

Prognostic significance of lymph node ratio in node-positive cervical cancer patients

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Abstract

To determine whether the pelvic lymph node ratio (LNR) has significant prognostic value for survival and disease recurrence in node-positive, early stage cervical cancer patients.

The medical records of 872 consecutive women who received postoperative adjuvant chemoradiotherapy were reviewed. Of these, 397 women with pathologically proven lymph nodal metastasis were included in this analysis and categorized into 3 groups according to their LNR: low (<0.1, n=251), intermediate (0.1–0.4, n=121), and high (>0.4, n=25). The association between LNR and oncological outcome was evaluated using the Kaplan–Meier method and multivariate analysis.

A total of 13,491 LNs were retrieved from 397 women, with a median harvest of 32 nodes per patient. There was a strong positive correlation between the number of metastatic LNs and LNR ($r=0.83$, $P<.01$). With a median follow-up duration of 48 months, the 5-year overall survival (OS) and disease-free survival (DFS) rates were 73% and 67%, respectively. The OS and DFS curves among the pelvic LNR groups significantly differed: the 5-year OS rates of the low, intermediate, and high pelvic LNR groups were 83%, 66%, and 17% ($P<.01$), and the 5-year DFS rates were 77%, 56%, and 20% ($P<.01$), respectively.

LNR is an important prognostic factor for survival outcomes in patients with uterine cervical cancer who underwent radical hysterectomy followed by adjuvant chemoradiotherapy.

Abbreviations: CT = computed tomography, DFS = disease-free survival, FIGO = federation of gynecology and obstetrics, LN = lymph node, LNR = lymph node ratio, LODD = log odds of positive lymph node, OS = overall survival, PAN = para-aortic node, PET = positron emission tomography, PFS = progression-free survival, PLND = pelvic lymph node dissection, RT = radiotherapy, RTOG = radiation therapy oncology group, SEER = surveillance epidemiology and end results, SNB = sentinel node biopsy.

Keywords: lymph node, prognosis, uterine cervical neoplasm

1. Introduction

Radical hysterectomy is the standard therapy for early stage cervical cancers, and adjuvant treatment is often needed depending on the pathological risk factors determined in previous clinical trials;^[1,2] in patients with major risk factors, such as lymph node (LN) metastasis, positive resection margins, and parametrial invasion, adjuvant chemoradiotherapy should be considered.^[1] Postoperative radiotherapy (RT) is recommended for patients with ≥ 2 minor risk factors, such as deep stromal invasion, lymphovascular space involvement, or large tumor diameter.^[2]

LN metastasis is one of the most powerful prognostic parameters for patients with cervical cancer.^[3] Additionally, the number of metastatic LNs also significantly affects patient outcomes.^[4,5] Because the International Federation of Gynecology and Obstetrics (FIGO) system is mainly based on clinical examination, ignoring the pathological results, particularly LN metastasis, is a major weakness of the system for predicting prognosis.

The ratio of metastatic to dissected LNs, known as the LN ratio (LNR), has been shown to be an important prognostic factor in various malignancies.^[6–8] Recently, LNR has been proposed as a prognostic tool in cervical cancer. A significant correlation between LNR and survival has also been shown in small-scale retrospective analyses.^[3,9] The purpose of the present study was to use a large single-institutional database to determine if LNR has prognostic value for survival and disease recurrence in patients with early stage cervical cancer who underwent hysterectomy followed by adjuvant chemoradiotherapy.

2. Methods

From 1997 to 2015, a total of 872 consecutive patients with early stage cervical cancer underwent surgery followed by adjuvant RT and chemotherapy; pelvic LN metastasis was pathologically proven in 397 patients. The medical records of these 397 women were retrospectively reviewed. This study was approved by the local institutional review board, and informed consent was waived.

