

# Review of the efficacy and safety of cryoablation for the treatment of small renal masses

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## Abstract

**Purpose:** Small renal masses are increasingly being discovered incidentally on imaging for another reason. The standard of care of these masses involves excision by open or laparoscopic techniques. Recently, ablative techniques, such as radiofrequency ablation (RFA) and cryoablation, have taken a more prominent role in the treatment algorithm of these masses. We evaluate the effectiveness and safety of cryoablation to treat renal tumours.

**Methods:** A review of the literature was conducted. There was no language restriction. Studies were obtained from the following sources: the Cochrane Library, PUBMED, EMBASE and LILACS.

**Results:** There was no clinical trial identified in the literature. Thus, we described the results from 23 case series and retrospective studies with a reasonable sample size (number of reported patients in each study  $\geq 30$ ), with a total of 2104 analyzed tumours from 2038 patients. There was wide variability in the outcomes reported, but success rates were generally good. Follow-up was generally short, but some series reported outcomes at 5 years. The most common complications reported were hemorrhage (some of the patients requiring transfusion), perinephric hematoma and urine leaks.

**Conclusion:** Cryoablation presents a feasible treatment for patients with small renal masses. Only short-term data are available and, as such, meaningful conclusions regarding long-term cancer control cannot be made. More rigorous studies are needed.

## Introduction

In Canada, the incidence of renal cancer is 4500 new cases per year, with 1500 dying of the disease.<sup>1</sup> Small renal masses are increasingly being discovered incidentally on imaging for another reason.<sup>2,3</sup> The natural history of these incidentally discovered masses remains unclear. When surgically excised, the masses are shown to be 70% to 80% renal cell carcinoma (RCC), and the rest are benign.<sup>4-7</sup>

When technically feasible, the standard of care for these masses has been partial and radical nephrectomy. Local and distant oncological control has been well-established

with surgical excision.<sup>8</sup> In the last 10 years, a minimally invasive approach with laparoscopy has largely supplanted open surgery. The question of whether in situ ablative technologies<sup>9,10</sup> can replace excision for the treatment of small renal tumours remains unanswered. The main advantage of ablative techniques would be to offer treatment to patients who are otherwise not candidates for invasive extirpative techniques.<sup>11,12</sup>

Several ablative technologies have been investigated, including cryoablation (CA), radiofrequency ablation (RFA), microwave,<sup>13</sup> high-intensity focused ultrasound,<sup>14,15</sup> laser interstitial thermotherapy,<sup>16</sup> microwave thermotherapy and radiosurgery.

Cryoablation has been used to treat human cancers since the 19th century, with the use of ice-salt mixtures to treat cervical and breast cancers.<sup>17</sup> In urology, CA has long been used to treat prostatic diseases: first for benign prostatic hyperplasia in the 1960s,<sup>18</sup> and later for prostate cancer.<sup>19</sup> Freezing and thawing causes alteration in various biological processes that ultimately result in cell death. CA targets and kills specific cells and spares surrounding tissue, which can be critical in patients with compromised renal function and small RCC.

In the last few years, several series have reported the results of CA for small renal masses with short to intermediate follow-up. A meta-analysis of case series studies evaluating CA and RFA showed no significant difference regarding clinical efficacy (the authors defined it as cancer-specific survival rate, radiographic success, no evidence of local tumour progression or distant metastases) and intraoperative and postoperative complications rates between both interventions.<sup>20</sup>

In this review, we examine the efficacy of CA to treat renal tumours. The efficacy of this technology in terms of oncological control and prevention of local recurrence and metastasis is reviewed. Complications and safety concerns as they relate to CA will also be reported.

## Methods

There was no language restriction. Trials were obtained from the following sources: Cochrane Central Register of Controlled Trials (Central, The Cochrane Library, issue 1, 2011), US National Library of Medicine (PUBMED; 1966-2011), Excerpta Medica database (EMBASE; 1980-2011), Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS; 1982-2011) and the Current Controlled Trials to identify all studies regarding cryoablation in RCC.

