12-1-2022

Evaluation of Practice Patterns and Outcomes after Implementing SMART for Pancreatic Cancer

Eric Schaff

Parag J. Parikh

Pin Li

Rupen Shah

Gazala Khan

See next page for additional authors

Authors

Eric Schaff, Parag J. Parikh, Pin Li, Rupen Shah, Gazala Khan, Farzan Siddiqui, Benjamin Movsas, and David Kwon

events of Real-time Online Adaptive Magnetic Resonance-Guided SBRT (MRgSBRT).

Materials/Methods: This IRB approved retrospective study included inoperable pancreas cancer patients who were treated consecutively with MRgSBRT from 2020 to 2021. Most patients (89%) received 50Gy prescribed to gross tumor volume (GTV), two patients (11%) received 40 Gy to GTV. Ten patients (56%) received elective nodal irradiation (ENI) to celiac and super mesenteric lymph nodes, & 8 patients (44%) did not receive ENI. Planning Target Volume (PTV) received a median dose of 35 Gy (range 25-50 Gy) and 40 Gy (range 40-50 Gy), in patients with, and without ENI respectively. PTV was defined as 3 mm expansion of either GTV, or a clinical target volume encompassing GTV and ENI areas when treated. Real-time Online Adaptive MRgSBRT was utilized in 59% of the treated fractions (53 of 90 fractions), while gated MRgSBRT was utilized in all fractions (100%). Real-time Online Adaptive MRgSBRT was utilized whenever the predicted radiation plan did not meet the organs at risk (OARs) constraints based on daily anatomic variations. Reoptimized plans were generated after re-contouring OARs within a 3 cm ring, & verifying GTV & PTV, & always met OARs constraints. All patients were treated twice weekly.

Results: The study included 18 eligible patients with median age of 72.5 years (range 56-85). Patients had local-regional advanced (44%), borderline (33%) & metastatic (22%) diseases. At a median follow up of 10 months from MRgSBRT (range 2-17 months), in patients with & without ENI local-regional progression was 20% versus 67% (p 0.12 Fisher's Exact Test), distant progression was 30% versus 67% (p 0.3), & overall survival was 80% and 37.5% (p 0.14) respectively. Of those who developed disease progression, first site of progression was distant metastases (75%), versus regional nodal progression (75%) in patients with & without ENI respectively. In the non-ENI group, 50%, 12.5%, 12.5%, & 25% were dead of disease (DOD), dead without disease progression (DWODP), alive with disease (AWD), & alive without disease progression (AWODP) respectively. In the ENI group, 10%, 10%, 60%, & 20% were DOD, DWODP, AWD, & AWODP respectively. Median follow up from diagnosis was 19 months (range 6-103 months). Acute & chronic toxicities were uncommon, & included grade 1-2 nausea (22%), fatigue (17%), & abdominal discomfort (11%). No grades 3-5 toxicities were reported.

Conclusion: Real-time Online Adaptive MRgSBRT is a feasible, & safe approach with minimal treatment related toxicities & promising local-regional control in a cohort of advanced pancreas cancer patients. ENI is safe & shows a trend for improved local-regional control. Larger controlled prospective trials are recommended.

Author Disclosure: T.R. Abdelrhman: None. N.H. Darwish: None. K. Gomez: None. B.H. Lee: None. A. Sethi: None. G. Abood: None. A. Badami: None. A. Haseeb: None. L.M. Knab: None. K. Micetich: None. W. Small: Research Grant; Zeiss. Honoraria; Zeiss. Travel Expenses; Zeiss. Board representative for ASTRO and Radiation Oncology Commission Chair - advocate for our society and patients and for Radiation Oncology throughout the college including research; ACR, NRG Oncology.

2445

Expression of Ki67 and p53 and their Relationship with the Survival Time of High-Dose Hypofractionated Radiotherapy in Pancreatic Cancer

G. Ren,[1,2] Y. Wang,[1] L. Feng,[1] J. Zhang,[1] and Y. Wang[1]; *[1]Department of Radiotherapy, Air Force Medical Center, Beijing, China, [2]Department of Radiotherapy, Peking University Shougang Hospital, Beijing, China*

Purpose/Objective(s): To analyze the expression of Ki67 and p53 in pancreatic cancer and their relationship with the survival time of high-dose hypofractionated radiotherapy.

