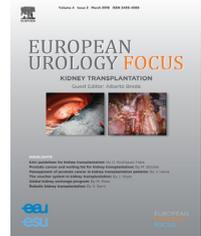


available at [www.sciencedirect.com](http://www.sciencedirect.com)  
journal homepage: [www.europeanurology.com/eufocus](http://www.europeanurology.com/eufocus)



Mini Review

# The Harms of Overdiagnosis and Overtreatment in Patients with Small Renal Masses: A Mini-review

Erica M. Sohlberg<sup>a</sup>, Thomas J. Metzner<sup>a,b</sup>, John T. Leppert<sup>a,b,c,\*</sup>

<sup>a</sup> Department of Urology, Stanford University School of Medicine, Stanford, CA, USA; <sup>b</sup> The Stanford Kidney Cancer Research Program, Stanford, CA, USA;

<sup>c</sup> Veterans Affairs Palo Alto Health Care System, Palo Alto, CA, USA

## Article info

### Article history:

Accepted March 10, 2019

Associate Editor: Malte Rieken

### Keywords:

Renal mass  
Kidney cancer  
Overdiagnosis  
Overtreatment

## Abstract

Overdiagnosis and overtreatment refer to the detection and treatment of conditions that would not ultimately affect an individual's health. With increasing detection of small renal masses there is growing awareness of the overdiagnosis and overtreatment of these tumors, supported by studies showing that 15–30% of nephrectomy specimens are pathologically benign, and that many small renal cell carcinomas are indolent. The harms of overdiagnosis and overtreatment are numerous, including psychosocial stressors and renal morbidity, in addition to unnecessary surgical complications. A greater understanding of the potential harms of overdiagnosis and overtreatment is crucial as clinicians focus on optimizing patient selection for renal mass biopsy, active surveillance protocols, and minimally invasive surgery.

**Patient summary:** In this mini-review we discuss the issues of overdiagnosis and overtreatment in patients with kidney cancer. We enumerate the risks of overdiagnosis and overtreatment, and examine the next steps towards preventing these harms.

Published by Elsevier B.V. on behalf of European Association of Urology.

\* Corresponding author. Department of Urology, Stanford University School of Medicine, 300 Pasteur Drive, Stanford, CA 94305, USA.

E-mail address: [jleppert@stanford.edu](mailto:jleppert@stanford.edu) (J.T. Leppert).

## 1. Introduction

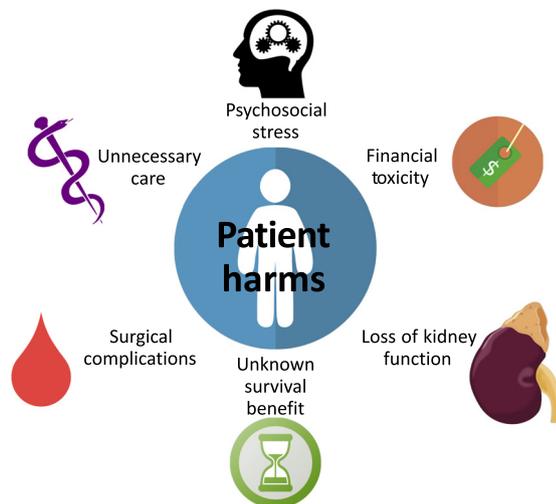
The incidence of renal cell carcinoma (kidney cancer) has been increasing worldwide, with more than 300 000 new cases now diagnosed annually [1]. This rising incidence is probably due in part to the widespread use and increasing sensitivity of abdominal imaging. The detection of small renal masses has caused a stage migration for patients diagnosed with kidney cancer such that the majority of patients are diagnosed with localized disease, which has a 5-yr survival of >90%. In addition, small renal masses and kidney cancers are often diagnosed in the sixth decade of life, when competing risks of mortality are common. While

more kidney cancers are being detected and treated, survival among patients with kidney cancer has not improved as dramatically [1].

For these reasons, there is a need to increase awareness of the potential overdiagnosis and overtreatment of patients diagnosed with kidney cancer. Overdiagnosis refers to the detection of a small renal mass that would not go on to cause symptoms or death [2]. Similarly, overtreatment refers to the removal of a benign renal mass or a kidney cancer that would either never progress or progress “slowly enough that the patient would die of other causes before the cancer becomes symptomatic” [2]. A patient diagnosed with a renal mass can be exposed to many harms (Fig. 1).

<https://doi.org/10.1016/j.euf.2019.03.006>

2405–4569/Published by Elsevier B.V. on behalf of European Association of Urology.



