

Table S1 Correlation between TLS and clinical characteristics of patients with ccRCC in the cohort (n=720)

Characteristics, n(%)	Total		TLS		χ^2	P value
	(n=720)	No TLS (n=607)	TLS-low (n=57)	TLS-high (n=56)		
Age						
≤65 years	549 (76.3)	467 (76.9)	39 (68.4)	43 (76.8)	2.096	0.351
>65 years	171 (23.8)	140 (23.1)	18 (31.6)	13 (23.2)		
Gender						
Male	497 (69)	416 (68.5)	42 (73.7)	39 (69.6)	0.657	0.720
Female	223 (31)	191 (31.5)	15 (26.3)	17 (30.4)		
WHO/ISUP grade						
I & II	623 (86.5)	527 (86.8)	47 (82.5)	49 (87.5)	0.901	0.637
III & IV	97 (13.5)	80 (13.2)	10 (17.5)	7 (12.5)		
TNM stage						
1	623 (86.5)	525 (86.5)	47 (82.5)	51 (91)	2.304	0.680
2	38 (5.3)	33 (5.4)	3 (5.3)	2 (3.6)		
3 & 4	59 (8.2)	49 (8.1)	7 (12.3)	3 (5.4)		
T stage						
T1	619 (86)	523 (86.2)	45 (78.9)	51 (91.1)	5.666	0.226
T2	31 (4.3)	28 (4.6)	2 (3.5)	1 (1.8)		
T3 & T4	70 (9.7)	56 (9.2)	10 (17.5)	4 (7.1)		
Necrosis						
Absent	598 (83.1)	506 (83.4)	44 (77.2)	48 (85.7)	1.714	0.425
Present	122 (16.9)	101 (16.6)	13 (22.8)	8 (14.3)		
Sarcoma						
Absent	712 (98.9)	600 (98.8)	57 (100)	55 (98.2)	0.882	0.643
Present	8 (1.1)	7 (1.2)	0 (0)	1 (1.8)		
Cystic architecture						
Absent	581 (80.7)	493 (81.2)	43 (75.4)	45 (80.4)	1.122	0.571
Present	139 (19.3)	114 (18.8)	14 (24.6)	11 (19.6)		
Multifocality						
Absent	695 (96.5)	583 (96)	56 (98.2)	56 (100)	2.936	0.230
Present	25 (3.5)	24 (4)	1 (1.8)	0 (0)		
Size						
≤4 cm	464 (64.4)	390 (64.3)	35 (61.4)	39 (69.6)	0.900	0.637
>4 cm	256 (35.6)	217 (35.7)	22 (38.6)	17 (30.4)		
Overall survival						
-	656 (91.1)	557 (91.8)	45 (78.9)	54 (96.4)	12.687	0.002
+	64 (8.9)	50 (8.2)	12 (21.1)	2 (3.6)		
Progression-free survival						
-	643	543 (89.5)	46 (80.7)	54 (96.4)	7.407	0.025
+	77	64 (10.5)	11 (19.3)	2 (3.6)		

WHO/ISUP World Health Organization/International Society of Urologic Pathologist; TLS tertiary lymphoid structure

Table S2 Correlation between TLS maturity and clinical characteristics of patients with ccRCC in the naïve cohort (n=720)

