C-105

Clinicopathological features of atypical renal cell carcinoma histological subtypes: a study of 1,686 cases spanning over three decades

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Background

- Rising renal cell carcinoma (RCC) incidence globally due to:
  - Rising prevalence of risk factors – hypertension, smoking, obesity
  - Commonplace use of cross-sectional abdominal imaging[1]
- Commonest types: clear cell (ccRCC) & papillary (pRCC) – often grouped as conventional RCC (**cRCC**) – ~80% cases
- ISUP[2] classification recognizes rarer atypical RCC (**aRCC**) subtypes[3], which are as yet not well characterized epidemiologically

Methods

- Retrospective review from large prospectively maintained, single-institution, electronic uro-oncological registry
- Time period : 1990-2019
- Inclusion criteria: All patients who underwent nephrectomy for renal masses
- Exclusion criteria: Incomplete records, non-malignant histology

Results

RCC subtypes	N (%)
Conventional RCC	
Clear cell	1283 (76.1%)
Papillary	194 (11.5%)
Atypical RCC	
Chromophobe	49 (2.9%)
Mixed clear cell-papillary	50 (3.0%)
Collecting duct	2 (0.1%)
Multilocular cystic	46 (2.7%)
Oncocytic papillary	4 (0.2%)
RCC NOS	33 (2.0%)
Sarcomatoid	12 (0.7%)
Translocation	5 (0.3%)
Tubulocystic	8 (0.5%)

- Demographics of overall cohort
  - **1477 conventional RCCs** (87.6%) + **209 atypical RCCs** (12.4%)
  - 66% male; mean age at diagnosis 58.4 ± 11.6 years
  - Mean follow-up time 38.8 ± 42.5 months
  - Mean age, BMI, ESRF prevalence lower in aRCC
  - Stage I, II, III, IV: 62.3%. 9.1%, 19.2%, 8.7% respectively
  - aRCC generally had a lower pathological T & N stage
- Surgical details
  - Laparoscopic approach favored over open & robotic
  - More radical than partial nephrectomies
  - aRCC: higher proportion underwent radical nephrectomies; shorter mean op time with less blood loss
- Notable subtype findings
  - Multilocular cystic RCC: highest association with ESRF (73.9%) & hypertension (82.6%)
  - Sarcomatoid RCC: largest mean size among aRCCs (12.2 ± 7.82 cm). 92% symptomatic, 50% metastasized at presentation. 83% stage 3 or 4 – highest of any subtype. Higher mean operative time and blood loss.
  - Xp11 translocation RCC: youngest mean age at presentation (45.6 ± 12.8 years) & excellent CSS
- Survival analysis
  - Absolute follow-up OS and CSS lower for aRCC; survival for first ~5 years consistently higher in cRCC
  - 5-year OS estimates higher in cRCC (0.74, 95%CI: 0.71-0.77) compared to aRCC (0.57, 95%CI: 0.46-0.70)
  - 5-year OS highest in chromophobe RCC (0.90, 95%-CI: 0.79-1.0)
  - In aRCC group: shorter operative time, partial nephrectomy, lower tumor stages, absence of contiguous tumor invasion were associated with increased survival

Discussion

- One of the largest comprehensive retrospective reviews focusing on aRCC
- Trends consistent with histologic subtype proportions in previous studies
- cRCC: consistently better 5-year OS & CSS
- aRCC: may have better long-term OS & CSS but statistically non-significant
- Limitations: single-center retrospective study (might not be widely generalizable); predominantly surgical cohort (may under-represent advanced/de-novo metastatic disease)
- **Conclusion:**
  - **Contributes towards tailored patient counseling and healthcare resource planning**
  - **Guides follow-up protocols after resection – current guidelines are mainly based on pathologic stage**

