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Original Article

Safety and Efficacy of Cryoablation of Renal Tumors in a High-Risk Patient Population at a Community Hospital

Abstract

Purpose: The purpose of the study was to evaluate the safety and efficacy of percutaneous cryoablation for the treatment of renal masses in a high surgical risk population stratified by Charlson Comorbidity Index treated at a community hospital and to determine parameters associated with higher complication rates. **Materials and Methods:** A retrospective chart review of patients with renal masses treated with image-guided percutaneous cryoablation between 2007 and 2013 was performed. **Results:** A total of 121 tumors were ablated in 105 patients. The mean patient age was 70 years old. Comorbidities included morbid obesity, hypertension, diabetes mellitus, coronary artery disease, pulmonary disease, cigarette use, and renal insufficiency. Mean tumor size treated was 3.15 cm in largest diameter, ranging from 1.4 to 6.5 cm. Complications were observed in 16 cases. The most common complication was perinephric and/or pararenal hemorrhage. Procedures with >3.5 probes, hemoglobin >12.5 g/dl, tumor size >3.55 cm, and age >75 years were all associated with greater likelihood of complications. **Conclusions:** Our experience with percutaneous cryoablation of small renal masses offers similar results in efficacy to published data in patients with significant comorbidities. In addition, the results of our study show that percutaneous cryoablation is relatively safe in patients with renal cancer who are poor surgical candidates but warrants special consideration. Parameters associated with higher rates of complications have been established, which may be used by physicians as a guide.

Keywords: *Interventional oncology, percutaneous renal cryoablation, renal cell carcinoma*

Martin Oselkin[1,2], Nathan Cornish[1], Peter Homel[3], Shaun Honig[1,4], David Silver[5], Sergei Sobolevsky[1,6]

Departments of [1]Radiology and [5]Urology, Maimonides Medical Center, Brooklyn, [2]Department of Radiology-Neuroradiology, St. Luke's University Hospital, Bethlehem, PA, [3]Department of Medicine, Albert Einstein College of Medicine, Bronx, [6]Presbyterian Columbia University Medical Center, NY, [4]Department of Radiology, Mount Sinai Brooklyn, Brooklyn, USA

Introduction

Incidental discovery of renal masses has been increasing with the widespread integration of cross-sectional imaging. In addition, more patients are detected at an early stage (Stage 1A or 1B). The increased incidence in patients with additional comorbidities has led to the development of nephron-sparing techniques.[1] Partial nephrectomy has been the gold standard for the treatment of resectable disease.[2] Percutaneous renal cryoablation has emerged as a minimally invasive, nephron-sparing treatment suitable for the treatment of renal masses in a select subgroup of patients who are poor candidates for resection or when preservation of renal function is essential due to comorbid conditions or multiple tumors.[3] Several studies have demonstrated that ablative techniques can achieve effective local tumor control with less risk and morbidity than partial nephrectomy.

This report represents our experience with image-guided percutaneous cryoablation of renal tumors in 105 patients treated at a community hospital, where resources our often scarce. The goal of this study was to evaluate our experience with percutaneous cryoablation as a means of treating renal tumors in high surgical risk patients who require maximal preservation of renal function. The patient's risk was stratified using the Charlson Comorbidity Index (CCI), which is one of the most widely used clinical indices for the evaluation of comorbidities. We also aimed to identify variables that correlated with the highest incidence of postoperative complications to add to the current accepted literature.

Materials and Methods

An Institutional Review Board exempt retrospective chart review of patients with renal masses treated with image-guided percutaneous cryoablation between August 2007 and January 2013 at our institution

Address for correspondence:
*Dr. Nathan Cornish, Department of Radiology, Maimonides Medical Center, 4802 10th Avenue, Brooklyn, NY 11219, USA.
E-mail: nathanacornish@gmail.com*

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was performed. Informed consent was obtained before the procedure. Candidates were selected after consultation with a multidisciplinary team that included urologists, nephrologists, oncologists, and interventional radiologists. Patients selected were those with renal masses who were not candidates for surgery either because of advanced aged, poor baseline renal function, comorbid conditions, or refusal to undergo surgery. The only percutaneous technique that was offered was cryoablation. All of the patients included had imaging follow-up for at least 24 months following the ablation procedure. US and computed tomography (CT) imaging were used to guide cryoprobe insertion. Ice ball formation was monitored with CT. A procedure was considered technically successful when an ice ball margin was at least 5 mm on the final freeze cycle. A percutaneous needle biopsy was performed at the time of cryoablation in most cases unless a previous biopsy demonstrated renal cell carcinoma. Experienced interventional radiologists with at least 5 years of practice performed all procedures.

