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Changes in management of patients with cancer during COVID-19 pandemic

Katarzyna Kosz, Natalia Zarankiewicz, Martyna Zielińska, Aleksandra Kuchnicka

1. Katarzyna Kosz

ORCID iD: <https://orcid.org/0000-0001-6848-0598>

Affiliation: Student Scientific Group of Oncological Surgery, Radziwiłłowska 13 (SPSK Nr 1) 20-080 Lublin Medical University of Lublin

2. Natalia Zarankiewicz

ORCID iD: <https://orcid.org/0000-0001-9203-3376>

Affiliation: Student Scientific Group of Oncological Surgery, Radziwiłłowska 13 (SPSK Nr 1) 20-080 Lublin Medical University of Lublin

3. Aleksandra Kuchnicka

ORCID iD: <https://orcid.org/0000-0001-8481-7592>

Affiliation: Student Scientific Group of Oncological Surgery, Radziwiłłowska 13 (SPSK Nr 1) 20-080 Lublin Medical University of Lublin

4. Martyna Zielińska

ORCID iD: <https://orcid.org/0000-0001-8886-8274>

Affiliation: Student Scientific Group of Oncological Surgery, Radziwiłłowska 13
(SPSK Nr 1) 20-080 Lublin Medical University of Lublin

ABSTRACT

Introduction: As of March 11, 2020, COVID-19 has been declared as a global pandemic. It has spread rapidly and profoundly impact the function of health care system all around the world. As a result, management and organisation of oncology units had to be altered in order to provide security measures and safe care for patients.

Purpose: The aim of this paper is to review current knowledge involving management of patients with malignancies during COVID-19 pandemic. Particular attention has been paid to changes in diagnosis, treatment and follow-up of patients with cancer.

Material and methods: The review includes publications released in 2019 and 2020. The data has been collected by the use of PubMed, WHO website and other online published guidance.

Results: As a lot of clinical trials has been suspended, current therapy options for patients with cancer has been also limited. Moreover, patients became fearful of becoming infected by SARS-CoV-2 and accordingly they were less likely to attend screening programmes. Additionally, as the amount of surgeries has been reduced, the need for radiotherapy service has increased. Chemotherapy has been found to be risky for patients with cancer as it may favour them to SARS-CoV-2 infection.

Conclusions: Appropriate security measures need to be implemented in order to protect against SARS-CoV-2 infection but optimal health care access should be provided as well. There is a high necessity to share knowledge and experience on the impact of pandemic on patients with malignancies. However, a lot of patients are fearful of COVID-19, adverse effects of delayed diagnosis, treatment and follow-up should not be diminished.

Key words: cancer; covid-19; malignancy

INTRODUCTION AND PURPOSE

In December 2019, the novel Coronavirus Disease (COVID-19) was first found in Wuhan, China. It has spread rapidly to other Chinese provinces and further all around the world [1]. On March 11, 2020, WHO declared COVID-19 as a global pandemic. Until then, it spread in 114 countries, where as of today 28 202 363 cases and 910 140 deaths has been confirmed [2,3]. However, coronaviruses have been known since 1960, giving rise to concern in recent years. From 2002 to 2003, severe acute respiratory syndrome coronavirus (SARS-CoV) infected 8,000 people and its mortality rate reached approximately 10% [4]. A decade later, Middle Eastern respiratory syndrome coronavirus (MERS-CoV) infected 1,700 people and reached a mortality rate of 36% [4]. Nowadays, the world struggles with COVID-19 pandemic caused by another *Coronavirus* designated as SARS-CoV-2 [5].

Initial analyses from China showed that hypertension, diabetes, cardiovascular disease and malignancy were the most common coexisting conditions among patients with COVID-19 [6]. Cancer patients, specifically, are usually immunosuppressed, undernourished and suffering from various side-effects of their treatment [7]. They are more liable to COVID-19 development than those without cancer history and are at the higher risk of severe COVID-19 course and might have a poorer prognosis [8,9]. COVID-19 pandemic affects not only the medical units directly involved in treating patients with COVID-19 but the entire health care system, including its management and organisation.

The aim of this paper was to review and summarize current literature related to management of patients with cancer during COVID-19 pandemic. Particular attention was paid to changes in diagnosis, treatment and follow-up of cancer patients.