Characteristics, n (%)	Total		TLS		χ^2	P value
	(n=720)	No TLS (n=607)	Less mature (n=54)	Mature (n=59)		
Age						
≤65 years	549 (76.2)	467 (76.9)	38 (70.4)	44 (74.6)	1.280	0.527
>65 years	171 (23.8)	140 (23.1)	16 (29.6)	15 (25.4)		
Gender					0.456	0.796
Male	497 (69)	416 (68.5)	39 (72.2)	42 (71.2)		
Female	223 (31)	191 (31.5)	15 (27.8)	17 (28.8)		
WHO/ISUP grade					0.518	0.772
I & II	623 (86.5)	527 (86.8)	45 (83.3)	51 (86.4)		
III & IV	97 (13.5)	80 (13.2)	9 (16.7)	8 (13.6)		
TNM stage					0.556	0.968
1	623 (86.5)	525 (86.5)	46 (85.2)	52 (88.1)		
2	38 (5.3)	33 (5.4)	3 (5.5)	2 (3.4)		
3 & 4	59 (8.2)	49 (8.1)	5 (9.3)	5 (8.5)		
T stage					2.880	0.578
T1	619 (86)	523 (86.2)	44 (81.5)	52 (88.1)		
T2	31 (4.3)	28 (4.6)	2 (3.7)	1 (1.7)		
T3 & T4	70 (9.7)	56 (9.2)	8 (14.8)	6 (10.2)		
Necrosis					2.471	0.291
Absent	598 (83.1)	506 (83.4)	41 (75.9)	51 (86.4)		
Present	122 (16.9)	101 (16.6)	13 (24.1)	8 (13.6)		
Sarcoma					0.942	0.624
Absent	712 (98.9)	600 (98.8)	53 (98.1)	59 (100)		
Present	8 (1.1)	7 (1.2)	1 (1.9)	0 (0)		
Cystic architecture					0.684	0.710
Absent	581 (80.7)	493 (81.2)	42 (77.8)	46 (78)		
Present	139 (19.3)	114 (18.8)	12 (22.2)	13 (22)		
Multifocality					2.965	0.227
Absent	695 (96.5)	583 (96)	53 (98.1)	59 (100)		
Present	25 (3.5)	24 (4)	1 (1.9)	0 (0)		
Size					1.814	0.404
≤4 cm	464 (64.4)	390 (64.3)	32 (59.3)	42 (71.2)		
>4 cm	256 (35.6)	217 (35.7)	22 (40.7)	17 (28.8)		
Overall survival					10.162	0.006
-	656 (91.1)	557 (91.8)	43 (79.6)	56 (94.9)		
+	64 (8.9)	50 (8.2)	11 (20.4)	3 (5.1)		
Progression-free survival					2.978	0.226
-	643 (89.3)	543 (89.5)	45 (83.3)	55 (93.2)		
+	77 (10.7)	64 (10.5)	9 (16.7)	4 (6.8)		

WHO/ISUP World Health Organization/International Society of Urologic Pathologist; TLS tertiary lymphoid structure

Table S3 Information of the antibodies used in our research

Antibodies	Company	Catalogue	Dye
CD21	Abcam	ab75985	PPD620
CD3	Abcam	ab135372	PPD650
CD56	CST	CST3576	PPD520
CD4	ZSGB-Bio	ZM-0418	PPD570
CD8A	CST	CST70306	PPD480
CD20	Abcam	ab78237	PPD780
CD163	CST	CST93498	PPD520
CD31	CST	CST3528	PPD570
CD68	CST	CST76437	PPD480

Table S4 Correlation between tumor-infiltrating T cells and clinical characteristics of patients with ccRCC in the naïve cohort (n=720)

Characteristics	Tumor-infiltrating T cells			χ^2	P value
	Total (n=720)	T-low (n=199)	T-high (n=521)		
Age					
≤65 years	549 (76.3)	150 (75.4)	399 (76.6)	0.116	0.734
>65 years	171 (23.8)	49 (24.6)	122 (23.4)		
Gender					
Male	497 (69)	137 (68.8)	360 (69.1)	0.004	0.948
Female	223 (31)	62 (31.2)	161 (30.9)		
WHO/ISUP grade					
I & II	623 (86.5)	185 (93)	438 (84.1)	9.775	0.002
III & IV	97 (13.5)	14 (7)	83 (15.9)		
TNM stage					
1	623 (86.5)	179 (90)	444 (85.2)	4.929	0.085
2	38 (5.3)	11 (5.5)	27 (5.2)		
3 & 4	59 (8.2)	9 (4.5)	50 (9.6)		
T stage					
T1	619 (86)	179 (90)	440 (84.5)	5.513	0.064
T2	31 (4.3)	9 (4.5)	22 (4.2)		
T3 & T4	70 (9.7)	11 (5.5)	59 (11.3)		
Necrosis					
Absent	598 (83.1)	174 (87.4)	424 (81.4)	3.752	0.053
Present	122 (16.9)	25 (12.6)	97 (18.6)		
Sarcoma					
Absent	712 (98.9)	197 (99)	515 (98.8)	0.028	0.867
Present	8 (1.1)	2 (1)	6 (1.2)		
Cystic architecture					
Absent	581 (80.7)	156 (78.4)	425 (81.6)	0.936	0.333
Present	139 (19.3)	43 (21.6)	96 (18.4)		
Multifocality					
Absent	695 (96.5)	191 (96)	504 (96.7)	0.246	0.620
Present	25 (3.5)	8 (4)	17 (3.3)		
Size					
≤4 cm	464 (64.4)	130 (65.3)	334 (64.1)	0.093	0.760
>4 cm	256 (35.6)	69 (34.7)	187 (35.9)		
Overall Survival					
-	656 (91.1)	191 (96)	465 (89.3)	8.050	0.005
+	64 (8.9)	8 (4)	56 (10.7)		
Progression-free survival					
-	643 (89.3)	186 (93.5)	457 (87.7)	4.987	0.026
+	77 (10.7)	13 (6.5)	64 (12.3)		

