

“Door to Treatment” Outcomes of Cancer Patients during the COVID-19 Pandemic

Naziye Ak^{a, b} Sezai Vatansever^{a, b}

^aDepartment of Medical Oncology, Institute of Oncology, Istanbul University, Istanbul, Turkey; ^bDepartment of Internal Medicine, Division of Medical Oncology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

Keywords

Chemotherapy · Coronavirus · Novel coronavirus disease 2019 · Oncology clinics · Outcome · Quality of life · Quality of service

Abstract

Background: The novel coronavirus disease 2019 has become a worldwide threat. We aimed to explore reflections of these unexpected changes to newly diagnosed cancer patients. **Method:** We searched the 2 months after the index case of our country. The first admission day and the first day of intravenous treatment of newly diagnosed patients were recorded. **Results:** In the 60 days measured during the pandemic, the total number of patients on polyclinics was 159/weekdays, and the total applied chemotherapy cycles were 276/week. For comparison, the total numbers in the previous year were 267/weekday and 363/week for polyclinic and applied chemotherapy cycles, respectively. The total number of newly admitted patients in 2020 was 283. For comparison, the number of new patients in the same 60-day period in 2019 was 495. Patients who were admitted for adjuvant treatment required a median of 8 days for the first course, those who were admitted for neoadjuvant treatment required 12 days, and metastatic patients required 14 days; there were no significant differences between treatment types ($p = 0.233$). However, the median treatment time was 11.5 and 17 days, in 2020 and in 2019, respectively. A significant difference was observed between the 2 groups ($p < 0.001$). **Conclusion:** The effective shift of workers and accu-

rate regulations have not resulted in apparent delays in patient care. While a decrease in the number of patients has detected, faster healthcare service was introduced to newly diagnosed patients. The reason for the decrease in the number of patients should be investigated with new studies.

© 2020 S. Karger AG, Basel

Introduction

The novel coronavirus SARS-Cov-2, also known as novel coronavirus disease 2019 (COVID-19), is the major healthcare concern of 2020 and represents a significant threat to human health worldwide [1–3]. The outbreak began in China at the end of 2019, and the first case in Turkey was diagnosed on March 11, 2020. As of April 1, 2020, the Ministry of Health of Turkey announced that COVID-19 had spread throughout Turkey, exhibiting the highest spread in Istanbul [4]. Until this point, there were no changes to routine practice in healthcare facilities; however, following this date, hospital regulations changed immediately as a result of the implementation of Ministerial regulations to maintain public healthcare. Out of the oncologic and hematologic outpatient clinics, routine polyclinics were changed to acute polyclinics in an attempt to focus on addressing issues in followed-up patients, while unnecessary or elective visits were postponed.

The first report of oncological patients in Wuhan stated the increased risk of infection in this specific patient group, although other studies have since shown that this

Table 1. Number of outpatient clinic and chemotherapy infusions during the first and last 5 weekdays of COVID-19 pandemic in our country

Outbreak days	Patients with COVID-19, n	Deaths from COVID-19, n	Outpatient clinic, n	Chemotherapy infusions, n
1	1	0	257	59
2	1	0	257	70
3	5	0	153	66
4*	6	0	na	na
5*	18	0	na	na
6	47	0	354	60
7	98	1	247	71
54	1,832	59	189	46
55	2,253	64	121	59
56	1,977	57	164	45
57	1,848	48	62	36
58*	1,546	50	na	na
59*	1,542	47	na	na
60	1,114	55	217	49

na, not applicable. * Weekend.

cannot be attributed only to “cancer” without the consideration of other factors, such as age, comorbidities, or performance score [5, 6]. Since oncologic diseases have severe mortality, oncology clinics have not changed their practice if the patient has no symptoms of COVID-19 infection according to current guidelines [7–9].

Officially, new patient polyclinics and chemotherapy or radiotherapy visits have continued as normal. However, the working hours of hospital staff has changed, and some patients have strict regulations with respect to local curfews. Furthermore, since Istanbul is a crowded city and near 60% of the COVID-19 cases in Turkey originated from Istanbul [4], some of our patients preferred to not visit the hospital, believing that it was unsafe. Unfortunately, these issues may have led to unplanned delays in the treatment schedules of patients. Therefore, we aimed to determine whether there was any difference in oncologic clinic service in a tertiary pandemic hospital within a crowded city during this unexpected crisis.

