



Comparison of Lymph Node Involvement in Carcinomas during Precovid and Covid Era

P. Manasvi¹ and V. Rishi Gowtham^{2*}

¹Saveetha Medical College and Hospital, Chennai-602105, Tamil Nadu, India.

²Department of General Surgery, Saveetha Medical College and Hospital, Chennai-602105, Tamil Nadu, India.

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Background: This is a clinicopathological study comparing the involvement of lymph nodes in various carcinomas before and during the COVID-19 period. During the pandemic the access to healthcare and timely detection and intervention of carcinomas were severely affected. This delay in treatment has led to the progression of malignancies and metastasis to lymph nodes.

Methods: A retrospective study was conducted of 40 patients (20 from 2019 and 20 from 2021) with carcinomas who were treated by surgical excision of tumour combined with lymph node resection. Histopathological examination of the nodes was done to detect malignant metastasis and the average node positivity rate was calculated.

Results: Lymph node metastasis was observed in 10 patients in 2019 (50%) and 16 patients in 2021 (80%). The average node positivity rate is significantly higher in 2021 than in 2019, in 2019 it is 31% and in 2021 it is 43%. Lymph node metastasis is expected to increase by 43% in 2021.

Conclusion: In the Covid-19 pandemic, a significant decrease and delay of patients presenting to the OPD for neoplasms, resulting in a delay in the diagnosis and treatment of advanced-stage neoplasms that manifest as metastases in the regional lymph nodes. Surgeons need to be vigilant and extensively explore the all draining affected lymph nodes and resect them.

Keywords: Pandemic; COVID-19; cancer; lymph node; metastasis; histopathology.

1. INTRODUCTION

The development of Coronavirus disease 2019 (COVID-19), which is caused by the severe acute respiratory illness coronavirus 2 (SARS-CoV-2), has caused a global public health catastrophe that has never been seen before. After the World Health Organization (WHO) declared COVID-19 a public health emergency on March 11, 2020,[1] numerous nations stepped up their efforts to stop the virus from spreading and to treat COVID-19 patients. The pandemic significantly influenced the healthcare system, as many other ailments that require attention were overlooked due to resource allocation. Cancers stand out among the diseases that have been unable to obtain adequate treatment, with significant consequences [2].

Locoregional LNs are the earliest and commonest sites of metastasis of solid tumors such as breast carcinoma [3]. As tumors grow and evolve, and they undergo metastasis to regional lymph nodes. Lymph node involvement is of prognostic importance. Persistent disease in lymph nodes can be the source of subsequent fatal metastases if not resected completely. Recurrence of the disease primarily affects lymph nodes, which may necessitate additional surgery or radioiodine ablation therapy, lowering the patient's quality of life. Improvement in local therapy is associated with a better prognosis [4]. This study highlights the increased burden to healthcare due to late presentation of malignancy in a tertiary care centre during this pandemic. The study also aims to create awareness for surgeons while approaching oncology case.

2. MATERIALS AND METHODS

This study conducted between January to March of 2019 and 2021 among patients who underwent surgeries for carcinomas in the general surgery department of Saveetha Medical College and Hospital, Chennai. A total of 40 patients were taken in this study, out of which 20 cases were taken before the covid-19 pandemic in 2019 and 20 cases during the covid-19 pandemic in 2021. We included carcinoma of breast, thyroid, stomach and rectum for this study.

The patients were included and excluded according to the following criteria: - Inclusion criteria: All operable carcinomas during the peak

of pandemic and before pandemic. Exclusion criteria: Sarcomas, Nonoperable cases.

Radical resection of tumour along with lymph node dissection was done. The resected lymph nodes were sent for histopathological examination and the average node positivity rate was calculated. The study was conducted as per the guidelines and approval of the Institutional Ethics Committee, the ethical clearance number of which is: SMC/IEC/2021/03/088. Informed consent was obtained from the patient. Odds ratio was used to measure the association between pre covid era [PCE] and covid era [CE]. p value < 0.05 was considered as statistically significant. All statistical analysis was done by using SPSS software Version 21.