The databases were searched using a comprehensive search strategy for kidney cancers and cryoablation, along with MeSH and text words, including an exhaustive list of synonyms (Table 1). The search strategy was adapted for each database to achieve more sensitivity. The bibliographic references in relevant review articles were also examined for eligible trials. The search was performed up to January 2011. In total, 696 titles were identified from the electronic databases. After screening by title and then abstract by two reviewers, full paper copies for 64 studies that were potentially eligible for inclusion in the review were obtained. The remaining 632 were off-topic, animal research, narrative reviews or *in vitro* studies. No randomized trials were identified, and therefore, the results from case series and retrospective studies with a reasonable sample size (number of reported patients in each study  $\geq 30$ ) were included in this review.

The following clinical outcome measurements were examined: cancer-specific survival, radiographic success, tumour recurrence, local tumour progression or distant metastases, need for repeat ablation, complications, adverse events and renal function.

## Results

Table 2 summarizes the characteristics of published studies on CA. Most patients undergoing CA had T1a disease with a mean tumour size ranging from 1.8 to 4.2 cm. The laparoscopic approach was the most commonly used approach, although the percutaneous and open approaches were also employed. The maximum mean and median follow-up reported was 45.7 months and 36 months, respectively.

Table 3 shows the clinical outcomes and complications reported in the examined CA studies. Cancer-specific survival, recurrence tumour rates and radiographic or technical success were the most commonly used outcomes to evaluate oncological control. Lack of contrast enhancement, decrease in tumour size, or lack of growth on serial imaging were considered signs of complete and successful ablation. The maximal and minimal percentage of cancer-specific survival reported was 100% and 84.3% in a follow-up of 11.4 months (median) and 64 months (mean), respectively. The most commonly reported complications were: hemor-

**Table 1. Summary of the bibliographic search strategies for type of clinical situation and intervention of interest.**

(Kidney Neoplasm) OR (Renal Neoplasms) OR (Renal Neoplasm) OR (Kidney Neoplasms) OR (Cancer of Kidney) OR (Kidney Cancers) OR (Renal Cancer) OR (Renal Cancers) OR (Cancer of the Kidney) OR (Kidney Cancer) OR (Kidney Cancers) OR (Renal masses) OR (Renal cell carcinoma) AND (Cryosurgeries OR Cryosurgery OR Cryoablation OR Cryoablations OR Cryotherapy)

rhage (some of the patients requiring transfusion), perinephric hematoma and urinary leak. Nonetheless, the procedures seem to be well-tolerated.

## Discussion

The principle of tissue freezing with CA involves the Joule Thomson phenomenon, whereby rapid cooling results from the rapid phase change of a highly compressed liquid expanding through a restricted orifice to a gaseous state. The mechanism of cellular injury by CA is a result of direct and indirect physiological processes. When the extracellular fluid freezes, there is an increase in osmotic pressure in the extracellular compartment. The resulting fluid shift causes cellular dehydration, accumulation of toxins within the cells, change in pH and denaturation of proteins. The disruption of the cellular membrane leads to crystallization of the intracellular fluid. In addition, endothelial damage leads to ischemia, thrombosis and coagulative necrosis, synergizing cell death.<sup>21,22</sup>

Imaging with computed tomography (CT) scans or magnetic resonance imaging (MRI) is the typical follow-up for cryoablated tumours, although a specific follow-up protocol has not been widely accepted. Tumour size may increase in early follow-up due to peri-tumour hemorrhage, and the difficulty in determining tumour margin from surrounding fibrosis and stranding.<sup>23-25</sup> However, any enhancement on CT scan ( $>10$  HU) or a progressive increase in tumour size is a sign of inadequate ablation. On MRI, 61% of adequately treated tumours are isointense to renal parenchyma on T1-weighted images, and 95% are either isointense or hypointense on T2 weighted images.<sup>26</sup> It remains unclear if radiological follow-up either by CT scan or MRI constitutes an adequate surrogate for local cancer control. Preoperative biopsies of these renal masses were uncommon in most series, even less so postoperative biopsies. One exception was the series by Gill and colleagues; the authors routinely performed biopsies at 6 months post-CA. In this series, 2 out of 56 tumours proved to be positive at 6 months post-CA, for a rate of 3.6%.<sup>27</sup> In a prostate cancer model, where CA has been more extensively studied, positive biopsies post-CA have been found in up to 23.1% of patients in a post-radiotherapy CA model.<sup>28</sup> While it may be stipulated that the prostate cancer model is not necessarily an apt comparison given the multi-focal nature of prostate cancer versus a solid

