

Supplementary Materials: Characteristics and Outcome of Children with Renal Cell Carcinoma: A Narrative Review

Justine N. van der Beek, James I. Geller, Ronald R. de Krijger, Norbert Graf, Kathy Pritchard-Jones, Jarno Drost, Arnould C. Verschuur, Dermot Murphy, Satyajit Ray, Filippo Spreafico, Kristina Dzhuma, Annemieke S. Littooij, Barbara Selle, Godelieve A.M. Tytgat and Marry M. van den Heuvel-Eibrink

Table S1. Search strategy in Pubmed and Embase/Medline.

Pubmed
((((((("Adenocarcinoma of Kidney"[Title/Abstract]) OR "Grawitz Tumor"[Title/Abstract]) OR "Grawitz Tumour"[Title/Abstract]) OR "Collecting Duct Carcinoma"[Title/Abstract]) OR Hypernephroma*[Title/Abstract]) OR "Renal-Cell Carcinoma"[Title/Abstract]) OR "Carcinoma, Renal Cell"[Mesh])) OR (((((Carcinoma*[Title/Abstract]) OR Adenocarcinoma*[Title/Abstract]) OR Cancer*[Title/Abstract])) AND (((Renal[Title/Abstract]) OR "Renal Cell"[Title/Abstract]) OR Nephroid[Title/Abstract]) OR Hypernephroid[Title/Abstract]))
AND
((((((Children[Title/Abstract]) OR Pediatric*[Title/Abstract]) OR Paediatric*[Title/Abstract]) OR "Child"[Mesh]) OR "Child, Preschool"[Mesh]) OR "Adolescent"[Mesh]) OR "Pediatrics"[Mesh])
Embase/Medline
((((((('Adenocarcinoma of Kidney':ab,ti) OR 'Grawitz Tumor':ab,ti) OR 'Grawitz Tumour':ab,ti) OR 'Collecting Duct Carcinoma':ab,ti) OR 'Hypernephroma':ab,ti) OR 'Renal-Cell Carcinoma':ab,ti) OR 'renal cell carcinoma'/exp)) OR (((('Carcinoma':ab,ti) OR 'Adenocarcinoma':ab,ti) OR 'Cancer':ab,ti)) AND (((('Renal':ab,ti) OR 'Renal Cell':ab,ti) OR 'Nephroid':ab,ti) OR 'Hypernephroid':ab,ti)))
AND
((((((('Child':ab,ti) OR 'Children':ab,ti) OR 'Pediatric':ab,ti) OR 'Paediatric':ab,ti) OR 'child'/exp) OR 'adolescent'/exp))

* searched for singular and plural terms.

Table S2. Transparency regarding patients in the articles identified after title and abstract screening using the in- and exclusion criteria.

Author (Year)	Year(s) of Inclusion	Demographic Information (Registry and/or Country and/or City)	Included (IN)/Excluded (EX)
National Cancer Database (NCD/NCDB)			
Akhavan (2015) [1]	1998–2011	NCDB (<30 years)	EX
Rialon (2015) [2]	1998–2011	NCDB (0–17 years)	EX
AREN03B2			
Cajaiba (2018) [3]	August 2006–July 2016	AREN03B2	IN
Geller (2015) [4]	Unknown	AREN03B2	EX
United States of America			
Ambalavanan (2019) [5]	2000–2015	Cincinnati Children's Hospital and Medical Center (Cincinnati)	EX
Wang (2012) [6]	1995–2011	2 academic institutions (Atlanta / Indianapolis)	IN
Geller (2008) [7]	Unknown	Cincinnati Children's Hospital and Medical Center (Cincinnati)	IN
Silberstein (2009) [8]	1988–2004	California cancer registry	IN
Wu (2008) [9]	January 1986–June 2006	Michigan School of Medicine	IN