2.1 Statistical Analysis

For all continuous variables, descriptive statistics such as Mean/Median with SD were provided, and for all categorical variables, frequency with percentages were expressed. The X^2 test, t test, or Mann-Whitney U test were used to compare patient characteristics, as applicable. The t test was used to compare monthly case counts. $P < 0.05$ was used to determine statistical significance, and all tests were two-tailed. The odds ratio was used to compare continuous variables in the Pre-COVID and Early COVID periods, based on the normality assumption. Statistical significance was defined as a p value of less than 0.05.

3. RESULTS

A total of 40 cancer patients underwent surgery from our department in the time period used for the study; 20 during the COVID period and 20 from the Pre-COVID era. A tabulation of the type of cancers and patient demographic characteristics in our study is given in Table 1. Graph 1 represents different types of cancer involved in the present study.

There were no significant differences between the 2 periods in terms of the proportions of male patients (2 patients [10%] vs 5 patients [25%]; $P = 0.08$) or mean (SD) age (51.3 [10.9] years vs 51.8 [10.7] years; $P = 0.19$) for CA stomach and CA rectum. There were also significant differences in mean ages and sex ratios according to cancer type. As a result, there was female predominance in both these groups because females were the most affected by

breast and thyroid cancer. (18 patients [90%] vs 15 patients [75%]).

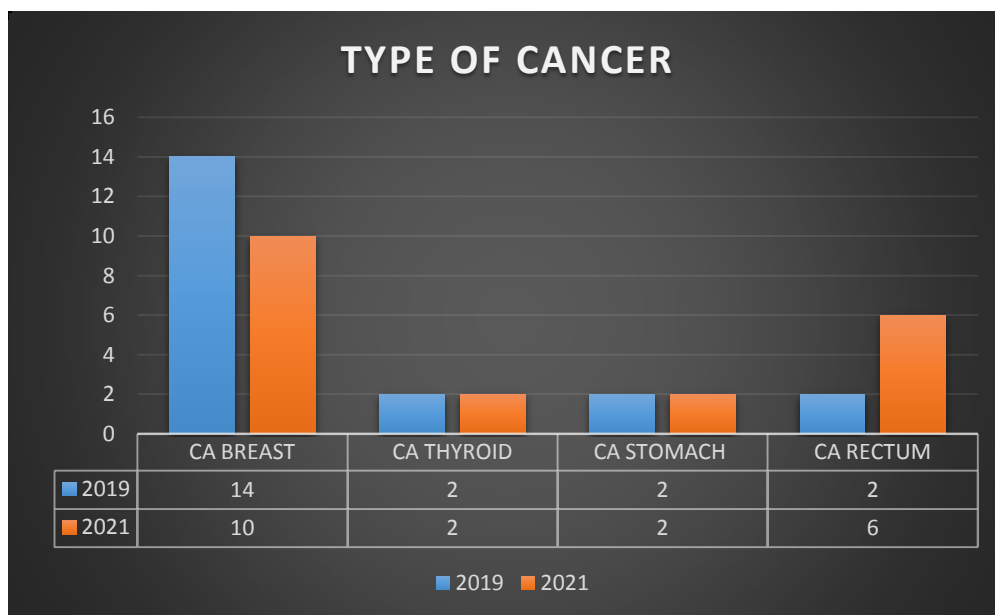
Graph 2 depicts the average node positivity in the years 2019, 2021.

The probability of lymph node involvement among cancer patients in 2019 and 2021 is shown in Table 2.

Table 3 and graph 3 depicts the average node positivity rate for individual cancers in PCE and CE:

Table 1. Patients characteristics [n =40]