ccRCC clear cell renal cell carcinoma; WHO/ISUP World Health Organization/International Society of Urologic Pathologist

Table S5 Correlation between tumor-infiltrating B cells and clinical characteristics of patients with ccRCC in the naïve cohort (n=720)

Characteristics, n (%)	Tumor-infiltrating B cells			χ^2	P value
	Total (n=720)	B-low (n=297)	B-high (n=423)		
Age					
≤65 years	549 (76.3)	224 (75.4)	325 (76.8)	0.192	0.661
>65 years	171 (23.8)	73 (24.6)	98 (23.2)		
Gender					
Male	497 (69)	198 (66.7)	299 (70.7)	1.318	0.251
Female	223 (31)	99 (33.3)	124 (29.3)		
WHO/ISUP grade					
I & II	623 (86.5)	268 (90.2)	355 (83.9)	5.962	0.015
III & IV	97 (13.5)	29 (9.8)	68 (16.1)		
TNM stage					
1	623 (86.5)	258 (86.8)	365 (86.3)	1.373	0.503
2	38 (5.3)	18 (6.1)	20 (4.7)		
3 & 4	59 (8.2)	21 (7.1)	38 (9)		
T stage					
T1	619 (86)	257 (86.5)	362 (85.6)	2.793	0.247
T2	31 (4.3)	16 (5.4)	15 (3.5)		
T3 & T4	70 (9.7)	24 (8.1)	46 (10.9)		
Necrosis					
Absent	598 (83.1)	252 (84.8)	346 (81.8)	1.155	0.283
Present	122 (16.9)	45 (15.2)	77 (18.2)		
Sarcoma					
Absent	712 (98.9)	295 (99.3)	417 (98.6)	0.881	0.348
Present	8 (1.1)	2 (0.7)	6 (1.4)		
Cystic architecture					
Absent	581 (80.7)	239 (80.5)	342 (80.9)	0.016	0.899
Present	139 (19.3)	58 (19.5)	81 (19.1)		
Multifocality					
Absent	695 (96.5)	285 (96)	410 (96.9)	0.487	0.485
Present	25 (3.5)	12 (4)	13 (3.1)		
Size					
≤4 cm	464 (64.4)	179 (60.3)	285 (67.4)	3.846	0.050
>4 cm	256 (35.6)	118 (39.7)	138 (32.6)		
Overall Survival					
-	656 (91.1)	284 (95.6)	372 (87.9)	12.707	<0.001
+	64 (8.9)	13 (4.4)	51 (12.1)		
Progression-free survival					
-	643 (89.3)	279 (94)	364 (86.1)	11.366	0.001
+	77 (10.7)	18 (6)	59 (13.9)		

ccRCC clear cell renal cell carcinoma; WHO/ISUP World Health Organization/International Society of Urologic Pathologist

Table S6 Correlation between tumor-infiltrating lymphocytes and clinical characteristics of patients with ccRCC in the naïve cohort (n=720)

