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Research Article

Radiofrequency Ablation for the Management of Sudanese Population with Hepatocellular Carcinoma: A Longitudinal Study

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Abstract

Hepatocellular carcinoma (HCC) is one of the most common primary malignant tumors that affect the liver. In management of small HCC, Multiple studies suggested local ablative techniques as the treatment of choice for HCC. We conducted a longitudinal study at GI and Endoscopy unit from 2012 to 2020. We aimed to evaluate the long-term outcomes of RFA as a first-line therapy for management of HCC and to determine the prognostic factors for survival. Results showed that nearly half of patients after RFA (46%) had a survival of more than one and a half year and nearly 20% of the study population survived more than two years. RFA proves to be an efficient mode of treatment for HCC. However, the management of HCC in Sudan still facing several obstacles from patient's monitoring to early detection and management. We will continue our study by increasing number of population and will aim into implementing a new screening and treatment program for those with such debilitating disease.

Keywords: Longitudinal Study; Hepatocellular Carcinoma; Sudan

Introduction

Hepatocellular carcinoma (HCC) is one of the most common primary malignant tumors that affect the liver. The annual incidence of HCC is estimated to be at least one per million, with an average survival rate of about 4-6 months from onset of diagnosis if left untreated. The only possible curative option until today is surgical resection as HCC has shown poor response to systemic chemotherapy and/or radiation therapy. However, despite the success of surgical resection [1], limited patient can go through surgery as they are usually considered not fit or have contraindications for surgeries. These contraindications may include HCC close to vital structures that are difficult to remove, multiple scattered tumors, poor hepatic reserve such as Cirrhosis and patients with other co morbid conditions like cardiac, renal and/or other conditions that makes them not suitable for surgery. Recent surveys showed that only 5-15% of patients with HCC or liver METs are eligible for surgical resection. And the 5 years survival rate post resection for those patients is 20-40% [1]. Other options for management of malignant hepatic tumors include Chemoembolisaion, ethanol injection and thermal ablation techniques in form of freezing (Cryoablation) or heating Radiofrequency (RFA) ,Laser or High-intensity focused sonography [2-4].

Radiofrequency ablation is a localized thermal technique result in tumor destruction by high temperature exceeding 60°C [5]. This ablation process of liver tumors removes both intra and extracellular water from malignant cells that result in coagulative necrosis and tissue damage [6]. When temperature increases above 60°C, intracellular proteins become denatured, lipid bilayers melt, and destruction of cell is inevitable [3,7]. Malignant cells are more resistant to fatal injury from freezing compared to normal cells, but are more sensitive to high temperature damage than normal cells

[8]. RFA has become preferable over surgery and intra-arterial therapies for treatment of HCC at an early stage and primary for small tumors [9,10]. In management of small HCC, A meta-analysis by jansen., *et al*. suggested local ablative techniques as the treatment of choice for HCC [11], which then recommended by (NICE) guidelines [12]. RFA may be used as alternative management for patients who are not fit or has contraindications for surgery or for those who are awaiting liver transplantation. Despite the good response of HCC to RFA, RFA may be considered unsafe in patients with tumors occupying more than 40% of the liver, as the remaining liver cannot sustain sufficient function [13]. Adverse effects of In long term analysis reported in several studies showed that most common major complications include biliary tract damage (4.9%), liver failure (2.8%), hepatic abscess formation (2.1%), peritoneal infection (1.4%), intrahepatic hematoma and pulmonary embolism (below1%) [14,15]. However, the long-term survival rate after RFA of colorectal liver metastases can range from 3-5 year for up to 10 years [16]. RFA has proven to show significant decrease in recurrence when good ablation with proper margins was obtained [4].

Aims and Methods

We conducted a longitudinal study at GI and Endoscopy unit from 2012 to 2020, the National Ribat University Hospital, Khartoum, Sudan. We aimed to evaluate the long-term outcomes of RFA as a first-line therapy for management of HCC and to determine the prognostic factors for survival. Patient with HCC referred from different hospitals for further management are considered for this study. Patient with mild or no chronic liver disease (Child-Pugh Class A,B) who developed hepatocellular carcinoma either solitary lesion of 6 cm in greater diameter or smaller, three or less multiple lesions with greater diameter of 3 cm or less have been included in this study. We excluded all patients with vascular invasion and extrahepatic metastasis as well as patient who received other modalities for management of HCC such as TACE, PEI or medical treatment such as Sorafenib.