Materials/Methods: The biopsies of 55 patients with pancreatic cancer were collected retrospectively before receiving high-dose hypofractionated radiotherapy. Immunohistochemical SP method was used to detect the expression of Ki67 and p53 in pancreatic cancer. Log-rank test was used to compare the difference of survival time between different expression levels. Cox model was analyzed by multivariate analysis.

Results: The expression rates of Ki67 and p53 protein in puncture tissues were 41.8% and 47.3%, respectively. Univariate survival analysis showed that the survival time of Ki67 and p53 negative expression group was significantly longer than that of positive group ($P < 0.05$). Multivariate analysis showed that Ki67, p53 and distant metastasis were independent prognostic factors of pancreatic cancer patients receiving high-dose hypofractionated radiotherapy.

Conclusion: The expression level of Ki67 and p53 protein in pathological tissue before treatment is an important index to predict the survival time of high-dose hypofractionated radiotherapy for pancreatic cancer.

Author Disclosure: G. Ren: None. Y. Wang: None. L. Feng: None. J. Zhang: None. Y. Wang: None.

2446

Evaluation of Practice Patterns and Outcomes after Implementing SMART for Pancreatic Cancer

E.M. Schaff,[1] P.J. Parikh,[1] P. Li,[2] R. Shah,[2] G. Khan,[3] F. Siddiqui,[1] B. Movsas,[1] and D. Kwon[4]; *[1]Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, [2]Henry Ford Health System, Detroit, MI, [3]Department of Medical Oncology, Henry Ford Cancer Institute, Detroit, MI, [4]Department of Surgical Oncology, Henry Ford Cancer Institute, Detroit, MI*

Purpose/Objective(s): Stereotactic MRI-guided adaptive radiation therapy (SMART) enables safe dose escalation for locally advanced, borderline resectable, and medically inoperable pancreatic cancer and has shown favorable toxicity and survival outcomes. In late 2018, our institution commissioned SMART for these patients, making it available to all patient referrals. We wanted to review changes in our patient population and differences in clinical outcomes for patients before and after the implementation of SMART.

Materials/Methods: In this IRB approved analysis, we retrospectively reviewed 167 consecutive patients from 2015-2021 with locally advanced, borderline resectable, or medically unresectable pancreatic cancer who were treated with radiation therapy. Chemoradiation (chemoRT) was defined as any 28-30 fraction radiation regimen that included concurrent chemotherapy. SMART was defined as 50 Gy over 5 consecutive daily fractions without concurrent chemotherapy. Baseline patient characteristics were compared between groups. Overall survival (OS) was evaluated by Kaplan-Meier (KM) and log-rank test. Univariate (UVA) and multivariate analysis (MVA) were also performed on multiple treatment variables.

Results: Of the patients included, 58 received chemoRT (2015-2018) and 109 received SMART (2018-2021). Median follow up from time of diagnosis for the chemoRT and SMART cohorts were 53.7 months and 29.2 months respectively. Cohorts did not have significant differences in age, gender, race, T or N staging, rates of surgery or surgical margin status. Patients receiving SMART had overall worse performance ($p = 0.011$) including a lower percentage of PS 0 patients (22.9% vs 44.8%) and a higher percentage of PS 2+ patients (34% vs 15.5%). Similarly, the SMART patients did numerically more often have locally advanced (50% vs 43%) and medically inoperable (26% vs 21%) disease ($p = 0.294$). The SMART cohort did have longer neoadjuvant chemotherapy with mean of 3.5 months vs 2.3 months in the chemoRT cohort ($p = 0.002$). There was no OS difference between each group when measured from diagnosis (p=0.79) or from first day of radiation (p=0.2). Median survival in the chemoRT and SMART groups was 18.7 vs 17.4 months from diagnosis. When including only PS 0-1 patients, the median survival in the chemoRT and SMART groups was 18.8 vs 22.3 months (p=0.37). There was also no difference in locoregional control, distant control, or progression free survival using KM. On MVA positive prognostic factors for OS from diagnosis included ECOG <2 (HR 0.54, p=0.015), increasing months of neoadjuvant chemo (HR 0.88, p=0.004) and pancreatectomy (HR 0.14, p <0.001).

