# Localization patterns and survival of extranodal NK/T-cell lymphomas in the United States: A population-based study of 945 cases

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## Background

Extranodal natural killer/T-cell lymphomas (eNK/TCLs) are aggressive, angioinvasive, necrotizing EBV-associated lymphomas with a 5-year overall survival ranging from 30-50%. Approximately 80% of eNK/TCLs develop in the nose/upper aerodigestive tract and 20% at non-nasal sites (skin, viscera, lymph nodes [LN]).1,2 Mean age of onset is 44 years, and it is 2-3 times more common in men.

**Figure 1. Nasal extranodal NK/T-cell lymphoma (eNK/TCL) with facial ulceration.**

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**Figure 2. Nasal extranodal NK/T-cell lymphoma (eNK/TCL) with cutaneous involvement**. This patient demonstrates cutaneous involvement by the patient's known nasal eNK/TCL (Goyal, et al, Atlas of Cutaneous Lymphomas, 2015).

## Objective

In this analysis we evaluated the impact of initial diagnosis on prognosis. we examined data from the Surveillance, Epidemiology, and End Results Program (SEER-18) database for patients diagnosed with eNK/TCL from 2000-2016 (n=945). We analyzed demographics and survival based on the site of initial diagnosis.

## Table 1: Patient Characteristics

| | | All Sites n=936 | Oro/Nasal n=678 | Visceral n=102 | Lymph Node n=104 | Skin n=52 | p-values |
|---|---|---|---|---|---|---|---|
| Distribution | | | 678 (72.4%) | 102 (10.9%) | 104 (11.1%) | 52 (5.6%) | |
| Age | | | | | | | |
| | Median (range) years | 54 (3-103) | 54 (4-93) | 54.5 (3-96) | 51.5 (3-87) | 62 (15-103) | Skin vs. all others p<0.05 |
| | Mean (std. dev.), years | 53.4 (18.6) | 53.3 (17.9) | 53.1 (19.7) | 50.9 (19.1) | 61.0 (23.0) | |
| Gender | | | | | | | |
| | Male | 602 (64.3%) | 432 (63.7%) | 69 (67.6%) | 72 (69.2%) | 29 (55.8%) | Skin vs. all others p<0.05 |
| | Female | 334 (35.7%) | 246 (36.3%) | 33 (32.4%) | 32 (30.8%) | 23 (44.2%) | |
| Race | | | | | | | |
| | Hispanic (all races) | 335 (35.8%) | 254 (37.5%) | 33 (32.4%) | 37 (35.6%) | 11 (21.2%) | NS |
| | Non-Hispanic American Indian/Alaska Native | 11 (1.2%) | 6 (0.9%) | 4 (3.9%) | 1 (1.0%) | 0 (0.0%) | |
| | Non-Hispanic Asian or Pacific Islander | 202 (21.6%) | 151 (22.3%) | 23 (22.5%) | 16 (15.4%) | 12 (23.1%) | |
| | Non-Hispanic Black | 46 (4.9%) | 32 (4.7%) | 6 (5.9%) | 7 (6.7%) | 1 (1.9%) | |
| | Non-Hispanic White | 339 (36.2%) | 232 (34.2%) | 36 (35.3%) | 43 (41.3%) | 28 (53.8%) | |
| | Non-Hispanic Unknown Race | 3 (0.3%) | 3 (0.4%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | |

## Table 2: Survival

| Survival | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Median follow-up (range), months | 10 (0-190) | 14 (0-187) | 4 (0-190) | 4 (0-175) | 9.5 (0-172) | NS |
| | # Alive (%) at end of follow-up | 375 (40.1%) | 326 (48.1%) | 26 (25.5%) | 16 (15.4%) | 7 (13.5%) | |
| | # Dead (%) at end of follow-up | 561 (59.9%) | 352 (51.9%) | 76 (74.5%) | 88 (84.6%) | 45 (86.5%) | Skin vs. oro/nasal p<0.0001 Skin vs. Visceral p=0.085 Skin vs. LN p=0.75 |
| | 2-year OS (95% CI) (Non-age adjusted) | 0.46 (0.42, 0.49) | 0.61 (0.55, 0.69) | 0.26 (0.19, 0.37) | 0.26 (0.19, 0.36) | 0.24 (0.15, 0.39) | Oro/Nasal vs. all others p<0.05 Skin vs. LN and visceral NS |
| | 5-year OS (95% CI) (Non-age adjusted) | 0.37 (0.34, 0.41) | 0.53 (0.50, 0.57) | 0.24 (0.16, 0.34) | 0.18 (0.12, 0.28) | 0.17 (0.09, 0.32) | Oro/Nasal vs. all others p<0.05 Skin vs. LN and visceral NS |
| | 2-year DSS (95% CI) (Non-age adjusted) | 0.55 (0.51, 0.58) | 0.62 (0.58, 0.66) | 0.34 (0.25, 0.47) | 0.35 (0.27, 0.47) | 0.36 (0.23, 0.54) | Oro/Nasal vs. all others p<0.05 Skin vs. LN and visceral NS |
| | 5-year DSS (95% CI) (Non-age adjusted) | 0.47 (0.44, 0.51) | 0.54 (0.49, 0.58) | 0.32 (0.23, 0.45) | 0.26 (0.18, 0.38) | 0.32 (0.20, 0.51) | Oro/Nasal vs. all others p<0.05 Skin vs. LN and visceral NS |

