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Testicular cancer survivors are at risk of developing testosterone deficiency, which can result in metabolic syndrome and poor cardiac health.\(^1\)\(^-\)\(^5\)

The European Society for medical Oncology recommends measurement of testosterone levels during follow-up.\(^6\)

References:
1. [List of references related to testicular cancer and testosterone deficiency.]
2. [Another reference related to metabolic syndrome and cardiac health.]

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Growth and renal function dynamics of renal oncocytomas in patients on active surveillance

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Objectives
To study the natural history of renal oncocytomas and address indications for intervention by determining how growth is associated with renal function over time, the reasons for surgery and ablation, and disease-specific survival.

Patients and Methods
The study was conducted in a retrospective cohort of consecutive patients with renal oncocytoma on active surveillance reviewed at the Specialist Centre for Kidney Cancer at the Royal Free London NHS Foundation Trust (2012 to 2019). Comparison between groups was performed using Mann–Whitney U-tests and chi-squared tests. A mixed-effects model with a random intercept for patient was used to study the longitudinal association between tumour size and estimated glomerular filtration rate (eGFR).

Results
Longitudinal data from 98 patients with 101 lesions were analysed. Most patients were men (68.3%) and the median (interquartile range [IQR]) age was 69 (13) years. The median (IQR) follow-up was 29 (26) months. Most lesions were small renal masses, and 24% measured over 4 cm. Over half (64.4%) grew at a median (IQR) rate of 2 (4) mm per year. No association was observed between tumour size and eGFR over time ($P = 0.871$). Nine lesions (8.9%) were subsequently treated. Two deaths were reported, neither were related to the diagnosis of renal oncocytoma.

Conclusion
Natural history data from the largest active surveillance cohort of renal oncocytomas to date show that renal function does not seem to be negatively impacted by growing oncocytomas, and confirms clinical outcomes are excellent after a median follow-up of over 2 years. Active surveillance should be considered the ’gold standard’ management of renal oncocytomas up to 7 cm.

Keywords
active surveillance, cohort study, renal function, renal neoplasm, renal oncocytoma

Introduction
Renal oncocytomas are the most commonly excised benign renal tumour [1], representing 4% to 7% of lesions in surgical series [2,3]. Incidence is higher when considering clinical T1 tumours, as the average oncocytoma size is between 4 and 5 cm [2,3]. Renal oncocytomas are frequently diagnosed incidentally [3] and have excellent prognosis [4]. Several reports showcase the safety of active surveillance for renal oncocytomas diagnosed after renal tumour biopsy [5–12]. Nonetheless, the
adoption of renal tumour biopsy for the diagnosis of renal masses has been slow. Consequently, the vast majority of oncocytomas are still diagnosed after surgical excision [2].

The underutilization of renal tumour biopsy, the overtreatment of renal oncocytomas and the iatrogenic morbidity of surgery have been well documented [2]. Nevertheless, a number of concerns with regards to the natural history of renal oncocytoma mean that clinicians are still divided, with many opting for interventional management rather than a period of surveillance. Amongst these concerns, is the fear that tumour growth will lead to a decrease in renal function and to the development of symptoms, and that there is a risk of metastatic disease and death from undiagnosed hybrid tumours. Previous reports have suggested that renal oncocytomas measuring more than 5 cm or that grow 5 mm or more per year on surveillance should be definitively treated [6].

In the present study, we report on the follow-up of the largest cohort of patients with renal oncocytoma on active surveillance to increase our understanding of the natural history of these lesions. Our objective was to address the concerns currently provided as indications for definitive treatment of renal oncocytomas, including assessment of tumour growth effects on renal function over time, reasons for definitive treatment, and disease-specific and overall survival on active surveillance.

