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The Impact of COVID-19 Within Stage Migration and Upstage in Multiple Cancer Lineages

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Abstract

Background:

The COVID-19 pandemic altered access to healthcare. This resulted in fewer number of

patients who received cancer screening, prompt evaluation, and management, while delaying diagnosis and treatment of multiple cancer types. Currently, there is limited information on staging trends observed after the COVID-19 pandemic. Therefore, we set to evaluate patterns of disease staging at diagnosis and treatment within multiple cancer types by comparing pre, during and post COVID eras. We seek to understand whether there is a COVID effect on the current guidelines for diagnosis, treatment, and surveillance.

Method:

We performed a retrospective review from a high-volume, Commission on Cancer certified institute. Cohorts were grouped into three separate eras, Pre-COVID (PreC) (2013-2020), During COVID (DC) (2020-2021), and Post-COVID (PosC) (2021-present). Clinical and pathological stages were compared across the COVID eras amongst breast, colorectal, prostate, lung, pancreas and gastric cancers. Multivariant analysis, factorial ANOVAs, independent t-test, and chi square analysis evaluated statistic relationships, with a p-value of <0.05 noted as significant.

Results:

Our study population consisted of 16119 individuals with a median age of 67 (SD±12). Staging trends indicated those with breast cancer had a significantly lower clinical stage DC (T1a) and PosC (T1a) compared to PreC era (T1b), (p<0.05). Conversely, lung cancer indicated a significant clinical upstage DC (T3a) when compared to PreC (T2b) (<0.001) but not during PosC (T2b). Further, there was a significant increase in clinical stage DC (T2b) and PosC (T2b) when compared to PreC (T2a) within prostate cancer (<0.001). Similar trends were reflected in colorectal cancer, to which a significant increase in clinical stage DC (T2b) and PosC (T2b) was observed compared to PreC (T2a) (<0.001). No significant difference in staging for pancreatic and gastric cancer was observed.

Conclusion:

Significant staging trends were observed throughout the cancer types when comparing PreC, DC, and PosC cohorts, but the trend depended on cancer type. This potentially highlights awareness of a changing population and healthcare system post pandemic depending on cancer types.

Introduction

The COVID-19 pandemic impacted the world socially, economically, politically, and individually. Due to generalized public health policies, a decrease in access to health care was observed across the globe. A

mandated “social distancing” advised communities to limit interaction, which included clinics and hospitals. A remarkable decrease in regular doctors’ visits and screening appointments, with an increase in emergency healthcare numbers was recorded. This economic crisis led to unemployment and poor household income, enhancing barriers and accentuating inequalities within healthcare access (1).

13,000 deaths per week were attributed to cancer as the underlying diagnosis throughout the pandemic. (2) The rigorous management protocols, required clinic /hospital visits for treatments, and balancing screening recommendations with social distancing, all appear to have contributed to late diagnosis and progression of disease. Several studies have reported an advanced stage at diagnosis, inoperable metastatic disease, and lower five-year survival rate when comparing pre verses during COVID era (3–5). Additionally, those with new cancer diagnosis experienced a reduction and suspension in treatment, whether inpatient or outpatient, due to limited resources initially diverted towards treating patients for COVID-19 (6).

As society focuses on returning to a new “normal”, little has been identified on whether trends persist within cancer care. We believe there is a continuation of a higher clinical and pathological stage observed today. Therefore, we aimed to assess whether there is a clinical/pathological staging upgrade/migration when comparing Pre-COVID (PreC), during COVID (DC), and Post-COVID (PosC) eras in breast, colorectal, prostate, lung, pancreas, and gastric malignancies.