Conclusion: Despite the fact that the patient cohort receiving radiation therapy per the SMART approach had poorer performance status compared with chemoRT, OS was not significantly different. The multidisciplinary team was highly supportive of SMART with increased patients being treated.

Author Disclosure: E.M. Schaff: None. P.J. Parikh: Research Grant; Viewray. Honoraria; Viewray. Stock; Nuvaira. P. Li: None. R. Shah: None. G. Khan: None. F. Siddiqui: Research Grant; Varian Medical Systems, Inc. Honoraria; Varian Medial Systems Inc, Varian Medical Systems, Inc., American College of Radiology. Speaker's Bureau; Varian Medial Systems Inc. Advisory Board; Varian Noona. Travel Expenses; Varian Medial Systems Inc, Varian Medical Systems, Inc.; HFHS Bylaws and Governance Committee, Henry F. B. Movsas: None. D. Kwon: None.

2447

Neoadjuvant Chemotherapy and Stereotactic Body Radiation Therapy in Patients with Early Onset Pancreatic Cancer: Clinical Outcomes and Toxicity

S. Sehgal,[1] A.V. Reddy,[2] C. Hill,[2] T.A. Lin,[3] L. Zheng,[4] J. He,[5] J.M. Herman,[6] J.J. Meyer,[2] and A. Narang[2]; [1]*Philadelphia College of Osteopathic Medicine, Philadelphia, PA,* [2]*Department of Radiation Oncology and Molecular Radiation Sciences, Johns Hopkins University School of Medicine, Baltimore, MD,* [3]*The University of Texas MD Anderson Cancer Center, Houston, TX,* [4]*Department of Medical Oncology, Johns Hopkins University School of Medicine, Baltimore, MD,* [5]*Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD,* [6]*Department of Radiation Medicine, Northwell Health Cancer Institute, Lake Success, NY*

Purpose/Objective(s): Little is known on optimal management of patients with early onset pancreatic cancer (EOPC), including the role of radiation therapy. As such, we report on a cohort of patients with EOPC (age <55 years) who was treated with neoadjuvant chemotherapy and stereotactic body radiation therapy (SBRT).

Materials/Methods: This was a single institution retrospective review of patients with EOPC who were treated with upfront chemotherapy followed by SBRT with or without surgical resection. Endpoints included overall survival (OS), local progression-free survival (LPFS), distant metastasis-free survival (DMFS), progression-free survival (PFS), and treatment-related toxicity. Next-generation sequencing (NGS) was performed on select patient tumor specimens.

Results: From 2016-2021, 47 patients met the inclusion criteria. Median age was 50.4 years (range, 36.4 − 54.7 years). Median induction chemotherapy duration was 4 months (range, 2.5 − 9 months). The majority (46/47, 97.9%) of patients received 33 Gy in 5 fractions. Following SBRT, 43 patients (91%) underwent surgical exploration, with extent of vascular involvement on post-SBRT imaging precluding exploration in 4 patients (9%). Gross resection was achieved in 33 patients (70.2%), with intraoperative metastatic disease precluding resection in 8 patients (17%) and intraoperative extent of vascular involvement of the primary tumor precluding resection in 4 patients (9%). Median OS, LPFS, DMFS, and PFS were 14.2 months, 11.6 months, 8.9 months, and 8.1 months respectively. Six-month and 1-year LPFS were 88.3% and 45.4%, respectively. Chemotherapy duration (≥ 4 months) was associated with improved median OS (16.5 vs 10.1 months, p=0.005), LPFS (10.1 vs 4.9 months, p=0.002), DMFS (9.7 vs 5.2 months, p=0.014), and PFS (9.7 vs 5.2 months, p=0.020). Normalization of CA 19-9 (≤ 34 vs > 34 U/ml) after chemotherapy was associated with improved median DMFS (not reached vs 5.6 months, p=0.003) and PFS (11.3 vs 5.6 months, p=0.022). Grade 3+ rates of chemotherapy and radiation-related toxicity were 14.9% and 2.1% respectively. Clavien-Dindo 3b toxicity rate was 3.0%. A total of 15 patients underwent NGS, with mutations being found in *KRAS* (10/15, 66.7%), *TP53* (7/15, 46.7%), *NOTCH 1/2* (3/15, 20%), *CDK2NA* (2/15, 13.3%), and *SMAD4* (1/15, 6.7%).

