

**Table 1.** Expression of nuclear and cytoplasmic Smad3 in comparison to clinicopathological parameters

	Smad3-nuclear			Smad3-cytoplasmic		
	Negative (n=7)	Positive (n=194)	<i>p</i> value	Negative (n=5)	Positive (n=196)	<i>p</i> value
Gender			1.000			1.000
Male	5 (71.4%)	127 (65.5%)		3 (60.0%)	129 (65.8%)	
Female	2 (28.6%)	67 (34.5%)		2 (40.0%)	67 (34.2%)	
Age at diagnosis (years)	54.9 ± 13.5	58.8 ± 11.8	0.396	56.0 ± 12.5	58.7 ± 11.9	0.619
Tumor size (cm)	2.9 ± 2.6	4.7 ± 1.9	0.016	2.0 ± 1.0	4.7 ± 1.9	0.003
AJCC stage			0.537			0.753
IIIA	0 (0%)	20 (10.3%)		0 (0%)	20 (10.2%)	
IIIB	5 (71.4%)	141 (72.7%)		4 (80.0%)	142 (72.4%)	
IIIC	2 (28.6%)	33 (17.0%)		1 (20.0%)	34 (17.3%)	
Cell differentiation			0.007			0.135
WD / MD	3 (42.9%)	171 (88.1%)		3 (60.0%)	171 (87.2%)	
PD / Others	4 (57.1%)	23 (11.9%)		2 (40.0%)	25 (12.8%)	
Lymphatic invasion			0.247			0.159
No	6 (85.7%)	115 (59.3%)		5 (100%)	116 (59.2%)	
Yes	1 (14.3%)	79 (40.9%)		0 (0%)	80 (40.8%)	
Vascular invasion			1.000			1.000
No	7 (100%)	172 (88.7%)		5 (100%)	174 (88.8%)	
Yes	0 (0%)	22 (11.3%)		0 (0%)	22 (11.2%)	
Perineural invasion			0.350			0.585
No	7 (100%)	155 (79.9%)		5 (100%)	157 (80.1%)	
Yes	0 (0%)	39 (20.1%)		0 (0%)	39 (19.9%)	
Number of harvested lymph nodes			0.005			0.003
< 12	6 (85.7%)	58 (29.9%)		5 (100%)	59 (30.1%)	
12 ≤	1 (14.3%)	136 (70.1%)		0 (0%)	137 (69.9%)	
Proximal resection margin (cm)	13.9 ± 4.3	11.8 ± 8.8	0.516	12.3 ± 3.8	11.8 ± 8.7	0.903
Distal resection margin (cm)	1.1 ± 1.1	2.4 ± 1.3	0.009	1.0 ± 1.2	2.4 ± 1.3	0.016
Circumferential resection margin			1.000			1.000
Negative	7 (100%)	187 (96.4%)		5 (100%)	189 (96.4%)	
Positive	0 (0%)	7 (3.6%)		0 (0%)	7 (3.6%)	
Preoperative CCRT			< 0.001			< 0.001
No	1 (14.3%)	170 (87.6%)		0 (0%)	171 (87.2%)	
Yes	6 (85.7%)	24 (12.4%)		5 (100%)	25 (12.8%)	
Adjuvant treatment			0.080			0.040 <sup>1</sup>
No	0 (0%)	10 (5.3%)		0 (0%)	10 (5.2%)	
Chemotherapy	6 (85.7%)	81 (42.9%)		5 (100%)	82 (42.9%)	
CCRT	1 (14.3%)	98 (51.9%)		0 (0%)	99 (51.8%)	
Preoperative CEA (ng/mL)			1.000			0.658
≤ 5	5 (71.4%)	118 (64.5%)		4 (80.0%)	119 (64.3%)	
5 <	2 (28.6%)	65 (35.5%)		1 (20.0%)	66 (35.7%)	