**Fig. 1 – Potential patient harms from overdiagnosis and overtreatment of small renal masses.**

## 2. Harms of overdiagnosis

Abdominal imaging has the ability to incidentally detect small, asymptomatic renal masses. As current imaging techniques are unable to definitively distinguish benign tumors, many patients receive a diagnosis of kidney cancer based solely on the detection of a small renal mass. This can subsequently cause psychological stress stemming not only from concern about survival, but also from uncertainty and changes in identity. In a recent study, 27% of patients undergoing treatment for kidney cancer were found to require psychosocial care [3]. Even patients with early-stage kidney cancer described anxiety, pain, sadness, and difficulty in sleeping [3]. Furthermore, a cancer diagnosis often leads patients to seek additional medical care, may adversely alter patients' financial and social planning, and can increase the odds of suicide [3]. The understanding of the impact of a cancer diagnosis and its potential to lead to unnecessary testing has increased calls to restrain the use of unnecessary imaging studies [4].

## 3. Underutilization of active surveillance

The detection of a small renal mass often leads to surgical treatment. In the USA, regional rates of abdominal imaging are strongly associated with the rates of kidney surgery [5]. Sadly, as many as one-third of patients treated with partial nephrectomy discover that they underwent surgery to remove a benign lesion [6]. The diffusion of robotic kidney surgery appears to be associated with increasing surgical treatment of small renal masses, which is outpacing active surveillance even among elderly patients [7]. Prospective data show that active surveillance of small renal masses is associated with 100% 5-yr cancer-specific survival [8]. Moreover, initial active surveillance can also help in identifying tumors with worrisome growth and in guiding selection for definitive treatment. Clearly, active surveillance—the ultimate nephron-sparing approach—remains underutilized [9].

## 4. Underutilization of renal mass biopsy

While renal mass biopsy has the potential to provide histological confirmation of cancer, it is underutilized. From 1992 to 2007, only one in five patients undergoing radical or partial nephrectomy underwent renal mass biopsy before surgery, although rates of biopsy are slowly increasing [10]. With current techniques, renal mass biopsy is safe and has a diagnostic accuracy of >90%. However, routine renal mass biopsy may not be appropriate for all patients with a small renal mass. Renal mass biopsy remains limited in its ability to reliably determine tumor grade. In addition, efforts are needed to determine when treatment can be avoided in healthy patients with long life expectancy. Moreover, a renal mass biopsy itself may represent overtreatment in older frail patients, for whom active surveillance might be the default management regardless of histologic confirmation of renal cell carcinoma.

## 5. Harms of overtreatment: surgical complications

While operative complications are the most obvious danger resulting from overtreatment of small renal masses with surgery, complications associated with partial and radical nephrectomy have decreased over time [11]. However, while most patients tolerate kidney surgery well, the risks of kidney surgery include blood transfusion (5% of minimally invasive surgeries, and up to 20% of open surgeries), reoperation (2–5%), prolonged ventilation and respiratory complications (1–7%), and even death [11]. The 90-d mortality rate following partial or radical nephrectomy has been reported to be as high as 4.3% [5]. For older or comorbid patients, the risks of surgery may significantly outweigh the risks of undertreatment of a small renal cell carcinoma.

## 6. Renal morbidity following kidney cancer surgery

In addition to surgical complications, the long-term health effects of a decrease in kidney function after kidney surgery remain an ongoing issue. Small changes in kidney function have been associated with significant adverse health outcomes, such as cardiovascular events, hospitalization, and death. While the benefits of preserving kidney function remain unclear, partial nephrectomy has become a standard surgical approach for preserving renal parenchyma and kidney function. However, patients who undergo partial nephrectomy are typically younger and healthier [12]. This suggests that the patients most vulnerable to renal insult are being left out.

## 7. Strategies to minimize overdiagnosis and overtreatment

Until there is a proven screening test for kidney cancer, efforts to minimize the harms of overdiagnosis and overtreatment will require patient-centered approaches (Fig. 2). Curbing inappropriate abdominal imaging studies may limit the overdiagnosis of asymptomatic small renal masses.

