



# Comparison of surgical effectiveness: kidney sparing surgery for upper tract urothelial carcinoma

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## Purpose of review

This review provides an overview of the recent publications on kidney-sparing-surgery (KSS) for upper tract urothelial carcinoma (UTUC), an alternative to radical nephroureterectomy (RNU) for an increasing number of indications

## Recent findings

Recent studies highlight comparable survival outcomes between KSS [ureterorenoscopy with tumour ablation (URS) or segmental ureteral resection (SUR)] and RNU, even in high-risk UTUC patients. KSS has shown to preserve renal function without significantly compromising oncologic control in appropriately selected patients. Included literature also researched surgical complications, surveillance strategies, such as second-look ureteroscopy, and comparative cost analyses.

## Summary

Over the past two and a half years, studies have emphasized the growing usage of URS and SUR in treating selected UTUC patients. Recent literature has remarkably included relatively large numbers of typically high-risk patients with features such as high-grade tumours, stage >Ta, multifocality, and hydronephrosis with acceptable results. Further research should expand on the different indications for KSS, its postoperative surveillance and comparative economic analyses.

## Keywords

kidney-sparing surgery, review, segmental resection, upper tract urothelial carcinoma, ureterorenoscopy

## INTRODUCTION

Upper tract urothelial carcinoma (UTUC) is a rare disease with an annual incidence of up to two per 100 000 individuals in Western countries [1]. Treatment of nonmetastatic UTUC can be determined using the risk-stratification provided by the European Association of Urology (EAU) Guidelines on UTUC [2]. For low-risk disease, the EAU Guidelines recommend treatment by kidney-sparing surgery (KSS). Additionally, these recommendations can extend to patients with high risk UTUC in case of an impaired renal function or solitary kidney, to preserve renal units and prevent dialysis. Management of UTUC by means of KSS, such as segmental ureter resection (SUR), ureterorenoscopy (URS), or percutaneous tumour resection (PCTR), can provide survival rates comparable to radical nephroureterectomy (RNU).

Over the past decades, there has been a notable increase in the number of patients treated

endoscopically. A 14-year epidemiological study of the German cancer registry showed an increase of management with URS of 61% for tumours in the renal pelvis and 108% of ureteral tumours. Similarly, the number of SURs has increased by 65%. Additionally, the mean age of patients undergoing URS for UTUC has risen significantly. The ratio of RNU to

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## KEY POINTS

- Kidney-sparing-surgery (KSS) is applied for a growing number of patients with upper tract urothelial carcinoma, also for those with high-risk disease.
- KSS preserves renal function effectively with no major compromise in oncologic control in selected patients.
- Results on the relevance of second-look ureteroscopy post-KSS are nonconclusive.

endoscopic therapy shifted from 5.1 : 1 in 2006 to 2.5 : 1 in 2019 in Germany [3]. It is reported that 76% of low-risk tumours are treated using KSS, and 19% of high-risk tumours are managed similarly, with an overall adherence rate to guideline recommendations for endoscopic treatment of 51% [4,5]. While KSS offers the clear benefit of preserving renal units and renal function, it is associated with higher rates of ipsilateral and intravesical recurrence compared to RNU and comes at the cost of regular endoscopic follow-up procedures under anaesthesia [6–9,10<sup>¶</sup>].

The goal of this review is to provide a comprehensive overview of the publications on KSS of the last 2.5 years for patients with UTUC to inform readers on the new additions to the body of literature on this rare disease.

## METHODS

For this review, we included papers from peer-reviewed journals and published in English, consisting of original patient data concerning KSS for UTUC published between 01-01-2022 and 01-06-2024. We focused on papers providing information on survival outcomes, complications, surveillance and economic burden of patients treated by KSS vs. RNU. We excluded review papers and case reports.

An extensive literature search was conducted on 3 June 2024 by an experienced medical librarian and encompassed four major medical databases; MEDLINE (Ovid), Embase (Ovid), the Cochrane Library, and Web of Science and was made by an experienced medical librarian (F.J.). We employed a combination of search terms, including “Kidney-sparing surgery” and its synonyms, as well as “UTUC” and its synonyms, duplicated papers were removed, and the remaining papers were exported into EndNote.

In total, 512 titles and abstracts were screened for eligibility of which we reviewed the full text of 74 papers. Titles and abstracts as well as the selected full text papers were independently reviewed by two reviewers (O.F. and H.S.) using the Rayyan screening

tool [11]. A total of 22 papers were included in this review, all of them observational studies.