Materials and Methods

The current study was based on systemic research acquired from the hospital registration system of Istanbul University, Institute of Oncology. In our clinic, patients can only access the hospital for scheduled appointments, and a telephone triage is performed to guarantee safety, especially for patients with cancer who are under surveillance. Moreover, there was a hospital vacancy rate

Table 2. Comparison of patients by treatment time

	2019 median days (range)	2020 median days (range)	p value
All patients	17 (1–70)	11.5 (1–53)	<0.001
<i>Treatment intent</i>			
Adjuvant	15 (1–68)	8 (1–53)	<0.001
Neoadjuvant	15 (1–40)	12 (3–24)	0.158
Metastatic line	20 (1–64)	14 (1–48)	0.065
p value	0.958	0.233	

of 20%, which was reserved for patients with acute problems. Although there were no official changes to the new patient appointment capacity, we aimed to determine whether there was any negative effect on the polyclinic service as a result of the pandemic.

We searched the 2 months after the index case of our country, with the intention to elucidate the consequences of the most challenging days of the pandemic. In line with this, new patients who were admitted to our clinic, both outpatients and inpatients, between March 10, 2020, and May 10, 2020, were recorded retrospectively. In addition, new patients between March 10, 2019, and May 10, 2019, were recorded as a control group. The Ethical Committee approved this study (No. 70973125-604.01.01/62733).

Statistical analyses were performed with SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). Patient characteristics including age, pathology, stage, date of first admission, date of the first day of therapy, and the type of chemotherapy were recorded for both groups. The time between admission and the first day of treatment was defined as “treatment time.” The primary endpoint of the study was to detect differences in treatment time between the 2 groups. Adjuvant treatment included primary chemotherapy (including for head and neck cancer, cervical cancer, and lymphoma) and chemotherapy after surgery. Neoadjuvant treatment included chemotherapy with the aim of a curative intent surgery, and metastatic line treatment included palliative therapies. Continuous variables analyzed for the normality of distribution. Treatment time difference between treatment groups was compared using Kruskal-Wallis *H* test. Treatment time difference between 2-years was compared using Mann-Whitney *U* test. Probability values <0.05 were considered statistically significant.

Results

In the 60 days measured during the pandemic, the total number of patients who visited polyclinics was 159/weekday, and the total applied chemotherapy cycles were 276/week. For comparison, the total numbers in the previous year were 267/weekday and 363/week for routine polyclinic visits and applied chemotherapy cycles, respectively. Table 1 shows the declining trend in the first and last 5 weekdays. After the data of previously followed pa-

Table 3. Disease characteristics of patients with treatment

	Stage				Treatment intent		
	I	II	III	IV	adjuvant	neoadjuvant	metastatic
Lung cancer	0	1	3	17	3	1	17
Breast cancer	2	3	5	2	5	5	2
Colorectal cancer	1	0	10	5	11	0	5
Genitourinary cancer	1	2	1	5	3	1	5
Gynecological cancers	0	1	8	3	10	2	0
Melanoma	0	0	1	0	1	0	0
Sarcoma	0	1	0	1	1	0	1
Esophagogastric cancer	0	0	5	6	3	2	6
Nervous system tumors	0	1	0	0	1	0	0
Head and neck cancers	0	0	1	0	1	0	0
Pancreatobiliary system	0	0	2	7	0	2	7
Others	0	0	1	0	1	0	0

tients were excluded, the total number of newly admitted patients in 2020 was 283. For comparison, the number of new patients in the same 60-day period in 2019 was 495. The most significant decrease detected in gynecological cancers, then sarcomas. The median age of all patients was 54 (range, 18–92) years and 57 (18–90) years for 2019 and 2020, respectively. With regard to the sex distribution, slightly more male patients were admitted in 2020 than in 2019 (M:F ratio for 2019:0.98; M:F ratio for 2020:1.12). In the 2 pandemic months of 2020, a total of 96 new patients visiting the polyclinic received their first cycle of systemic cytotoxic intravenous treatment, and 17 patients received their initial dose of first-line oral cytotoxic treatment. Active follow-up or noncytotoxic treatments, such as endocrine treatment for breast cancer or antiandrogen treatment for prostate cancer, were decided for the remaining patients in accordance with the current guidelines, regardless of the pandemic situation. Over the same time period in the previous year, 51.4% of patients were treated with an adjuvant, while 15.2 and 33.3% of the patients were treated with a neoadjuvant and metastatic line treatment. During the pandemic, 41.7, 13.5, and 44.8% of patients were treated with adjuvant, neoadjuvant, and metastatic line therapies, respectively. Patients who were admitted for adjuvant treatment required a median of 8 days for the first course, those who were admitted for neoadjuvant treatment required 12 days, and metastatic patients required 14 days; there were no significant differences between treatment types ($p = 0.233$, Table 2). The most preferred treatment regimen was Xelox/Folfox, followed by a combination of Paclitaxel and Carboplatin. A summary of the disease characteristics of patients with

