

Chemoradiotherapy Tolerability Results in Geriatric Pancreatic Cancer Patients

Abstract

Pancreatic cancer poses unique challenges in elderly patients, given comorbidities, performance status concerns, and the absence of clear treatment guidelines. Understanding treatment outcomes and tolerability in this age group is vital. In this retrospective study (2012-2019), 24 elderly pancreatic cancer patients (≥ 65 years) underwent chemoradiotherapy. Patients were categorized into adjuvant or definitive groups, with overall survival (OS) as the primary endpoint. The median follow-up was 13.57 months; the median age was 71.46 ± 5.55 years. Of these, 9 received definitive chemoradiation, while 15 had surgery followed by chemoradiation. Median OS was 13.07 months (definitive) and 23.4 months (adjuvant) ($p=0.061$). No significant associations were found between OS and radiotherapy doses, pT stage, pN stage, tumor grade, or presence of invasion/microscopic disease. All completed radiotherapy; no grade 4-5 hematologic toxicity occurred. In conclusion, our findings suggest well-tolerated chemoradiotherapy in elderly patients, supporting its use in both adjuvant and definitive settings within this selected patient group.

Keywords: Pancreatic cancer, Chemoradiotherapy, Geriatrics, Aged, Pancreatic neoplasms

Introduction

Pancreatic adenocarcinoma is a significant cause of cancer-related mortality, particularly in Western countries. Surgical resection offers the only potential cure, but the majority of tumors are unresectable at diagnosis. Despite advances in multimodal therapy, the five-year overall survival (OS) for pancreatic cancer remains dismal at approximately 5%.^[1, 2] Standard care for resectable pancreatic cancer involves surgery followed by adjuvant chemotherapy, and the role of postoperative radiotherapy (PORT) continues to be a subject of debate.^[3] While some studies demonstrate increased OS with adjuvant radiotherapy,^[4-6] others show no clear benefit.^[7-9]

For locally advanced unresectable pancreatic cancer, chemoradiation has become an accepted form of definitive treatment. However, this approach is associated with significant treatment-related morbidity and poor outcomes.^[10-13] With an aging population globally, the majority of pancreatic cancer patients are over the age of 65. Yet, this age group is underrepresented in clinical trials, and the efficacy and tolerability of treatments in

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: Support_reprints@ccij-online.org

older patients remain unclear. Retrospective studies, like ours, become essential for examining outcomes and tolerability in this elderly cohort.^[14] Therefore, we aimed to investigate the treatment outcomes and tolerability of full-dose chemoradiation therapy in patients aged 65 years or older with pancreatic cancer.

Materials and Methods

This retrospective study was conducted at a single radiation oncology center in Turkey, and the protocol was approved by the local ethics committee. Patients aged 65 years or older with curative or adjuvant pancreatic cancer treated with chemoradiation therapy between 2013 and 2018 were retrospectively reviewed. Exclusion criteria included M1 disease, age < 65 , and histopathologic diagnoses other than ductal adenocarcinomas. Adjuvant external beam radiotherapy was delivered with linear accelerators, and concurrent chemotherapy (CT) was applied with capecitabine or gemcitabine. Statistical analysis was performed using SPSS Statistics 22.0, comparing treatment groups with various tests.

How to cite this article: Sarıcanbaz İ, Kayalı İ, Habiboğlu R. Chemoradiotherapy Tolerability Results in Geriatric Pancreatic Cancer Patients. Clin Cancer Investig J. 2023;12(6):19-22. <https://doi.org/10.51847/2Q1kXsLpy2>

**İrem Sarıcanbaz¹,
İlknur Kayalı^{1*},
Rahşan Habiboğlu¹**

¹Radiation Oncology Clinic,
Ankara Numune Training and
Research Hospital, Ankara,
Turkey.

Address for correspondence:
İlknur Kayalı,
Radiation Oncology Clinic,
Ankara Numune Training and
Research Hospital, Ankara,
Turkey.
E-mail: ilknurkayali@yahoo.com

Access this article online

Website: www.cci-j-online.org

DOI: [10.51847/2Q1kXsLpy2](https://doi.org/10.51847/2Q1kXsLpy2)

Quick Response Code:



Results and Discussion

We analyzed 24 patients, with 9 in the definitive group and 15 in the adjuvant group. The median follow-up was 13.57 months, and the median age was 71.46±5.55 years. In the definitive group, the median age and the dose of RT were significantly higher compared to the adjuvant group. No differences were observed in ECOG, gender, CT given with RT, and the number of CT given before RT or RT technique. Tumor characteristics varied between the groups, with the majority located in the pancreatic head for the adjuvant group and in the corpus for the definitive group. Patient characteristics are shown in **Table 1** and tumor characteristics of the patients are listed in **Table 2**.

