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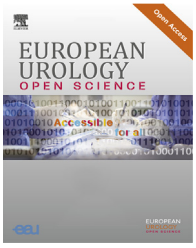

European Association of Urology

Kidney Cancer

Diagnostic Biopsy for Small Renal Tumours: A Survey of Current European Practice

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Article info

Article history:
Accepted February 2, 2024

Associate Editor:
M. Carmen Mir

Keywords:
Biopsy
Kidney cancer
Small renal mass

Abstract

Background and objective: Renal tumour biopsy (RTB) can help in risk stratification of renal tumours with implications for management, but its utilisation varies. Our objective was to report current practice patterns, experiences, and perceptions of RTB and research gaps regarding RTB for small renal masses (SRMs).
Methods: Two web-based surveys, one for health care providers (HCPs) and one for patients, were distributed via the European Association of Urology Young Academic Urologist Renal Cancer Working Group and the European Society of Residents in Urology in January 2023.
Key findings and limitations: The HCP survey received 210 responses (response rate 51%) and the patient survey 54 responses (response rate 59%). A minority of HCPs offer RTB to >50% of patients (14%), while 48% offer it in <10% of cases. Most HCPs reported that RTB influences (61.5%) or sometimes influences (37.1%) management decisions. Patients were more likely to favour active treatment if RTB showed high-grade cancer and less likely to favour active treatment for benign histology. HCPs identified situations in which they would not favour RTB, such as cystic tumours

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https://doi.org/10.1016/j.euros.2024.02.002

and challenging anatomic locations. RTB availability (67%) and concerns about delays to treatment (43%) were barriers to offering RTB. Priority research gaps include a trial demonstrating that RTB leads to better clinical outcomes, and better evidence that benign/indolent tumours do not require active treatment.
Conclusions and clinical implications: Utilisation of RTB for SRMs in Europe is low, even though both HCPs and patients reported that RTB results can affect disease management. Improving timely access to RTB and generating evidence on outcomes associated with RTB use are priorities for the kidney cancer community.
Patient summary: A biopsy of a kidney mass can help patients and doctors make decisions on treatment, but our survey found that many patients in Europe are not offered this option. Better access to biopsy services is needed, as well as more research on what happens to patients after biopsy.

1. Introduction

The expanding use of cross-sectional imaging throughout medicine has led to a rise in the detection of incidental small renal masses (SRMs) [1]. Contemporary imaging cannot reliably differentiate benign from malignant renal tumours [2], with 18–30% of surgically excised SRMs found to be benign on final pathology [3,4]. Surgery represents overtreatment for benign SRMs and has a potential risk of morbidity. A national audit of surgical outcomes following surgery for benign renal masses in the UK revealed perioperative complications in 20% of cases, including major complications in 4% (Clavien-Dindo grade $\geq$3), and 30-d mortality of 0.3% [5].

Core renal tumour biopsy (RTB) is diagnostic in ~90% of cases, and diagnostic samples have sensitivity and specificity of >99% for detection of malignancy in comparison to surgical specimens [6]. Morbidity associated with RTB is low [6]. Observational studies have shown that pretreatment RTB reveals benign histology for ~20% of SRMs, and the likelihood of benign pathology after surgical resection is lower among patients who undergo RTB [7,8]. Preoperative diagnostic RTB is recommended by international guidelines whenever it may influence SRM management [9–11]. Interpretation of this statement is at the discretion of health care providers (HCPs) and therefore uptake of RTB in the SRM setting is variable.

The aim of this study was to investigate current practice in Europe and perceptions of diagnostic RTB in the SRM setting, as well as barriers to and facilitators of its adoption. Opinions were collected from HCPs and patients.