Table 4. Patients with primary GCSF prophylaxis

	N
<i>Treatment</i>	
Adriamycin + cyclophosphamide	5
Adriamycin + iphosphamide	1
Cisplatin + etoposide	7
FLOT regimen	5
Cisplatin + gemcitabine	2
CHOP regimen + rituximab	1
Paclitaxel + carboplatin	4
VAC regimen	1
<i>Histology</i>	
Lung cancer	10
Breast cancer	4
Colorectal cancer	1
Genitourinary cancer	2
Gynecological cancers	3
Sarcoma	1
Esophagogastric cancer	4
Others	1
<i>Stage</i>	
I	1
II	2
III	8
IV	15
GCSF, granulocyte colony-stimulating factor.	

intravenous cytotoxic treatment during the pandemic is shown in Table 3. We then explored whether the treatment decisions of physicians were affected by the pandemic. We found that there were changes in the treat-

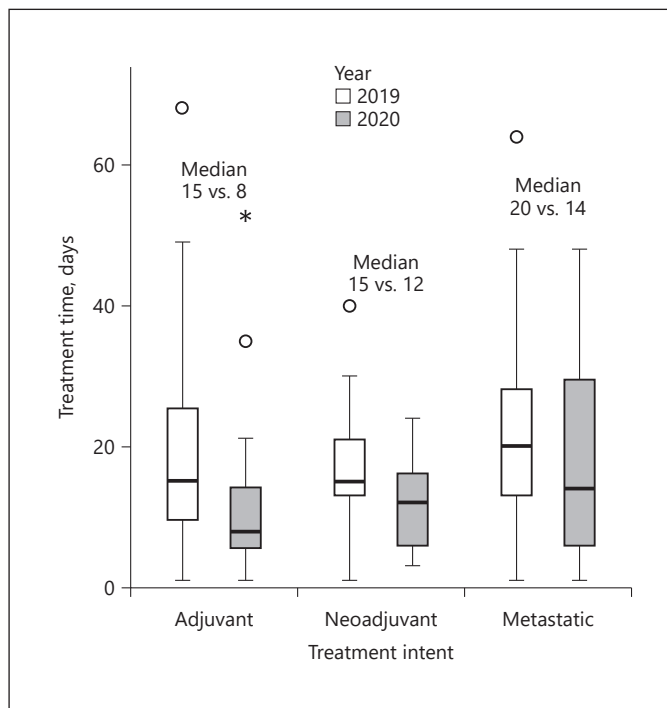


Fig. 1. Distribution of patients according to treatment time.

ment plans of 6 patients; 4 patients declined chemotherapy due to an increased risk of infections, and clinicians chose the same treatment regimen with reduced dosing for 2 patients because of the pandemic. A total of 26 patients received primary granulocyte colony-stimulating factor prophylaxis, mostly those who underwent the cisplatin + etoposide regimen (Table 4). Of note, none of the new patients were diagnosed with COVID-19 infection up until the study cutoff date. In all patients, the median treatment time in 2020 was 11.5 (range, 1–53) days, and the median treatment time of patients in 2019 was 17 (range, 1–70) days; a significant difference was observed between the 2 groups ($p < 0.001$, Table 2). Also, treatment time difference in all treatment subgroups is shown in Figure 1.

Discussion

Istanbul University, Institute of Oncology is unique oncology institute in Istanbul and is affiliated with Istanbul Medical Faculty Hospital, which is the leading hospital in the fight against COVID-19 in our country. This critical location of the hospital during the pandemic led to a reduction in the number of cancer patient appoint-

ments (by approximately 1/3), which also resulted in a significant decrease in the time to the first treatment cycle. Although cancer patients are at risk of critical infections, none of our new patients were diagnosed with COVID-19, which may be due to an increased awareness of hygiene and the requirement to self-quarantine.