To create an overview of the survival outcomes of patients treated by KSS, including endoscopic treatment and segmental resection, we abstracted data on patient characteristics (age and sex), tumour characteristics (stage, grade, size, focality and signs of hydronephrosis on imaging), type of treatment (SUR, PCTR, URS and RNU), and the survival outcomes [recurrence-free survival (RFS), intravesical-RFS (IV-RFS), upper tract RFS (UT-RFS), progression-free survival (PFS), metastasis-free survival (MFS), RNU-free survival (RNU-FS), overall survival (OS), cancer-specific survival (CSS)]. Additionally, we abstracted data from included papers to create an overview of known complications after URS for UTUC and the post-KSS surveillance. For the post-KSS surveillance we abstracted data regarding the second-look URS and the timing of recurrences during surveillance.

## RESULTS

### (Comparative) survival outcomes of kidney-sparing-surgery

In total, 17 studies examining recurrences, progression, OS and/or CSS following KSS for UTUC were identified. Twelve out of 17 studies comparing these outcomes to a cohort treated with RNU.

Patient, treatment, and tumour characteristics from these studies are detailed in Table 1. Since KSS encompasses several essentially different surgical procedures (URS, PCTR, SUR), the results are presented per treatment modality. The averages of the age of patients in the included studies at UTUC diagnosis were 64 years or older, with a majority being male. Tumour characteristics varied across cohorts, which in turn influenced the indication for KSS; however, these indications were rarely specified in the articles. Survival outcomes are presented in Table 2. The average (mean or median) duration of follow-up since surgery varied between 17 and 138 months. To better analyse the association between treatment and outcome, eight studies used patient matching on baseline covariates: propensity score matching (PSM) was applied in five studies [10<sup>¶</sup>,12,13<sup>¶</sup>,14<sup>¶</sup>,15], score overlap weighting (PSOW) in two studies [16,17<sup>¶</sup>], and inverse probability of treatment weighting (IPTW) by Shen *et al.* [18].

URS with tumour laser ablation was the predominant KSS modality in six of the included studies.

The tumour grade ranged from 26% to 54% low-grade tumours and 18% to 74% high-grade tumours. The percentage of patients with Ta-stage tumours