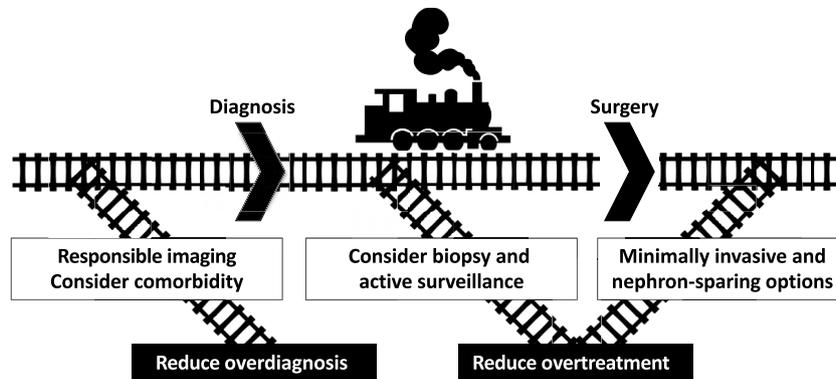


Fig. 2 – While the detection of a renal mass often leads directly to treatment, there are opportunities to limit the overdiagnosis and overtreatment of small renal masses.

Overtreatment can be minimized by encouraging the use of active surveillance for patients with limited life expectancy and multimorbidity. Renal mass biopsy can also help in risk-stratifying patients and in guiding treatment selection. Finally, ongoing research efforts to develop biomarkers that can personalize care for kidney cancer patients will be critical.

8. Conclusions

The harms resulting from both overdiagnosis and overtreatment are diverse, and there is now a greater onus on clinicians to both recognize these risks and to appropriately counsel patients. Shared decision-making and better patient selection tools will ultimately help in guiding treatment selection and in minimizing the morbidity in patients diagnosed with a small renal mass.

**Author contributions:** John T. Leppert 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:** Sohlberg, Metzner, Leppert.

**Acquisition of data:** None.

**Analysis and interpretation of data:** None.

**Drafting of the manuscript:** Sohlberg, Metzner, Leppert.

**Critical revision of the manuscript for important intellectual content:** Sohlberg, Metzner, Leppert.

**Statistical analysis:** None.

**Obtaining funding:** None.

**Administrative, technical, or material support:** Sohlberg, Metzner, Leppert.

**Supervision:** None.

**Other:** None.

**Financial disclosures:** John T. Leppert 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: None.

**Funding/Support and role of the sponsor:** None.

**Acknowledgments:** The content here does not represent the views of the US Department of Veterans Affairs or the US Government.

References

- [1] Scelo G, Larose TL. Epidemiology and risk factors for kidney cancer. *J Clin Oncol* 2018;26:3574–81.
- [2] Welch HG, Black WC. Overdiagnosis in cancer. *J Natl Cancer Inst* 2010;102:605–13. <http://dx.doi.org/10.1093/jnci/djq099>.
- [3] Draeger DL, Sievert KD, Hakenberg OW. Analysis of psychosocial stress factors in patients with renal cancer. *Adv Urol* 2018;10:175–82.
- [4] Oren O, Kebebew E, Ioannidis JPA. Curbing unnecessary and wasted diagnostic imaging. *JAMA* 2019;321:45–6. <http://dx.doi.org/10.1001/jama.2018.20295>.
- [5] Welch HG, Skinner JS, Schroeck FR, Zhou W, Black WC. Regional variation of computed tomographic imaging in the United States and the risk of nephrectomy. *JAMA Intern Med* 2018;178:221–777. <http://dx.doi.org/10.1001/jamainternmed.2017.7508>.
- [6] Kim JH, Li S, Khandwala Y, Chung KJ, Park HK, Chung BI. Association of prevalence of benign pathologic findings after partial nephrectomy with preoperative imaging patterns in the United States from 2007 to 2014. *JAMA Surg* 2019. <http://dx.doi.org/10.1001/jamasurg.2018.4602>, in press.
- [7] Shah PH, Alom MA, Leibovich BC, et al. The temporal association of robotic surgical diffusion with the overtreatment of the small renal mass. *J Urol* 2018;200:981–8.
- [8] Pierorazio P, Johnson M, Ball M, et al. Five-year analysis of a multi-institutional prospective clinical trial of delayed intervention and surveillance for small renal masses: the DISSRM registry. *Eur Urol* 2015;68:408–15.
- [9] Nguyen K, Nolte A, Alimi O, et al. Determinants of active surveillance in patients with small renal masses. *Urology* 2019;123:167–73.
- [10] Leppert JT, Hanley J, Wagner TH, et al. Utilization of renal mass biopsy in patients with renal cell carcinoma. *Urology* 2014;83:774–9.
- [11] Liu JJ, Leppert JT, Maxwell BG, Panousis P, Chung BI. Trends and perioperative outcomes for laparoscopic and robotic nephrectomy using the National Surgical Quality Improvement Program (NSQIP) database. *Urol Oncol* 2014;32:473–9.
- [12] Leppert JT, Mittakanti HR, Thomas IC, et al. Contemporary use of partial nephrectomy: are older patients with impaired kidney function being left behind? *Urology* 2017;100:65–71.