ISSN (e): 2250 – 3005 || Volume, 14 || Issue, 4|| Jul. - Aug. – 2024 ||
International Journal of Computational Engineering Research (IJCER)

Case study for The COVID-19 and cancer human

Narjis Yassir Khudir ,Fatma Yassir Khudir

Abstract: *The COVID-19 pandemic has created major disruptions in cancer care, with reductions in diagnostic tests and treatments. We evaluated the impact of these health care–related changes on cancer staging by comparing cancers staged before and during the pandemic. We performed a retrospective cohort study at London Health Sciences Centre and St. Joseph's Health Care London, London, Ontario, Canada. We evaluated all pathologically staged breast, colorectal, prostate, endometrial and lung cancers (the 5 most common cancers by site, excluding non-melanoma skin cancer) over a 3-year period (Mar. 15, 2018–Mar. 14, 2021). The pre-COVID-19 group included procedures performed between Mar. 15, 2018, and Mar. 14, 2020, and the COVID-19 group included procedures performed between Mar. 15, 2020, and Mar. 14, 2021. The primary outcome was cancer stage group, based on the pathologic tumor, lymph node, metastasis system. We performed univariate analyses to compare demographic characteristics, pathologic features and cancer stage between the 2 groups. We performed multivariable ordinal regression analyses using the proportional odds model to evaluate the association between stage and timing of staging (before v. during the pandemic).*

Date of Submission: 14-07-2024 Date of acceptance: 30-07-2024

I. Introduction

Cancer refers to any one of a large number of diseases characterized by the development of abnormal cells that divide uncontrollably and have the ability to destroy normal body tissue. Cancer often has the ability to spread throughout the body. Cancer is the second-leading cause of death in the world.Cancer cells need a blood supply to survive and develop into a tumor. Vascularization can be achieved in several ways. When cancer cells induce angiogenesis, the blood supply is provided by newly formed vessels. In rare occasions, cancer cells do not induce the formation of new vessels but instead line blood-perfused channel, a process called vas congenic mimicry. A more common mechanism of no antigenic tumor growth relies on the co-option of the normal preexisting vasculature.[1]

- Nomenclature of cancer The origin of the word cancer is credited to the Greek physician Hippocrates (460-370 BC), who is considered the "Father of Medicine." Hippocrates used the terms carbines and carcinoma to describe non-ulcer forming and ulcer-forming tumors. In Greek, these words refer to a crab, most likely applied to the disease because the finger-like spreading projections from a cancer called to mind the shape of a crab. another Greek physician, used the word oncos (Greek for swelling) to describe tumors.[2]
- Causes and risk factors of cancer

In 1977, four scientists, Higginso, Muir, Doll, and Peto explained the evidences that 80% of all cancers were caused by environmental factors. Their studies included the epidemiological data relating to migrants, geographical variation, changes in risk over time, correlation studies, clusters and case reports. In the past 30 years, there have been several efforts to estimate the proportion of cancer due to these involuntary exposures to environmental factors. Carcinogenesis refers to an underlying cancer causing elements that lead to cancer. Several models of carcinogenesis have been proposed. Two widely cited models of carcinogenesis are those of Vogelstein and Kinzler as well as Hanahan and Weinberg. The model of Vogelstein and Kinzler emphasizes that cancer is a disease of damaged DNA, comprised of a series of genetic mutations that can transform normal cells to cancerous cells.

The genetic mutations include inactivation of tumor suppressor genes and activation of oncogenes. The model of Hanahan and Weinberg focuses on the hallmark events at the cellular level that lead to a malignant tumor. In this model, the hallmarks of cancer include sustained angiogenesis, unlimited replication, evading apoptosis, self-sufficiency in growth signals, and insensitivity to antigrowth signals, leading to the defining characteristics of malignant tumors by giving them the ability to invade and metastasize. This theory is based on the dual premise that carcinogenesis is driven by defects in tissue organization and that all cells are inherently in a proliferative state.[8]

The following factors were selected that appear to increase the risk of different types of human cancers:

1. Aging

The most important risk factor for cancer is growing older. Most cancers occur in people over the age of 55, but cancer can occur in younger ages as well. Both cancer and ageing result from accumulating damage to the stem and progenitor cells. Certain genetic mutations cause the stem cells to divide out of control which lead to cancer. Normal somatic cells telomere losses are coupled with increasing age of the organism. Due to mutations in the TERC and TERT telomerase genes, telomeres will shorten in human premature ageing syndromes and dyskeratosis congenital (10). Environmental factors such as; stress, social status, smoking and obesity can also accelerate telomere shortening due to reduced telomerase activity. In contrast to normal somatic cells, most human tumors have activated telomerase to achieve immortal growth.[8]