2. Patients and methods

2.1. Design and data collection

A survey was developed and reported in line with the EQUATOR Network consensus-based Checklist for Reporting of Survey Studies (CROSS) [12]. Ethics approval was obtained from the UK Health Research Authority (reference 20/SC/0244) for development of the survey, which was then distributed internationally in line with local policies. Two cross-sectional surveys, one for HCPs and one for patients, were co-designed by researchers, HCPs, and patients. Survey items and responses were informed by a parallel qualitative study exploring RTB barriers and facilitators in England (ISRCTN16455338). Participation in the survey was voluntary and responses were anonymous. The survey link was not publicly available and was only shared directly with the intended sample. No additional mechanisms were in place to avoid unauthorised access or multiple responses.

2.2. Survey instruments

2.2.1. HCP survey

The 28-question instrument for HCPs is available in the Supplementary material. It included six questions on respondent demographics (Q1–6), 15 on local service provision for SRM diagnostics (Q7–16, Q18–20, Q23–24), four on perceptions of RTB (Q21–22, Q25–26), preferences for offering RTB in relation to 14 different patient- or tumour-related factors (Q17), four questions on research gaps (Q27), and an option to leave free-text comments (Q28).

2.2.2. Patient survey

The 28-question instrument for patients is available in the Supplementary material. It included six questions on respondent demographics (Q1–6), 14 on the diagnostic and initial management pathway applicable only to respondents with personal experience of an SRM (Q7–20), two on general preferences for health service provision (Q21–22), four on preferences in different hypothetical clinical scenarios (Q23–26), one on willingness to participate in research (Q27), and an option to leave free-text comments (Q28).

2.3. Sample characteristics and survey administration

Surveys were translated into 11 European languages and distributed to HCPs via the professional networks of collaborators from the European Association of Urology Young Academic Urologist (EAU YAU) Renal Cancer Working Group and the European Society of Residents in Urology (ESRU). Collaborators were requested to seek responses from practising urology, radiology, oncology, pathology, and nursing staff to capture responses from all the disci-

plines involved in SRM management and to approach HCPs working in a range of health care settings. Collaborating HCPs also approached patients undergoing SRM investigation and management and their accompanying friends and relatives during or shortly before the study period. Patients were approached directly. The survey was open to responses from January 1 to January 31, 2023. Study data were collected and managed using REDCap electronic data capture tools hosted by University College London, London, UK [13,14].

2.4. Statistical analysis

The aim of this project was to provide a qualitative and quantitative description of current practice and perceptions. Responses to each survey item are presented as a proportion of the respondents for that item. For continuous variables, the sample mean and standard deviation are reported. Data were analysed using Stata version 17 (Stata Corp., College Station, TX, USA).

Table 1 – Demographic data for respondents to the health care provider survey

Parameter	Respondents, *n*/*N* (%)
Profession	
Pathologist	9/210 (4.3)
Radiologist	13/210 (6.2)
Urologist	159/210 (75.7)
Oncologist	14/210 (6.7)
Nurse	11/210 (5.2)
Administrator	0
Health care manager	0
Other	4/210 (1.9)
Experience	
<5 yr	102/209 (48.8)
5–10 yr	56/209 (26.8)
>10 yr	51/209 (24.4)
Country of practice	
Belgium	1/205 (0.5)
Estonia	13/205 (6.3)
France	1/205 (0.5)
Germany	13/205 (6.3)
Greece	11/205 (5.4)
Ireland	3/205 (1.5)
Italy	101/205 (49.3)
Netherlands	6/205 (2.9)
Portugal	1/205 (0.5)
Spain	4/205 (2.0)
Sweden	1/205 (0.5)
UK	13/205 (6.3)
Turkey	22/205 (10.7)
Other	15/205 (7.3)
Practice setting	
University teaching hospital	160/210 (76.2)
Regional hospital	22/210 (10.48)
Community setting	9/210 (4.3)
Private hospital	19/210 (9.1)
Other	3/210 (1.4)
Annual case volume	
0–10 SRMs	18/210 (8.5)
10–20 SRMs	53/210 (25.5)
20–50 SRMs	61/210 (29.1)
50–100 SRMs	38/210 (18.1)
>100 SRMs	34/210 (16.1)
Unknown	6/210 (2.9)

SRM = small renal mass.

