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ORIGINAL ARTICLE

"Swords and Shields" against COVID-19 for patients with cancer at "clean" and "pandemic" hospitals: are we ready for the second wave?

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Abstract

Purpose COVID-19 will continue to disrupt the diagnosis-treatment process of cancer patients. Dr. Abdurrahman Yurtaslan Ankara Oncology Hospital has been considered as a 'non-pandemic' center ('*clean*') in Ankara, the capital city of Turkey. The other state hospitals that also take care of cancer patients in Ankara were defined as '*pandemic*' centers. This study aimed to evaluate hospital admission changes and the precautionary measures in *clean* and *pandemic* centers during the pandemic. The effect of these measures and changes on COVID-19 spreading among cancer patients was also evaluated.

Methods The patients admitted to the medical oncology follow-up, new diagnosis, or chemotherapy (CT) outpatient clinics during the first quarter of pandemic period (March 15–June 1, 2020) of each center were determined and compared with the admissions of the same frame of previous year (March 15–June 1, 2019). COVID-19 PCR test results in clean and pandemic centers were compared with each other. Telemedicine was preffered in the clean hospital to keep on follow-up of the cancer patients as 'noninfected'.

Results In the *clean* hospital, COVID-19-infected patients that needed to be hospitalized were referred to pandemic hospitals. COVID-19 test positivity rate was eight-fold higher for outpatient clinic admissions in pandemic hospitals ($p < 0.001$). The number of patients admitted new diagnosis outpatient clinics in both clean and pandemic hospitals decreased significantly during the pandemic compared with the previous year.

Conclusion We consider that local strategic modifications and defining '*clean*' hospital model during infectious pandemic may contribute to protect and treat cancer patients during pandemic.

Keywords COVID-19 · Cancer · Hospital · Pandemic · Telemedicine

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Introduction

The novel coronavirus disease (COVID-19) has led a pandemic this year. Patients with cancer on active chemotherapy, radiotherapy, immunotherapy, targeted therapy, and immunosuppressants for bone marrow transplantation in the previous 6 months were considered to have higher risk for COVID-19 [1]. In addition, cancer patients over 60 years old and those with comorbidities, such as cardiovascular or cardiopulmonary diseases, have higher mortality rates [1, 2]. COVID-19 infection rate was reported to be two-fold higher for cancer patients in a tertiary center in Wuhan (0.79% vs 0.37 and OR: 2.31) [3, 4]. It was almost higher for patients over 60 years old and/or with lung cancer (4.3%). The case fatality rate was almost higher in patients with cancer (5.6–7.6%) [4, 5]. In addition, patients with cancer were also found to have a higher risk for severe events such as the

need for intensive care unit [6]. Italians reported that 19.5% of the patients with COVID-19 had a cancer diagnosis in the previous 5 years [7]. So, a strategy is needed for patients with cancer because of increased mortality and morbidity during the COVID-19 outbreak.

The first case was diagnosed with COVID-19 on 10 March 2020, in Turkey. One-fifth of deaths are attributed to cancer, and approximately 170,000 people have cancer diagnoses every year in Turkey [8]. Therefore, the management of cancer patients should not be interrupted even during the COVID-19 pandemic. However, novel modifications in diagnostic and therapeutic approaches besides follow-up strategies for these patients are needed to minimize possible hitches during the COVID-19 pandemic. Since it is an emergency, there is no well-established guideline to overcome the COVID-19 pandemic. So, local committees besides national and global authorities have been struggling to manage it.

Cancer management needs experienced centers, and it has been more significant during the COVID-19 pandemic to keep on the management of patients with cancer. Daily routine procedures should have been modified to treat and follow up patients with cancer successfully during this period since there is no guideline for cancer management during an infectious pandemic [4]. So, local committees had to take action plans to deal with COVID-19 at oncology clinics. Valenza et al. reported their action plan to counteract COVID-19 in a cancer center in Italy [9]. Their clinical experience to fight with COVID-19 pandemic at a cancer center in Milano, a part of Lombardy region, has contributed to the management of cancer patients in other cancer clinics. Dr Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital is a comprehensive cancer center in Turkey. It has been considered that this center should have been kept as a '*non-pandemic*' center ('*clean hospital*') during the COVID-19 pandemic. On the other hand, there are almost experienced centers that take care of patients with cancer behaved as '*pandemic*' centers.