**Table 1.** Patient, treatment and tumour characteristics

| Reference  |          | No of patients |      |      |      | Age (years)                         | Male % | Low grade % | High grade % | G1% | G2% | G3% | Ta % | T1% | >T1% | Tis %                | Tumour size (cm)     | Unifocal % | Multifocal % | Hydro-nephrosis % |
|--|----------|----------------|------|------|------|-------------------------------------|--------|-------------|--------------|-----|-----|-----|------|-----|------|----------------------|----------------------|------------|--------------|-------------------|
|  |          | URS            | SUR  | PCTR | RNU  |                                     |        |             |              |     |     |     |      |     |      |                      |                      |            |              |                   |
| Studies mainly detailing treatment with URS        |          |                |      |      |      |                                     |        |             |              |     |     |     |      |     |      |                      |                      |            |              |                   |
| Baboudijian 2023 [26]                              | KSS      | 60             |      |      |      | 74                                  | 83     | 50          | 30           |     |     |     | NR   | NR  | NR   | 5.0                  | <2.0 43%<br>>2.0 43% | 62         | 38           | 30                |
| Chen 2024 [15]                                     | RNU      | 13             |      |      |      | 68                                  | 62     | 47          | 53           |     |     |     | 55   | 45  |      | <2.0 48%<br>>2.0 52% | 47                   | 53         | 56           |                   |
|  | KSS      |                |      |      | 103  | 73                                  | 69     | 54          | 46           |     |     |     | 62   | 38  |      | <1.0 54%<br>>2.0 46% | 39                   | 62         | 77           |                   |
| Chen 2023 [25]                                     | KSS      | 274            |      | 5    |      | 70                                  | 43     | 34          | 42           |     |     |     | 42   | 1.1 |      | <2.0 88%<br>>2.0 12% | 48                   | 45         | 52           |                   |
| Shen 2022 [18]                                     | RNU      |                |      |      | 42   | 69                                  | 45     | 40          | 60           |     |     |     | 74   | 26  |      |                      | >3.0 36%             | 0          | 100          | 79                |
|  | KSS      | 23             |      |      |      | 66                                  | 47     | 26          | 74           |     |     |     | 61   | 39  |      |                      | >3.0 18%             | 26         | 74           | 30                |
| Tsujino 2023 [22]                                  | RNU      |                |      |      | 108  | 71                                  | 69     | 21          | 79           |     |     |     | 32   | 58  |      | 9.3                  | NR                   | 84         | 16           | NR                |
|  | KSS      | 35             |      |      |      | 73                                  | 66     | 46          | 54           |     |     |     | 63   | 26  |      | 11                   | NR                   | 60         | 40           | NR                |
| Ye 2023 [14 <sup>■</sup> ]                         | RNU      |                |      |      | 397  | 40–59 20%;<br>60–79 50%;<br>>80 30% | 61     | 47          | 32           |     |     |     | 65   | 30  |      | 5.0                  | <2.0 58%<br>>2.0 42% | NR         | NR           | NR                |
|  | KSS      | 397            |      |      |      | 40–59 13%;<br>60–79 59%;<br>>80 29% | 65     | 47          | 18           |     |     |     | 70   | 26  |      | 3.5                  | <2.0 61%<br>>2.0 38% | NR         | NR           | NR                |
| Studies detailing treatment with SUR               |          |                |      |      |      |                                     |        |             |              |     |     |     |      |     |      |                      |                      |            |              |                   |
| Abbate 2022 [19]                                   | RNU      |                |      |      | 150  | 80                                  | 72     |             |              | 2.7 | 34  | 64  | 43   | 56  |      | NR                   | 64                   | 36         | 59           |                   |
|  | KSS      |                | 27   |      |      | 80                                  | 63     |             |              | 3.8 | 19  | 77  | 56   | 44  |      | NR                   | 82                   | 18         | 71           |                   |
| Lee 2024 [21]                                      | RNU      |                |      |      | 127  | 67                                  | 77     |             |              | 44  | 54  | 12  | 24   | 61  | 1.6  | 3.1                  | NR                   | NR         | NR           |                   |
|  | KSS      |                | 46   |      |      | 65                                  | 85     |             |              | 54  | 39  | 24  | 20   | 50  | 6.5  | 1.7                  | NR                   | NR         | NR           |                   |
| Masson-Lecomte 2022 [34]                           | KSS      |                | 155  |      |      | 73                                  | 73     | 28          | 66           | 10  | 25  | 58  | 47   | 21  | 28   | 0.3                  | 2.6                  | 95         | 4.5          | 74                |
| Paciotti 2023 [16]                                 | RNU      |                |      |      | 9016 | 72                                  | 62     | 14          | 35           |     |     |     | 38   | 16  |      | <2.0 25%<br>>2.0 56% | NR                   | NR         | NR           |                   |
|  | KSS      |                | 4045 |      |      | 72                                  | 39     | 17          | 31           |     |     |     | 42   | 13  |      | <2.0 35%<br>>2.0 36% | NR                   | NR         | NR           |                   |
| Yang Qiu 2023 [13 <sup>■</sup> ]                   | RNU      |                |      |      | 1844 | <70 37%;<br>>70 63%                 | 60     | 8.6         | 79           |     |     |     | NR   | NR  | NR   | NR                   | <2.0 23%<br>>2.0 76% | NR         | NR           | NR                |
|  | KSS      |                | 664  |      |      | <70 34%;<br>>70 66%                 | 68     | 18          | 83           |     |     |     | NR   | NR  | NR   | NR                   | <2.0 36%<br>>2.0 63% | NR         | NR           | NR                |
| Wei 2023 [35]                                      | KSS      |                | 20   |      |      | 64                                  | 75     | 50          | 50           |     |     |     | 60   | 5   | 35   |                      | <2.0 20%<br>>2.0 80% | NR         | NR           | 100               |
| Studies detailing various KSS treatment modalities |          |                |      |      |      |                                     |        |             |              |     |     |     |      |     |      |                      |                      |            |              |                   |
| Hendriks 2022 [10 <sup>■</sup> ]                   | RNU      |                |      |      | 97   | 69                                  | 69     | 32          | 73           |     |     |     | 51   | 17  | 33   |                      | <2.0 30%<br>>2.0 70% | 80         | 11           | 49                |
|  | KSS n=89 | NR             | NR   | NR   |      | 68                                  | 76     | 75          | 25           |     |     |     | 87   | 4.5 | 9.0  |                      | <2.0 54%<br>>2.0 46% | 82         | 5.6          | 26                |

Table 1 (Continued)