Patients were routinely admitted to the hospital following the cryoablation procedure. Length of stay was determined by the consecutive amount of overnight hospital days following cryoablation; a single overnight stay was counted as 1 day. No routine laboratory examinations or imaging were performed immediately following the procedure unless clinically indicated. The most recent preprocedural patient laboratory values were recorded within 1 month before cryoablation. Long-term follow-up blood analysis values were recorded if available.

Unenhanced and contrast-enhanced CT or magnetic resonance imaging (MRI) was used to assess efficacy of treatment and was obtained at 1, 3, 6, and 12 months posttreatment and annually thereafter. This was based on the postablative therapy recommendations of the American College of Radiology.[4] Residual tumor was determined as focal enhancement in the tumor ablation zone at initial postprocedural imaging performed 3 and/or 6 months after cryoablation. Recurrent tumor was determined as a focal enhancement in the tumor ablation zone at postprocedural imaging performed at 12 months or later after cryoablation but clearly not seen on the initial postprocedural examination [Figure 1].

The effects of multiple independent variables on tumor residual/recurrence and complications were evaluated such as characteristics of the mass, patient clinical status, and amount of probes used. Complications were assessed in accordance with the Common Terminology Criteria for Adverse Events (CTCAE). A major complication was defined as any morbidity associated with the procedure, which resulted in the length of hospital stay >2 days (CTCAE Grade 3). Major hemorrhage was defined as any amount of blood loss that resulted in hemodynamic compromise and/or required transfusion therapy (CTCAE Grade 4).[5] Results were reported using the Society of Interventional Radiology guidelines.[6]

From 2007 to 2013, a total of 121 ablation procedures performed in 105 patients were included in our analysis. Seventy-one patients (67.6%) had confirmed tissue diagnosis of renal cell carcinoma. The mean patient age was 70 years old. One patient had a congenital solitary kidney, nine patients had a prior contralateral total nephrectomy, three patients had a previous ipsilateral partial nephrectomy, six had contralateral partial nephrectomy, and one patient with a horseshoe kidney. Common comorbidities among the majority of subjects included morbid obesity, hypertension, diabetes mellitus, coronary artery disease, pulmonary disease, cigarette use, and renal insufficiency; 75 patients (71.4%) at the very minimum had both diabetes mellitus and coronary artery disease. The CCI was used as a risk-stratifying tool. The average CCI was 6.6 (2–13) among the patients.

Mean tumor size treated was 3.15 cm in largest diameter, ranging from 1 to 7.5 cm [Table 1]. One patient had simultaneous bilateral cryoablation. One patient, who presented with a 7 cm tumor, had a planned staged ablation and therefore was excluded from the efficacy analysis.

Statistical analysis

Data were described in terms of mean ± standard deviation in the case of normally distributed variables and in terms of frequency (percent) in the case of categorical variables.

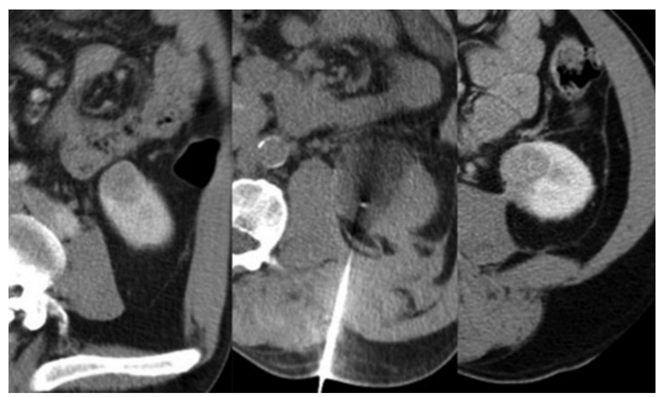

Figure 1: Tumor recurrence. Precryoablation enhancement (left); Ice ball formation encompasses the tumor (middle); computed tomography at 19 months postablation shows focal enhancement within the tumor (right)

