Journal of Clinical and Investigative Surgery

https://doi.org/10.25083/2559-5555
https://proscholar.org/jcis/
ISSN: 2559-5555

Evaluation of lymph node status in cancer patients during pandemic period

Nandhana Prashanth V[1*], Saravanan P[2], Vivekananda Subramania Nathan[3]

[1] *Associate Professor, Shri Sathya Sai Medical College and Research Institute, Ammapettai, Chengalpattu, Taluk, Kanchippuram district, Tamil, Nadu, India*
[2] *Hod and Professor, Meenakshi Medical College, India*
[3] *Professor, Chettinad Medical College, Chennai, India*

ABSTRACT

Background. This is a clinicopathological study comparing lymph node involvement in breast carcinomas before and during the COVID-19 period. During the pandemic, access to healthcare was limited, which led to a delay in the diagnosis and treatment of malignant tumors, which often presented in advanced stages, with lymph node metastases. *Methods*. A retrospective study was performed on 40 patients with carcinomas treated by surgical excision of the tumor combined with lymph node resection. Histopathological examination of lymph nodes was performed to detect malignant metastases, and the mean lymph node positivity rate was calculated. Odds ratio was used to measure the association between pre covid era and covid era (p value < 0.05 being considered statistically significant). *Results*. Lymph node metastasis was observed in 10 patients in 2019 (50%) and in 16 patients in 2021 (80%). The average node positivity rate was significantly higher in 2021 (39.4%) than in 2019 (21.1%). *Conclusion*. During the Covid-19 pandemic, there was a considerable delay in presenting patients for symptoms of malignancy. This led to a delay in the diagnosis of malignancies, which were treated in advanced stages, frequently with metastases in the regional lymph nodes. Patient awareness should be improved to ensure early presentation and reporting of symptoms. Surgeons must be more vigilant and fully explore the dissection field to ensure that all involved lymph nodes are resected, thus avoiding recurrence and improving the patient's overall prognosis.

Category: Original Research Paper

Received: May 22, 2022
Accepted: July 19, 2022
Published: November 20, 2022

Keywords:

pandemic, Covid-19, cancer, lymph node, metastasis, histopathology

* **Corresponding author:**

Nandhana Prashanth V,

Shri Sathya Sai Medical College and Research Institute, Ammapettai, Chengalpattu, Taluk, Kanchippuram district, Tamil, Nadu, India

E-mail: nandprash@gmail.com

Introduction

The development of Coronavirus disease 2019 (COVID-19), which is caused by the severe acute respiratory disease coronavirus 2 (SARS-CoV-2), has produced 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, numerous nations stepped up their efforts to stop the virus from spreading and to treat COVID-19 patients [1]. The pandemic had a significant influence on the health-care 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 lymph nodes/ LNs are the earliest and commonest sites of metastasis of solid tumors such as carcinoma of the breast [3]. As tumors grow and evolve, they metastasize to regional lymph nodes, which are of significant prognostic importance. Persistent disease in lymph nodes can be the source of subsequent fatal metastases if not resected completely [4]. Therefore, improvement in local therapy is associated with better prognosis.

Materials and Methods

This is a retrospective 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. Radical resection of tumour along with lymph node dissection was performed. The resected lymph nodes were sent for histopathological examination and the average node

To cite this article: Prashanth VN, Saravanan P, Nathan VS. Evaluation of lymph node status in cancer patients during pandemic period. *J Clin Investig Surg*. 2022;7(2):169-173. doi: 10.25083/2559.5555/7.2.9

positivity rate was calculated. The study was conducted as per the guidelines and approval of the Institutional Ethics Committee, the ethical clearance study number being: SMC/IEC/2021/03/088. Informed consent was obtained from the patients. 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.

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 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

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 in our study is given in Table 1 and Figure 1.