| Reference                           | No of patients |     |      |      | Age (years)        | Male % | Low grade % | High grade % | G1% | G2% | G3% | Ta % | T1% | >T1% | Tis % | Tumour size (cm)     | Unifocal % | Multifocal % | Hydronephrosis % |
|-------------------------------------|----------------|-----|------|------|--------------------|--------|-------------|--------------|-----|-----|-----|------|-----|------|-------|----------------------|------------|--------------|------------------|
|                                     | URS            | SUR | PCTR | RNU  |                    |        |             |              |     |     |     |      |     |      |       |                      |            |              |                  |
| Jiang 2023 [36]                     | 5              | 17  |      |      | 69                 | 68     | 23          | 77           |     |     |     |      | 55  | 45   |       | <2.0 41%<br>>2.0 59% | NR         | NR           | 73               |
| Kim 2023 [20]                       |                |     |      | 708  | 68                 | 71     | 16          | 81           |     |     | 23  | 23   | 25  | 49   | 2.5   | 3.7                  | 69         | 31           | NR               |
| Liu 2024 [12]                       | 10             | 52  | 0    |      | 68                 | 79     | 27          | 61           |     |     | 32  | 32   | 21  | 19   | 4.8   | 2.3                  | 92         | 8.1          | NR               |
|                                     |                |     | 309  | 71   | 73                 | 73     |             |              | 14  | 22  | 52  | 21   | 22  | 47   | 2.3   | <2.0 29%<br>>2.0 67% | 86         | 14           | NR               |
| Jianhui Qiu 2023 [17 <sup>a</sup> ] | 28             | 54  |      |      | 73                 | 71     |             |              | 27  | 22  | 23  | 40   | 17  | 16   | 3.7   | <2.0 49%<br>>2.0 35% | 92         | 8.5          | NR               |
|                                     |                |     |      | 1510 | <75 61%<br>>75 39% | 61     | 33          | 67           |     |     |     |      | 65  | 53   |       | NR                   | NR         | NR           | NR               |
| KSS                                 | NR             | NR  | NR   |      | <75 55%<br>>75 45% | 67     | 29          | 53           |     |     |     |      | 70  | 30   |       | NR                   | NR         | NR           | NR               |
|                                     | n = 459        |     |      |      |                    |        |             |              |     |     |     |      |     |      |       |                      |            |              |                  |

KSS, kidney-sparing surgery; mm, millimetre; NR, not reported; PCTR, percutaneous tumour resection; RNU, radical nephroureterectomy; SUR, segmental ureteral resection; URS, ureteroscopic tumour ablation. Totals are less than 100% if data was missing.

undergoing URS ranged from 32% to 70%, multifocal disease ranged from 38% to 74%, and hydronephrosis was observed in 30% to 77%. IV-RFS was reported in three studies, with 5-year rates ranging from 69% to 75%. Comparison between URS and RNU did not reveal statistically significant differences in IV-RFS or overall RFS. OS was reported in four of the six URS studies, with 5-year OS rates ranging from 57% to 95%. Comparative analysis found no differences in survival outcomes between KSS and URS in all, but one study: Ye *et al.* reported a significant difference in OS and CSS between the URS and RNU cohort. This study, which included 397 patients in each treatment arm and used PSM for comparison, found a 5-year OS of 80% for RNU and 66% for KSS ( $P < 0.001$ ), and a 5-year CSS of 94% for RNU and 83% for URS ( $P < 0.001$ ). Further stratification by tumour grade and stage in their study showed comparable tumour control between URS and RNU for low-grade, nonmuscle-invasive ureteral tumours only.

Six studies reported on the outcomes of SUR. Patients treated with SUR generally had a high-grade tumour (range 31–85%) and a high proportion of invasive disease (T2 or higher: 13% to 50%). Focality was rarely reported. Hydronephrosis, noted in three studies, was present in 71% to 100% of patients undergoing SUR. The 5-year IV-RFS for SUR ranged from 41% to 55%. Two studies compared IV-RFS between SUR and RNU, with no significant difference observed. No differences were found for CSS (two comparative studies) or PFS (one comparative study). Four studies compared OS between SUR and KSS, finding no significant differences, with 5-year OS ranging from 51% to 70%.

Five studies grouped various KSS modalities or did not specify the type of surgery. Notably, only one of these studies reported differences in outcomes. Hendriks *et al.* described a higher rate of intravesical recurrences during follow-up in patients treated with KSS, but this did not lead to differences in PFS, MFS, OS, or CSS.

Only one study noted the use of post-KSS adjuvant upper tract instillation and in only patient [12].

Seven papers reported the comparative postoperative renal function changes, of which five papers reported a significant difference in postoperative renal function in favour of KSS [10<sup>a</sup>,15,18–22].

## Postoperative complications

In total, eight studies described the occurrence of complications after KSS. We found a postoperative complication rate for URS of 13–42% and for SUR of 7–33%. All included papers assessed the complications using the Clavien Dindo classification [23].

