

Supplemental Table S1. Association of TSR with clinicopathological characteristics in the training, validation, and EUS-FNA cohort

Variables	Training Cohort				Validation Cohort				EUS-FNA Cohort			
	N	TSR-Low	TSR-High	P	N	TSR-Low	TSR-High	P	N	TSR-Low	TSR-High	P
Age				0.811				0.442				0.123
0	42	21(50.0)	21(50.0)		120	75(62.5)	45(37.5)		34	21(61.8)	13(38.2)	
1	63	30(47.6)	33(52.4)		152	88(57.9)	64(42.1)		41	18(43.9)	23(56.1)	
Sex				0.946				0.086				0.912
0	47	23(48.9)	24(51.1)		125	68(54.4)	57(45.6)		37	19(51.4)	18(48.6)	
1	58	28(48.3)	30(51.7)		147	95(64.6)	52(35.4)		38	20(52.6)	18(47.4)	
Differentiation				0.214				0.252				
G1-G2	70	31(44.3)	39(55.7)		171	98(57.3)	73(42.7)			NA		
G3-G4	35	20(57.1)	15(42.9)		101	65(64.4)	36(35.6)					
Location				0.503				0.008				0.143
Head	55	25(45.5)	30(54.5)		166	110(66.3)	56(33.7)		48	28(58.3)	20(41.7)	
Body & Tail	50	26(52.0)	24(48.0)		106	53(50.0)	53(50.0)		27	11(40.7)	16(59.3)	
CA199				0.690				0.082				0.834
<37	29	15(51.7)	14(48.3)		58	29(50.0)	29(50.0)		20	10(50.0)	10(50.0)	
≥37	76	36(47.4)	40(52.6)		214	134(62.6)	80(37.4)		55	29(52.7)	26(47.3)	
PNI				0.214				0.095				0.617
Yes	70	37(52.9)	33(47.1)		183	116(63.4)	67(36.6)		48	26(54.2)	22(45.8)	
No	35	14(40.0)	21(60.0)		89	47(52.8)	42(47.2)		27	13(48.1)	14(51.9)	
LVI				0.042				0.213				0.608
Yes	43	26(60.5)	17(39.5)		102	66(64.7)	36(35.3)		29	14(48.3)	15(51.7)	
No	62	25(40.3)	37(59.7)		170	97(57.1)	73(42.9)		46	25(54.3)	21(45.7)	
ACT				0.692				0.506				0.091
Yes	78	37(47.4)	41(52.6)		191	112(58.6)	79(41.4)		49	22(44.9)	27(55.1)	
No	27	14(51.9)	13(48.1)		81	51(63.0)	30(37.0)		26	17(65.4)	9(34.6)	
pT Stage				0.208				0.331				0.729
T1-T2	74	33(44.6)	41(55.4)		201	117(58.2)	84(41.8)		57	29(50.9)	28(49.1)	
T3-T4	31	18(58.1)	13(41.9)		71	46(64.8)	25(35.2)		18	10(55.6)	8(44.4)	
pN Stage				<0.001				<0.001				0.003
N0	49	13(26.5)	36(73.5)		103	32(31.1)	71(68.9)		41	15(36.6)	26(63.4)	
N1-N2	56	38(67.9)	18(32.1)		169	131(77.5)	38(22.5)		34	24(70.6)	10(29.4)	
pM Stage				0.525				0.675				0.333
M0	102	49(48.0)	53(52.0)		263	157(59.7)	106(40.3)		74	38(51.4)	36(48.6)	
M1	3	2(66.7)	1(33.3)		9	6(66.7)	3(33.3)		1	1(100.0)	0(0.0)	
AJCC				0.005				<0.001				0.001
I-II	89	38(42.7)	51(57.3)		215	116(54.0)	99(46.0)		64	28(43.8)	36(56.3)	
III-IV	16	13(81.3)	3(18.8)		57	47(82.5)	10(17.5)		11	11(100.0)	0(0.0)	

AJCC, American Joint Committee on Cancer; PNI, perineural invasion; LVI, lymphovascular invasion; ACT, adjuvant chemotherapy; TSR, tumor-stroma ratio; EUS-FNA, Endoscopic ultrasound - guided fine needle aspiration; NA, not available.
p values < 0.05 are bolded.

Supplemental Table S2. Association of TSR with clinicopathological characteristics in the Pre-Neoadjuvant therapy EUS-FNA biopsy cohort

Variables	N	Low	TSR High	P
Age				0.958
<60, yrs	38	15(39.5)	23(60.5)	
≥60, yrs	65	26(40.0)	39(60.0)	
Sex				0.046
Female	45	13(28.9)	32(71.1)	
Male	58	28(48.3)	30(51.7)	
Location				0.025
Head	59	29(49.2)	30(50.8)	
Body & Tail	44	12(27.3)	32(72.7)	
Pre-Neoadjuvant therapy CA19-9				0.763
<37	26	11(42.3)	15(57.7)	
≥37	77	30(39.0)	47(61.0)	
pT Stage				<0.001
T1-T2	40	7(17.5)	33(82.5)	
T3-T4	63	34(54.0)	29(46.0)	
pN Stage				0.044
N0	87	31(35.6)	56(64.4)	
N1	16	10(62.5)	6(37.5)	
AJCC				<0.001
I	28	0(0.0)	28(100.0)	
II	75	41(54.7)	34(45.3)	
Neoadjuvant therapy				0.529
Gemcitabine + Radiation	96	39(40.6)	57(59.4)	
Gemcitabine + S-1 + Radiation	7	2(28.6)	5(71.4)	
Pathological response				<0.001
Non-responder	58	34(58.6)	24(41.4)	
Responder	45	7(15.6)	38(84.4)	

AJCC, American Joint Committee on Cancer; EUS-FNA, Endoscopic ultrasound - guided fine needle aspiration; TSR, tumor-stroma ratio.

p values < 0.05 are bold.