For baseline evaluation before hysterectomy, pelvic examination, laboratory tests, chest radiography, intravenous pyelography, cystoscopy, sigmoidoscopy, and magnetic resonance imaging or

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positron emission tomography-computed tomography (PET-CT) were routinely performed in all patients. Most patients underwent type III radical hysterectomy. Para-aortic lymphadenectomy was not routinely performed as a part of surgical nodal staging, but was performed to remove enlarged or suspicious nodes at the surgeon's discretion. Prior to RT, planning CT using intravenous contrast agents and free breathing (AcQSim, Philips Medical System, Andover, MA and Light Speed RT, GE Healthcare, St Giles, UK) was performed in each patient in the supine position, with arms on their chest. Three-dimensional conformal or intensity-modulated RT to the pelvis was administered at a median dose of 50.4 Gy with conventional fractionation unless the para-aortic node (PAN) was involved. The superior border of the pelvic field was located at the aortic bifurcation. In patients with PAN metastasis, extended-field RT with the same dose and fractionation schedule encompassing pelvic and retroperitoneal lymphatics below the T12/L1 junction was performed. Additional vaginal brachytherapy boost, which was mainly 10 Gy in 2 fractions, was performed in patients with positive or close resection margins. There were 340 (86%) concurrent patients who received platinum-based chemotherapy during adjuvant RT at the physician's discretion. The most popular regimen was weekly cisplatin (n=261) followed by cisplatin and 5-fluorouracil (n=47) and cisplatin and taxane (n=32). After completion of the adjuvant treatment, the patients were evaluated at 3-month intervals for 2 years and at 6-month intervals thereafter. Pelvic examinations were performed at each follow-up, including liquid-based cytological analysis of tissue samples from vaginal stump. Imaging studies, such as CT or PET-CT, were performed every 6 to 12 months or as clinically indicated.

Overall survival (OS) time was calculated from the start of adjuvant RT to death or last follow-up. Disease-free survival (DFS) was calculated from the start of RT to the development of recurrence, death, or last follow-up. The Kaplan–Meier method was used to construct survival curves. A Cox proportional hazards model was used for multivariate analysis. Multivariate analysis was performed on factors with a *P* value of <.2 in the

univariate analysis. Chi-square tests and analysis of variance were used to compare the characteristics between the LNR groups. *P* value of <.05 was considered statistically significant. All statistical analyses were performed using the SPSS software, version 21.0 (IBM, Armonk, NY).

3. Results

The clinical and pathological characteristics of patients are summarized in Table 1. The median age was 45 years, and 154 (39%) patients were aged ≥50 years. Most patients had squamous cell carcinoma with stage IB (n=282) and IIA (n=74) pathologies. In the surgical specimens, unilateral and bilateral parametrial invasion was diagnosed in 121 (30%) and 98 (25%) patients, respectively. Bulky tumor (≥ 4 cm) was diagnosed in 172 (43%) patients. Adjuvant chemotherapy was concurrently administered in 358 (90%) patients.

A total of 13,491 LNs from 397 patients were examined, with a median harvest of 32 LNs per specimen; of these, 1697 (13%) were diagnosed as positive (median, 2 LNs per patient). A strong positive correlation was observed between metastatic LNs and LNR as a continuous variable (*r*=0.83, *P*<.01). The patients were categorized into 3 groups according to their pelvic LNR: low (<0.1, n=251), intermediate (0.1–0.4, n=121), and high (>0.4, n=25). The patients in the high pelvic LNR group had significantly higher stage disease than those in other groups (*P*=.04). There was no significant difference in the number of harvested pelvic LNs among the 3 groups. Para-aortic LN sampling or dissection was performed in 304 (77%) patients. Median number of retrieved LNs was 4. Totally, 1770 para-aortic LNs were harvested and 243 (14%) were diagnosed as positive. For analysis, patients were grouped as low PAN-LNR (<0.1, n=264), intermediate PAN-LNR (0.1–0.4, n=19), high PAN-LNR (>0.4, n=21). Both number of retrieved PAN (*P*<.01) and metastatic PAN (*P*<.01) was higher in high pelvic LNR group.