Table 2. Recurrence, survival and progression outcomes

| Reference                                   | FU mean or median (months) | Overall RFS % | Recurrences                |          |                            |                            |                    |                            | Survival           |       |             | Progression             |                         |             |       |  |
|---|----------------------------|---------------|----------------------------|----------|----------------------------|----------------------------|--------------------|----------------------------|--------------------|-------|-------------|-------------------------|-------------------------|-------------|-------|--|
|   |                            |               | RNU vs. KSS                | IV-RFS % | IVRNU vs. KSS              | UT-RFS %                   | RNU vs. KSS        | OS %                       | RNU vs. KSS        | CSS % | RNU vs. KSS | PFS %                   | RNU vs. KSS             | RNU vs. KSS | MFS % |  |
| Studies mainly detailing treatment with URS |                            |               |                            |          |                            |                            |                    |                            |                    |       |             |                         |                         |             |       |  |
| Baboudjian 2023 [26]                        | KSS                        | 36            | 1yr 87<br>3yr 80<br>5yr 69 |          | 1yr 83<br>3yr 70<br>5yr 56 | 1yr 94<br>3yr 75<br>5yr 57 |                    | 1yr 98<br>3yr 95<br>5yr 75 |                    |       |             | 1y 87<br>3y 84<br>5y 81 | 1y 98<br>3y 94<br>5y 86 |             |       |  |
| Chen 2024 [15]                              | RNU                        | 28            | 2yr *81                    |          |                            | 2yr *84                    | HR 0.94<br>p>0.9   |                            |                    |       | 2y 71       | HR 104<br>p>0.9         |                         |             |       |  |
|   | KSS                        | 28            | 2yr *83                    |          |                            | 2yr *82                    |                    |                            |                    |       | 2y 73       |                         |                         |             |       |  |
| Chen 2023 [25]                              | KSS                        | 44            |                            |          |                            |                            |                    | 80                         |                    |       |             |                         |                         |             |       |  |
| Shen 2022 [18]                              | RNU                        | 34            | 5yr *56                    |          | p = 0.3                    | 5yr *95                    | p > 0.9            |                            |                    |       | 5y *56      | p=0.9                   |                         |             |       |  |
|   | KSS                        | 34            | 5yr *75                    |          |                            | 5yr *95                    |                    |                            |                    |       | 5y *59      |                         |                         |             |       |  |
| Tsujino 2023 [22]                           | RNU                        | 39            | HR 1.8<br>p=0.16           |          |                            |                            | HR 2.4<br>p=0.058  |                            |                    |       |             |                         |                         |             |       |  |
|   | KSS                        | 17            |                            |          |                            |                            |                    |                            |                    |       |             |                         |                         |             |       |  |
| Ye 2023 [14]                                | RNU                        | 56            |                            |          |                            | 5yr *80                    | *p<0.001           | 5y *94                     | P<0.001            |       |             |                         |                         |             |       |  |
|   | KSS                        | 56            |                            |          |                            | 5yr *66                    |                    | 5y *83                     |                    |       |             |                         |                         |             |       |  |
| Studies detailing treatment with SUR        |                            |               |                            |          |                            |                            |                    |                            |                    |       |             |                         |                         |             |       |  |
| Abbate 2022 [19]                            | RNU                        | 26            |                            |          |                            | 3yr 66                     | HR 0.35<br>P=0.15  |                            |                    |       |             |                         |                         |             |       |  |
|   | KSS                        | 26            |                            |          |                            | 3yr 87                     |                    |                            |                    |       |             |                         |                         |             |       |  |
| Lee 2024 [21]                               | RNU                        | 53            | 3yr 55                     |          | p = 0.9                    | 3yr 83                     | P=0.5              | 3yr 94                     | p = 0.17           |       | 3y 74       | p = 0.7                 |                         |             |       |  |
|   | KSS                        | 40            | 5yr 51                     |          |                            | 3yr 89                     |                    | 3yr 91                     |                    |       | 3y 80       |                         |                         |             |       |  |
| Masson-Lecomte 2022 [34]                    | KSS                        | NR            | 2yr 58<br>5yr 44           |          | 2yr 83<br>5yr 74           | 5yr 72                     |                    | 5yr 84                     |                    |       |             |                         |                         |             |       |  |
| Paciotti 2023 [16]                          | RNU                        | 38            |                            |          |                            | 5yr *53                    | HR 0.98<br>p = 0.5 |                            |                    |       |             |                         |                         |             |       |  |
|   | KSS                        | 38            |                            |          |                            | 5yr *53                    |                    |                            |                    |       |             |                         |                         |             |       |  |
| Yang Qiu 2023 [13]                          | RNU                        | 46            | 73                         |          | HR 1.0<br>p > 0.9          | 5yr *53                    | p = 0.3<br>p = 0.4 | 5y 58                      | P = 0.5<br>p = 0.3 |       |             |                         |                         |             |       |  |
|   | KSS                        | 46            | 79                         |          |                            | 5yr *51                    |                    | 5y 57                      |                    |       |             |                         |                         |             |       |  |
| Wei 2023 [35]                               | KSS                        | NR            |                            |          |                            | 3yr 70                     |                    |                            |                    |       | 3y 50       |                         |                         |             |       |  |

