Review Article

Reduction in the Number of Diagnoses of Upper Digestive Tract Cancer during the Covid-19 Pandemic: An Integrative Literature Review

Redução do Número de Diagnóstico de Câncer do Trato Digestivo Alto durante a Pandemia Covid-19: Revisão Integrativa de Literatura

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Goi APC, Dalbosco AK, Vedana B, Pilatti D, Garcia MC, Alt LL. Reduction in the Number of Diagnoses of Upper Digestive Tract Cancer during the Covid-19 Pandemic: An Integrative Literature Review / Redução do Número de Diagnóstico de Câncer do Trato Digestivo Alto durante a Pandemia Covid-19: Revisão Integrativa de Literatura. Rev Med (São Paulo). 2024 Jan-Feb;103(1):e-210147.

ABSTRACT: Introduction: In 2019, the World Health Organization was alerted about cases of infection with COVID-19. Due to the measures taken to prevent contamination, many pre-scheduled consultations, treatments and exams were suspended or cancelled. Objectives: This study aims to identify literature data on upper digestive tract cancer diagnosis numbers in patients that had performed endoscopy during the COVID-19 pandemic, along with a pre-pandemic control group. Methods: A literature review was performed through searches on the SciELO, Science Direct, PubMed, and BVS Regional Portal platforms. After applying the inclusion and exclusion criteria, 8 articles were selected for the study. Results: All articles reported a decrease in diagnoses of upper digestive tract cancer (reduction ranged from 76.3% to 19.28%) and in endoscopies performed (reduction ranged from 87.5% to 43.1%) during the pandemic. Conclusion: The COVID-19 pandemic reduced the accessibility of resources and; consequently, increased the number of underdiagnoses of pathologies with no direct relationship with the coronavirus. Thus, a significant reduction in the number of diagnoses of upper digestive tract cancer was observed due to the decline in the number of endoscopies performed.

KEY WORDS: Gastrointestinal Neoplasms, Diagnosis, Endoscopy, COVID-19.

RESUMO: Introdução: Em 2019, a Organização Mundial de Saúde foi alertada sobre casos de infecção por COVID-19. Devido às medidas adotadas para prevenção de contaminação, muitas consultas, tratamentos e exames pré-agendados foram suspensos ou cancelados. Objetivos: Este estudo visa identificar dados na literatura sobre a número de diagnóstico de câncer do trato digestivo superior em pacientes que realizaram endoscopia durante a pandemia por COVID-19, com grupo controle pré-pandêmico. Métodos: Foi realizada uma revisão de literatura, por meio de buscas nas plataformas SciELO, Science Direct, PubMed, Portal Regional da BVS. Após os critérios de inclusão e exclusão aplicados, foram selecionados 8 artigos para o estudo. Resultados: Todos os artigos relataram diminuição de diagnósticos de câncer do trato digestivo superior (indicando reduções entre 76,3% a 19,28%) e de endoscopias realizadas (reduções variaram entre 87,5% a 43,1%) durante a pandemia. Conclusão: A pandemia por COVID-19 diminuiu a acessibilidade de recursos e, sendo assim, aumentou o número de subdiagnósticos de doenças sem relação direta com o coronavírus. Dessa forma, observou-se uma significativa redução de diagnósticos de câncer de trato digestório superior, em consequência ao declínio no número de endoscopias realizadas.

DESCRITORES: Neoplasias Gastrointestinais, Diagnóstico, Endoscopia, COVID-19.

Work presented at the event: IX Academic Week of Knowledge UPF - University of Passo Fundo on September 29, 2022.

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INTRODUCTION

On December 31, 2019, the World Health Organization (WHO) was alerted about pneumonia in the city of Wuhan, China. As a result, cases of a new strain of coronavirus that had not previously been identified in humans spread to several countries and regions around the world, characterizing the COVID-19 pandemic¹.

In addition to the difficulties caused by the new disease, other health sectors were affected during the pandemic period. The impact of COVID-19 on the accessibility of investigations, patterns of other diseases and the volume of patients undergoing tests significantly decreased, making early diagnosis difficult and causing negative consequences in the prognosis of pathologies².

Directing this perspective to the oncology area, it is notable that pre-scheduled appointments, treatments and exams were suspended or canceled both at the patient's request and due to security measures adopted by health institutions. The direct effect of the pandemic lockdown on the number of endoscopies affects initial staging, therapeutic options and patient survival³.