**Patient and Methods**

**Data Collection**

We conducted a retrospective study of consecutive patients reviewed at the Specialist Centre for Kidney Cancer at Royal Free London NHS Foundation Trust between 2012 and 2019. Data collection was last performed on 6 January 2021. Inclusion criteria included age ≥18 years, one or more renal lesions histologically diagnosed as renal oncocytoma, management with active surveillance, and availability of longitudinal data (i.e. at least two radiological assessments performed more than 1 month apart). Patients with renal oncocytosis mentioned on the histopathological report and with discordant biopsy/surgery histopathological results were excluded from the analyses. Histological diagnosis was obtained using renal tumour biopsy or after surgery. At our unit, we routinely offer renal tumour biopsy to all patients diagnosed with small renal masses, as well as to patients with larger lesions if the results would change the patient’s choice of management, if there are competing comorbidities increasing the risk of surgery, or if there is chronic kidney disease (CKD). We do not perform tumour biopsy in patients who consider surgical excision their preferred treatment, regardless of whether their tumour was benign or cancer. Excluding non-diagnostic renal tumour biopsies, the overall benign biopsy diagnostic rate is 17.7% at our unit, with rates of 21.8% and 9.0% for lesions measuring up to 4 cm, and over 4 cm, respectively [13]. Patients diagnosed with a renal oncocytoma on biopsy are routinely offered active surveillance.

Demographic data, age-adjusted Charlson comorbidity index, symptomatic status, estimated GFR (eGFR), tumour size, complexity and multifocality, time of follow-up (time from first to last scan), management decisions and reasons, and clinical outcomes were collected. Paired tumour size and eGFR data were collected for each patient if the scan and blood test were carried out in the same 3-month period.

**Definitions**

The diagnosis of renal oncocytoma was made by specialist uropathologists after analysis of biopsy and surgical specimens using the classically described criteria. Tumours were often unencapsulated and composed of small solid nests of uniform polygonal cells arranged in clusters within a loose connective tissue stroma; cells had abundant, eosinophilic granular cytoplasm, small round nuclei and, evenly dispersed chromatin [14]. Nuclear atypia of varying degrees was accepted as well as vascular and perinephric fat invasion [14]. Immunohistochemical staining criteria were: positivity for CD117; weak or incomplete membranous staining with E-cadherin; negativity or <5% expression of CK7; and; negative RCC and vimentin staining [14].

Tumour size was defined as the largest axis as provided on the radiological report. A small renal mass (cT1a) was defined as a lesion with the largest axis measuring 4 cm or less. A large renal mass (≥cT1b) was defined as a lesion with the largest axis measuring more than 4 cm. A lesion that grew at a rate of 5 mm or more per year was deemed fast growing. Categorization into CKD stages was based solely on eGFR. CKD stage III was defined as 30 ≤ eGFR < 60 ml/min/1.73m², CKD stage IV as 15 ≤ eGFR < 30 ml/min/1.73m², and CKD stage V as eGFR < 15 ml/min/1.73m², as defined by international guidelines [15].

**Statistical Analysis**

Continuous variables are presented as median, first quartile (Q1), third quartile (Q3), interquartile range (IQR), minimum (min) and maximum (max) values. Categorical variables are presented as absolute (n) and relative (%) frequencies.

Comparison between groups was tested using the Mann–Whitney U-test for continuous variables and the chi-squared test for categorical variables.

A linear mixed-effects model with a random intercept for patient was used to study the association between tumour size and eGFR over time. Variables included in the model were paired tumour size and eGFR, sex, age, and age-adjusted
Charlson comorbidity index. Only patients with paired tumour size and eGFR data over at least two time points were included in the model. Patients with more than one renal lesion were excluded from this analysis. Paired data were only available for lesions measuring between 10 and 80 mm, so the model was limited to the same size frame.

Statistical significance was set at $P = 0.05$. Analysis was performed using STATA/SE 13.0. Plots were created using Microsoft Excel, STATA/SE 13.0 and SankeyMATIC (http://sankeymatic.com).

Results

The total cohort of histological diagnoses of renal oncocytona comprised 192 lesions in 185 patients. One hundred and thirteen lesions (110 patients) were managed using active surveillance. Longitudinal data were available for 98 patients with 101 lesions (Figure S1).

