ISSN 1392–0995, ISSN 1648–9942 (online)

http://www.chirurgija.lt
LIETUVOS CHIRURGIJA
Lithuanian Surgery
2016, 15 (2–3), p. 96–103

Repeated percutaneous cryoablation and radiofrequency ablation for renal tumors in a solitary kidney: report of two cases

Pakartotinė inkstų navikų krioabliacija ir radijo dažnio abliacija esant vieninteliam inkstui: dviejų klinikinių atvejų aprašymas

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Introduction

Percutaneous cryoablation and radiofrequency ablation are options of minimally invasive treatment while maximizing nephron preservation. It is increasingly used in patients with comorbid conditions, multiple renal cell carcinomas, for patients with a single kidney and/or inherited renal cancer syndromes especially in situations when there is a need to preserve renal function. The aim of this presentation is to show the benefits (effectiveness and safety) of cryoablation for the patients with a solitary kidney from our experience.

Case reports

We present 2 cases of the patients with a solitary kidney and solid renal masses of <4 cm who underwent percutaneous cryoablation and radiofrequency ablation multiple times. A follow up computed tomography was performed at 1 day, 3, 6 and 12 months and every 6 months thereafter, along with physical examination, urine analysis and serum creatinine. Both patients tolerated renal cryoablation and radiofrequency therapy well with no postoperative complications and no change in renal function, there was no significant change in serum creatinine from preoperative values. Both patients had complete tumor ablation after the treatment.

Conclusion

Although it is not possible to draw definite conclusions about the safety and efficacy of these techniques from two successful cases, however, these cases demonstrate that these minimally invasive treatment techniques allow kidney cancer to be treated with much less disruption of patients' lives and helps to achieve acceptable oncological results.

Key words: minimally invasive therapies, renal tumors, interventional radiology

Įžanga

Perkutaninė inkstų navikų krioabliacija ir radijo dažnio abliacija yra minimaliai invazyvūs gydymo metodai, leidžiantys maksimaliai išsaugoti inkstų funkciją. Jie vis dažniau naudojami pacientams, sergantiems sunkiomis gretutinėmis ligomis, esant daugybiniams inkstų navikams, pacientams, turintiems tik vieną inkstą ir (ar) turintiems didelį genetinį polinkį susiformuoti dauginiams inkstų navikams, ypač tais atvejais, kai labai svarbu išsaugoti inkstų funkciją. Straipsnyje siekta įvertinti šių minimaliai invazyvių gydymo metodų naudą (efektyvumą ir saugumą) pacientams, turintiems vienintelį inkstą.

Klinikiniai atvejai

Aprašome ir aptariame du klinikinius atvejus pacientų, kuriems buvo diagnozuoti maži inkstų navikai (<4 cm) vieninteliame likusiame inkste ir kurie buvo pakartotinai gydyti krioabliacijos bei radijo dažnio abliacijos metodais Nacionaliniame vėžio institute. Kontrolinė kompiuterinė tomografija buvo atlikta kitą dieną po procedūros, po 3, 6 ir 12 mėnesių po procedūros ir toliau kas 6 mėnesius, kartu buvo atliekamas fizinis ištyrimas, šlapimo tyrimas ir nustatoma kreatinino koncentracija serume. Abu pacientai inkstų navikų krioabliaciją ir radijo dažnio abliaciją toleravo gerai, pooperacinių komplikacijų, ryškesnių inkstų funkcijos pokyčių nebuvo. Serumo kreatinino koncentracija mažai skyrėsi nuo priešoperacinių verčių. Abiem ligoniams pasiekta visiška / radikali naviko abliacija po vienos gydymo procedūros.

Išvada

Nors neįmanoma daryti tikslių galutinių išvadų apie navikų vieninteliame inkste gydymo minimaliai invaziniais metodais veiksmingumą ir saugumą tik iš dviejų sėkmingų atvejų, tačiau jie parodo, jog inkstų navikų krioabliacija ir radijo dažnio abliacija leidžia minimaliai invazyviu būdu gydyti inkstų navikus ir siekti gerų onkologinių rezultatų.