Table 2 – Contemporary local practice details reported by respondents to the health care provider survey

Local practice options	Respondents, *n*/*N* (%)
CT	204/210 (97.1)
Magnetic resonance imaging	188/210 (89.5)
Ultrasound	187/210 (89.1)
Contrast-enhanced ultrasound	123/210 (58.6)
^{99m}Tc-sestamibi single-photon emission CT/CT	159/210 (75.7)
Other	3/210 (1.4)
Treatments routinely available to patients with SRMs	
Radical nephrectomy	150/204 (74.5)
Partial nephrectomy	207/208 (99.5)
Percutaneous ablation	158/206 (76.7)
Laparoscopic ablation	72/198 (36.4)
Active surveillance	192/206 (93.7)
Treatments routinely explained to all patients with SRMs	
Radical nephrectomy	179/206 (86.9)
Partial nephrectomy	198/205 (96.6)
Percutaneous ablation	148/205 (72.2)
Laparoscopic ablation	69/197 (35.0)
Active surveillance	189/206 (91.8)
Time required to counsel a new patient with an SRM	
Up to 10 min	57/207 (27.5)
11–20 min	93/207 (44.9)
21–30 min	45/207 (21.7)
31–40 min	8/207 (3.9)
>40 min	4/207 (1.9)

CT = computed tomography; SRM = small renal mass.

3. Results

3.1. HCP survey

A total of 210 HCPs responded, representing a response rate of 51%. The demographics of respondents are reported in Table 1. Responses to question on practice related to SRMs are shown in Table 2.

The proportion of patients in their current practice offered RTB for an SRM is <10%, 10–30%, 30–50%, 50–70%, and >70% according to 48%, 22%, 9%, 8%, and 6% of the respondents, respectively. The remaining 6% did not know the proportion of patients offered RTB. The proportion of patients who ultimately undergo RTB was reported as <10%, 10–30%, 30–50%, 50–70%, and >70% by 57%, 19%, 8%, 5%, and 3% of the respondents, respectively. The remaining 8% did not know the proportion of patients who actually undergo RTB.

Respondents indicated the patient- and tumour-related factors they consider to favour or not favour biopsy (Fig. 1). Other service-related factors that influence decisions on whether to offer or recommend biopsy were biopsy availability (138/207, 66.7%) and concerns regarding delays in treatment (89/207, 43.0%) and missed time targets for cancer treatment (84/205, 41.0%). The turnaround time for RTB pathology reporting was <1 wk, 1–2 wk, 2–3 wk, and >3 wk according to 12.1%, 51.0%, 29.6%, and 7.3% of respondents, respectively. On a 10-point Likert scale rating their confidence in the RTB result for decision-making regarding SRM management, the mean score was 7.3 (standard deviation 1.97; Fig. 2). When asked if a biopsy result could change their clinical decision-making, 126/205 respondents (61.5%) indicated yes, 76/205 (37.1%) indicated sometimes, and three of 205 (1.5%) indicated no.

