicine and in modern world full of advanced technology is more than ever crucial topic for philosophical, theological, legal, sociological, bioethical and other debates in society [32,33]. Seems that medicine here has no last word in this field.

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