Artificial Ascites in Radiofrequency Ablation for Liver Cancer

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ABSTRACT

Background: *Radio frequency ablation (RFA) is one of the treatment modality for liver tumor either as primary tumor as well as secondary malignancy. Occasionally, a good ablation can't be performed due to the tumor location. To assists the ablation in this particular case, some fluid can be deposited inside the abdomen which is called as artificial ascites. The aim of this study is to report and evaluate the method of artificial ascites in RFA*

Method: *This was a case series study consist of 19 consecutive patients that had been treated with ultrasound-guided RFA using artificial ascites from 2014 to 2017.*

Results: *Artificial ascites was successfully performed in all 19 patients (100%) with total of 53 hepatocellular carcinoma (HCC) lesions in 34 RFA's sessions and tumor size ranges from 10 mm to 50 mm. Most of the tumors were primary tumor (14/19). Nine patients had single tumor and 10 patients had multiple tumors and most of the tumor were located in segment 5 (14/53). Artificial ascites was performed using 5% dextrose in water (D/W) solution ranging from 500 mL to 1500 mL. No adverse effect occurred during and after the procedure.*

Conclusion: *Percutaneous RFA using artificial ascites technique was safe and effective for treating HCC*

Keywords: *artificial ascites, hepatocelullar carcinoma, radiofrequency ablation*

ABSTRAK

Latar belakang: *Radiofrequency ablation (RFA) merupakana salah satu modalitas terapi untuk tumor hati baik primer maupun sekunder. Pada beberapa kondisi, ablasi tidak dapat dilakukan akibat lokasi tumor. Untuk memfasilitasi ablasi pada kondisi seperti ini, ronga abdomen dapat diisi dengan cairan atau dikenal dengan artificial ascites. Tujuan dari studi ini adalah mengevaluasi metode artificial ascites pada RFA.*

Metode: *Studi ini merupakan studi case series yang terdiri dari 19 pasien konsekutif yang telah diterapi dengan RFA terpimpin ultrasonografi menggunakan artificial ascites dari tahun 2014 hingga 2017.*

Hasil: *Artificial ascites sukses dilakukan pada seluruh pasien (19 pasien, 100%) dengan total 53 lesi karsinoma sel hati (KSH) pada 34 sesi RFA dan ukuran tumor berkisar antara 10mm hingga 50mm. Sebagian besar tumor adalah tumor primer (14/19). Tumor tunggal ditemukan pada 9 pasien dan 10 pasien memiliki tumor multipel. Sebagian besar tumor berada di segmen 5 (14/53). Teknik artificial ascites dilakukan menggunakan cairan 5% dextrose in water (D/W) dengan volume berkisar antara 500 mL hingga 1500 mL. Tidak ditemukan efek samping baik pada sebelum maupun sesudah terapi.*

Simpulan: *RFA perkutan dengan artificial ascites merupakan modalitas terapi KHS yang aman dan efektif.*

Kata kunci: *artificial ascites, karsinoma hepatoselular, radiofrequency ablation*

INTRODUCTION

Hepatocellular carcinoma (HCC) is the world fifths most common malignancy in male subjects. This malignancy is rank the 2nd most common cause of death related to malignancy in the world. In Indonesia, incidence of HCC is estimated will increased until 2030 because of increasing number of patients with liver cirrhosis due to hepatitis B virus infection.[1] One study revealed that only 34% patients with HCC that potentially cured and that because most patients came to the hospital with already advanced disease.[2] Until now, curative treatment for HCC can be done with a very few modalities.

Radio frequency ablation (RFA) is one of the curative methods for HCC. It is not clear whether RFA is as effective as liver resection which until now still considered as the treatment of choice for HCC. There are two meta-analyses that showed hepatic resection is superior to RFA in small HCCs, particularly for tumors < 3 cm.[3,4] But one meta-analysis showed no difference between hepatic resection and RFA in terms of overall survival rates.[5] One randomized controlled trial revealed that percutaneous RFA is as effective as liver resection.[6] Because RFA is a minimally invasive treatment, it can be used in patients who have an increased risk of complications for hepatic resection, including a decrease liver reserve of Child Pugh B status and suboptimal general condition with co-morbidities. However, several conditions may influence the decision to perform RFA such as tumors abutting the diaphragm or near vital organs like the colon, bile duct, or gallbladder. These position not only cause difficulty in performing percutaneous ablation, but also increase the risk of thermal injury to adjacent organs. To perform RFA in this situation one may have to consider assistant technique that include artificial ascites, artificial pleural effusion, or other means of procedure that can attenuate the heat damage by RFA. These assistant technique may protect the adjacent organ or give a clearer path for the RFA electrode to be put in desired posititio to give a total ablation of the tumor.