Methods

This was a single-center retrospective review of a high-volume Commission on Cancer Institute from 2013 to 2024. Inclusion criteria consisted of those 18 years or older, with a recorded TMN clinical and pathological staging of lung, prostate, breast, colorectal, pancreas or gastric cancer, and those who underwent elective workup and surgery (emergent surgical interventions were excluded). TMN clinical stage was confirmed via biopsy/imaging results, and pathological stage was classified via post-surgical resection with pathology review. Demographic parameters (age, BMI, smoking status, average stage, etc.) were recorded for each participant. This was exempt from full IRB review due to the non-human subject delineation of our study cohort but did go through the IRB process for non-human subjects research and was approved. We did not require patient consent as identifying factors were de-identified. No experimental process occurred due to the study design and we followed the institutional guidelines and study protocol.

Participant Cohort:

The cohort was divided by cancer type and sub-divided into groups based on the time of clinical diagnosis via biopsy and time of pathological staging post-surgical intervention. These two groups were further divided by dates into three separate eras, PreC (January 2013-Febuary 2020), DC (March 2020-Decemeber 2021), and PosC (December 2021-August 2024) for comparison of staging.

Statistical Analysis:

Factorial ANOVAs were utilized to assess treatment efficacy and pathological staging by era as they uniquely relate to each cancer site. The PosC era had a limited number of cases and could not be included in the full factorial models. Alternatively, one-way ANOVAs with Bonferoni posthoc tests assessed the differences in clinical stage within the three eras among each of the six cancer types. Further, demographic characteristics were evaluated with average, median and percentage calculations, in addition to one-way ANOVA for any statistical relationship between stage and demographic profiles. A p-value of < 0.05 was classified as significant.

Results

Population Characteristics

A total of 16199 patients were included in this study. The average age was 67 years old (SD, 12), and the majority of patients received neoadjuvant or adjuvant treatment for their cancer (73%) (Table 7). The PreC had a total of 11719 (72%) patients within this era; 4342 (27%) were in the DC, and 138 (1%) in the PosC era. In total, there were 5980 (37%) patients diagnosed with breast cancer (PreC, 4403 (74%); DC, 1532 (26%); PosC, 45 (1%)). 3384 (21%) patients diagnosed with colorectal cancer (PreC, 2438 (72%); DC, 908 (27%): PosC, 38 (1%)). 3722 (23%) diagnosed with lung cancer (PreC, 2733 (73%); DC, 959 (26%), PosC, 30 (1%)). 3113 (19%) patients diagnosed with prostate cancer (PreC, 2145 (69%); DC, 943 (30%): PosC, 25 (1%). 780 (5%) patients diagnosed with pancreatic cancer (PreC group, 569 (72.9%), DC, 206 (26.4), PosC, 5 (.06%)). A total of 421 (3%) with gastric cancer (PreC, 328 (77.9%), DC, 90 (21.4%), PosC, 3 (0.07%) Table 1–7).

Cancer Sites:

Breast

The average age was 64 (SD, 12.69) years old with a median cancer stage of T1a (Table 1). There was a significant difference in the clinical stages between the three eras, with Posthoc tests indicating a higher clinical stage in the PreC era (T1b) relative to DC (T1a), and PosC ((T1a) p = < .05) (Graph 1). A multifactorial analysis indicated there was no pathological stage difference between those who received treatment in the PreC (T1a) and DC (T1a) era (p value = .520 (graph 2)). There was a significantly higher stage for those who did not receive treatment in the DC group (T3a) compared to the PreC group (T2b) (P-value < 0.05 (graph 2)). There was a significantly lower stage in the DC group for those who did receive treatment (T1a) compared to those who did not (T3a), which was also reflected in the PreC group (T1a) compared to those who did not receive treatment (T2b) (p-value 0.05).

