

Critical Evaluation of Emergency Department Management in Oncology Patients with Chemotherapy- Induced Complications

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ABSTRACT

Admission to the emergency department can be uncomfortable for patients with advanced cancer. There is limited research on the clinical characteristics of these patients and the amount of psychological and physical problems of patients after admission to the emergency department (ED). Efforts to improve patient-caregiver communication and increase patient support are crucial to save time in ED. Triage in the emergency department plays an important pivotal role in the quality and delivery of medical services because the number of cancer patients referred to ED is unpredictable and it is generally very difficult for them to wait. Therefore, more efforts are needed to reduce the waiting time of cancer patients due to their condition. There is a need to increase cooperation between emergency room, emergency nurses, and the primary oncology team for improving patient care. In general, the existence of oncology emergency and dedicated hospitalization is an essential service for people with cancer. Trained nurses can make a great help in identifying and providing specific services to these patients by diagnosing and treating them and providing appropriate care in the first minutes of the patients' admission.

KEYWORDS

Neoplasm, Triage, Emergencies, Oncology Service, Hospital, Drug Therapy Toxicity.

Introduction

The first attempt to use chemotherapy in oncology was in 1942 using nitrogen mustard in malignant lymphoma [1]. Since then, many efforts have been made to improve chemotherapy agents, analyze their effect. Currently, anti-cancer drugs are available in cytostatic or cytotoxic forms. Cytostatic drugs focus on preventing tumor cell proliferation; on the other hand, cytotoxic drugs focus on cell destruction, but these drugs have various side effects [2]. Neoplasms are still one of the top 10 causes of death on the World Health Organization list and a major public health problem worldwide. The National Cancer Institute estimates that 14.5 million people in the United States have cancer, and this number could rise to 19 million by 2024 [3]. Currently, prostate, colorectal, and skin melanoma are the three most common cancers in men, while breast, uterine, and colorectal cancers are the most common in women. Approximately two-thirds (64%) of survivors have 65 years of age or older, while only 1 in 10 is younger than 50 years [3, 4]. Five percent of patients with solid tumors and up to 15 percent of patients with hematologic malignancies need to be admitted to the intensive care unit (ICU), due to acute medical complications in the early stages of their disease[5, 6].

With the increase of the elderly population, the number of patients with malignancies is increased. This has led to a great number of referrals to the emergency department, which are mostly due to the local effects of tumors and metastases, paraneoplastic syndromes, or treatment complications[7]. In many patients, the cancer is not diagnosed until the disease is in advanced stages. Usually, the different clinical symptoms of cancer are not an emergency. Identifying and treating these conditions is critical for physicians, especially in areas where the hospitalization of cancer patients is not possible. Therefore, a patient-centered approach that includes special education and monitoring of cancer is necessary for the awareness of emergency personnel. Major oncologic emergencies can be classified as metabolic, hematological, structural, or side effects of chemotherapy agents [8-11].

When cancer patients are referred to emergency department (ED) with chemotherapy-induced complications,

identifying the problems soon can be effective in providing better health services. For this purpose, the patient should be identified and treated in a short time to reduce the complications and mortality due to the disease. Unfortunately, patients with oncological emergencies must wait too long, even if they suffer from difficult conditions. However, EDs are designed for care of clinical emergency and health problems. For example, many people with acute health problems should be evaluated and treated to achieve this goal, various triage systems have been introduced around the world to ensure that patients' health status is properly identified for providing timely care and treatment [12, 13].

Presently, emergency triage is a very important issue and has been considered in Iranian hospitals. However, little attention has been paid to oncologic emergencies especially in Iran. Therefore, conducting studies on the management of oncology patients with chemotherapy-induced complications in ED can improve the knowledge and performance of health care workers.