Some artificial ascites technique offer a relatively expensive or difficult to find appliances. The objective of this article is to elucidate the feasibility and effectiveness of artificial ascites in difficult-to-ablate HCCs with the modification technique that suitable and cost effective for most clinical conditions because the use of apparatus that already in use in every day situation (such as spinal needle instead of special needle, and without any guide wire). Therefore, the purpose of this study is to evaluate the method of artificial ascites using technique that we developed to suit our condition and the availability of apparatus in our procedure room.

METHOD

This was a case series study consist of 19 patients treated with radiofrequency ablation using artificial ascites technique. The patients in this study required to perform artificial ascites because of difficult location to put the electrode or to avoid thermal injury to the adjacent organ. The inclusion criteria for the patients were: tumor accessible via a percutaneous approach, can be visualized using ultrasonography, absence of portal/ hepatic vein main branch tumor thrombus; INR >1.6, platelet count > 50,000/ll, tumor size +/- 5.0 cm, and no tumor invasion of major surrounding structures. Baseline characteristic of the patients and reports of the procedure were recorded and summarized in result section of this study. We summarized all the patients data in Table 1.

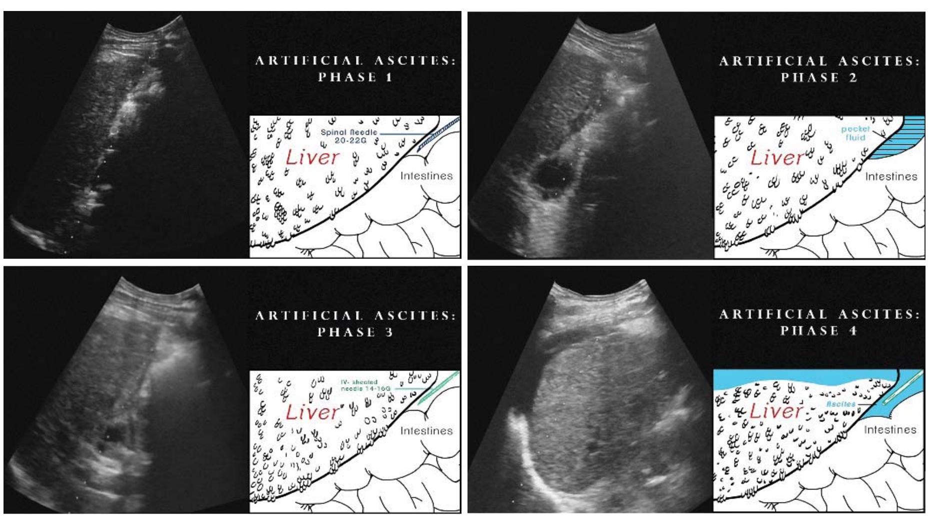
Artificial ascites was performed by introduce some fluid into the perihepatic peritoneal space provides a thermal barrier insulating the ablation zone from surrounding structures. Tumor visualization with ultrasound is often improved, as the surrounding fluid displaces the liver inferiorly and provides a sonographic window. At our institution, artificial ascites is utilized if a patient is determined to have a tumor adjacent to critical structures, such as the diaphragm, stomach, bowel, or occasionally the lungs. D5W is typically used for artificial ascites in radiofrequency ablation as it is less ionic and presumed less likely to conduct electrical current.

We use 22G and 20G-spinal needle as local anesthetic needle as well as introduction needle for a small pocket of fluid along the edge of the liver. As the formation of the small pocket of fluid established, 14G or 16G iv-canulla needle can be safely inserted to allow the deposition of 500-1000 mL or more 5% dextrose. 5% dextrose will be preferred because more non-ionic.