Colorectal

Patients who presented with colorectal cancer were on average 66 years old (SD, 12.93) and presented at a median stage T2a (Table 2). A one- way ANOVA indicated a significant difference in the clinical stage between the three eras, and Posthoc tests determined clinical stages were significantly lower during PreC era (T2a) compared to DC era (T2b). However, DC was no different than PosC due to the same clinical stage in both cohorts (T2b; p-value < 0.05 (Graph 3)).To further assess results, a multivariant analysis resulted in a significant difference in pathological stage of both PreC and DC eras. DC group had a significant upstage for those who received treatment (T2b) compared to PreC (T2a) era (p-value = 0.05 (graph 4)), but the same stage in both cohorts for those who did not receive treatment (T3a). Further, those who received systemic treatment in both eras had a significantly lower pathological stage (PreC T2a & DC T2b) compared to those who did not receive systemic therapy (T3a; p-value < 0.05). The interaction term was not significant between treatment and era, $p = 0.340$, suggesting that the effect of receiving treatment was not dependent on the era.

Lung

The average age within the lung group was 70 years old (SD, 10.29) and with a median cancer stage of T2b (Table 3). One-way ANOVA indicated, there was a significant difference in the clinical stage between the eras, which Posthoc tests determined the cancer stages were significantly lower in PreC (T2b), compared to DC (T3a) (p-value = < 0.05). However, neither PreC nor DC differed from PosC (T2b) (p = 1.00) (graph 5). DC and PreC cohorts who received treatment had a significant decrease in pathological stage compared to those who did not (DC = T3a vs. T3b and PreC = T2b versus T3a) (p<.05 (graph 6)). When comparing DC and PreC groups, DC had a significantly higher pathological stage, whether receiving treatment or not, compared to PreC cohorts (p-value = < 0.05 (graph 6)).

Prostate

Patients with prostate cancer were on average 68 years old (SD, 8.63) and with a median cancer stage of T2a (Table 4). Results indicated a statistical difference between the three eras, with Post hoc test suggesting clinical stage was significantly lower in PreC (T2a) compared to DC or PosC groups (T2b; p-Value = < 0.05 (graph 7)). A multivariant analysis assessed the PreC and DC eras in regards to treatment and stage correlation. There was a significantly higher stage in the DC group (T2b) for those who received treatment compared to the PreC group (T2a; p-value = < 0.05 (graph 8)). The DC group had a significant difference in staging when comparing those who received (T2b) and did not receive treatment (T2a) (p-value < 0.005). The PreC group had the same stage regardless of whether they received treatment or not.

Pancreas

The median stage for the total cohort was T2b (Table 5). Those in the PreC and DC eras had the same stage of (T2b), compared to PosC era (T2a) (p-value = .354) (graph 9).

Gastric

The median stage for the total gastric cohort was T2a (Table 6). Gastric cancer indicated a down trending stage when comparing PreC (T3a), DC (T2b) and PosC eras (T1a) (graph 10), although not significant (p-value = 0.318).

Discussion

This study analyzed clinical and pathological stages in multiple cancer types throughout pre, during and post COVID periods. To our knowledge, this is the first study to evaluate these factors. Trends appeared to vary between the cancer stages depending on the era. Contradictory to what has previously been described, breast cancer was observed to have a significantly higher clinical and pathological stage in PreC era, and a lower stage in both DC and PosC era. Breast cancer is known to have a well-delineated clinical management pathway, and national education promotion pertaining to screening and treatments. Although screening visits halted during COVID-19, this was only for a short week to month period during this time, and currently has rebounded back to pre-COVID screening numbers (7). For example, when breast cancer screening halted it decreased to 80.6% throughout February and April 2020, but once recommendations to continue screening were promoted, in June 2020 rates increased to 77.7% of those undergoing follow up screening appointments (8). Further, breast cancer screening in 2023 compared to 2019 had a 7% increase in visits (9). Additionally, Berardi et al evaluated 6 institutions from March to December 2020 and found no negative impact on staging, diagnosis or treatment due to COVID-19 on post-COVID breast cancer population (10). They further concluded there was no time difference between symptom onset and radiographic or cytohistological diagnosis during COVID-19, and diagnosis and treatment were maintained or improved post-COVID, which may correlate with our staging results.