Reikšminiai žodžiai: minimaliai invazyvi terapija, inkstų navikai, intervencinė radiologija

Introduction

Renal cell carcinoma (RCC) is the most common solid tumor of the kidney which accounts for approximately 90% of all primary renal neoplasms in adults [1]. The incidence of RCC is increasing worldwide. In 2012, there were approximately 84,400 new cases of RCC within the European Union. According to International Agency for Research on Cancer, Lithuania is at a second place of the list of the 20 countries with the highest rate of kidney cancer in 2012 [2]. Due to increasingly used cross-sectional imaging techniques, the diagnosis is being made in an earlier stage. Usually these are small renal masses and more than a half of new cases are detected incidentally without the typical triad of symptoms: flank pain, haematuria and a palpable abdominal mass [3].

Due to the lack of treatment response to chemotherapy and radiation therapy, surgery is the treatment of choice managing the patients with RCC. Partial nephrectomy is considered as a first-line therapy (whenever possible) for the patients with a localised tumor less than 4 cm in maximum diameter [4]. However, surgical treatment can be often a cause of consecutive renal failure with the need for hemodialysis. Therefore for some patients, poor candidates for an open surgery or with small peripheral tumors, a less invasive treatment, e.g. cryoablation (CRYO), microwave or radiofrequency (RF) ablation could be a better choice. Being performed using open, laparoscopic and percutaneous approaches these nephron-sparing surgery (NSS) techniques are widely used among patients with a small renal tumors and who have significant co-morbidities or compromised renal function, multiple bilateral kidney tumors, inherited renal cancer syndromes or in case of a solitary kidney [5]. It offers advantages by reducing perioperative morbidity, decreasing pain and shortening the hospital stay, promoting faster recovery, and importantly preserving the renal function [6]. Studies show ablative therapies to be promising techniques in managing selected cases of renal cell carcinoma [7]

Case reports

In the National Cancer Institute during the period from 2012 to 2014 a total of 10 cryoablation and 81 radiofrequency ablation procedures were performed. We present two successful clinical cases of the patients with RCC in a solitary kidney who underwent multiple percutaneous CRYO and RF procedures.

All tumors were imaged on contrast enhanced computed tomography (CT) before percutaneous CRYO or RF ablation. Under general anaesthesia combined CT and ultrasound guidance was used to place the cryoprobes into the targeted renal tumor. The total number

of probes placed was based on tumor size. CT monitoring during the procedure was performed. An argon helium based cryoablation system was used with two freeze-thaw cycles, at a probe tip temperature of –40°C. RF ablation was performed with an RF generator using multipolar applicators which were inserted through the skin into the kidney tumor using the real-time sonoscopy**.** The high frequency alternating current causes tissue molecular vibrations. As a result, the temperature exceed to 80–100° which resulted in cancer cells destruction. The length and number of applicators was chosen by the operator on the basis of tumor size and location.

Both procedures were performed by experienced interventional radiologist as an inpatient operation. Additionally, a day before the operation titanium markers were placed around renal tumors. All tumors were treated with the intention of providing at least a 0.5 cm tumor-free margin.

Both patients were hospitalized from 3 to 9 days for observation. Follow-up imaging using contrast enhanced CT and physical examination were done at the first day after ablation, later at 3–6 months and every 6 months afterward. Treatment was considered successful when tumors gradually shrunk and showed no sign of contrast enhancement, in the treated area on follow-up CT.

Renal function was analyzed with serum creatinine concentration measured before ablation, on the first day after ablation, 3 months after ablation and every 6 months afterward.

The 1st patient – 77 year-old man with a clear cell RCC metastasis in a solitary right kidney. In 2001 he underwent open radical left nephrectomy for the left kidney clear cell RCC pT2 G2. In March 2010, he began to complain with hemoptysis. Bronchoscopy was performed in order to obtain the tissue for biopsy but unfortunately acute hemorrhage occurred and it failed to get the histological answer. He was admitted to National Cancer Institute in June 2010. Contrast enhanced CT of the chest revealed a 3cm diameter suspicious as a metastatic lesion in the S8 segment of the right lung with no evidence of lymphatic nodes invasion. Multidisciplinary team meeting, consisting of urologist, medical oncologist, radiation oncologist and thoracic surgeon, recommended beginning with the surgical treatment because of persisting coughing with blood. Right lower lobectomy was performed. Pathological examination of the resected tissue revealed a diagnosis of the metastasis of clear cell RCC in the right lung. He was followed up routinely performing abdominal and chest CT scans.