The COVID-19 pandemic has emerged to be a significant global health threat as a result of the immediate adaptations required by the healthcare system, especially, with regard to cancer patients. The implementation of public health protection measures led to concerns of disruptions to cancer treatment, which may prove to be life-threatening. Several medical societies worldwide have mobilized and attempted to create recommendations for navigating the COVID-19 crisis without jeopardizing the provision of cancer treatments [7–9]. The majority of these guidelines state that maximum effort should be made to maintain standard treatment modalities, with a few changes relating to priority patients, based on symptoms of disease or intent of therapy. Indeed, the aim of treatment was another concern, due to the desire to decrease patient exposure to COVID-19. Given the immunocompromised nature of cancer patients, cancer centers have adhered to strict infection control guidelines, and outpatient visits, including ambulatory clinics and chemotherapy infusion visits, have been reduced [10]. Although our clinic has not changed its outpatient clinic service, especially for new patients, only patients in surveillance had tele-visits before admission. Given the lack of knowledge about their condition, the new patient appointment system was the same as that used in the previous year. However, the risk of patients not applying to the hospital, either for cancer diagnosis or treatment, especially those with asymptomatic conditions, cannot be excluded. Consequently, treatment delays or unavailability remain concerns. Indeed, as previously stated by Wang and Zhang [11], the main risk factor for cancer patients during the COVID-19 pandemic is their inability to receive appropriate medical treatment and care.

Since it is the time period that is least affected by the disease progression and disease-related factors, focusing on the statistics of new patients seems to represent a more useful and accurate tool to measure the quality of services. In line with this, we aimed to determine whether changes in the lives of the public and healthcare workers due to the pandemic have an impact on oncological services and patient care. Our results showed there were no delays in treatment, at least as a result of “in hospital” causes. In our cohort, the first treatment time was significantly shorter than that for the previous year. Considering the high pa-

tient density of the health system in our country, which is much more than is recommended by quality guidelines, the pandemic may have improved care as a result of the reduction in the number of patients. Unfortunately, it is very difficult to establish the quality of the care and experiences of the patients who could not apply to the hospital.

Surgery is another vital component in cancer management, and previous studies have indicated that patients who underwent surgery and contracted COVID-19 concomitantly were at a greater risk of severe clinical events than those who did not receive surgery [12, 13]. In some instances, particularly in early stage cancers where surgery is often the initial step in management, patients may be offered neoadjuvant therapy; consequently, surgery could be delayed without adversely affecting patient outcomes [7, 14, 15]. Based on this hypothesis, we anticipated an increase in neoadjuvant therapies but found that only 13.5% of our patients received neoadjuvant therapy in 2020, while the previous year had 15.2%. This result may be due to the cohort number and the decrease in the number of surgeons who worked at the polyclinic due to their redistribution to pandemic services. Since decisions relating to neoadjuvant treatments are made in councils that are in contact with surgeons, and patients tend to want to be examined by their usual surgeon, there is likely to be a slight shift to private hospitals. Furthermore, patients may consider private hospitals, or other public hospitals that do not provide pandemic services, to be safer. In addition, our hospital previously accepted applications from all countries due to its location and extensive experience in oncology. Travel restrictions are likely to have caused a reduction in the number of applications and a change in our patient population. We also observed a slight increase in the percentage of metastatic patients, likely as a result of their symptoms. Metastatic patients have more cancer-related symptoms, and consequently, tend to seek diagnostic and therapeutic support, even during the pandemic; this may also explain the decrease in the adjuvant patient population. The majority of early stage patients do not have symptoms, and screening procedures may be omitted during quarantine.

The most important finding of the current study is that none of our new patients had confirmed COVID-19 infection by the cutoff date. However, on-treatment patients may also be more difficult to assess given ongoing treatment-related side effects that may resemble signs of infection, such as fatigue and dyspnea. However, it is unlikely to omit COVID-19 infection in cancer patients with high sensitivity of the whole medical staff. We attribute this finding to the high preventive measures in our coun-

try, as well as to the extra care taken by cancer patients with regard to self-hygiene. In addition, we used granulocyte colony-stimulating factor with high-risk regimens, since there is no clear recommendation about the routine use for all cancer patients [16].

There are some limitations to study. First, this was a retrospective and mainly registry-based study, which may lead to ungeneralized results. However, this type of an observational study, which examines the consequences of unexpected pandemic time, is difficult to carry out prospectively. Furthermore, to the best of our knowledge, this is one of the first studies to present the outcomes of newly diagnosed cancer patients among studies of oncological patients. Large-scale epidemiological studies by public health services should be conducted in order to clarify the impact of this period on oncological care in the future.