Table 1
Clinical and pathologic characteristics of the patients.

| Variables | Total (N = 397) | Low (<0.10, N = 251) | Intermediate (0.10–0.40, N = 121) | High (>0.40, N = 25) | <i>P</i> |
|------------------------|-----------------|----------------------|-----------------------------------|----------------------|----------|
| Age | | | | | |
| <50 | 243 (61) | 145 | 78 | 20 | .06 |
| ≥50 | 154 (39) | 106 | 43 | 5 | |
| Histology | | | | | |
| SqCC | 291 (73) | 189 | 86 | 16 | .38 |
| Non-SqCC | 106 (27) | 62 | 35 | 9 | |
| Stage | | | | | |
| IA/IB | 7/282 | 4/187 | 1/82 | 2/13 | .04 |
| IIA/IIB | 74/34 | 44/16 | 25/13 | 5/5 | |
| SCC-Ag (median) | 6.6 ± 13.6 | 6.0 ± 13.5 | 6.9 ± 12.6 | 12.0 ± 18.5 | .09 |
| Metastatic PAN* | 0.8 ± 3.5 | 0.1 ± 0.5 | 0.6 ± 1.8 | 7.9 ± 10.3 | <.01 |
| Harvested PAN* | 5.8 ± 6.6 | 4.7 ± 4.4 | 6.0 ± 6.7 | 14.8 ± 12.5 | <.01 |
| Metastatic pelvic node | 4.3 ± 5.5 | 1.9 ± 1.1 | 6.1 ± 3.3 | 19.7 ± 10.1 | <.01 |
| Harvested pelvic node | 34.0 ± 12.3 | 34.8 ± 12.4 | 31.9 ± 10.9 | 36.0 ± 15.9 | .33 |
| PMI | | | | | |
| No | 158 (42) | 105 | 48 | 5 | .02 |
| Unilateral | 121 (32) | 80 | 35 | 6 | |
| Bilateral | 98 (26) | 53 | 32 | 13 | |
| LVI | | | | | |
| Negative | 92 (24) | 76 | 16 | 0 | <.01 |
| Positive | 298 (76) | 169 | 104 | 25 | |
| DOI | | | | | |
| ≤1/2 | 37 (9) | 24 | 12 | 1 | .63 |
| >1/2 | 356 (91) | 223 | 109 | 24 | |
| Size | | | | | |
| ≤4 cm | 225 (57) | 147 | 68 | 10 | .19 |
| >4 cm | 172 (43) | 104 | 53 | 15 | |

CCRT = concurrent chemoradiation, DOI = depth of invasion, LNR = lymph node ratio, LVI = lymphovascular invasion, PAN = para-aortic node, PMI = parametrial invasion, RH = radical hysterectomy, RM = resection margin, RT = radiotherapy, SCC-Ag = squamous cell antigen, SqCC = squamous cell carcinoma.

*Para-aortic lymph node sampling or dissection was performed in 304 patients.

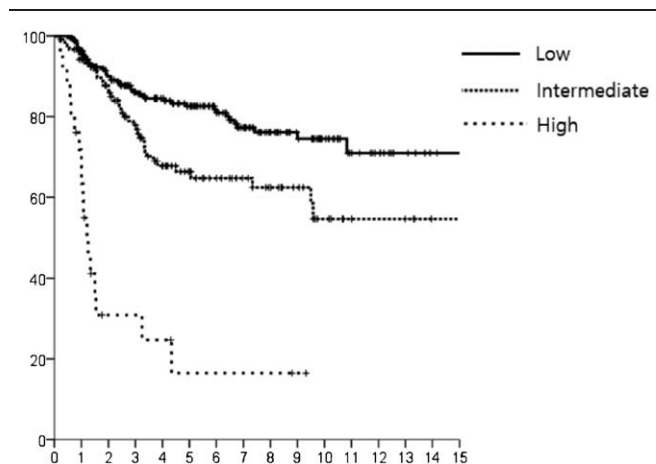


Figure 1. Overall survival curves of the lymph node ratio (LNR) groups. The 5-year rates of each group are shown.