Despite the strategies used during the pandemic, the reduction in endoscopies performed may have led to a reduction in the diagnoses of upper digestive tract cancer. Considering this scenario, a lower number of diagnoses during this period could result in late diagnoses later. Therefore, this study sought to identify data in the scientific literature on the number of diagnoses of upper digestive tract cancer in patients who underwent endoscopy during the COVID-19 pandemic with a pre-pandemic control group.

METHOD

This study is an integrative literature review in which searches were conducted in the SciELO, Science Direct, PubMed, and VHL Regional Portal databases from May to July 2021. The searches were conducted to find articles which demonstrate data on the number of diagnoses of upper digestive tract cancer in patients who underwent endoscopy during the COVID-19 pandemic with a pre-pandemic control group; first, the main Health Sciences Descriptor terms related to the topic and some uncontrolled vocabulary terms which appear with certain frequency in these articles were chosen to construct the search string. Thus, two strings were selected, and two searches were conducted on the platforms: search 1- [(Diagnosis) AND (Stomach Neoplasm) OR (Gastric Cancer) Or (Esophageal Neoplasm) OR (Esophageal Cancer) AND (COVID-19) OR (SARS-CoV-2)]; search 2- [Diagnosis AND (Gastrointestinal Neoplasms OR Gastrointestinal Cancer OR Digestive System Neoplasms OR Digestive System Cancer) AND (COVID-19 OR SARS-CoV-2)1.

Only retrospective observational works that contain real data on cancer diagnoses of the upper digestive tract during the COVID-19 pandemic with a control group from the prepandemic period published in the period 2019 to 2021 were selected as the pre-determined criteria for including articles in this integrative literature review. Furthermore, articles from all languages were included. Comments, preprints, correspondence, position statements, guidelines, literature reviews, conference abstracts, articles that did not report data on diagnoses of upper digestive tract cancers during the COVID-19 pandemic were excluded.

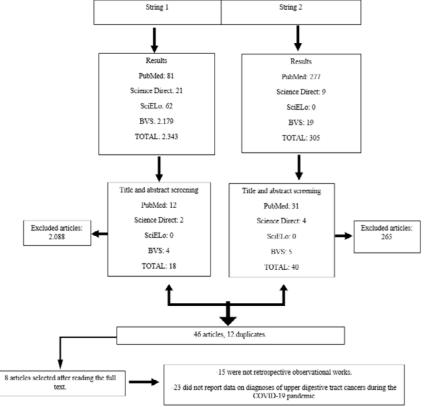


Figure 1 - Article search and selection flowchart.

RESULTS

After reading the articles and applying the exclusion and inclusion criteria, 8 articles were selected (Table 1). We can highlight that all authors showed a reduction in the diagnoses of

upper digestive tract cancer during the pandemic in these studies, as demonstrated in Table 2. Furthermore, the quantification of the reduction in the number of endoscopies performed during the pandemic period (demonstrated in the second column in Table 2) shows the significant results found.

Table 1 - Articles selected.

