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BACKGROUND:

Prospective randomized trials of neoadjuvant chemoimmunotherapy followed by surgery have demonstrated markedly improved pathologic response and survival outcomes in resectable stage II–III non-small cell lung cancer (NSCLC). While nodal downstaging is frequently observed, the prognostic relevance of its extent, particularly in the context of the 9th TNM edition, distinguishing single-station (N2a) from multi-station (N2b) mediastinal disease, remains incompletely defined.

METHODS:

We retrospectively analyzed 90 consecutive patients with baseline node-positive (cN1–2) resectable NSCLC treated with neoadjuvant chemoimmunotherapy followed by curative-intent resection. Nodal downstaging was defined as any reduction in nodal stage between clinical (cN) and pathologic (ypN) assessment, and was classified according to the 8th and 9th TNM editions. Disease-free survival (DFS) was analyzed according to downstaging extent and residual nodal burden. Predictors of nodal downstaging were evaluated.

CONCLUSION:

The extent of nodal downstaging after neoadjuvant chemoimmunotherapy is strongly associated with outcome. Patients with baseline mediastinal disease achieving complete nodal clearance demonstrate particularly favorable outcomes. The 9th TNM classification further refines prognostic stratification by distinguishing single- and multi-station residual mediastinal disease, suggesting persistent ypN2b as a particularly high-risk subgroup.

RESULTS:

Median age was 63 years (IQR 58–69), and 60.0% were male. Baseline nodal stage was cN1 in 26.7%, cN2a in 60.0%, and cN2b in 13.3%. Overall nodal downstaging occurred in 68.9%, including complete nodal clearance in 58.9% and partial downstaging in 10.0%. Patients with nodal downstaging had significantly improved DFS compared with those without downstaging (3-year DFS 73.6% vs 42.2%; $p = 0.009$). DFS differed significantly by depth of nodal response ($p = 0.009$), with 3-year DFS rates of 77.3%, 57.1%, and 42.2% after complete nodal clearance, partial downstaging, and no downstaging, respectively. DFS differed according to postoperative nodal response in patients with baseline cN1 ($p = 0.015$), cN2a ($p = 0.097$), and cN2b disease ($p = 0.005$). Higher PD-L1 expression was associated with increased odds of nodal downstaging (OR 3.25, 95% CI 1.19–8.61; $p = 0.022$), and nodal downstaging was significantly associated with MPR (OR 4.31, 95% CI 1.42–13.09; $p = 0.010$).