In present multicentric study, our purpose was to evaluate the strategies for management of cancer patients in '*clean*' and '*pandemic*' centers besides local changes in admissions. We also aimed to evaluate COVID-19 rate in cancer patients, the changes in treatment and follow-up modalities compared with previous daily routine, the effect of these changes on COVID-19 positivity rates besides comparison of COVID-19 positivity rates, and challenges against COVID-19 spread at these centers. We consider that our study might contribute to the management of cancer patients during other unexpected infectious healthcare breakdowns as of COVID-19 pandemic.

Method

This study was approved by Ethical Comittee of Dr Abdurrahman Yurtaslan Oncology Training and Research Hospital. It was also approved by Republic of Turkey Ministry of Health.

Definitons of '*clean*' and '*pandemic*' hospitals

Ankara, capital city of Turkey, is a metropolitan city. It is among the most affected regions from COVID-19 pandemic in Turkey. Strategies and precautionary measures taken for COVID-19 at four big centers in Ankara were evaluated in this study. All of these centers have experienced Medical Oncology clinics at which cancer patients have been followed up for many years. These centers are Dr Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital (Hos-A), Ankara City Hospital (Hos-B), Ankara Diskapi Yildirim Beyazit Training and Research Hospital (Hos-C), and Gulhane Training and Research Hospital (Hos-D). Hos-A is a comprehensive cancer center that mainly aims to follow up cancer patients. During COVID-19 pandemic, there has been a pandemic outpatient clinic for the patients with COVID-19 suspicions. The patients with confirmed COVID-19 diagnosis who did not need hospitalization followed up from their home. Hos-A also had a pandemic inpatient service for COVID-19-suspected patients who were hospitalized with suspicious COVID-19 symptoms rather than documented COVID-19. The patients with confirmed COVID-19 diagnosis and need hospitalization were transferred to pandemic hospitals as soon as possible. So, Hos-A was defined as a '*non-pandemic*' ('*clean*') hospital. Hos-B, Hos-C, and Hos-D are also big centers that are experienced at oncology. Hos-B, Hos-C, and Hos-D were defined as '*pandemic*' hospitals since they allowed admission of all cancer and non-cancer patients with documented COVID-19 while they kept on management of the cancer patients without COVID-19.

Telemedicine application

Telemedicine for cancer patients receiving chemotherapy

Telemedicine application was applied only in the '*clean*' hospital for cancer patients' safety in terms of protection from COVID-19 and cancer management without any interruption. With this application, patients who had a CT appointment were called by a medical oncologist. All of the patients were questioned for symptoms of COVID-19 (i.e., fever, cough, sputum, dyspnea). Chemotherapy was postponed for the patients with suspected COVID-19 and these patients were referred to the pandemic outpatient clinic. On the other hand, the patients receiving CT could also access the medical oncologist whenever they needed a professional help via telemedicine. So, telemedicine could contribute to a decrease in '*cancer patient traffic*' at the hospital. The patients were also informed about protection from COVID-19 (i.e., wearing mask,

hygiene, and keeping social distance) and COVID-19 status in our healthcare center as of the day on which the phone call was made upon their demand.

Telemedicine application for cancer patients not receiving CT

Telemedicine practice was also applied for the cancer patients not receiving CT in only two centers, the clean hospital and one of the pandemic hospitals. During the interviews on the phone, the patients informed the medical oncologist if they had active complaints. Evaluating the patients' complaints besides examination of their previous follow-up notes on the hospital database gave an opportunity to reduce the risk of exposure to COVID-19 by ensuring that only the patients who really needed to be evaluated face-to-face in the outpatient clinic. Some of the patients are referred from nearby cities and they mostly reach the centers by public transport. So, telemedicine also contributed to lessen public transport of these patients in terms of risk reduction for COVID-19 exposure.

Precautionary strategy

Precautions against COVID-19 were classified as logistic modifications, healthcare staff daily routine modification, filiation, referral of COVID-19-infected patients to pandemic hospitals, and telemedicine.

COVID-19 PCR test

COVID-19 testing was applied by using rRT-PCR ('*real-time reverse transcription polymerase chain reaction*') method for detection of SARS-CoV2 nucleic acid in nasopharyngeal and oropharyngeal swabs.