Baseline demographic, clinical and lesion characteristics are depicted in Table 1. The majority of patients were male ($n = 69, 68.3\%$) and the median (IQR) age was 69 (13) years. The median (IQR) age-adjusted Charlson comorbidity index was 3 (3; 77\% estimated 10-year survival rate). The majority of patients were diagnosed incidentally ($n = 84, 83.2\%$).

Most lesions were unifocal ($n = 66, 65.3\%$). The median lesion size was 34 (15) mm; 76.2\% of lesions were small renal masses ($n = 77$), and 23.8\% were large renal masses (4–7 cm: $n = 22$; >7 cm: $n = 22$). Most lesions were diagnosed using renal tumour biopsy (95.0\%, $n = 96$), but a few initially managed with active surveillance were diagnosed after surgery without previous biopsy (5\%, $n = 5$). Patients with 22 of the large lesions did not proceed to upfront surgery and the lesions were initially biopsied for the following reasons: bilateral renal lesions ($n = 6$), patient choice ($n = 4$), single functioning kidney ($n = 1$), chronic kidney disease ($n = 1$), and presence of comorbidities ($n = 10$). After biopsy confirming renal oncocytona, these patients opted to pursue active surveillance instead of surgery.

Table 1 Baseline demographic, clinical and lesion characteristics.

| Total number of patients | 98 |
|--------------------------|----|
| Women, n (%)             | 29 (38.7) |
| Median (Q1, Q3; min, max) age, years | 69 (62, 75; 39, 87) |
| Median (Q1, Q3; min, max) age-adjusted | 3 (2, 5; 0, 11) |
| Charlson Comorbidity Index | Asymptomatic, n (%) | 84 (83.1) |
| Total lesions, n         | 101 |
| Unifocal lesion, no other renal lesions, n (%) | 66 (65.3) |
| Histologically proven multifocal | 3 (3) |
| Oncocytoma, n (%)        | 34 (25, 40, 5, 88) |
| Median (Q1, Q3; min, max) lesion size, mm | 34 (25, 40, 5, 88) |
| Small renal masses (cT1a), n (%) | 77 (76.2) |
| Large renal masses (≥cT1b), n (%) | 24 (23.8) |

Growth Dynamics

Renal oncocytona longitudinal growth data is detailed in Table 2 and shown in Fig. 1. The median (IQR) follow-up was 29 (26) months. Over half ($n = 65, 64.4\%$) of renal oncocytonas grew during active surveillance, but 13.7\% ($n = 14$) reduced in size over time. Growing lesions grew at a median (IQR) rate of 2 (4) mm per year.

Approximately a quarter ($n = 19, 24.7\%$) of all small renal masses grew over the 4-cm threshold, 13\% ($n = 10$) were fast growers and 9.1\% ($n = 7$) fitted both categories. One in seven small renal masses decreased in size ($n = 11, 14.3\%$).

Out of all large renal masses, 20.8\% ($n = 5$) grew at a fast rate $\geq$5 mm/year. Interestingly, 12.5\% ($n = 3$) of cT1b lesions decreased in size and 8.3\% ($n = 2$) were small renal masses at the last follow-up. One lesion (4.2\%) decreased more than 1 cm in size during follow-up (from 47 to 36 mm in 12 months).

At the last follow-up, a total of 41 lesions (40.6\%) were large renal masses.

Longitudinal Assessment of Renal Function

Baseline eGFR and CKD stage were available for 89 patients (90.8\%). The median (Q1, Q3; min, max) eGFR was 75 (62, 87; 16, 156) mL/min/1.43m$^2$. One patient already on haemodialysis prior to diagnosis had CKD stage V. Five patients (5.1\%) had a single kidney at diagnosis.

Estimated GFR and CKD stage at last follow-up were available for 66 patients (67.7\%). The median (Q1, Q3; min, max) eGFR was 71 (64, 86; 18, 130) mL/min/1.43m$^2$.