Materials and Methods

The present study investigated the important clinical characteristics of patients treated with chemotherapy who are referred to the emergency department. In order to study the patterns of care and quality of care, studies conducted in this regard during the last 20 years were reviewed. Databases of Nature, PubMed, Medline WHO, NCBI, PsycINFO, and other important databases were used to access the articles. This study was conducted in December 2020. To gather information in the field of oncology and emergency management, keywords such as cancer, cancer and emergency, emergency management, instructions and cancer, etc. were searched in the mentioned databases. The research was categorized into the number of people undergoing cancer treatment, emergency in Iran, cancer complications management, the importance of the health care system for cancer patients, care patterns and quality of care, and the best guidelines provided.

Cancer Statistics

In European countries, one out of eight ICU patients has malignant cancer [14]. Many of these patients are encountered with specific cancer complications. Most of them may have drug reactions, infectious complications after immunotherapy or chemotherapy. Sometimes cancer regrowth and spread, impaired organ function, tumor lysis syndrome occurs. Some side effects are not necessarily specific but are more common in cancer patients such as thrombotic microangiopathies, electrolyte imbalance such as hypercalcemia or antidiuretic hormone secretion syndrome, hemorrhagic and thrombotic diathesis. In addition, common ICU problems such as acute respiratory distress syndrome or septic complications require specific diagnostic and therapeutic approaches in cancer patients [6, 14, 15].

Cancer is the major cause of death in Canada and accounts for 30% of the overall mortality rate. The incidence of cancer is also increasing as survival improves due to better life style. However, treatment remains highly limited and causes severe complications, and contributes to the prevalence of cancer-related emergencies [16, 17].

In Iran, neoplasms are the third leading cause of death and disabilities in the population [18]. Smoking and poor diet along with other cancer risk factors such as air pollution, exposure to occupational pollutants, and drug use have increased significantly in urban areas [19, 20]. In many patients, the cancer is not diagnosed until the advanced disease; therefore, a patient-centered approach that includes education, cancer-specific screening, and constant health care provider education is highly recommended [21].

Emergency Conditions and Cancer

Due to better quality of health care, mortality has decreased worldwide significantly. On the other hand, with the increase in the elderly population, the number of patients with malignant diseases also increase. Such patients often have more complications and come to the emergency department. Cancer patients may face distinctive problems; such as local effects of tumors or metastases, paraneoplastic syndromes, or treatment adverse effects. Identifying and treating these conditions is critical for physicians, especially in areas where inpatient oncology services are not available [8].

Sometimes patients are referred to emergency department due to oncologic emergencies such as brain metastasis, spinal cord compression. These conditions need to be diagnosed immediately. Treatment of these emergencies usually requires the treatment of underlying malignancy. Physicians should think about malignancies in the differential diagnosis of persistent symptoms that do not resolve with routine treatment [8].

Any acute event that potentially has a direct or indirect effect on the life of a cancer patient or is related to the treatment of the patient is defined as an oncologic emergency. Despite the significant number of deaths caused by cancer, survival improvements are growing due to advances in cancer treatment. Accordingly, it is predicted that the number of cancer patients who are referred to the emergency department (ED) due to the complications of treatment will increase. In order to simplify the work process, emergencies are divided into four categories: mechanical emergencies, metabolic emergencies, hematological emergencies, and treatment-related emergencies [8, 22].

The ED is one of the most important departments of the general hospitals that provides emergency services to patients, 24 hours a day, seven days a week. Although especial palliative care services are important in the treatment of cancer, most of those seen in palliative care clinics are advanced cancer patients at the end of their lives. In addition, referring to the emergency room in the last few months, weeks, or days of life can cause severe discomfort to cancer patients, families and their caregivers. Despite these concerns, the difficulty of cancer treatment in the elderly population leads to a growing number of ED visits due to complications and comorbidities. This problem is increasing in the United States and Canada. However, studies show that the total number of advanced cancer patients with multiple ED visits in the United States is higher than in Canada [21, 23, 24].

Management of Complications

Some of the patients who are treated with chemotherapy and radiotherapy have weakness, anemia or nausea and vomiting [25]. They can be treated prophylactically with supportive care prescribed by their oncologists. These can prevent unnecessary refer of these patients to ED for example for serum therapy and remaining in ED for hours.