Demographics	cRCC (N=1477)	aRCC (N=209)	P-value
Male sex	986 (66.8%)	126 (60.3%)	0.077
Age at diagnosis (years)	58.8 ± 11.5	55.7 ± 11.9	**<0.001**
Smoking history			
Non-smoker	962 (65.1%)	141 (67.5%)	0.3
Ex-smoker	251 (17.0%)	30 (14.4%)	
Current smoker	189 (12.8%)	18 (8.6%)	
Passive smoker	3 (0.2%)	0	
BMI	25.1 ± 4.36	24.3 ± 4.47	0.04
Hypertension	886 (60.0%)	135 (64.6%)	0.125
Charlson comorbidity index			
0-1	710 (48.1%)	84 (40.2%)	0.068
≥2	734 (49.7%)	116 (55.5%)	
End-stage renal failure	149 (10.1%)	67 (32.1%)	**<0.001**
Symptomatic at presentation	751 (50.8%)	101 (48.3%)	0.619
Follow-up time (months)	39.8 ± 42.3	32.2 ± 43.3	0.019
Operation characteristics			
Nephrectomy approach			
Laparoscopic	811 (54.9%)	123 (58.9%)	0.274
Open	478 (32.4%)	55 (26.3%)	
Robotic	167 (11.3%)	23 (11.0%)	
Nephrectomy type			
Radical	1037 (70.2%)	158 (75.6%)	**0.041**
Partial	439 (29.7%)	46 (22.0%)	
Nephrectomy time (min)	194 ± 74.8	184 ± 64.8	**0.04**
Blood loss (ml)	427 ± 636	328 ± 478	**0.035**
Clavien-Dindo score			
0-II	1296 (87.7%)	178 (85.2%)	0.41
≥III	93 (6.3%)	9 (4.3%)	
Length of stay (days)	5.19 ± 4.93	5.19 ± 5.00	0.985
Overall survival	1194 (80.8%)	156 (74.6%)	**0.045**
Cancer-specific survival	1298 (87.9%)	171 (81.8%)	**0.025**
Pathological findings			
Pathological T			
T1	936 (63.4%)	134 (64.1%)	**0.0242**
T2	159 (10.8%)	21 (10.0%)	
T3	353 (23.9%)	39 (18.7%)	
T4	25 (1.7%)	10 (4.8%)	
TX	3 (0.2%)	0	
Pathological N			
N0	1110 (75.2%)	151 (72.2%)	**0.007**
N1	28 (1.9%)	11 (5.3%)	
NX	339 (22.9%)	42 (20.1%)	
Pathological M			
M0	1353 (91.6%)	186 (89.0%)	0.509
M1	115 (7.8%)	18 (8.6%)	
MX	8 (0.5%)	0	
Pathological stage			
Stage 1	919 (62.2%)	131 (62.7%)	0.438
Stage 2	135 (9.1%)	19 (9.1%)	
Stage 3	291 (19.7%)	32 (15.3%)	
Stage 4	125 (8.5%)	22 (10.5%)	
Pathological size (cm)	5.34 ± 3.47	5.54 ± 4.83	0.574
Collecting duct invasion	54 (3.7%)	10 (4.8%)	0.484
Lymphovascular invasion	184 (12.5%)	27 (12.9%)	0.811
Renal sinus invasion	96 (6.5%)	15 (7.2%)	0.753
Perinephric fat invasion	236 (16.0%)	37 (17.7%)	0.490