Figure 2 shows changes in eGFR categories during follow-up for patients with both baseline and final eGFR available for analysis ($n = 59, 60.2\%$). A total of 20 patients (33.9\%) changed CKD category during follow-up. No patient progressed from CKD stage III to IV or V, or started renal replacement treatment or had a renal transplant during follow-up.

The association between tumour size and eGFR over time was explored using a mixed-effects model with a random intercept for patient, and adjusted for sex, age and age-adjusted Charlson comorbidity index. All paired tumour size and eGFR datapoints available were used for analysis. No association was observed between the two variables ($P = 0.871$). The model is plotted in Fig. 3. Individual longitudinal paired data are plotted in Figure S2.

Definitive Intervention

Nine lesions (8.9\%) had interventional treatment after follow-up: one (1\%) with percutaneous cryoablation, three (3\%) with
minimally invasive partial nephrectomy and five (4.9%) with minimally invasive radical nephrectomy. Of the eight surgically treated patients, five did not have a biopsy prior to surgery. All surgical cases had a final diagnosis of renal oncocytoma.

Seven lesions were treated due to lesion growth; five were sized over 4 cm at time of surgery, including four that exhibited fast growth (≥5 mm/year). Growth between diagnosis and surgery ranged from 3 mm in 12 months to 18 mm in 42 months.

Two of the treated patients had no previous biopsy or any lesion growth; active surveillance had been chosen as the initial strategy because of relative contraindications for intervention (pulmonary embolism, and need for lobectomy for lung cancer, respectively). Patients opted to proceed directly to surgery when the contraindications no longer existed (6 months after diagnosis). No patient chose interventional treatment as a result of new or ongoing symptoms attributable to the renal oncocytoma.

All patients treated with radical nephrectomy had lesions that were not amenable to nephron-sparing surgery on initial radiological diagnosis. Thus, in this study cohort no patient lost the opportunity to undergo partial nephrectomy rather than radical nephrectomy by virtue of being on active surveillance.

Table 2 Baseline size and growth pattern of renal oncocytomas, grouped by size.

| Follow-up (months) | All | Small renal masses | Large renal masses | P value |
|--------------------|-----|--------------------|--------------------|---------|
| n                  | 101 | 77                 | 24                 | NA      |
| Size at diagnosis (mm) | Median (Q1, Q3, min, max) | 34 (25, 40, 5, 88) | 30 (22, 35, 5, 40) | 47 (43, 57, 41, 88) | <0.001 |
| Size at last follow-up (mm) | Median (Q1, Q3, min, max) | 36 (28, 45, 12, 92) | 33 (26, 40, 12, 99) | 51 (44, 59, 36, 92) | <0.001 |
| Overall growth rate (mm/year) | Median (Q1, Q3, min, max) | 1 (0.3, -10, 17) | 1 (0.3, -5, 13) | 1 (0.4, -10, 17) | 0.899 |
| Growing lesions n (%) | 65 (64.4) | 50 (64.9) | 15 (62.5) | 0.828 |
| Yeary growth rate (mm/year) | Median (Q1, Q3, min, max) | 2 (1, 5, 0, 17) | 2 (1, 4, 0, 13) | 3 (1, 5, 0, 17) | 0.584 |
| Growth ≥5 mm/year n (%) | 15 (23.1) | 10 (20.0) | 5 (33.3) | 0.282 |
| Growth to cT1b n (%) | 19 (29.2) | 19 (38.0) | NA | NA |
| Growthover 4 cm and ≥5 mm/year n (%) | 7 (10.8) | 7 (14.0) | NA | NA |
| Stable lesions n (%) | 22 (21.8) | 16 (20.8) | 6 (25.0) | 0.662 |
| Regressing lesions n (%) | 14 (13.9) | 11 (14.3) | 3 (12.5) | 0.825 |
| Regress to cT1a n (%) | 2 (14.3) | NA | 2 (66.7) | NA |

Small renal masses: ≤4cm, cT1a. Large renal masses: >7cm, cT1b. NA, not applicable. Bold indicates statistically significant value.

