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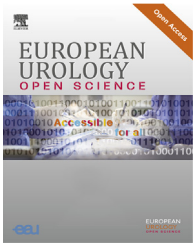

European Association of Urology

Review – Urothelial Cancer

Navigating the Aftermath: A Comprehensive Scoping Review on Follow-up Strategies After Kidney-sparing Surgery for Upper Tract Urothelial Carcinoma

Hugo W. Schuil [a,b,c,*], *Orlane J.A. Figaroa* [a,c,d], *Nora Hendriks* [a,b,c], *Barbara M.A. Schout* [b], *Harrie P. Beerlage* [a,c], *Faridi S. van Jamaludin* [e], *Michaël M.E.L. Henderickx* [a,c], *R. Jeroen A. van Moorselaar* [c,f], *Guido M. Kamphuis* [a,c], *Joyce Baard* [a,c]

[a] *Department of Urology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands;* [b] *Department of Urology, Alrijne Hospital, Leiderdorp, The Netherlands;* [c] *Cancer Center Amsterdam, Amsterdam UMC, Amsterdam, The Netherlands;* [d] *Department of Medical Oncology, Amsterdam UMC, Amsterdam, The Netherlands;* [e] *Medical Library AMC, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands;* [f] *Department of Urology, Amsterdam UMC, Vrije Universiteit, Amsterdam, The Netherlands*

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Abstract

Background and objective: Upper tract urothelial carcinoma (UTUC) can be managed efficiently and safely through kidney-sparing surgery (KSS) in selected patient groups. However, the most effective and efficient postoperative surveillance strategy remains undetermined. We aimed to provide a comprehensive synopsis of the follow-up strategies and survival outcomes in patients diagnosed with UTUC treated by KSS.
Methods: Following the systematic methodology outlined in the Preferred Reporting Items for Systematic Reviews and Meta-analyses Extension for Scoping Reviews, we conducted searches in four databases (MEDLINE [Ovid], Embase [Ovid], Cochrane Library, and Web of Science) up until December 11, 2023.
Key findings and limitations: A total of 3121 articles underwent screening, of which 19 were selected for inclusion in this review. The follow-up schedules after KSS exhibited considerable variability among the included studies. Diagnostic modalities employed consisted of computed tomography urography (present in 84% of protocols), X urography (21%), ultrasound (21%), thoracic imaging (26%), voided urine cytology (89%), selective upper tract cytology (5.3%), cystoscopy (84%), and ureterorenoscopy (53%) at varying frequencies. At 5 yr of follow-up, the reported recurrence-free survival rate ranged from 30% to 86%, overall survival was 50–92%, and metastasis-free survival was 77–90%.
Conclusions and clinical implications: This review unveils significant heterogeneity in clinical practices and survival outcomes, indicating disparities between real-world approaches and guideline recommendations. The lack of consensus on follow-up schemes is evident, emphasising the necessity for future initiatives aimed at developing a comprehensive protocol.

* Corresponding author. Department of Urology, Amsterdam UMC location, location VUmc, De Boelelaan 1117, 1081HV Amsterdam, The Netherlands. Tel. +31 20 444 02 61, +31 6 46 43 48 02; Fax: +31 20 444 6031.
E-mail address: H.W.Schuil@amsterdamumc.nl (H.W. Schuil).

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Patient summary: This review shows significant heterogeneity in follow-up strategies after kidney-sparing surgery for upper tract urothelial carcinoma. A lack of evidence contributes to discrepancies between guidelines and real-world approaches. Thus, future endeavours should aim at establishing a comprehensive protocol.

1. Introduction

Upper tract urothelial carcinoma (UTUC) is a rare condition and affects approximately two per 100 000 persons in Western countries [1]. Management of UTUC with kidney-sparing surgery (KSS) can consist of segmental ureteral resection (SUR), ureterorenoscopy (URS), or percutaneous tumour resection (PCTR) and shows similar survival rates to radical nephroureterectomy (RNU) in patients with low-risk disease. While these methods aim to conserve renal units, they pose increased risk of disease recurrence [2–7]. The European Association of Urology (EAU) and the American Urological Association (AUA) guidelines advocate for KSS as the primary approach for managing low-risk disease. This recommendation extends to patients with high-risk disease, with solitary kidneys or with impaired renal function, aiming to prevent the necessity of dialysis [8,9].

Owing to the risk of disease recurrence after KSS in both the affected upper tract and the bladder, a stringent and frequent follow-up schedule is recommended. According to current EAU guidelines, the follow-up for low-risk disease includes URS within 3 mo, followed by cystoscopy and computed tomography (CT)-urography at 3 and 6 mo, and subsequently each year for 5 yr. High-risk tumours necessitate additional URS and in situ cytology at 3 and 6 mo [8]. Notably, the AUA guideline recommends a more comprehensive scheme for endoscopy, advising URS within 3 mo, and at 6 and 12 mo [9]. A summary of the current recommendations can be found in Table 1. The guidelines assign a low level of evidence to these follow-up recommendations, as there is limited knowledge regarding the optimal methods for monitoring these patients. The rarity of UTUC renders conducting large prospective trials on the topic impractical. Consequently, the existing guidelines rely on evidence derived mainly from compiled retrospective case series and cohort studies.