2. Family history

Most cancers develop because of genetic mutations. Some genetic changes that increase the risk of cancer are passed from parent to child. Certain types of cancer do occur more often in some families than in the rest of the population, such as; colon cancer. Familial adenomatous polyposis (FAP) is a good example of hereditary colon cancer. People with FAP may have over hundred polyps in their colon. If it is untreated, one of these polyps will develop to cancer. Removing the polyps by early surgery will enhance the recovery. Another inherited syndrome that increases colon cancer is hereditary non-polyposis colorectal cancer (HNPCC) or Lynch syndrome. People with this syndrome have a higher risk of colorectal cancer. People with HNPCC have only a few polyps with a high risk of developing uterus, ovary, bladder, kidney and brain cancers. Inheriting a gene change does not mean that you will definitely develop cancer. It means that you have an increased chance of developing the disease. Following indications can increase the risk of developing cancers. Such as; tumor on the same side of the family, two cases of rare cancers in the same family and family history of multiplicity of primary tumors. [8]

3. Smoking

Tobacco use is the most preventable cause of death. Each year, more than 180,000 Americans die from cancer as a result of smoking. More than 85% of all lung cancers and 30% of all deaths are caused by smoking. Second hand smoke can also increase 5% the risk of cancer. Smokers are more likely than nonsmokers to develop different types of cancers, such as; lung, larynx, mouth, esophagus, bladder, kidney, throat, stomach, pancreas, cervix and acute myeloid leukemia. Among 4000 chemicals that have been identified in tobacco smoke, at least 400 are known to be harmful to human health, such as; hydrogen cyanide, carbon monoxide, and ammonia. Almost 40(10%) of these toxic chemicals are shown to be carcinogenic. [8]

4. Alcohol

Alcohol consumption causes 3.6 % of all human cancers. Having more than two drinks each day for many years will increase the chance of developing cancers of the mouth, throat, esophagus, stomach, liver, colon, lymphomas, prostate, kidney, breast and ovaries. Alcohol has been classified by World Health Organization (WHO) as group-1- carcinogen. Liver can process 7 grams of ethyl alcohol each hour. When liver processes alcohol, it will produce acetaldehyde which is carcinogenic. Higher exposure to acetaldehyde will induce a defect in alcohol dehydrogenase gene and tumor suppressor gene (BRCA) inactivation that can lead to the upper gastrointestinal tract, breast and liver cancers. Iron accumulation, retinoic acid impairment, acetaldehyde genotoxicity, increased estrogen concentration, free radical production and folate metabolic alterations are induced by chronic alcohol abuse. Liver cirrhosis caused when liver cells are replaced with scars due to chronic alcohol use. Almost 5% of people with cirrhosis lead to liver cancer .The risk is 35% higher for drinkers with simultaneous smoking habits. [8]

5. Sunlight and ionizing radiation

Ultraviolet (UV) radiation comes from the sun, sunlamps, and tanning booths. It causes early aging of the skin that can lead to skin cancer. UV radiation can penetrate light clothing, windshields, and windows. Three types of sun radiations include the visible (color), infrared (heat) and UV lights (UVA, UVB, UVC). The UV light from sun and tanning can cause skin damages, such as; benign, pigmentation, discoloration, freckles, sunburn, cancers (Basal cell carcinoma, squamous carcinoma and Melanoma) and destruction of elastin and collagen proteins. Exposure to UV sunlight produces the same skin damages in winter as well as summer time. Skin damages could be reduced and /or prevented by: 1. Avoiding direct sunlight exposure between 10:00 a.m. and 3:00 p.m. 2. Use sun protection factor cream (SPF-50) 30 minutes before sun exposure. 3. Proper use of clothing protection and sunglasses with UV protection. 4. Regular self-skin examination. Ionizing radiation can cause cell damage that leads to cancer. [8]

6. Viruses and Bacteria

Infectious micro-organisms have been estimated to cause 18% of all cancer cases. The burden of cancers caused by infections is much greater in developing nations (26%) than in developed nations (8%).Human papilloma-viruses (HPVs): HPV infection is the main cause of cervical cancer. Infection with an oncogenic strain of human papillomavirus (HPV) is considered a necessary event for subsequent cervix cancer, and vaccine-conferred immunity results in a marked decrease in precancerous lesions.Hepatitis B and hepatitis C viruses: Both viruses can cause liver cancerHuman immunodeficiency virus (HIV): HIV is the virus that causes AIDS. People who have HIV infection are

at great risk of lymphoma and Kaposi's sarcoma cancers (20).Epstein-Barr virus (EBV): Infection with EBV has been linked to Burkitt's lymphoma.
Human herpesvirus-8 (HHV8): This virus is a main risk factor for Kaposi's sarcoma cancer.Helicobacter pylori: This bacterium can cause stomach ulcers that can lead to MALT-lymphoma in the stomach and esophageal cancer (22).
Salmonella typhoid: This bacterium can cause gallbladder cancer.