Figure 1 Waterfall plot depicting baseline and size change for all lesions. Each lesion is represented by a bar. Baseline size is represented in blue. Size change at last follow-up is depicted in orange.
Disease-free and Overall Survival

Two deaths (2%) were reported, one due to an ischaemic leg, the other as a result of glioblastoma. No deaths were related to the diagnosis of renal oncocytoma.

Discussion

We report on a comprehensive analysis of natural history data from the largest active surveillance cohort of renal oncocytomas to date [5–12], and provide strong evidence that whilst the majority of oncocytomas grow over time, lesion growth is not associated with renal function decline for lesions measuring up to 7 cm. In addition, no patient elected to undergo interventional treatment because of the development of symptoms. These analyses challenge long-standing concerns that often underly the upfront routine surgical (over)treatment of renal oncocytomas, and provide clinicians with evidence to support an active surveillance management strategy for these benign tumours.

We show, in line with other reports, that more than half of renal oncocytomas grow during active surveillance [5,7–9,11] with a quarter of these fitting the criteria for fast growth (≥5 mm/year) [10,11]. Also, similarly to previous reports [10,11], we note that approximately one in seven oncocytomas decrease in size during follow-up. Uniquely, we also provide natural history data for the largest subcohort of oncocytomas larger than 4 cm, which is clinically relevant as approximately 80% of renal oncocytomas measure up to 7 cm [2]. Our analysis is consistent with previously published excellent outcomes for large oncocytomas on active surveillance [8,16]. A large oncocytoma seems to be as likely to grow as a smaller one. In the present cohort, the development of symptoms was not a trigger for intervention. Indeed, previous reports cite a similar experience [6,7,10].

Oncocytosis is a very rare phenomenon characterized by multiple oncocytic tumours and diffuse infiltration of the kidney by oncocytes and has been associated with renal failure [17,18]. Renal oncocytosis has a distinct morphological, immunohistochemical and cytogenetic profile compared to oncocytoma and is considered a separate entity [19]. For this reason, patients diagnosed with renal oncocytosis were excluded from the present study.

Our longitudinal analysis of paired lesion growth and eGFR provides evidence that, for single oncocytomas, growth is not associated with deterioration of renal function and supports similar findings from other groups [12]. A recent publication suggested that active surveillance for renal oncocytomas is associated with higher renal function decline than partial nephrectomy, and advocated surgery over monitoring [20]. However, in our view, the unreported and unmeasured confounding biases that led to the choice of initial management strategy (active surveillance vs partial nephrectomy) [21] is likely to have contributed significantly to the decline in renal function in the cohort studied.

Limitations of the present analysis include the lack of central pathology or radiology review. The cohort may be biased by the exclusion of patients with lesions treated with upfront...
surgery or ablation, which are likely to be larger in size. Another limitation may have been the use of the largest axis measurement as a surrogate for tumor volume; however, previous reports suggest that these correlate well [6]. A median follow-up of 29 months also limits predictions of long-term outcomes. Finally, analyses and precision may have been influenced by data scarcity for both renal function and large renal lesions.

To conclude, in this paper we report clinically relevant outcomes that can aid in patient and clinician decision making and consultation. We show in the present study that fears of deteriorating renal function, or symptom development due to oncocytoma growth seem to be unfounded for lesions up to 7 cm. Although longer-term outcomes need to be established, the present study adds significantly to the accruing body of evidence that active surveillance is safe and should be the ‘gold standard’ management for renal oncocytomas measuring up to 7 cm.

Conflicts of Interest
None declared.

