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Change in Renal Function as Measured by Technetium^{99m} MAG-3 Scintigraphy and Biochemical Endpoints Following Abdominal Chemoradiation for Gastrointestinal Malignancies

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Background: Information on differential renal function following abdominal chemoradiation (CRT) as measured by renal scintigraphy (RS) is limited. This study was conducted to evaluate the association between renal function, as measured by biochemical endpoints and scintigraphy, and dose volume parameters in patients following abdominal CRT in the treatment of gastrointestinal malignancies.

Methods: Patients who received abdominal RT with concurrent chemotherapy between 2002 and 2009 were identified to study the association of renal functional imaging with change in renal function following abdominal CRT. Technetium^{99m} MAG-3 scintigraphy and laboratory data were obtained prior to CRT and after CRT in 6-month intervals. Factors assessed included age, gender, hypertension, diabetes, and dose volume parameters. Renal function was assessed by serum creatinine, creatinine clearance (CrCl) calculated by the Cockcroft-Gault formula, and renal perfusion measured using scintigraphy. Endpoints analyzed include relative renal function, biochemical endpoints, and dose volume parameters. Normal tissue complication probability (NTCP) for the primarily irradiated kidney (PK) was calculated using a tolerance dose for 5% probability of complications at 5 years (TD 5/5) of 23 Gy and α/β ratio = 2.5. The PK was defined as the kidney that received the greater mean kidney dose.

Results: Of 136 patients evaluated, median age was 64 years. The majority of primary disease sites were pancreas and periampullary tumors (75.7%). Median follow up was 9.61 months. Median radiation dose was 50.4 Gy. All patients received concurrent chemotherapy, most with 5-fluorouracil-, capecitabine-, or gemcitabine-containing regimens, and had a baseline RS performed prior to CRT. Significant reductions

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in relative renal function of the PK and global renal function were seen following CRT. Changes in split renal function, creatinine, and CrCl are shown in the table below.

	Pre-CRT (n=136)	6 -12 months post CRT (n=25)	>12 months post CRT (n=8)	P value
Mean RS of PK (%)	49.75(5.30)	47.74(6.48)	41.28(7.38)	0.0184
RS Ratio (PK/non PK)	1.01(0.22)	0.94(0.25)	0.73(0.23)	0.0606
Creatinine (mg/dl)	0.87(0.26)	0.94(0.23)	1.05(0.09)	*<0.0001
CrCl (ml/min)	90.67(33.43)	82.23(30.97)	74.54(23.00)	*<0.0001

*P values obtained using log-transformed values

Univariate analysis did not show age, gender, hypertension, diabetes, or pre CRT CrCl, to be associated with decrease in split perfusion of the PK following CRT. Percent volumes of the PK receiving ≥ 25 Gy (V_{25}) and 40 Gy (V_{40}) were significantly associated with $\geq 5\%$ decrease in relative renal function of the PK in patients who had at least one post CRT renogram ($P = .0387$ and $P = .0438$ respectively). The difference in NTCP for the PK was significantly different between patients with $<5\%$ change in split renal function on RS versus those with $\geq 5\%$ decrease (11.4 % vs. 24.2%, $P = .0097$).

Conclusions: Decline in split renal function using Technetium^{99m} MAG-3 scintigraphy correlates with decrease in CrCl and radiation dose-volume parameters following abdominal radiation with concurrent chemotherapy. Change in split perfusion can be detected as early as 6 months post CRT. Scintigraphy may provide early determination and quantification of subclinical renal injury prior to clinical evidence of nephropathy.