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Tolerability of Chemoradiotherapy in Geriatric Patients with Pancreatic Cancer

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ABSTRACT

Pancreatic cancer in older adults presents distinct challenges due to underlying comorbidities, functional status, and the lack of universally accepted treatment protocols. It is essential to assess the tolerability and efficacy of treatment in this demographic. The goal of our study was to evaluate the outcomes and tolerability of full-dose chemoradiation in pancreatic cancer patients aged 65 years and older. This retrospective study (2012-2019) involved 24 patients aged 65 years and older diagnosed with pancreatic cancer, all of whom underwent chemoradiotherapy. The cohort was divided into two groups: one receiving adjuvant therapy following surgery, and the other receiving definitive chemoradiotherapy. The primary endpoint was overall survival (OS). The median follow-up period was 13.57 months, with a mean age of 71.46 ± 5.55 years. Of the participants, 9 were treated with definitive chemoradiotherapy, while 15 underwent surgery followed by chemoradiotherapy. The median OS was 13.07 months for the definitive group and 23.4 months for the adjuvant group (P = 0.061). There were no significant associations between OS and factors such as radiotherapy dose, pT stage, pN stage, tumor grade, or the presence of microscopic disease or invasion. All patients completed the radiotherapy regimen, without any severe hematologic toxicity (grade 4-5). In conclusion, this study supports the use of chemoradiotherapy in elderly pancreatic cancer patients, demonstrating its feasibility and tolerability in both adjuvant and definitive treatment contexts.

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

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Introduction

Pancreatic adenocarcinoma is a leading cause of cancer-related deaths, especially prevalent in Western countries [1, 2]. Surgical resection remains the only potentially curative treatment; however, the majority of pancreatic tumors are diagnosed as inoperable. Despite advances in combined therapy approaches, the five-year survival rate for pancreatic cancer remains disheartening, at approximately 5% [3, 4]. The standard approach for resectable cases involves surgery followed by adjuvant chemotherapy, though the use of postoperative radiotherapy (PORT) remains contentious [5]. Some studies report improved survival with adjuvant radiotherapy [6-8], while others find no significant benefit [9-11].

For patients with locally advanced and non-resectable pancreatic cancer, chemoradiotherapy has become a widely accepted treatment option [12, 13]. Unfortunately, this treatment is often associated with high levels of morbidity and suboptimal outcomes [14-17]. With an aging global population, a significant proportion of pancreatic cancer patients are now over the age of 65 years [18, 19]. However, elderly patients are underrepresented in clinical trials, and there is limited information regarding the efficacy and tolerability of treatment in this demographic [20]. Retrospective studies, such as the one presented here, provide crucial insights into treatment outcomes and tolerability for elderly patients [21]. The goal of our study was to evaluate the outcomes and tolerability of full-dose chemoradiation in pancreatic cancer patients aged 65 years and older.

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Materials and Methods

This retrospective study was carried out at a radiation oncology center in Turkey, with ethical approval from the local committee. We reviewed the medical records of patients aged 65 years and older, diagnosed with pancreatic cancer, who received chemoradiotherapy between 2013 and 2018 in either a curative or adjuvant setting. We excluded patients with metastatic disease (M1), those younger than 65 years, or those with histopathological diagnoses other than ductal adenocarcinoma. Adjuvant radiotherapy was delivered using linear accelerators, with concurrent chemotherapy (CT) involving capecitabine or gemcitabine. Data analysis was performed using SPSS Statistics 22.0 to compare the treatment groups using appropriate statistical tests.

Results and Discussion

The study cohort consisted of 24 patients, divided into two groups: nine in the definitive treatment group and fifteen in the adjuvant treatment group. The median follow-up period was 13.57 months, with a median patient age of 71.46 ± 5.55 years. Patients in the definitive treatment group were significantly older and received higher radiotherapy doses compared to the adjuvant group. No significant differences were found between the groups regarding ECOG performance status, gender, chemotherapy used with radiotherapy, number of chemotherapy cycles before radiotherapy, or radiotherapy techniques employed. Tumor locations differed between the groups, with the most of tumors in the adjuvant group being located in the pancreatic head, while those in the definitive group were more commonly found in the pancreatic body. Additional details on patient characteristics can be found in **Table 1**, and tumor characteristics are provided in **Table 2**.