Conclusion: Multi-modality therapy for EOPC was administered with low toxicity, but outcomes remain suboptimal. Induction chemotherapy duration ≥ 4 months and normalization of CA 19-9 after chemotherapy were associated with improved outcomes, suggesting a role for extended durations of systemic therapy titrated to CA 19-9 response before transitioning to local therapy. The high rate of local failure and the low rate of grade 3+ toxicity also suggest a role for intensifying local therapy in this population, such as radiation dose escalation, expansion of the radiation target volume, and more aggressive surgical techniques.

Author Disclosure: S. Sehgal: None. A.V. Reddy: None. C. Hill: None. T. A. Lin: None. L. Zheng: None. J. He: None. J.M. Herman: None. J.J. Meyer: Honoraria; Springer. Royalty; Springer, UpToDate. A. Narang: Research Grant; Boston Scientific.

2448

Retrospective Clinical Outcomes of Proton Beam Therapy for Unresectable Locally Advanced Pancreatic Cancer

I. Seto,[1] H. Yamaguchi,[1] Y. Takagawa,[1,2] M. Suzuki,[1] K. Takayama,[1] T. Tominaga,[1] M. Machida,[1] and M. Murakami[1]; [1]*Department of Radiation Oncology, Southern TOHOKU Proton Therapy Center, Koriyama, Japan,* [2]*Department of Minimally Invasive Surgical and Medical Oncology, Fukushima Medical University, Fukushima, Japan*

Purpose/Objective(s): We retrospectively researched on the treatment outcomes and assessed the efficacy of proton beam therapy (PBT) for unresectable locally advanced pancreatic cancer (LAPC).

Materials/Methods: Fifty-four patients who were diagnosed unresectable LAPC and administered PBT between April 2009 to March 2020 at our institution. Patients who could not completed PBT, had new distant metastases during treatment, and did not have enough follow-up time were excluded in this study. Statistical analyses were performed by calculating overall survival rate (OS) and local control rate (LC). Median survival time (MST) was analyzed by several following factors; maximum standardized uptake values (SUV_{max}) of FDG-PET evaluation, performance status (PS), tumor site, total irradiation dose, and combination use of chemotherapy. Treatment toxicities were evaluated by Common Terminology Criteria for Adverse Events (CTCAE ver.5.0). OS, MST, and LC were analyzed using the Kaplan-Meier method and log-rank test. The cut-off values for SUV_{max} and tumor diameter were estimated using the receiver operating characteristic (ROC) curve and area under the curve (AUC) based on MST.

Results: This study included 28 men and 26 women whose median age was 67.5 years (range, 40 to 88 years). All patients were clinical stage III LAPC according to the Union for International Cancer Control (UICC) TNM staging system (8th edition). Median follow-up time was 17.4 months (range, 4.0 to 89.7 months). The median total dose was 67.5GyE (range, 50-77 GyE/25-35 fractions). The median tumor diameter was 36.5mm (range, 15 to 90 mm). The median SUV_{max} was 5.85 (range, 2.1 to 27.6). Chemotherapy regimens during PBT were following; 24 patients were gemcitabine alone, 5 were tegafur-gimeracil-oteracil (TS-1) alone, 17 were paclitaxel and TS-1. Eight patients did not receive chemotherapy because of their poor general condition. The One-year, 2-year, 3-year OS were 74.1%, 33.3%, 10.8%, respectively. The One-year, 2-year, 3-year LC were 89.0%, 84.6%, 84.6%, respectively. The MST was 17.1 months. Only one patient survived longer than 5 years. The cut-off values were estimated for SUV_{max}: 4.8 and tumor diameter: 37mm. Two-year OS based on PS-score group were following; PS 0/1/2: 26.1/ 13.4/8.0 months, respectively with significant differences (each group P<0.01). Treatment related acute toxicities were neutropenia (Grade1/2/3: 2/6/17 patients), leukopenia (Grade1/2/3: 1/4/11 patients), thrombocytopenia (Grade1/2: 1/4 patients), respectively. Late toxicity was gastrointestinal ulcer (Grade1/2: 2/2 patients). No Grade 3 or higher late adverse events were observed.