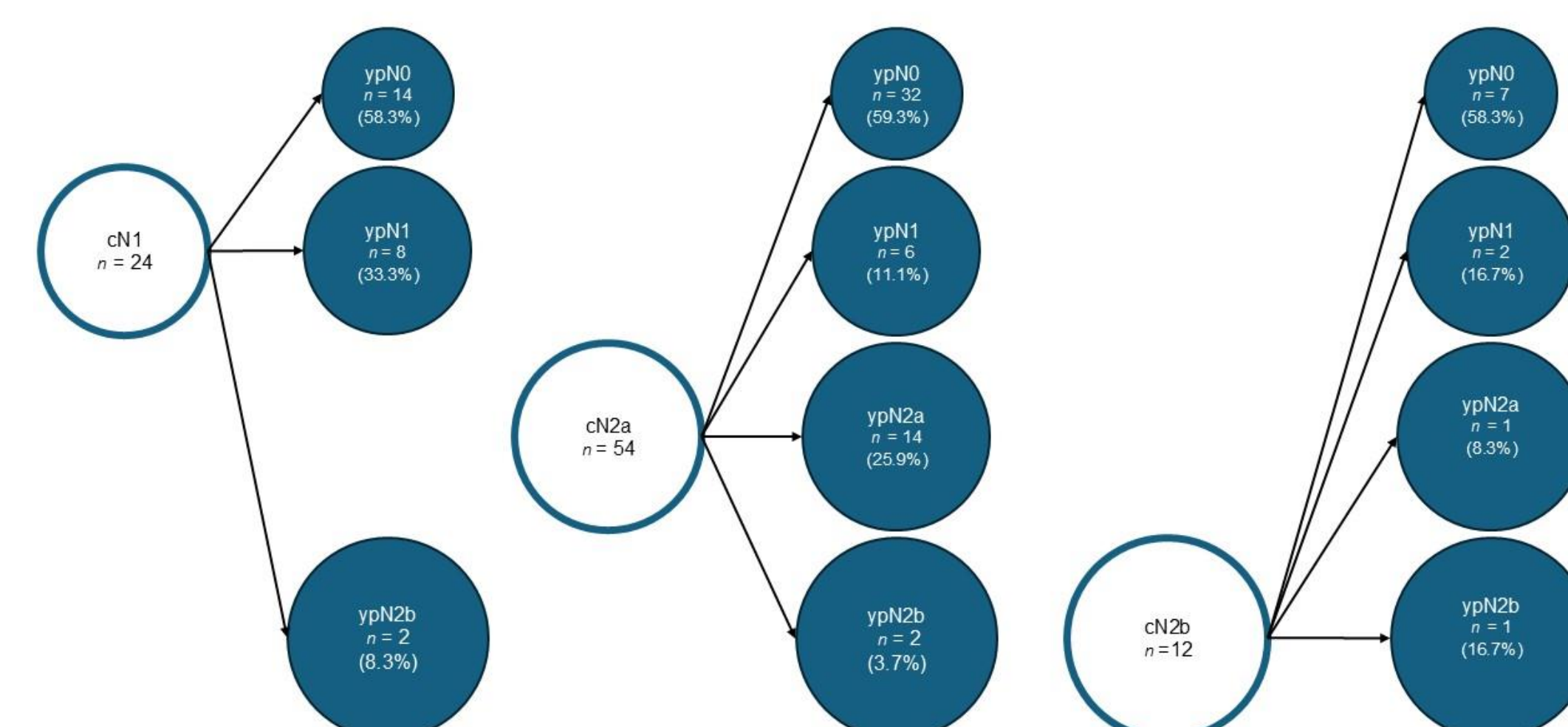


Figure 1. Transition flow chart between baseline clinical nodal stage and postoperative pathologic nodal stage

Variable	Downstaged, n/N (%)	p-value
Baseline PD-L1 expression		0.042
PD-L1 <1%	6/10 (60.0)	
PD-L1 1–49%	24/41 (58.5)	
PD-L1 ≥50%	32/39 (82.1)	
Complete nodal clearance (ypN0)		0.033
PD-L1 <1%	5/10 (50.0)	
PD-L1 1–49%	20/41 (48.8)	
PD-L1 ≥50%	28/39 (71.8)	

