Treatment strategies in node-negative gastric cancer

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Lymph node metastasis is the most important prognostic factor in gastric cancer (1-3). Curative resection including adequate lymphadenectomy provided the chance of a cure for localized disease. However, node-negative gastric cancer patients undergoing extensive lymphadenectomy also experience recurrence and distant metastases (4,5). In the issue of *Journal of Gastrointestinal Surgery*, Liu and colleagues (6) show that the invasion in lymphatic or vascular vessels, and depth of tumor invasion were independent prognostic factors in node-negative gastric cancer and therefore suggest considering the use of adjuvant therapies in patients with high risk for recurrence. However, it should be argued that only 234 (5.3%) gastric cancer patients undergoing curative D2 gastrectomy were free of lymph node metastasis and 67 T1 tumors (28.6%) and none of T4 tumor reported in their study. Quite different from their findings, our previous study (tumor staged according to the seventh edition of the American Joint Committee on Cancer Staging Manual) demonstrated that node-negative gastric cancer with more than 15 lymph nodes dissected accounted for 41.3% of patients undergoing radical resection and there were 358 T1 (48.4%) and 226 T4 tumors (30.5%) (5). Furthermore, our results indicated that tumor size >5 cm, T4 status and perineural invasion were independent prognostic factors in T1-4 node-negative gastric cancer (*Table 1*). Patients with T1-T3 lesions had 95.0% of 5-year overall survival rates, higher than 85.0% reported by Liu *et al.* (6). Given the fact that T1 gastric cancer without nodal involvement has an excellent prognosis and an extremely low recurrence rate, adjuvant therapy is not beneficial (5,7). In this regard, Chou *et al.* reported predictive factors for recurrence patterns in node-negative advanced (T2-4) gastric cancer and revealed that depth of tumor invasion predicted locoregional recurrence and peritoneal seeding; tumor size and perineural invasion were associated with hematogenous spread (4). Our recent study also suggested that extensive lymphadenectomy with >25 lymph nodes retrieval has survival benefit in patients with node-negative advanced gastric cancer (5). Furthermore, a recent systemic review showed that the presence of intraperitoneal free cancer cells documented by washing cytology test is associated with peritoneal recurrence and worse overall survival in gastric cancer patients (8). Taken together, adjuvant therapies should be considered in node-negative advanced gastric cancer patients with unfavorable factors for recurrence and those with inadequate lymphadenectomy to improve patient outcome (*Figure 1*).

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Table 1 Multivariate analysis of prognostic factors in node-negative gastric cancer patients with >15 lymph nodes dissected

Factors	N (%)	5-year survival rate (%)	Hazard ratio (95% CI)	P value
Tumor size (cm)				
≤5	619 (85.4)	92.4	1	
>5	106 (14.6)	75.1	1.987 (1.209-3.266)	0.007
T status*				
T1	356 (48.6)	96.4	1	
T2	119 (16.3)	90.2	1.695 (0.800-3.594)	0.169
T3	36 (4.9)	97.0	0.443 (0.059-3.329)	0.429
T4	221 (30.2)	77.4	3.008 (1.602-5.647)	0.001
Location				
Upper	97 (13.3)	89.3	0.865 (0.387-1.934)	0.725
Middle	154 (21.0)	93.7	1	
Lower	469 (64.1)	89.1	1.370 (0.761-2.464)	0.294
Whole	12 (1.6)	63.6	3.865 (0.848-17.604)	0.081
Lymphatic invasion				
No	679 (95.4)	90.0	1	
Yes	33 (4.6)	80.2	1.004 (0.422-2.389)	0.992
Perineural invasion				
No	588 (17.9)	92.6	1	
Yes	128 (82.1)	76.2	1.728 (1.034-2.889)	0.037

*, according to the seventh edition of the American Joint Committee on Cancer Staging Manual; CI, confidence interval

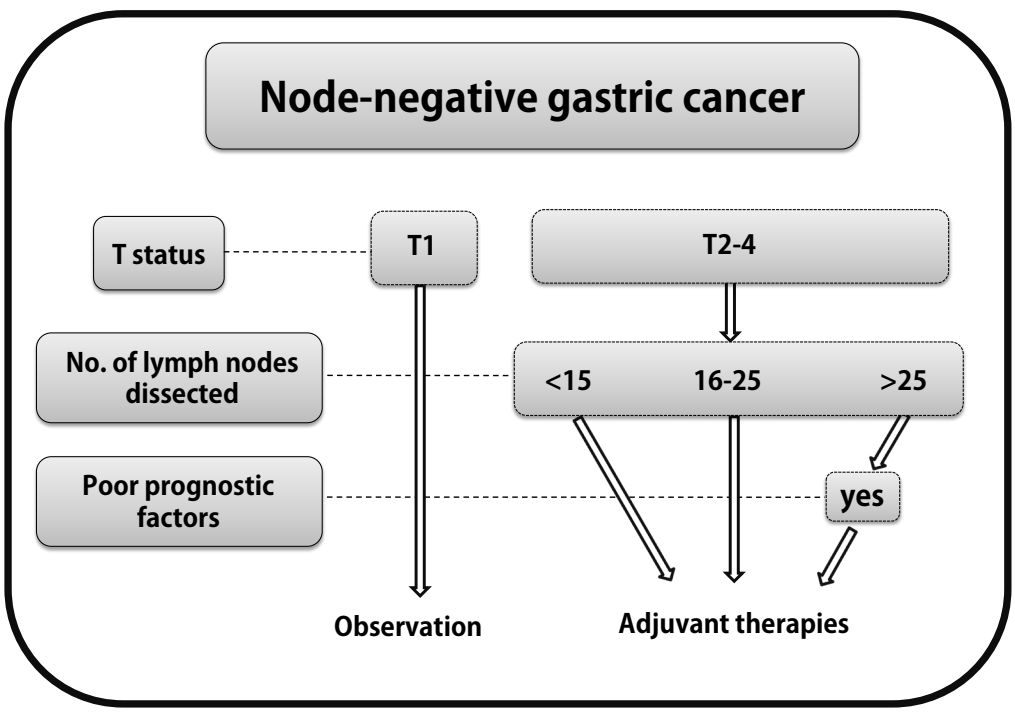

Figure 1 Strategies in managing node-negative gastric cancer

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