Step by step method as follows: (1) Patient breath normally, no need to perform deep inspiration. In this stage light sedation can be applied to the patient. A 22G-Spinal needle (Spinocan) is placed just under the inferior edge of the liver tip with ultrasound guidance. Aspiration of the needle should not contained any aspirate nor gases; (2) 5-10 mL of 5% dextrose solution pushed to form a small pocket of hypoechoic area along the edge of the liver tip; (3) The needle can be changed to a 20G spinal needle (Spinocan) that by the help of

Table 1. Summary of data from case series

Patient No	Initial	Sex	Age	Etiology	Nodule HCC	Tumor Size	Lesion Amount	Freq RFA	Segmen
1	BLS	Male	64	NBNC	Secondary	23 mm	Multiple	3	V V V
2	S	Female	70	HCV	Primary	38 mm	Single	1	VI
3	EP	Male	57	HCV	Primary	25 mm	Single	1	VIII
4	A	Male	59	HCV	Primary	39 mm	Multiple	9	V, VII V, VII V, VII, VIII I, II, III II, III V, VI, VIII II, IV V, VI, VII VIII
5	WSJ	Male	63	HCV	Primary	29 mm	Single	1	IV
6	N	Female	66	NBNC	Secondary	25 mm	Single	1	VII
7	SS	Female	70	NBNC	Primary	29 mm	Single	1	IV
8	TSK	Male	65	HBV	Primary	14 mm	Multiple	2	VII IV
9	DS	Female	67	HCV	Primary	43 mm	Multiple	1	VI, VIII
10	EW	Female	65	HCV	Primary	15 mm	Single	1	VIII
11	SP	Male	34	NBNC	Secondary	20 mm	Single	1	VIII
12	DD	Male	65	NBNC	Secondary	50 mm	Multiple	2	V, VII VI
13	HW	Male	64	HBV	Primary	37 mm	Single	1	III
14	KL	Male	53	HBV	Primary	25 mm	Multiple	1	V
15	LMD	Male	64	HBV	Primary	29 mm	Multiple	1	VIII
16	IAN	Female	56	NBNC	Secondary	NA	Multiple	4	V, VI V, VIII IV III, V
17	AK	Male	46	HCV	Primary	NA	Multiple	1	II, III
18	RA	Female	25	HBV	Primary	10 mm	Multiple	1	II, III
19	PN	Male	56	HBV	Primary	15 mm	Single	1	V



Picture 1. Phases of creating artificial ascites

the small pocket can introduce more fluid until about 100 mL. At this stage usually the area inferior the liver edge appeared hypoechoic; (4) A 16G or 14G iv canule put inside the hypoechoic area just under the infrior edge of the liver. This allow for more rapid inflow of 5% dextrose into the abdominal cavity; (5) The amount of fluid introduce to the abdominal cavity is depends on the goal such as to separate the liver and the adjacent organ or to bring out clearer visualization of the target nodule in the liver in order to give a good needle path. These objectives usually can be accomplished by 500 – 1500 mL of solution; (6) The iv canule may be left indwelling during the procedure but care must be taken not to puncture or ablate the canule. At the end of the procedure the iv canule can be used to drain the fluid if necessary.

This study qualified under the category of exempt human subjects research, 45 CFR 46.101(b) (4): 'Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects'. The confidentiality and anonymity of all participating subjects was ensured at all times. Subject participation was completely voluntary and the patients did not come to any harm during the course of the study. The research was conducted in an independent and impartial manner.

RESULTS

A total of 34 artificial ascites were conducted in 19 patients treated with RFA. 12 (63.2%) patients were male and 7 were female (36.7%). The mean age of this patients was 64 years old with range of 29-70 years old. 7 patients were infected with hepatitis C virus, 6 patiens were infected with hepatitis B virus, and 6 patiens were negative from hepatitis B and C virus infection (Table 2).

Liver function of the patiens were described. The mean of platelet counts ($10^3/\mu L$) was 188 with range of 53-974 and the mean of prothrombin time (%) was 11.6 with range of 9.4-17.2. The mean of albumin (g/dL) was 3.61 with range of 2.50-4.90 and the mean of total bilirubin (mg/dL) was 1.8 with range of 0.31-2.70 (Table 2).

Most of the patients had cirrhosis (11/8) with the mean of Child Pugh (CP) Score was 5 with the range of 5-8. 12 patients were CP(A) and 7 patients were CP(B). The mean of MELD score was 7 with the range of 6-16.

Nodule characteristic were also described. Most of the nodule were primary tumor (14/5) with mean size of 25mm. 9 patients had single nodule and 10 patients had multiple nodule. Total of 53 lesions had been treated in 34 RFA's sessions. Most of the nodule were located in segment 5 (14/19) and only 1 nodule located in segment 1. All 53 nodules were successfully treated with RFA using artificial ascites with no retention of fluid after procedure (Table 3).