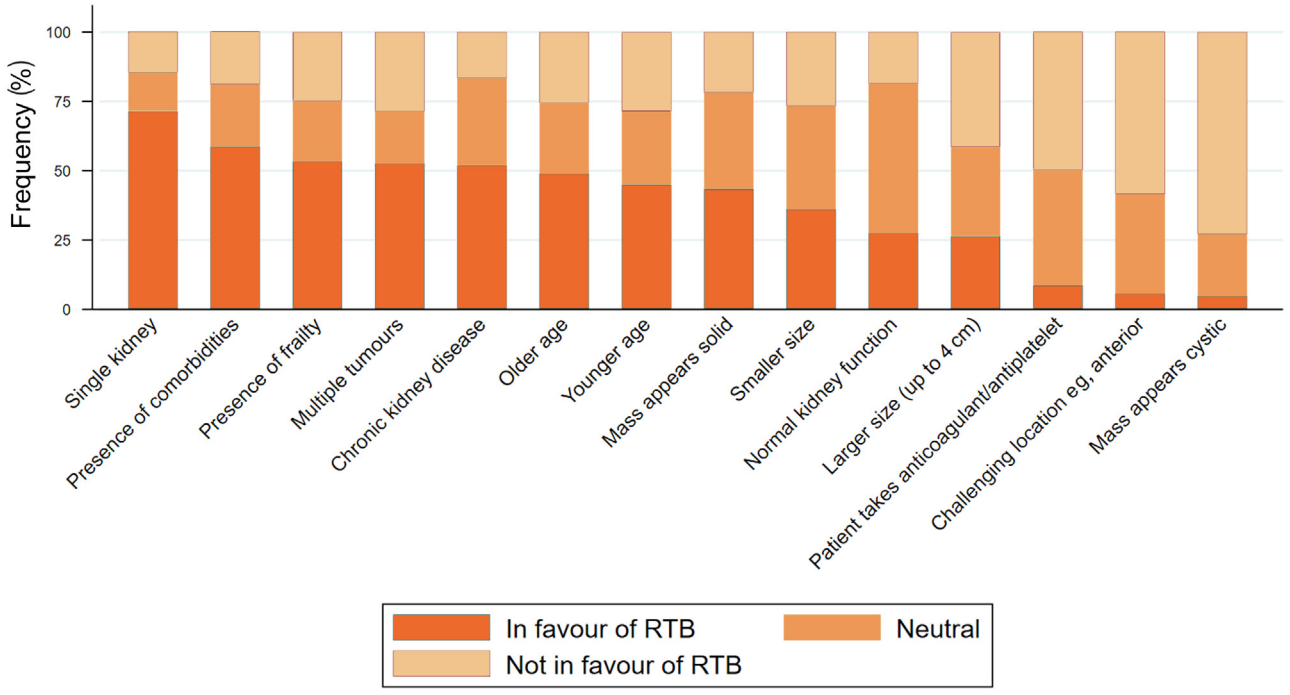

Fig. 1 – Patient- and tumour-related factors considered important when deciding on whether to perform renal tumour biopsy (RTB) for small renal masses.

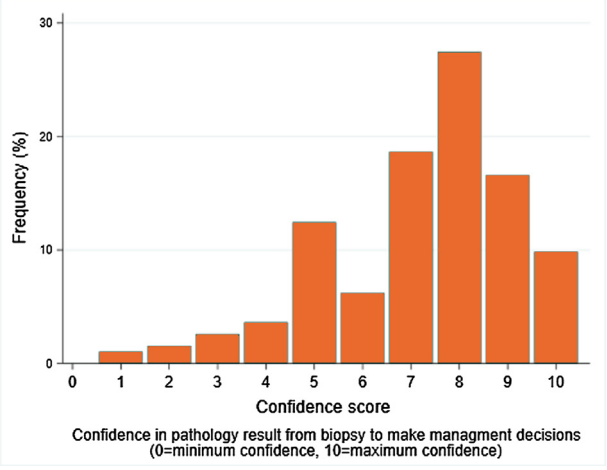

Fig. 2 – Confidence in the pathology result for a renal tumour biopsy to be able to make management decisions for small renal masses on a 10-point Likert scale, where 0 = minimum confidence and 10 = maximum confidence. The mean score was 7.3 (standard deviation 2.0).

In their current practice, RTB is a radiologist-delivered service according to 75% of respondents, urologist-delivered according to 17%, a mixture according to 2%, and other/unknown according to 6%. When asked which professional(s) should perform RTB (with appropriate training), 54% of the respondents identified urologists and 75% identified radiologists.