Characteristics, n (%)	Tumor-infiltrating lymphocytes			χ^2	P value
	Total (n=720)	TIL-low (n=377)	TIL-high (n=343)		
Age					
≤65 years	549 (76.3)	288 (76.4)	261 (76.1)	0.009	0.925
>65 years	171 (23.7)	89 (23.6)	82 (23.9)		
Gender					
Male	497 (69)	256 (67.9)	241 (70.3)	0.467	0.494
Female	223 (31)	121 (32.1)	102 (29.7)		
WHO/ISUP grade					
I & II	623 (86.5)	346 (91.8)	277 (80.8)	18.707	<0.001
III & IV	97 (13.5)	31 (8.2)	66 (19.2)		
TNM stage					
1	623 (86.5)	341 (90.5)	282 (82.2)	11.904	0.003
2	38 (5.3)	17 (4.5)	21 (6.1)		
3 & 4	59 (8.2)	19 (5)	40 (11.7)		
T stage					
T1	617 (85.7)	340 (90.2)	279 (81.3)	12.954	0.002
T2	31 (4.3)	14 (3.7)	17 (5)		
T3 & T4	70 (9.7)	23 (6.1)	47 (13.7)		
Necrosis					
Absent	598 (83.1)	323 (85.7)	275 (80.2)	3.862	0.049
Present	122 (16.9)	54 (14.3)	68 (19.8)		
Sarcoma					
Absent	712 (98.9)	374 (99.2)	338 (98.5)	0.716	0.397
Present	8 (1.1)	3 (0.8)	5 (1.5)		
Cystic architecture					
Absent	581 (80.7)	295 (78.2)	286 (83.4)	3.037	0.081
Present	139 (19.3)	82 (21.8)	57 (16.6)		
Multifocality					
Absent	695 (96.5)	364 (96.6)	331 (96.5)	0.001	0.971
Present	25 (3.5)	13 (3.4)	12 (3.5)		
Size					
≤4 cm	464 (64.4)	255 (67.6)	209 (60.9)	3.525	0.060
>4 cm	256 (35.6)	122 (32.4)	134 (39.1)		
Overall Survival					
-	656 (91.1)	366 (97.1)	290 (84.5)	38.840	<0.001
+	64 (8.9)	11 (2.9)	53 (15.5)		
Progression-free survival					
-	643 (89.3)	356 (94.4)	287 (83.7)	21.756	<0.001
+	77 (10.7)	21 (5.6)	56 (16.3)		

ccRCC clear cell renal cell carcinoma; WHO/ISUP World Health Organization/International Society of Urologic Pathologist; TIL tumor-infiltrating lymphocyte

Table S7 Correlation between combination of TLS-T expression and clinical characteristics of patients with ccRCC in the naïve cohort (n=720)

Characteristics, n (%)	TLS-T expression				χ^2	P value
	Total (n=720)	Double high/low (n=235)	TLS-low-T-high (n=475)	TLS-high-T-low (n=10)		
Age						
≤65	549 (76.3)	179 (76.2)	363 (76.4)	7 (70)	0.224	0.894
>65	171 (23.7)	56 (23.8)	112 (23.6)	3 (30)		
Gender					0.005	0.997
Male	497 (69)	162 (68.9)	328 (69.1)	7 (70)		
Female	223 (31)	73 (31.1)	147 (30.9)	3 (30)		
WHO/ISUP grade					8.309	0.016
I & II	623 (86.5)	214 (91.1)	399 (84)	10 (100)		
III & IV	97 (13.5)	21 (8.9)	76 (16)	0 (0)		
TNM stage					6.371	0.173
1	623 (86.5)	210 (89.4)	413 (86.9)	10 (100)		
2	38 (5.3)	13 (5.5)	25 (5.3)	0 (0)		
3 & 4	59 (8.2)	12 (5.1)	47 (9.9)	0 (0)		
T stage					6.556	0.161
T1	619 (86)	210 (89.4)	399 (84)	10 (100)		
T2	31 (4.3)	10 (4.3)	21 (4.4)	0 (0)		
T3 & T4	70 (9.7)	15 (6.4)	55 (11.6)	0 (0)		
Necrosis					4.531	0.104
Absent	598 (83.1)	202 (86)	386 (81.3)	10 (100)		
Present	122 (16.9)	33 (14)	89 (18.7)	0 (0)		
Sarcoma					0.186	0.911
Absent	712 (98.9)	232 (98.7)	470 (98.9)	10 (100)		
Present	8 (1.1)	5 (2.1)	5 (1.1)	0 (0)		
Cystic architecture					1.109	0.574
Absent	581 (80.7)	187 (79.6)	387 (81.5)	7 (70)		
Present	139 (19.3)	48 (20.4)	88 (18.5)	3 (30)		
Multifocality					0.379	0.827
Absent	695 (96.5)	227 (96.6)	458 (96.4)	10 (100)		
Present	25 (3.5)	8 (3.4)	17 (3.6)	0 (0)		
Size					1.190	0.552
≤4 cm	464 (64.4)	153 (65.1)	303 (63.8)	8 (80)		
>4 cm	256 (35.6)	82 (34.9)	172 (36.2)	2 (20)		
OS					10.811	0.004
-	656 (91.1)	225 (95.7)	421 (88.6)	10 (100)		
+	64 (8.9)	10 (4.3)	54 (11.4)	0 (0)		
PFS					8.537	0.014
-	643 (89.3)	220 (93.6)	413 (86.9)	10 (100)		
+	77 (10.7)	15 (6.4)	62 (13.1)	0 (0)		

