Purpose/Objective(s): Lymphovascular space invasion (LVI) is an established negative prognostic factor in many solid tumors and guides recommendations regarding adjuvant radiation therapy in many malignancies including head and neck cancer, cervical cancer, and endometrial cancer. LVI does not currently influence therapeutic decision making in non-small cell lung cancer (NSCLC). The purpose of this study was to evaluate LVI in patients with early-stage NSCLC undergoing initial surgical resection, specifically to evaluate the relationship between LVI and regional lymph node involvement and the risk of local failure after resection.

Materials/Methods: As part of an IRB-approved study, all patients who underwent surgery for pathological T1-3N0-2 NSCLC at Duke University Medical Center from 1995-2008 were identified. Medical records were reviewed and pathologic and clinical data extracted. A multivariate ordinal regression was used to assess the relationship of LVI and pathologic hilar and mediastinal lymph node involvement. A multivariate Cox regression analysis was used to evaluate the relationship of LVI and other clinical and pathologic factors on local failure (LF), distant metastasis-free survival (DMFS), and overall survival (OS). Kaplan Meier methods were used to generate estimates of local failure in patients with and without LVI in a stage-dependent manner.

Results: 1559 patient were identified. Median follow-up for all patients was 34 months, and 40 months for surviving patients. On multivariate ordinal regression, LVI was independently associated with the presence of regional lymph node involvement (p<0.001) along with lobar (versus sublobar) resections (p<0.001), and open (versus VATS) approaches (p<0.001). LVI was associated with a 36% risk of pN1 disease and a 12% risk of pN2 disease. LVI was associated with a higher risk of local failure after surgery, with 5-year local control of 79% in patients without LVI vs. 71% in patients with LVI (p=0.001). LVI was also significantly associated with a lower 5-year DMFS (HR 1.52, p=0.005) and OS (HR 1.26, p=0.015). Chemotherapy was associated with improved OS (HR 0.35, p<0.001). Adjuvant chemotherapy was associated with improved 5 year OS for both patients with LVI (from 32% to 60%, p = 0.001) and without LVI (from 50% to 69%, p<0.001).

Conclusions: LVI is associated with an increased risk of harboring regional lymph node involvement (N1 and N2 disease). This may aid in determining adjuvant therapies in patients who do not undergo full surgical staging. Additionally, LVI is associated with a higher risk of local failure after surgical resection. Lastly, LVI is a poor prognostic factor for development of distant metastasis and long-term survival and in the future could be used to guide adjuvant therapy recommendations.