Study design

Hos-B, C, and D were pandemic hospitals while Hos-A was a clean hospital. The precautionary measures and practices for COVID-19 at these centers were recorded. Primary outcome of our study was to determine how the pandemic process affected the number of patients admitted to oncology centers. In this regard, cancer patients who were admitted to the medical oncology follow-up outpatient clinic (F-OC), new diagnosis outpatient clinic (ND-OC), and chemotherapy outpatient clinic (CT-OC) during the first quarter of the pandemic period (March 15–June 1, 2020) of each center were determined and compared with the admissions of the same frame of last year (March 15–June 1, 2019).

Secondary outcome was to determine whether there was a difference for COVID-19 positivity rate between '*clean*' and '*pandemic*' hospitals. COVID-19 PCR test results performed for COVID-19 suspicious were evaluated and compared with each other in '*clean*' and '*pandemic*' hospitals.

Statistical analysis

Statistical analysis was performed by using IBM SSPS Statistics for Windows v.20.0 software (IBM, NY, USA). Qualitative variables were reported as number and percentage. Comparison of categorical data was performed by Pearson chi-square test or Fischer's exact test. Wilcoxon test was used to compare dependent group variables. Statistical analyses were '*two-way*' and '*p value*' less than 0.05 was considered as statistically significant.

Results

Precautions

Precautionary strategy against COVID-19 at clean and pandemic hospitals is summarized in Table 1. In the clean hospital, COVID-19-infected patients were referred to pandemic hospitals to keep on being a 'clean' hospital.

COVID-19 PCR results

While 124 of 19,010 cancer patients who were admitted to the outpatient clinics of '*pandemic*' hospitals were positive for COVID-19 test, only 7 of 8909 cancer patients at outpatient clinics in the '*clean*' hospital had positive test results, respectively ($\chi^2 = 42.443$, $p < 0.001$). It was significantly eight fold higher for pandemic hospital. In the clean hospital, one patient who was diagnosed with COVID-19 and needed hospitalization was transferred to the pandemic hospital.

Changes in admissions to the outpatient clinics

The number of patients who were admitted to F-OC, CT-OC, and ND-OC in both '*clean*' and '*pandemic*' hospitals significantly decreased during the first quarter of pandemic compared with the same frame of previous year. Seven hundred and forty-one newly diagnosed cancer patients were admitted to ND-OC between 15 March 2019 and 01 June 2019 in the clean hospital whereas it was only 438 in the same period of 2020 (p=0.047). However, it was not different from the pandemic hospitals in terms of newly diagnosed patients (1739 vs. 917, p=0.044; Figs. 1 and 2). On the other hand, outpatient clinic cancer patient admissions to F-OC and CT-OC in both clean (n: 2976 vs n: 7334, n: 5495 vs n: 8201) and pandemic (n: 14321 vs n: 20853, n: 3772 vs n: 4480) hospitals were almost significantly lower in 2020 (p=0.011, p=0.021, p=0.035, p=0.027, respectively).

Table 1 Precautionary strategy against COVID-19

	Clean hospital	Pandemic hospitals
Logistic modifications		
Information documents for COVID-19 prevention	Yes	Yes
Attempts to keep physical (social) distance	Yes	Yes
Triage desks (body temperature measurement before entering the hospital)	Yes	Yes
Localization arrangement for inpatient and outpatient clinics at Medical Oncology Departments	Yes	Yes
Distance arrangement between medical oncology inpatient/outpatient clinics and infectious disease inpatient/outpatient clinics	Yes	Yes
Restriction for visitors and the others accompanying with the patients	Yes	Yes
Healthcare staff (i.e., doctors, nurses, assistant staff, medical secretaries) daily routine modifications		
Shift arrangement	Yes	Yes
Working hours modification	Yes	Yes
Personal protective equipments (PPE; locally routine recommendation, additional personal preference)	Yes	Yes
COVID-19 case detection and control: "*filiation*"	Yes	Yes
Transfer of COVID-19 positive cases to a pandemic center	Yes	No
Telemedicine application for cancer patients receiving CT	Yes	No
Telemedicine application for other patients	Yes	Yes[a]

[a] Telemedicine practice applied for the cancer patients not receiving CT in only one of the pandemic hospitals