With a median follow-up duration of 48 months (range, 3–215 months), the 5-year survival rates of the patients in the low, intermediate, and high pelvic LNR groups were 83%, 66%, and 17%, respectively ($P < .01$ by log-rank test) (Fig. 1). The DFS rate also differed significantly between the groups (Fig. 2); the 5-year DFS rates were 77%, 56%, and 20%, respectively ($P < .01$). Likewise the absolute number of metastatic pelvic LN showed correlation with survival as well as disease recurrence. Using Cox-regression, the hazard ratios (HR) for death and recurrence were 1.09 (1.07–1.11, $P < .01$) and 1.09 (1.07–1.11, $P < .01$), respectively, meaning the probability of death and recurrence would be 1.09 times more likely when the number of positive lymph node increased by one. Additionally, OS and DFS significantly differed according to PAN-LNR groups. For low, intermediate, and high PAN-LNR groups, the 5-year OS rates were 80%, 50%, and 14%, respectively ($P < .01$). The 5-year DFS rates were 73%, 48%, and 22%, respectively ($P < .01$). The results of prognostic factor analysis for OS and DFS are summarized in Table 2. In the multivariate analysis the significant prognostic factors were histology, stage, pelvic LNR, and parametrial invasion for OS, and histology, pelvic LNR, and parametrial invasion for DFS. Subgroup analyses were performed

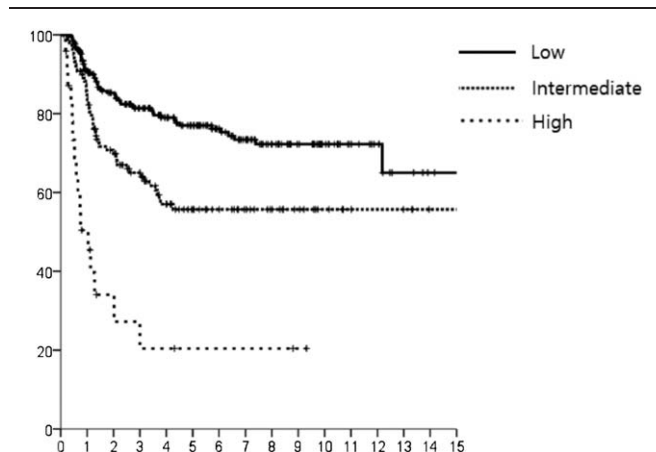


Figure 2. Disease-free survival curves of the lymph node ratio (LNR) groups. The 5-year rates of each group are shown.

to determine if survival differences associated with pelvic LNR persisted after grouping the patients according to the disease stage. The probability of recurrence and death was higher in the higher LNR group for all stages than in other groups (Fig. 3). The hazard ratios for pelvic LNR according to FIGO stages are presented in Table 3. In both squamous cell carcinoma or non-squamous cell carcinoma, higher LNR was associated to poorer treatment outcomes. The results are presented in Table 4.

4. Discussion

We investigated the prognostic value of LNR for disease recurrence as well as survival in patients with node-positive early stage uterine cervical cancer. We found that LNR was a strong prognosticator for both the outcomes. When the patients were grouped according to low (<0.1), intermediate (0.1–0.4), and high (>0.4) pelvic LNRs, substantial differences in the DFS and OS rates were observed. Previous studies have investigated the association between LN positivity and prognosis in patients with uterine cervical cancer who underwent radical hysterectomy.^[3,9] A study by Polterauer et al^[9] found associations between LN density (same as LNR in the current study) and DFS and OS. According to their report, patients with LN density of $<10\%$ and $\geq 10\%$ had 5-year OS rates of 67% and 38%, respectively; these findings were consistent with those of our study. Fleming et al^[3] suggested that LNR was a useful tool for identifying patients with worse prognosis in node-positive early stage cervical cancer. They showed that LNR of $>6.6\%$ was associated with worse progression-free survival (PFS), and LNR of $>7.6\%$ was associated with worse OS. Unlike the results of Polterauer et al^[9] and the current study, they did not find any significant association between LNR of $>10\%$ and any survival, possibly due to difficulty in determining the optimal cutoff values in small retrospective studies.