In this study, our objective is to examine the current follow-up schedules after KSS. To achieve this, we have conducted a comprehensive scoping review of the existing literature to establish the extent and nature of available evidence regarding follow-up practices and survival outcomes. Owing to the heterogeneous nature of evidence, our study's objective is not to compare experimental and control groups, rendering a systematic review less applicable. Instead, our emphasis lies in mapping and reporting past and current practices, thus making a scoping review the more suitable approach [10,11].

2. Methods

2.1. Protocol

The research protocol was drafted by the research team in accordance with the Preferred Reporting Items for Systematic Review and Meta-analyses Protocols (PRISMA-P) and is provided in the Supplementary material [12].

2.2. Eligibility criteria

We included papers on original patient data providing detailed information on follow-up strategies and survival outcomes following KSS for UTUC by URS, PCTR, or SUR. A clear description of the diagnostic modalities used during follow-up, along with the frequency of their utilisation, needed to be outlined. Additionally, censored data on recurrence, progression, or survival expressed over a defined time period should have been available. We selected data from peer-reviewed journal papers, published in English, with no restriction of publication year.

Papers were excluded if they involved studies with fewer than ten patients or specifically addressed atypical patient groups, such as studies exclusively focussing on patients

Table 1 – Guidelines on follow-up strategies

Reference	Low-risk tumours			High-risk tumours			
	CT-urography	Cystoscopy	URS	CT-urography	Cystoscopy	URS	Selective upper tract cytology
EAU guideline 2023 [8]	At 3 and 6 mo, then yearly Strength rating: weak	At 3 and 6 mo, then yearly Strength rating: weak	At 6 wk or 3 mo Strength rating: weak	At 3 and 6 mo, then yearly Strength rating: weak	At 3 and 6 mo, then yearly Strength rating: weak	At 3 and 6 mo Strength rating: weak	At 3 and 6 mo Strength rating: weak
AUA guideline 2023 [9]	At 6–9 mo for 2 yr, then annually Expert opinion	At 1–3 mo, then 6–9 mo for 2 yr, and then annually Expert opinion	At 1–3 mo, 6 mo, and 1 yr Expert opinion	At 1–3 mo, then 3–6 mo for 3 yr, then annually Expert opinion	At 1–3 mo, then 3–6 mo for 3 yr, then annually Expert opinion	At 1–3 mo, 6 mo, and 1 yr Expert opinion	Once within 1–3 mo Expert opinion

AUA = American Urological Association; CT = computed tomography; EAU = European Association of Urology; URS = ureterorenoscopy.

with imperative indications for KSS or metastasised disease, or cohorts where additional treatments such as upper tract chemotherapeutic instillations were evaluated. Additionally, studies that did not present distinct information for patients who were managed primarily with KSS separately from patients who underwent RNU as initial treatment were also excluded.

2.3. Information sources

Following the systematic methodology outlined in the Preferred Reporting Items for Systematic Reviews and Meta-analyses Extension for Scoping Reviews (PRISMA-ScR), an extensive literature search was conducted on December 11, 2023, to identify relevant publications [11]. The search encompassed four major medical databases—MEDLINE (Ovid), Embase (Ovid), Cochrane Library, and Web of Science, and was enrolled by an experienced medical librarian (F.J.). The results were exported into EndNote, and duplicates were removed. The literature search was completed by searching the reference lists of the included studies for potentially relevant studies.

We employed a combination of search terms, including "kidney-sparing surgery" and its synonyms, as well as "UTUC" and its synonyms. The detailed search query for MEDLINE (Ovid) is presented in Supplementary Table 1.

2.4. Selection of sources of evidence

Two reviewers (O.F. and H.S.) independently screened all titles and abstracts using the Rayyan screening tool, adhering to the criteria outlined in the screening protocol to retrieve relevant articles [13]. Following this, full-text versions of relevant articles were evaluated for final inclusion in the study. Any discrepancies in the decision to include an article were resolved through discussion between the two reviewers. In cases where consensus could not be reached, a third reviewer (J.B.) was consulted to make a final decision.

2.5. Data charting process and data items

A data charting form in Microsoft Excel (version 2302; Microsoft Corp, Redmond, WA, USA) was constructed, which was revised repeatedly in collaboration with the study team as data items were encountered and discussed during the examination of the included studies. We abstracted data on patient characteristics (sex and age), tumour characteristics (grade, T stage, size, focality, and hydronephrosis), type of KSS (URS, PCTR, or SUR), frequency and type of diagnostics (imaging, endoscopy, and cytology), length of follow-up, and survival outcomes (survival, recurrences, and progression).

We refrained from attempting to interpret survival outcomes from Kaplan-Meier survival curves when no specific time period for censored survival data was reported. When outcomes were presented based on subgroups (eg, low- and high-grade subgroups), we consistently followed this reporting approach in our documentation. Moreover, we did not differentiate between studies reporting mean or median values for variables, as both were employed as descriptive statistics across the articles included in our analysis.

The abstracted data from the data-charting form are presented in three tables, displaying the patient and tumour characteristics, follow-up strategies, and survival outcomes (Tables 2–4). The included studies were ordered by their publication year, to visualise possible changes over time.