Table 1: Baseline study characteristics

Characteristics	Values
Procedures	121
Patients	105
Age (years), mean (range)	70.3 (42-90)
CCI, mean (range)	6.6 (2-13)
Tumor size (cm), mean (range)	3.15 (1.0-7.5)
Tumor location	
Central	35
Exophytic	53
Probes (# used), mean (range)	2.75 (1-8)

CCI: Charlson Comorbidity Index

Univariate analysis of predictors of complication was carried out using Student's *t*-tests for normally distributed predictors and using Chi-square tests for categorical ones. Logistic regression was used to calculate univariate and multivariate odds ratios and to determine whether univariate predictors were independent of each other. In addition, receiver operator characteristic (ROC) analysis was performed to determine optimal cutoffs for variables found to have statistically significant effects on outcomes. Statistical tests were carried out using a level of significance <0.05. All analyses were done using SPSS 20 (IBM Corp., Armonk, NY, USA).

Results

There were 11 tumor recurrences (9.1%), of which six received a repeat cryoablation procedure. A case of tract seeding with a disease-free ablation zone was considered a recurrence. There was a mean time of 29 months until imaging detected recurrence. Two patients (1.9%) had repeat cryoablation at 3 months for residual tumor. The five patients who had tumor recurrence but did not have repeat ablation went on to have a surgical resection.

The average length of stay was 2 days and 91 patients (86.7%) were discharged within 24 h. There were no deaths. Major complications were observed in 16 cases (13.2%). Major hemorrhage [Figure 2] or hematuria was observed in 12 cases (9.9%), one of which was a simultaneous bilateral ablation procedure. In one case, a patient developed bilateral hydronephrosis due to hematuria, which resolved spontaneously. Another patient developed unilateral hydronephrosis secondary to ureteropelvic junction (UPJ) obstruction postcryoablation [Figure 3]. One patient was readmitted for small bowel ileus, which resolved spontaneously; one patient developed bowel ischemia leading to hemicolectomy and progressed to end-stage renal disease (ESRD); and one patient had a non-ST elevation myocardial infarction requiring no intervention before discharge.

Several study variables were found to have a statistically significant association with postprocedure complications [Table 2]. ROC analyses showed that (1) procedures with >3.5 probes (area under the curve [AUC] = 0.90, $P < 0.001$); hemoglobin <12.5 g/dl (AUC = 0.72, $P = 0.005$); (2) tumor size >3.55 cm (AUC = 0.82, $P < 0.001$); (3) ablation performed in the lower pole (32% vs. 5%, $P < 0.001$); and (4) age >75 years (AUC = 0.66, $P = 0.04$) were all significantly associated with greater likelihood of complications. With all five factors in a multivariate logistic regression, only a number of probes (odds ratio = 5.61, 95% confidence interval [CI] = 2.28–13.83, $P < 0.001$) and lower pole (odds ratio = 12.42, 95% CI = 2.42–63.90, $P = 0.003$) remained significant. In the 12 patients with major bleeding complications requiring transfusions, average preoperative hemoglobin was 11 g/dl. Incidence of complications did not correlate with tumor location within the kidney or proximity to vital structures.

A subanalysis of the study's two interventional radiologists revealed differences in their techniques. The operator that typically employs a greater probe density also resulted in a lower recurrence rate. This benefit was offset by more complications (19% vs. 6%). However, the same operator also performed cryoablations on the larger tumors on average (3.3 vs. 3.0).

Discussion

Our experience with percutaneous cryoablation of renal masses offers similar results in efficacy to published data in patients who were high risk. Studies have shown that high CCI scores are associated with impaired survival and increased risk of death. More specifically, Simon *et al*. showed that a CCI >5 was associated with significantly worse mortality rates in patients undergoing lung ablations.[7] In this study, CCI was 6.6, placing these patients at significant risk. A tumor recurrence rate of 9% is comparable with the 12.5% rate published by Babaian *et al*.[8] or the 14% rate published by Kim *et al*.[9] Furthermore, none of the patients which

Figure 2: The most common complication of cryoablation was perinephric and/or pararenal bleeding