Table 1. Patient and treatment characteristics

Characteristic	Definitive (n = 9)	Adjuvant (n = 15)	P-value
Median age (y)	73 ± 7.4	70.53 ± 4.1	0.017
Gender			
Female	33.33% (3/9)	40% (6/15)	0.74
Male	67.67% (6/9)	60% (9/15)	
Pre-CRT ECOG			
0	11.11% (1/9)	13.33% (2/15)	0.643
1	56.56% (5/9)	66.67% (10/15)	
2	33.33% (3/9)	20.00% (3/15)	
CT given with RT			
gemcitabine	77.78% (7/9)	66.67% (10/15)	0.339
Capacitabine	22.22% (2/9)	20.00% (3/15)	
none	-	13.33% (2/15)	
CT given before RT			
1-4	44.44% (4/9)	73.33% (11/15)	0.326
5-6	33.33% (3/9)	20.00% (3/15)	
none	22.22% (2/9)	6.67% (1/15)	
RT dose (Gy)			
45	11.11% (1/9)	53.33% (8/15)	0.039
50.4	88.89% (8/9)	46.67% (7/15)	
RT mean dose (Gy)	49.8	47.52	0.04
RT technique			
3D conformal	77.78% (7/9)	86.67% (13/15)	0.57
IMRT	22.22% (2/9)	13.33% (2/15)	

Abbreviations: CRT = chemoradiotherapy, ECOG = eastern cooperative oncology group, IMRT = intensity-modulated radiation therapy, CT = chemotherapy, and RT= radiotherapy

Table 2. Tumor characteristics of patients

Characteristic	Definitive	Adjuvant

	(n = 9)	(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)
Moderately differentiated	---	60% (9/15)
Poorly differentiated	---	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		
Pozitive	---	46.67% (7/15)

Abbreviations: LVI = lymphovascular invasion, and PNI = perineural invasion

In terms of treatment tolerance, toxicity levels remained manageable, with no instances of severe hematologic toxicity (grade 4-5). The most common adverse reactions were those directly related to the therapy, such as nausea, vomiting, and appetite loss. Nutritional support was initiated for 20 of the patients in the form of oral supplementation, with none requiring more invasive methods like feeding tubes or parenteral nutrition during treatment.

Survival data revealed a median overall survival (OS) of 13.07 months for the definitive treatment group, while the adjuvant treatment group had a median OS of 23.4 months. However, this difference was not statistically significant (P = 0.061). Univariate analysis indicated no meaningful associations between OS and variables such as radiotherapy dosage, tumor staging (pT, pN), tumor grade, lymphovascular invasion (LVI), perineural invasion (PNI), or microscopic disease presence, as outlined in **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	
Moderately	-		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, and RT= radiotherapy

Pancreatic cancer remains a disease with a generally poor prognosis across all age groups, with typical survival estimates ranging from 17 to 20.1 months [9, 10, 14, 22, 23]. Research specifically focusing on elderly patients is limited, often relying on retrospective data due to fewer treatment options for this age group.

In our research, the adjuvant cohort, with a median age of 70.5 years, had a median overall survival (OS) of 23.4 months, which is higher than the 13 months observed in the definitive treatment group, where the median age was 73. Notably, the OS in the adjuvant group was similar to what has been reported in younger patient populations.

Miyamoto and colleagues examined patients aged 75 years and older (n = 42) who received chemoradiotherapy (CRT) in either a curative or palliative context, reporting a median OS of 20.6 months for those who underwent surgery followed by CRT, which aligns with our findings [24]. Horowitz's research involving 655 patients revealed a two-year survival benefit in patients aged 75 or older who received adjuvant CRT (49% vs. 31.6%, P = 0.013), with no significant difference in the five-year survival rates [25]. On the other hand, Frakes *et al*. [26] identified factors contributing to higher mortality in elderly patients, while no such correlations were found in our adjuvant group.

Although Miyamoto's work noted treatment-related adverse events, our findings demonstrated that chemotherapy and radiotherapy were well-tolerated in the elderly group, with no significant interruptions due to toxicity [24]. Advances in radiation techniques, which have helped reduce adverse effects, are echoed in Ciabatti *et al*.'s work [27].

Despite some limitations, including the retrospective nature of the study, a relatively small sample size, and patient heterogeneity, our data suggest that chemoradiotherapy is a tolerable and viable treatment option for elderly pancreatic cancer patients, both in adjuvant and definitive treatment contexts, when carefully selected. Further research is required to refine treatment regimens and achieve better survival rates while minimizing side effects.

Conclusion

This study highlights that full-dose chemoradiation therapy is both feasible and well-tolerated among elderly patients diagnosed with pancreatic cancer. Although the median overall survival rates between the definitive and adjuvant treatment groups did not show statistically significant differences, the results indicate that the treatment could still offer promising efficacy for this demographic. With manageable side effects and a positive safety profile, full-dose chemoradiation represents an important option for treatment consideration in elderly patients with pancreatic cancer. Additional research with larger patient populations is necessary to further confirm and refine these results, ultimately enhancing personalized treatment approaches for elderly pancreatic cancer patients.

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