Conclusion

The COVID-19 pandemic can be considered as the greatest public health crisis since the last decade. This crisis has led to considerable challenges in the management of patients, by overwhelming healthcare systems and causing significant stress to the healthcare workforce. During the COVID-19 pandemic, the major risk for cancer patients is considered to be the inability to receive appropriate medical treatment and services. In the current study, we have provided a brief overview of the oncology services within our institute over the course of the pandemic, with the intention to measure the disruption to these patients in our hospital. Our results showed that the effective shift of workers and accurate regulations to protect patients and staff have been effective, and as a result, there have been no apparent delays in patient care.

Acknowledgements

The authors would like to thank all healthcare professionals who working devotedly at all costs in this difficult process.

Statement of Ethics

This study held by full compliance with Ethical Standards. Ethical approval stated in the text with number.

Conflict of Interest Statement

Authors state that there are no conflicts of interest and no disclosures about this study.

Funding Sources

There is no funding.

Author Contributions

Conceptualization and methodology: S.V. and N.A.; software, validation, formal analysis, data curation, and writing – original draft: N.A. and; writing – review and editing, visualization, supervision, project administration, investigation, and resources: S.V. and N.A.

References

- 1 ProMED, ISID. Report of Undiagnosed pneumonia – China. [cited 2020 July 9]. Available from: <https://promedmail.org/promed-post/?id=6864153>.
- 2 WHO. Disease outbreak news. [cited 2020 Jun 29]. Available from: www.who.int/csr/don/05-january-2020-pneumonia-of-unknown-cause-china/en/.
- 3 Bogoch II, Watts A, Thomas-Bachli A, Huber C, Kraemer MUG, Khan K. Pneumonia of unknown aetiology in Wuhan, China: potential for international spread via commercial air travel. *J Travel Med*. 2020 Mar 13(2):27.
- 4 T.C. Ministry of Health. Current Status of Turkey. [cited 2020 July 9]. Available from: <https://covid19.saglik.gov.tr/>.
- 5 Dai M, Liu D, Liu M, Zhou F, Li G, Chen Z, et al. Patients with cancer appear more vulnerable to SARS-CoV-2: a multicenter study during the COVID-19 outbreak. *Cancer Discov*. 2020 Jun;10(6):783–91.
- 6 Zhang L, Zhu F, Xie L, Wang C, Wang J, Chen R, et al. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. *Ann Oncol*. 2020 Jul;31(7):894–901.
- 7 ASCO. ASCO coronavirus resources. [cited 2020 Jun 29]; Available from: <https://www.asco.org/asco-coronavirus-information>.
- 8 ESMO. ESMO COVID-19 and cancer. [cited 2020 Jun 29]; Available from: <https://www.esmo.org/covid-19-and-cancer>.
- 9 NCCN. Coronavirus disease 2019 (COVID-19) resources for the cancer care community. [cited 2020 Jun 29]. Available from: <https://www.nccn.org/covid-19/>.
- 10 Al-Shamsi HO, Alhazzani W, Alhurajji A, Coomes EA, Chemaly RF, Almuhanna M, et al. A practical approach to the management of cancer patients during the novel coronavirus disease 2019 (COVID-19) pandemic: an international collaborative group. *Oncologist*. 2020 Jun;25(6):e936–e45.
- 11 Wang H, Zhang L. Risk of COVID-19 for patients with cancer. *Lancet Oncol*. 2020 Apr; 21(4):e181.
- 12 Liang W, Guan W, Chen R, Wang W, Li J, Xu K, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol*. 2020 Mar;21(3):335–7.
- 13 Moletta L, Pierobon ES, Capovilla G, Costantini M, Salvador R, Merigliano S, et al. International guidelines and recommendations for surgery during Covid-19 pandemic: a systematic review. *Int J Surg*. 2020 Jul;79:180–8.
- 14 Surgery, A.E.G. (2020). Joint Society Statement on Elective Surgery during COVID-19 Pandemic. Published March. [cited 2020 July 9]. Available from: <https://www.aagl.org/news/covid-19-joint-statement-on-elective-surgeries>.
- 15 Mansfield SA, Abdel-Rasoul M, Terando AM, Agnese DM. Timing of breast cancer surgery—how much does it matter? *Breast J*. 2017 Jul; 23(4):444–51.
- 16 Alkan A, Uncu A, Taşkıran I, Tanrıverdi Ö. Double-edged sword: Granulocyte colony stimulating factors in cancer patients during the COVID-19 era. *Clinics*. 2020;75:e2033.