In addition to LNR, several other LN-related factors have been tested for their prognostic values in patients with uterine cervical cancer. In a study by Monk et al,^[10] patients with ≥ 2 positive LNs had a significantly lower survival rate after radical surgery followed by only adjuvant RT (5-year OS, 55% vs 79%; $P = .01$). Tsai et al^[11] demonstrated that the number and location of nodal involvement independently influenced the prognosis of uterine cervical cancer. The 5-year DFS rates for patients with 0, 1, and >1 LN metastases were 87%, 84%, and 61%, respectively ($P = .0001$). Patients with common iliac node metastasis had a higher incidence of distant metastasis (50%) than that (16%) in patients with external and internal iliac node metastases ($P = .03$). Similarly, Takeda et al^[12] found that when the tumor extended to the common iliac nodes or PANs, the patients' survival became very poor irrespective of other histological characteristics. Kwon et al^[13] compared the prognostic efficacies of various LN-associated variables, including number, location, LNR, and log odds of positive LNs (LODDs, the log of odds between the numbers of positive and negative LNs). Among the methods used for the assessment of LN status, they proposed that LODD was the most powerful indicator associated with DFS. Patients with LODDs of ≥ -1.05 had significantly shorter DFS rates than those without it (5-year DFS rate, 93.8% vs 54.2%, $P = .015$). However, LODD is not simple to use in daily practical setting. Additionally, the number of LNs and LNR have been used together to construct prognosis-predicting nomograms in several studies.^[4,5,14,15] The advantages of LNR over other parameters are as follows: underestimation because of less aggressive dissection can be avoided,^[16] thoroughness of the surgical

Table 2
Univariate and multivariate analysis for disease-free and overall survival.

| Variables | OS | | DFS | |
|------------------------------|--------------------------|--------------------|--------------------------|-------------------|
| | Univariate HR | Multivariate HR | Univariate HR | Multivariate HR |
| Age (<50 vs ≥50) | 1 (1–1.01) | | 1 (0.99–1.01) | |
| Histology (SqCC vs non SqCC) | 2.57* (1.72–3.82) | 2.9* (1.66–5.06) | 3.23* (2.25–4.64) | 3.39* (2.06–5.56) |
| Stage (I vs II) | 1.35 (0.88–2.07) | 1.8* (1.07–3.04) | 1.05 (0.69–1.59) | 1.2 (0.7–2.05) |
| SCC-Ag (normal vs elevated) | 1.01 (1–1.02) | 1.01 (1–1.02) | 1.01 (1–1.02) | 1.01 (1–1.02) |
| Metastatic LN | 1.09* (1.07–1.11) | | 1.09* (1.07–1.11) | |
| Pelvic LNR (low vs) | | | | |
| Intermediate (0.10–0.40) | 1.85* (1.21–2.85) | 1.55 (0.9–2.68) | 1.99* (1.35–2.93) | 1.77* (1.03–3.03) |
| High (>0.40) | 9.57* (5.48–16.71) | 4.74* (1.68–13.39) | 7.13* (4.06–12.52) | 3.4* (1.3–8.87) |
| PAN-LNR (low vs)† | | | | |
| Intermediate (0.10–0.40) | 2.75* (1.31–5.8) | 1.31 (0.51–3.37) | 2.76* (1.42–5.38) | 0.98 (0.32–2.97) |
| High (>0.40) | 7.79* (4.35–13.97) | 3.15* (1.22–8.12) | 6.01* (3.34–10.8) | 1.98 (0.66–5.91) |
| PMI (none vs) | | | | |
| Unilateral | 1.79* (1.07–2.97) | 1.43 (0.76–2.68) | 1.5 (0.93–2.41) | 2.04* (1.05–3.96) |
| Bilateral | 3.13* (1.9–5.16) | 2.75* (1.51–5.01) | 3.08* (1.98–4.8) | 4.36* (2.36–8.06) |
| LVI (– vs +) | 2.32* (1.31–4.08) | 0.94 (0.42–2.12) | 1.74* (1.08–2.78) | 0.89 (0.44–1.82) |
| DOI (≤1/2 vs >1/2) | 2.97* (1.09–8.08) | 1.42 (0.42–4.84) | 1.69 (0.82–3.47) | 0.93 (0.34–2.52) |
| Size (≤4 vs >4 cm) | 1.06 (0.93–1.21) | | 1.05 (0.93–1.19) | |