Streptococcus bovid: This bacterium can cause colon cancer. [8]

7. Organic and inorganic chemicals

A number of chemical substances revealed to be dangerous at high concentrations. These cancer causing agents are called carcinogens. We have more than 100,000 chemical elements in our environment in which 30,000 of them have been analyzed. Out of 30,000 analyzed ones, only 275 of them proved to be carcinogenic. People who have certain jobs such as; painting, construction, pesticide and petroleum workers have an increased risk of cancer. Many studies have shown that exposure to asbestos, benzene, Benzedrine, cadmium, nickel, arsenic, radon and vinyl chloride in the workplace can cause cancer. [8]

8. Diet and obesity

People who have a poor diet with reduced physical activity may be at increased risk of several diseases. Obese people will be at higher risk of coronary heart disease, stroke, high blood pressure, diabetes, and cancers (esophagus, breast, uterus, colon, rectum and prostate). Fat tissue produces high quantity of estrogen which is linked to increased risk of cancers. Also, obese people may produce high amount of insulin-like growth factor-1 (IGF-1) in their blood which may lead to certain cancers. Leptin and adiponectin are produced by fat cells which can promote and inhibit cell proliferation, respectively.Having a healthy diet, and being physically active may help to reduce cancer risks. [8]

- Diagnosis of cancer

The goal of cancer screening and early detection is to cure cancer by detecting the malignancy, or its precursor lesion, at an early stage prior to the onset of symptoms.
The most successful cancer screening programs lead to the identification of precursor lesions where the treatment of the precursor lesion leads to a decrease in the incidence of invasive cancer over time.[9]
High or low levels of certain substances in the body can be a sign of cancer. So, lab tests of blood, urine, or other body fluids that measure these substances can help doctors make a diagnosis. [10]

Imaging Tests

Imaging tests create pictures of areas inside your body that help the doctor see whether a tumor is present. These pictures can be made in several ways:

CT scan

A CT scan can help doctors find cancer and show things like a tumor's shape and size. CT scans show a slice, or cross-section, of the body. The image shows the bones, organs, and soft tissues more clearly than standard x-rays. By layering CT image slices on top of each other, the machine can create a 3-dimensional (3-D) view. The 3-D image can be rotated on a computer screen to look at different angles.CT scans can show a tumor's shape, size, and location. They can even show the blood vessels that feed the tumor – all without having to cut into the patient.Also by comparing CT scans done over time, doctors can see how a tumor is responding to treatment or find out if the cancer has come back after treatment.[11]

MRI

MRI creates cross-section pictures of the insides. But MRI uses strong magnets to make the images – not radiation. It helps doctors find cancer in the body and look for signs that it had metastasized. MRI also can help doctors plan cancer treatment, like surgery or radiation. [12]

II. Setting and design

We performed a 3-year (March 2018–March 2021) retrospective cohort study at London Health Sciences Centre and St. Joseph's Health Care London, a network of academic tertiary hospitals in London, Ontario, Canada. In Canada, all medically necessary health care services are covered under a publicly funded health care system; the delivery and administration of health care services, including those related to the pandemic, generally occurs at the provincial level. The London Health Sciences Centre and St. Joseph's Health Care London cancer program is the regional referral center for southwestern Ontario, serving a catchment area of more than 1.5 million people. We reported the study in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[12] In Ontario, the pathologic staging of primary cancers is reported via an electronic standardized synoptic format, based on the College of American Pathologists Cancer Protocols templates.[13,14] These protocols are generally organized by disease site, with each protocol containing an established set of mandatory reporting items. We first used our institutional cancer

reporting data to identify the 5 most common cancers by site (excluding no melanoma skin cancer). Using our departmental laboratory information system, we identified all cancer staging procedures for these sites performed between Mar. 15, 2018, and Mar. 14, 2021. We based the comparison groups on the surgery date: procedures performed between Mar. 15, 2018, and Mar. 14, 2020, were included in the pre-COVID-19 group, and procedures performed between Mar. 15, 2020, and Mar. 14, 2021, were included in the COVID-19 group. We used the cutoff of Mar. 15, 2020, because it was the start of the first province-wide ramping down of elective operations and nonemerging activities.[15] During these periods, hospitals in the province implemented measures to maintain readiness for a potential surge in COVID-19 cases, including reserving at least 10% of acute bed capacity and maintaining at least 15 days' worth of personal protective equipment. Guidelines for triaging and prioritizing cancer care were also developed.[16] Generally, surgical management for patients with cancer was prioritized in cases with greater risk of imminent morbidity or death, lower risk of COVID-19-related critical illness and lack of effective alternative treatments.