**Table 2. Case series and retrospective studies on cryoablation for renal tumours**

Study	Design of study	Comparative intervention	Patients (n)	Tumours (n)	Mean tumour size or range on preoperative (cm)	Tumour type Exophytic Parenchymal, central, mixed or others	Laparoscopic or Percutaneous Cryoablation	Follow-up (months)	
Atwell 2008 <sup>33</sup>	Retrospective	N/A	110	115	3.3	56	59	Percutaneous	13.3 <sup>b</sup>
Finley 2008 <sup>34</sup>	Retrospective	N/A	37	43	2.9	6	36	Percutaneous and laparoscopic	12.8 <sup>b</sup>
Georgiades 2008 <sup>35</sup>	Case series	N/A	46	40	3.0 <sup>c</sup>	NR		Percutaneous	28 <sup>c</sup>
Hinshaw 2008 <sup>36</sup>	Retrospective	N/A	90	90	Perc. 2.1 Lap. 2.5	NR		Percutaneous and laparoscopic	Perc. 14.5 <sup>b</sup> Lap. 16.5 <sup>b</sup>
Lehman 2008 <sup>37</sup>	Retrospective	N/A	44	51	Group 1 <sup>d</sup> 1.8 Group 2 <sup>d</sup> 4.0	32	19	Laparoscopic	Group 1: 9.0 <sup>b</sup> Group 2: 11.0 <sup>b</sup>
Nguyen 2008 <sup>38</sup>	Retrospective comparative	RFA	CA 14 RFA 22	CA 25 RFA 38	CA 3.0 RFA 2.8	NR		Laparoscopic and open	NR
Weight 2008 <sup>39</sup>	Retrospective comparative	RFA	CA 176 RFA 88	CA 192 RFA 109	CA 2.4 RFA 2.5	NR	CA 30 NR RFA 42	Laparoscopic	6
Atwell 2007 <sup>a,b,39-41</sup>	Retrospective	N/A	40	40	4.2	15	25	Percutaneous	9 <sup>b</sup>
Bandi 2007 <sup>42</sup>	Retrospective	N/A	78	88	2.6	NR		Percutaneous and laparoscopic	19 <sup>b</sup>
Cestari 2007 <sup>43</sup>	Retrospective	N/A	86	56	2.3	NR		Laparoscopic	24
Littrup 2007 <sup>44</sup>	Retrospective	N/A	48	49	3.3	30	19	Percutaneous	1.1 <sup>c</sup>
Lokken 2007 <sup>30</sup>	Retrospective comparative	RFA	253	287	3.0	NR		Percutaneous	52
Weld 2007 <sup>45</sup>	Case series	N/A	31	36	2.1	27	09	Laparoscopic	45.7 <sup>b</sup>
Wright 2007 <sup>29</sup>	Retrospective	N/A	32	35	1.9	32	03	Laparoscopic	18 <sup>c</sup>
Davol 2006 <sup>46</sup>	Retrospective	N/A	48	48	2.6	44	04	Laparoscopic and open	64 <sup>b</sup>
Hegarty 2006 <sup>47</sup>	Retrospective comparative	RFA	CA 161 RFA 72	CA 179 RFA 81	CA 2.56 RFA 2.51	NR NR	CA 6% RFA 37%	Laparoscopic	CA 36 <sup>c</sup> RFA 13 <sup>c</sup>
Lawatsch 2006 <sup>48</sup>	Case series	N/A	59	81	2.5	NR		Laparoscopic	26.8 <sup>c</sup>
Matin 2006 <sup>49</sup>	Retrospective comparative	RFA	CA 8 <sup>f</sup> RFA 55 <sup>f</sup>	N	3.85	39%	61%	Percutaneous and laparoscopic	24.2 <sup>b</sup>
Schwartz 2006 <sup>50</sup>	Retrospective	N/A	84	85	2.6	NR		Laparoscopic and open	10 <sup>b</sup>
Desai 2005 <sup>51</sup>	Retrospective comparative	LPN	CA 78 LPN 153	CA 89 LPN 153	CA 2.05 LPN 2.25	NR		Laparoscopic	CA 24.6 <sup>b</sup> LPN 5.8 <sup>b</sup>
Gill 2005 <sup>27</sup>	Case series	N/A	56	60	2.3	NR		Laparoscopic	36
Cestari 2004 <sup>52</sup>	Case series	N/A	37	NR	2.5	NR		Laparoscopic	20.5 <sup>b</sup>
Gill 2000 <sup>53</sup>	Case series	N/A	32	34	2.3	NR		Laparoscopic	12