Regarding research gaps, we asked what evidence would increase the likelihood of recommending a diagnostic RTB to patients with an SRM. The most favoured option was a trial demonstrating that RTB results in better clinical outcomes (93.3%), followed by evidence that benign/indolent tumours do not require active treatment (85.7%), a trial demonstrating better quality of life for patients undergoing RTB (71.7%), and cost-effectiveness (52.0%).

3.2. *Patient survey*

A total of 54 patients responded to the survey, representing a 59% response rate. The demographics of the respondents are reported in Table 3. Of 31/54 (57%) respondents with a personal history of a renal mass, 13/31 (42%) recalled being offered RTB, 15/31 (48%) were not offered RTB, and three of 21 (10%) were unsure if they had been offered RTB.

Respondents were asked to report their preferences for a range of hypothetical clinical scenarios (Fig. 3). In the event of an initial nondiagnostic attempt at RTB, 29/54 (54%) would opt for a second attempt, nine of 54 (17%) would prefer to proceed to active treatment, 11/54 (20%) would opt for a period of surveillance, and five of 54 (9%) were unsure.

Regarding participation in research, 28/54 respondents (52%) indicated they would be willing and 13 (24%) that they might be willing to take part in a trial of RTB for SRMs (meaning that they had a 50:50 chance of undergoing RTB) to help in deciding on the best treatment option.

4. Discussion

We report responses to a cross-sectional survey of European practice and perception relating to RTB from a range of multidisciplinary HCPs and patients. Respondents to both surveys indicated that the result of an RTB for an SRM could influence management decisions. Patients would be more likely to choose active treatment of an SRM if RTB histology

Table 3 – Demographic data for respondents to the patient survey

Parameter	Respondents, *n*/*N* (%)
Age	
<18 yr	0
18–30 yr	8/54 (14.8)
31–40 yr	8/54 (14.8)
41–50 yr	6/54 (11.1)
51–60 yr	13/54 (24.1)
61–70 yr	12/54 (22.2)
71–80 yr	6/54 (11.1)
>80 yr	1/54 (1.85)
Gender (n = 54)	
Male	36 (66.7)
Female	18 (33.3)
Other/Prefer not to say	0 (0)
Ethnicity	
White	53/54 (98.2)
Black	0
Asian	0
Mixed or multiple ethnicity	1/54 (1.9)
Other	0
Prefer not to say	0
Country of residence	
Estonia	2/54 (3.7)
Germany	10/54 (18.5)
Greece	10/54 (18.5.)
Italy	25/54 (46.3)
UK	7/54 (13.0)
Personal experience of a kidney mass	
Yes	31/54 (57.4)
No	23/54 (42.6)
Lesion detection	
Incidental	19/31 (61)
On investigation of related symptoms (eg, blood in urine)	7/31 (23)
Unsure	1/31 (3.3)
Setting	
Hospital	25/31 (81)
Community	6/31 (19)
Anticoagulant use	
Yes	8/31 (26)
No	23/31 (74)

was suggestive of high-grade disease, and less likely to choose active treatment if their SRM was benign. However, our survey results suggest that only a minority of patients are offered RTB in contemporary European practice.

Our HCP survey results show similar variation to regional and national surveys of urologists from the USA and Canada, which revealed that HCPs pursue RTB for a cT1a renal masses in anything from <25% (53–59% of respondents) to >50% of cases (13–25% of respondents) [15,16]. In comparison, 70% of our HCPs respondents reported that <30% of patients are offered RTB, while 14% reported that >50% of patients are offered this option. To the best of our knowledge, our survey represents the first report on multidisciplinary practice and the first in a European setting regarding RTB for SRMs. Furthermore, this is the first survey to include responses from patients as important stakeholders.

Our HCP respondents tended to favour RTB for patients with comorbidities, a single kidney, chronic kidney disease, or multiple tumours, while RTB was not favoured for cystic tumours, SRMs in a challenging location (eg, anterior), or for patients taking anticoagulant medication. These tendencies are in keeping with current guidelines [9,11] and reported practice [15,17].