3. Results

3.1. Selection of sources of evidence

The outcomes of the search strategy and the selection process are visualised in the PRISMA flow chart (Fig. 1). After removing duplicates, 3121 titles and abstracts were screened for eligibility, of which we reviewed the full text of 224 papers. Absence of a clear description of the follow-up protocol and a lack of survival data over a specific time period were the main reasons for subsequent exclusion (106/224, 47%). A total of 19 papers matched our criteria and were included in this review [14–32].

3.2. Characteristics of sources of evidence

Included studies (n = 19) were published between 2001 and 2023, and were either case series or cohort studies. All studies had a retrospective design; only Yoshida et al [30] and Baboudjian et al [32] collected their patient data prospectively. Most papers originated from single-centre studies. Three studies included patients from two medical centres [15,17,19], one study encompassed data from five hospitals [20], and one collected data from a European multi-institutional collaborative database containing data of 34 European centres [22].

Study groups occasionally published updates on articles concerning a selection of the same patient group at different time intervals, resulting in partial overlap. Moreover, study groups occasionally published updates on patients from their medical centres at different time intervals or with varied patient selections. Consequently, among the studies included in this review, there appears to be some overlap in the patient descriptions between the two studies by Rouprêt et al [15,17] and between the studies of Thompson et al [18] and Elliot et al [14].

The results of the individual sources of evidence are presented in Table 2 (patient, tumour, and treatment characteristics), Table 3 (follow-up strategies), and Table 4 (survival outcomes).

3.3. Synthesis of results

3.3.1. Patient, tumour, and treatment characteristics

Table 2 presents a comprehensive overview of the patient and tumour characteristics. The included studies contain cohorts ranging from 12 to 176 patients, predominantly male, with a reported mean or median age spanning from 64 to 75 yr. Reported tumour grading system varied between the use of either the 1973 World Health Organization (WHO) grading system (7/19, 37%) in studies published between 2001 and 2020, or the 2004/2016 WHO grading system (12/19, 63%) in studies published between 2006 and 2023 [33,34].

Table 2 – Patient, tumour, and treatment characteristics

Reference	No. of KSS patients	Male (%)	Age (yr)	Low grade, n (%)	High grade, n (%)	G1, n (%)	G2, n (%)	G3, n (%)	G missing, n (%)	Ta, n (%)	T1, n (%)	>T1, n (%)	Tis, n (%)	T missing, n (%)	Tumour size, mm (range or SD)	Unifocal, n (%)	Multifocal, n (%)	Hydronephrosis, n (%)	URS, n (%)	PCTR, n (%)	SUR, n (%)
Elliott (2001) [14]	21	76	69			4 (19)	5 (24)	2 (9.5)	10 (48)	8 (38)	4 (19)			9 (43)	4-20	NR	NR	NR	21 (100)		
Rouprêt (2006) [15]	43	69	68	30 (70)	13 (30)					22 (51)	11 (26)	7 (16)	3 (7.0)		URS 14 (2–26) PCTR 19 (3–33)	NR	NR	NR	27 (63)	16 (37)	
Giannarini (2007) [16]	19	NR	69			1 (5.3)	13 (68)	5 (26)		13 (68)	0	6 (32)			20 (5–25)	NR	NR	NR			19 (100)
Rouprêt (2007) [17]	24	63	71	17 (71)	7 (29)					10 (42)	8 (33)	4 (17)	2 (8.3)		18 (8–29)	22 (92)	2 (8.3)	NR		24 (100)	
Thompson (2008) [18]	22	50	64			15 (68)	7 (32)			22 (100)					10 (3–26)	NR	NR	NR	22 (100)		
Tada (2010) [19]	15	67	75			10 (67)	2 (13)	3 (20)		13 (87)	2 (13)				25 (11–55)	12 (80)	3 (20)	NR	15 (100)		
Simonato (2012) [20]	73	85	69			15 (21)	28 (38)	30 (41)		31 (43)	23 (32)	19 (26)			18 (5–23)	NR	NR	34 (47)			73 (100)
Seisen (2016) [22]	176	76	69	100 (57)	76 (43)					NR	NR	NR	NR		URS 11 (4–27) SUR 13 (6–34)	NR	NR	99 (56)	42 (24)		134 (76)
Villa (2015) [21]	41	63	74	16 (39)	8 (20)				17 (42)	23 (56)	1 (2.4)			17 (42)	13.2 (8.5)	36 (88)	3 (12)	NR	41 (100)		
Lee (2017) [23]	19	68	69	3 (16)	13 (68)				3 (16)	3 (16)	2 (11)	12 (63)	1 (5.3)	1 (5.3)	NR	NR	NR	NR			19 (100)
Kato (2018) [25]	12	64	74	6 (50)	6 (50)					4 (33)	1 (8.3)	6 (50)	1 (8.3)		21 (9.7)	12 (100)	0	NR			12 (100)
Jia (2018) [24]	40	43	70			0 (0)	23 (58)	17 (43)		0	18 (45)	22 (55)			34 (21)	NR	NR	NR			40 (100)
Hsieh (2020) [26]	34	29	71	9 (26)	25 (74)					9 (26)	23 (68)		2 (5.9)		<20, *N* = 20 >20, *N* = 14	NR	NR	NR	34 (100)		
Scotland (2020) [27]	168	64	70			42 (25)	98 (58)	28 (17)		NR	NR	NR	NR		17 (1–60)	NR	NR	NR	168 (100)		
Yoshida (2021) [30]	10	70	77	6 (60)	4 (40)					9 (90)	1 (10)				24 (13–30)	9 (90)	1 (10)	NR	10 (100)		
Shenhar (2022) [28]	24	72	71	24 (100)						23 (96)					13 (4.8)	13 (54)	11 (46)	NR	24 (100)		
Lindner (2023) [29]	14	71	72	6 (43)	8 (57)					6 (43)	2 (14)	4 (29)	2 (14)		NR	NR		NR	NR	0	NR
Figaroa (2023) [31]	71	80	68	58 (81)	13 (19)					71 (100)					<20, *N* = 39 >20, *N* = 32	58 (82)	13 (18)	NR	71 (100)		
Baboudjian (2023) [32]	60	83	74	30 (50)	18 (30)				12 (20)	NR	NR	NR	3 (5.0)		<20, *N* = 26 ≥20, *N* = 26 NR, *N* = 8	37 (62)	23 (8)	18 (30)	60 (100)		