Also, some of adverse effects of chemotherapy can be managed prophylactically. There are several studies working on chemotherapy-induced nausea and vomiting. Some of the studies used anti-emetic drugs while others used music therapy [26]. If these complications can be managed during radiotherapy or chemotherapy, the patients come to ED less.

Also, immunosuppression induced by chemotherapy drugs or immunosuppressive conditions can exacerbate complication such as serious viral or bacterial infections which need immediate management or sometimes need admission [27].

Oncological emergencies can occur at any time during the disease and in some patients can be a primary manifestation. Progression of the underlying disease is the most common cause for ED visits of cancer patients, followed by infection and treatment complications [7, 28].

According to a study by HIGDON et al. in 2006, Oncological emergencies are divided into four categories, which are metabolic, hematological, structural, and treatment-related (Tables 1) [9, 29]. Metabolic emergencies, such as hypercalcemia, acute tumor lysis syndrome, hyponatremia, and lactic acidosis, febrile neutropenia, hyper-viscosity syndrome, and disseminated intravascular coagulation are primarily diagnosed and treated based on clinical features and laboratory findings without the aid of radiological studies. However, structural emergencies, such as those that lead to thrombosis or hemorrhage, invasion or compression of the involved organs, and obstruction require imaging studies to diagnose.

Oncological emergencies include the central nervous system emergencies, cardiopulmonary and uterine emergencies need clinical imaging for accurate diagnosis and optimal patient care. In addition, complications of chemotherapy and radiation therapy can be well detected with the help of standard imaging [28]. Oncologic

emergencies are summarized in table 1.

Table 1.Summary of oncological emergencies (13)

Emergency	Cancer site	Common signs and symptoms	Consulting considerations
Metabolic Tumor lysis syndrome Malignant hypercalcemia Syndrome of inappropriate antidiuretic hormone secretion	Hematologic malignancies, especially acute leukemia and high-grade lymphomas; Multiple myeloma solid tumors; Breast; head and neck, lung, kidney, or cervix, small cell lung cancer	Azotemia, Hyperphosphatemia, Hyperkalemia, Hyperuricemia, Acute Kidney Failure, Hypocalcemia, mild cognitive impairment, Weakness, Anorexia, Thirst, Constipation, Nausea, Vomiting, Decreased Urine Production, Hyponatremia (Coma), Nausea, Vomiting	Oncology, nephrology, surgical care Oncology, endocrinology, nephrology nephrology, palliative care
Hematological Febrile neutropenia Hyperviscosity syndrome	Current chemotherapy Waldenström macroglobulinemia (10-30%), leukemia, multiple myeloma	Underarm or oral temperature $\geq 101.3^{\circ}\text{F}$ (38.5°C) or stable temperature $\geq 100.4^{\circ}\text{F}$ (38°C) for one hour and absolute neutrophil count <500 cells per 3 mm^3 Spontaneous bleeding, dyspnea, neurological defects (peripheral neuropathy), sausage-like retinal bleeding vessels, serum viscosity > 4	Oncology, Infectious Diseases, Palliative Care Hematology, oncology
Structural Superior vena cava syndrome Malignant epidural spinal cord compression Malignant pericardial effusion	Lung cancer, lymphoma, metastatic mediastinal mass or lymph node, static venous catheters (port) Breast cancer, multiple myeloma, lymphoma, lung and prostate cancer Lung, esophageal, and breast cancer. Leukemia lymphoma; Melanoma infection complication therapy; Autoimmune reaction	Swelling of the face, cough, dyspnea at rest, hoarseness, chest and shoulder pain, collateral blood circulation (chest wall) New back pain (worse when lying down), paraplegia (late presentation) Dyspnea, chest pain, or palpitations; pulsus paradoxus; tachycardia, orthopnea, and water-bottle heart	Oncology, heart surgery, palliative care Oncology, Neurosurgery, Palliative Care Oncology, heart surgery, palliative care
Treatment related Chemotherapy (extravasations) Gastrointestinal problems Radiotherapy Immunotherapy	chemotherapy cancer treatment radiation therapy immunotherapy	Pain, erythema, and angioedema, blistering, discoloration, and necrosis of the skin Abdominal pain, nausea, vomiting, diarrhea, constipation, and dehydration; Obstruction; Weight loss, hemorrhage; Dehydration Dermatitis, cardiovascular disease, esophagitis, cystitis, sexual dysfunction, depression Ambiguous symptoms, such as fever and rash	Oncology, dermatology, plastic surgery Oncology, Gastroenterology, General Surgery, Infectious Diseases, Radiology Oncology, Dermatology, Cardiovascular, Gastroenterology, Urology / Gynecology Oncology, a targeted subspecialty