Lack of availability was a factor that influenced the decision to offer RTB (66.7%). The turnaround time for pathology results was acceptable, with 63.1% available within 2 wk and 92.7% within 3 wk. Shifting the setting in which RTB is delivered from overnight admission to day-case and outpatient settings may improve access in scenarios in which inpatient capacity is a limiting factor. Bringing RTB into the practice of urologists in addition to radiologists may be appropriate in addressing access limitations, and was supported by 54% of the HCP respondents. Alternatively, or in addition, "one-stop" diagnostic clinics that combine consultation, imaging, and biopsy could be trialled; these have been used for other solid organs for many years, with high levels of patient satisfaction [18].

Alternative methods for risk stratification of renal tumours using multiparametric magnetic resonance imaging [19], novel radionucleotide imaging techniques [20–22], radiomics [23], and urine and serum biomarkers [24] are currently being investigated. Such tests could overcome some of the limitations of RTB, such as the inability to account for tumour heterogeneity, and are noninvasive. While current recommendations restrict the use of such tools to research settings, we note that 75% of clinicians responding to our survey had access to ^{99m}Tc-sestamibi single-photon emission computed tomography/computed tomography, which is routinely used for diagnostic imaging of other organs such as the parathyroid and myocardium.

Limitations of our survey include a small sample size relative to the number of HCPs working in this field, lack of representations of some European countries, lack of validation for the survey translations, and over-representation of academic institutions. In a universal health care setting, Richard et al [15] found no association between the clinical setting (academic vs nonacademic) and the proportion of patients offered biopsy. It has been shown that RTB utilisation varies between private and academic hospital settings [7], and our relatively few responses from clinicians in the private sector limit any conclusions that can be drawn for that setting. Approximately half of our respondents had <5 yr of clinical experience, which is not reflective of clinical decision-makers in urological oncology. According to a UK urology workforce report, 80% of consultants in urological oncology are aged >45 yr [25]. This discrepancy is probably because the survey was distributed via professional networks of young academic urologists and residents. However, we would expect less experienced respondents to report practice that is reflective of their departments and mentors, and the results are therefore still of value and potentially more generalisable. Approximately half of the HCPs who responded to the survey (101/205, 48%) practice in Italy, albeit from 16 different cities/regions, meaning that this country was over-represented.

SRM diagnosis, risk stratification, and management are becoming increasingly nuanced, with options that include RTB, active surveillance (as supported by an expanding evidence base) [26,27], thermal ablation [28,29], and surgery, which is currently the preferred recommendation in guidelines [9–11]. Core outcomes for informed consent to treatment have been defined and include patient satisfaction with the quality and amount of information disclosed during the consent process, feeling that there was a choice, and an opportunity to ask questions [30]. Results from our

