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Prognostic value of the CRM-status in pancreatic ductal adenocarcinoma - data from a regional cancer registry.

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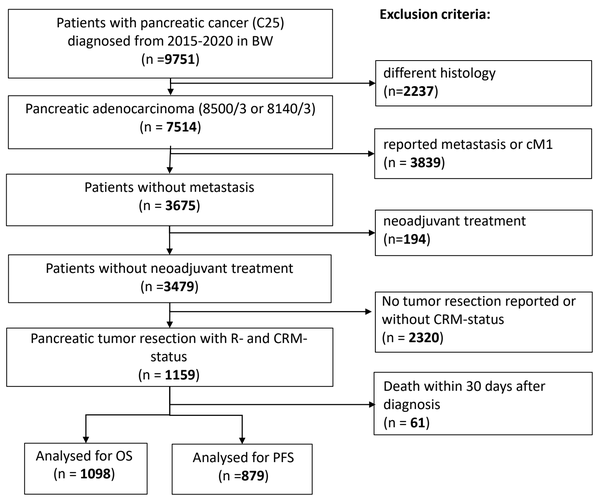
Background

- Ductal pancreatic adenocarcinoma (PDAC) still has a dismal prognosis even when deemed resectable
- A cancer free resection margin (R0) is associated with a more favorable prognosis
- The precise definition of the R0 status is still a matter of debate
- For a more accurate determination of R0 in PDAC the concept of circumferential resection margins (CRM) has been introduced[1]
- However, the clinical value of the CRM concept is not yet fully established
- Here we evaluate whether the CRM status is an independent prognostic factor using data from the regional cancer registry of the State of Baden Württemberg in Germany

Methods

- Patients with diagnosed PDAC between 2015 and 2020 were selected
- The R-status was assessed according to the national German S3 guideline with R0 wide when CRM is > 1mm, R0 narrow when CRM is ≤ 1 mm from the tumor and R1 when tumor cells are found at the resection margin
- Overall survival were assessed using Kaplan-Meier statistics and Cox proportional hazard models (adjusted by age, gender, tumor location and systemic treatment)



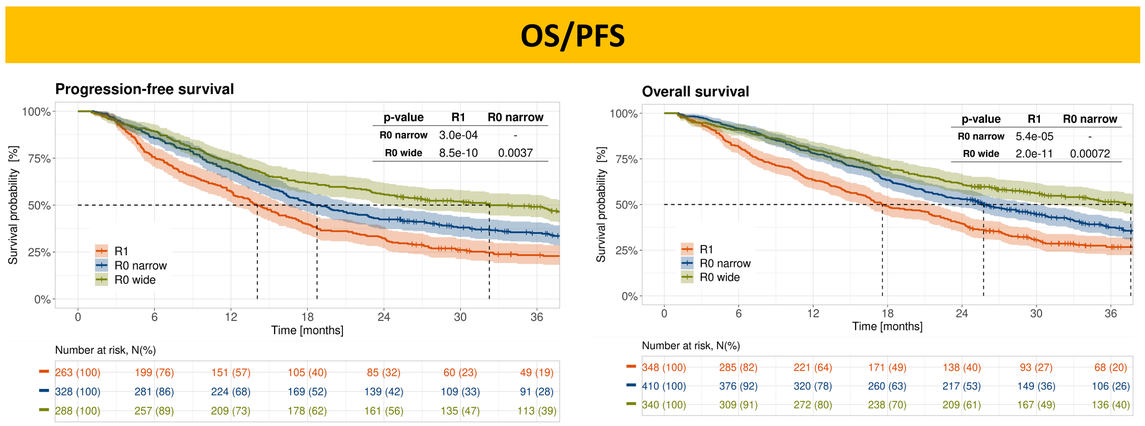
*) It is noteworthy, that since PFS analysis requires a complete follow-up in addition to the death record, the size of the PFS group is smaller than OS one.

Patient demographics and clinical information

		overall	R1	R0 narrow	R0 wide	p-test
N		**1098**	**348**	**410**	**340**	
R status (%)						
	R1	348 (31,7)	348 (100.0)	0 (0.0)	0 (0.0)	<0.001
	R0 narrow	410 (37.3)	0 (0.0)	410 (100.0)	0 (0.0)	
	R0 wide	340 (31.0)	0 (0.0)	0 (0.0)	340 (100.0)	
age (mean (SD))						
		69.73 (10.11)	70.16 (9.76)	69.07 (10.55)	70.09 (9.92)	0.246
sex (%)						
	M	542 (49.4)	170 (48.9)	207 (50.5)	165 (48.5)	0.844
	W	556 (50.6)	178 (51.1)	203 (49.5)	175 (51.5)	
location (%)						
	body	66 (6.0)	27 (7.8)	25 (6.1)	14 (4.1)	0.252
	head	888 (80.9)	284 (81.6)	326 (79.5)	278 (81.8)	
	overlapping	67 (6.1)	19 (5.5)	29 (7.1)	19 (5.6)	
	tail	77 (7.0)	18 (5.2)	30 (7.3)	29 (8.5)	
pN (%)						
	pN0	287 (26.1)	58 (16.7)	97 (23.7)	132 (38.8)	<0.001
	pN1	456 (41.5)	147 (42.2)	175 (42.7)	134 (39.4)	
	pN2	355 (32.3)	143 (41.1)	138 (33.7)	74 (21.8)	
pT (8th ed) (%)						
	pT1	74 (9.6)	8 (3.4)	19 (6.6)	47 (18.7)	<0.001
	pT2	439 (56.9)	113 (48.3)	178 (62.2)	148 (59.0)	
	pT3	246 (31.9)	102 (43.6)	89 (31.1)	55 (21.9)	
	pT4	12 (1.6)	11 (4.7)	0 (0.0)	1 (0.4)	
pT (7th ed) (%)						
	pT1	4 (1.2)	0 (0.0)	2 (1.6)	2 (2.2)	0.065
	pT2	8 (2.4)	2 (1.8)	1 (0.8)	5 (5.6)	
	pT3	308 (94.2)	107 (93.9)	120 (96.8)	81 (91.0)	
	pT4	7 (2.1)	5 (4.4)	1 (0.8)	1 (1.1)	
adjuvant therapy (%)						
	Gem-based	364 (33.2)	113 (32.5)	146 (35.6)	105 (30.9)	0.236
	5-FU-based	144 (13.1)	37 (10.6)	59 (14.4)	48 (14.1)	
	missing	590 (53.7)	198 (56.9)	205 (50.0)	187 (55.0)	