**Table 2** (Continued)

|  |     | FU mean or median (months) | Recurrences      |             |          |                 |                  | Survival                    |                    |                           | Progression       |                                |                  |             |          |                                |
|--|-----|----------------------------|------------------|-------------|----------|-----------------|------------------|-----------------------------|--------------------|---------------------------|-------------------|--------------------------------|------------------|-------------|----------|--------------------------------|
|  |     |                            | Overall RFS %    | RNU vs. KSS | IV-RFS % | IVRNU vs. KSS   | UT-RFS %         | RNU vs. KSS                 | OS %               | RNU vs. KSS               | CSS %             | RNU vs. KSS                    | PFS %            | RNU vs. KSS | RNU-FS % | MFS %                          |
| Reference  |     |                            |                  |             |          |                 |                  |                             |                    |                           |                   |                                |                  |             |          |                                |
| Studies detailing various KSS treatment modalities |     |                            |                  |             |          |                 |                  |                             |                    |                           |                   |                                |                  |             |          |                                |
| Hendriks 2022 [10 <sup>■</sup> ]                   | RNU | 37                         |                  |             | 69 %68   | *p=0.029        | 88 %92           | 11yr 71 %84                 | *p=0.7             | 11yr 79 %76               | *p=0.5            | 96 %96                         | *p=0.15          | 67 %72      |          | *p=0.2                         |
|  | KSS | 48                         |                  |             | 49 %48   |                 | 29 %21           | 11yr 81 %86                 |                    | 11yr 90 %76               |                   | 87 %86                         |                  | 87 %82      |          |                                |
| Jiang 2023 [36]                                    | KSS | NR                         |                  |             |          |                 |                  | 5yr 54                      |                    |                           |                   | 39                             |                  |             |          |                                |
| Kim 2023 [20]                                      | RNU | 68                         | 3yr 43<br>5yr 38 | p=0.8       |          |                 |                  | 3yr 80<br>5yr 71<br>10yr 51 | P=0.4              | 3yr 80<br>5yr 74          | p=0.6             |                                |                  | 3y 71 5y 64 |          | p=0.8                          |
|  | KSS | 66                         | 3yr 45<br>5yr 41 |             |          |                 |                  | 3yr 85<br>5yr 72<br>10yr 57 |                    | 3yr 84<br>5yr 70          |                   |                                |                  | 3y 67 5y 67 |          |                                |
| Liu 2024 [12]                                      | RNU | NR                         |                  |             |          | P=0.7<br>*p>0.9 | p=0.2<br>*p=0.15 |                             | P=0.17 %0.5        |                           |                   | KSS > RNU<br>p=0.028<br>*p=0.5 | P=0.11<br>*p=0.6 |             |          | KSS > RNU<br>p=0.011<br>*p=0.3 |
|  | KSS | NR                         |                  |             |          |                 |                  |                             |                    |                           |                   |                                |                  |             |          |                                |
| Jianhui Qiu 2023 [17 <sup>■</sup> ]                | RNU | 138                        |                  |             |          |                 |                  | 5yr 62 %61<br>10yr 38 %37   | p=0.15 %<br>p=0.15 | 5yr 80 %79<br>10yr 68 %67 | P=0.11<br>*p=0.11 |                                |                  |             |          |                                |
|  | KSS | 138                        |                  |             |          |                 |                  | 5yr 58 %58<br>10yr 35 %36   |                    | 5yr 77 %77<br>10yr 64 %64 |                   |                                |                  |             |          |                                |

CSS, cancer-specific survival rate; FU, follow-up; IV, intravesical; MFS, metastasis-free survival rate; OS, overall survival rate; PFS, progression-free survival rate; RFS, recurrence-free survival rate; RNU-FS, radical nephroureterectomy-free survival rate; UT, upper tract. Outcomes are presented as results of the FU duration or at a specific year of FU. P-values are results of log-rank tests or cox regression survival.

\*Outcomes marked with an asterisk are results obtained after patient matching between cohorts, using methods propensity score matching, propensity score overlap weighting, or inverse probability weighting.