RFA: Radiofrequency ablation; LPN: Laparoscopic partial nephrectomy; CA: cryoablation; N/A: not applicable; NR: not reported.

<sup>a</sup>A subset of these patients have been included in 2 prior publications (Atwell 2007a and Atwell 2007b); <sup>b</sup>Mean; <sup>c</sup>Mean; <sup>d</sup>In Group 1 the patients presented with a maximum tumour diameter less than 3.0 cm and, group 2 patients had a maximum tumour diameter of 3.0 cm or larger; <sup>e</sup>Atwell 2007 has two publications with the same participants; <sup>f</sup>Patients with residual or recurrent disease.

**Table 3. Clinical outcome and complications of each included studied**

Study	Outcomes		Complications*	
	Clinical outcome studied	Occurrence (%)	Major complications	Minor complications
Atwell 2008 <sup>33</sup>	Technical success <sup>a</sup> following a single ablation session	97%	Worsening preexisting hypertension (0.90%); pulmonary edema (0.90%); large hematomas requiring angiography and transfusion of red blood cells (2.7%); pulmonary embolus (0.90%) and hematuria requiring ureteral stent placement (0.90%)	
Finley 2008 <sup>34</sup>	CSS among patients with biopsy proven RCC during a median follow-up of 11.4 and 13.4 months	100% and 100%	Hemorrhage requiring transfusion (13.5%); blood transfusions (16.2%); internal jugular vein thrombus (2.7%); small bowel injury (2.7%) and loss of kidney (2.7%)	
	Treatment failure rate <sup>b</sup> among patients with biopsy proven RCC during a median follow-up of 11.4 and 13.4 months	5.3% and 4.2%		
Georgiades 2008 <sup>35</sup>	Technical success <sup>c</sup> Overall CR <sup>d</sup>	100% 97.5%	Silent, small perinephric hematoma; large, painful perinephric hematomas; intercostal nerve injury; genitofemoral nerve injury;	
Hinshaw 2008 <sup>36</sup>	Effectiveness rate <sup>e</sup> for laparoscopic CA	93.3%	Severe respiratory distress (1.1%); intraoperative bowel injury (1.1%) and postoperative atrial fibrillation (1.1%)	Asymptomatic perinephric hematoma; asymptomatic and self-limited urine leak; self-limited flank paresthesia and neuralgia; and intercostal neurapraxia (4.4%).
Lehman 2008 <sup>37</sup>	Tumour recurrences	Group 1: 0%	Group 1: no complications (0%)	
		Group 2: 4.8%	Group 2 (62%): mortality (4.5%); cerebrovascular accident; myocardial infarction; pulmonary embolism and; hemorrhage with blood transfusion	
Nguyen 2008 <sup>38</sup>	Tumour recurrences	CA 7.4% RFA 25%	Intraoperative complications: CA: renal arterial injury (21%); RFA: no major intraoperative complications reported on this group (0%)  Postoperative complications: CA: no major postoperative complications reported on this group (0%). RFA: no major postoperative complications reported on this group (0%).	Intraoperative complications: CA: diaphragmatic injury (7.1%); pleurotomy (requiring chest tube) (7.1%) and peritoneotomy (21%) RFA: no major intraoperative complications reported on this group (0%)  Postoperative complications: CA: urinary leak and anephric state (7.1%). RFA: no major postoperative complications reported on this group (0%).
Weight 2008 <sup>39</sup>	Radiographic success <sup>f</sup> at 6-months follow-up Radiographic success <sup>f</sup> with biopsy and 6-months imaging	CA 90% RFA 85%  CA 89% RFA 81%	NR	NR
Atwell 2007 <sup>a,b40,41</sup>	Technical success <sup>g</sup>	95%	Large hemorrhage and transient renal failure (necessitated temporary dialysis) (2.5%)	
Bandi 2007 <sup>42</sup>	Overall, CSS <sup>h</sup> and RFS <sup>i</sup> rates	88.5%, 100% and 98.7%, respectively	Atrial fibrillation (1.2%); respiratory failure (1.2%) and; urine leak (1.2%); bleeding (1.2%); bowel injury (1.2%); symptomatic perirenal haematoma (1.2%) and neurophatic pain (1.2%)	