Discussion

In this multicentric study, the precautions against COVID-19 taken by clean and pandemic hospitals in the COVID-19 pandemic were evaluated. Precautional tools were defined and their effect on cancer management during the first quarter of pandemic led us to go on more confidently on the following weeks. Among the cancer patients admitted to the outpatient clinics in both clean and pandemic hospitals, COVID-19 positivity rate in the clean hospital was significantly lower than pandemic ones as well. It might be related to be known as 'clean' hospital. The people were aware of the fact that they would be referred to 'pandemic' hospitals as soon as they were diagnosed with COVID-19. So, it might have been easier

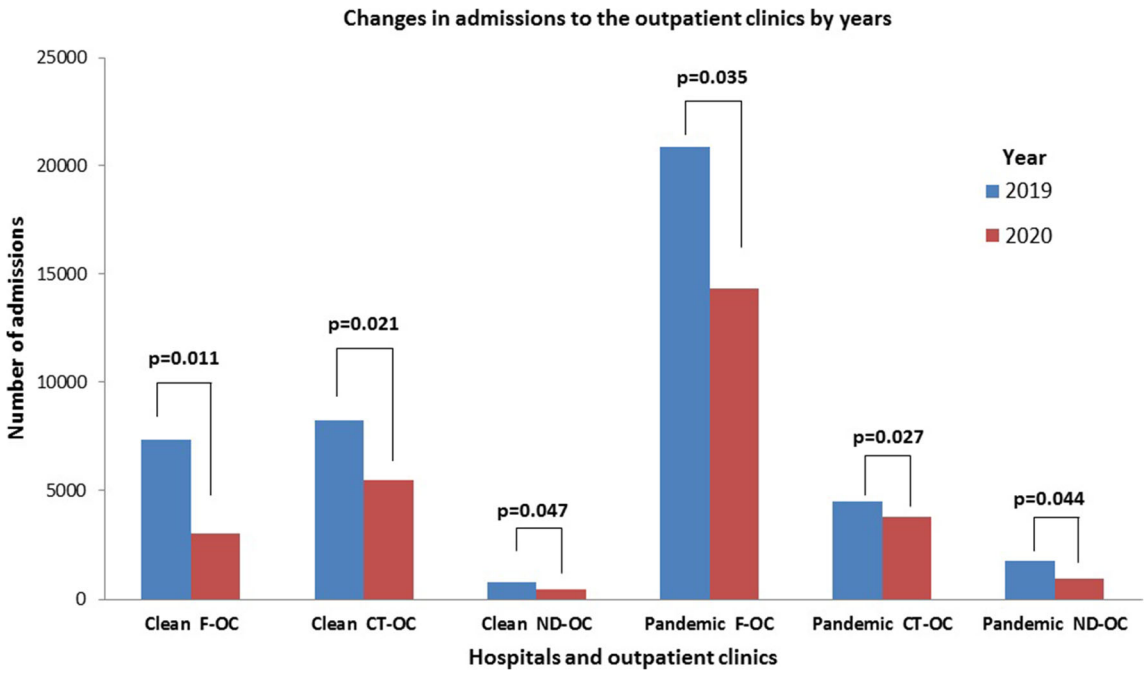

Fig. 1 Changes in admissions to the outpatient clinics

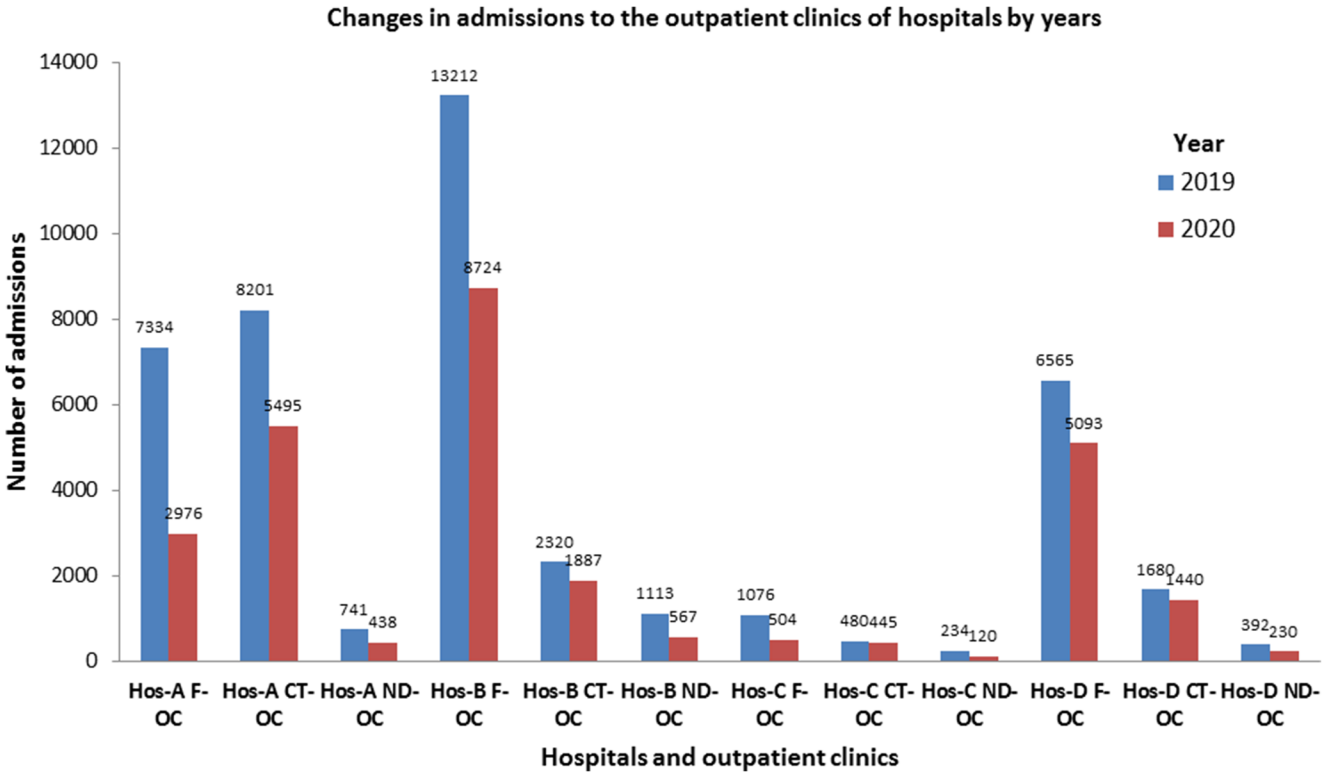

Fig. 2 Changes in admissions to the outpatient clinics according to hospitals

for them to attend to pandemic hospitals at first whenever they had suspicious symptoms for COVID-19. This awareness facilitated additional work-up for COVID-19 management of these patients in pandemic hospitals while keeping them away from 'clean' hospital.

As we mentioned before, telemedicine application was widely used during pandemic for management of the cancer patients [10]. Telemedicine access for follow-up visits was preferred in both clean and one of pandemic hospitals. It was a chance for the patients especially for those who reside in other cities and rural regions to escape from additional COVID-19 exposure risk during travel to the hospitals for follow-up visits [11, 12]. Relapse rate is higher in the first 2 or 3 years for most cancer types and the