Authors	Title	Publication date	Journal, Volume and Pages	DOI	Study design
Thomas K. L. Lui, Kathy Leug, Chuan- Guo Guo et al.	"Impacts of the Coronavirus 2019 Pandemic on Gastrointestinal Endoscopy Volume and Diagnosis of Gastric and Colorectal Cancers: A Population-Based Study."	May 16, 2020	Gastroenterology. Vol. 159 Pág. 1164-1166	10.1053/j. gastro.2020.05.037	Cross-sectional Observational Study
Mauele Furnari, Leonardo Henry Eusebi, Edoardo Savarino et al.	"Effects of Sars-CoV-2 emergency measures on High-risk lesion detection: multicentre cross-sectional study."	Sept. 28, 2020	Gut. Vol 70 Pág 1241-1243	10.1136/ gutjnl-2020-323116	Cross-sectional Observational Study
Matthew D. Rutter, Matthew Brokes, Thomas J Lee	"Impact of the COVID-19 pandemic on UK endoscopy activity and cancer detection: a National Endoscopy Database Analysis."	July 20, 2020	Gut. Vol 70. Pág 537-543	10.1136/ gutjnl-2020-323116	Cross-sectional Observational Study
Xavier Bosh Aina Capdevila, Ignacio Grafia et al	"The impact of COVID-19 on patients with suspected cancer: An analysis of ED presentation and referrals to a quick diagnosis unit."	April 2, 2021	The American Journal of Emergency Medicine. Vol 48, Pág 1-11.	10.1016/j. ajem.2021.03.087	Cross-sectional Observational Study
Gais LongCroft- Whean Natalie Tolfree, Anmol GAngi et al.	"Data from a large Western centre exploring the impact of COVID-19 pandemic on endoscopy services and cancer diagnosis."	July 30, 2020	Gastroenterology. Vol 12. Pág 193-199	10.1136/ flgastro-2020-101543	Cross-sectional Observational Study
Ahmad Khan, Mohammad Bilal, Vicent Morrow et al.	"Impact of the Coronavirus Disease 2019 Pandemic on Gastrointestinal Procedures and Cancers in the United States: A Multicenter Research Network Study."	March 1, 2021	Gastroenterology. Vol 160. Pag 2602- 2604.	10.1053/j. gastro.2021.02.055	Cross-sectional Observational Study
Marten A. Lantinga, Felix Teunissen, Pieter C. J. ter Bong et l.	"Impact of the COVID-19 pandemic on gastrointestinal endoscopy in the Netherlands: analysis of a prospective endoscopy database."	Oct. 20, 2020	Endoscopy. Vol 53. Pág 166-170	10.1055/a-1272-3788	Cross-sectional Observational Study
L Zhu, M Y Cai, Q Shi et al.	"Analysis of selective endoscopy results during the epidemic of coronavirus disease 2019 (COVID-19)	April 25, 2020	Chinese Journal of Gatrointestinal surgery. Vol 23. Pág 327-331.	10.3760/ cma.j.issn.1671- 0274.2020- 0316-00147	Retrospective cohort

Among the studies, Lui et al.⁴ analyzed the period between 01/10/2019 and 31/03/2020 in Hong Kong, and found a reduction of 46.2% in cancer diagnoses and 51% in the number of endoscopies among the studied population. Thus, a weekly average of 22.9 diagnoses was found in the pre-pandemic period and an average of 12.3 during the pandemic, totaling 123. Regarding the number of endoscopies, 1,813 were performed per week before the pandemic and 887/week during the pandemic (total of 8,878).

In line with Lui et al.⁴, the authors Furnari et al.⁵ compared

the period from 03/09 to 05/04 of 2019 to the same equivalent period in 2020 in the city of Genova, Italy, and found similar results, with the reduction in cancer diagnoses equal to 62.4% and the number of endoscopic exams of 71.4%. The researcher obtained a number of 1,661.6 endoscopies per week in the prepandemic period and diagnosed gastroesophageal cancer in 3.4% of these patients. An average of 474.9 endoscopies were performed/week (3,799 in total) and 3.6% diagnosed during the pandemic. A weekly average was taken (total/number of weeks) to arrive at these endoscopic exam results.

Table 2 - Results.

Authors	Date	Reduction in diagnoses	Diagnoses in the pre-pandemic period	Diagnoses during the pandemic	Reduction in the number of endoscopies	Endoscopies in the pre- pandemic period	Endoscopies during the pandemic
Lui et al.	May. 2020	46.2%	22.9 diagnoses/week.	12.3 diagnoses/ week (123 total).	51%	1,813 endoscopies/week.	887 endoscopies/week during the pandemic (8,878 total).
Furnari et al.	Sept. 2020	62.4%	3.4% of exams were diagnosed with cancer of the upper digestive tract.	3.6% of the tests were diagnosed with upper digestive tract cancer.	71.4%	1,661.6 endoscopies/week. (13,293 total)	474.9 endoscopies/week (3,799 total).
Rutter et al.	Jul. 2020	40.6%	266 diagnoses/ week.	158 diagnoses/ week.	86%	14,985 endoscopies/week.	2,091 endoscopies/week.
Bosch et al.	Apr. 2021	56.9%	0.29 diagnoses/ week. (2 diagnoses total).	0.125 diagnoses/ week. (1 diagnosis total).	45.3%	19.43 endoscopies/ week (136 endoscopies total).	10.625 endoscopies/week (85 endoscopies total)
Longcroft- Wheaton et al.	Oct. 2020	76.3%.	4.9 diagnoses/ week.	1.16 diagnoses/ week. (7 total).	87.5%	151 endoscopies/ week (3,631 total).	18.8 endoscopies/week (113 total).
Khan et al.	Jun. 2021	March -July: 26.96% July -November: 19.78%	March - July: 10.57 diagnoses/ 100,000 patients. July -November: 9.45 diagnoses/ 100,000 patients.	March - July: 7.72 diagnoses/100,000 patients. July - November: 7.58 diagnoses/100,000 patients.	March - July: 71.84% July - November: 64.74%	March - July: 186.38 endoscopies performed/100,000 patients. July - November: 179.84 endoscopies performed/100,000 patients.	March - July: 52.48 endoscopies performed/ 100,000 patients. July - November: 63.41 endoscopies performed/ 100,000 patients.
Lantinga et al.	Oct. 2020	30.2%	20.9 suspicious cancer findings/ week (182 total).	14.6 suspicious cancer findings/ week. (127 total).	43.1%	901.8 endoscopies/ week (7,846 total).	513.4 endoscopies/week (4,467 total).
			38.6 diagnoses/	19 diagnoses/		1.716.5	272 endoscopies/week.