Diagnosis

Cancer Research UK note that COVID-19 pandemic has a negative impact on diagnostic procedures in oncology [10]. Many countries have suspended cancer screening programmes for bowel, cervical and breast cancer. Such a decision has been taken inter alia in Wales, Scotland or Northern Ireland [11,12,13]. In the USA screening programmes were advised to be postponed as a low-priority service [14]. Moreover, endoscopies have been classified as procedures increasing the risk of transmission of SARS-CoV-2 [15]. Recommendations from the European Society of Gastrointestinal Endoscopy, the American College of Gastroenterology and the Asian Pacific Society for Digestive Endoscopy suggest that elective endoscopies should be postponed [16]. On the contrary, as the number of endoscopic procedures has decreased, the market for non-invasive procedures has grown. Another concern causing the increased number of delayed diagnosis of malignancies is the patients' fear of SARS-CoV-2 exposure and infection. For that reason, the number of referrals to oncological departments has decreased [17]. According to Cancer Research UK, these factors may result in around 2.000 less cancer diagnoses each week [18]. Such a decrease has been already found in the number of thyroid biopsies, which were performed relevantly less often during COVID-19 pandemic in comparison to former years [19]. It is crucial to emphasize that as in many countries COVID-19 peak is passed, all implemented limitations should be reconsidered. [17].

Treatment

To minimize the risk for COVID-19 exposure, the treatment pathways for oncological patients had to be altered. Authors have suggested that cancer-care facilities should be located separately from acute-care hospitals or at least with dedicated access and admissions processes for patients in mixed-care hospitals [20,21]. Only patients after self-isolation and with no symptoms of COVID-19 should be admitted to the hospitals [22]. There are many difficulties in terms of surgeries, radiotherapy and systemic treatment in the times of COVID-19 [20]. First of all, amount of surgeries has been limited as Intensive Care Units has been occupied by patients with COVID-19 and as a result the role of radiotherapy has expanded [20]. Nevertheless, radiotherapy is allowed and recommended to continue, there is still a rising demand on this procedure and according to that, it has been advised to rationed radiotherapy courses [20]. Finally, there is a lot of uncertainty in terms of chemotherapy,

which can possibly expose patients with cancer to infection and worsen COVID-19 course [20].

As there is a rising necessity to provide safe theater space and ventilators for patients with COVID-19, the other surgeries had to be postponed or reduced. In order to ration surgeries, countries developed schedules depending on several stages of pandemic [22,23,24]. The American College of Surgeons have decided that at the peak of the pandemic only emergency operations should be performed (e.g. perforated, bleeding cancers) [22]. According to the National Health System in England, hospitals should only admit patients who will require surgery within the next 24–72hours [23]. In order to minimize the risk of infection, low-risk cancers should be treated with minimally invasive surgical procedures, while open surgeries should be replaced with transoral procedures [25]. Particular precautions should be taken among patients with tracheostomy or total laryngectomy, who are at the high risk of virus aerosolization [25].

Yu et al. suggested that colorectal cancer (CRC) patients should undergo laparoscopy-assisted radical surgery [26]. They advise Natural Orifice Specimen Extraction (NOSE) and Transanal Total Mesorectal Excision (taTME) to be performed with caution, as well as they recommend to strengthen protection of operating room personnel [26]. Di Saverio et al. advise that COVID-19 positive patients with CRC need to be treated with conservative approach and that high priority cases, which include only surgical emergencies, should be performed within 2 weeks [27].

Studies addressing influence of COVID-19 on lung and thoracic malignancies management presented a high discordance in the recommendations. The standard of treatment should be maintained but also adjusted to the rising trend of COVID-19 [28]. The opposite view has been presented by Rathod et al. And Wu et al. who do not recommend surgery in case of early lung cancers and instead advise to use stereotactic body radiotherapy [29,30].

In reference to gastric cancer (GC), it is advised to delay surgical treatment for benign tumors. Patients at low operative risk may be offered a partial gastrectomy, while for invasive GC, non-surgical anti-tumor therapies are recommended. It is also advised that GC stage \geq T2 should be managed with neoadjuvant therapy and those with obstruction can be treated with stent placement or gastric tube decompression [31].

In breast cancer, radiotherapy should be delayed or omitted, as suggested by experts from the Memorial Sloan Kettering Cancer Center in New York [25]. They suggest abandoning the radiation treatment in the case of ductal carcinoma in situ, among women aged 70 or more, invasive estrogen-receptor positive cancer, tumour smaller than 3 cm, without nodal metastasis and with negative resection margins. On the other hand, the diagnosis of inflammatory breast or triple negative node-positive disease and the presence of node-positive (N2) disease are high priority indications for breast radiotherapy [25].

Implications for systemic treatment are a topic of difficult conversations between patients and healthcare professionals. Chemotherapy is considered to be a dangerous method which may expose patients for COVID-19 [20]. That is why European Society for Medical Oncology and American Society of Clinical Oncology recommend performing chemotherapy cycles in the case of predicted significant improvements in outcomes. Acute hematological malignancies, testicular, ovarian, and small cell lung cancers are included in this group. When the benefits of performing chemotherapy are not that certain, treatment should be delayed, for example during palliative care [20,31]. These decisions seem to be reasonable as previous reports showed that patients who underwent chemotherapy in the past 4 weeks had significantly higher risk of severe COVID-19 course in comparison to those who did not. Moreover, receiving chemotherapy within 4 weeks has been found as an independent risk factor for COVID-19 mortality. Possibly, it is because of an already impaired immune system of the host and further SARS-CoV-2 worsening this antiviral immunity. As chemotherapy results in the decrease in the amount of lymphocytes, it contributes to the infection of SARS-CoV-2 [32]. It has been also advised to switch from intravenous to oral correspondent formulations such as etoposide and vinorelbine [25].

