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Review / Derleme

Changes in medical oncology practice due to the COVID-19 pandemic in Turkey, and the risk of neglect of cancer patients

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Abstract

Cancer patients are among patient groups most affected by the COVID-19 outbreak. During the COVID-19 pandemic, rearrangement of oncological services and adaptation to the pandemic process has become mandatory. In this review, we mentioned the changes in medical oncology practice and adaptive treatment modifications. COVID-19 infection will continue to affect and change the practice of oncology unless the COVID-19 outbreak ends.

Keywords: COVID-19 pandemia,oncology,cancer patients

Türkiyede COVID-19 pandemisine bağlı medikal onkoloji pratiğindeki değişiklikler ve kanser hastalarının ihmal edilme riski

Öz

Kanser hastaları COVID-19 pandemi sürecinden en çok etkilenen hasta grupları arasında yer almaktadır. COVID-19 salgın sürecinde onkolojik hizmetlerin yeniden düzenlenmesi ve pandemi sürecine adapte olması zorunlu hale gelmiştir.Biz bu derlemede Turkiye'de medikal onkoloji pratiğindeki değişikliklerden ve adaptif tedavi modifikasyonlarından bahsettik. COVID-19 salgını sürdükçe COVID-19 enfeksiyonu onkoloji pratiğimizi etkilemeye ve değiştirmeye devam edecektir.

Anahtar kelimeler: COVID-19 pandemisi,onkoloji,kanser hastaları.

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INTRODUCTION

Cancer patients have been identified as being at high-risk during the COVID-19 pandemic, as is the case for patients with other chronic diseases[1-3]. The greater risk to cancer patients from COVID-19 is associated with such factors as hypertension, diabetes, and cardiac and pulmonary diseases. SARS-CoV2 (severe acute respiratory syndrome-coronavirus 2) is associated with far worse outcomes in cancer patients than in those without cancer due to advanced age, frailty, comorbidity and treatment-related immunosuppression[3]. This patient group is at further risk of COVID-19 infection due to the treatment applications and frequent hospital visits associated with their disease[4].

Upon the declaration of first case of COVID-19 in Turkey on March 10, 2020, the entire healthcare system entered into the fight against COVID-19, as was the case in many countries around the world, with most healthcare service providers reorganized to treat COVID-19 patients[5]. Turkey is among the countries that dynamically managed this process, and that succeeded in implementing the necessary precautions on time and in an appropriate manner. Cancer patients are among those most affected by the COVID-19 outbreak. Many non-urgent surgical procedures were postponed, the routine follow-up of patients with cancer in remission were postponed and cancer screenings were suspended during this period. Oncology services, intensive care units, ventilators, blood products, healthcare personnel and certain medical resources (medications, medical materials) were reassigned to COVID-19 patients during the pandemic, leaving oncology patients with difficulties in accessing the necessary resources. Certain services were suspended to relieve the burden on the healthcare system[6]. The reduced access to healthcare resources, the limited access to healthcare services and the difficulties faced in planning treatment strategies for cancer patients are thought have resulted in negative outcomes not just in the short term, but also in the medium and the long terms. International surveys conducted in large-scale cancer centers have reported that the COVID-19 pandemic has affected the way medical oncologists and surgical oncologists approach the management of cancer and cancer patients[7].

Changes in medical oncology practice in Turkey

Taking into account the extent of the outbreak in Turkey and our own experiences, important changes have been made in the routine practices of oncology units in Turkey to counter this unexpected situation. There has been a prominent decrease in the number of admissions to emergency departments and to outpatient clinics by follow-up patients during the first three months of the pandemic. Many patients can apply to hospitals only after being granted special permission, as a result of the limitations placed on interprovincial travel and curfews. The bed capacity of oncology units has been reduced, having been reassigned in many hospitals for the use of COVID-19 patients. Additionally, the fear of becoming infected with COVID-19 has contributed to decreased rates of admission to oncology units among all cancer patients. A study by Karaçin et al. reported that COVID-19-related anxiety and fear has increased the rate of chemotherapy treatment postponements, while telemedicine has contributed to a decrease in the rates of chemotherapy[8,9].