Furthermore, in agreement with the other authors, a study published by Rutter et al.⁶ observed a decrease of 40.6% in comparing the pre-pandemic and pandemic periods. In total, 266 cancer diagnoses were recorded per week, falling to 158 during COVID-19. In this study, the number of esophageal cancer diagnoses was added to the gastric cancer diagnosis to obtain a percentage of the number of diagnoses. Regarding the decrease in endoscopic exams (86%), 14,985 endoscopies were performed per week before the pandemic, and then 2,091 per week during the pandemic.

In Barcelona, Spain, statistics studied by Bosch et al.² show that the reduction was 56.9%, calculating an average of 0.29 diagnoses/week (2 in total) during the pre-pandemic and 0.125% (1 in total) during the pandemic. Following the same line of reasoning, the number of endoscopies fell by 45.3% - from 19.43 per week (136 in total) to 10.625 per week (85 in total), obtaining a relevant result with a P>0.001. The calculations were performed based on the weekly average of each research result (diagnosis and endoscopies), as the article compared a period

Furthermore, in agreement with the other authors, a of 7 weeks (before the pandemic) with a period of 8 weeks published by Rutter et al.⁶ observed a decrease of 40.6% (pandemic period).

Among the selected studies, the study by Longcroft-Wheaton et al.⁷ conducted in the United Kingdom showed a 76.3% decrease in diagnoses - with a pre-pandemic weekly average of 4.9, there was a drop to 1.16/week. Similar to diagnoses, endoscopies also suffered a reduction (87.5%), with 151 performed/week (3,631 in total) pre-pandemic, becoming 18.8/week (113 total) during the pandemic. In this study, the reduction percentages in diagnoses of upper GIT cancer and endoscopies were calculated based on weekly averages.

Without a doubt, the work carried out by Khan et al.⁸ added even more to the thesis that the number of diagnoses and endoscopies has decreased. They carried out the evaluation on two dates during the pandemic between the months of March to July and from July to November 2019, with the most significant reduction in diagnoses and endoscopies carried out in the period from March to July, representing 26.96% and 71.84%,

respectively, and 19.78% and 64.74% in the period from July to November.

In an article published in the Netherlands by Lantinga et al.³, the decrease in diagnoses was 30.2% (182 cases with a weekly average of 20.9 before the pandemic, and 127 cases and a weekly average of 14.6 during the pandemic). Endoscopies follow the same pattern, with a reduction of 43.1%, with 901.8 exams performed per week before the pandemic and 513.4/week during it. The percentage reduction in diagnoses in the article by Lantinga et al.³ was calculated based on all weekly averages.

In addition, Zhu et al. 9, established a reduction in diagnoses in Shanghai, China, of 49.3% and 84.1% in endoscopies, with a weekly average of 38.5 diagnoses and 1,716.5 endoscopies (total of 3,433) pre-pandemic, which became 19.5 and 272 (total of 544) during the pandemic. However, duodenal cancer was excluded from the diagnoses during the pandemic period in this study for calculation purposes, as our study only considers esophagogastric cancer. Percentages regarding the data were made based on the weekly average calculated by the total number of diagnoses and endoscopies reported in the article.

Thus, it is noted that all authors corroborate their theses with each other, obtaining similar results with regard to the reduction in the number of diagnoses of gastroesophageal cancer and the number of endoscopies performed during the pandemic.