<sup>1</sup> Adjusted *p* value is 0.120

**Table 2.** Expression of nuclear and cytoplasmic Smad4 in comparison to clinicopathological parameters

	Smad4-nuclear			Smad4-cytoplasmic		
	Negative (n=96)	Positive (n=105)	<i>p</i> value	Negative (n=78)	Positive (n=123)	<i>p</i> value
Gender			0.036			0.498
Male	56 (58.3%)	76 (72.4%)		49 (62.8%)	83 (67.5%)	
Female	40 (41.7%)	29 (27.6%)		29 (37.2%)	40 (32.5%)	
Age at diagnosis (years)	57.8 ± 11.8	59.4 ± 11.9	0.342	56.7 ± 11.7	59.8 ± 11.9	0.067
Tumor size (cm)	4.4 ± 1.9	4.8 ± 1.9	0.177	4.7 ± 2.0	4.6 ± 1.9	0.598
AJCC stage			0.083			0.504
IIIA	5 (5.2%)	15 (14.3%)		6 (7.7%)	14 (11.4%)	
IIIB	75 (78.1%)	71 (67.6%)		56 (71.8%)	90 (73.2%)	
IIIC	16 (16.7%)	19 (18.1%)		16 (20.5%)	19 (15.4%)	
Cell differentiation			0.432			0.839
WD / MD	85 (88.5%)	89 (84.8%)		68 (87.2%)	106 (86.2%)	
PD / Others	11 (11.5%)	16 (15.2%)		10 (12.8%)	17 (13.8%)	
Lymphatic invasion			0.524			0.757
No	60 (62.5%)	61 (58.1%)		48 (61.5%)	73 (59.3%)	
Yes	36 (37.5%)	44 (41.9%)		30 (38.5%)	50 (40.7%)	
Vascular invasion			0.824			0.498
No	85 (88.5%)	94 (89.5%)		68 (87.2%)	111 (90.2%)	
Yes	11 (11.5%)	11 (10.5%)		10 (12.8%)	12 (9.8%)	
Perineural invasion			0.894			0.961
No	77 (80.2%)	85 (81.0%)		63 (80.8%)	99 (80.5%)	
Yes	19 (19.8%)	10 (19.0%)		15 (19.2%)	24 (19.5%)	
Number of harvested lymph nodes			0.002			0.055
< 12	41 (42.7%)	23 (21.9%)		31 (39.7%)	33 (26.8%)	
12 ≤	55 (57.3%)	82 (78.1%)		47 (60.3%)	90 (73.2%)	
Proximal resection margin (cm)	11.2 ± 6.0	12.4 ± 10.5	0.325	12.3 ± 11.3	11.6 ± 6.4	0.560
Distal resection margin (cm)	2.4 ± 1.3	2.4 ± 1.3	0.831	2.4 ± 1.3	2.4 ± 1.3	0.904
Circumferential resection margin			1.000			0.708
Negative	93 (96.9%)	101 (96.2%)		76 (97.4%)	118 (95.9%)	
Positive	3 (3.1%)	4 (3.8%)		2 (2.6%)	5 (4.1%)	
Preoperative CCRT			0.508			0.505
No	80 (83.3%)	91 (86.7%)		68 (87.2%)	103 (83.7%)	
Yes	16 (16.7%)	14 (13.3%)		10 (12.8%)	20 (16.3%)	
Adjuvant treatment			0.392			0.148
No	3 (3.2%)	7 (6.9%)		1 (1.3%)	9 (7.6%)	
Chemotherapy	45 (47.9%)	42 (41.2%)		35 (45.5%)	52 (43.7%)	
CCRT	46 (48.9%)	53 (52.0%)		41 (53.2%)	58 (48.7%)	
Preoperative CEA (ng/mL)			0.009			0.428
≤ 5	51 (55.4%)	72 (73.53%)		46 (61.3%)	77 (67.0%)	
5 <	41 (44.6%)	26 (26.5%)		29 (38.7%)	38 (33.0%)	

**Table 3.** Expression of nuclear Smad7 in comparison to clinicopathological parameters

	Smad7-nuclear Negative (n=62)	Smad7-nuclear Positive (n=132)	<i>p</i> value
Gender			0.382
Male	38 (61.3%)	94 (67.6%)	
Female	24 (38.7%)	45 (32.4%)	
Age at diagnosis (years)	57.5 ± 11.5	59.1 ± 12.0	0.382
Tumor size (cm)	4.7 ± 2.1	4.6 ± 1.9	0.918
AJCC stage			0.884
IIIA	7 (11.3%)	13 (9.4%)	
IIIB	45 (72.6%)	101 (72.7%)	
IIIC	10 (16.1%)	25 (18.0%)	
Cell differentiation			0.297
WD / MD	56 (90.3%)	118 (84.9%)	
PD / Others	6 (9.7%)	21 (15.1%)	
Lymphatic invasion			0.680
No	36 (58.1%)	85 (61.2%)	
Yes	26 (41.9%)	54 (38.8%)	
Vascular invasion			0.917
No	55 (88.7%)	124 (89.2%)	
Yes	7 (11.3%)	15 (10.8%)	
Perineural invasion			0.125
No	46 (74.2%)	116 (83.5%)	
Yes	16 (25.8%)	23 (16.5%)	
Number of harvested lymph nodes			0.808
< 12	19 (30.6%)	45 (32.4%)	
12 ≤	43 (69.4%)	94 (67.6%)	
Proximal resection margin (cm)	11.9 ± 7.4	11.8 ± 9.2	0.928
Distal resection margin (cm)	2.4 ± 1.2	2.4 ± 1.3	0.878
Circumferential resection margin			0.441
Negative	61 (98.4%)	133 (95.7%)	
Positive	1 (1.6%)	6 (4.3%)	
Preoperative CCRT			0.591
No	54 (87.1%)	117 (84.2%)	
Yes	8 (12.9%)	22 (15.8%)	
Adjuvant treatment			0.342
No	1 (1.7%)	9 (6.6%)	
Chemotherapy	27 (45.0%)	60 (44.1%)	
CCRT	32 (53.3%)	67 (49.3%)	
Preoperative CEA (ng/mL)			0.242
≤ 5	34 (68.6%)	89 (67.4%)	
5 <	24 (41.4%)	43 (32.6%)	