## Kaplan-Meier Survival Curve

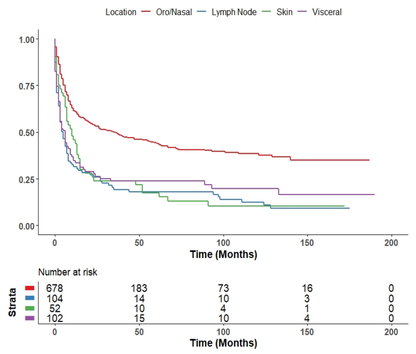


**Figure 2**. Overall survival by location of extranodal NK/T-cell lymphoma (eNKTCL). Cases diagnosed based on oro/nasal involvement demonstrate better survival than those diagnosed at lymph node, skin, or visceral sites.

## Cox Multivariate Regression Modeling

- Patients with skin-diagnosed eNK/TCL disease were 1.56 times (95% CI 1.17-2.09, p=0.023) more likely to die than those with oral/nasal diagnoses
- This was similar to lymph node diagnosed disease (relative risk [RR] 1.57, 95% CI 1.17-2.09, p=0.002) and visceral disease (RR 1.65, 95% CI 1.23-2.21, p<0.001).
- Age was a significant factor, with a 9% increase risk of death due to eNK/TCL per decade of increased age (RR 1.09, 95% CI 1.04-1.15, p<0.001).
- Extent of disease was also significant, localized and regional disease being protective factors compared to distant disease. Gender was not a significant contributor.

| Cox Regression Model ` | | | | |
|---|---|---|---|---|
| | Disease-Specific Survival | | Overall Survival | |
| Covariate | RR (95% CI) | p-value | RR (95% CI) | p-value |
| Site | | | | |
| Skin vs. oro/nasal | 1.55 (1.06, 2.27) | 0.023 | 1.63 (1.19, 2.25) | 0.003 |
| LN vs. oro/nasal | 1.57 (1.17, 2.09) | 0.002 | 1.50 (1.16, 1.94) | 0.002 |
| Visceral vs. oro/nasal | 1.65 (1.23, 2.21) | <0.001 | 1.65 (1.27, 2.13) | <0.001 |
| LN vs. skin | 1.01 (0.65, 1.55) | 0.971 | 0.92 (0.63, 1.33) | 0.654 |
| Visceral vs. skin | 1.06 (0.68, 1.65) | 0.783 | 1.01 (0.69, 1.47) | 0.970 |
| Age (10 years) | 1.09 (1.04, 1.15) | <0.001 | 1.15 (1.09, 1.20) | <0.001 |
| Sex, Male vs. Female | 0.85 (0.70, 1.04) | 0.107 | 0.98 (0.82, 1.17) | 0.819 |
| Stage | | | | |
| Regional vs. localized | 1.77 (1.33, 2.33) | <0.001 | 1.66 (1.31, 2.11) | <0.001 |
| Distant vs. localized | 3.25 (2.53, 4.17) | <0.001 | 2.74 (2.21, 3.41) | <0.001 |
| Unknown/Unstaged vs localized | 1.18 (0.72, 1.93) | 0.513 | 1.60 (1.11, 2.31) | 0.011 |

## Conclusions

- Patients with eNK/TCL diagnosed in the skin had markedly poorly prognosis compared to those diagnosed in the oral/nasal area
- Survival of patients with skin-diagnosed disease was similar to patients diagnosed via visceral or lymph node disease

## References

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