DISCUSSION

Cancer diagnosis and care services reduced their flow of patients during the COVID-19 pandemic, aiming to contain the spread of the virus¹⁰. These measures are important as some studies show that cancer patients are more likely to acquire more severe forms of the disease with fatal consequences¹¹. On the other hand, by reducing the number of people undergoing diagnostic tests, many cancers are no longer diagnosed¹², evolving into more serious and often palliative forms.

Corroborating this definition, all studies evaluated in this integrative review demonstrate a reduction in the number of diagnoses of upper digestive tract cancers during the pandemic. This fact is due to the suspension of routine procedures from restructuring health services, which prioritized prevention and control of the epidemic. Furthermore, because endoscopy is a potentially aerosol-generating procedure, several professional associations have issued recommendations to postpone selective procedures, except in urgent or emergency cases¹³, a fact which has had a global impact on the diagnosis of gastrointestinal cancer. In this sense, many asymptomatic cancers were possibly not investigated⁷, so the main negative outcome was the possible increase in the pathology stage together with the possibility of greater patient mortality^{3,8}.

In comparing the decrease in diagnoses of upper gastrointestinal cancer with other types of cancer such as breast and lower gastrointestinal, we observed that the average decrease is similar¹², which is also reported due to the decrease in screening tests, although endoscopy is still the test with the

greatest capacity for spreading aerosols when compared to mammography or colonoscopy¹³.

The most prominent among the secondary outcomes considered in the present review was the increase in the detection rate per procedure for esophageal and gastric cancer^{3,6,7,9}, meaning even with a reduction in total diagnoses and the number of endoscopies, exams that were carried out had a higher percentage of positive diagnoses. This fact can be attributed to the selective nature of endoscopic procedures performed during the pandemic, focusing on patients whose symptoms and initial tests indicate the highest risk of cancer^{5,6}. Other authors who were not selected in this study report similar trends¹³. Based on mathematical models, Lui et al.⁴ estimated that 4.6% of patients with gastric cancer would have an increase in cancer stage within 6 months.

Furthermore, there was an increase in diagnoses in the post-pandemic period, which can be explained by both the return to operation of endoscopy services and by the return of patients to the health system, many with more advanced disease, due to a decrease in the number of COVID-19 cases^{2,5}.

Another interesting outcome which also reveals an impact on post-pandemic clinical practice is the increase in the virtual consultation rate^{2,8}, constituting a practice which became widespread with the pandemic and has gained ground in the health sector.

Finally, it is important to highlight that this literature analysis does not include any study carried out in Brazil, so that although the pandemic also reached Brazil and possibly reduced the number of cancer diagnoses during this period, this relationship cannot be confirmed due to lack of data. Therefore, the production of more studies in this area is encouraged so that the impact of the pandemic and its relationship with the decrease in diagnoses in Brazil can also be analyzed.

CONCLUSION

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Therefore, it is clear that the COVID-19 pandemic caused several impacts on health, such as difficulty in accessing resources and underdiagnosis of pathologies not directly related to the coronavirus. As demonstrated in this study, a significant reduction in the number of diagnoses of upper gastrointestinal tract cancer was observed, indicating negative consequences due to the decline in the number of endoscopies performed.

In this scenario, it should be noted that developing adequate health management plans is essential to monitor cases and provide care in order to infer the diagnosis and appropriate therapy for everyone. Furthermore, according to the Pan American Health Organization (PAHO)¹⁴, the repercussions of underdiagnosis can result in increased morbidity and mortality, worsened prognosis and higher health costs in the coming years; therefore, the work of a multidisciplinary team in providing healthcare in the pandemic is decisive to ensure the following of protocols and the need for continuous research aimed at numerically proving this data and minimizing these impacts.

Authors' participation: Alt, L.L.: Project planning, supervising professor, final review of the article.

Goi, A.P.C.: Project planning, article search, methodology design, creation of the diagram and results table, project submission. Dalbosco, A.K.: Project planning, reading and selection of articles, development of discussion. Vedana, B.: Project planning, search for articles, reading and selection of articles, outlining the methodology and writing the results. Pilatti, D: project planning, reading and selection of articles, development of the discussion. Garcia, M: Project planning, reading and selection of articles, writing the introduction and conclusion.

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Received: 2023, April 10 Accepted: 2024, February 28