G = grade; KSS = kidney-sparing surgery; NR = not reported; PCTR = percutaneous tumour resection; SD = standard deviation; SUR = segmental ureteral resection; URS = ureterorenoscopic tumour ablation.

Table 3 – Follow-up strategies

Reference	Abdominal imaging			Chest imaging		Cytology		Endoscopy	
	CT urography	X urography	Ultrasound	CT thorax	X thorax	Bladder	Selective upper tract	Cystoscopy	URS
Elliott (2001) [14]		Y1-Y2: 3–4 mo Y3+: 6 mo				Y1-Y2: 3–4 mo Y3+: 6 mo		Y1-Y2: 3–4 mo Y3+: 6 mo	
Rouprêt (2006) [15]	Y1: 6 mo Y2+: 12 mo					Y1: 6 mo Y2+: 12 mo		Y1-Y3: 6 mo Y4+: 12 mo	Y1-Y3: 6 mo Y4+: 12 mo
Giannarini (2007) [16]	Y1+: 12 mo (if stage ≥pT2)	Y1: 12 mo		Y1+: 12 mo (if stage ≥pT2)		Y1: 6 mo Y2+: 12 mo			
Rouprêt (2007) [17]	Y1-Y3: 6 mo Y4+: 12 mo					Y1-Y3: 6 mo Y4+: 12 mo		Y1-Y3: 6 mo Y4+: 12 mo	Y1-Y3: 6 mo Y4+: 12 mo
Thompson (2008) [18]	Y1-Y2: 3–4 mo Y3+: 6 mo "UT imaging" [a]					Y1-Y2: 3–4 mo Y3+: 6 mo		Y1-Y2: 3–4 mo Y3+: 6 mo	
Tada (2010) [19]	Y1+: 6–12 mo	Y1+: 6–12 mo				Y1+: 3 mo		Y1+: 3 mo	Y1: 6–12 mo Y2+: 12 mo
Simonato (2012) [20]	Y1+: 12 mo		Y1-Y3: 3 mo Y4+: 12 mo			Y1-Y3: 3 mo Y4+: 12 mo			
Seisen (2016) [22]	Y1: 3 mo, 6 mo Y2-Y5: 6 mo Y6+: 12 mo			Y1: 3 mo, 6 mo Y2-Y5: 6 mo Y6+: 12 mo		Y1: 3 mo, 6 mo Y2-Y5: 6 mo Y6+: 12 mo		Y1: 3 mo, 6 mo Y2-Y5: 6 mo Y6+: 12 mo	
Villa (2015) [21]	Y1: 3 mo, 6 mo Y2+: 12 mo					Y1: 3 mo, 6 mo Y2+: 12 mo	Y1: 3 mo, 6 mo Y2-Y3: 6 mo Y4+: 12 mo	Y1: 6 wk, 3 mo, 6 mo Y2-Y3: 6 mo Y4+: 12 mo	Y1: 6 wk, 3 mo, 6 mo Y2-Y3: 6 mo Y4+: 12 mo
Lee (2017) [23]			Y1-Y2: 3 mo Y3+: 12 mo			Y1-Y2: 3 mo Y3+: 12 mo			
Kato (2018) [25]	Y1+: 12 mo		Y1-Y5 6 mo Y6+: 12 mo	Y1+: 12 mo		Y1-Y5: 3 mo Y6+: 6 mo		Y1-Y5: 3 mo Y6+: 6 mo	
Jia (2018) [24]	Y1-Y2: 3 mo Y3-Y5: 6 mo Y6+: 12 mo [a]		Y1-Y2: 3 mo Y3-Y5: 6 mo Y6+: 12 mo [a]		Y1-Y2: 3 mo Y3-Y5: 6 mo Y6+: 12 mo	Y1-Y2: 3 mo Y3-Y5: 6 mo Y6+: 12 mo		Y1-Y2: 3 mo Y3-Y5: 6 mo Y6+: 12 mo	
Hsieh (2020) [26]	Y1-Y2: 6 mo Y3-Y5: 12 mo Or MRI	Y1-Y5: 3 mo or URS				Y1-Y5: 3 mo		Y1-Y5: 3 mo	Y1-Y5: 3 mo or x-ray
Scotland (2020) [27]								Y1: 6 wk, 3 mo, 6 mo Y2-Y5: 6 mo Y6+: 12 mo	Y1: 6 wk, 3 mo, 6 mo Y2-Y5: 6 mo Y6+: 12 mo
Yoshida (2021) [30]	Y1+: 4 wk, 3 mo					Y1+: 3 mo		Y1+: 3 mo	Y1+: 6 mo
Shenhar (2022) [28]	Y1-Y2: 6 mo Y3+: 12 mo					Y1: 3 mo once		Y1-Y2: 3 mo, 6 mo Y3+: 12 mo	Y1-Y2: 6 mo Y3+: 12 mo
Lindner (2023) [29]	Y1-Y2: 3 mo Y3-Y5: 6 mo Y6+: 12 mo			Y1-Y2: 3 mo Y3-Y5: 6 mo Y6+: 12 mo		Y1: 3 mo Y2-Y5: 6 mo Y6+: 12 mo		Y1: 3 mo Y2-Y5: 6 mo Y6+: 12 mo	Y1: 3 mo Y2-Y5: 6 mo Y6+: 12 mo
Figaroa (2023) [31]	Y1: 6 mo Y2+: 12 mo							Y1: 6w, 3 mo Y2-Y3: 6 mo Y4+ 12 mo	Y1: 6w, 3 mo Y2-Y3: 6 mo Y4+ 12 mo
Baboudjian (2023) [32]	Y1+: 6 mo					Y1+: 6 mo		Y1+: 6 mo	