Like all countries around the world engaged in the fight against the coronavirus pandemic, the Ministry of Health of the Republic of Turkey has made various arrangements to ensure the minimum impact on the provision of oncological healthcare services. It has been ensured that teams providing services to oncology patients are kept separate from, and do not work in, COVID-19 services and

outpatient clinics, and that the oncology departments maintain their existing work system, if only at a minimum. Outpatient clinic visits are restricted except in the event of urgent oncological situations and ongoing active treatments. Outpatient clinic visit have been postponed, unless patients on follow-up develop complaints or symptoms of recurrence. The Ministry of Health of the Republic of Turkey has published general instructions informing all physicians to cease surgeries other than urgent interventions and those for cancer, aiming to minimize the risk of infection, to shorten hospital stays and to free up hospital beds for the use of patients with COVID-19. Some health facilities have been assigned as pandemic hospitals, where cancer surgeries have continued, but at a reduced level. Aerosol-associated procedures (endoscopy, endoscopic ultrasonography, bronchoscopy) and diagnostic biopsies have been suspended, with eligible patients referred to computed tomography-guided biopsies where possible. There has also been a decrease in the interventional procedures that form part of oncological care due to the increased workload of the radiology clinics resulting from the COVID-19 pandemic. COVID-19 patients have been given priority access to palliative care services during this period, leaving oncology patients with insufficient access to such services.

In addition to the delays in cancer treatment, disruptions have been experienced in the use of cancer screening methods such as mammography, cervical smear and colonoscopy. Clinical research studies into cancer have also been negatively affected by the COVID-19 pandemic in Turkey, to a significant degree. Studies in the future will be able to quantify the extent of the damage caused by the pandemic. Güven et al. analyzed the functions of outpatient clinics, clinics and palliative care services, as well as interventional procedures, within the first month of the COVID-19 outbreak in Turkey, and made a detailed comparison of their findings with data from the same period over in the previous three years. No prominent decrease was noted in the number of inpatients making use of such services when compared to the previous three years, while a prominent reduction was observed in the mean length of hospital stay and new oncology admissions. An approximately 30% reduction was observed, especially in breast and gastrointestinal cancers, although the decrease in the number of cancer screening tests performed are believed to be a factor affecting this outcome[10].

Delays and problems related to screening, diagnosis, and therapeutic and surgical approaches pose a serious risk to cancer patients in particular. Although there is general consensus on this matter, unfortunately there is still a shortfall of scientific evidence and experience indicating how to properly conduct patient management and apply solution-oriented strategies. National and international organizations (ESMO, ASCO and NCCN) have published guidelines for the diagnosis, follow-up and treatment management of cancer patients during the COVID-19 pandemic, as well as measures to counter the COVID-19 pandemic and implementation methods[11-14]. Due to the lack of scientific evidence and experience, health institutions are being advised to act in accordance with the recommendations of national guidelines and internationally recognized cancer institutions[15].

In Turkey, some of the restrictions that were introduced in the early days of the pandemic started to be removed gradually on May 11, 2020 as part of a gradual normalization process, and this expanded to oncology clinics, with a workload increase in outpatient clinics and other services, resulting in a transition to the former working order. The effect of the normalization process on oncology patients and on the provision of oncological care will become clearer in time.

Adaptive Treatment Modifications

During the COVID-19 pandemic, many hospitals need to rearrange the oncological services they provide to adapt to the pandemic. Our goal is to ensure that both our patients and our healthcare workers are protected from COVID-19, and to manage diagnoses, therapies and follow-up processes in such a way that they are least affected by the outbreak. The factors affecting treatment modifications have included disease prognosis and stage, the expected benefit from treatment and toxicity risk, the patient's choice, age, performance status and the presence of comorbidities, as well as the capacity, resources and accessibility of the hospital[16].

