# A Study of Metastatic Lymph Node Ratio and Staging of Tumor in Primary Organ Malignancy

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**Abstract**

**Background:** Lymph Node Ratio (LNR) is considered to be more important and precise than TNM staging for prognosis in management of cancer patients. LNR is defined as the ratio of number of positive lymph nodes (Lymph Node Metastasis, LNM) to the total number of lymph nodes harvested (LNH). It is used as an important prognostic factor. **Aims :** 1) To measure LNH,LNM and LNR in primary organ malignancy.2)To know significance of relation of lymph node ratio and tumor stage in cancer patients. **Materials & Method :** A study of total 101 cancer resections including breast, gastro-intestinal tract, genitourinary tract, head and neck were done over a period of two years at NHL medical college. Total 1148 lymph nodes were reviewed for metastasis. LNR was calculated from LNM and LNH. Data regarding age, gender, tumor stage of primary organ malignancy, total lymph node dissected per case was accessed from histopathology records.LNH and LNR were calculated per specimen done. **Result :** LNH was highest in head and neck malignancy (25.16) and lowest in periampullary region (6.58). Mean LNR was highest in stomach (0.85) and breast (0.8) malignancies. Lowest LNR was in colon malignancy (0.008).Maximum number of malignant cases were of breast and stomach in stage II,GIT in stage III, Head and neck and GUT in stage IV. The largest and smallest metastatic lymph node was 3.2cm and 0.4cm, respectively. **Conclusion :** LNR can serve as a prognostic indicator in cancer patients. Additional research and diagnostic examinations using LNR would be   a potential tool for management of patients.

**Keywords :** Lymph node ratio, Primary organ malignancy, Tumor stage.

## Introduction:

Lymph node metastasis is a common problem for patients and those involved in their management. Patients with lymph node metastasis from various cancers are often at a higher risk of death from cancer than those whose lymph nodes are free of cancer. Clinical and pathologic staging of cancer is dependent upon identification of lymph node metastases. Recent studies have suggested that LNR is a prognostic indicator for various malignancies.[1] LNR is defined as the number of metastatic lymph nodes divided by total number of retrieved lymph nodes. Insufficient number of lymph nodes examined in a tumor is called stage migration. LNR has been confirmed to be simple and reproducible prognostic tool even in cases of limited lymph node dissection.[2]

## Aims:

1) To measure LNH, LNM and LNR in primary organ malignancies.

2) To know significance of relation of lymph node ratio and tumor stage in cancer patients.

## Materials and Method:

In the present retrospective study, cancer patients were included who underwent surgery between July 2017 to June 2019 over a period of 2 years at NHLMMC. Most patients received adjuvant chemotherapy, radiotherapy or hormone therapy. System wise cases were divided among GIT, GUT, Head and neck and breast malignancies. Data regarding age, gender, tumor stage of primary organ malignancy, total lymph nodes dissected per case and lymph node sizes were accessed from surgical histopathology records. Then total number of lymph

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nodes harvested and total number of positive lymph nodes for metastasis were calculated. Age and gender distribution, staging of tumor, highest and lowest LNR according to primary organ malignancy was calculated. The recorded data was subjected to statistical analysis using appropriate statistical formulae and results were inferred. p value was calculated using stage of tumor with LNR value.

## Results:

Total 101 cancer resections with their dissected 1148 lymphnodes were reviewed over a period of two years. In present study, there were 34 cases of breast malignancies. Among gastrointestinal tract malignancies(n=43), primary organ malignancies were as follows : stomach(n=13), colon(n=12), periampullary region(n=11) and gall bladder(n=7). In head and neck (n=14), malignant lesions of tongue (n=6), buccal mucosa (n=6) and thyroid (n=2) were included. Among genitourinary tract malignancies (n=10), prostate (n=3), urinary bladder(n=5), renal pelvis(n=1) and ovary (n=1) were included.

As shown in Table 1, maximum number of primary organ malignancies were of gastrointestinal tract(42.57 %) and breast(33.66 %); while maximum number of LNH were from breast(n=381) followed by gastrointestinal tract(n=373) and head and neck(n=308)malignancies. Though LNH in head and neck malignancies were high in number but LNM (n=50) was very low. Table 2 shows the age and gender of cancer patients. The male (n=44) to female (n=57) ratio was 1:1.29. Higher female ratio was due to more number of cases of breast malignancy. Male preponderance was found in gastrointestinal and genitourinary cases.