Based on our results, colorectal cancer (CRC) had an increased clinical stage when comparing PreC, DC, and PosC. This is seen in other studies, such as Domper-Arnel also observed a higher stage during COVID when compared to pre-COVID (11). This increase in staging during COVID may be related to screening options for CRC. A 43% decrease in colonoscopy referral, 65.7% decrease in completion colonoscopies, and an increase from 2 to 9% in emergent colonoscopies were reported throughout the pandemic (12). This was similar across additional colonoscopy centers (13–14). Further, there was an uptrend within emergent abdominal presentations of CRC, such as bowel perforations and obstructions stemming from malignant colonic pathology (15). Currently, CRC screening visits continue to be lower than pre-pandemic levels (16). It is postulated if CRC screening is delayed by less than 12 months, patients with advance disease increase from 26 to 29% at presentation, and if delayed further will increase by 33%. (17). During the pandemic, home test were available for CRC screening, and therefore may have been (and still may be) beneficial to increase promotion and education to the general population of the varying screening options to decrease missed appointments.

Both prostate and lung cancer resulted in similar staging trends as CRC, with a higher pathological stage DC and PosC compared to PreC eras. Both rely on imaging modalities for diagnostic identification and

confirmation via biopsies of observed tumors. Lung cancer screening recommends CT imaging and prostate cancer relies on MRI for diagnostic and prognostic identification, but overall, imaging (CT, MRI, PET) is vital within cancer care as the modality for disease surveillance and monitoring. During COVID, there was a 55% decrease in total imaging and 88% within emergency departments alone (18), which is a common area many incidental cancers are discovered. Further, both prostate and lung cancer, in addition to all other types, require access to primary care physicians for monitoring, surveillance, and referral status. Ambulatory care practices had a 60% decrease in visits throughout March and April of 2020 (19). Although there has been an increase in doctor visits since the time of pandemic, we still have yet to return to pre-pandemic levels. (20). A common substitute during the pandemic was Tele-health communication. Tele-health continues to indicate similar pandemic trends with a 22% increase in communication compared to pre-pandemic levels, but studies still inqure an inferior level of care compared to in person check-ups (21). Due to tele-health visits as a continuing option, education in effective communication for clinicians and patients when assessing signs/symptoms in regards to co-morbid conditions, such as cancer, is warrented.

Limitations

Limitations of the study include the retrospective nature and its inherent bias. Accuracy of data is dependent on individual practitioners and our data registry team for extraction. Nevertheless, these factors remained constant for the entire time studied. This study also involved one institution and may not represent a broader general population or geographical area. Public health policies and the severity of the pandemic were not uniform from state to state and may have impacted other geographical areas differently. Finally, various confounding factors could exist as patient demographics, and other social determinants can differ significantly from region to region, which can impact the degree of access to general health care during this period.

Conclusions

This is the first study to assess current trends observed post-Pandemic in multiple cancer types. Despite limitations, this study provides valuable insight on COVID-19's impact on migration and upgrade at diagnosis and treatment of various cancer types. Access was granted to a large cohort of data points at an accredited Cancer on Commission center, which provided a high statistical power for analysis. In regards to this, we observed a varying uptrend within the migration and upgrade of several cancer types.

Ultimately, COVID-19 will have a permanent mark in history and has changed our society in multiple ways. We believe after assessment there was and is a “COVID Effect” when pertaining to clinical and pathological cancer staging. Even though cancer diagnosis and management were only one of many health conditions affected by the pandemic, we hope to promote a focus on elucidating an improved approach to cancer screening, diagnosis, and management in an ever-changed society.

Declarations

Author Contribution

T.N was involved in study idea and direction for study cohort selection with manuscript review. L.M coordinated data/patient cohort retrieval, generated direction of statistical analysis, and then writing the manuscript. E.C was involved in statistical analysis and writing the methods and statistical results. D.D and M.M helped with guidance throughout cohort selection and review of manuscript.

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Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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