Studies in 2020 show that ED is one of the most important health care centers for people in need of cancer treatment. In ED, patients are classified according to the priority of the triage process, which plays a critical role, since the volume of patients and nurses is not predictable. All ED patients, after assurance of stable conditions for emergency care and treatment, should be triaged and treated according to their disease condition. However, the evaluation and identification of serious cancer patients are problematic because such patients may have no specific symptoms. This can lead to widespread delays in treating these patients and adverse health consequences. Findings from existing studies show that most cancer patients have significant delays in seeking emergency care, even in emergency cases of cancer [12].

Accurate diagnosis and appropriate treatment of oncology patients referred to ED can significantly increase their quality of life and reduce their mortality rate. It was shown in a review study by Masjedi et al. that with the increase in tumor rates, cancer has become one of the most important health concerns in Iran [30].

The Importance of the Health Care System for Cancer Patients

Although cancer is a chronic disease, patients generally refer to ED because of treatment complications or acute condition of the disease. There are several common problems which are due to the radiotherapy such as mucositis with the incidence about 40 percent in cases with head and neck cancers [31]. The frequency of ED use among cancer patients is calculated by considering the number of patients undergoing chemotherapy or radiotherapy. Despite the number of visits, cancer patients constitute a small number of the total number of emergency room visitors. In a study on the characteristics of ED visits by cancer patients, the number of visits by cancer patients was between 2 and 6 percent of the total ED visits. This small percentage of patients is likely to pose a challenge to triage nurses [12, 32].

Studies show that there are many factors that complicate oncological emergencies and make triage a challenge. For example, older cases have comorbidities. Therefore, this makes triage and, consequently, the treatment of the patient more difficult. It has also been found that among cancer patients, cases that are in the acute phase of the disease are much more likely to refer to ED. A study in Canada found that people with cancer had the highest number of ED visits in the last six months of life; while in the last two weeks of their lives, this rate reaches 83% [24].

Gorham et al. reported that patients with advanced and metastatic cancer accounted for 95% of all ED referrals of cancer patients. Therefore, the importance of triage and the availability of adequate medical supplies and drugs should be greatly considered, otherwise some cancer patients who need palliative care or hospital admission may not be identified [33, 34].

In another study by Patel et al., the results of telephone triage services to help people with cancer showed that 62% of those who had a telephone call could manage their symptoms. Also, due to the fact that cancer patients usually require further emergency care such as radiological imaging, invasive procedures, and medication, there are many oncological complaints in ED. In this regard, another study showed that more than two-thirds of patients referred to ED with oncological complaints [35, 36].

Care Patterns and Quality of Care

A high percentage of people with cancer are hospitalized several times, indicating the need for more care. Results from the Canadian Institute of Health Information (CIHI) showed that oncology complications are one of the top five causes of re-admission [33]. A study of patients with head and neck cancer reported that 22% of patients were re-admitted to the hospital two times [37]. Studies also show that cancer patients stay longer in hospitals and ED which may vary between 5 hours to 9 days. Also, about 53% of cancer patients are readmitted for more than a week; Therefore, having an appropriate pattern and quality of care is very important [38].