Maximum number of cases were in age group of $4^{th}$(n=28)and $5^{th}$(n=31)decade. Lesser frequency was found in age group of $2^{nd}$ (n=4)and $7^{th}$(n=4)decade. Both genders had comparable presence in the $5^{th}$decade. No patient was registered below 20 years in our study.

Maximum number of Breast malignancies were in $4^{th}$ decade(n=13) while GIT malignancy in

### Table 1: Total no of system wise cases with LNH, LNM, Mean LNH

| Primary organ malignancy | No. of cases(n) | LNH(n) | LNM(n) | Mean LNH |
|---|---|---|---|---|
| Breast | 34(33.66 %) | 381 | 108 | 11.2 |
| GIT | 43(42.57 %) | 373 | 98 | 8.4 |
| Head and neck | 14(13.86 %) | 308 | 50 | 22.0 |
| GUT | 10(9.90 %) | 86 | 15 | 7.8 |
| Total(N) | 101(100 %) | 1148 | 271 | - |

### Table 2: Age and Gender distribution of cases

| Age Group(years) | Male(n) | Female(n) |
|---|---|---|
| 21-30 | 01 | 03 |
| 31-40 | 07 | 08 |
| 41-50 | 08 | 20 |
| 51-60 | 15 | 16 |
| 61-70 | 11 | 08 |
| 71-80 | 02 | 02 |
| Total | 44 | 57 |

### Table 3: Analysis of Age and Primary organ malignancy

| Age Group (years) | Breast (n) | GIT(n) | Head and Neck(n) | GUT(n) |
|---|---|---|---|---|
| 21-30 | 02 | 01 | 01 | - |
| 31-40 | 04 | 06 | 02 | 02 |
| 41-50 | 13 | 12 | 02 | 02 |
| 51-60 | 10 | 09 | 07 | 05 |
| 61-70 | 03 | 14 | 01 | 01 |
| 71-80 | 02 | 01 | 01 | 00 |
| Total | 34 | 43 | 14 | 10 |

### Table 4: Primary organ malignancy and Tumor stage

| Primary organ malignancy | Number of cases in Stage I | Number of cases in Stage II | Number of cases in Stage III | Number of cases in Stage IV | Total number of cases |
|---|---|---|---|---|---|
| Breast | 4 | 19 | 10 | 1 | 34 |
| GIT | 4 | 18 | 21 | 0 | 43 |
| Head and neck | 2 | 2 | 4 | 6 | 14 |
| GUT | 1 | 3 | 2 | 4 | 10 |

### Table 5: Comparison of stage with highest and lowest LNR in different primary organ malignancy

| Primary organ malignancy | Highest LNR with stage of tumor | Lowest LNR with stage of tumor |
|---|---|---|
| **Breast** | IIIC-0.8 | IIB-0.05 |
| **GIT cases** | | |
| **Stomach** | IIIB-0.85 | IIIA-0.06 |
| Colon | IIIC-0.68 | IIIB-0.008 |
| Periampullary region | III-0.62 | IIIA-0.08 |
| Gall bladder | IVB-0.75 | IIIB-0.13 |
| **Head and Neck cases** | | |
| Tongue | IVA-0.2 | III-0.04 |
| Buccal mucosa | IVA-0.58 | IVA-0.06 |
| Thyroid | I-0.4 | I-0.125 |
| **GUT cases** | | |
| Prostate | IVA-0.25 | IVA-0.18 |
| Bladder | IVA-0.28 | IIIB-0.2 |

6th decade(n=14), head and neck (n=7)and genitourinary malignancy in 5th decade (n=5).

In primary organ malignancies of GIT maximum numbers of cases were in stage III while in breast stage II was found. In malignancies of GUT and Head and Neck maximum number of cases were in stage IV except thyroid malignancies in which stage I was found. We calculated LNR from LNH and LNM. Total number of LNH with maximum number of LNM considered as highest LNR while total number of LNH with lowest LNM considered as lowest LNR. We calculated highest and lowest LNR in all stages of primary organ malignancies.

Mean LNR was highest in stomach (0.85) and breast (0.8) malignancies. Lowest LNR was in colon malignancy (0.008). As there is only single case in kidney and ovary LNR cannot be defined as highest or lowest. It was found to be 0.1(stage IV A) in kidney and 0.7(stage I) in ovary.

**Discussion:**

In recent years, LNR has provided superior prognostic information over the 'N' category according to TNM classification in cancer patients.LNR, as a new research direction has been shown to have value in estimating prognosis.