Table 1. Type of cancer [n =40]

	2019	2021
CA breast	14	10
CA thyroid	2	2
CA stomach	2	2
CA rectum	2	6

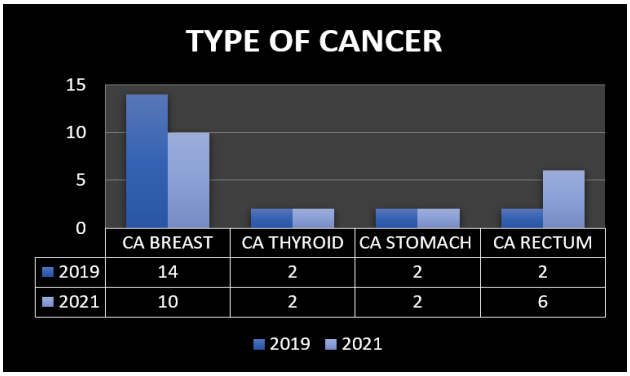

Figure 1. Type of cancer

The probability of lymph node involvement among cancer patients in 2019 and 2021 is shown in Table 2. Figure 2 depicts the prevalence of node positivity in cancer patients during the years 2019 and 2021.

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

Type of cancer	2019 node positivity N=20	2021 node positivity N=20	Odds ratio (95%confidence interval)	P value
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

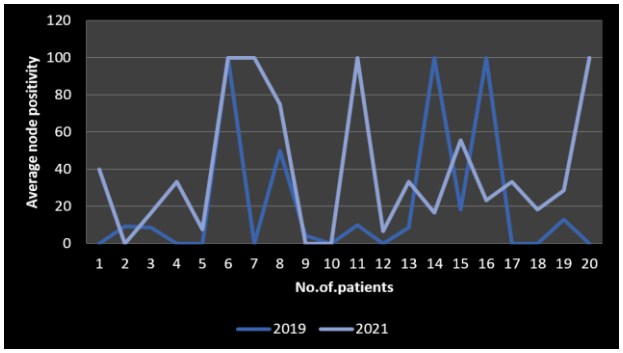

Figure 2. Average node positivity rate in pre covid era compared with covid era

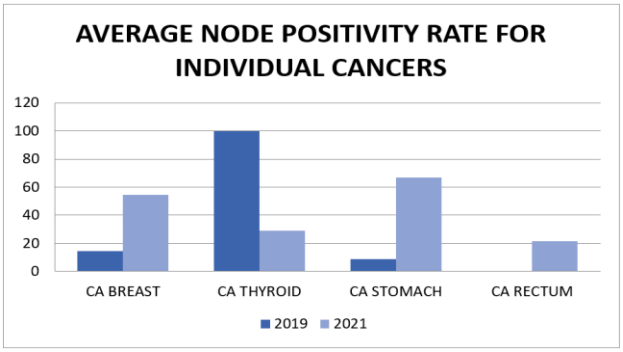

Figure 3. Average rate of node positivity according to the type of cancer

Table 3 and Figure 3 depicts the average node positivity rate for individual cancers in PCE and CE.

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

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 [5-7].

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 [8,9]. 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 a year ago.

The presence of metastasis to regional lymph nodes is of special importance as it determines treatment protocol and overall prognosis of the patient [10-12]. 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 so, by the time they underwent surgery for resection of the tumour along with removal of regional lymph nodes, there was already significant nodal metastasis.

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 tumor size. Lymph node status serves as an indicator of the tumor's ability to spread to distant sites [13-15]. 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 [16-18].

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 only subtotal thyroidectomy was done wherein only 1 lymph node was resected which was positive for metastasis. But in 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. The bias may be attributed to the low number of cases as well. 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 [19-21].

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 [22,23].

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 [24-26]. 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 [27-29].

Our study helps surgeons to be 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.

Conclusions

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.