CT = computed tomography; MRI = magnetic resonance imaging; URS = ureterorenoscopy; UT = upper tract; Y = year.
Follow-up strategies presented as intervals during that year of postoperative follow-up, for example, "Y1–Y2: 6 mo, Y3+: 12 mo" means "performed semiannually during the first 2 yr of follow-up and then continued annually".
[a] Type of upper tract imaging was not specified in the study.

Table 4 – Survival outcomes

Reference		FU (mo)	Recurrences														Survival										Progression									
			Overall RFS (%)				IV-RFS (%)				UT-RFS (%)				OS (%)					CSS (%)					PFS (%)			RNU-FS (%)				MFS (%)			
			1 yr	2 yr	3 yr	5 yr	1 yr	2 yr	3 yr	5 yr	1 yr	2 yr	3 yr	5 yr	1 yr	3 yr	5 yr	10 yr		1 yr	2 yr	3 yr	5 yr	10 yr	1 yr	2 yr	5 yr	1 yr	2 yr	3 yr	5 yr	1 yr	2 yr	3 yr	5 yr
Elliott (2001) [14]		73															66						100	70											
Rouprêt (2006) [15]	URS	52				72																	71												
	PCTR	58				72																	80												
Giannarini (2007) [16]		50															52	43					64	64											
Rouprêt (2007) [17]		62				68																	80												
Thompson (2008) [18]		59			35		76		59	46	53		48	48						95		90	90												
Tada (2010) [19]		25					80	60	60		80	60	60									100													
Simonato (2012) [20]		87								82							85						89	77											
Seisen (2016) [22]	URS	29				36				59							75						83												
	SUR	31				86				53							80						88												
Villa (2015) [21]		28																							81										
Lee (2017) [23]		28				68											74																		
Kato (2018) [25]		49				34											78						88												81
Jia (2018) [24]		64								46				86, 93 [a]																					90
Hsieh (2020) [26]	LG	25						100				89									100											100			
	HG							63				39									87											86			
Scotland (2020) [27]		66				30											81						93				75								
Yoshida (2021) [30]		NR		57																						100									
Shenhar (2022) [28]		60															85													83					81
Lindner (2023) [29]		100	85	77		36									92		92			92	92		92								85	77		77
Figaroa (2023) [31]	All	50						86			50	22					82						86		96	85	79	86	80		67				84
	LG										44	29																84	67		57				
	HG											35																							
Baboudjian (2023) [32]		36					87		80	69	83		70	56	94	75	57			98		95	75					87		84	81	98		94	86

CSS = cancer-specific survival rate; FU = follow-up; HG = high grade; IV = intravesical; LG = low grade; MFS = metastasis-free survival rate; NR = not reported; OS = overall survival rate; PCTR = percutaneous tumour resection; PFS = progression-free survival rate; RFS = recurrence-free survival rate; RNU-FS = radical nephroureterectomy-free survival rate; SUR = segmental ureteral resection; URS = ureterorenoscopic tumour ablation; UT = upper tract.

[a] Ipsilateral, contralateral.