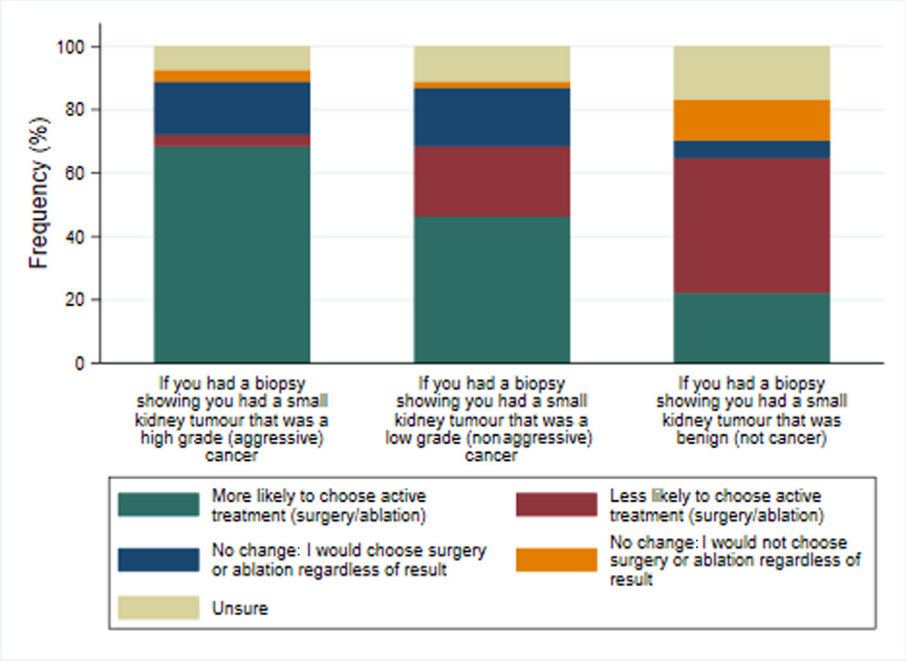

Fig. 3 – Patient preferences when considering biopsy results in different hypothetical clinical scenarios (*n* = 54).

HCP and patient surveys suggest that the majority of patients with SRMs are not offered RTB as an option. In the event of a biopsy-confirmed low-grade renal cancer, 65% of responding patients stated that they would choose some form of active treatment, despite evidence supporting the safety of surveillance in this setting [26,27]. Public health messaging on the importance of early diagnosis and treatment of cancer can make it challenging for patients to accept active surveillance of confirmed cancer. In order to avoid overtreatment, clinicians have a duty to discuss the safety and prognostic value of an initial period of surveillance with their patients. In our survey, 72% of HCPs reported that the time they spend in counselling a new patient with an SRM is <20 min. It is possible that this is simply not enough time to raise all the available options appropriately.

HCPs reported that further research is needed to demonstrate that RTB use improves patient outcomes, and that benign and indolent tumours do not require active treatment. The former could be addressed via a prospective randomised controlled trial of RTB, which 74% of patients responded that they would or might agree to participate in. The latter will be addressed as prospective cohort studies of patients on active surveillance for SRMs mature [26,27].

5. Conclusions

In conclusion, risk stratification and treatment of SRMs are increasingly nuanced. Patients should be offered RTB for SRM where it is feasible to aid in treatment decision-making. Further work is required to ensure timely access to an RTB service, and further research is needed to support expansion of RTB.

Author contributions: Riccardo Campi and Hannah Warren had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Warren, Campi, Tran.
Acquisition of data: Warren, Rautio, Marandino, Pyrgidis, Tzelves, Roussel, Muselaers, Erdem, Palumbo, Amparore, Wu, Ciccarese, Diana, Borregales, Pavan, Pecoraro, Caliò, Klatte, Carbonara, Marchioni, Bertolo, Campi, Tran.
Analysis and interpretation of data: Warren.
Drafting of the manuscript: Warren.
Critical revision of the manuscript for important intellectual content: Warren, Rautio, Marandino, Pyrgidis, Tzelves, Roussel, Muselaers, Erdem, Palumbo, Amparore, Wu, Ciccarese, Diana, Borregales, Pavan, Pecoraro, Caliò, Klatte, Carbonara, Marchioni, Bertolo, Campi, Tran.
Statistical analysis: Warren.
Obtaining funding: None.
Administrative, technical, or material support: None.
Supervision: Campi, Tran.
Other: None.

Financial disclosures: Riccardo Campi certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: Hannah Warren is supported by research fellowships from The Urology Foundation, The Pan London Cancer Alliance, and the Royal College of Surgeons of England. Maxine G.B. Tran is a member of the European Association of Urology kidney cancer guidelines panel and the National Institute for Health and Care Excellence kidney cancer guideline committee and has received honoraria for educational engagements and events from MSD and Boston Scientific. The remaining authors have nothing to disclose.

Funding: None.

Acknowledgments: We would like to thank all the health care providers and patients who completed this survey.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2024.02.002.

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