



Predictors of growth kinetics and outcomes in small renal masses (SRM ≤ 4 cm in size): Tayside Active Surveillance Cohort (TASC) Study[☆]

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Abstract

Objective: To determine outcomes of small renal masses (≤ 4 cm) on active surveillance and explore factors which can influence their growth.

Patients and methods: Two hundred twenty six patients between January 2007 and December 2014 were analysed using cross-linked methodology of healthcare data and independent review. Cancer specific and non-specific survival were the primary outcomes. Growth kinetics, factors influencing growth and need for interventions were secondary outcomes.

Results: 101 (64.4%) solid and 4 (5.9%) cystic SRMs showed growth. 43 (19.02%) of SRMs required treatment interventions. Seven patients (7/158; 4.4%) died due to renal cancer at a median follow-up of 21.7 (SD 10.6, min 6–42) months, all in solid category. Independent review of serial radiological imaging of these seven cases showed two patients had subtle metastatic disease at the initial presentation, and 5 of the 7 did not adhere to recommended imaging regime. 33 (33/158; 20.8%) died due to other causes including non-renal cancers (14/158; 8.8%). Multivariate analyses showed that lower eGFR at baseline, co-morbidities and tumour location were independently associated with growth in size.

Conclusions: A higher cancer-specific mortality was seen in the present study compared to the reported literature. Independent critical review of imaging of cases with poor outcome underscored the importance of adherence to a robust protocol including follow up. Comorbid conditions had a significant impact on growth and overall survival of patients with SRMs.

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Keywords: Small renal masses; Active surveillance; Co-morbidities; Outcomes; Growth patterns

Introduction

Predictors of growth and progression in SRMs on active surveillance remain poorly defined mainly due to a dearth of good quality longitudinal observational data.^{1–4} The universal healthcare model in the National Health Services (NHS) of the United Kingdom has the advantage of studying longitudinal observational data, especially through linkage methodology using a common identifier such as unique Community Health Care Index (CHI) number. The universal healthcare cover to a population in a well-defined geographical area provides an ideal environment to study natural history of diseases such as early renal cancer (SRMs), in particular outcomes of continued surveillance. Electronic

[☆] Abstracts of this work partly presented at: 1. American Urology Association Meeting, May 6–10, 2016; San Diego, USA. Podium-PD46-08: Factors that predict growth kinetics in solid renal masses (< 4 cm) on active surveillance. *J Urol*; vol. 195, 4S Supplement, 2016. 2. Academic Urology meeting, British Association of Urological Surgeon Meeting, December 2015, London, United Kingdom. Podium: Growth Kinetics in small renal masses on active surveillance. *Clin. J Urol* (in press). 3. World Congress of Endourology, 15th Oct. 2015, London, United Kingdom. Poster presentation e944: Baseline estimated glomerular filtration rate influences need for intervention in small renal masses.

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patient records including demographic, clinical episodes, imaging and histopathology data can easily be linked to answer research question. Third party certification and review by independent body of the data where researchers have little influence remains a significant advantage. One of the key questions in SRMs remains cancer-specific and non-cancer specific mortality in patients opting for active surveillance. What influences growth of these masses is also not known, in particular influence of co-morbid conditions has not been reported.^{5,6} Multiple chronic medical ailments are associated with poorer outcomes, morbidities of treatment, complications following surgery, poorer quality of life, psychological distress, and higher mortality. This knowledge base should inform the appropriate follow-up for patients diagnosed with SRMs. In a large population based cohort in a well-defined geographical area we aimed to address the following objectives:

1. Assess progression and outcomes (cancer specific and overall survival) in both cystic and small renal masses.
2. Explore factors which can influence progression of these masses including impact of co-morbid conditions.

Patients and materials

Study cohort

The TUCAN (Tayside Urological Cancers Network Database) collects routine data from the patient population affected by urological cancers in Tayside, Scotland. NHS Tayside serves a population of more than 405,721 based on mid-year 2011 population estimates published by the General Register Office for Scotland. Each inhabitant of this area has a 10 digit CHI number and health records can be accessed using this common identifier. Patients were identified from TUCAN Database using validated record linkage methodology as described previously.⁷ All patients with SRM in this defined population were recorded in a database after discussion in multidisciplinary tumours board meetings using an agreed data sheet (Supplementary material). The study had an initial and updated Institutional approval (Caldicott/CSAppGN021211; Caldicott/IGTCAL2973). Two hundred twenty six patients who opted for active surveillance for SRMs after review at multidisciplinary meetings and face-to-face meetings with an urologist between January 2007 and December 2014 were identified and recruited into the study. One hundred fifty eight patients were diagnosed with solid SRMs. Sixty eight were identified as cystic masses.

Outcome data

Patients opting for active surveillance for SRMs were imaged at regular interval (6–12 months) using CT/MR scans and reviewed in multidisciplinary meetings if reported any change in size. All imaging data and reports were available on CARESTREAM Vue Picture Archiving and

Communication System (PACS) (<http://www.carestream.com/specials/campaign/search-pacs>) for review and follow-up. Similarly clinic letters and other communications including re-admissions, blood investigations were available on Clinical Portal System of the organization. There were only a few patients where ultrasound was used for follow-up with immediate conversion to CT scan in case of any suspicious of growth or poor visualization. The information was retrieved for a number of demographic variables: age, gender, and Scottish Index of Multiple Deprivation (SIMD). The SIMD is a scoring system utilized by Scottish Government to identify areas of deprivation (www.scotland.gov.uk/topics/statistics/SIMD). The system uses a quintile scoring system, which classifies geographical areas as most deprived¹ to least deprived.⁵ Clinical factors included growth in size, initial presentation (symptomatic versus asymptomatic), multiplicity, Charlson index, location of tumour, and baseline eGFR (at least 3 months prior to the diagnosis) and most recent eGFR (within last 3 months of most recent scan).

Primary outcomes and interventions

Primary outcome of the study was cancer-specific and non-cancer specific survival of patients on active surveillance. Secondary outcomes were growth of SRMs. Cystic SRM growth was defined as an increase in cyst complexity and migration of a class to a higher level and was determined by the uro-radiologist mainly based on changes in the wall or septal enhancement, increased nodularity, or calcifications over a time period on follow-up scans. Tumour growth of solid SRM was defined as any increase in the maximum axial dimensional size (two axial measurements perpendicular to each other) found on scans over a time period. All SRMs were reviewed in multidisciplinary tumour meetings at the time of initial diagnosis and on follow-up, if there was increase in growth.

Surgical excision/interventions were offered for solid SRMs more than 4 cm in size, those opting for change in surveillance protocol following increase in size on imaging (but still less than 4 cm) and in younger patients with reluctance to follow-up. Similarly, surgical intervention was offered in cystic masses classified following MDT review for Bosniak III or IV and follow-up for Bosniak IIF (see Fig. S1 for TASC management algorithm, Supplementary files). The type of surgical procedure, pathological outcome including benign or malignant, presence of metastases and progression, and cause of death was recorded as an indicator of outcome.

Independent review of records and imaging data

Patients developing metastases were reviewed in multidisciplinary meetings (radiologist, urologists, pathologist and renal oncologist) and their record linkage was reviewed by at least two experienced researchers to ascertain the clinical events. Cancer-specific deaths were reviewed by an

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