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

References

1. Coronavirus Act 2020, c7. (2020). Accessed: March 11, 2021 https://www.legislation.gov.uk/ukpga/2020/7/contents/enacted/data.htm.
2. Akula SM, Abrams SL, Steelman LS, Candido S, Libra M, Lerpiriyapong K, Cocco L, Ramazzotti G, Ratti S, Follo MY, Martelli AM, Blalock WL, Piazzi M, Montalto G, Cervello M, Notarbartolo M, Basecke J, McCubrey JA. Cancer therapy and treatments during COVID-19 era. *Adv Biol Regul*. 2020 Aug;77:100739. doi: 10.1016/j.jbior.2020.100739
3. Punglia RS, Morrow M, Winer EP, Harris JR. Local therapy and survival in breast cancer. *N Engl J Med*. 2007 Jun 7;356(23):2399-405. doi: 10.1056/NEJMra065241
4. Kawada K, Taketo MM. Significance and mechanism of lymph node metastasis in cancer progression. *Cancer Res*. 2011 Feb 15;71(4):1214-8. doi: 10.1158/0008-5472.CAN-10-3277
5. COVIDSurg Collaborative. Global guidance for surgical care during the COVID-19 pandemic. *Br J Surg*. 2020;107(9):1097-1103. doi: 10.1002/bjs.11646
6. Aboueshia M, Hussein MH, Attia AS, Swinford A, Miller P, Omar M, Toraih EA, Saba N, Safah H, Duchesne J, Kandil E. Cancer and COVID-19: analysis of patient outcomes. *Future Oncol*. 2021 Sep;17(26): 3499-3510. doi: 10.2217/fon-2021-0121
7. Keskin A, Karslioglu B. Did Covid-19 pandemic narrow the spectrum of surgical indications?. *J Clin Investig Surg*. 2021;6(1):58-63. doi: 10.25083/2559.5555/6.1.11
8. Wu XR, Zhang YF, Lan N, Zhang ZT, Wang XS, Shen B, Lan P, Kiran RP; Chinese Society of Colorectal Surgery of China Medical Association. Practice Patterns of Colorectal Surgery During the COVID-19 Pandemic. *Dis Colon Rectum*. 2020 Dec;63(12):1572-1574. doi: 10.1097/DCR.0000000000001840
9. COVIDSurg Collaborative. Effect of COVID-19 pandemic lockdowns on planned cancer surgery for 15 tumour types in 61 countries: an international, prospective, cohort study. *Lancet Oncol*. 2021;22(11): 1507-1517. doi: 10.1016/S1470-2045(21)00493-9
10. Foster RS Jr. The biologic and clinical significance of lymphatic metastases in breast cancer. *Surg Oncol Clin N Am*. 1996 Jan;5(1):79-104.
11. Lee YJ, Huh JW, Shin JK, Park YA, Cho YB, Kim HC, Yun SH, Lee WY. Risk factors for lymph node metastasis in early colon cancer. *Int J Colorectal Dis*. 2020 Aug;35(8):1607-1613. doi: 10.1007/s00384-020-03618-7
12. Georgescu TA, Bohiltea R, Munteanu O, Grigoriu C, Paunica I, Sajin M. A mini-review regarding the carcinogenesis and morphology of serous tumors of the ovary, fallopian tube and peritoneum. *J Mind Med Sci*. 2021;8(1):44-52. doi: 10.22543/7674.81.P4452
13. Jatoi I, Hilsenbeck SG, Clark GM, Osborne CK. Significance of axillary lymph node metastasis in primary breast cancer. *J Clin Oncol*. 1999 Aug;17(8): 2334-40. doi: 10.1200/JCO.1999.17.8.2334
14. Yamada A, Hayashi N, Kumamaru H, Nagahashi M, Usune S, Asaga S, Iijima K, Kadoya T, Kojima Y, Kubo M, Miyashita M, Miyata H, Ogo E, Tamura K, Tanakura K, Tada K, Niikura N, Yoshida M, Ohno S, Ishikawa T, Narui K, Endo I, Imoto S, Jinno H. Prognostic impact of postoperative radiotherapy in patients with breast cancer and with pT1-2 and 1-3 lymph node metastases: A retrospective cohort study based on the Japanese Breast Cancer Registry. *Eur J Cancer*. 2022 Sep;172:31-40. doi: 10.1016/j.ejca.2022.05.017
15. Chen J, Luo B, Gao M, Cai G, Luo X, Zhang-Cai Y, Ke S, Chen Y. Regional Lymph Node Metastasis and Axillary Surgery of Microinvasive Breast Cancer: A Population-Based Study. *Diagnostics (Basel)*. 2022 Apr 21;12(5):1049. doi: 10.3390/diagnostics12051049
16. Carter CL, Allen C, Henson DE. Relation of tumor size, lymph node status, and survival in 24,740 breast cancer cases. *Cancer*. 1989;63(1):181-7. doi: 10.1002/1097-0142(19890101)63:1<181::aid-cncr2820630129>3.0.co;2-h
17. Andring LM, Diao K, Sun S, Patel M, Whitman GJ, Schlembach P, Arzu I, Joyner MM, Shaitelman SF, Hoffman K, Stauder MC, Smith BD, Woodward WA. Locoregional Management and Prognostic Factors in Breast Cancer With Ipsilateral Internal Mammary and Axillary Lymph Node Involvement. *Int J Radiat Oncol Biol Phys*. 2022 Jul 1;113(3):552-560. doi: 10.1016/j.ijrobp.2022.02.037
18. Lazar AL, Vulturar R, Fodor A, Orasan OH, Crișan CH, Login C, Para I, Negrean V, Tiperciuc B, Cozma A. The molecular mechanisms linking metabolic syndrome to endometrial and breast cancers. *J Mind Med Sci*. 2021; 8(2):167-178. doi: 10.22543/7674.82.P167178
19. Harwood J, Clark OH, Dunphy JE. Significance of lymph node metastasis in differentiated thyroid cancer. *Am J Surg*. 1978 Jul;136(1):107-12. doi: 10.1016/0002-9610(78)90209-x
20. Zhan L, Feng HF, Yu XZ, Li LR, Song JL, Tu Y, Yuan JP, Chen C, Sun SR. Clinical and prognosis value of the number of metastatic lymph nodes in patients with papillary thyroid carcinoma. *BMC Surg*. 2022 Jun 20; 22(1):235. doi: 10.1186/s12893-022-01635-7
21. Wang Y, Deng C, Shu X, Yu P, Wang H, Su X, Tan J. Risk Factors and a Prediction Model of Lateral Lymph Node Metastasis in CN0 Papillary Thyroid Carcinoma Patients With 1-2 Central Lymph Node Metastases. *Front Endocrinol (Lausanne)*. 2021 Oct 15;12:716728. doi: 10.3389/fendo.2021.716728
22. Maehara Y, Orita H, Okuyama T, Moriguchi S, Tsujitani S, Korenaga D, Sugimachi K. Predictors of