III. Data collection

We used the pathologic cancer stage group, determined with the tumour, lymph node, metastasis system of the eighth edition of the *AJCC Cancer Staging Manual*,[17] as the outcome variable. In cases in which pathologic staging was performed over multiple procedures, most commonly in breast cancers with separate sentinel lymph node sampling, we collated this information to determine the final stage group. We documented whether the case was staged as a tumors recurrence or after neoadjuvant therapy, and whether there were multiple primary tumor's. In the case of multiple primary tumor's, we used the tumors with the most advanced stage for analysis.For all cases, we collected demographic information, including patient age and sex, as well as information regarding the specimen and procedure. For all primary cancers, we also extracted macroscopic and microscopic features that are included in the synoptic report but are not directly used for staging, with the variables specific to each cancer site. Generally, these features are indicators of tumors aggressiveness and may be used to inform prognosis or guide treatment decisions, or both. For breast and colorectal cancers, which have population-wide screening programs, we reviewed the patients' electronic medical records to determine the clinical presentation and whether the cancer was initially detected via screening.We used the pathology reports and electronic medical records to extract data for analysis, and all cases were identified by means of a unique study identifier. The pathology reports and demographic information for the included cases were retrieved from our laboratory information system. Within the synoptic reports, the data fields containing the pathologic stage and cancer features were automatically extracted for analysis. The collected data were reviewed with the original pathology report to confirm accurate extraction.

IV. Results

There were 4055 cases across the 5 cancer sites. The average number of breast cancer staging procedures per 30 days increased during the pandemic compared to the yearly average in the pre-COVID-19 period (41.3 v. 39.6), whereas decreases were observed for endometrial cancer (15.9 v. 16.4), colorectal cancer (21.8 v. 24.3), prostate cancer (13.6 v. 18.5) and lung cancer (11.5 v. 15.9). For all cancer sites, there were no statistically significant differences in demographic characteristics, pathologic features or cancer stage between the 2 groups ($p > 0.05$). In multivariable regression analysis, for all cancer sites, cases staged during the pandemic were not associated with higher stage (breast: odds ratio [OR] 1.071, 95% confidence interval [CI] 0.826–1.388; colorectal: OR 1.201, 95% CI 0.869–1.661; endometrium: OR 0.792, 95% CI 0.495–1.252; prostate: OR 1.171, 95% CI 0.765–1.794; and lung: OR 0.826, 95% CI 0.535–1.262).

V. Conclusion

We did not find a statistically significant shift in cancer stage in the first year of the COVID-19 pandemic compared to the 2 years before the pandemic. There were variable reductions in the number of cases across cancer sites, which likely reflect differences in clinical presentation, disease detection and treatment. Long-term surveillance is required to fully understand the impact of COVID-19-related health care changes on cancer outcomes at the population level.

References

[1] "Tumor Vascularization | ScienceDirect." Accessed: Feb. 13, 2021. [Online]. Available: https://www.sciencedirect.com/book/9780128194942/tumor-vascularization#book-description.
[2] "Early History of Cancer | American Cancer Society." https://www.cancer.org/cancer/cancer-basics/history-of-cancer/what-is-cancer.html (accessed Feb. 13, 2021).
[3] "What Is Cancer? - National Cancer Institute," Sep. 17, 2007. https://www.cancer.gov/about-cancer/understanding/what-is-cancer (accessed Feb. 13, 2021).
[4] "Sarcoma - PubMed." https://pubmed.ncbi.nlm.nih.gov/17976362/ (accessed Feb. 13, 2021).
[5] S. A. Bird and K. Boyd, "Multiple myeloma: an overview of management," *Palliat. Care Soc. Pract.*, vol. 13, Oct. 2019, doi: 10.1177/1178224219868235.