**Table 3.** Overview of the post-KSS complication rates overall and using the Clavien Dindo classification

| Reference                | Type of KSS | FU (months) mean or median (SD or IQR) | Overall complication rate | Complication rate per CD score                                      |
|--------------------------|-------------|--|---------------------------|---|
| Baboudjian 2023 [26]     | URS         | 36                                     | 13%                       | CD2 10%<br>CD3a/b 3.3%  |
| Basile 2024 [24]         | URS         | NR                                     | 15%                       | CD1 1.7%<br>CD2 10%<br>CD3a 1.7%<br>CD3b 0<br>CD4a 1%               |
| Chen 2024 [15]           | URS         | 28 (21–32)                             | 42%                       | CD1 17% CD2 17%<br>CD3a 0<br>CD3b 8%                                |
| Chen 2023 [25]           | URS         | 44 (23–76)                             | 8.2%                      | CD1 3.6%<br>CD2 3.6%<br>CD3a/b 1.1%                                 |
| Abrate 2022 [19]         | SUR         | 26                                     | 7%                        | CD1 7%  |
| Masson-Lecomte 2022 [34] | SUR         | NR                                     | 33%                       | CD1 9%<br>CD2 16%<br>CD3a 0.6%<br>CD3b 5.8%<br>CD4 1.9%<br>CD5 0.6% |
| Wei 2023 [35]            | SUR         | NR                                     | 20%                       | CD 1 10%<br>CD2 5%<br>CD3 5%  |
| Jiang 2023 [36]          | URS and SUR | 138                                    | 28%                       | CD1 27%<br>CD2 4.5%   |

CD, Clavien Dindo; FU, follow-up; IQR, interquartile range; NR, Not reported; SD, standard deviation; SUR, segmental ureteral resection; URS, ureterorenoscopic tumour ablation.

The postoperative complication rates are presented in Table 3. The most common reported complications were haematuria, urinary tract infections and postoperative bleeding. Only two of the included papers reported a post-KSS complication classified as grade 4 or higher, with a percentage of 1.9%. Two studies reported post-URS ureteral stricture rates, with 29% of patients in the study by Chen *et al.* developing strictures compared to 6.9% in a study by Basile *et al.*, indicating a notable difference [24,25].

### Post-kidney-sparing-surgery surveillance

Of the abovementioned 17 studies on survival outcomes, six described their follow-up protocols [10<sup>¶</sup>,15,21,22,25,26]. We additionally found three recently published studies specifically researching post-KSS surveillance [27,28<sup>¶</sup>,29<sup>¶</sup>]. All but one [26] included ureteroscopy as part of their follow-up procedures.

The article by Gallioli *et al.* aimed to compare the effect of performing or omitting an early second-look URS (URS ≤8 weeks vs. >8 weeks) in the surveillance of patients with UTUC after endoscopic

treatment on oncological outcomes [28<sup>¶</sup>]. In total, 85 patients treated by URS and who underwent a second-look URS, were included in this study. Tumour grade was low in 49% and missing in 25% of cases. The overall cancer detection rate at second-look was 45%. Patients with a positive second-look URS had a significantly higher rate of UTUC recurrence at a median follow-up of 35 months. Finally, there was no significant difference regarding the oncological outcomes seen analysing the timing of the second-look URS. This article concluded that a second-look URS is a key step in the follow-up schedule of patients after endoscopic treatment.

In contrary, an article by Figaroa *et al.*, including 71 patients with 81% low-grade tumours, showed that the second-look URS lacks prognostic value for tumour recurrence or treatment conversion to RNU after a median follow-up of 50 months [29<sup>¶</sup>].

### Comparative economic burden

Only one paper described the overall and categorical cost components in the management of patients



with nonmetastatic UTUC according to the given treatment [30<sup>¶</sup>]. To analyse these costs, 4,114 patients were identified retrospectively. Patients were stratified in two different groups, the KSS vs. the RNU group. The total costs within 1 year of diagnosis were compared using the inverse probability of treatment-weighted propensity score (IPTW) models.

Overall, 26% and 74% of the identified patients underwent KSS and RNU, respectively. After propensity score matching, all variables were well balanced. Median costs were lower for KSS vs. RNU up to one year, with significantly lower costs at 90 days and 365 days. Median costs according to categories of services were significantly less for KSS vs. RNU patients. The only category which was significantly higher for KSS vs. RNU was inpatient visits. This article concludes that the total median costs were significantly less for KSS vs. RNU up to 1 year after diagnosis.

## DISCUSSION

We aimed to provide an overview of the recent publications in the field of KSS for UTUC. We found 22 articles, mainly retrospective cohort studies, reporting on survival outcomes, complications of surgery, the postoperative surveillance and the economic implications.