In the light of the current guidelines, cancer patients have been categorized into cases undergoing treatment (adjuvant, neoadjuvant and palliative), new cases, cases receiving palliative care and those not receiving treatment (those whose treatments have been completed or discontinued after the disease has been brought under control), and recommendations have been established for each clinical picture. Many modifications have been made to the treatment and follow-up procedures of patients in this period, in line with the guidelines. Certain changes have also been made to strategies in the treatment planning stage for cancer patients actively undergoing treatment, and those who have been newly diagnosed. Priority has been given to treatment regimens that require the minimum of hospital visits, that can be administered appropriately in a short time, and that have the minimum immunosuppressive effect among the available treatment options. Alternative dose schemes have been applied in systemic therapies, with the aim being to reduce the number of hospital visits required. In cases where the expected contribution of adjuvant chemotherapy is low, immunosuppressive therapies that can increase the risk of infection have been avoided. Palliative therapies have been postponed to the maximum possible extent. For patients with difficulties in accessing the hospital, oral applications have been preferred over infusion therapies, where possible. Additionally, it has been ensured that patients prescribed with oral medications continue their treatment without the need to visit the hospital through the provision of a minimum three-month supply of medication by the Ministry without prescription, thus reducing the frequency of outpatient follow-ups to the lowest level at which the health of the patient is not jeopardized. Several oncology clinics have implemented such practices as reducing the frequency of or discontinuing certain maintenance treatments. GCSF therapies have been increased to avoid febrile neutropenia and immunosuppression, which require hospitalization, for patients with an ongoing risk of neutropenia. Certain treatments, such as subcutaneous or intramuscular procedures, and GnRH analogues have been administered in the home care nurses. Oral forms of intravenous bisphosphonate have been preferred, or while zoledronic acid is being administered once every 12 weeks, rather than once every four weeks.

The interactions of immune checkpoint inhibitors and COVID-19 infection are not exactly known[17]. The TERAVOLT study, presented at ASCO 2020, reported the treatment of cancer patients with chemotherapy to be a risk factor for mortality associated with COVID-19 infection, while treatment with tyrosine kinase inhibitors and immunotherapy were not risk factors.18 During the pandemic, our oncology centers have made arrangements to reduce clinic visits for immunotherapies, as is the case with chemotherapy regimens. Nivolumab has been administered once every 4 weeks rather than every 2 weeks; pembrolizumab has been administered once every 6 weeks rather than

every 3 weeks, and atezolizumab has been administered once every 4 weeks rather than every 3 three weeks. For radiotherapy programs, hypofractionated programs have been preferred where appropriate.

Alternative strategies, such as neoadjuvant therapies, are prioritized so as to minimize the perioperative and intraoperative risk of COVID-19 and to postpone surgery for a while, in line with international guidelines. Most oncology clinics in Turkey prefer neoadjuvant therapies for several cancer types, where possible, although medical oncologists have some reservations in this regard, including the increased risk of developing metastasis, overtreatment and potential toxicities due to neoadjuvant chemotherapy within this period. There is a need for new treatment approaches and strategies that are suited to the normalization period at this time, as the current situation may prevail for several months, or even years.

Patients undergoing cancer treatments have the potential to be susceptible to infections through hospital admission, as well as treatment toxicity, while other risk factors become an issue for newly diagnosed cases.The main problems faced by these patients are the delays in diagnosis and treatment. The early diagnosis and initiation of treatment are of vital importance for patients who can be cured (such as lymphoma and germ cell histology), especially those with early stage disease. For new cancer cases, treatment plans and decisions to initiate treatment are made considering the urgency of the situation and the benefit-harm balance.For cases in the advanced stage, the benefit and goal of the treatment should be assessed and discussed based on a multidisciplinary approach, and considering the risk of COVID-19 transmission.

Significant changes have been made also in the provision of clinical services in the hospital so as to provide the best and safest possible cancer care. A large number of measures have been taken to ensure isolation and hygiene. The number of doctors attending patient visits has been decreased. Patients admitted to the hospital, especially those with symptoms related to the respiratory tract, are assessed for COVID-19, and are accepted for treatment and tests in the oncology clinic only after COVID-19 has been ruled out. Suspected cases are admitted to the department depending on the result of their COVID-19 test. Isolation rooms have been established for patients with suspected COVID-19. Patients testing positive for COVID-19 are transferred to COVID-19 departments or intensive care units. Hospitalization priority is given to those whose conditions demand it (severe anemia, thrombocytopenia, febrile neutropenia, grade 3-4 mucositis) and to patients with oncological urgency (e.g. hypercalcemia, spinal cord compression, increased intracranial pressure). The length of stay has been kept as short as possible, again considering the recommendations laid out in the guidelines. Patients requiring palliative care are advised to utilize home care services if possible, and are ensured to receive home care.