Table 1. Patient and Treatment Characteristics

Characteristic	Definitive (n=9)	Adjuvan (n= 15)	P value
Median age (y)	73±7.4	70.53±4.1	0.017
Gender			0.74
Female	33.33%(3/9)	40%(6/15)	
Male	67.67%(6/9)	60%(9/15)	
Pre-CRT ECOG			0.643
0	11.11% (1/9)	13.33% (2/15)	
1	56.56% (5/9)	66.67% (10/15)	
2	33.33% (3/9)	20.00% (3/15)	
CT given with RT			0,339
gemcitabine	77.78% (7/9)	66.67% (10/15)	
Capacitabine	22.22% (2/9)	20.00% (3/15)	
none	-	13.33% (2/15)	
CT given before RT			0,326
1-4	44.44% (4/9)	73.33% (11/15)	
5-6	33.33% (3/9)	20.00% (3/15)	
none	22.22% (2/9)	6.67% (1/15)	
RT dose (Gy)			0,039
45	11.11% (1/9)	53.33% (8/15)	
50.4	88.89% (8/9)	46.67% (7/15)	
RT mean dose (Gy)	49.8	47.52	0,04
RT technique			0,57
3D conformal	77.78% (7/9)	86.67% (13/15)	
IMRT	22.22% (2/9)	13.33% (2/15)	

Abbreviations: CRT=chemoradiotherapy; ECOG= Eastern Cooperative Oncology Group; IMRT= intensity-modulated radiation therapy; CT= chemotherapy; RT= radiotherapy

Table 2. Tumor Characteristics of Patients

Characteristic	Definitive (n= 9)	Adjuvan (n=15)
Location in pancreas		
head	33.33% (3/9)	86.67% (13/15)
body	44.44% (4/9)	00.00% (0/15)
tail	22.22% (2/9)	13.33% (2/15)
Tumor diameter (cm)	3,95±1.097	3,65±1.32
Tumor grade		
Well differentiated	---	13.33% (2/15)
Modarately differentiated	---	60% (9/15)

Poorly differantiated	---	26.67% (4/15)
Stage		
T2	-	6.67% (1/15)
T3	44.44% (4/9)	73.33% (11/15)
T4	56.56% (5/9)	20.00% (3/15)
Lymph nodes		
Positive	---	86.67% (13/15)
Number assessed(median)	---	13 (3-25)
Number positive(median)	---	2(0-18)
LVI	---	46.67% (7/15)
PNI	---	80.00% (12/15)
Surgical Margins		
Positive	---	46.67% (7/15)

Abbreviations: LVI = lymphovascular invasion; PNI = perineural invasion

Toxicity was generally manageable, with no grade 4-5 hematologic toxicity observed. Adverse events were mostly related to treatment, including sickness, vomiting, and lack of appetite. Oral nutritional support was initiated in 20 patients, and no patient required a feeding tube or parenteral nutritional support during treatment.

The median overall survival was 13.07 months in the definitive group and 23.4 months in the adjuvant group, although this difference did not reach statistical significance (p=0.061). Univariate analysis did not reveal significant associations between OS and various factors, including RT dose, pT stage, pN stage, tumor grade, and the presence of lymphovascular invasion (LVI), perineural invasion (PNI), and microscopic disease (**Table 3**).

Table 3. Univariate Analysis of Median Survival Time and Log-rank p-value in Definitive and Adjuvant groups.

Variable	Definitive		Adjuvant	
	Median OS (months)	P value	Median OS (months)	P value
Gender		0.63		0.927
Female	11.6		17.2	
Male	13.7		24.5	
Pre-CRT ECOG		0.14		0.147
0	22.1		12	
1	10.4		17.4	
2	12.2		50	
Location in pancreas		0.024		0.843
head	7.9		25.9	
body -tail	15		14	
CT given before RT		0.301		0.203
1-4	16.2		15.3	
5-6	9.4		50	
none	8.9		23.4	
RT dose (Gy)		0.005		0.965
45	4.8		18.1	
50.4	13.6		31.9	
pT-stage				0.745
T3	-		23.3	
T4	-		17.5	

pN-stage			0.735
N0	-	23.4	
N+	-	30.8	
Tumor grade			0.158
Well	-	10.2	
Modarately	-	27.1	
Poorly	-	16	
LVI			0.729
No	-	26.5	
Yes	-	13.9	
PNI			0.555
No	-	35.5	
Yes	-	17.6	
Mic. Res. disease			0.47
No	-	19.8	
Yes	-	26.8	

Abbreviations: CRT=chemoradiotherapy; ECOG= Eastern Cooperative Oncology Group; LVI = lymphovascular invasion; PNI = perineural invasion; CT= chemotherapy; RT= radiotherapy

Pancreatic adenocarcinoma presents a challenging prognosis across various age groups, with prospective studies indicating a median overall survival (OS) of 17 to 20.1 months.^[7, 8, 10, 15, 16] Limited literature focuses on the elderly, often relying on retrospective studies due to constrained treatment options for this demographic.

