Comparison of Radiotherapy Techniques for Unresectable Pancreatic Cancer: A retrospective study of outcomes at a single institution

Dr. Daniel Tesolin MD MSc[1,2], Dr. Vimoj Nair MBBS MD MSc FRCPC[1,2,3]

1. The Ottawa Hospital Cancer Center, University of Ottawa, Ottawa, ON K1H 8L6, Canada, 2. Faculty of Medicine, University of Ottawa, Ottawa, ON K1H 8M5, Canada, 3. The Ottawa Hospital Research Institute, Ottawa, ON K1Y 4E9, Canada

Introduction and Rationale

- Unresectable pancreatic cancer (UPC), is associated with especially dismal survival outcomes, with a reported median survival of 8-12 months. (1)
- Although the role of chemotherapy in improving overall survival (OS) and progression free survival (PFS) is vivid, the role of radiotherapy (RT) remains unclear.
- Due to conflicting data in the literature, there exists a therapeutic quandary among various dose fractionation and radiation technique options with variety in choice amongst different centres.
- The standard RT techniques employed include stereotactic body RT (SBRT), conventional fractionation RT (CFRT) or hypofractionated RT with lower doses (HypoRT). (2-6)
- In this retrospective study we intend to compare the outcomes of patients with UPC who have been treated with RT.
- We also present the outcomes from use of radiotherapy in patients who had distant metastasis at time of RT (de novo M1)

Objectives

A. Primary objective

i. To determine the OS difference between different RT techniques in UPC patients.

B. Secondary objectives

i. To determine which RT technique provide best local-regional control (Freedom From Progression/FFP) and Treatment specific survival (TSS).

ii. To determine clinicopathologic factors associated with the above variables to allow us to potentially select subpopulations that will benefit from different techniques of radiotherapy.

Methods

* Disclaimer: More data has been collected since submission of abstract. There are discrepancies.

From a database of 257 radiation plans of patients treated for pancreatic cancer in a single institution between August 2007 to December 2022, patients with UPC were selected for this REB approved retrospective study.

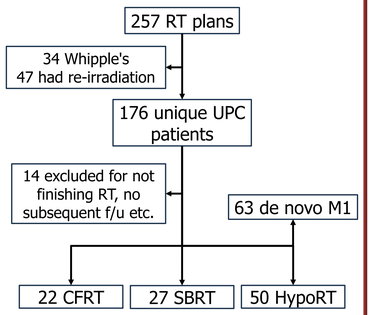

Figure 1): CONSORT Diagram of the current retrospective study. Total of 176 patients were analyzed. 63 patients had metastatic disease at presentation and received local RT.

For the purpose of this study, we defined;

- CFRT - (defined as > 15 fractions)
- HypoRT - (defined as ≤ 15 fractions and EQD2 <40Gy for a/b=3)
- SBRT - (defined as ≤ 5 fractions and EQD2 ≥ 40Gy for a/b=3)
- OS – Overall Survival (diagnosis to death)
- FFP – Freedom from Progression (RT to radiographic evidence of progression on imaging)
- TSS - Treatment specific survival: RT to death

The patient charts were analyzed by accessing them through our institutional electronic medical records.

Kaplan Meier survival curves as well as multivariable analysis using Cox Correlation method was done using the statistical software R (version 4.3.1; R Core Team 2023).

Results

Table 1): Demographic and Baseline Characteristics of Patients Treated With Radiotherapy For UPC

	Cohorts (mean value unless otherwise specified)			
Variables	**HypoRT**	**SBRT**	**CFRT**	**de novo M1**
No. of patients	50	27	22	63
Male (%)	50.0%	63.0%	63.6%	57.1%
Ca 19-9 (U/mL)	2321.8	819.4	204.7	6419.1
PS (ECOG)	1.7	1.5	1.1	1.9
T4 status (%)	74%	63%	91%	84%
Age (years)	70.4	71.5	65.4	67.0
Stent +ve (%)	50.0%	33.3%	50.0%	33.3%
No chemo (%)	48.0%	51.9%	0%	46.0%
Fractions (Range)	1-15	3-5	18-28	1-14
BED α/β=3 (Gy)	46.5	81.6	76.4	51.1
EQD2 α/β=3 (Gy)	27.9	48.9	45.9	30.7

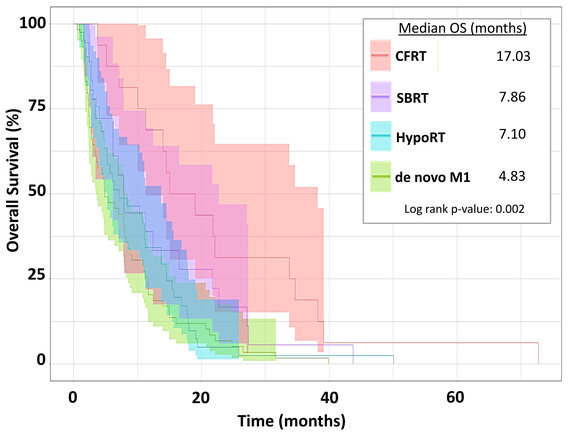

Figure 2): Kaplan Meier Estimates of OS between the various RT techniques and De novo M1 cohort.