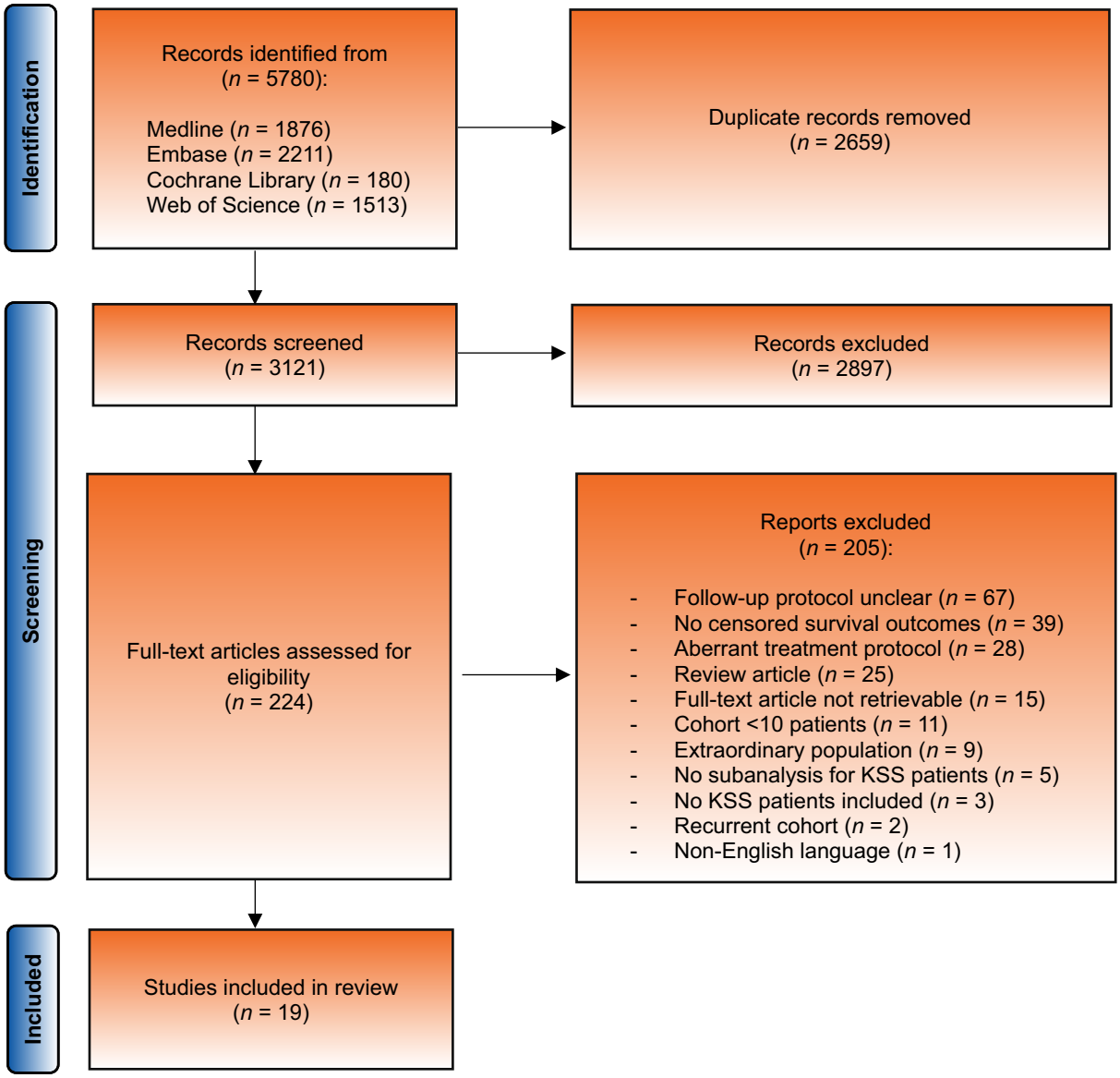

Fig. 1 – Literature search and study selection process according to the PRISMA statement criteria. KSS = kidney-sparing surgery; PRISMA = Preferred Reporting Items for Systematic Review and Meta-analyses.

The initial presurgical diagnostics were described in most studies, except two [18,28], and consisted of a combination of abdominal imaging (X-urography, 9/19, 47% [14,15,17,19,21,23,24,26,27,30]; CT urography, 16/19, 84% [15–17,19–27,29–32]; and/or magnetic resonance imaging, 5/19, 26% [22–26]), voided urine cytology (11/19, 58%) [14–17,21,22,24,26,30,31], upper tract urine cytology (3/19, 16%) [16,18,25], and cystoscopy (13/19, 68%) [15–17,19–21,24,26–28,30–32]. Diagnostic URS with endoscopic biopsy was performed in nine of the included studies (47%) [19,21,26–32]. No studies described diagnostic URS without biopsy.

The studies were heterogeneous regarding the characteristics of the tumours included. For example, Shenhar et al [28] exclusively involved patients with small (mean size 13 mm), low-grade tumours at Ta stage. In contrast, the cohort reported by Jia et al [24] comprised solely G2 and G3 tumours, with an average size of 34 mm and at least T1 stage.

The prognostic factors essential for risk stratification as outlined in the EAU guidelines were not reported completely in all the included studies: focality (8/19, 42%), tumour size (17/19, 89%), grade (19/19, 100%), local invasion (16/19, 84%), hydronephrosis (3/19, 16%), previous radical cystectomy for high-grade bladder cancer (7/19, 37%) [16,19,20,25,28,29,31], and histological subtype (2/19, 11%) [8,23,32].

The techniques applied for KSS were predominantly URS (13/19, 68%) and SUR (7/19, 37%). Two studies detailed PCTR (11%). Shenhar et al [28] described the use of both URS and SUR, but not the proportion in which these modalities were used. Cohorts focussing on adjuvant treatment as part of the treatment protocol (eg, upper tract instillations) were excluded. However, incidental upper tract instillation usage was applied in a small number of patients ($n = 2$ and $n = 3$) in two included studies [15,17].