WHO/ISUP World Health Organization/International Society of Urologic Pathologist;

TLS tertiary lymphoid structure

Table S8 Correlation between combination of TLS-B expression and clinical characteristics of patients with ccRCC in the naïve cohort (n=720)

Characteristics, n (%)	Total	TLS-B expression			χ^2	P value
	(n=720)	Double high/low (n=331)	TLS-low-B-high (n=378)	TLS-high-B-low (n=11)		
Age						
≤65	549 (76.3)	249 (75.2)	291 (77)	9 (81.8)	0.492	0.782
>65	171 (23.7)	82 (24.8)	87 (23)	2 (18.2)		
Gender					1.031	0.597
Male	497 (69)	223 (67.4)	267 (70.6)	7 (63.6)		
Female	223 (31)	108 (32.6)	111 (29.4)	4 (36.4)		
WHO/ISUP grade					5.930	0.052
I & II	623 (86.5)	295 (89.1)	317 (83.9)	11 (100)		
III & IV	97 (13.5)	36 (10.9)	61 (16.1)	0 (0)		
TNM stage					3.167	0.530
1	623 (86.5)	287 (86.7)	325 (86)	11 (100)		
2	38 (5.3)	20 (6)	18 (4.8)	0 (0)		
3 & 4	59 (8.2)	24 (7.3)	35 (9.2)	0 (0)		
T stage					3.970	0.410
T1	619 (86)	286 (86.4)	322 (85.2)	11(100)		
T2	31 (4.3)	17 (5.1)	14 (3.7)	0 (0)		
T3 & T4	70 (9.7)	28 (8.5)	42 (11.1)	0 (0)		
Necrosis					2.909	0.233
Absent	598 (83.1)	278 (84)	309 (81.7)	11(100)		
Present	122 (16.9)	53 (16)	69 (18.3)	0 (0)		
Sarcoma					0.404	0.817
Absent	712 (98.9)	328 (99.1)	373 (98.7)	11(100)		
Present	8 (1.1)	3 (0.9)	5 (1.3)	0 (0)		
Cystic architecture					0.464	0.793
Absent	581 (80.7)	268 (81)	305 (80.7)	8 (72.7)		
Present	139 (19.3)	63 (19)	73 (19.3)	3 (27.3)		
Multifocality					0.420	0.811
Absent	695 (96.5)	319 (96.4)	365 (96.6)	11 (100)		
Present	25 (3.5)	12 (3.6)	13 (3.4)	0 (0)		
Size					3.265	0.195
≤4 cm	464 (64.4)	202 (61)	254 (67.2)	8 (72.7)		
>4 cm	256 (35.6)	129 (39)	124 (32.8)	3 (27.3)		
OS					16.579	<0.001
-	656 (91.1)	316 (95.5)	329 (87)	11 (100)		
+	64 (8.9)	15 (4.5)	49 (13)	0 (0)		
PFS					16.428	<0.001
-	643 (89.3)	311 (94)	321 (84.9)	11 (100)		
+	77 (10.7)	20 (6)	57 (15.1)	0 (0)		

WHO/ISUP World Health Organization/International Society of Urologic Pathologist;

TLS tertiary lymphoid structure

Table S9 Correlation between combination of TLS-TIL expression and clinical characteristics of patients with ccRCC in the naïve cohort (n=720)