During the follow up in April 2013 the contrast enhanced abdominal CT scan showed two tumors of about 1.6 cm diameter at the dorsal surface of the middle part of the right kidney. At presentation his creatinine level was (92 μmol/l). Titanium markers were implanted and percutaneous cryoablation procedure was performed (Figure 1). The postoperative creatinine level was (98 μmol/l). Biological therapy with sunitinib was administrated to the patient at a dose of 50 mg orally once daily for 4 weeks, followed by 2 weeks of treatment – 2 cycles.

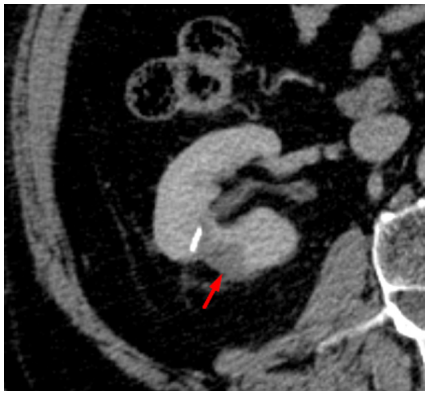

Figure 1. 1st clinical case. Contrast enhanced CT axial view of a solitary right kidney after the 1st cryoablation

Another percutaneous CRYO procedure was performed in March 2014 for the new tumor of a size of 1.4 cm in the middle part of the right kidney (Figure 2) with serum creatinine levels 90 μmol/l before and 110 μmol/l after the procedure. In June 2015 abdominal CT showed two newly onset tumors in the remaining kidney. The first was 2.2 cm in maximum diameter in the dorsal surface of the lower pole of the kidney and another was 1.9 cm in the anterior surface of the upper pole of the right kidney. RF was performed with no postoperative complications and serum creatinine levels were from 99 μmol/l preoperatively and 120 μmol/l postoperatively. The last RF ablation was carried out

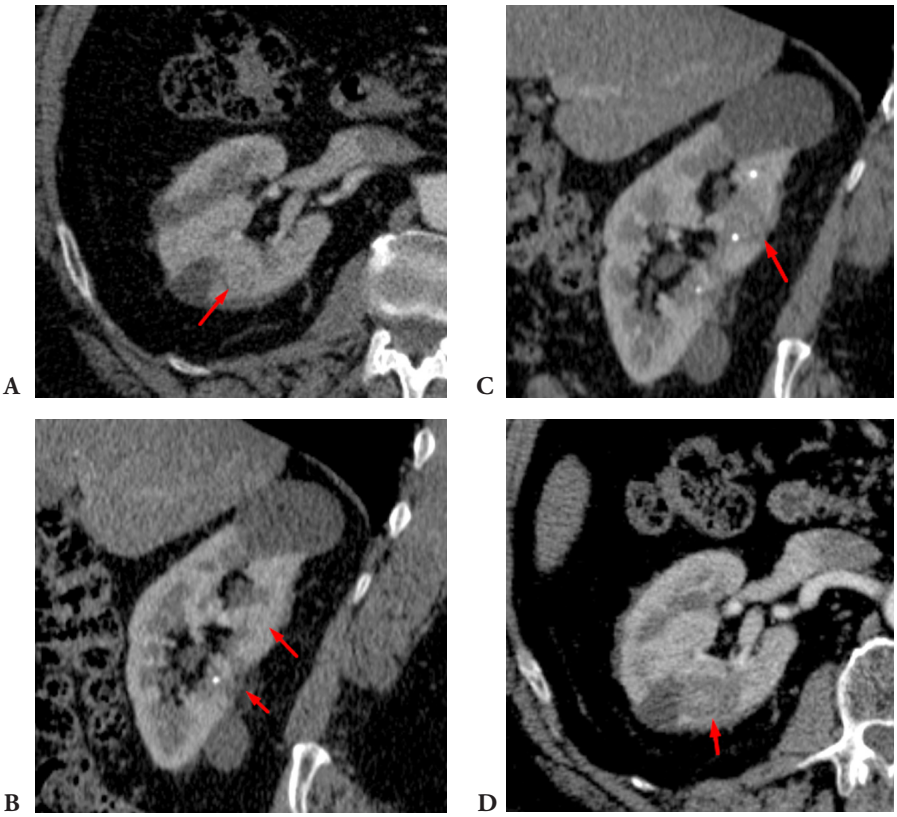

Figure 2. 1st clinical case. Contrast enhanced CT before (A – axial view, B – sagittal view) and after (C – axial view, D – sagittal view) repeated cryoablation of solitary right kidney tumor in March 2014

in January 2016 for the tumor of 2 cm, located in the dorsal surface of the middle part of the right kidney (Figure 3). The postoperative serum creatinine level was 131 μmol/l.