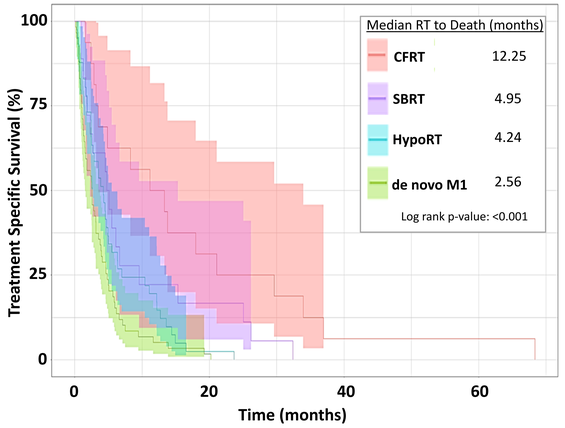

Figure 3): Kaplan Meier Estimates of Treatment Specific Survival between the various RT techniques and De novoM1 cohort.

Table 2): Differences in Outcomes between HypoRT, SBRT and de novo M1 cohorts, adjusting for receipt of chemotherapy (All CFRT patients got chemo).

		Cohorts (Median months)					
Variables (months)	**Chemo**	**HypoRT**	p	**SBRT**	p	**de novo M1**	p
OS	Yes	**31.66**	<0.001	**19.09**	0.04	**10.91**	<0.001
	No	**9.34**		**6.16**		**2.33**	
TSS	Yes	**5.02**	0.02	**8.12**	0.1	**4.62**	<0.001
	No	**2.98**		**3.60**		**1.25**	
FFP	Yes	**3.91**	0.2	**7.35**	0.004	**3.51**	<0.001
	No	**1.32**		**2.83**		**0.89**	

Table 3): Multivariable analysis demonstrating variables influencing OS adjusted for Chemotherapy Use

Variables	**Odds Ratio** (95% CI)	P value
Age	1.028 (0.153, 6.916)	**0.025**
Total Bili	1.001 (0.995, 1.006)	0.812
Ca 19-9	1.000 (1.000, 1.000)	0.039
PS (ECOG)	2.228 (1.610, 3.082)	**<.001**
EQD2	0.982 (0.964, 0.999)	0.048
Chemo	0.243 (0.145, 0.406)	**<.001**

Discussion

- OS, TSS and FFP post RT are all significantly improved in patients who received chemotherapy. These patients also had a higher performance status overall
- FFP is not statistically significant between the various radiation techniques. A trend towards better local control with SBRT over CFRT was demonstrated (5.26 v 4.16 respectively, p=0.1).
- Even de novo M1 patients had significantly improved outcomes if they were well enough to receive chemotherapy. If they did not receive chemotherapy, the benefit of RT is questionable due to the poor survival.
- Survival outcomes seem to be best for CFRT cohort. The potential reasons for this could be better PS, use of chemotherapy as well as tendency to treat nodal drainage in these patients.
- The SBRT cohort performed only marginally better than the HypoRT arm but also had better performance scores on average.
- OS of patients who received SBRT after chemotherapy, approaches the CFRT cohort; which is in agreement with the CRiSP Meta-analysis (7).
- Being a retrospective study, our data also suffers from having a small sample size and shorter follow up time given less historical experience with SBRT at our centre compared to CFRT.
- In the multivariate analysis, the performance status and use of chemotherapy are most predictive of patient OS.

Conclusion

- UPC patient with good performance status and who receive chemotherapy are the best survivors and will likely benefit from RT. The best performers should receive CFRT.
- Even metastatic UPC patients who received chemotherapy and have good PS may live long enough to see local control benefits from RT.
- RT benefit in poor performing patients or metastatic patients who do not receive chemotherapy is insignificant on all accounts.
- More local studies comparing SBRT to CFRT in UPC patients are required.

Acknowledgements

- Christian Hache – For data retrieval
- Tabitha Lavallee – for administrative support
- Yuxin Zhang – For statistical support and analysis

Contact Info

Daniel Tesolin MD, MSc Rad Onc Resident PGY3, University of Ottawa
Corresponding Author
email: dtesolin@toh.ca

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