Characteristics, n (%)	Total		TLS-TIL expression		χ^2	P value
	(n=720)	Double high/low (n=403)	TLS-low-TIL-high (n=302)	TLS-high-TIL-low (n=15)		
Age						
≤65	549 (76.3)	309 (76.7)	229 (75.8)	11 (73.3)	0.140	0.932
>65	171 (23.7)	94 (23.3)	73 (24.2)	4 (26.7)		
Gender						
Male	497 (69)	273 (67.7)	213 (70.5)	11 (73.3)	0.760	0.684
Female	223 (31)	130 (32.3)	89 (29.5)	4 (26.7)		
WHO/ISUP grade						
I & II	623 (86.5)	371 (92.1)	240 (79.5)	12 (80)	24.031	<0.001
III & IV	97 (13.5)	32 (7.9)	62 (20.5)	3 (20)		
TNM stage						
1	623 (86.5)	362 (89.8)	246 (81.5)	15 (100)	14.316	0.006
2	38 (5.3)	19 (4.7)	19 (6.3)	0 (0)		
3 & 4	59 (8.2)	22 (5.5)	37 (12.3)	0 (0)		
T stage						
T1	619 (86)	361 (89.6)	243 (80.5)	15 (100)	15.255	0.004
T2	31 (4.3)	15 (3.7)	16 (5.3)	0 (0)		
T3 & T4	70 (9.7)	27 (6.7)	43 (14.2)	0 (0)		
Necrosis						
Absent	598 (83.1)	343 (85.1)	241 (79.8)	14 (93.3)	4.609	0.100
Present	122 (16.9)	60 (14.9)	61 (20.2)	1 (6.7)		
Sarcoma						
Absent	712 (98.9)	399 (99)	298 (98.7)	15 (100)	0.345	0.841
Present	8 (1.1)	4 (1)	4 (1.3)	0 (0)		
Cystic architecture						
Absent	581 (80.7)	316 (78.4)	253 (83.8)	12 (80)	3.192	0.203
Present	139 (19.3)	87 (21.6)	49 (16.2)	3 (20)		
Multifocality						
Absent	695 (96.5)	390 (96.8)	290 (96)	15 (100)	0.839	0.657
Present	25 (3.5)	13 (3.2)	12 (4)	0 (0)		
Size						
≤4 cm	464 (64.4)	272 (67.5)	181 (59.9)	11 (73.3)	4.834	0.089
>4 cm	256 (35.6)	131 (32.5)	121 (40.1)	4 (26.7)		
OS						
-	656 (91.1)	390 (96.8)	251 (83.1)	15 (100)	41.278	<0.001
+	64 (8.9)	13 (3.2)	51 (16.9)	0 (0)		
PFS						
-	643 (89.3)	380 (94.3)	248 (82.1)	15 (100)	28.621	<0.001
+	77 (10.7)	23 (5.7)	54 (17.9)	0 (0)		

WHO/ISUP World Health Organization/International Society of Urologic Pathologist; TLS tertiary lymphoid structure; TIL tumor-infiltrating lymphocyte

Table S10 Influencing factors of patient survival of ccRCC among TLS-TIL expression of patients with ccRCC in the naïve cohort (n=720)

Characteristics	Total	Outcome	Average survival (months)	Log-Rank χ^2	P value
	(n=720)	(death)			
TLS-T					
Double high/low	235 (32.6)	10 (16)	56.19	11.090	0.004
TLS-low-T-high	475 (66)	54 (84)	53.01		
TLS-high-T-low	10 (1.4)	0 (0)	59.10		
TLS-B					
Double high/low	331 (46)	15 (23.4)	55.93	17.135	<0.001
TLS-low-B-high	378 (52.5)	49 (76.6)	52.41		
TLS-high-B-low	11 (1.5)	0 (0)	59.18		
TLS-TIL					
Double high/low	403 (56)	13 (20.3)	56.19	43.090	<0.001
TLS-low-TIL-high	302 (41.9)	51 (79.7)	51.12		
TLS-high-TIL-low	15 (2.1)	0 (0)	59.40		

TLS tertiary lymphoid structure; TIL tumor-infiltrating lymphocyte

Table S11 Concordance index analysis of the prognostic accuracy of TIL and prognostic models for overall survival in the naïve cohort (n=720)

Characteristics	Overall survival	Progression-free survival
Nuclear grade (1-2 vs. 3-4)	0.6631 (0.6039~0.7226)	0.6547 (0.6008~0.7086)
TNM stage (1-2 vs. 3-4)	0.6364 (0.5801~0.6928)	0.6539 (0.6018~0.7061)
T stage (1-2 vs. 3-4)	0.6539 (0.5959~0.7120)	0.6608 (0.6078~0.7138)
SSIGN score (0-5 vs. ≥ 6)^a	0.6370 (0.5812~0.6928)	0.6342 (0.5837~0.6846)
Leibovich score (0-5 vs. ≥ 6)^a	0.6399 (0.5846~0.6952)	0.6333 (0.5832~0.6834)
TIL_T (low vs. high)	0.5843 (0.5434~0.6252)	0.5613 (0.5190~0.6036)
TIL_B (low vs. high)	0.6135 (0.5634~0.6637)	0.5988 (0.5509~0.6468)
TIL (low vs. high)	0.6901 (0.6436~0.7366)	0.6408 (0.5913~0.6902)
SSIGN+TIL	0.7441 (0.6879~0.8002)	0.7197 (0.6641~0.7753)
Leibovich+TIL	0.7471 (0.6912~0.8030)	0.7102 (0.6529~0.7675)