Seventeen studies reported on the survival outcomes of KSS in UTUC, primarily focusing on two surgical modalities: URS with laser ablation and SUR. PCTR was mentioned in only one study, accounting for just 5 out of 279 cases. Interestingly, studies included a large proportion of patients with traditionally high-risk features – such as high-grade tumours, stage >Ta, multifocality, and hydronephrosis – who underwent KSS, not only via SUR but also URS. This inclusion is notable, as it deviates from current guidelines, which generally recommend KSS for low-risk patients. Despite this, the majority of studies found no significant reduction in MFS, RFS, CSS or OS among these high-risk patients, suggesting that patient selection might have been appropriate and that KSS could be a viable option for some high-risk individuals, warranting further investigation on this selection criteria.

It should be noted however that the largest study on URS, conducted by Ye *et al.*, found that its oncological effectiveness was comparable to RNU only in low-grade, noninvasive disease, but not in cases with high-grade or more advanced tumours. This study aligns with the conclusions of a 2016 systematic review by Seisen *et al.*, which suggested that URS offers comparable outcomes to RNU in low-grade, low-stage disease and should be considered for more

advanced cases only in imperative or palliative settings [6]. The studies included studies on SUR have showed no significant difference in survival outcomes when compared to RNU, even though they included more patients with high-grade and invasive tumours. This indicates that SUR is a feasible option for certain high-risk patients, even in elective treatment settings.

In the included articles on survival outcomes, upper tract instillation as adjuvant treatment after KSS was described in only one patient in one study, indicating no significant role for instillations as ancillary treatment in KSS in this selection of literature [12].

In total, eight studies reported complications. We found an overall postoperative complication rate between 7% and 42%, with most of the complications classified as Clavien Dindo grade 3 or lower.

In two of the included studies, the timing and predictive value of the second-look URS was researched. On the one hand, the article by Gallioli *et al.* found patients with a positive second-look URS had a significantly higher rate of UTUC recurrence. On the contrary, Figaroa *et al.* found that a second-look URS lacks prognostic value for tumour recurrence or treatment conversion to RNU in patients treated by URS. Possible explanations for this difference could be the longer follow-up or higher proportion of low-grade tumours described by Figaroa. An earlier study on this topic published in 2016 by Villa *et al.* found a prognostic value of a positive second-look on tumour recurrence [31]. However, tumour grading data was also missing in 42% of the cases, raising the possibility that the included patient population may have had a higher proportion of high-grade tumours than reported. Because of the conflicting results from these studies, it is our opinion that the EAU guidelines advise, to perform a second-look URS after initial KSS by URS and adjust further follow-up based on its outcome, is still a matter of debate.

We found 1 article in the time period included in our search on costs. This article described the overall and categorical cost components in the management of patients with nonmetastatic UTUC according to the given treatment within 1 year of follow-up and found KSS to be less costly than RNU. However, the omission of a clear follow-up schedule makes it hard to interpret these findings, since it is not clear how many follow-up visits were executed and what diagnostic modalities were used during follow-up in the two treatment groups. Moreover, it could be that large cost differences occur after one year. On the one hand, patients who were treated with KSS, may have had many repeat URS during



follow-up and some of these patients eventually still had to undergo RNU. On the other hand, KSS preserves renal function, and a portion of these patients could possibly be spared dialysis with substantial annual costs [32]. When comparing these outcomes with known literature, an earlier study by Shenhar and Lifshitz found higher costs in the KSS group over a follow-up period of 4.9 years [9].

## Strengths and limitations

For this article we performed a systematic literature search by an experienced medical librarian, making it unlikely that relevant publications were missed. Unfortunately, as can be expected with a rare disease, most data are based on retrospective studies, no prospective randomized studies were found. Selection bias is therefore inevitable and any comparison between KSS and RNU cohorts is limited. Beside this, KSS can be either by ureterorenoscopic treatment or segmental resection. Patient selection for both treatment modalities differs as we have shown. Percutaneous tumour resection is another option but was barely included in recent publications. Some studies had small sample sizes. Larger studies were based on databases such as the SEER, which has its own limitations. Notably the lack of data on repeat endoscopic interventions, bladder recurrence as well as which patients eventually had to undergo RNU.

We set out to explore KSS for different indications of treatment, this was however often impossible to distill from papers since universal definitions of indication (elective, imperative or palliative) for KSS are lacking. Lastly, survival data was not always presented at defined time intervals using censoring, but over the follow-up period, has limited value [33].

## CONCLUSION

Over the past two and a half years, studies have highlighted the significant role of KSS in treating selected UTUC patients. Notably, recent literature has focused not only on low-risk patients undergoing KSS but also on those with high-risk characteristics, including high-grade, stage >Ta, multifocality, and hydronephrosis undergoing URS or SUR and shows mainly favourable outcomes. This trend should be continued to be scrutinized carefully and its safety should be the subject of further long-term studies.

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## Conflicts of interest

*There are no conflicts of interest.*

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- of special interest
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