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EUO Collaborative Review – Kidney Cancer

Role of Active Surveillance for Localized Small Renal Masses

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Abstract

Context: Stage migration of organ-confined renal masses is occurring as a result of incidental diagnosis, especially in the elderly. Active surveillance (AS) is gaining clinical traction as a treatment alternative to surgery and focal therapy.

Objective: To assess contemporary data and evaluate AS risk trade-offs in the treatment of organ-confined kidney cancer.

Evidence acquisition: A comprehensive search of the Embase, Medline and Cochrane databases was carried out. A systematic review of the role of AS for organ-confined renal masses was performed. A total of 28 studies were included in the systematic review.

Evidence synthesis: The median linear tumor growth rate for clinically localized renal masses (CLRMs) was 0.37 cm/yr (interquartile range 0.15–0.7), with 0.22 cm/yr in the cT1a subgroup and 0.45 cm/yr in the cT1b––2 subgroup. The metastatic progression rate was 1–6% and was similar for cT1a (1–6%) and cT1b (0–5%); other-cause mortality for patients with CLRMs was 0–45% (1–25% for cT1a vs 11–13% for cT1b–2); cancer-specific mortality ranged between 0% and 18%. According to the 2011 Oxford scale, AS as a treatment option for CLRMs remains supported by level 3 evidence.

Conclusions: Although no randomized clinical data are available, current data support oncologic safety for AS in the management of CLRMs, particularly for small renal masses and among elderly and/or comorbid patients.

Patient summary: In this review we looked at the outcomes for patients with small kidney masses managed with surveillance. We found that surveillance is a safe initial option for tumors of less than 2 cm, especially in elderly and sick patients.

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1. Introduction

The incidence of renal cell carcinoma (RCC) steadily increased from 1975 through 2008, mostly because of incidental detection via cross-sectional imaging [1,2]. In Western European countries, this incidence rise has plateaued over the past decade; however, the number of cases diagnosed has continued to increase in Eastern Europe [3]. Globally, approximately 380 000 cases of kidney cancer are diagnosed yearly and 116 000 people die from the disease. The greatest increase in diagnosis of kidney cancer has been in the last decade of life [4]. Most patients now present with a small renal mass (SRM), defined as a renal mass of $\leq$4 cm in diameter. As many as 20–30% of such masses are benign, but 20% exhibit potentially aggressive biologic behavior [5]. However, even in patients with aggressive tumors, the risk of other-cause mortality often overshadows the risk of RCC death [6,7]. Thus, the optimal treatment strategy for patients with s renal mass requires a nuanced balance of risks, with active surveillance (AS) often representing a superior strategy over intervention.

In the present review, available data on the role of AS for clinically localized renal masses (CLRMs) are systematically analyzed to obtain clinically relevant evidence for evaluating the AS risk trade-offs for the treatment of organ-confined kidney cancer.

2. Evidence acquisition

2.1. Search strategy

A comprehensive search of the Embase, Medline, and Cochrane databases was performed. The search included English language articles reporting on renal masses and surveillance from January 2000 to December 2017. The query search terms “surveillance”, “renal mass”, “renal cell carcinoma”, “kidney cancer”, “watchful waiting”, and “observation” yielded 6403 abstracts.

2.2. Inclusion criteria

As recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines, we used the population, intervention, comparator and outcomes (PICO) approach to define study eligibility [8]. Studies were considered relevant to the current systematic review when they included adult patients (age $>$18 yr) diagnosed with a CLRM and enrolled on AS to compare growth rates and oncologic outcomes.

The following study types were considered eligible for inclusion in our systematic review: (1) randomized control trials (RCTs) or quasi-RCTs; and (2) in the absence of available RCTs, comparative nonrandomized prospective or retrospective studies reporting on oncologic outcomes for patients under AS for CLRM (suspicious for cT1 or cT2 RCC). Studies had to include at least ten participants with minimum follow-up of 1 yr to assess the primary outcome. Pathologic confirmation by means of renal tumor biopsy (RTB) was not mandatory for consideration; radiological features indicating an enhancing renal mass were deemed sufficient. Therefore, this review does not include just patients with RCC undergoing AS. Case reports, editorials, letters, and conference abstracts were not eligible and were excluded during the systematic review process. Review articles were used to identify potential informative data not included in the paper selection. Only articles published in English were considered. Finally, if two or more studies reported results for overlapping AS series, the one with the largest sample was selected for inclusions.

2.3. Systematic review process

After duplicates were removed, two authors (M.C.M. and U. C.) completed an independent review of 136 abstracts and selected 35 articles for separate full-text evaluation, in accordance with the aforementioned inclusion criteria. A PRISMA flow chart outlining the systematic literature search and selection of studies for inclusion is shown in Fig. 1. A total of 28 manuscripts were included.

The primary outcome was overall survival (OS) at 2 and 5 yr. The secondary outcomes were cancer-specific survival (CSS) at 2 and 5 yr, tumor growth kinetics, delayed surgical intervention rates, and progression to metastatic disease during follow-up.

2.4. Data extraction

A standardized data extraction form was created a priori to collect study-level data, including the study design, number of participants, age, staging, length of follow-up, pathology features, and rates of growth and metastatic progression.

2.5. Data analysis

In the absence of RCTs, a narrative synthesis of the studies included was performed using descriptive statistics to summarize the extracted data on baseline characteristics. Continuous outcomes were described using the median and interquartile range (IQR) or the mean and standard deviation, as appropriate. Categorical outcomes were described using frequencies and percentages. Crude rates of relevant outcomes at available time points, as well as unadjusted and adjusted hazard rations (HRs) with 95% confidence intervals (CIs), were extracted. Two-sided statistical significance was set at a p value of $<$0.05 for all studies included.

2.6. Assessment of the risk of bias and confounding

The risk of bias for each study included was assessed by two reviewers (M.C.M. and U.C.) working independently. The quality of the studies was assessed using the standard Cochrane Collaboration risk of bias tool, which comprises seven domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias [9]. The risk of confounding bias was high (Fig. 2, red) if the confounder

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