DFS=disease-free survival, DOI=depth of invasion, HR=hazard ratio, LN=lymph node, LNR=lymph node ratio, LVI=lymphovascular invasion, OS=overall survival, PAN=para-aortic node, PMI=parametrial invasion, SCC-Ag=squamous cell antigen, SqCC=squamous cell carcinoma
 *Statistically significant values.
 †Para-aortic lymph node sampling or dissection was performed in 304 patients.

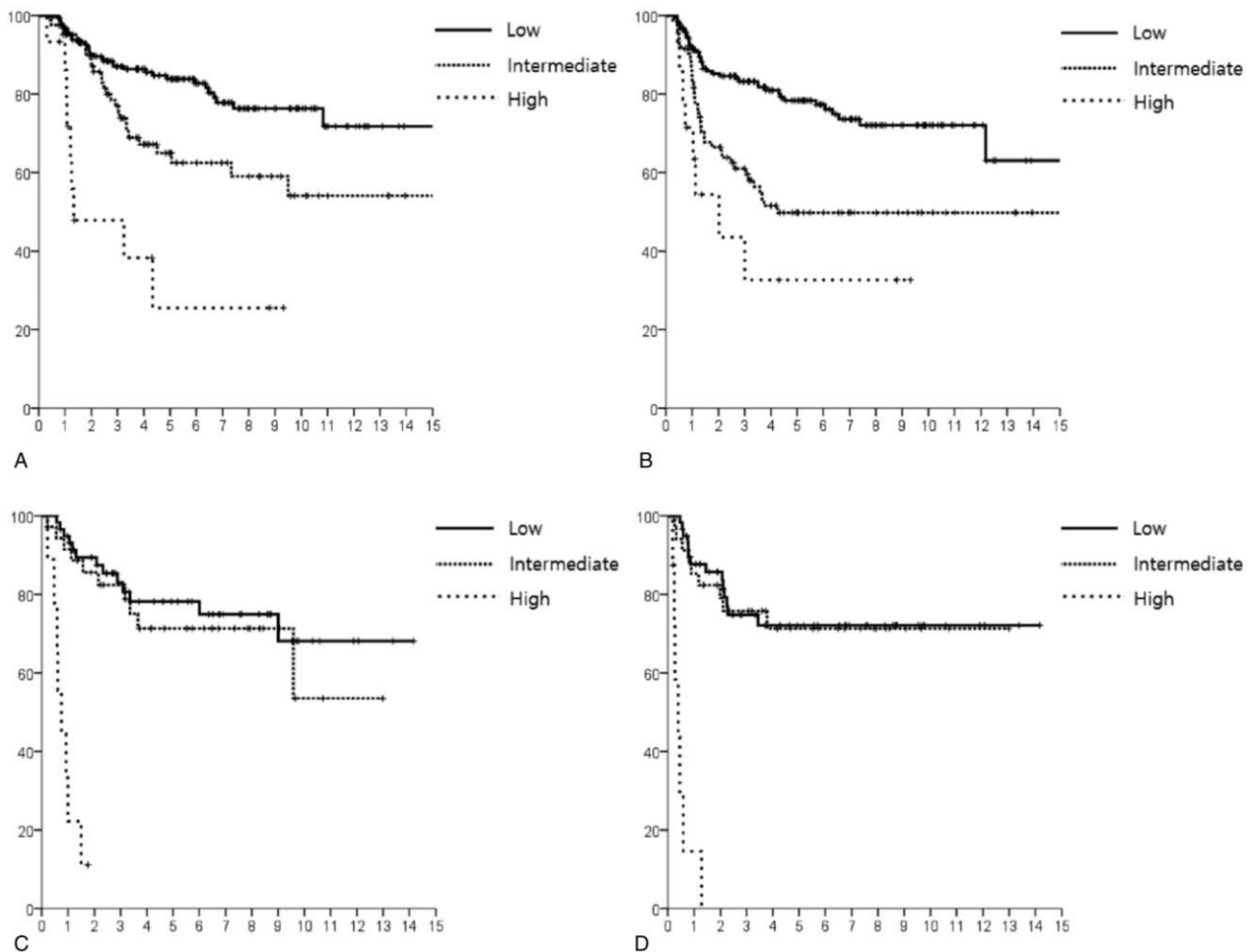


Figure 3. (A) Overall survival curve in stage I. (B) Disease-free survival curve in stage I. (C) Overall survival curve in stage II. (D) Disease-free survival curve in stage II.

Table 3
Hazard ratios by pelvic LNR for overall and disease-free survival, according to FIGO stages.

| | LNR | N | OS (HR) | P | DFS (HR) | P |
|----------|--------------|-----|--------------------|------|--------------------|------|
| Stage I | Low | 191 | 1 | | 1 | |
| | Intermediate | 83 | 2.01 (1.24–3.44) | .01 | 2.42 (1.55–3.76) | <.01 |
| | High | 15 | 6.64 (3.16–13.98) | <.01 | 4.39 (2.05–9.39) | <.01 |
| Stage II | Low | 60 | 1 | | 1 | |
| | Intermediate | 38 | 1.29 (0.56–2.95) | .54 | 1.08 (0.46–2.48) | .87 |
| | High | 10 | 17.37 (6.34–47.61) | <.01 | 22.02 (7.99–60.66) | <.01 |

DFS=disease-free survival, HR=hazard ratio, LNR=lymph node ratio, OS=overall survival.

Table 4
Hazard ratios by pelvic LNR for overall and disease-free survival, according to pathology.

| | LNR | N | OS (HR) | P | DFS (HR) | P |
|----------|--------------|-----|--------------------|------|--------------------|------|
| SqCC | Low | 189 | 1 | | 1 | |
| | Intermediate | 86 | 1.87 (1.07–3.27) | .03 | 2.41 (1.42–4.09) | <.01 |
| | High | 16 | 11.85 (5.62–24.99) | <.01 | 10.60 (4.92–22.84) | <.01 |
| Non-SqCC | Low | 62 | 1 | | 1 | |
| | Intermediate | 35 | 1.68 (0.86–3.31) | .13 | 1.51 (0.85–2.68) | .16 |
| | High | 9 | 5.00 (2.15–11.62) | <.01 | 3.70 (1.60–8.56) | <.01 |

DFS=disease-free survival, HR=hazard ratio, LNR=lymph node ratio, OS=overall survival, SqCC=squamous cell carcinoma.

dissection and pathological examination is reflected, and it is the most intuitive factor and is easy to calculate.