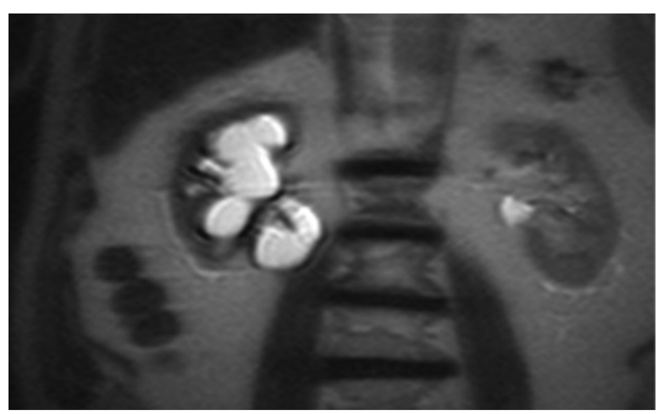

Figure 3: Delayed complication following cryoablation. Noncontrast T2-weighted coronal magnetic resonance through the abdomen reveals delayed complication where normal postablation tumor enlargement resulted in ureteropelvic junction obstruction and hydronephrosis

required (and received) a repeat cryoablation had a recurrence. Of note, all patients treated by cryoablation had biopsy-proven renal neoplasms. Many of our renal biopsies were performed as standalone procedures well in advance of the cryoablation. This contributed to the elimination of benign entities from our study population.

The amount of residual disease is also lower in our study compared to other reports. One of our (out of two total) residual tumor cases occurred early on in our institution's experience with cryoablation and postoperative imaging. The first postoperative MRI was diagnosed as a residual tumor, which leads to immediate repeat cryoablation. In retrospect, the lesion displayed typical characteristics of postablated tumors. Familiarity with normal postablation imaging characteristics and pitfalls [Figure 4] is important to prevent false-positives and unnecessary repeat tumor ablation.

Table 2: Univariate predictors of significant complication

Predictor	No complication (%)	Complication (%)	*P*
Physician			
1	56 (81)	13 (19)	0.06
2	49 (94)	3 (6)	
Laterality			
Left	53 (87)	8 (13)	1.00
Right	52 (87)	8 (13)	
Next to vital structure			
No	55 (83)	11 (17)	0.28
Yes	50 (91)	5 (9)	
Upper pole			
No	72 (84)	14 (16)	0.15
Yes	33 (94)	2 (6)	
Midpole			
No	62 (82)	14 (18)	0.03
Yes	43 (96)	2 (4)	
Lower pole			
No	80 (95)	4 (5)	<0.001
Yes	25 (68)	12 (32)	
Anterior			
No	82 (86)	13 (14)	1.00
Yes	23 (88)	3 (12)	
Medial			
No	70 (86)	11 (14)	1.00
Yes	35 (88)	5 (12)	
Lateral			
No	72 (86)	12 (14)	0.77
Yes	33 (89)	4 (11)	
Sinus			
No	75 (87)	11 (13)	0.78
Yes	30 (86)	5 (14)	
Exophytic			
No	60 (88)	8 (12)	0.60
Yes	45 (85)	8 (15)	
Endophytic			
No	75 (84)	14 (16)	0.23
Yes	30 (94)	2 (6)	
Partially exo			
No	99 (88)	14 (12)	0.28
Yes	6 (75)	2 (25)	
Age	69.50±10.36	75.31±9.94	0.04
Size (cm)	2.94±1.6	4.38±1.31	<0.001
Number of probes	2.50±0.92	4.44±1.31	<0.001
HgB	13.50±1.52	12.31±1.21	0.007

We posit that more probes per centimeter of lesion logically results in greater efficacy. In this study, the interventional radiologist who typically deployed a greater probe density also had a lower recurrence rate. However, he also had a higher rate of complications. This could be related to the increased probe density, but it can also be explained by the fact that the same operator performed cryoablations on larger tumors on average (3.3 vs. 3.0).

Although our recurrence rate is low, our complication rate appears higher than other published studies. As mentioned above, this may be partially explained by increased probe: mass density. Most of our complications were related to hemorrhage although a few unique complications did arise. For example, following successful ablation, a cyst eventually developed in the ablation zone 1 year postprocedure at the UPJ, which gradually expanded in size leading to unilateral hydronephrosis [Figure 3]. One patient developed aspiration pneumonia immediately following the procedure, and the resultant septic shock lead to renal failure. Another patient developed bowel ischemia leading to hemicolectomy and progressed to ESRD.