A cohort of patients with HCC were identified and referred from different regional hospitals in Sudan to National Ribat University Hospital, data were collected in a form of interview questionnaire and clinical data obtained pre and post RFA. All gathered data has been validated to ensure patients have met inclusion/exclusion criteria. Collected information has been entered into IBM SPSS software package v23.0 for statistical analysis, number of value and its percentage as well as survival rate were calculated. Association between survival and RFA as well as AFP was assessed using correlation and univariate and multivariate regression analysis.

Results

Fifty patients has been referred from different hospital for suspension of HCC that may need RFA as a form of management, 5 patients were excluded as they already underwent PEI, 3 patients excluded as they underwent TACE and 6 patients were having either huge lesion or other contraindication that may interfere with the results and have been excluded. We included 36 patients in the study.

Patient demographics and baseline characteristics

Out of 36 patients included in this study, around 61% were above the age of 60 years and 33% were between the age 41-60 years and only 5% were below 40 years. Majority of the study population were males (80.5% n = 29). More than one third of the study population were from west Sudan (38.8% n = 14). 30.5% were from central area and rest of population were from north, east and south of Sudan (16.67%,11.11%,2.7% respectively). When we screened for viral hepatitis, 72.2% tested positive for either Hepatitis B (n = 13) or Hepatitis C (n = 12).

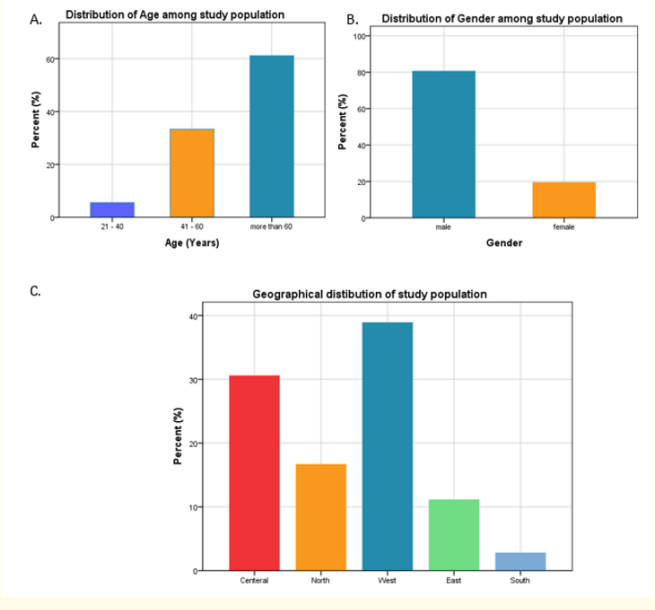

Figure 1: Demographic distribution of recruited patients (A. Distribution of different age groups among study population. B. Gender distribution C. Distribution of study population according to geographical residence in Sudan.)

Disease status and severity among study population

While assessing patient's history, we discover that only 30.6% of patients who have viral hepatitis received antiviral treatment, while 69.4% were novel to any kind of treatment. More than two third of the study population have liver cirrhosis (71.43%) and high levels of alpha feto protein (AFP more than 100 U/L) (77.8%).Looking at the current disease situation, nearly half of study population were Child-pugh class A (47.6%) and other half were Child-pugh class B(47.6%) . only one patient was with child pugh class C. As for number of lesions presented in each of our study population, more than two third of study population had only one lesion (76.2%) while only few had two or more lesions (23.8%).

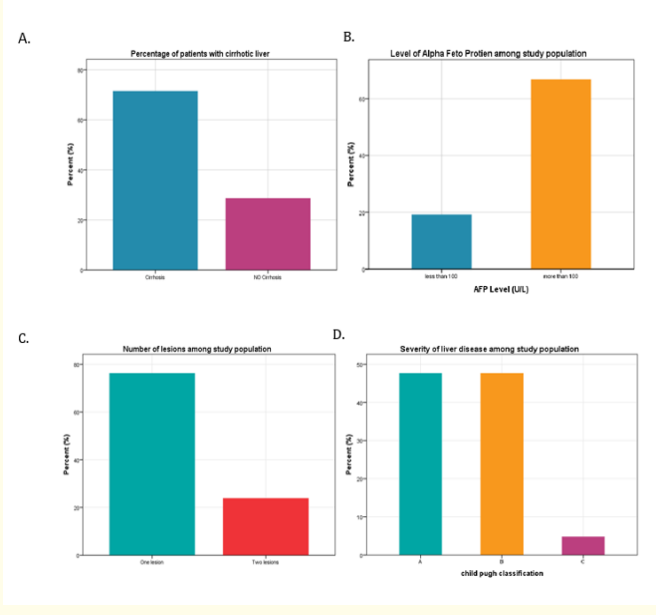

Figure 2: Status and severity of liver disease among study population (A. Presence of liver fibrosis and cirrhosis among study population B. levels of Alpha Feto Protein among study population. C. Number of lesions found on patients' liver among screening D. Severity of liver disease among study population based on Child Pugh classification.)