lymph node metastasis in early gastric cancer. *Br J Surg*. 1992;79(3):245-7. doi: 10.1002/bjs.1800790320

23. Dumitriu B, Valcea S, Andrei G, Beuran M. Evaluation of anemia as a postoperative risk factor in the evolution of patients with gastric resection for malignancies. *J Clin Investig Surg*. 2021 Nov 25;6(2):136-140. doi: 10.25083/2559.5555/6.2.8
24. Ueno M, Oya M, Azekura K, Yamaguchi T, Muto T. Incidence and prognostic significance of lateral lymph node metastasis in patients with advanced low rectal cancer. *Br J Surg*. 2005 Jun;92(6):756-63. doi: 10.1002/bjs.4975
25. Kang BM, Park JS, Kim HJ, Park SY, Yoon G, Choi GS. Prognostic Value of Mesorectal Lymph Node Micrometastases in ypN0 Rectal Cancer After Chemoradiation. *J Surg Res*. 2022 Aug;276:314-322. doi: 10.1016/j.jss.2022.02.040
26. Zhou S, Jiang Y, Pei W, Liang J, Zhou Z. Prognostic significance of lateral pelvic lymph node dissection for middle-low rectal cancer patients with lateral pelvic lymph node metastasis: a propensity score matching study. *BMC Cancer*. 2022 Feb 3;22(1):136. doi: 10.1186/s12885-022-09254-4
27. Katsura Y, Yamada K, Ishizawa T, Yoshinaka H, Shimazu H. Endorectal ultrasonography for the assessment of wall invasion and lymph node metastasis in rectal cancer. *Dis Colon Rectum*. 1992 Apr;35(4): 362-8. doi: 10.1007/BF02048115
28. Agger E, Åkerlund V, Ekberg O, Jörgren F, Lydrup ML, Buchwald P. Management, treatment and prognostic significance of lateral lymph node metastases in rectal cancer-a regional cohort study. *Int J Colorectal Dis*. 2021 Dec;36(12):2707-2714. doi: 10.1007/s00384-021-04018-1
29. Kuo YT, Tsai WS, Hung HY, Hsieh PS, Chiang SF, Lai CC, Chern YJ, Hsu YJ, You JF. Prognostic value of regional lymph node involvement in patients with metastatic colorectal cancer: palliative versus curative resection. *World J Surg Oncol*. 2021 May 13;19(1): 150. doi: 10.1186/s12957-021-02260-z