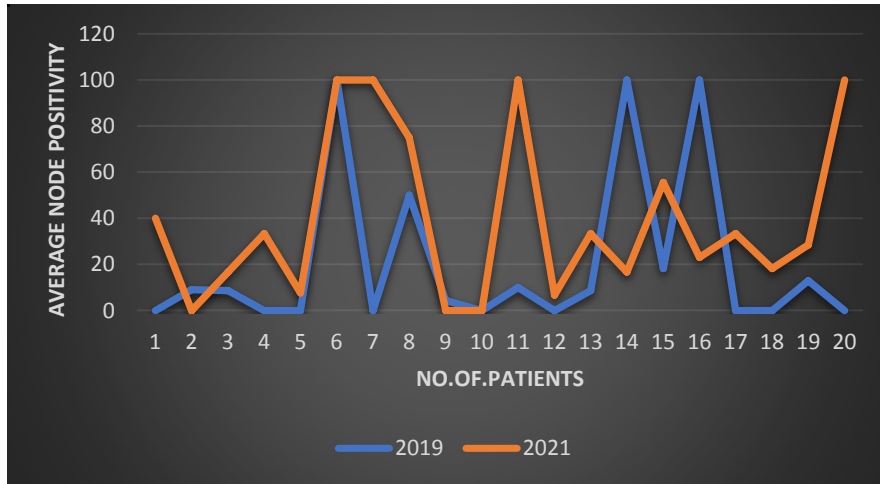
Characteristics	2019 Pre covid era [n=20]	2021 Covid era [n=20]	P value
CA BREAST			
Total	14	10	NA
Age [Mean]	50.4	51.2	0.19
Men	0	0	0.04
Women	14	10	
CA THYROID			
Total	2	2	NA
Age [Mean]	49.7	50.3	0.21
Men	0	0	0.05
Women	2	2	
CA STOMACH			
Total	2	2	NA
Age [Mean]	50.2	51.4	0.16
Men	1	2	0.11
Women	1	0	
CA RECTUM			
Total	2	6	NA
Age [Mean]	50.4	51.9	0.22
Men	1	3	0.08
Women	1	3	



Graph 1. Type of cancer

Table 2. Risk association of lymph node involvement between PCE and CE

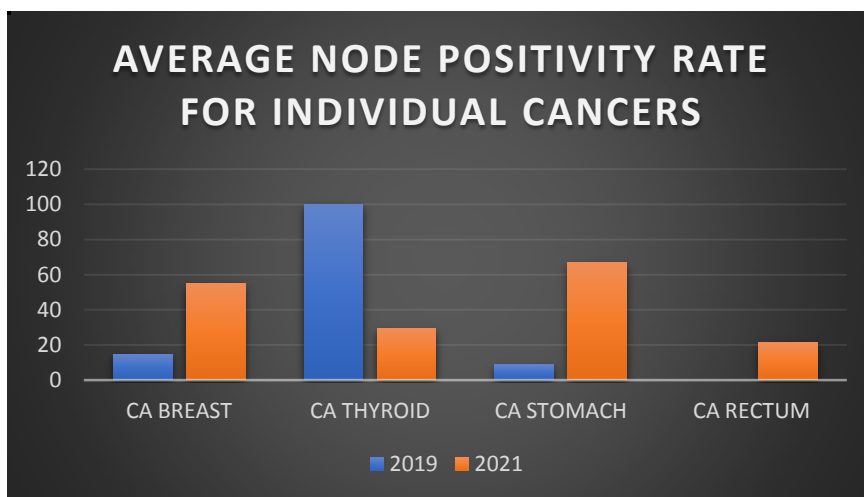
	2019 positivity N=20	node	2021 positivity N=20	node	Odds ratio (95%confidence interval)	Pvalue
Breast cancer	7		8		0.25 (0.04,1.62)	<0.05
Thyroid cancer	1		1		1 (0.02,50.5)	>0.05
Stomach cancer	1		2		0.55 (0.03,29.81)	0.052
Rectal cancer	1		5		0.2 (0.01,6.66)	<0.05



Graph 2. Average node positivity rate in precovid era compared with covid era

Table 3. Average node positivity rate for individual cancers in PCE and CE

Type of Cancer	Average Node Positivity Rate in Pce in 2019	Average Node Positivity Rate in Ce in 2021
CA Breast	14.61%	54.65%
CA Thyroid	100%	29.09%
CA Stomach	8.69%	66.66%
CA Rectum	0%	21.42%
Mean Total	31%	43%



Graph 3. Average node positivity rate for individual cancers

4. DISCUSSION

The outbreak of COVID-19 posed major healthcare, scientific, and economic challenges globally. These ranged from shortage of personal protective equipment and testing kits to lack of clear guidelines on the management of non-COVID patients during the pandemic. This required a thorough consideration and risk assessment on a case-to-case basis along with re-prioritizing of current waiting lists [5].

Early experience from China suggested that the COVID-19 pandemic clearly influenced the care of patients with cancer surgeries were especially more affected than emergency surgeries [6].

