

Stomach Dose-Volume Parameters and Clinical Factors Predict Acute Toxicity in Pancreatic Cancer Chemoradiotherapy

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Purpose/Objective(s)

Gastrointestinal (GI) toxicity impedes dose escalation and likelihood of cure in chemoradiotherapy (CRT) for hepatobiliary malignancies. The risk of toxicity can depend on clinical and radiotherapy (RT) dose-volume metrics. We aimed to identify predictive factors using data from two prospective phase-II clinical trials of locally-advanced pancreatic cancer (LAPC).

Materials/Methods

91 patients with available dose cubes from the ARCII (EudraCT 2008-006302-42, 59.4 Gy in 33 # with gemcitabine, cisplatin and nelfinavir, n=23) and SCALOP (NCT 01032057, 50.4 Gy in 28 # with capecitabine or gemcitabine, n=74) trials. Independent variables: clinical factors (age, sex, performance status (PS), baseline symptoms, tumour size, weight loss, chemo regimen) and DVH parameters (stomach, duodenum and small bowel) in 5-Gy bins. Outcome measures: grade / risk of CTCAE grade ≥ 2 RTOG acute upper-GI toxicity (UGIT) (anorexia, pain, nausea and/or vomiting); risk of diarrhoea grade ≥ 2 . Statistics: Correlation/prediction of grade - Spearman's rank/ordinal regression; risk of CTCAE grade ≥ 2 events - Kendall tau-b/multivariable logistic regression (MVA) with backwards stepwise selection, criteria $p < 0.1$, and selection by AIC and predictive accuracy; risk thresholds - ROC analysis.

Results

UGIT: CTCAE grade ≥ 2 symptoms occurred in 38 patients (42%) (Table). On univariate analysis increasing stomach $V_{35-45Gy}$ was predictive of risk (odds ratio 1.035, 95% CI 1.007- 1.063), and also grade (1.023, 1.003-1.044), of toxicity. AUC was 0.632 (0.516-0.747) with toxicity risk 33/66 (50%) above and 5/25 (20%) below the optimal discriminatory threshold (7.1 cc), sensitivity 0.892 and specificity 0.377. Using a threshold of 30cc, risk was 13/20 (65%) vs 25/71 (35%). Optimal MVA model incorporated patient sex, chemo regimen and stomach $V_{35-45Gy}$ and correctly classified 71.4% of patients. Concurrent chemotherapy (gemcitabine vs

capecitabine, odds ratio 3.965, 95% CI 1.274- 12.342) and weight loss during induction chemotherapy (1.216, 1.043-1.419) were significant predictors in MVA for the SCALOP cohort, while age was a significant predictor of toxicity risk among ARCI patients only (1.344, 1.015-1.780). Duodenum and small-bowel dose-volume did not predict toxicity risk or severity in any cohort. Diarrhoea: Grade ≥ 2 diarrhoea occurred in 19 patients (21%). For the combined cohort, GTV size and the presence of diarrhoea symptoms at baseline were significant predictors of risk of grade ≥ 2 diarrhoea.

Conclusion

In CRT for LAPC the volume of stomach irradiated to moderately high dose (35-45Gy) predicts incidence and severity of acute toxicity. Other predictive factors include age, sex, recent weight-loss and choice of concomitant chemotherapy.

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UGIT grade (CTCAE)	Patients	Median Stomach V _{35-45Gy} (IQR) [cc]
0	17 (19.1%)	9.70 (1.72-22.00)
1	36 (39.6)	12.93 (5.54-23.37)
2	26 (29.2%)	15.31 (9.95-31.51)
3	12 (13.2%)	28.02 (9.74-32.26)

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