3.3.2. Follow-up protocols

Absence of complete descriptions regarding follow-up protocols was the reason for exclusion in this review in 30% of the evaluated full-text articles (67/224; Fig. 1).

Table 3 presents the follow-up strategies described in the included studies. The follow-up schedules primarily comprised a mix of abdominal and thoracic imaging, endoscopic examinations, and cytology.

3.3.2.1. Imaging. A transition occurred from the sole use of X-urography (1/19, 5.3%) or ultrasound (1/19, 5.3%) seen in earlier publications to the current use of multiphase CT scans in recent studies (16/19, 84%). The first use of CT imaging during follow-up is at 3 mo (6/16, 38%), 6 mo (7/16, 44%), or 1 yr (3/16, 19%). Subsequently, intervals for CT scans are gradually prolonged to eventually be performed quarterly (1/16, 6.3%), semiannually (2/16, 13%), or annually (13/16, 81%).

Thoracic imaging is performed rarely during follow-up. Of the five studies (26%) that described its use, CT scans were the modality of choice, with the study of Jia et al [24] being the only study applying thoracic x-ray imaging.

In one study, by Giannarini et al [16], the follow-up strategy is determined based on tumour characteristics, with the application of only abdominal and thoracic CT for patients with a ≥pT2 tumour. Another study, by Scotland et al [27], did not detail the use of imaging in their follow-up strategy.

3.3.2.2. Cytology. Cytology was used in nearly all follow-up protocols (17/19, 89%), starting its use at either 3 mo (13/17, 76%) or 6 mo (4/17, 24%) after surgery and then broadening its interval to a frequency of every 3 mo (3/17, 18%), 6 mo (4/17, 24%), or 12 mo (9/17, 53%). Shenhar et al [28] described cytology as a one-time examination at 3 mo. Selective cytology was used only during follow up by Villa et al [21].

3.3.2.3. Endoscopy. Addressing the risk of intravesical recurrences, cystoscopy was integrated into the protocols of 16 out of the 19 included studies (84%). Cystoscopy during follow-up started at 6 wk (3/16, 19%), 3 mo (10/16, 63%), or 6 mo (3/16, 19%), Then, intervals for cystoscopies are gradually prolonged to eventually be performed every 3 mo (3/16, 19%), semiannually (4/16, 25%), or annually (9/16, 56%).

About half of the regimens (10/19) involved URS for monitoring upper tract recurrences. A "second-look" URS at 6 wk was performed in three of these studies (30%); otherwise, endoscopic upper tract surveillance was started at 3 mo (2/10, 20%) or after a half year (5/10, 50%). Followed by a period of quarterly (1/10, 10%), semiannual (8/10, 80%), or annual (1/10, 10%) URS, the strategies then conclude with an on-going semiannual (1/10, 10%) or annual (8/10, 80%) scheme for endoscopy.

3.3.3. Duration of follow-up

The majority of studies (18/19, 95%) did not specify defined endpoints for concluding follow-up in their protocols. The study by Hsieh et al [26] is an exception, mentioning the conclusion of follow-up after 5 yr without providing additional details.

3.3.4. Survival outcomes

The survival outcomes following KSS varied in terms of reported outcomes across the included studies, as shown in Table 4. The majority of the papers provided censored survival data spanning a 5-yr period (14/19, 74%).

Out of the 19 included studies, 15 reported upper tract and/or intravesical recurrence rates (79%). The overall recurrence-free survival (RFS) rates for urothelial cell carcinomas ranged from 30% to 86% at the 5-yr mark. Four studies (21%) presented separate RFS figures for intravesical and upper tract cases.

Overall (OS) and cancer-specific (CSS) survival rates were reported in 16 studies (84%). The 5-yr OS rates ranged from 52% to 92%, while the 5-yr CSS rates ranged between 64% and 100%. The lowest 5-yr survival rates were reported by Giannarini et al (OS 52% and CSS 64%) [16] and Baboudjian et al (OS 75%, CSS 75%) [32]. Both cohorts comprised a significant percentage of cases with high-risk disease. Giannarini et al [16] observed no deaths related to pTa or pT1 tumours in their cohort. Baboudjian et al [32] described a cohort composed exclusively of high-risk disease cases.

Disease progression was expressed by progression-free survival (PFS), RNU-free survival (RNU-FS), or metastasis-free survival (MFS) rates. At the 5-yr follow-up, PFS was 75–79%, RNU-FS was 57–83%, and MFS ranged from 77% to 90% across the six studies (32%) using this outcome measure.

Disease progression was expressed by PFS rates in 21% of studies, RNU-FS rates in 21% of studies, or MFS rates in 37% of studies. At the 5-yr follow-up, PFS was 75–79%, RNU-FS was 57–83%, and MFS ranged from 77% to 90%.

4. Discussion

4.1. Summary of evidence

In this scoping review, our aim is to present a comprehensive overview of the existing follow-up strategies and survival outcomes in published patient cohorts that underwent KSS for UTUC. Owing to the recurrent nature of UTUC, post-treatment surveillance requires adequate attention [6]. Despite this, a notable portion of studies had to be excluded from this review due to insufficient detail regarding patient monitoring after surgery. Ultimately, we identified 19 eligible studies spanning from 2001 to 2023, and identified and mapped the methods used for patient monitoring and evaluated their associated survival outcomes.