Commonly known associations with complications such as age, lesion size, and amount of probes were also shown to increase risk significantly.[10] Contrary to recent scoring systems for tumor location such as renal, lesion location within the kidney, or proximity to other structures did not reveal any correlation with complications. However, the clinical status of the patient revealed a significantly increased risk for complications. Interestingly, in the 12 patients with major bleeding complications requiring

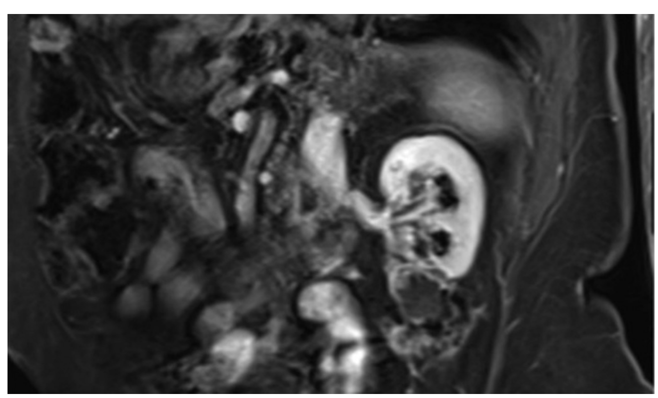

Figure 4: Mild peripheral enhancement of the ablation zone is normal in early postprocedural imaging. In addition, coursing vessels may be confused for residual tumor

transfusions, average preoperative hemoglobin was 11 g/dl. Aside from being at increased for hemorrhage, these patients are additionally more likely to suffer complications due to postprocedural anemia. Atwell *et al*. have previously suggested that "it may be reasonable to perform prophylactic transfusion before ablation to correct baseline anemia" and we believe our data support this preprocedural management.

The majority of reported cryoablation complications are hemorrhage. Excluding all other variables such as clinical status and tumor location, tumor size is still an important independent predictor for bleeding risk. Although our study and many other reports in the literature demonstrate the relationship between tumor size and bleeding risk, it is not definitively proven whether the amount of probes used or the intrinsic properties of the mass is responsible for bleeding. For example, is there perhaps greater vascularity or vessel fragility in tumors larger than 3 cm? Do more probes inserted simply lead to more chances for vessel injury? Although our study was not designed to prove that these two variables are mutually exclusive, we have demonstrated that probe density is associated with more complications. It may be of value to evaluate if the total amount of probe/needle insertions including repositions and immediate preablation biopsy, rather than the total amount of probes inserted, has a greater impact on the rate of hemorrhage.

At our institution, the only percutaneous technique offered was cryoablation. The rationale is that cryoablation offers advantages over radiofrequency ablation (RFA) and other thermal ablation techniques in that imaging permits direct visualization of the ice ball, allowing for more precise monitoring of the ablation zone. It also allows the simultaneous use of more than one probe and has been shown to have a reduced risk of thermal injury to the collecting system when treating centrally located tumors.[11] In a meta-analysis reported by Kunkle and Uzzo in October 2007, the results demonstrated that repeat ablation was performed more often after RFA (8.5% vs. 1.5%), and the rates of local tumor progression were significantly higher for RFA compared with cryoablation (12.9% vs. 5.2%).[12] The literature has reported a higher rate of hemorrhage in cryoablation compared to RFA. In one series, hemorrhage occurred in 4.8% of cryoablations compared to 1.2% with RFA procedures.[13] This can be explained by the thermal coagulation induced by RFA electrodes and the larger caliber of cryoprobes.[13]

Given the fact that the literature supports cryoablation as more efficacious than other percutaneous techniques but associates it with a higher rate of hemorrhage, as did this study, we look to further investigate the role of preprocedural embolization in future prospective studies. In a study by Miller *et al*., in 21 lesions treated in 19 patients, embolization was shown to significantly decrease complications without impacting renal function, biopsy quality, or recurrence.[14] These are promising results; however, their sample size is lacking. We hope to enroll more patients to see if these results hold with a larger sample size.

Study limitation

Several aspects of our study limit the long-term conclusions of safety and efficacy. First, there are many patients near the tail end of our study and maybe falsely deflating our recurrence rate. Since some of our cases only include follow-up imaging up to 24-month postablation, the time frame recurrence rate could be assessed over was limited. We also have a large amount of missing data on follow-up blood urea nitrogen and Cr; therefore, we could not assess for renal function. However, many previous studies have shown that percutaneous cryoablation is an excellent nephron-sparing technique. In addition, the study was a retrospective, single-arm analysis. No comparison was made to other surgical or interventional techniques.