Table 2. Baseline characteristics of study population

	Artificial ascites (n = 19)
Sex (%)	
Male	12 (63.2%)
Female	7 (36.7%)
Age - range (years)	64 years (29-70 years)
Etiology (%)	
HBV Virus	6 (31.6%)
HCV Virus	7 (36.8%)
Non-B Non -C	6 (31.6%)
Platelet counts - range (10^3/ µL)	188 (53-974)
Prothrombin time - range (%)	11.6 (9.4-17.2)
Albumin - range (g/dL)	3.61 (2.50-4.90)
Bilirubin total - range (mg/dL)	1.18 (0.31-2.70)
Liver cirrhosis (%)	
Yes	11 (57.9%)
No	8 (42.1%)
Child Pugh score (range)	5 (5-8)
Child Pugh (%)	
A	12 (63.2%)
B	7 (36.8%)
Meld score (range)	7 (6-16)
Nodules HCC (%)	
Primary	14 (73.7%)
Secondary	5 (26.3%)
Lesion (%)	
Single	9 (47.4%)
Multiple	10 (52.6%)

Table 3. Summary of results artificial ascites in patients treated by radiofrequency ablation

Tumor size (range)	25 mm (10-50 mm)
Amount of frequency RFA with artificial ascites	34
Total number of Session	53
Segmen of RFA session (%)	
S1	1 (1.8%)
S2	5 (9.4%)
S3	6 (11.5%)
S4	5 (9.4%)
S5	14 (26.4%)
S6	6 (11.5%)
S7	7 (13.2%)
S8	9 (16.8%)
Technical success rate (%)	
Success	53 (100%)
Unsuccess	0 (0%)
Fluid intra-abdomen post RFA (%)	
Absence	53 (100%)
Presence	0(0%)

DISCUSSION

RFA is accepted as one of effective method for treatment of liver tumor. This procedure were considered as effective as liver resection – the gold standard for treatment of liver cancer. Recent meta-analysis showed that in studies where all tumors are considered resectable and patients are not grouped into the different treatment groups by baseline characteristics, liver resection is not shown to have significantly improved 1- and 3-year overall survival and disease-free-survival when compared to RFA. Especially for tumor < 3 cm, no difference in terms of overall survival between liver resection and RFA.[7] Moreover, patient with already compromised liver function, RFA still can be done.

It is mandatory in patients with HCC, the tumor must be clearly visualized on US to avoid complications and to treat the tumor successfully.[8] Percutaneous RFA has become widely used in HCC patients owing to its safety and efficacy.[9,10,11] Recently, this modality for treatment of HCC is also included as one of the curative treatment in the expert consensus.[12] However, RFA is difficult to perform when the tumor is located under the hepatic dome or near the surface of the liver, since visibility of the tumor on ultrasonography is not really clear, or abutting adjacent structures, such as the diaphragm, skin or organs that can be burned because of thermal injury during the process of RFA. These are several drawback of RFA that hampered the decision to use this modality. Artificial ascites can be use and overcome most condition to fulfill the objective of RFA. The technique of artificial ascites was first introduced in 1995.

Artificial ascites technique use in the following cases: (1) Failure to detect the tumor by usual ultrasonography because of tumor location, below the diaphragm, at the hepatic dome or left edge of the left lobe; (2) The proximity of the tumor to other vital organs, digestive tract, heart or diaphragm RFA is not easily performed because these are heat-vulnerable organs, high risk for thermal damage (3) Lack of clarity in the ultrasonographic image of the whole tumor because of mesenteric interference or gasses in the intestine.[13] An artificial ascites (AA) can effectively solved these problems. The AA method is safe and practical when performing RF ablation for tumors adjacent to heat-vulnerable organs because it can separate the RF ablation zone from the adjacent organs and improve the visibility of an index tumor.[14,15]

There were four different options of entry point for artificial ascites according to the location of hepatic tumor. Perihepatic route through the right 7-8 intercostal space or a sub-hepatic route below the hepatic angle along the anterior axilary line is recommended for tumor located in right lobe and segment 4. Another entry point is sub-xiphoid for tumor located in segments 2,3, and 4 abutting the diaphragmgm.[16]