Table 1. Association of baseline PD-L1 expression with nodal response

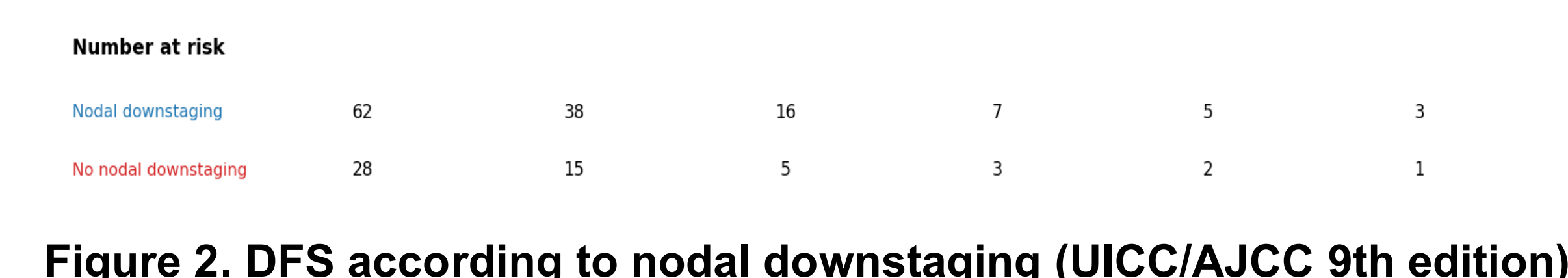
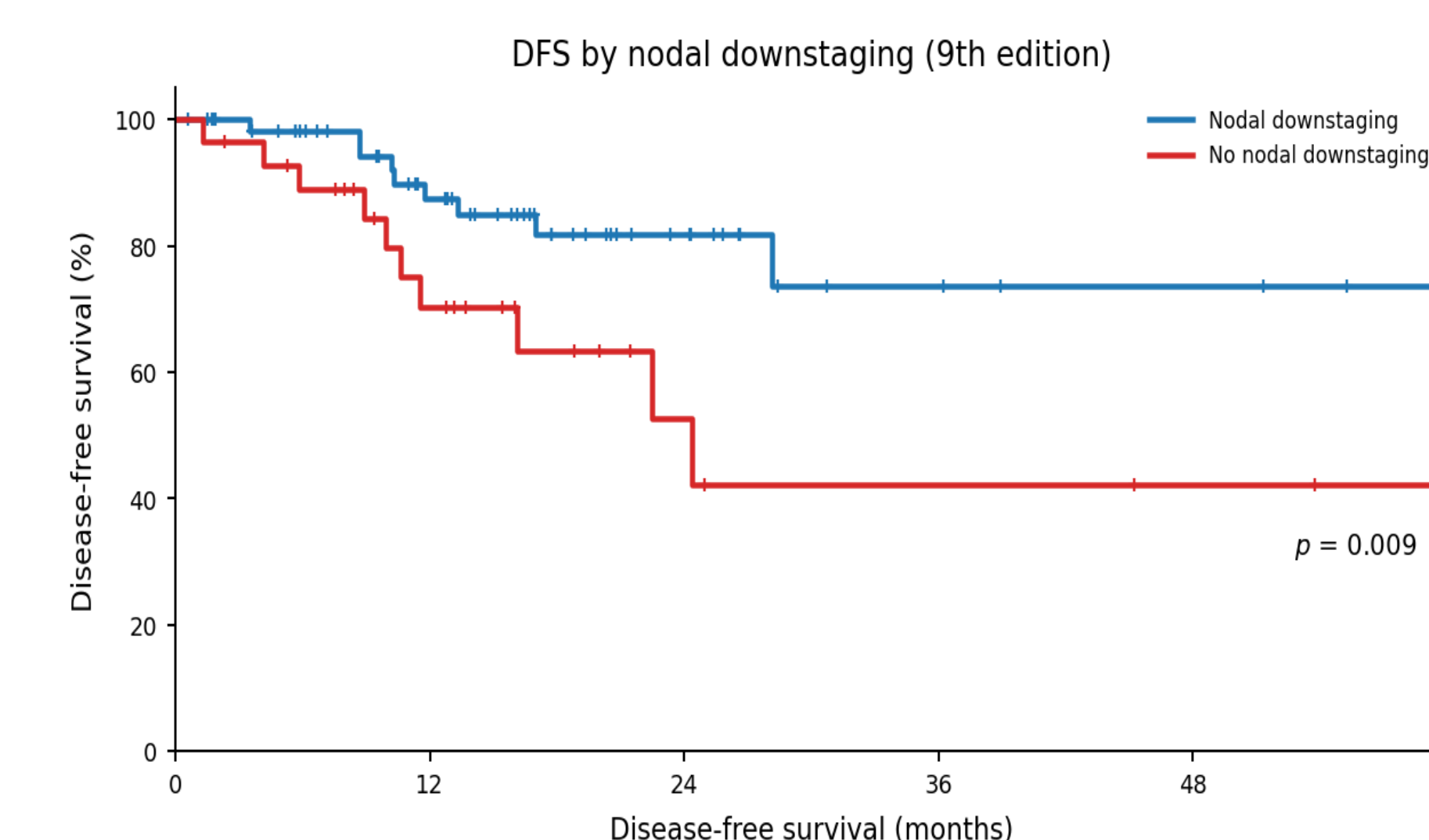