patients who covered the first 2 or 3 years of their disease without any relapse seem to be good candidates for telemedicine in daily routine [13, 14]. In this study, unlike pandemic hospitals, a separate telemedicine application was used for patients receiving active CT in clean hospital. By the way, potentially infected patients just because of any COVID-19-suspected symptoms and/or contact history with COVID-19 test positive ones were told not to have CT until clearing COVID-19 status. This measure might have contributed to reducing the COVID-19 positivity rate in 'clean' hospitals compared with 'pandemic' hospitals.

As we know, closer contact with infected people is the most critical risk factor in COVID-19 disease [15, 16]. Isolation and quarantine of infected patients, identification of the people with a possible contact history, and follow-up them closely are main factors for victory in this war [17]. Therefore, filiation teams are organized by the Ministry of Health in our country [17]. They operate COVID-19 action plans in all regions as a national manner. With this respect, the same strategy algorithms are applied in clean and pandemic hospitals. Definition of a comprehensive cancer center as a '*clean*' hospital is almost a part of this strategy. However, '*show must go on for cancer management*' in every circumstance without any interruption since cancer is still among leading causes of death all over the world. So, keeping comprehensive cancer centers as 'clean' centers even during pandemic is not a luxury. It also contributes to the breakdown of COVID-19 spread chain, especially among more frail immunosuppressive patients who tend to have poorer outcomes as if in COVID-19 pandemic.