Low LNR can result from more aggressive LN dissection, which has been shown to be correlated with improved survival. Some studies have found that removal of a larger number of regional LNs improved patient survival in several malignancies.^[17,18] These findings are most likely explained by the fact that examination of a greater number of LNs increases the likelihood of proper staging rather than providing a direct therapeutic effect.^[16] Proper LN assessment is critical because it affects the decision on adjuvant treatment, such as the addition of chemotherapy and radiotherapy. In cervical cancer, clinical assessment of LNs is performed using CT, magnetic resonance imaging, or PET-CT. However, the diagnostic performance of these modalities has not been found to be satisfactory.^[19,20] Therefore, pathological nodal staging often differs from clinical information and may change the course of the treatment. Marnitz et al^[21] reported the results of surgical staging. Using laparoscopic LN dissection/sampling, metastatic LN involvement was histopathologically proven in 75% of patients (25 out of 33) with stage IB to IIA cervical cancer. In a study by Lim et al,^[22] laparoscopic LN dissection was prospectively evaluated. Six (7.8%) of 77 patients suggestive of no metastases on preoperative imaging analysis had LN metastases in PAN on pathological diagnosis. As a result, the radiation field was enlarged to cover the para-aortic area. Furthermore, it has been proven that aggressive node dissection improves patient survival. Surveillance Epidemiology and End Results (SEER) analysis of 12,882 patients found that patients who underwent LN dissection had improved OS ($P=.001$), which was significant for each stage. OS increased for ≤ 15 resected LNs ($P=.01$).^[23] Another important finding was shown by Gold et al^[24] who reviewed the outcomes of 685 LN-negative patients enrolled in 3 Gynecology Oncology Group studies and compared PFS and OS between patients who underwent surgical and radiological staging. They found that PAN dissection was independently associated with better PFS and OS. Patients in the surgical staging group had better 4-year PFS (48.9% vs 36.3%) and OS (54.3% vs 40%) than those of patients