Several techniques have been described to percutaneously separate the ablation site from adjacent structures. Fluid can be put into the pleural space to create artificial pleural effusion in order to improve visualization of peridiaphragmatic hepatic tumors.[17,18] This method have risk of respiratory compromise which may be already co-morbidity with liver cancer. Furthermore, volume of fluid injected are limited, and unable to separate the diaphragm from the liver. Angiographic balloon catheters have been tried and can be deployed between the liver and adjacent tissue, with expansion of the catheter providing space and buffering from the ablation zone.[19,20,21] The use of the balloon can be advantageous as they are not gravity dependent but this method is cumbersome and need more resources because they can be difficult to position, especially in tumors located far from the body surface, may rupture because of thermal damage, or interfere with ultrasound imaging. Sometimes manual deflection of the ablation zone by applying torque or pushing/pulling on the ablation applicator may occasionally be successful in displacing the tumor ablation zone from adjacent structures.[19,22] However, this technique may be difficult in deep lesions or may fail to create an adequate gap between the liver and perihepatic structures. There is also potential risk of tissue injury from excessive applicator deflection.

Artificial ascites can be use to separate the adjacent structure in order to avoid thermal injury and give a clear electrode path to the tumor percutaneously.[23] Kang et al, study the role of AA in RFA of a single HCC abutting the diaphragm. They divided 44 patients into two groups: the artificial ascites group and control group. They found that right shoulder pain and transient lung injury were significantly more prevalent in the control group than in the artificial ascites group, indicating the protective effect of artificial ascites in RFA for HCCs abutting the diaphragm.[24]

Several method of performing AA have been done. Kondo et al use 14-G needle with a metallic flat-cut trocar and a diamond-cut inner stylet that was designed for infusion of artificial ascites under real-time ultrasonographic guidance as initial puncture needle, followed by infusion of 5% dextrose into perihepatic space just under the inferior border of the liver.[25]

We modified their technique because metallic needle with flat-cut trocar dan diamond-cut sylet is not availabe. In this series, we use 22G spinal needle to make a pocket of fluid just below the inferior border of the liver. After the pocket of fluid was formed, slightly bigger 20G-spinal needle inserted to ease the administration of more fluid and then 14G or 16G IV canule needle were put inside the fluid line that formed. Liu et al use 18G-PTC needle as introducer needle before they put verress needle to administered the fluid into peritoneal cavity.[26] As introducer needle we consider these needle were big and may potentially have bigger risk of perforate or damage to adjacent organ. Chen MH et al injected 30-200 mL aseptic solution between the tumor and diaphragm which may be not enough to form a good separation. They reported 3.2% of major complication during RFA.[27] Uehara et al insert a 21-gauge needle just in front of the surface of the liver to inject 5% glucose which is not clear whether the fluid fill in the peritoneal cavity or only restricted at the liver capsule.[28]

Nishimura et al use the needle like ours but they penetrated the liver surface which we consider have a higher risk of bleeding. Moreover, their method need patients full cooperation in order to regulate inspiration because they need maximum inspiration while they inserted the needle, such action that we cannot done because our patient were already sedated from the beginning of the procedure to give the patients some comfort.[29] Asvadi et al use 19G-coaxial needle that inserted with CT guidance to the anterior surface of the liver that we consider high risk to peneterate the liver.[30] Others use angiosheath and guide wire which are relatively more expensive.[31,32,33]

In majority, artificial ascites can be done successfully without any complication. In our series, 100% of cases artificial ascites can be accomplished and fulfill the objectives whether it was to separate the adjacent structure to avoid thermal damage, clear the path of electrode or bring up the nodule so it can be visualize by ultrasonography. Rhim et al showed that artificial ascites was successfully achieved in 22 (88%) of 25 patients. They reported marked improvement in the visibility in 93.4% (15/16) of the tumor and a better path for electrode in 77.8% (7/9). The primary technique effectiveness rate for hepatic dome tumors was 96% (24/25) and no diaphragmatic thermal injury in all but one case.[32] Nishimura et al also found high success rate (97.1%) of performing artificial ascites. In their series, no significant differences were observed with respect to age, tumor size, or number of treatment sessions.[29] Liu et al reported technical success rate for induction of artificial ascites were 100% (35/36). The procedures had achieved predefined goals in 52 (92.9%) patients. Others also reported the same high success rate of performing artificial ascites.[13,15]

Whether abdominal surgery have any influence on success rate of induction of artificial ascites, remain controversial. Kang et al reported that hepatic resection can severely impaired success rate of performing artificial ascites from 84.1% to 55.8%.[15] However, Kondo et al found no difference in the success of performing artificial ascites between patient with history of abdominal surgery or not.[25]