The patient is currently well and during the last check up in May 2016 CT revealed only postoperative changes in the right lung and neither local nor distant recurrence of the disease was seen. The serum creatinine concentration during the last visit was 115 μmol/l.

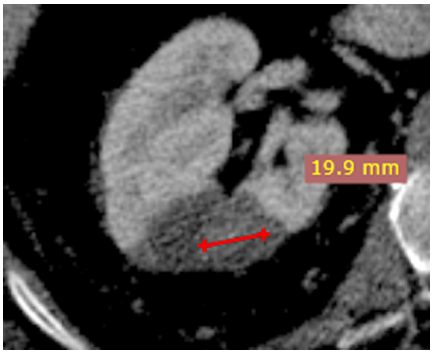

Figure 3. 1st clinical case. Solitary right kidney, new tumor in June 2016 (contrast enhanced CT, axial view)

The 2nd patient – 32 year old woman with von Hippel-Lindau (vHL) disease. In the history of the disease patient became blind with the right eye due to the retinal detachment and enucleation of the right eye, inserting the prostetic eye was performed. Two surgical resections of brain stem hemangioblastomas were performed. vHL syndrom was diagnosed in 2004. vHL molecular examination showed (Santa HOTC): VHL c.586A>T (p.L196*).

In August 2008 underwent a left nephrectomy for the left kidney RCC pT2 G2 and right partial nephrectomy with adrenelectomy for pT1 G2**.** In January 2012 the right partial nephrectomy was performed repeatedly with a histology of RCC pT1a G2. In November 2012 a CT scanning showed a 1.4 cm x1.7 cm size lesion in the lateral surface of the middle part of the right kidney. Percutaneous biopsy was obtained from the tumor and no specific alterations for vHL disease were noticed on histology (Figure 4). Her renal function was normal, with serum creatinine 81 μmol/l. Multidisciplinary team meeting consisting of urologist, medical oncologist and radiation oncologist considered percutaneous

CRYO as the treatment of choice and the procedure was performed (Figure 5). The patient had no immediate complications and the postoperative serum creatinine was 85 μmol/l.

During the regular check-up in February 2015 five new tumors in a solitary right kidney were seen on contrast enhanced CT with a size from 1.3 cm to 2.6 cm (Figure 5). A percutaneous CRYO was performed for all the new tumors (Figure 6). The postablation course in the hospital was uneventful with no significant changes in serum creatinine levels.

The last abdominal CT was performed in February 2016 and showed one new tumor in the dorsal surface of the middle part of the right kidney of a size of 1.4 x 1.9 cm. The patient underwent percutaneous radiofrequency ablation of the right renal mass.

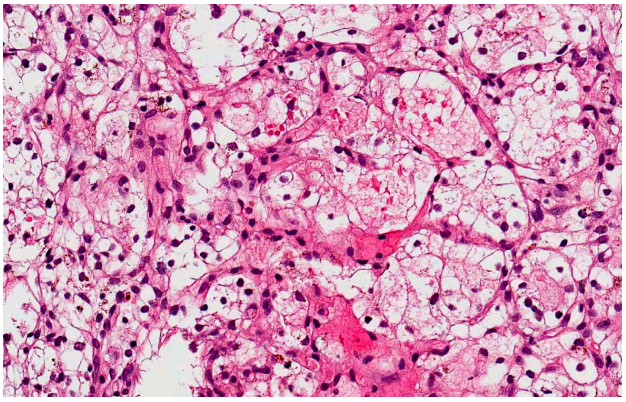

Figure 4. 2nd clinical case. Histological view of right kidney tumor percutaneous biopsy

Figure 5. 2nd clinical case. Solitary right kidney tumor (arrow) before cryoablation in November 2012 (contrast enhanced CT, axial view)

