Predictors of Local-Regional Failure and the Impact on Overall Survival in Patients With Resected Exocrine Pancreatic Cancer

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In our analysis of 458 patients with resected pancreatic cancer and adjuvant therapy, elevated preoperative CA 19.9 and no adjuvant RT were associated with increased risk of LRF. LRF was associated with poor OS. As such, RT should be considered as an adjunctive LR treatment modality for patients undergoing pancreatic cancer resection.

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PURPOSE: Resection of exocrine pancreatic cancer is necessary for cure, but most patients subsequently develop progressive disease. In prospective trials, rates of local-regional failure (LRF) range from 20% to 40%. We evaluated our institutional experience to better understand the risk factors for LRF and the impact on overall survival (OS).

METHODS: We reviewed 665 consecutive patients with nonmetastatic exocrine pancreatic carcinoma who underwent resection (R0 or R1) at our institution between March 1985 and January 2011 and received adjuvant therapy. A total of 458 patients had adequate follow-up and imaging to determine LR control (LRC) rates. All patients received adjuvant chemotherapy (n = 80, 17.5%) or chemoradiotherapy (CRT) (n = 378, 82.5%). Chemotherapy and CRT most frequently consisted of six cycles of gemcitabine and 50.4 Gy in 28 fractions with concurrent 5-fluorouracil (5-FU), respectively. In addition to CRT, 207 (45%) patients received additional chemotherapy. LRF was defined as tumor bed or regional node progression with or without distant metastatic progression. When available, CA19.9 values were used to validate radiographic findings. LRC and OS were estimated using the Kaplan-Meier method. Univariate and multivariate (MVA) analyses were performed using Cox proportional hazards regression models.

RESULTS: Median patient age was 64.5 years (range: 37–88 yr). Median follow-up for living patients was 84 months (range: 6–300 mo). Tumor location was pancreas head (80%), body (5%), and tail (8%) or unspecified (7%). Tumor grade was I (0.5%), II (11.5%), III (76%), or IV (12%). T-stage was T1 (7%), T2 (20%), T3 (70.5%), or T4 (2.5%). N stage was N0 (38%) or N1 (62%). Extent of resection was R0 (84%) or R1 (16%). The overall crude incidence of LRF was 17% (n = 79). Three-year rates of LRC for patients with and without RT were 81.6% vs 68.3%, respectively ($P = .003$; hazard ratio [HR] = 0.45; 95% confidence interval [CI], 0.28–0.76). On MVA, no radiation therapy ($P = .0097$; HR = 2.2; 95% CI, 1.22–3.79), elevated preoperative CA19.9 ($P = .046$; 95% CI, 1.02–3.59), and positive nodes/total nodes ratio ≥ 0.2 ($P = .059$; HR = 1.61; 95% CI, 0.98–2.65) were associated with LRF. When used as a time-dependent covariate for OS, LRF was associated with worse OS ($P < .0001$; HR = 4.07; 95% CI, 3.2–5.2) compared with no LRF.

CONCLUSIONS: In our analysis of 458 patients with resected pancreatic cancer and adjuvant therapy, elevated preoperative CA 19.9 and no adjuvant RT were associated with increased risk of LRF. LRF was associated with poor OS. As such, RT should be considered as an adjunctive LR treatment modality for patients undergoing pancreatic cancer resection.

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