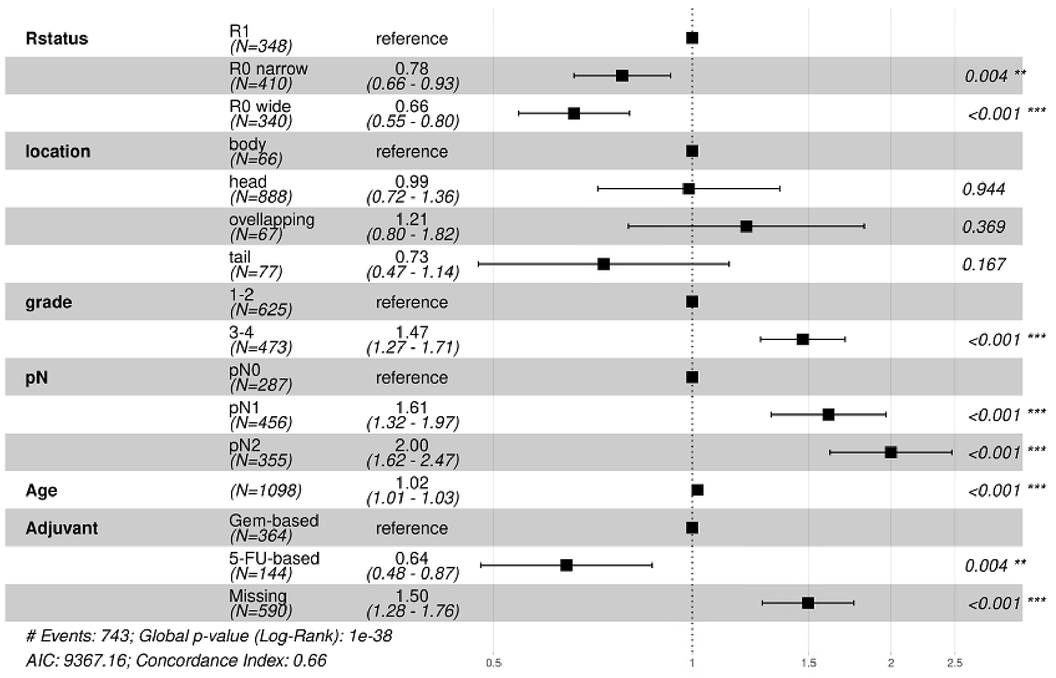
- Median age was 69.7 years
- The R0 wide group comprised more pT1 tumors and more patients with pN0
- The R1 group comprised more pT4 tumors and more patients with pN2
- Adjuvant chemotherapy was reported for 508 patients (46%)
- Gemcitabine-based regimens were reported for 71,6% and 5-FU-based regimens for 28,8 % of the patients

OS/PFS



- Median OS was 37.6 months in the R0 wide group, 25.7 months in the R0 narrow group and 17.6 months in the R1 resected group, respectively
- PFS was also statistically significant longer in R0 wide-resected patients compared to both R0 narrow and R1 resected patients. mPFS was 32.3 months, 19.1 months and 14.1 months in the respective groups
- The difference in mOS and mPFS between the R0 CRM+/- and R1 groups was observed independently of tumor grading (data not shown)

Cox Model



- HR for R0 wide/CRM- was 0.66 and 0.78 for R0 narrow/CRM+
- Apart from the R-status, the N-status, grading as well as adjuvant chemotherapy were important prognostic parameters
- Systemic adjuvant therapy modalities were equally distributed between the CRM groups

Discussion and Conclusion

- The present study was performed using real world data reflecting actual clinical settings
- The results obtained are in good agreement with the available data from clinical trials, including the prognostic role of the R-Status as well as the T- and N- stage and the efficacy of adjuvant chemotherapy protocols used [1,2]
- 5-FU based adjuvant treatment was mainly mFOLFIRINOX and showed better outcome as compared to gemcitabine-based treatments
- In conclusion, our data also demonstrate that population-based clinical cancer registries provide a valuable source of information when clinical trials are lacking or limited.

References

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[2] Conroy T et al. Five-Year Outcomes of FOLFIRINOX vs Gemcitabine as Adjuvant Therapy for Pancreatic Cancer: A Randomized Clinical Trial. JAMA Oncol. 2022 Nov 1;8(11):1571-1578.

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