CSS: cancer-specific survival; RCC: renal cell carcinoma; CR: complete response; CA: cryoablation; RFA: radiofrequency ablation; RFS: recurrence-free survival; CT: computed tomography; MRI: magnetic resonance imaging.

\*Percentages were calculated on a patient number basis; <sup>a</sup>Extension of the ice ball beyond the tumour margin and post-ablation images showing no contrast enhancement in the tumour parenchyma; <sup>b</sup>Not defined; <sup>c</sup>Completion of the cycle of a 10-minute freeze, 8-minute active thaw, and 10-minute repeat freeze with the ice ball covering the entire lesion and extending at least 5 mm beyond its border; <sup>d</sup>Complete lack of enhancement of a previously enhancing mass; <sup>e</sup>Complete ablation of macroscopic tumour as shown at imaging follow-up; <sup>f</sup>No evidence of central or nodular enhancement after treatment; <sup>g</sup>Extension of the ice ball beyond the tumour margin and postablation imaging findings of no contrast enhancement in the area encompassing the original tumour; <sup>h</sup>Absence of death from renal cancer; <sup>i</sup>No evidence of radiographic recurrence at the site of CA, regardless of the lesion pathology; <sup>j</sup>Not defined; <sup>k</sup>Continued contrast enhancement on postoperative CT; <sup>l</sup>An involuted scar or fibrosis without evidence of growth or enhancement on the most recently available imaging study; <sup>m</sup>Growth of a persistent renal mass, as well as the persistence or development of heterogeneous peripheral enhancement within any persistent mass.

**Table 3. Clinical outcome and complications of each included studied (cont'd)**

Study	Outcomes		Complications*	
	Clinical outcome studied	Occurrence (%)	Major complications	Minor complications
Cestari 2007 <sup>43</sup>	NR	NR	Minimal intraoperative blood loss (100%); intraoperative renal fracture (2.3%); postoperative anemia (8.1%); transitory hyperpyrexia (6.9%); hematoma (2.3%); pulmonary edema (1.1%); gross hematuria (1.1%) and ureteropelvic junction obstruction (1.1%)	
Littrup 2007 <sup>44</sup>	Technical success <sup>l</sup>	98%	Perinephric hematoma; hematuria and ureteral stricture. Major and minor complications were seen in 6% and 22% procedures, respectively	
Lokken 2007 <sup>30</sup>	Occurrence of applicator track nodules	CA 2.7% RFA 1.7%	CA: small perinephric hematoma (0.3%). RFA: self-limited hematuria and small perinephric hematoma (0.3%)	
Weld 2007 <sup>45</sup>	3-year CSS rate	100%	Hemorrhage (3.2%); urinary leak (3.2%); gross hematuria (3.2%); ileus (3.2%); perinephric urinoma (3.2%); hydronephrosis (3.2%); blood clots (3.2%); atrial fibrillation (3.2%); and heart failure (3.2%)	
	Mean increase of ablation zone size on follow-up CT or MRI at 3 months	14		
Wright 2007 <sup>29</sup>	Mean decrease of ablation zone size on follow-up CT or MRI at 3 months.	71	No major and minor complications were found (0%)	
	Treatment failures <sup>k</sup>	6%		
Daval 2006 <sup>46</sup>	Complete radiologic resolution <sup>l</sup> from a total of 40 patients available in the analysis	85%	There were no major adverse events found (0%) There were 7 minor adverse events (14.5%)	
	Treatment failure <sup>m</sup> from a total of 40 patients available in the analysis	12.5%		
	CSS rate in a total of 32 patients	100%		
	CSS rate after a single CA procedure in a total of 32 patients	84.3%		
Hegarty 2006 <sup>47</sup>	Radiologic evidence of tumour recurrence or persistence of disease;	CA 1.8% RFA 11.1%	CA: congestive heart failure (0.62%); myocardial infarct (0.62%); required thoracotomy for hemothorax (0.62%). RFA: no major complications were reported in the RFA group (0%).	
	CSS	CA 98% at a median 3-year follow-up RFA 100% at 1-year median follow-up		
Lawatsch 2006 <sup>48</sup>	Overall tumour recurrence rate per patient	5.9% in 34 patients	Intraoperative complications: open surgery conversion (3.3%); nephrectomy for bleeding (1.6%); myocardial infarction (1.6%); pneumothorax (3,3%) Postoperative complications: perinephric hematoma (1.6%); pulmonary embolus (1.6%) and ileus (3.3%)	
	Recurrence rate per lesion treated in patients with biopsy confirmed RCC	5.1% for 38 lesions		
Matin 2006 <sup>49</sup>	Overall survival rate in all patients from both groups	82.5%	NR	NR
	2-year metastasis-free survival rate in all patients from both groups	97.4%		
Schwartz 2006 <sup>50</sup>	No growth or evidence of recurrence on CT scan or MRI at 3 months	98.18%	Renal fracture (1.2%); stroke (1.2%) and hydronephrosis (1.2%)	
	Radiographic enhancement after the procedure	3.6%		