In our study, the adjuvant group, with a median age of 70.5 years, demonstrated a noteworthy median OS of 23.4 months. In the definitive group, with a median age of 73, the median OS was 13 months. Importantly, the adjuvant group's OS closely resembled values observed in non-elderly cohorts.

Miyamoto *et al.* investigated pancreatic cancer patients aged 75 or older (n=42) undergoing chemoradiotherapy (CRT) as adjuvant or definitive therapy. They reported a median OS of 20.6 months for those undergoing surgery followed by CRT, comparable to our findings.^[17]

Horowitz *et al.* studied 655 patients, noting improved two-year survival with adjuvant CRT for those ≥ 75 (49% vs. 31.6%, p=0.013), with similar five-year survival rates.^[18] Frakes *et al.* associated increased mortality in the elderly with specific factors, while our study did not find significant associations between OS and certain parameters in the adjuvant group.^[19]

Miyamoto *et al.* reported adverse events during CRT, with our study showing manageable toxicity and no treatment interruptions.^[17] Advanced radiotherapy techniques contribute to reduced toxicity, as suggested by Ciabatti *et al.*^[20]

Despite its limitations – including retrospective design, a small patient cohort, and heterogeneity – our study highlights the tolerability and outcomes of CRT in elderly patients. The results underscore CRT as a viable treatment option for the elderly in both adjuvant and definitive settings within carefully selected patient groups. Ongoing research in treatment strategies aims to achieve improved survival with diminished

toxicity.

Conclusion

In conclusion, our study supports the feasibility and tolerability of full-dose chemoradiation therapy for elderly patients with pancreatic cancer. While differences in median overall survival between definitive and adjuvant groups did not reach statistical significance, the comparable outcomes suggest the potential efficacy of this treatment in the elderly cohort. With manageable toxicities and a favorable safety profile, full-dose chemoradiation emerges as a valuable consideration in treatment decisions for elderly patients with pancreatic cancer. Further research in larger cohorts is warranted to validate and refine these findings, paving the way for improved and personalized therapeutic strategies in the management of pancreatic cancer in the elderly.

Acknowledgments

None.

Conflict of interest

None.

Financial support

None.

Ethics statement

The protocol was approved by the Ethics Committee of Ankara Numune Training and Research Hospital. (Approval No: E-19-2694, dated 09/05/2019).

References

1. Vincent A, Herman J, Schulick R, Hruban RH, Goggins M. Pancreatic cancer. *Lancet*. 2011;378(9789):607-20. doi:10.1016/S0140-6736(10)62307-0
2. Raimondi S, Maisonneuve P, Lowenfels AB. Epidemiology of pancreatic cancer: An overview. *Nat Rev Gastroenterol Hepatol*. 2009;6(12):699-708. doi:10.1038/nrgastro.2009.177
3. Hoffe S, Rao N, Shridhar R. Neoadjuvant vs adjuvant therapy for resectable pancreatic cancer: The evolving role of radiation. *Semin Radiat Oncol*. 2014;24(2):113-25. doi:10.1016/j.semradonc.2013.11.002
4. Corsini MM, Miller RC, Haddock MG, Donohue JH, Farnell MB, Nagorney DM, et al. Adjuvant radiotherapy and chemotherapy for pancreatic carcinoma: The Mayo Clinic experience (1975-2005). *J Clin Oncol*. 2008;26(21):3511-6. doi:10.1200/JCO.2007.15.8782
5. Mattiucci GC, Falconi M, VAN Stiphout RG, Alfieri S, Calvo FA, Herman JM, et al. Adjuvant chemoradiation in pancreatic cancer: A pooled analysis in elderly (≥ 75 years) patients. *Anticancer Res*. 2015;35(6):3441-6.
6. Hayman TJ, Strom T, Springett GM, Balducci L, Hoffe SE, Meredith KL, et al. Outcomes of resected pancreatic cancer in patients age ≥ 70 . *J Gastrointest Oncol*. 2015;6(5):498-504. doi:10.3978/j.issn.2078-6891.2015.038
7. Neoptolemos JP, Dunn JA, Stocken DD, Almond J, Link K, Beger H, et al. European study group for pancreatic cancer. Adjuvant chemoradiotherapy and chemotherapy in resectable pancreatic cancer: A randomized controlled trial. *Lancet*. 2001;358(9293):1576-85. doi:10.1016/s0140-6736(01)06651-x
8. Neoptolemos JP, Stocken DD, Friess H, Bassi C, Dunn JA, Hickey H, et al. European study group for pancreatic cancer. A randomized trial of chemoradiotherapy and chemotherapy after resection of pancreatic