Supplemental Table S3. Univariate Cox analysis of TSR and clinicopathological characteristics in the training, validation, and EUS-FNA cohort

Variables	Training		Validation		EUS-FNA	
	HR(95%CI)	<i>p</i>	HR(95%CI)	<i>p</i>	HR(95%CI)	<i>p</i>
Age						
<60, yrs	reference		reference		reference	
≥60, yrs	1.55 (0.93 - 2.58)	0.092	1.18 (0.87 - 1.60)	0.283	1.02 (0.57 - 1.83)	0.946
Sex						
Female	reference		reference		reference	
Male	1.11 (0.68 - 1.78)	0.683	1.36 (1.00 - 1.84)	0.048	1.03 (0.58 - 1.82)	0.918
Differentiation						
moderate & well	reference		reference		NA	
Poor	2.17 (1.33 - 3.53)	0.002	2.01 (1.49 - 2.72)	<0.001	NA	
Location						
Head	reference		reference		reference	
Body & tail	0.91 (0.56 - 1.46)	0.687	0.64 (0.46 - 0.87)	0.005	0.62 (0.33 - 1.14)	0.122
Preoperative CA19-9						
<37	reference		reference		reference	
≥37	0.75 (0.45 - 1.27)	0.291	1.11 (0.77 - 1.60)	0.573	1.54 (0.79 - 3.02)	0.205
PNI						
No	reference		reference		NA	
Yes	1.58 (0.93 - 2.70)	0.094	1.14 (0.83 - 1.57)	0.420	NA	
LVI						
No	reference		reference		NA	
Yes	1.05 (0.65 - 1.71)	0.841	1.20 (0.89 - 1.63)	0.240	NA	
ACT						
No	reference		reference		reference	
Yes	0.53 (0.31 - 0.89)	0.018	0.52 (0.38 - 0.70)	<0.001	0.69 (0.38 - 1.25)	0.219
pT Stage						
T1-T2	reference		reference		reference	
T3-T4	1.79 (1.07 - 3.00)	0.028	1.76 (1.28 - 2.44)	<0.001	2.84 (1.49 - 5.42)	0.002
pN stage						
N0	reference		reference		reference	
N1-N2	1.49 (0.92 - 2.43)	0.106	1.75 (1.26 - 2.41)	<0.001	1.53 (0.85 - 2.74)	0.153
AJCC						
I-II	reference		reference		reference	
III-IV	3.13 (1.68 - 5.82)	<0.001	2.08 (1.49 - 2.92)	<0.001	3.17 (1.55 - 6.49)	0.002
TSR						
High	reference		reference		reference	
Low	3.97 (2.38 - 6.63)	<0.001	4.41 (3.10 - 6.25)	<0.001	4.49 (2.35 - 8.57)	<0.001

EUS-FNA, Endoscopic ultrasound - guided fine needle aspiration; AJCC, American Joint Committee on Cancer; PNI, perineural invasion; LVI, lymphovascular invasion; ACT, adjuvant chemotherapy; TSR, tumor-stroma ratio; HR, hazard ratio; CI, confidence interval; NA, not available.

p values < 0.05 are bolded.

Supplemental Table S4. Univariate Cox analysis of TSR and clinicopathological characteristics in the Pre-Neoadjuvant therapy EUS-FNA biopsy cohort

Variables	HR(95%CI)	<i>p</i>
Age		
<60, yrs	reference	
≥60, yrs	1.06 (0.62 - 1.82)	0.835
Sex		
Female	reference	
Male	1.22 (0.72 - 2.05)	0.465
Location		
Head	reference	
Body & tail	0.58 (0.34 - 1.00)	0.051
Pre-Neoadjuvant therapy CA19-9		
<37, U/mL	reference	
≥37, U/mL	1.30 (0.69 - 2.45)	0.424
ypT Stage (post-Neoadjuvant therapy)		
T1-T2	reference	
T3-T4	6.07 (3.04 - 12.12)	<0.001
ypN Stage (post-Neoadjuvant therapy)		
N0	Reference	
N1	1.38 (0.69 - 2.73)	0.361
AJCC		
I	Reference	
II	7.61 (3.43 - 16.90)	<0.001
Pathological response		
CAP0-2	reference	
CAP3	5.46 (2.94 - 10.14)	<0.001
Neoadjuvant treatment		
Gemcitabine + Radiation	reference	
Gemcitabine +S1+Radiation	0.35 (0.08 - 1.44)	0.146
TSR		
High	reference	
Low	6.81 (3.74 - 12.41)	<0.001

AJCC, American Joint Committee on Cancer; EUS-FNA, Endoscopic ultrasound - guided fine needle aspiration; TSR, tumor-stroma ratio; HR, hazard ratio; CI, confidence interval.

p values < 0.05 are bolded.

Supplemental Figure S1. Molecular Characteristics of Different TSR in Patients with PDAC. A and B, Top 20 significantly mutated genes in the samples of different TSR subgroups obtained from the TCGA cohort. C, Co-occurrence among the top 20 mutated genes in the TSR-low (C) and -high (D) subgroups of patients with PDAC from the TCGA dataset. *P*-values < .05 are marked in red. TSR, tumor-stroma ratio; PDAC, pancreatic ductal adenocarcinoma; and TCGA, The Cancer Genome Atlas.