The subject of biologic and monoclonal-antibody therapies is not clearly explained. Some of them are considered to be valuable in the inflammatory storm observed in COVID-19 [30]. However, it should be mentioned that there are reported cases of severe adverse effects while using immune checkpoint inhibitor therapy. Bonomi et al. described the case of a patient with lung cancer treated with nivolumab, whose condition suddenly deteriorated within five days after COVID-19 diagnosis. He presented a rapid evolution of respiratory failure and died [33].

Follow-up

As social distancing has been implemented, public health had to respond and adjust to the COVID-19 pandemic. Thereupon, office visits have been substituted for telemedicine, hospital-at-home approach and early discharge [34]. Until COVID-19 appeared, telemedicine was just an addition, rather than a primary form of health care. Schaffert et al. introduced an online tutorial for decision-making and communication with cancer patients, which was tested in a pilot study afterwards [35]. This approach was also evaluated by the Personal Patient Profile-Prostate (P3P) in a multicentre randomised trial and gave promising results as it significantly decreased decisional conflict in comparison to “usual care” [36]. Moreover, no significant difference has been found between nurse-led and standard follow-up visits satisfaction among patients after radiotherapy [37].

Belarmino et al. had recently demonstrated a mobile application for monitoring postoperative recovery for men following prostatectomy. Most of the patients (85%) complied with ambulation, hydration and Kegel’s exercising app notification. Patients found this mobile app comprehensible and easy to use, which gives an opportunity for improving compliance in perioperative instructions [38]. On the contrary, Lange and colleagues draw attention that guided online peer chat was not an effective support tool and demonstrated poorer psychological outcomes in patients using this app compared to control group [39].

Another relevant issue is a clinical examination, which used to be an indispensable component of medical appointments. However, physical examination has a crucial value, it does not apply for all patients. Even though, digital rectal examination (DRE) is widely performed in prostate cancer management, its value is still questionable. In one of the studies, DRE showed low sensitivity and specificity and thus its omission among patients with prostate cancer seems to be reasonable [40]. Moreover, for patients with kidney or bladder cancer, in-office physical examination is rarely crucial in treatment decisions and patients’ surveillance. However, nowadays cystoscopy has an influence on diagnosis or monitoring patients with bladder cancer, though recent data indicate that biomarker-based surveillance may replace it shortly [41].

According to the ESMO guidelines follow up for cancer patients is divided in three categories according to the risk of relapse: low, medium and high priority [24]. However, these recommendations should be used as a guidance in prioritizing patients and conditions which need urgent service. Nonetheless, the reprioritization can have long-term consequences

in terms of detection of disease progression and following complications. Development of telemedicine seems to be promising and helpful for patients who are already treated and require only routine check-up but cannot replace all medical services. Although, changes in healthcare management are inevitable, risks and benefits of these actions need to be carefully considered.

SUMMARY:

COVID-19 pandemic affected health care system worldwide on an unprecedented scale. The burden of SARS-CoV-2 has important implications also for the cancer care. As patients with cancer are especially vulnerable to SARS-CoV-2, the impact of COVID-19 on cancer outcome is substantial. Beyond that patients with cancer seem to have higher prevalence and worse COVID-19 course, while the access to optimal care for them is limited. Diagnostic and treatment pathways should be adjusted to minimize the risk of SARS-CoV-2 infection, but on the other, suboptimal care provision may effect delayed diagnoses and have a negative impact on cancer outcomes. In addition, as all the world focused on struggling with COVID-19, a lot of clinical trials have been suspended, which results in limiting of current therapy options for patients with cancer. It is highly important to continue research and share experiences of different medical centres in order to provide much-needed data concerning influence of COVID-19 on patients with cancer. It will help to identify patients that are at particularly high risk of worse COVID-19 course and exclude those for whom those special protective measures are not necessary. Although fear of SARS-CoV-2 is immense, adverse effects of delayed diagnosis and treatment of oncological patients should not be diminished. Deprioritization of patients with cancer can have longitudinal and irreversible effects on their well-being. As many patients have been fearful of potential exposure to SARS-CoV-2, they were also less likely to attend screening programmes. Given the circumstances, there is a high need to educate society and prevent delayed diagnosis and treatment.

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