Artificial ascites can give space between the liver surface and adjacent organs. The fluid between the liver and the gastrointestinal tract plays a role in insulating thermal energy transmission and lowering the temperature around the liver, thus protecting the adjacent structure from thermal injury. Although artificial ascites insulate adjacent structure from thermal injury but Kim et al. found that artificial ascites did not cause a heat-sink effect, which can affect the efficacy of RF ablation.[31] Kang et al study to compare between patient with artificial ascites and control group and they found that the mean diaphragmatic thickness on CT scans immediately after RF ablation was 1.88 mm in the artificial ascites group and 3.05 mm in the control group diaphragmatic thickness increase from the condition before radiofrequency ablation to that immediately after was 0.56 mm for the artificial ascites group and 1.55 mm for the control group; these differences were statistically significant ($p = 0.01$). Follow-up CT scans showed that swelling of the diaphragm in both groups decreased with time. Seven patients in the control group (7/24 = 29,2%) but only one patient (1/20 = 20%) in the artificial ascites group had right shoulder pain after radiofrequency ablation.[24] Hakime et al, reported that artificial ascites significantly decreases post-operative pain for peripheral large ablation by avoiding peritoneal burning.[34]

Although artificial ascites is beneficial to reduce the heat injury to the adjacent structure, artificial ascites does not have any heat-sink effect. Nam et al evaluate one group with artificial ascites and the other group as control. They found that mean volume of the RFA zone was 31.6 ± 11.9 cm 3 in group artificial ascites patients and 30.9 ± 11.0 cm 3 in control group ($p = 0{,}871$). Their conclusion were that artificial ascites does not have heat-sink effect and therefore it does not influence the efficacy of ablation.[35]

Artificial ascites improves tumor visibility because it pushed the intestine that is usually filled with air and change it with fluid that is more beneficial in terms of conductivity of ultrasound. This is really true in case of small tumor at the dome of the liver. In a previous study of 25 patients with HCCs in the hepatic dome, substantial improvement in visibility was achieved in 93.4 % (15/16) of the patients, and a more favorable electrode path was obtained in 77.8 % (7/9) of the patients.[14]

HCCs at difficult locations are technically more demanding to ablate than centrally located HCCs even after the infusion of artificial ascites. Therefore, more sessions of RFA are required to achieve the complete ablation of HCCs at difficult locations. However, the complete ablation and local tumor progression rates are comparable. In brief, RFA with artificial ascites is an effective therapy for HCCs at difficult locations. However, a conclusion has not been reached because of limited studies with few case.[23]

Artificial ascites procedure may lead to complications such as intraperitoneal bleeding or intestinal perforation, however no major complications have been reported in the literature. In their study, Jeong YS et al found no severe complications such as peritoneal bleeding, intestinal perforation, liver abscess, liver infarction, pneumothorax, biliary tract injury, skin burns, lung burns, uncontrolled ascites, or uncontrolled pleural effusion were observed. The stomach is the most frequent injured organ (28/ 52, 53.8%), followed by colon (17/52, 32.7%) and small bowel (7/52, 13.5%). Patients with complication tend to had thicker bowel wall than those with minor complication (1.8 ± 0.1 vs. 1.1 ± 0.3 cm, p = NS). They found that gastrointestinal tract (GIT) injury after hepatic RFA is rare (1.32%, 52/3933) and that major GIT complication requiring bowel surgery is extremely uncommon (0.05%, 2/3933). This result follows previous literature that reports the complication incidences of 0.1–0.3%. All of these complications may be related to RFA procedure rather than the artficial ascites.[36]

Complication of peritoneal cavity bleeding also analyzed in several studies. Hakime et al, found that artificial ascites did not increase the rate of bleeding. Several study also reported that artificial ascites does not have major complication.[13,25,29,34]

Long-term local tumour control and risk of peritoneal seeding were comparable for RFA with or without artificial ascites when used as a first-line therapy for subcapsular HCC. A recent study showed that the rate of peritoneal seeding was 6.8 % (3/44) in an artificial ascites group and 2.6 % (3/ 116) in a control group. No significant difference was noted between these two groups, suggesting that RFA with artificial ascites for the ablation of subcapsular HCCs did not increase the risk of peritoneal seeding.[24]

CONCLUSION

In this study we conclude that ultrasound-guided percutaneous RFA using artificial ascites technique was safe and effective for treating primary and secondary hepatic tumours. Artificial ascites offer good separation from other vital organ to further enhance the safety of the procedure. We did not find any serious complication to this thecnique, however the authors believe that more studies required to be perform in order to convince the safety and efficacy of this technique.

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