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Integration of Stereotactic MR-Guided Online Adaptive Radiation Therapy (SMART) in Management of Inoperable Pancreatic Cancer

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Abstract
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Abstract

Objectives:

Insufficiency of current treatments for inoperable pancreatic cancer has led to incorporation of new modalities in the treatment protocols. In this retrospective study, we aimed to analyse the oncological outcomes and toxicity of integration of SMART to the standard therapy.

Methods:

Patients treated with SMART for primary inoperable non-metastatic adenocarcinoma of the pancreas were analyzed retrospectively. Overall survival (OS), metastasis free survival (MFS), local recurrence free survival (LRFS) were estimated with Kaplan Meier method and log rank test was used to estimate the effect of age, sex, tumor markers, ECOG, tumor location, chemotherapy (ChT) type, RT technique (elective nodal RT or not), presence of pain, surgery status and RT dose. Total doses of 50 Gy, 45 Gy and 40 Gy in 5 fractions were used as cut off values. Cox regression was performed for multivariate analyses. Toxicity was reported according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.

Results:

A total of 48 patients were included in the analyses. After a median follow up of 12 months (Range: 2-43 months) after SMART, median OS was 14.2 months. Forty patients were given FOLFIRINOX (83.3%), three (6.3%) had Gemcitabine, five (10.4%) did not receive ChT. Nine (18.75%) patients were treated with a total dose of 50 Gy, 15 (31.25%) with 45 Gy, 19 (39.6%) with 40 Gy and five (10.4%) with lower doses. After SMART, operation was attempted in 16 (33.3%) patients, 10 (20.8%) of which resulted in successful R0 resection. R0 resection correlated with total dose of 50 Gy (55.6% of patients given 50 Gy and 12.8% of patients given lower doses had R0 resection, p=0.012). All R0 resections were in the FOLFIRINOX group. Adding elective nodal RT did not influence OS. None of the tested doses showed any effect on survival. In univariate analyses, patients with R0 resection had longer OS (median OS was not reached in the R0 group and it was estimated as 7 months in the non-operated and non R0 group, p=0.005). Use of FOLFIRINOX also significantly increased survival; 11.6 months for no or other ChT protocols to 27 months for FOLFIRINOX (p=0.035). Factors such as ECOG and tumour location also significantly influenced survival (lower ECOG and head location correlated with lower survival, p=0.026 and p=0.024). Presence of pain after RT was also marginally associated with lower OS (p=0.08). On multivariate analyses only FOLFIRINOX use and no pain after RT correlated with higher OS (p=0.009 and 0.05). Median LRFS was not reached, 1- and 2-year LRFS was 90.7% and 64.2%, respectively. No factor influenced LRFS, including tumour location and size, RT dose and technique, use of ChT, R0 resection or presence of pain after RT. Median MFS was 11.3 months and none of the factors analysed influenced MFS. There were two patients with grade 3 acute toxicity (nausea and vomiting) and two patients with grade >3 late toxicity (bleeding), none of which was in the 50 Gy receiving group.

Conclusion(s):

SMART given to inoperable pancreatic cancer patients in doses of 50 Gy leads to higher rate of R0 resection and acceptable toxicity. Use of FOLFIRINOX improved survival and persistence of pain after treatment was associated with poor prognosis.