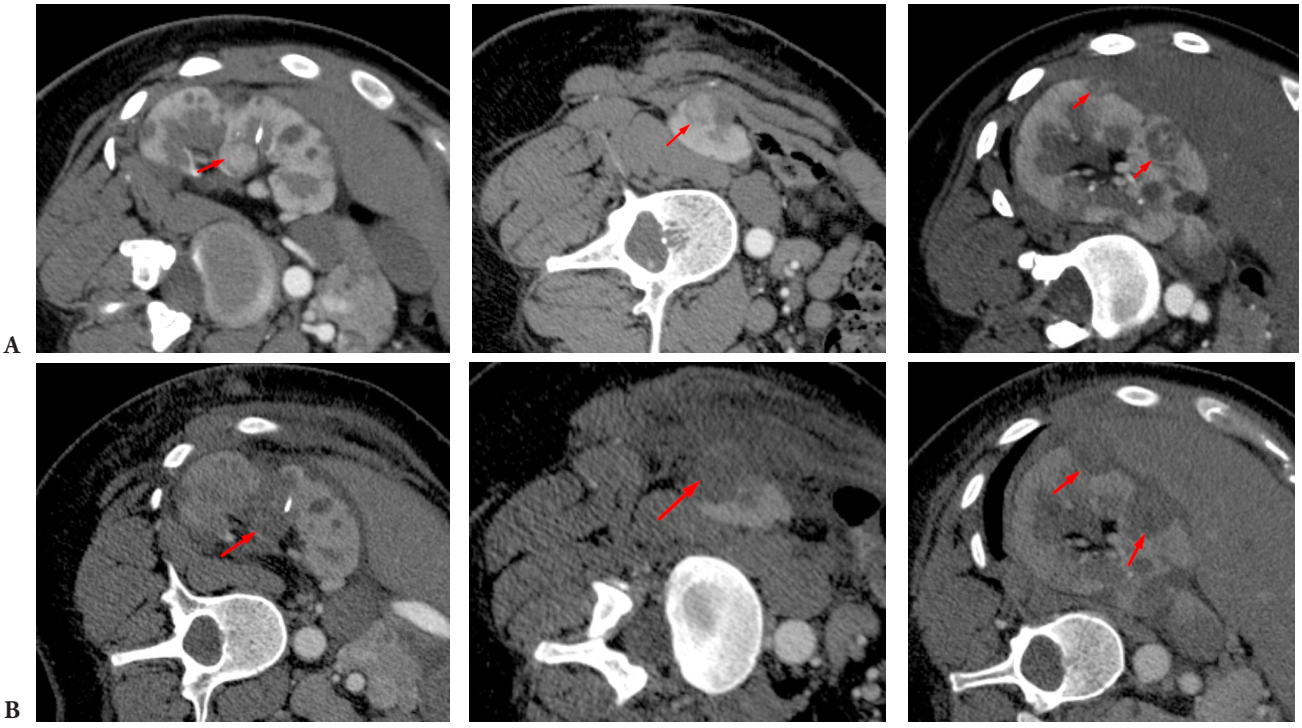

Figure 6. 2nd clinical case. Solitary right kidney tumors (arrows) before cryoablation (A) and after cryoablation (B) in February 2015 (contrast enhanced CT)

After tumor ablation procedures both patients were designated for absolute bed rest for minimum 4 hours under vital-sign monitoring. Both of them had no postoperative complications. Serum creatinine and hemoglobin levels were checked the next morning. No significant change occurred in the laboratory findings and the mean hospital stay was 4,3 days (3–8 days). The preprocedure and postprocedure serum creatinine levels were recorded and there were only small changes in serum creatinine from pretreatment values.

Complete tumor ablation was seen after one treatment session. Repeated ablation session was not necessary. Contrast enhanced CT after ablation was performed and the images were compared with the preablation images. Immediately following ablation, the ablation zone appeared larger than the original tumor but decreased in size over time. No contrast enhancement and no enlargement at the site of ablation was seen.

Discussion

The new accepted standard treatment for small renal tumours (<4 cm) is a nephron sparing surgical approach technique or image-guided ablative therapy [8]. Radiofrequency ablation and cryoablation are increasingly used in patients with a solitary kidney, because these patients are not ideal candidates for surgical resection as their renal function must be preserved [9].

The management of patients with inherited renal cancer syndromes or with multifocal renal tumors is usually complicated by the recurrence of the disease, especially in those with a solitary kidney. Even if these patients are treated with aggressive nephron sparing surgery they are still at risk for *de novo* tumor formation [10]. For example, as many as 85% of patients with vHL will experience tumor recurrence at 10 years and may need multiple surgical interventions [11].