References
1 Ljunghberg B, Hedin O, Lundstam S et al. Nephron sparing surgery associated with better survival than radical nephrectomy in patients treated for unforeseen benign renal tumors. Urology. 2016; 93: 117–21
2 Neves JB, Withington J, Fowler S et al. Contemporary surgical management of renal oncocytoma: a nation’s outcome. BJU Int. 2018; 121: 893–9
3 Amin MB, Amin MB, Tamboli P et al. Prognostic impact of histologic subtyping of adult renal epithelial neoplasms: an experience of 405 cases. The American Journal of Surgical Pathology. 2002; 26(3): 281–291
4 Van der Kwast T, Perez-Ordonez B. Renal oncocytoma, yet another tumour that does not fit in the dualistic benign/malignant paradigm? J Clin Pathol. 2007; 60: 585–6
5 Bosniak MA, Birnbaum BA, Krinsky GA, Waisman J. Small renal parenchymal neoplasms: further observations on growth. Radiology. 1995; 197: 589–97
6 Neuzillet Y, Lechevallier E, Andre M, Daniel L, Nahon O, Coulange C. Follow-up of renal oncocytoma diagnosed by percutaneous tumor biopsy. Urology. 2005; 66: 1181–5
7 Siu W, Hafez KS, Johnston IWK, Wolf JS Jr. Growth rates of renal cell carcinoma and oncocytoma under surveillance are similar. Urologic Oncology 2007; 25: 115–9
8 Kawaguchi S, Fernandes KA, Finelli A, Robinette M, Fleshner N, Jewett MA. Most renal oncocytomas appear to grow: observations of tumor kinetics with active surveillance. The Journal of urology. 2011; 186: 1218–22
9 Kurup AN, Thompson RH, Leibovich BC et al. Renal oncocytoma growth rates before intervention. BJU international. 2012; 110: 1444–8
10 Liu S, Lee S, Rashid P et al. Active surveillance is suitable for intermediate term follow-up of renal oncocytoma diagnosed by percutaneous core biopsy. BJU Int. 2016; 118(Suppl 3): 30–4
11 Richard PO, Jewett MA, Bhatt JR, Evans AJ, Timilsina N, Finelli A. Active surveillance for renal neoplasms with oncocytic features is safe. The Journal of urology. 2016; 195: 581–6
12 Miller BL, Mankowski Gettle L, Van Roo JR et al. Comparative analysis of surgery, thermal ablation, and active surveillance for renal oncocytic neoplasms. Urology. 2018; 112: 92–7
13 Tanabal C, Neves J, Patki P et al. Routine renal mass biopsy in diagnosis of renal cancer. European Urology Supplements. 2018; 17: e420–e1
14 Wobker SE, Williamson SR. Modern pathologic diagnosis of renal oncocytoma. J Kidney Cancer VHL. 2017; 4: 1–12
15 Stevens PE, Levin A. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. Ann Intern Med. 2013; 4(158): 825–30
16 Mehrzad R, Smalldone MC, Kutikov A et al. Growth kinetics and short-term outcomes of cT1b and cT2 renal masses under active surveillance. Journal of Urology. 2014; 192: 659–64
17 Warfel KA, Eble JN. Renal oncocytomatosis. J Urol. 1982; 127: 1179–80
18 Tickoo SK, Reuter VE, Amin MB et al. Renal oncocytosis: a morphologic study of fourteen cases. Am J Surg Pathol. 1999; 23: 1094–101
19 Gobbo S, Eble JN, Delahunt B et al. Renal cell neoplasms of oncocytosis have distinct morphologic, immunohistochemical, and cytogenetic profiles. Am J Surg Pathol. 2010; 34: 620–6
20 Meagher MF, Lane BR, Capitanio U et al. Comparison of renal functional outcomes of active surveillance and partial nephrectomy in the management of oncocytoma. World Journal of Urology. 2021; 39: 1195–1201.
21 Warren H, Neves JB, Tran MGB. Oncocytoma: risk of promoting unnecessary surgery. World Journal of Urology. 2020. http://doi.org/10.1007/s00345-020-03347-0

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Abbreviations: CKD, chronic kidney disease; eGFR, estimated GFR; IQR, interquartile range.

Supporting Information
Additional Supporting Information may be found in the online version of this article:

Figure S1. CONSORT diagram of cases.
Figure S2. Plot of longitudinal paired tumour size and estimated glomerular filtration rate (eGFR) data.