The presence of metastasis to regional lymph nodes is of importance as it determines treatment protocol and overall prognosis of the patient [7]. During the covid-19 pandemic there was a delay in the presentation of patients with undetected malignancies to the outpatient department. This delay can be attributed to several factors some of which are the lockdown which was enforced, travel restrictions, logistical constraints and so on.

And thus, by the time they underwent surgery for resection of the tumour along with removal of regional lymph nodes, there was already significant nodal metastasis. The present study evaluated the association of the COVID-19 pandemic with the different cancer stage at diagnosis not only in the first phase of the pandemic (ie, March to June) but also until the end of 2020. Previous studies have shown that the numbers of patients decreased significantly for almost all cancer types [8,9].

4.1 Breast Cancer

The average node positivity rate in CE (54.65%) is higher than PCE (14.61%). In our experience, no major difference was observed in management of breast cancer patients in comparison with the Pre-COVID era. This was a concern in our team as well but our results show that there was no compromise in provision of standard of care to other cancer patients when compared with pre-COVID era.

The survival rate of patients moderately increased as lymph node involvement decreased regardless of tumorsize. Lymph node status serves as an indicator of the tumor's ability to spread to distant sites. Patients with four or more

involved nodes at initial diagnosis have a significantly worse outcome after relapse than patients without nodal involvement. Nodal metastasis is also a marker of an aggressive phenotype [10].

4.2 Thyroid Cancer

On the contrary, in our study the average node positivity rate in PCE (100%) is higher than CE (29.09%). This can be explained by the procedure underwent on the patient. In the PCE it was found to be follicular carcinoma and papillary carcinoma respectively. Hence, total thyroidectomy was done. Where in only 1 lymph node was resected which was positive for metastasis. But during CE, thyroidectomy was done along with neck dissection and several lymph nodes were resected among which minimal positivity was found, which brought down the average node positivity rate. In a study conducted by Harwood et al in malignancies of thyroid, there was a recurrence in 32% of patients with lymph node metastasis and in 14% of those without lymph node metastases. Nodal involvement shows an adverse outcome in the prognosis of patients [10].

4.3 Stomach Cancer

The average node positivity rate in CE (66.66%) is considerably higher than PCE (8.69%). In a study conducted by Maehara et al, the survival rate was lower for patients with metastasis to lymph nodes than for those without metastasis. Lymph node metastasis was associated with larger tumour, a higher incidence of submucosal invasion and a higher rate of lymphatic vessel involvement [11,12].

4.4 Rectal Cancer

The average node positivity rate in CE is 21.42%. There was no lymph node metastasis in PCE. Patients with lateral node metastases had a significantly poor 5-year survival rate and an increased risk of local recurrence compared with those without lateral node metastases [13]. Endorectal ultrasonography is a very useful tool for the assessment of the depth of cancer invasion in the rectal wall and pararectal lymph node metastasis [14,15].

Similar to the present study, Kuzuu K et al., [16]. evaluate stage at diagnosis among patients with gastrointestinal cancer in Japan. Given the ongoing nature of the COVID-19 pandemic, it

may have further negative effects on patients with cancers that are asymptomatic and/or typically detected via screening.

Utilizing our newly designed list prioritization and careful patient selection, we were able to increase our cancer resection numbers almost same when compared to the same time frame 2 years ago.

As a result, it is critical to ensure that patients receive essential screening and monitoring without having to wait for the pandemic to subside, particularly those who require colonoscopy to potentially identify colorectal cancer. Furthermore, given the rapid advancement of cancer, the negative impacts of the COVID-19 pandemic may grow more evident with time, and additional study is needed to adequately analyse this issue.

5. CONCLUSION

During the covid-19 pandemic there was a considerable reduction and delay in patients that presented to the OPD for symptoms of malignancies. This has led to a delay in diagnosing and treating malignancies in advanced stages which is reflected as metastasis to regional lymph nodes which were resected along with the tumour during surgery. Awareness among patients should be improved to ensure early presentation and reporting of symptoms. Surgeons must be more vigilant and explore the dissecting field completely to ensure all involved lymph nodes are resected during surgery to avoid recurrence and to improve overall prognosis of the patient in the forthcoming months.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT AND ETHICAL APPROVAL

The study was conducted as per the guidelines and approval of the Institutional Ethics

Committee, the ethical clearance number of which is: SMC/IEC/2021/03/088. Informed consent was obtained from the patient.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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