The treatment success depends on tumor location and size. The ideal renal tumor for the percutaneous approach is small (<3 cm), partially exophytic, and posteriorly located in a patient who cannot tolerate a partial nephrectomy [12]. Relative contraindications include younger patient age, larger than 4cm tumors, hilar or centrally located tumors, cystic tumors with the absolute contraindications of untreatable or irreversible coagulopathy or severe medical instability [13]. Usually tumors next to or involving the collecting system cannot be treated with ablation techniques because of the possibility of either incomplete tumour destruction or injury to the collecting system. However, sometimes patients who have solitary kidneys and have tumours >4 cm, can also be treated in this way to prevent dialysis [14].

Studies have shown, that complications of ablative therapies in the treatment of RCCs are usually clinically insignificant and that the rate of serious complications is very low [15]. Complications may occur as a result of injury to the kidney, including it's vasculature and the upper urinary tract collecting system, or injury to the surrounding structures. Urologic complications include hemorrhage, ureteral stricture, urine leak, and urinary tract infection. Non-urologic complications include pneumothorax, nerve injury, skin burn, tract seeding and other less common medical events [16]. A multi-institutional review identified complications associated with percutaneous and laparoscopic ablative treatment of renal tumors. Of these cases 139 were cryoablation and 133 were radio frequency ablation. They reported a total of 30 complications (11.1%) including 25 minor (9.2%) and 5 major (1.8%) complications [17]. Another prospective review of complications following 573 renal ablation procedures included 254 RF ablation, 311 cryoablation procedures, and 8 combined procedures. The overall complication rate was 11.3% (65/573), and the major complication rate was 6.6% (38/573). Major complications occurred more commonly following cryoablation (7.7%; 24/311) than RF ablation (4.7%; 12/254) ($p = 0.15$) [18].

Literature demonstrate that ablative therapies could be an acceptable alternative for the patients with small RCCs in a solitary kidney. Mylona SL et al evaluated clinical outcomes of the 18 patients with solitary kidney and renal cell carcinoma, who underwent percutaneous CT-guided radiofrequency ablation with the tumors in maximum diameter from 1 to 7 cm. All the tumors were treated with totally 24 RF ablation sessions. In small (1-3 cm) exophytic tumors technical success was 85.7%. Residual disease was totally seen in 6/18 tumors which required a 2nd RF ablation session. The recurrence rate was 11.1%, but no recurrence was noticed in tumors less than 3 cm in diameter. No major complications were observed. Serum creatinine values were

normal in 17/18 patients and survival ranged from 12 to 72 months [19]. Another study of 14 patients with renal masses in a solitary kidney had been treated with percutaneous cryoablation showed no complications during treatment. Two patients had gross haematuria afterward that resolved within 24 h. The mean follow-up was 17 (2–30) months, with three patients requiring re-treatment for incomplete tumour ablation. There was no radiographic evidence of local tumour recurrence to date [20].

In retrospective analysis Altunrende F and colleagues between the period from April 2002 to March 2010 evaluated the oncological and functional outcomes of computerized tomography guided percutaneous cryotherapy and radiofrequency ablation for renal tumors in patients with a solitary kidney. Overall 65 patients were included 29 (44.6%) underwent cryotherapy and 36 (55.4%) underwent radiofrequency ablation. Median follow-up was 15.1 and 38.8 months. The 3 primary treatment failures, including 1 after cryotherapy and 2 after radiofrequency ablation, were successfully re-treated with thermal ablation. There were 14 recurrences after radio frequency ablation and 3 after cryotherapy. Two-year overall survival rates for cryotherapy vs radiofrequency ablation were 89% vs 93%, the cancer specific 100% vs 96%, recurrence-free 69% vs 58% and metastasis-free survival 86% vs 91%, respectively [21].

As in our presented cases it was important to avoid major surgical interventions and to prolong the period till radical surgery, especially in the case of the patient with vHL disease. The ablative therapies gave the greatest benefit because they didn't harm healthy tissue and the treatment could be repeated several times. Both RF ablation and cryoablation have demonstrated acceptable outcomes.

Conclusions

Patients with a history of RCC have higher risk to develop another RCC in their remaining kidney. In these two demonstrated cases the patients were poor candidates for open surgery. And the main goal was to avoid consecutive renal failure with the need for hemodialysis. After few ablation therapies no significant change occurred in the laboratory finding for both patients and the mean hospital stay was short enough. Although it is not possible to draw definite conclusions about the safety and efficacy of these techniques from two successful cases however, it demonstrates that percutaneous ablation technique allows achieve acceptable oncological results. A long-term follow-up will be required to confirm these results.

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