CSS: cancer-specific survival; RCC: renal cell carcinoma; CR: complete response; CA: cryoablation; RFA: Radiofrequency ablation; RFS: recurrence-free survival; CT: computed tomography; MRI: magnetic resonance imaging.

\*Percentages were calculated on a patient number basis; <sup>a</sup>Extension of the ice ball beyond the tumour margin and post-ablation images showing no contrast enhancement in the tumour parenchyma; <sup>b</sup>Not defined; <sup>c</sup>Completion of the cycle of a 10-minute freeze, 8-minute active thaw, and 10-minute repeat freeze with the ice ball covering the entire lesion and extending at least 5 mm beyond its border; <sup>d</sup>Complete lack of enhancement of a previously enhancing mass; <sup>e</sup>Complete ablation of macroscopic tumour as shown at imaging follow-up; <sup>f</sup>No evidence of central or nodular enhancement after treatment; <sup>g</sup>Extension of the ice ball beyond the tumour margin and postablation imaging findings of no contrast enhancement in the area encompassing the original tumour; <sup>h</sup>Absence of death from renal cancer; <sup>i</sup>No evidence of radiographic recurrence at the site of CA, regardless of the lesion pathology; <sup>j</sup>Not defined; <sup>k</sup>Continued contrast enhancement on postoperative CT; <sup>l</sup>An involuted scar or fibrosis without evidence of growth or enhancement on the most recently available imaging study; <sup>m</sup>Growth of a persistent renal mass, as well as the persistence or development of heterogeneous peripheral enhancement within any persistent mass.

**Table 3. Clinical outcome and complications of each included studied (cont'd)**

Study	Outcomes		Complications*	
	Clinical outcome studied	Occurrence (%)	Major complications	Minor complications
Desai 2005 <sup>51</sup>	Local recurrence at a mean follow-up time of 5.8 months in LPN group and 24.6 months in CA group	LPN 0.6% CA 3%	LPN associated with greater blood loss and a higher incidence of delayed complications after hospital discharge compared with CA 16.3% versus 2.2%, respectively	
Gill 2005 <sup>27</sup>	3-year CSS (in a total of 51 patients with sporadic unilateral renal tumour)	98%	NR	NR
Cestari 2004 <sup>52</sup>	Mean reduction of cryolesions on MRI 12 and 18 months of follow-up	73% and 76% (in a total number of patients 32 and 30, respectively)	Transitory hyperthermia (8.1%); hematoma (8.1%); gross hematuria (2.7%); low postoperative pain (100%); and ureteropelvic junction obstruction (2.7%)	
Gill 2000 <sup>53</sup>	Follow-up CT-directed needle negative biopsies at 3 to 6 months in a total of 23 patients	100%	Perirenal hematoma (3.1%) and herpes esophagitis (3.1%)	

CSS: cancer-specific survival; RCC: renal cell carcinoma; CR: complete response; CA: cryoablation; RFA: radiofrequency ablation; RFS: recurrence-free survival; CT: computed tomography; MRI: magnetic resonance imaging.