Healthcare professionals are cornerstones of the health system [18]. They take care of the patients; on the other hand, they might be undesirable vectors for infectious spread especially during unexpected pandemic [18]. Healthcare staff at oncology clinics should be also well protected to protect themselves and to decrease the risk of COVID-19 spread from one to another [18]. Furthermore, healthcare staff especially at special units such as oncology and hematology clinics should be educated for protection of both themselves and the patients.

The pandemic harmed cancer patients in many ways [19–25]. Fear and anxiety associated with COVID-19 caused the patients to delay their treatment by disrupting adherence to therapy [22]. In addition, delaying diagnostic tests was another issue during pandemic leading to the presentation of cancer patients at

advanced stage [20, 21]. Guven et al. evaluated the effect of COVID-19 on admissions of cancer patients and determined that there was a significant decrease in the number of newly diagnosed cancer cases when compared with the previous year [19]. De Vincentiis et al. reported that the average number of newly diagnosed cancer patients in the 2018–2019 period decreased by approximately 39% during the 2020 pandemic period [21]. Similarly, another study conducted in Slovenia showed that diagnostic-screening tests and newly diagnosed cancer patients decreased in the COVID-19 pandemic [20]. In all four experienced centers included in this study, the number of newly diagnosed patients during the pandemic process decreased significantly compared with the previous year as of in our study, in correlation to the literature. The number of new patients diagnosed with cancer might have decreased due to the delay in screening-diagnostic tests and increased COVID-19 anxiety in the pandemic. Healthcare professionals also might have been worried about the infection risk at health centers during the diagnostic and treatment process [24, 26]. In addition, the COVID-19 fear and anxiety of the patients may have caused the diagnosis-screening and treatment process to be delayed [22]. We consider that the number of newly diagnosed cancer patients might have decreased significantly in the pandemic as a result of these concerns of both healthcare professionals and patients. Delay in cancer diagnosis and treatment is negatively correlated with survival [27]. The possible effect of pandemic on cancer mortality has been investigated in the USA and an approximately 1% increase in mortality due to delays in cancer screening and treatment has been predicted (approximately 10,000 more deaths) [28]. We consider that a clean hospital model seems to have role in overcoming of delays in cancer diagnosis and treatment during pandemic by minimizing the risk of COVID-19 spread.

The present study has some limitations. Follow-up period is not so long; however, we aimed to share our experience with comparing '*clean*' and '*pandemic*' hospitals in the first quarter of this unexpected pandemic to enlighten our roadmap. Secondly, only cancer patients who had undergone COVID-19 PCR test for COVID-19 suspicious symptoms and/or COVID-19 contact history on admission to the outpatient medical oncology clinics were included in our study. Transfer of patients diagnosed with COVID-19 who need hospitalization from clean hospitals to pandemic hospitals may have affected the COVID-19 positivity rate. However, in our study, it was thought that transferring only one patient from a clean hospital to a pandemic hospital would not affect the result of the study.

Conclusions

Unfortunately, the COVID-19 pandemic has not been taken under control and it seems to go on as a globally health problem for a long time. The daily number of cases shows that the first wave is not over yet. Even if the first wave ends, the following waves will continue to adversely affect the healthcare system and disrupt the diagnosis-follow-up process of cancer patients. It should be our priority to protect cancer patients especially for those with other risk factors such as cardiopulmonary comorbidities from COVID-19 infection during diagnostic and treatment process. In this respect, further development and universalization of the '*clean*' hospital project in our study may contribute to the protection and better management of cancer patients.

Authors' contributions CK and MD authors contributed to the study conception and design. Material preparation, data collection were performed by CK, RA, OB, TE, MANS, YA, NK, GII, OBO, MD. Statistical analyses were performed by CK. The first draft of the manuscript was written by CK, and MD commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data availability All the database and results of the study are available in the corresponding author and in the center of Dr. Abdurrahman Yurtaslan oncology.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest

Ethics approval This study was approved by Ethical Comittee of Dr Abdurrahman Yurtaslan Oncology Training and Research Hospital (2020/04).

Consent to participate All the methods in the present study were carried out in accordance with guidelines of the Declaration of Helsinki. All participants provided written informed consent.

Consent for publication This study was approved by Republic of Turkey Ministry of Health.

Code availability Not applicable.

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