Since most patients refer to ED have serious complications, the quality of services can be a symbol of the general state of the hospital [39, 40].

Studies in Iran have shown that one of the problems of patients referred to the emergency department is

overcrowding in ED[41]. Appropriate measures need to be taken to prevent and resolve the congestion problem. The triage of all patients referred to ED should be managed carefully specially the cases with trauma considering the capacity of ED in each hospital. Some of the patients come to ED by themselves like cancer cases; Therefore emergency staff should have guidelines to manage ED well[39, 42, 43].

Strategies Suggestions

There is limited studies on the clinical characteristics of advanced cancer patients being treated in palliative setting who are referred to ED, and whether these visits can be avoided. In a study using administrative data from the Ontario Cancer Registry, showed that 2.8% of ED visits in cancer patients who were in the last six months of their life could be avoided. Although the exact reasons of refer in each of these cases were not well known in this study[44]. In another study by Wallace et al. analyzed 35 ED visits in 30 advanced cancer patients at Limerick Mid-Western Regional Hospital and reported that 52% of these visits were potentially preventable [45].

At M.D. Anderson Outpatient Palliative Care Clinic, patients are administered by an interdisciplinary palliative care team (PCT) consisting of palliative care specialists, physicians, palliative care nurses, social workers, clergy, psychologists, and pharmacists [46].

The Canadian Triage and Acuity Scale (CTAS) guidelines are used to standardize triage decisions in Canada. Upon entering the ED ward, the triage nurse divides the patient's health condition into one of five categories using CTAS guidelines. These categories indicate the patient's urgency level, which indicates the state of health. The categories are determined by waiting time so that the patient can calmly wait before the medical intervention[47, 48]. The five categories of CTAS are:

1. Resuscitation (immediate rescue treatment by both nurse and physician)
2. Emergency (maximum 15 minutes to see a physical therapist)
3. Urgent (between 15 and 30 minutes)
4. Less immediate (60 minutes)
5. Non-immediate (more than 120 minutes)

Following the standards of developed countries can be effective in better classifying cancer patients for treatment. Numerous interventions have been proposed to reduce the time of taking antibiotics (TTA) in patients with fever and neutropenia (FN) after chemotherapy. Other useful strategy to improve the diagnosis of cancer emergencies is the use of fever alert cards (FAC). Kapil et al. evaluated FACs as a tool to reduce TTA in patients with FN who referred to ED. Implementation of FACs helps improve FN diagnosis in a higher percentage of patients who receive a correct CTAS score [49].

Such strategies can be combined with clinical protocols and rapid pathways in patients with specific conditions. For example, the fever neutralization pathway (FNP) was performed in an ED, and an almost 66% reduction in antibiotic use was reported, which can be a major success for cancer patients' triage. However, similar strategies cannot be devised to improve early diagnosis or treatment of other cancer emergencies in ED. It is best for oncology emergencies to follow CTAS guidelines for monitoring the triage of cancer patients and to determine their sources, accordingly [50, 51].

Conclusion

The existence of an oncology emergency room and dedicated hospitalization of cancer patients is an essential service and these patients require faster triage compared to other patients. Also, they experience a high rate of hospital admissions and an increased risk of death. Trained nurses can greatly help in this issue by timely diagnosis and treatment of these patients and providing appropriate care in the first minutes of the patient's visit. However, most cancer patients experience significant delays when referring to the emergency department, and even in oncological emergencies. Many of these emergencies are time-sensitive and require prompt treatment. All studies provide background and opportunities for improvement in the management of this population. It is very important to check the symptoms of the patients who referred to the emergency department including fever, nausea, headache, and

weakness. Patients' awareness can also be effective in preventing oncology complications and improving the quality of care so that their awareness of chemotherapy symptoms such as nausea, vomiting, constipation, anorexia can be helpful in emergencies. Patients aware of the predictable side effects of chemotherapy can use anti emetics or analgesics as needed to reduce complications before going to the emergency room.

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