\*Percentages were calculated on a patient number basis; <sup>a</sup>Extension of the ice ball beyond the tumour margin and post-ablation images showing no contrast enhancement in the tumour parenchyma; <sup>b</sup>Not defined; <sup>c</sup>Completion of the cycle of a 10-minute freeze, 8-minute active thaw, and 10-minute repeat freeze with the ice ball covering the entire lesion and extending at least 5 mm beyond its border; <sup>d</sup>Complete lack of enhancement of a previously enhancing mass; <sup>e</sup>Complete ablation of macroscopic tumour as shown at imaging follow-up; <sup>f</sup>No evidence of central or nodular enhancement after treatment; <sup>g</sup>Extension of the ice ball beyond the tumour margin and postablation imaging findings of no contrast enhancement in the area encompassing the original tumour; <sup>h</sup>Absence of death from renal cancer; <sup>i</sup>No evidence of radiographic recurrence at the site of CA, regardless of the lesion pathology; <sup>j</sup>Not defined; <sup>k</sup>Continued contrast enhancement on postoperative CT; <sup>l</sup>An involuted scar or fibrosis without evidence of growth or enhancement on the most recently available imaging study; <sup>m</sup>Growth of a persistent renal mass, as well as the persistence or development of heterogeneous peripheral enhancement within any persistent mass.

renal neoplasm, the lack of data confirming complete ablation and necrosis of the treated renal tumours leaves this technique open to question regarding equivalence to more accepted extirpative methods.

This review demonstrates a wide variability in the definition of outcomes (i.e., technical success, radiographic success, local recurrence and cancer specific survival). Cancer-specific survival can be as low as 84.3%,<sup>29</sup> and radiographic resolution as low as 71%,<sup>30</sup> even with relatively short follow-up intervals. When juxtaposed with the fact that 20% to 30% of small renal masses are found to be benign when excised, the true efficacy of CA should be assumed to be lower than reported.<sup>4-7</sup> This highlights the need for longer follow-up, and for comparative trials with partial nephrectomy, or other ablative technologies, such as RFA.

CA is generally well-tolerated, but laparoscopic access is the most common technique. When compared to a partial nephrectomy, it has the advantage of not requiring hilar clamping, vascular and collecting system repair. However, a general anesthetic, and a pneumoperitoneum with all inherent complications remain essential. Hemorrhage, urinary leaks and injury to adjacent organs are all potential adverse events.

From a financial standpoint, CA compares favourably with other modalities for treatment of renal tumours. A financial analysis compared minimally invasive surgery procedures, such as laparoscopic cryoablation, laparoscopic partial nephrectomy and hand-assisted laparoscopic nephrectomy, versus conventional surgery. The open radical nephrectomy had higher total hospital costs (\$15 498), followed by laparoscopic partial nephrectomy (\$15 458). The lowest total

hospital costs was laparoscopic cryoablation (\$10 105) for renal tumours smaller or equal than 3.5 cm.<sup>31</sup> However, in a more robust Markov model which factored the costs of follow-up and re-treatment, an immediate laparoscopic ablation procedure was found to be dominated by laparoscopic, and open partial nephrectomy for healthy patients less than 74 years old in terms of Quality Adjusted Life Years (QALY). Even in patients with multiple comorbidities, observation followed by possible delayed percutaneous ablation dominated immediate laparoscopic ablation.<sup>32</sup>

## Conclusions

The results of this review show that cryoablation is a feasible treatment for patients with small renal masses. Long-term follow-up is lacking, but the available short-term data demonstrate a significant re-treatment rate. Given the lack of long-term follow-up, the technique should be reserved for elderly patients, or those with significant comorbidities, whose masses have demonstrated growth after a period of observation. Otherwise, partial nephrectomy remains the gold standard.

Continued research on cryoablation in the treatment of small renal tumours is needed, especially comparative trials with partial nephrectomy and other ablative technologies, such as RFA.

**Competing interests:** None declared.

This paper has been peer-reviewed.

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