Figure 2. DFS according to nodal downstaging (UICC/AJCC 9th edition)

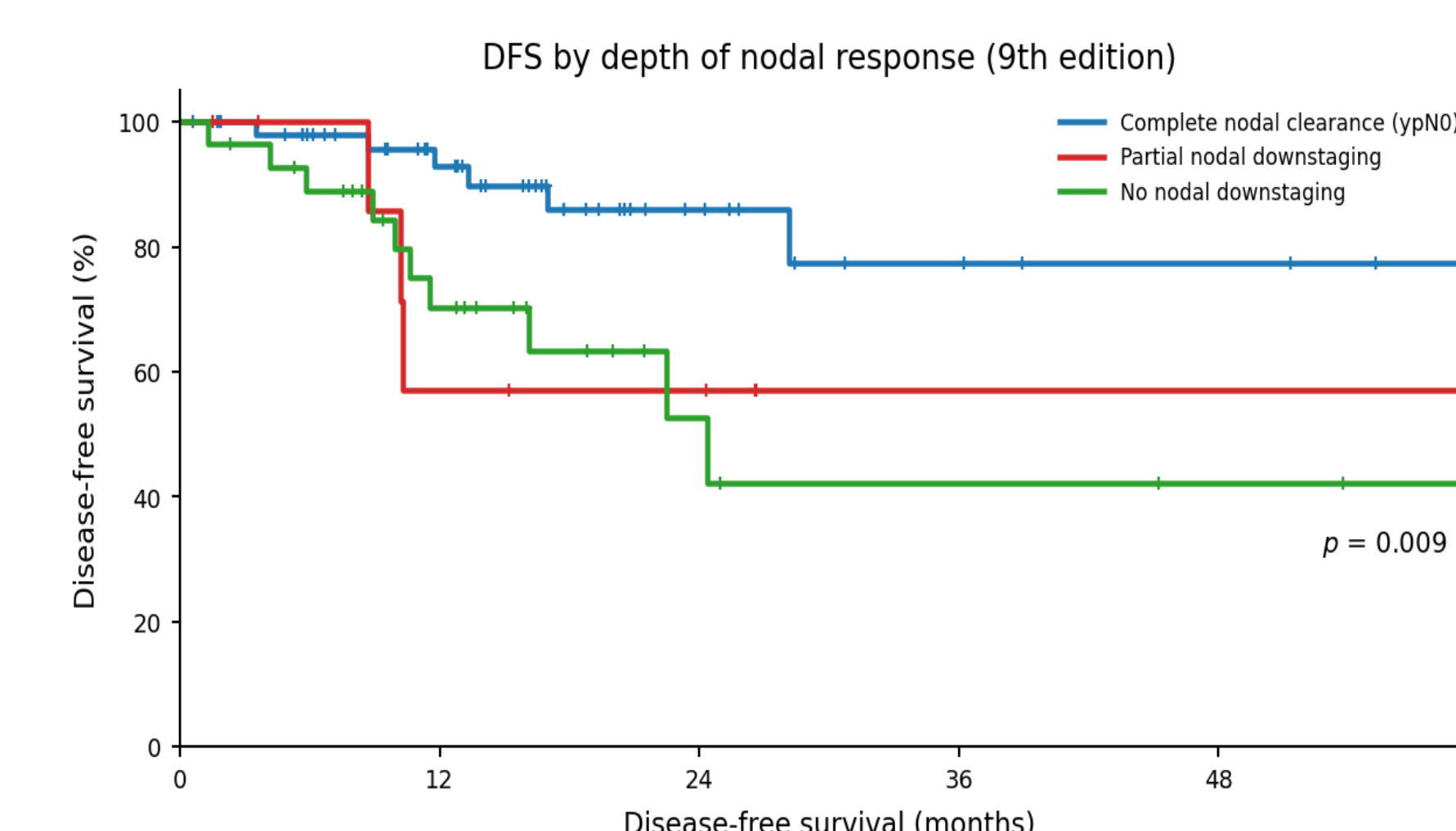


Figure 3. Disease-free survival according to depth of nodal response