Conclusions

The results of our study show percutaneous cryoablation of renal tumors are relatively safe in patients with renal cancer who are poor surgical candidates and with significant comorbidities but warrants special consideration. We delineated a set of parameters including advanced age, amount of probes used, and tumor size that correlated with increased occurrence of complications, specifically hemorrhage. These patients with significant adverse events also had the lowest baseline hemoglobin levels. This observation underscores the need for preoperative optimization of hemoglobin to decrease the incidence of postoperative complications associated with hemorrhage. In addition, patients of advanced age and those who will have four or more probes inserted should be carefully monitored in the postoperative period. There may be a role of preprocedural embolization to reduce the risk of hemorrhage, which will be investigated in further studies.

Future studies analyzing the relationship between hemorrhage risk and the total amount of probe/needle insertions, including repositions and immediate preablation biopsy, may be useful. If a relationship does exist, then there would likely be evidence to support the routine use of navigational instruments to prevent complications.

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Conflicts of interest

There are no conflicts of interest.

References

1. Homma Y, Kawabe K, Kitamura T, Nishimura Y, Shinohara M, Kondo Y, *et al.* Increased incidental detection and reduced mortality in renal cancer – Recent retrospective analysis at eight institutions. Int J Urol 1995;2:77-80.
2. Fergany AF, Hafez KS, Novick AC. Long-term results of nephron sparing surgery for localized renal cell carcinoma: 10-year followup. J Urol 2000;163:442-5.
3. Woldu SL, Thoreson GR, Okhunov Z, Ghandour R, Rothberg MB, RoyChoudhury A, *et al.* Comparison of renal parenchymal volume preservation between partial nephrectomy, cryoablation, and radiofrequency ablation using 3D volume measurements. J Endourol 2015;29:948-55.
4. Patel U, Sokhi H. Imaging in the follow-up of renal cell carcinoma. AJR Am J Roentgenol 2012;198:1266-76.
5. Common Terminology Criteria for Adverse Events (CTCAE). U.S. Department of Health and Human Services. National Institutes of Health. National Cancer Institute; 28 May, 2009. Available from: https://www.evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf. [Last accessed on 2017 Dec 17; Last updated on 2010 Jun 14].
6. Ahmed M, Solbiati L, Brace CL, Breen DJ, Callstrom MR, Charboneau JW, *et al.* Image-guided tumor ablation: Standardization of terminology and reporting criteria – A 10-year update. J Vasc Interv Radiol 2014;25:1691-705.
7. Simon TG, Beland MD, Machan JT, Dipetrillo T, Dupuy DE. Charlson comorbidity index predicts patient outcome, in cases of inoperable non-small cell lung cancer treated with radiofrequency ablation. Eur J Radiol 2012;81:4167-72.
8. Babaian KN, Okhunov Z, Juncal S, Ordon M, Lusch A, Zand T, *et al.* Clinical outcomes of patients with nondiagnostic biopsy during cryoablation of small renal masses. Urology 2015;85:605-9.
9. Kim EH, Tanagho YS, Bhayani SB, Saad NE, Benway BM, Figenshau RS, *et al.* Percutaneous cryoablation of renal masses: Washington university experience of treating 129 tumours. BJU Int 2013;111:872-9.
10. Atwell TD, Carter RE, Schmit GD, Carr CM, Boorjian SA, Curry TB, *et al.* Complications following 573 percutaneous renal radiofrequency and cryoablation procedures. J Vasc Interv Radiol 2012;23:48-54.
11. Maria T, Georgiades C. Percutaneous cryoablation for renal cell carcinoma. J Kidney Cancer VHL 2015;2:105-13.
12. Kunkle DA, Uzzo RG. Cryoablation or radiofrequency ablation of the small renal mass: A meta-analysis. Cancer 2008;113:2671-80.
13. Kurup AN. Percutaneous ablation for small renal masses-complications. Semin Intervent Radiol 2014;31:42-9.
14. Miller JM, Julien P, Wachsman A, Van Allan RJ, Friedman ML. The role of embolization in reducing the complications of cryoablation in renal cell carcinoma. Clin Radiol 2014;69:1045-9.