Estimation of survival post Radiofrequency ablation

Follow-up of patients after RFA showed that nearly half (46%) of treated patients had a survival of more than one and a half year and nearly 20% of the study population survived more than two years and among these 5 patients are still alive and in good health.

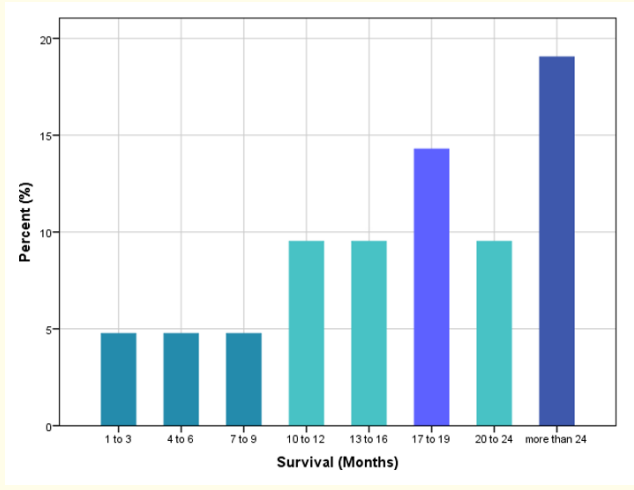

Figure 3: Survival outcome of study population after a successful Radiofrequency ablation of their liver lesions.

Discussion

Many studies that have been documented recently validate the superior of radiofrequency ablation over other techniques for the treatment of HCC [16-18]. With the current difficulty that is faced by Healthcare professional here in Sudan, it was prudent to study this mode of management locally to provide a clear and accurate description of patient demographics and survival after being treated with RFA.

It was recognized that the demographics of patients included in the study showed most of patients who presented with hepatic lesions were of middle to elderly groups, it was also apparent that those were coming from either Central or Western regions of Sudan. These regions are considered a known epidemic area for viral hepatitis, which constitute nearly three quarters of the study population [19]. A review on the number of patients with severe disease upon referral and causes of HCC among our study population, it was clear that all patients were having advanced liver disease with high levels of AFP, but what took us by surprise was only one third of patients who had viral hepatitis received treatment. In contrast, two third were novel to any kind of treatment despite having clear features of chronic liver diseases. These complications would have been prevented with proper management and treatment through medication and close follow up [20-23].

In our study, despite the advanced disease these patients were having, survival after RFA was more than one and a half years in nearly half of the study population, and five patients are still alive, we hypothesis that late presentation and poor management of these patients in the their early disease presentation may had a negative impact on treatment and survival. Sucandy., *et al*. a retrospective study to assess the survival rate after RFA of hepatocellular carcinoma concluded that treating HCC with RFA can lead to long term survival of up to 10 years in 25% of primary liver tumor [24,25]. Other study by Babawale., *et al.* to assess the survival rate after RFA of 105 patients with colorectal metastasis suggested early approach and management of liver tumors has a great impact on the survival rate [25].

Several limitations were considered in the study. The number of patients in this study was small compared to other studies due to the robust and strict inclusion and exclusion criteria implemented, another limitation was the inability to review past history of many included patient due to absence of documentation which affected the ability to pursue the reason for novelty of treatment. Nevertheless, this study provided critical information regarding the management of patient with viral hepatitis and its effect on patient survival that should be immediately recognized by clinician involved on their management. A national program for screening of viral hepatitis should be adopted and implemented by local authorities specially in western and central Sudan for early detection and management of discovered cases to decrease the development of HCC. Systemic screening of patient with liver fibrosis and cirrhosis for HCC should be actively considered to increase the effectiveness of RFA and thus survival.

We are aiming to continue in our study and to increase the number of populations. We also aim to involve other centers for early referral and early management of HCC cases.

Conclusion

RFA proves to be an efficient mode of treatment for HCC. However the management of HCC in Sudan still facing several obstacles from patient's monitoring to early detection and management. This study showed that despite the successful use of RFA for treatment of HCC; we require a proper screening program for more efficient and robust treatment plan. We will continue our study by increasing number of population and will aim into implementing a new screening and treatment program for those with such debilitating disease.

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