Outcome of Surgical Resection after Neoadjuvant Peptide Receptor Radionuclide Therapy (PRRT) for Pancreatic Neuroendocrine Neoplasms: a case-matched analysis

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Background: Peptide receptor radionuclide therapy (PRRT) can be an option for advanced pancreatic neuroendocrine neoplasms (PNENs). Whether or not neoadjuvant PRRT increases postoperative morbidity remains unclear.

Methods: 20 patients with initially metastatic and/or locally advanced PNEN who underwent neoadjuvant PRRT (neoadjuvant group) were compared with a group of 20 patients who underwent upfront surgery (control group). Patients were matched (1:1) for tumor size, grading, staging, and intent of resection.

Results: The reason for choosing neoadjuvant PRRT was the presence of liver metastases in 6 patients (30%), the presence of organ/vascular infiltration in the remaining 14 (70%). After PRRT the median tumor size decreases from 59 mm to 50 mm (P=0.047). Patients who underwent neoadjuvant PRRT had a lower risk of developing pancreatic fistula (25% versus 65%, P=0.011) (table 1). Patients who underwent upfront surgery were more likely to have nodes metastases (80% versus 35%, P=0.004) (table 2). The 2-year progression free survival rate was 67% for the neoadjuvant group versus 58% in the control group (P=0.166). Independent predictors of progression free survival were PNEC-G3 and stage IV tumor (table 3).

Variable	Neoadjuvant n (%)	Control n (%)	*P*
Gender			
Male	15 (75)	12 (60)	
Female	5 (25)	8 (40)	0.311
Age			
≤60 years	13 (65)	8 (40)	
>60 years	7 (35)	12 (60)	0.113
Operative Time, minutes*	275 (222; 330)	235 (165; 322)	0.343
Blood Transfusion			
No	16 (80)	16 (80)	
Yes	4 (20)	4 (20)	1.000
Postoperative complications			
No	11 (55)	8 (40)	
Yes	9 (45)	12 (60)	0.342
Pancreatic fistula			
No	15 (75)	7 (35)	
Yes	5 (25)	13 (65)	0.011

Table 1. Perioperative outcomes

Variable	Neoadjuvant n (%)	Control n (%)	*P*
Pathology			
G1 G2	17 (85)	16 (80)	
G3	3 (15)	4 (20)	0.677
R			
R0 R1	13 (65)	15 (75)	
R2	7 (35)	5 (25)	0.490
T-Stage			
T1 T2	4 (20)	1 (5)	
T3 T4	16 (80)	19 (95)	0.151
N-Stage			
N0	13 (65)	4 (20)	
N1	7 (35)	16 (80)	0.004
Stage			
II-III	14 (70)	13 (65)	
IV	6 (30)	7 (35)	0.736

Table 2. Pathological findings

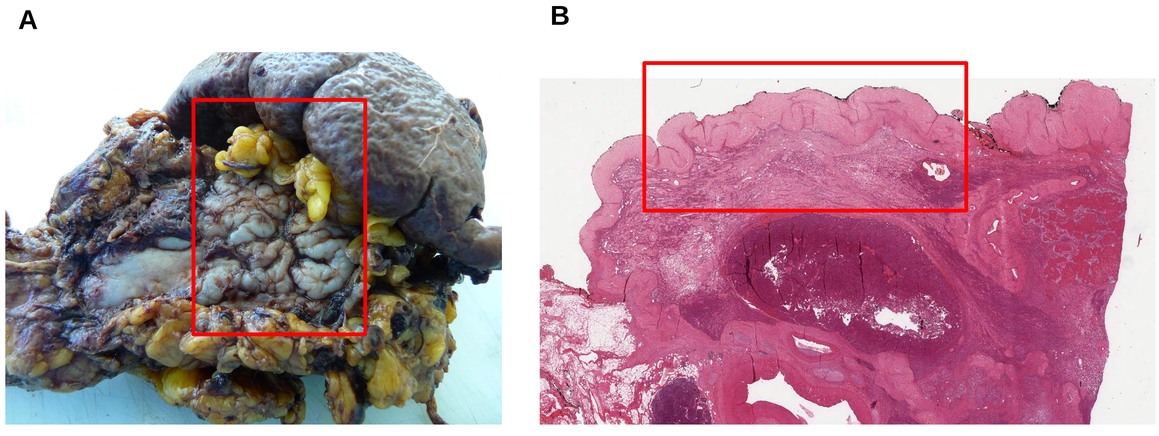

Figure 1. Macroscopic (A) and microscopic (B) appearance of surgical specimen after distal pancreatectomy for NET in a patient who underwent neoadjuvant PRRT. (A) Extensive fibrosis (red square) is seen macroscopically (A) and microscopically (B)

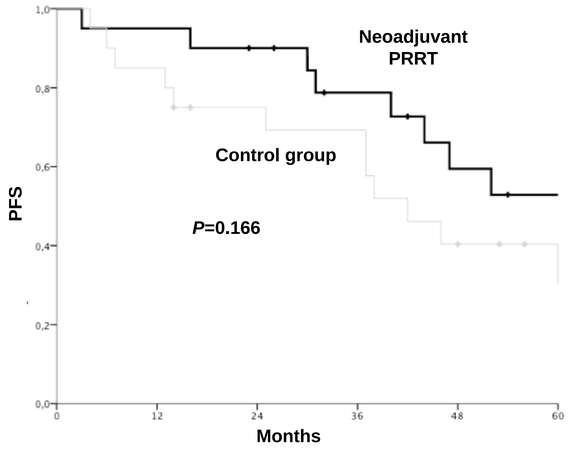

Figure 2. Comparison of progression-free survival from diagnosis between patients who underwent neoadjuvant PRRT and those who underwent upfront surgery (control group)

Variable	HR	95%CI	P
Tumor grading			
G1 G2	1	1	-
G3	3.040	1.076-8.593	0.036
TNM Stage			
Stage II-III	1	1	-
Stage IV	2.685	1.009-7.143	0.048
R			
R0 R1	1	1	-
R2	1.132	0.218-5.880	0.882

Table 3 . Multivariate analysis of progression-free survival

Conclusions: Pancreatic resection for PNEN after neoadjuvant PRRT is safe and associated with a lower risk of developing pancreatic fistula. A trend toward a better disease/progression-free survival was observed and it should be further evaluated in a larger population