in the radiological staging group. In other words, LN dissection is important for accurate diagnosis and treatment and is associated with improved survival.

However, in patients with FIGO stage IB to IIA disease, extensive lymphadenectomy leads to lymphocyst formation in approximately 20% and lymphedema in 10%.^[25,26] Cervical cancer tends to spread to pelvic nodes in a stepwise pattern.^[27] Cancer detection in the first draining LN (sentinel LN) can predict pelvic nodal metastasis and reduce unnecessary extensive nodal dissection. Several retrospective studies have investigated whether sentinel node biopsy (SNB) can safely replace pelvic LN dissection (PLND)^[28–30] and reported conflicting results. Kenter et al showed that completing LN dissection resulted in a longer OS and DFS for LN-positive cervical cancer patients but not LN-negative patients^[28]. Contrastingly, Shah et al^[29] showed that extensive lymphadenectomy had no effect on survival in LN-positive women (hazard ratio=0.75; 95% confidence interval, 0.47–1.22), but was associated with improved survival in LN-negative women. In a multicenter retrospective study by Zaal et al,^[30] only patients with micrometastases and isolated tumor cells benefited from PLND in terms of OS. Taken together, extensive PLND may have a therapeutic effect in patients with definitive pelvic LN metastases, and may help in proper staging in clinically diagnosed LN-negative patients. The Uterus-11 multicenter phase III intergroup trial is underway. It is designed to evaluate the role of surgical staging in patients with cervical cancer. Until then, attempts to substitute PLND with SNB remain challenged, regardless of the clinical nodal stage.

The current study had several limitations. First, many inherent biases stem from its nature as a retrospective study. Our study, however, was the result of a long-term follow-up at a single center with relatively homogeneous staging, and data were extracted from the largest database which was used by previous studies. Additionally, the number of harvested LNs (median, 32) was high. Second, the location of metastatic LNs could not be analyzed. Despite these drawbacks, very high risks of disease recurrence and mortality were found in patients with LNR of >0.4 , which suggested the need for additional chemotherapy in

these patients. A study of the role of additional adjuvant chemotherapy after radical hysterectomy and chemoradiotherapy in patients with high-risk early stage cervical carcinoma is underway (Radiation Therapy Oncology Group [RTOG] 0724). Third, this study lacks granular information about complications related to lymphadenectomy. A recent study involving sentinel LN mapping showed very high sensitivity (96%) and negative predictive value (99%) for early stage cervical cancer.^[31] Once validated by prospective randomized trials, sentinel LN mapping will replace complete lymphadenectomy in a highly selected patient group to decrease morbidity resulting from comprehensive lymphadenectomy. However, until SNB becomes a standard treatment, LNR following standard LN dissection can provide the necessary prognostic information.

In conclusion, this study found that LNR is an important prognostic factor in patients with uterine cervical cancer who underwent radical hysterectomy followed by chemoradiotherapy. LNR can be used to design future clinical trials on the potential benefit of additional chemotherapy in high-risk patient populations.

Author contributions

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Methodology: Ji Hyeon Joo, Young Seok Kim.

Project administration: Young Seok Kim.

Supervision: Young Seok Kim, Joo-Hyun Nam.

Validation: Young Seok Kim.

Writing – original draft: Ji Hyeon Joo.

Writing – review and editing: Young Seok Kim, Joo-Hyun Nam.

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