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Adverse Effect Of Radiation Delay In Locally Advanced Cervical Cancer In The Setting Of Definitive Concurrent Chemoradiation

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Purpose/Objective(s): The detrimental effect of radiation (RT) prolongation in cervical cancer patients is well established for RT alone, but has not been investigated for patients receiving concurrent chemotherapy. We evaluated the impact of overall RT time and timing of brachytherapy on outcomes for locally advanced cervical carcinoma treated with definitive chemoradiation.
Materials/Methods: From 1997 to 2009**,** 94 patients with FIGO stage II (69%) and III (31%) cervical cancer completed definitive concurrent chemoradiation and intracavitary brachytherapy boost at the University of Chicago Medical Center radiation facilities. Eligibility included ≥ 3 months of follow-up and no hysterectomy. Staging included CT scans in 91% of patients. Concurrent chemotherapy was weekly Cisplatin in 84%. Patients received whole pelvis RT via 3DCRT or IMRT (median dose 45 Gy) and 68% received parametrial boost (PMB). The median cumulative dose to Point A was 85 Gy. Total RT time was defined from the first to the last day of RT. Point A time was defined from the first day of RT to the day Point A received the total prescription dose, which usually corresponded to the completion date of the brachytherapy treatment. Freedom from local (ff-LF) or distant failure (ff-DF), and dead of disease (DOD) were calculated from the end of RT and were evaluated for associations with RT delay as well as other clinical factors. Kaplan-Meier and Cox-proportional hazard models were utilized for multivariate analyses (MVA).
Results: Patients were: median age 51, pelvic lymph nodes (LN) present on imaging 36%, and median initial hemoglobin (Hgb) 11.7 ng/ml. The median whole pelvis RT time was 36 days. The median total RT time was 69 days, with 19% ≤56 days, and 33% ≤63 days. The median Point A time was 60 days, with 43% ≤56 days, and 67% ≤63 days. With a median follow up of 26 months, local failure, distant failure, and DOD occurred in 15%, 22%, and 21% of the patients, respectively. ff-LF was associated with young age, prolonged Point A time and total RT time, LN status, and Hgb, but not with use of IMRT, stage, or use of PMB. On MVA for ff-LF, age (HR: 0.93; 95% CI 0.86-0.98; p=0.01) and Point A time >56 days (HR: 10.2; 95% CI 1.8-192; p=0.005) were significant. 2y ff-LF was 71% if Point A time >56 days v 96% if Point A time ≤56 days (p=0.004). Stage was the only significant predictor for ff-DF. DOD was associated with stage, LN status, and prolonged Point A time and total RT time. On MVA for DOD, only total RT time >63 days (HR: 4.2; 95% CI 1.2-26; p=0.02) was significant. 2y DOD was 14% if total RT time >63 days v 4% if total RT time ≤63 days (p=0.02).
Conclusions: Concurrent chemotherapy does not mitigate the negative effects of RT delay in locally advanced cervical cancer. We recommend completing RT to point A in ≤ 8 weeks, and total RT in ≤ 9 weeks.