Estrada (2005) [10]	1965–2003	Children’s Hospital Boston (Boston)	IN
Geller (2004) [11]	1962–Unknown	St. Jude Children’s Research Hospital (Memphis)	IN
Aronson (1996) [12]	May 1956–July 1990	Memorial Sloan Kettering (New York)	IN
Dehner (1970) [13]	Unknown	Kidney tumor registry and registry of pediatric pathology of the American registry of Pathology (Washington DC)	IN
Canada			
Ramphal (2006) [14]	January 1984–December 2003	The Hospital for Sick Children (Toronto)	IN
Cook (2006) [15]	1980–2005	The Hospital for Sick Children (Toronto)	EX
Carcao (1998) [16]	1979–1996	The Hospital for Sick Children (Toronto) Montreal Children’s Hospital (Montreal) Hospital st. Justine (Montreal)	EX
Chan (1983) [17]	1958–1982	The Hospital for Sick Children (Toronto) Princess Margaret Hospital (Toronto)	IN
Europe			
Indolfi (2012) [18]	January 1973–November 2010	AIEOP	EX
Varan (2007) [19]	1972–2004	Single center study (Ankara, Turkey)	IN
Selle (2006) [20]	1980–2005	GCCR & KTR (Germany)	IN
Indolfi (2003) [21]	January 1973–January 2001	AIEOP	IN
China/South Korea			
Kim (2015) [22]	1988–2014	Dongnam Institute of Radiological & Medical Sciences Cancer center (Busan) Samsung Medical Center (Seoul) Asan Medical Center (Seoul) Seoul National University Hospital (Seoul) Seoul St. Mary’s Hospital (Seoul)	IN
Rao (2011) [23]	1989–2008	Nanjing Jinling Hospital (Nanjing) Nanjing Drum Tower Hospital (Nanjing)	IN
Baek (2010) [24]	1997–2008	Samsung Medical Center Masan Samsung Hospital (Seoul/Masan)	EX

Table S3. The Modified Robson Staging System and TNM-Staging Systems of RCC. (a) Stage grouping of the Modified Robson Staging System and the TNM-Staging Systems of RCC [25–29]; (b). TMN-Staging Systems of RCC [25–29].

a	
Modified Robson Staging System of RCC	
Stage I	Limited to the kidney
Stage II	Involvement of perinephric fat or adrenal gland, but remains limited to Gerota fascia
Stage IIIa	Renal vein or caval involvement below and above the diaphragm
Stage IIIb	Lymph node involvement
Stage IIIc	Both IIIa and IIIb: combination of venous and nodal involvement
Stage IVa	Direct invasion of adjacent organs / structures: local extension beyond Gerota fascia

Stage IVb		Distant metastases	
1997 TNM Staging System of RCC			
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1	N1	M0
	T2	N1	M0
	T3	N0, N1	M0
Stage IV	T4	N0, N1	M0
	Any T	N2	M0
	Any T	Any N	M1
2002 TNM Staging System of RCC			
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1	N1	M0
	T2	N1	M0
	T3	N0, N1	M0
Stage IV	T4	Any N	M0
	Any T	N2	M0
	Any T	Any N	M1
2010 TNM Staging System of RCC			
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1	N1	M0
	T2	N1	M0
	T3	N0, N1	M0
Stage IV	T4	Any N	M0
	Any T	Any N	M1
b			
Year	1997	2002	2010
T—primary tumour			
Tx	Cannot be assessed	Cannot be assessed	Cannot be assessed
T0	No evidence	No evidence	No evidence
T1	≤7.0 cm, limited to kidney	≤7.0 cm, limited to kidney	≤7.0 cm, limited to kidney
T1a	-	≤4.0 cm, limited to kidney	≤4.0 cm in greatest dimension, limited to kidney
T1b	-	4–7 cm, limited to kidney	4–7 cm, limited to kidney
T2	>7.0 cm, limited to kidney	>7.0 cm, limited to kidney	>7.0 cm, limited to kidney
T2a	-	-	>7.0 cm, but ≤10 cm, limited to kidney
T2b	-	-	>10cm, limited to the kidney
T3	Extends into major veins or invades adrenal gland or perinephric tissues but not beyond Gerota fascia	Extends into major veins or invades adrenal glad or perinephric fat but not beyond Gerota fascia	Extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota fascia
T3a	Invades adrenal gland or perinephric tissues, but not beyond Gerota fascia	Invades adrenal gland or perinephral and/or renal sinus fat but not beyond Gerota fascia	Grossly extends into the renal vein or its segmental (muscle containing) branches, or invades perirenal