The patient and tumour characteristics varied considerably, with both low- and high-risk tumours included in the selected cohort studies for this review. With the exception of the study conducted by Giannarini et al [16], the follow-up procedures were not altered or impacted by tumour characteristics in the included studies.

Protocols used in the included studies for follow-up were evidently different, with hardly any two cohort studies employing identical diagnostics at corresponding intervals. Current EAU guidelines recommend CT urography and cys-

toscopy at 3 and 6 mo and then yearly for 5 yr, and AUA guidelines recommend cystoscopy and upper tract imaging at 6–9 mo for 2 yr and then yearly. These recommendations were largely followed by most of the included studies. This adherence highlights a degree of consistency between the practices in treatment centres and the guidelines recommended by the EAU and AUA on the use of cytology and imaging [8,9].

However, this consistency is not seen with the use of cytology and ureteroscopy in follow-up. The existing guidelines recommend cytology solely for the follow-up of treated high-risk tumours, with an emphasis by the EAU on obtaining urine from the upper tract [8,9]. Surprisingly, cytology of voided urine emerged as the most frequently used test across all included studies. This inconsistency underscores the ambiguity surrounding the role of cytology in follow-up, supported by recent studies indicating its limited reliability as a diagnostic tool for UTUC [35–38].

It should be noted that some of the studies were published before the establishment of the EAU and AUA guidelines. However, differences are apparent not only between more historic cohorts and recent publications, but also between contemporary studies.

Furthermore, regarding URS, recommendations have changed over the last decade. The first EAU guideline on UTUC, published in 2011, recommended to perform URS at 3 and 6 mo after KSS, then every 6 mo over 2 yr and then yearly for at least 5 yr [39]. Since 2018, URS is recommended by the EAU only once after treating low-risk tumours and twice after treating high-risk tumours [8]. AUA guidelines state to perform URS at least three times, within 1–3 mo, and at 6 and 12 mo after surgery. Ten out of the 19 included studies (53%) integrated URS in their monitoring, where it was implemented more frequently than the current recommendations.

In conclusion, there appears to be consistent adherence to guideline recommendations regarding the utilisation of CT urography and cystoscopy. However, there is notable inconsistency in adherence to guidelines regarding the utilisation of cytology and ureteroscopy. The use of voided urine samples is not recommended, but often performed, while selective upper tract sampling is recommended for follow-up of high-risk tumours, but seldom applied. URS is either never performed or performed far more frequently than recommended. The included study by Figaroa et al [31] details that if URS is utilised only at the current recommended time points, recurrences may be missed. It is important, however, to recognise that the guidelines might be interpreted as a minimum of examinations that should be performed and does not advise against a more stringent follow-up strategy.

Both the type and the results of the included survival outcomes differ substantially between studies. Moreover patient and tumour characteristics showed great heterogeneity. Follow-up is necessary to identify disease recurrence and progression, and eventually improve survival rates; however, due to the heterogeneity of the included studies, conclusions on the relation of the follow-up schedules to the survival outcomes cannot be made.

4.2. Future perspectives

The differences observed in follow-up approaches across studies underscore a notable gap between real-world practices and the recommended standards. Variation in practice is presumably partly due to the rarity of the disease. Low incidence rates do not permit large prospective trials comparing different follow-up schemes. Current guidance is therefore based on evidence gained from retrospective cohort studies and expert opinion. A consultation of expert clinicians and scientists in 2022 formulated the following statement: "Regular and long-term follow-up, including URS if organ-sparing treatment has been carried out is crucial for handling recurrences, intravesical recurrences, metastases and tumour progression" [40]. Our goal is to concretise and standardise surveillance practices following KSS. As the current review does not by itself allow for the proposal of an ideal follow-up schedule due to the heterogeneous nature of the included studies, we aim to attain consensus on post-KSS surveillance through a Delphi consensus project utilising the synthesised data from our review as a foundational starting point.

4.3. Limitations

An absence of description of the used follow-up protocol or a defined time-specific censored time outcome were predominant reasons for exclusion of studies, leading to an inevitable selection of articles from the available literature. The retrospective and often single-centre nature of the included studies may provide a selection bias in the patients described in the studies and may lead to weaker evidence on survival outcomes related to treatment. It does not have an effect however on the follow-up protocols followed. Owing to the variation in types of patients included in the study, we are not able to draw useful conclusions on the relationship of the used follow-up protocols and survival of these patients.

5. Conclusions

This scoping review highlights the absence of high-quality evidence regarding follow-up strategies, contributing to variations in clinical practices and discrepancies between guidelines and real-world approaches. As comparative prospective trials are not deemed feasible, we will initiate a Delphi project to construct a consensus-based follow-up protocol.

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Study concept and design: Schuil, Figaroa, Baard.
Acquisition of data: Schuil, Figaroa, van Jamaludin, Baard.
Analysis and interpretation of data: Schuil, Figaroa, Baard.
Drafting of the manuscript: Schuil, Figaroa, Baard.

Critical revision of the manuscript for important intellectual content: Hendriks, Schout, Beerlage, van Jamaludin, Henderickx, van Moorselaar, Kamphuis, Baard.
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Appendix A. Supplementary data

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