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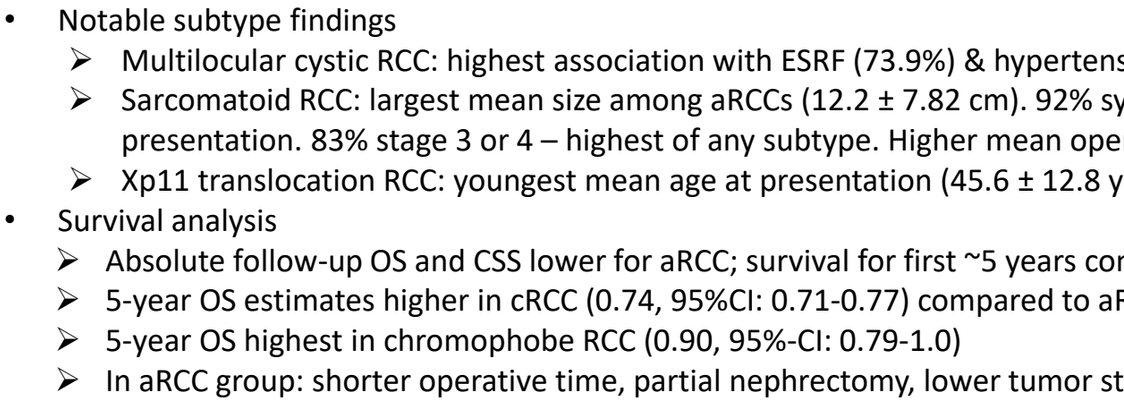
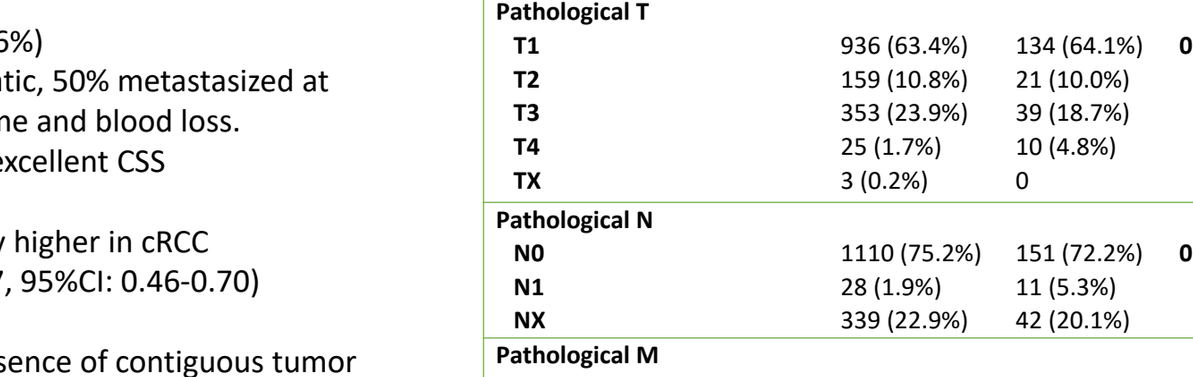
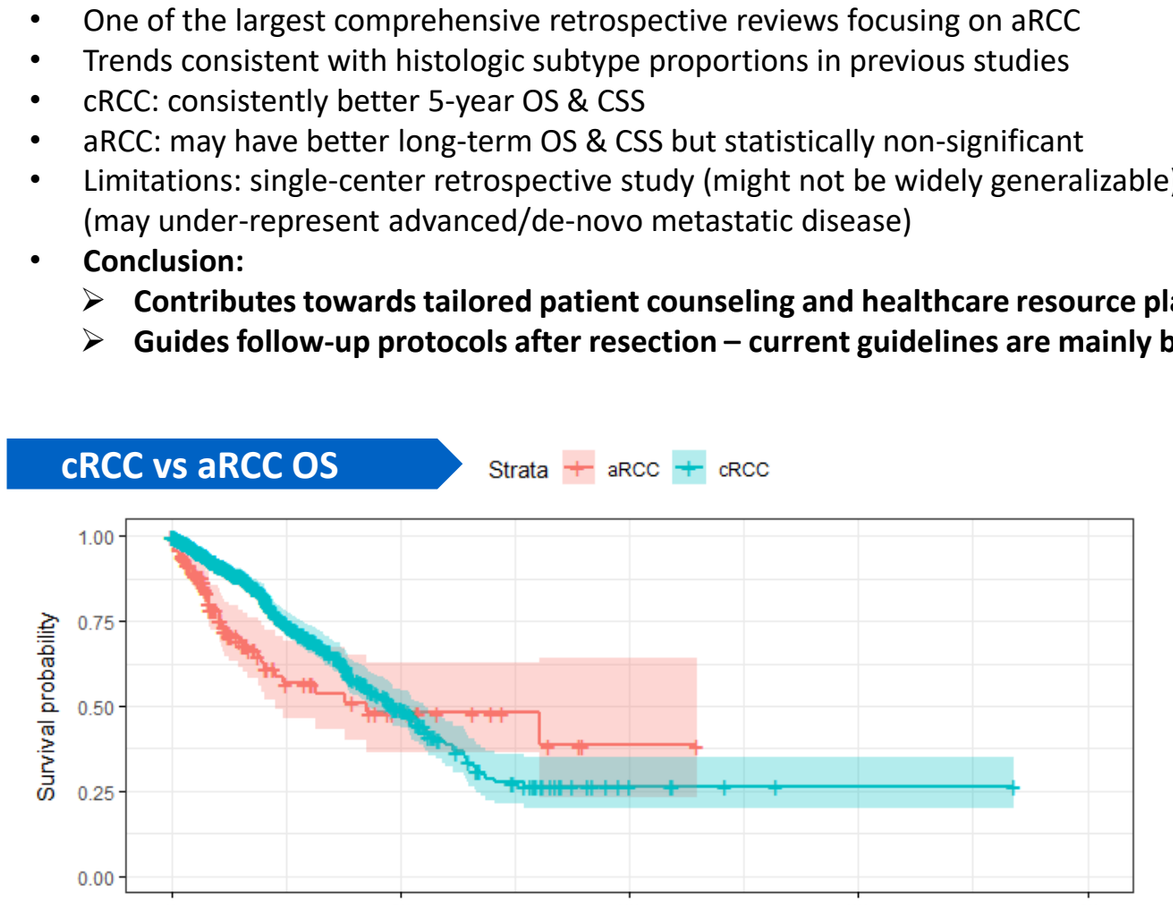
cRCC vs aRCC OS



cRCC vs aRCC CSS



Subtype OS



Subtype CSS