SSIGN=stage, size, grade, and necrosis; TIL tumor-infiltrating lymphocyte

^a: For clinical application, SSIGN and Leibovich score were defined as low risk (scores 0-2), intermediate risk (3-5), and high risk (6 or higher) [1].

Table S12 Correlation between clinical characteristics with the combination of Age-TLS density of patients with ccRCC in the naïve cohort (n=720)

Characteristics, n (%)	Total (n=720)	Age-TLS density				χ^2	P value
		Young-TLS low	Young-TLS high	Old- TLS low	Old- TLS high		
Gender							
Male	497 (69)	350 (69.2)	33 (76.7)	108 (68.4)	6 (46.2)	4.417	0.220
Female	223 (31)	156 (30.8)	10 (23.3)	50 (31.6)	7 (53.8)		
WHO/ISUP grade							
I & II	623 (86.6)	445 (87.9)	39 (90.7)	129 (81.6)	10 (76.9)	5.772	0.123
III & IV	97 (13.5)	61 (12.1)	4 (9.3)	29 (18.4)	3 (23.1)		
TNM stage							
1	623 (86.5)	443 (87.6)	41 (95.4)	129 (81.6)	10 (76.9)	9.120	0.167
2	38 (5.3)	27 (5.3)	1 (2.3)	9 (5.7)	1 (7.7)		
3 & 4	59 (8.2)	36 (7.1)	1 (2.3)	20 (12.7)	2 (15.4)		
T stage							
T1	619 (86)	442 (87.3)	41 (95.3)	126 (79.7)	10 (76.9)	10.468	0.106
T2	31 (4.3)	21 (4.2)	0 (0)	9 (5.7)	1 (7.7)		
T3 & T4	70 (9.7)	43 (8.5)	2 (4.7)	23 (14.6)	2 (15.4)		
Necrosis							
Absent	598 (83.1)	431 (85.2)	37 (86)	119 (75.3)	11 (84.7)	8.639	0.034
Present	122 (16.9)	75 (14.8)	6 (14)	39 (24.7)	2 (15.4)		
Sarcoma							
Absent	712 (98.9)	500 (98.8)	43 (100)	157 (99.4)	12 (92.3)	5.962	0.113
Present	8 (1.1)	6 (1.2)	0 (0)	1 (0.6)	1 (7.7)		
Cystic architecture							
Absent	581 (80.7)	406 (80.2)	32 (74.4)	130 (82.3)	13 (100)	4.520	0.211
Present	139 (19.3)	100 (19.8)	11 (25.6)	28 (17.7)	0 (0)		
Multifocality							
Absent	695 (96.5)	490 (96.8)	43 (100)	149 (94.3)	13 (100)	4.491	0.213
Present	25 (3.5)	16 (3.2)	0 (0)	9 (5.7)	0 (0)		
Size							
≤4 cm	464 (64.4)	331 (65.4)	30 (69.8)	94 (59.5)	9 (69.2)	2.560	0.465
>4 cm	256 (35.6)	175 (34.6)	13 (30.2)	64 (40.5)	4 (30.8)		
OS							
-	656 (91.1)	473 (93.5)	42 (97.7)	129 (81.6)	12 (92.3)	23.291	<0.001
+	64 (8.9)	33 (6.5)	1 (2.3)	29 (18.4)	1 (7.7)		
PFS							
-	643 (89.3)	463 (91.5)	42 (97.7)	126 (79.7)	12 (92.3)	20.947	<0.001
+	77 (10.7)	43 (8.5)	1 (2.3)	32 (20.3)	1 (7.7)		

WHO/ISUP World Health Organization/International Society of Urologic Pathologist; TLS tertiary lymphoid structure, YL young-low density, YH young-high density, OL old-low density, OH old-high density