- cancer. *N Engl J Med.* 2004;350(12):1200-10. doi:10.1056/NEJMoa032295
9. Van Laethem JL, Hammel P, Mornex F, Azria D, Van Tienhoven G, Vergauwe P, et al. Adjuvant gemcitabine alone versus gemcitabine-based chemoradiotherapy after curative resection for pancreatic cancer: A randomized EORTC-40013-22012/FFCD-9203/GERCOR phase II study. *J Clin Oncol.* 2010;28(35):4450-6. doi:10.1200/JCO.2010.30.3446
 10. Moertel CG, Frytak S, Hahn RG, O'Connell MJ, Reitemeier RJ, Rubin J, et al. Therapy of locally unresectable pancreatic carcinoma: A randomized comparison of high dose (6000 rads) radiation alone, moderate dose radiation (4000 rads + 5-fluorouracil), and high dose radiation + 5-fluorouracil: The gastrointestinal tumor study group. *Cancer.* 1981;48(8):1705-10. doi:10.1002/1097-0142(19811015)48:8<1705::aid-cnrcr2820480803>3.0.co;2-4
 11. Klaassen DJ, MacIntyre JM, Catton GE, Engstrom PF, Moertel CG. Treatment of locally unresectable cancer of the stomach and pancreas: A randomized comparison of 5-fluorouracil alone with radiation plus concurrent and maintenance 5-fluorouracil--An eastern cooperative oncology group study. *J Clin Oncol.* 1985;3(3):373-8. doi:10.1200/JCO.1985.3.3.373
 12. Shinchi H, Takao S, Noma H, Matsuo Y, Mataka Y, Mori S, et al. Length and quality of survival after external-beam radiotherapy with concurrent continuous 5-fluorouracil infusion for locally unresectable pancreatic cancer. *Int J Radiat Oncol Biol Phys.* 2002;53(1):146-50. doi:10.1016/s0360-3016(01)02806-1
 13. Sultana A, Tudur Smith C, Cunningham D, Starling N, Tait D, Neoptolemos JP, et al. A systematic review, including meta-analyses, on the management of locally advanced pancreatic cancer using radiation/combined modality therapy. *Br J Cancer.* 2007;96(8):1183-90. doi:10.1038/sj.bjc.6603719
 14. Maréchal R, Demols A, Van Laethem JL. Adjuvant pharmacotherapy in the management of elderly patients with pancreatic cancer. *Drugs Aging.* 2013;30(2):155-65. doi:10.1007/s40266-013-0049-0
 15. Garofalo MC, Regine WF, Tan MT. On statistical reanalysis, the EORTC trial is a positive trial for adjuvant chemoradiation in pancreatic cancer. *Ann Surg.* 2006;244(2):332-3. doi:10.1097/01.sla.0000229980.81505.44
 16. Regine WF, Winter KA, Abrams RA, Safran H, Hoffman JP, Konski A, et al. Fluorouracil vs gemcitabine chemotherapy before and after fluorouracil-based chemoradiation following resection of pancreatic adenocarcinoma: A randomized controlled trial. *JAMA.* 2008;299(9):1019-26. doi:10.1001/jama.299.9.1019
 17. Miyamoto DT, Mamon HJ, Ryan DP, Willett CG, Ancukiewicz M, Kobayashi WK, et al. Outcomes and tolerability of chemoradiation therapy for pancreatic cancer patients aged 75 years or older. *Int J Radiat Oncol Biol Phys.* 2010;77(4):1171-7. doi:10.1016/j.ijrobp.2009.06.020
 18. Horowitz DP, Hsu CC, Wang J, Makary MA, Winter JM, Robinson R, et al. Adjuvant chemoradiation therapy after pancreaticoduodenectomy in elderly patients with pancreatic adenocarcinoma. *Int J Radiat Oncol Biol Phys.* 2011;80(3):1391-7. doi:10.1016/j.ijrobp.2010.04.003
 19. Frakes J, Mellon EA, Springett GM, Hodul P, Malafa MP, Fulp WJ, et al. Outcomes of adjuvant radiotherapy and lymph node resection in elderly patients with pancreatic cancer treated with surgery and chemotherapy. *J Gastrointest Oncol.* 2017;8(5):758-65. doi:10.21037/jgo.2017.08.05
 20. Ciabatti S, Cammelli S, Frakulli R, Arcelli A, Macchia G, Deodato F, et al. Radiotherapy of pancreatic cancer in older patients: A systematic review. *J Geriatr Oncol.* 2019;10(4):534-9. doi:10.1016/j.jgo.2018.09.007