Gender and age wise distribution of cases:

Akagiet al[3] and Zenget al[4] reported male predominance in colorectal and gastric carcinoma,as did Chen et al[5] in oropharyngeal malignancy. Rubinstein et al [6] found 88.5% male preponderance in urinary bladder malignancy. In our study,we found a female preponderance because of more number of breast malignancies.The male predominance was in GIT and GUT cases in present study same as in other studies.

**Lymph node harvested**

The recommended mean LNH values are 10, 12, 12 and 40 in breast, GIT, GUT and HFNT, respectively(7-10)almost similar to 11.2,8.4,7.8 and 22 in present study. In Head and Neck, mean LNH is higher than other primary organ malignancy.

**Lymph node metastasis**

Nodal metastasis can coexist with reactive hyperplasia. Titipungulet al.[7] found mean LNM of 3.2 in breast

cases, while Freneaux et al[11] found 4.73.Mean LNM was 1-6 in GIT cases 0.2-4.5 in urinary bladder malignancies 5.8-7 in oral cancersand 4.5-10 in papillary thyroid carcinoma whereas it was 3.17,2.27,1.5,3.57 in breast, GIT, GUT and HFNT respectively in present study.

**Breast cases lymph node ratio, TNM stage**

Titipungal et al.[7] classified breast cancer as low risk(0.01-0.2),intermediate risk(0.21-0.65) high risk(0.66-1.0) with 5 year survival being 66.7%,50% and 0%,respectively.In our study, maximum number of cases of breast cancer were in stage II and III having mean LNR 0.175 and 0.529, respectively. So they were included in low and intermediate risk.

**GIT cases lymphnode ratio,TNM stage**

Dedavidet al.[8] found mean LNR 0.15 as the best predictor of recurrence in colon cancer.Zeng et al[4] found LNR to have high prognostic value in gastric cancers using cut off points as 0,0.5 and 0.8 to categorise as low,intermediate and high risk.From all GIT cancer, we considered stage II and III, as they were in maximum number having mean LNR 0.13 and 0.38, respectively.So they were in intermediate category.

Head and Neck cases lymphnode ratio,TNM stage

Chen et al[5] categorized head and neck cancer as low at LNR<0.06,medium with LNR 0.06-0.17 and high at LNR >0.17. They found low LNR to have longer 3 year survival and metastasis free survival. Sweety SV et al.[13] qualify as low LNR had highest LNH(more lymph nodes harvested) and staging of tumor was less so they had better survival. In present study, maximum numbers of cases were found in stage III and IV with mean LNR 0.04 and 0.24.So they were included in low and high risk. Number of lymph nodes harvested but positive nodes for malignancy were less,

**Genitourinary cases lymph node ratio, TNM stage**

Rubinsteinet al. wright et al[12] and Pedrosa et al.[10] used 2.4,0.12 and 0.2 LNR  as cut off for low, intermediate and high risk, respectively for urinary bladder malignancies. Mean LNR was found to be 0 in stage II, 0.2 in stage III and 0.28 in stage IV. Due to lesser number of cases, further study is required.

## LNR, TNM stage of tumor and prognosis

Maximum numbers of primary organ malignancies were in GIT and Breast so we considered them for statistical analysis. In both malignancies, the numbers of stage IV cases were negligible so we didn't consider them for statistical analysis. In present study, by using unpaired t-test between tumor stage and mean LNR, we calculated p-value in breast (stage II and III) which was significant ($<0.01$); which explains patients having higher stages of cancer with a high mean LNR. This suggests bad prognosis but higher stage of cancer with lower LNR has good prognosis.

p-value in GIT(stage II and III) was significant ($<0.01$) which explains patients having lower mean LNR but having higher stage of cancer. In such cases, prognosis is better.

As number of cases in head and neck malignancies were less and also it had different organ like thyroid, buccal mucosa, tongue. Maximum numbers of lymph nodes harvested are more and positive for malignancy were less. Our main purpose is to see stage of tumor with their LNR values but due to less number of cases in that respective time period and organ wise variation p value is not significant for our study for that more data is required to conclude for the prognosis.

In GUT malignancies, number of cases were also very less; so statistical analysis was not applicable. Longitudinal studies on large sample size would be appropriate for analysis.

Hence, we confirmed that LNR was a better prognostic marker in comparison to LN Staging and TNM classification.LNR can be adopted in follow up of various cancers because of it being more precise predictor of prognosis.

## Conclusion:

Higher predictive value has been observed with LNR than lymph node stage. Present study has several limitations. This study is limited by its retrospective design and single institution focus. Thus a well defined prospective study is needed to fully determine the value of LNR as a prognostic indicator.

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