			and/or renal sinus fat but not beyond Gerota fascia
T3b	Grossly extends into renal vein(s) or vena cava below diaphragm	Extends into renal vein or its segmental branches or infradiaphragmatic vena cava	Grossly extends into the vena cava below the diaphragm
T3c	Grossly extends into vena cava above diaphragm	Extends into superdiaphragmatic vena cava or invades wall of vena cava	Grossly extends into the vena cava above the diaphragm or invades wall of the vena cava
T4	Invades beyond Gerota fascia	Invades beyond Gerota fascia	Invades beyond Gerota fascia (including contiguous extension into the ipsilateral adrenal gland)
N-regional lymph nodes			
Nx	Cannot be assessed	Cannot be assessed	Cannot be assessed
N0	No metastasis	No metastasis	No metastasis
N1	Metastasis in single regional lymph node	Metastasis in single regional lymph node	Metastases in regional lymph node(s)
N2	Metastasis in >1 regional lymph node	Metastasis in >1 regional lymph node	-
M-Distant Metastasis			
Mx	Cannot be assessed	Cannot be assessed	Cannot be assessed
M0	Absent	Absent	Absent
M1	Present	Present	Present

Table S4. Studies based on multi-center registration and/or databases.

Author (Year)	Amount of Patients	Country	Registry	Years of Inclusion
Cajaiba (2018) [3]	208	USA	AREN03B2	August 2006–July 2016
Akhavan (2015) [1]	515	USA	NCDB	1998–2011
Geller (2015) [4]	120	USA	AREN03B2	NS, <2015
Rialon (2015) [2]	304	USA	NCDB	1998–2011
Indolfi (2012) [18]	14	Italy	AIEOP	January 1973–November 2010
Silberstein (2009) [8]	43	USA	California Cancer Registry	1988–2004
Selle (2006) [20]	49	Germany	GCCR & KTR	1980–2005
Indolfi (2003) [21]	41	Italy	AIEOP	January 1973–January 2001
Dehner (1970) [13]	14	USA	American registry of pathology	NS, <1970

The other studies were mainly single-center studies. USA = United States of America; AREN03B2 = The Children's Oncology Group (COG) renal tumor study; NCDB = National Cancer Database; AIEOP = Italian Association for Pediatric Hematology and Oncology; GCCR = German Childhood Cancer Registry; KTR = Kiel Paediatric Tumour Registry.

Table S5. Available included studies with information about survival according to tumor stage.

Author (Year)	Nr. ^r	Number of Patients	Staging System	Stage I		Stage II		Stage III		Stage IV	
				Nr. of Patients	Survival % (Range)	Nr. of Patients	Survival % (Range)	Nr. of Patients	Survival % (Range)	Nr. of Patients	Survival % (Range)
Silberstein (2009) [8]	5	43	TNM	23	88.5% (SE7.7%)		9	58.1% (SE 18.9%)	11	9.1% (SE 8.0%)	
Selle (2006) [20]	9	49	TNM	28	EFS: 96.4%		8 (N1/2+M0) 4 (M1)		EFS: 68.8% EFS: 25.0%		
Indolfi (2003) [21]	13	41	Modified Robson	19	20yEFS: 88.9% (95%CI 163–100%) 20yOS: 88.9% (95%CI 163–100%)		21	20yEFS: 18% (95%CI 10–36%) <i>p</i> = 0.0001 20yOS: 22.6% (95%CI 12–43%) <i>p</i> = 0.0001			
Geller (2004) [11] Systematic review	12	-	Modified Robson	243	92%	26	85%	66	73%	72	14%

^r Article number referring to Table 1. 95%CI = 95% confidence interval; 1yS = one-year survival; 5yS = five-year survival; SE = standard error; EFS = event-free survival; OS = overall survival; y = year; m = month; NS = not specified

Table S6. Genes and syndromes associated with RCC [9,20,23,30–33].

Genes	Associated Syndromes
VHL	Von Hippel-Lindau syndrome
TSC1	Tuberous sclerosis
TSC2	
TP53	Li-Fraumeni syndrome
FLCN	Birt-Hogg-Dubé syndrome
FH	Hereditary leiomyomatosis and renal cell cancer
PTEN	PTEN Hamartoma Tumor Syndrome / Cowden syndrome
SDHA	Hereditary paraganglioma-pheochromocytoma syndromes
SDHB	
SDHC	
SDHD	
TMEM127	
MLH1	Lynch syndrome
MSH2	
MSH6	
PMS2	
EPCAM	
BAP1	-
MET	Hereditary papillary renal cancer
CDKN2B	-

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