

Table SI. Correlation between CA-9 positivity and histological tumor necrosis.

	UFS group				NAT group		
	n	CA-9	P-value		n	CA-9	P-value
Histological necrosis							
Presence	133	23 (0-82)	<0.001		13	34 (7-58)	<b>&lt;0.001</b>
Absence	130	10 (0-41)			29	17 (6-35)	
Histological large necrosis							
Presence	53	33 (0-82)	<0.001		11	38 (7-58)	<b>&lt;0.001</b>
Absence	210	12 (0-67)			31	17 (6-35)	

Table SII.Univariate and multivariate risk analyses of prognostic factors associated with DSS in the UFS group (n=263).

Variable	n	Median DSS			Univariate analysis <sup>a</sup>			Multivariate analysis <sup>a</sup>
		(months)		RR (95% CI)	P-value		RR (95% CI)	P-value
Age (years)								
≥75	81	40.2		1.42 (0.90-2.19)	0.131			
<75	182	61.9						
Sex								
Male	159	55.6		1.12 (0.73-1.68)	0.599			
Female	104	61.9						
Body mass index (kg/m <sup>2</sup> )								
≥25	40	56.4		0.97 (0.53-1.66)	0.924			
<25	223	54.7						
Local tumor extent								
Potentially resectable	260	56.4		2.44 (0.14-11.09)	0.440			
Borderline resectable	3	NR						

Pathological tumor size (mm)							
≥20	188	43.9		1.93 (1.19-3.28)	<0.001	1.12 (0.68-1.93)	0.667
<20	75	NR					
Lymph node metastasis							
Positive	172	38.0		3.15 (1.95-5.32)	<0.001	2.21 (1.31-3.90)	0.003
Negative	91	NR					
Lymphatic invasion							
Positive	195	43.0		2.65 (1.53-4.99)	<0.001	1.50 (0.83-2.93)	0.183
Negative	68	NR					
Vascular invasion							
Positive	241	52.0		5.70 (1.80-34.59)	<0.001	3.05 (0.95-18.62)	0.064
Negative	22	NR					
Perineural invasion							
Positive	249	54.7		2.30 (0.86-9.36)	0.105		
Negative	14	75.2					

HTN							
Positive	133	31.5		3.90 (2.51-6.25)	<b>&lt;0.001</b>	3.28 (2.09-5.31)	<b>&lt;0.001</b>
Negative	130	NR					

Table SIII.Univariate and multivariate risk analyses of prognostic factors associated with RFS in the UFS group (n=263).

Variable	n	Median RFS (months)	Univariate analysis <sup>a</sup>		Multivariate analysis <sup>a</sup>	
			RR (95% CI)	P-valu	RR (95% CI)	P-valu
Age (years)						
≥75	81	14.0 <i>(10.05-18.6)</i>	1.34	0.093		
<75	182	20.1				
Sex						
Male	159	19.2	0.96	0.795		
Female	104	17.1				
Body mass index (kg/m <sup>2</sup> )						
≥25	40	20.8	0.96 <i>(0.61-1.44)</i>	0.858		
<25	223	17.1				
Local tumor extent						
Potentially resectable	260	17.2	0.39 <i>(0.12-2.35)</i>	0.249		
Borderline	3	9.7				
Pathological tumor size (mm)						
≥20	188	14.2	1.89 <i>(1.32-2.76)</i>	<b>&lt;0.001</b>	1.15 <i>(0.79-1.71)</i>	0.476
<20	75	31.9				
Lymph node metastasis						

Positive	172	13.0		3.48 <i>(2.41-5.15)</i>	<b>&lt;0.00</b> <b>1</b>		2.84 <i>(1.80-4.40)</i>	<b>&lt;0.00</b> <b>1</b>
Negative	91	74.0						
Lymphatic invasion								
Positive	195	14.9		2.16	<b>&lt;0.00</b>		1.06	0.788
Negative	68	48.1						
Vascular invasion								
Positive	241	16.1		3.44	<b>&lt;0.00</b>		1.99	0.076
Negative	22	NR						
Perineural invasion								
Positive	249	17.1		2.53	<b>0.018</b>		0.96	0.936
Negative	14	NR						
HTN								
Positive	133	10.9		3.06	<b>&lt;0.00</b>		2.59	<b>&lt;0.00</b>
Negative	130	42.0						

<sup>a</sup>Cox proportional hazards regression model. Upon multivariate analysis, lymph node metastasis and histological tumor necrosis were considered prognostic factors. P-values representing significant differences are indicated in bold print. RFS, relapse-free survival; UFS, upfront surgery; HTN, histological tumor necrosis; RR, risk ratio; CI, confidence interval.