Healthcare through telemedicine approaches (telephone, e-mail or videoconference) have gained a place in our daily practice in this period as a means of reducing the admission of patients with cancer in remission or with no symptoms, and those receiving oral cancer medications, to the pandemic hospitals. Telemedicine offers important advantages, in particular to immunosuppressive cancer patients, in preventing COVID-19 infections. Specifically, doctors working in private hospitals are making more intensive use of telemedicine approaches for the evaluation of treatment-related side effects and the discussion of laboratory tests with the patients. Recent guidelines have recommended that routine follow-up visits should be postponed, and that telemedicine

approaches should be used for patients in remission during this period[11-14]. Telemedicine has certain limitations. Given the conditions in our country, some patients may have difficulty in adapting to telemedicine in regions with a low socioeconomic status. Telemedicine reduces the risk of COVID-19 infection, but may lead to a sign of recurrence being missed that would have been identified in a physical examination or routine imaging.

As many cancer centers have restricted elective procedures and surgeries, multidisciplinary councils are today convening over the Internet for the planning of the optimal treatment of patients during this period. Many scientific activities, including research and training, have been moved online, and continue to be carried out in a virtual environment. Training services have been re-organized in this period. The Turkish Society of Medical Oncology and several cancer associations in Turkey have contributed to the training of oncologists by providing up-to-date information on approaches to the treatment and management of cancer patients during the pandemic through regular and irregular online meetings[14]. National and international guidelines for medical oncology clinics, and regularly updated websites containing treatment algorithms for COVID-19 and cancer, have become a valuable resource for oncologists, and have on the whole been welcomed[11-14].

Risk of neglect of cancer patients

Attempts have been made to maintain the diagnosis, treatment and follow-up of cancer patients in Turkey with the minimum of disruption during the COVID-19 pandemic, which has had an adverse effect on the healthcare systems, economies and social lives of all countries. Despite best efforts, cancer patients have been limited in their access to diagnostic/therapeutic services as a result of the COVID-19 pandemic due to the threat of infection and the problems experienced by healthcare systems as a result of the pandemic. Problems arising from delayed diagnoses and treatments may lead to even more severe outcomes than those related to COVID-19, with increased mortality and morbidity in the future. An increase in the number of cases detected at a more advanced stage and who will consequently require additional oncological treatment due to delays in diagnosis, surgery and examination, is inevitable[19].

The COVID-19 pandemic has increased the workload of hospitals, and healthcare systems are proving to be incapable of supporting this additional load. It has been found that cancer patients who contract COVID-19 are unable to benefit from the same level of emergency healthcare and intensive care services as those without cancer within this period[20].In order to avoid suffering in healthcare services, every patient should be assessed individually, and a joint decision should be made with the patient's oncologist on such issues as intensive care unit admission and ventilator applications.

We, as oncologists, must decide upon the most appropriate treatment for our cancer patients at risk of COVID-19 infection, as well as those at high risk of a severe course and mortality in the case of infection, by closely following the pandemic in our country; by not compromising on the treatment standards, to the greatest extent possible under the current conditions; and by considering the risk of infection and the potential contribution of treatment. Treatment decisions should consider the patient's city of residence, the need for hospital of admission and follow-up, and the patient's environmental conditions. The positive or negative outcomes of this major change in the fight against cancer and the modifications made within this period will be clarified by retrospective studies conducted in the future, and may have a profound effect on our daily practice in oncology.

In conclusion, COVID-19 infection will continue to affect and change the practice of oncology unless the COVID-19 outbreak ends. Cancer will develop into a far greater problem in the upcoming days unless the necessary changes are made.

Summary Points

- SARS-CoV2 (severe acute respiratory syndrome-coronavirus-2) infection is associated with poorer outcomes in cancer patients than in those without cancer, due to associated advanced age, frailty, comorbidities (hypertension, diabetes, cardiac and pulmonary diseases, etc.), malnutrition and treatment-related immunosuppression, and there is a further risk of COVID-19 infection due to the associated therapeutic applications and frequent hospital visits.
- Important changes have occurred in the routine practices of oncology units in Turkey.
- Attempts have been made to maintain the diagnosis, treatment and follow-up of cancer patients in Turkey during the COVID-19 pandemic in accordance with the recommended guidelines (ESMO, ASCO and NCCN)

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