[6] "Cancer Staging." https://www.cancer.org/treatment/understanding-your-diagnosis/staging.html (accessed Feb. 13, 2021).
[7] "Stages of Cancer," *WebMD*. https://www.webmd.com/cancer/cancer-stages (accessed Feb. 13, 2021).
[8] "Environmental Factors Inducing Human Cancers." https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3521879/ (accessed Feb. 16, 2021).
[9] "Cancer screening and early detection in the 21st century." https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5467686/ (accessed Feb. 16, 2021).
[10] "How Cancer Is Diagnosed - National Cancer Institute." https://www.cancer.gov/about-cancer/diagnosis-staging/diagnosis (accessed Feb. 16, 2021).
[11] "CT Scan for Cancer." https://www.cancer.org/treatment/understanding-your-diagnosis/tests/ct-scan-for-cancer.html (accessed Feb. 16, 2021).
[12] "MRI for Cancer." https://www.cancer.org/treatment/understanding-your-diagnosis/tests/mri-for-cancer.html (accessed Feb. 16, 2021).
[13] "Nuclear Medicine Scans for Cancer." https://www.cancer.org/treatment/understanding-your-diagnosis/tests/nuclear-medicine-scans-for-cancer.html (accessed Feb. 16, 2021).
[14] "Tumor Markers - National Cancer Institute." https://www.cancer.gov/about-cancer/diagnosis-staging/diagnosis/tumor-markers-fact-sheet (accessed Feb. 16, 2021).
[15] "Surgery for Cancer - National Cancer Institute." https://www.cancer.gov/about-cancer/treatment/types/surgery (accessed Feb. 17, 2021).
[16] "Radiation Therapy for Cancer - National Cancer Institute." https://www.cancer.gov/about-cancer/treatment/types/radiation-therapy (accessed Feb. 17, 2021).
[17] "Chemotherapy to Treat Cancer - National Cancer Institute." https://www.cancer.gov/about-cancer/treatment/types/chemotherapy (accessed Feb. 17, 2021).
[18] "Immunotherapy for Cancer - National Cancer Institute." https://www.cancer.gov/about-cancer/treatment/types/immunotherapy (accessed Feb. 17, 2021).
[19] "Hormone Therapy for Cancer - National Cancer Institute." https://www.cancer.gov/about-cancer/treatment/types/hormone-therapy (accessed Feb. 17, 2021).
[20] "Stem Cell Transplants in Cancer Treatment - National Cancer Institute." https://www.cancer.gov/about-cancer/treatment/types/stem-cell-transplant (accessed Feb. 17, 2021).
[21] "Targeted Therapy for Cancer - National Cancer Institute." https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies (accessed Feb. 17, 2021).
[22] "Precision Medicine in Cancer Treatment - National Cancer Institute." https://www.cancer.gov/about-cancer/treatment/types/precision-medicine (accessed Feb. 17, 2021).
[23] "Cancer is a Preventable Disease that Requires Major Lifestyle Changes." https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2515569/ (accessed Feb. 19, 2021).
[24] "Frontiers | Long Non-coding RNAs in Cancer: Implications for Diagnosis, Prognosis, and Therapy | Medicine." https://www.frontiersin.org/articles/10.3389/fmed.2020.612393/full#B13 (accessed Feb. 19, 2021).
[25] "Molecular mechanisms of long noncoding RNAs." https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3199020/ (accessed Mar. 05, 2021).
[26] "Long Noncoding RNAs as Biomarkers in Cancer." https://www.hindawi.com/journals/dm/2017/7243968/ (accessed Feb. 20, 2021).
[27] "Long Non-coding RNAs in Cancer: Implications for Diagnosis, Prognosis, and Therapy." https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7734181/ (accessed Feb. 23, 2021).
[28] "Gene therapy: advances, challenges and perspectives." https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5823056/ (accessed Feb. 24, 2021).
[29] "Nonviral Gene Delivery: Principle, Limitations, and Recent Progress." https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2782077/ (accessed Feb. 26, 2021).
[30] "Gene Therapy: Some History, Applications, Problems, and Prospects - Ana P. Cotrim, Bruce J. Baum, 2008." https://journals.sagepub.com/doi/full/10.1177/0192623307309925 (accessed Feb. 28, 2021).
[31] "Gene Therapy for Cancer Treatment: Past, Present and Future." https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1570487/ (accessed Mar. 02, 2021).
[32] "Gene therapy for cancer: present status and future perspective." https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4452068/ (accessed Mar. 02, 2021).
[33] "Gene Therapy Used in Cancer Treatment." https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5423469/ (accessed Mar. 02, 2021).
[34] "Gene Therapy Used in Cancer Treatment." https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5423469/ (accessed Feb. 28, 2021).