Evaluation of Cirrhotic Cardiomyopathy in Patients with Hepatocellular Carcinoma by Brain Natriuretic Peptide and Echocardiography Before and After Radiofrequency Ablation

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Abstract: Radiofrequency ablation (RFA) is a minimally invasive alternative therapeutic technique for hepatocellular carcinoma (HCC). Cirrhotic cardiomyopathy (CCM) is chronic cardiac dysfunction in patients with cirrhosis and one of its markers is brain natriuretic peptide (BNP). The aim of this study was to evaluate cirrhotic cardiomyopathy in hepatocellular carcinoma patients by brain natriuretic peptide and echocardiography before and after radiofrequency ablation. Patients and Methods: This study was conducted on 30 patients who were divided into: Group I which included twenty patients with hepatocellular carcinoma candidate for radiofrequency ablation as patient group. Group II which included ten patients with liver cirrhosis (child A) as control group. Evaluation of presence of cirrhotic cardiomyopathy in patient group was done by measuring serum BNP level by ELIZA and performing echocardiography before and after radiofrequency ablation by one week. Results: There was insignificant statistical difference between BNP and ejection fraction (EF%) in patient group before RFA (P=0.995). And insignificant correlation between BNP and parameters of cardiac dysfunction in echocardiography (E/A ratio, deceleration time) in patient group before RFA (P=0.117) (P=0.466). One week after RFA, there was insignificant correlation between BNP, EF%, E/A ratio and deceleration time before and after RFA (P>0.05). Conclusion: Serum BNP and echocardiography might not be conclusive or diagnostic for unmasking any mild cardiac dysfunction in (child A) cirrhotic patients after RFA.

Keywords: CCM, HCC, RFA, BNP, EF%.

1. Introduction

Hepatocellular carcinoma is one of the ten most common cancers worldwide. The tumor is either single or occurs as multiple nodules throughout the liver (Kumar et al., 2005). Liver cancer is the fifth most common cancer in men and the seventh in women (Golobocan, 2008).

Radiofrequency ablation has received great interest as a minimally invasive alternative therapeutic technique for hepatocellular carcinoma (HCC) for the past decade and has now gained a major role in the treatment of HCC with promising clinical outcome data (Rhim et al., 2003).

Cirrhotic cardiomyopathy is defined as chronic cardiac dysfunction in patients with cirrhosis characterized by blunted contractile responsiveness to stress and/or altered diastolic relaxation with electrophysiological abnormalities, in the absence of known cardiac disease and irrespective of the causes of cirrhosis, although some etiologies (e.g., iron overload and alcohol consumption) have further impact on myocardial structure and function. This syndrome is considered to be related to both portal hypertension and cirrhosis and is characterized by intrinsic alterations in myocardial function (Donovan et al., 1996).

Stresses such as liver transplantation, infection and procedures such as insertion of Transjugular intrahepatic portosystemic stent-shunts (TIPS) can convert latent to overt heart failure. Indeed, heart failure is responsible for 7%–15% of mortality following liver transplantation (Myers and Lee, 2000 & Therapondos et al., 2004).

In the setting of liver cirrhosis and portal hypertension, a wide spectrum of factors, such as volume expansion and hyperdynamic circulation, contribute to systolic and diastolic dysfunction. Cardiomyocyte plasma membrane abnormalities, cytokines, growth factors, and autonomic impairment are also implied in this process. With advanced liver disease, these factors can lead to cardiac failure (Zardi et al., 2010).

Several studies suggest that some level of diastolic dysfunction exists in most patients with cirrhosis therefore, it would be expected that this and other cardiac abnormalities would disappear after liver transplantation (LT). However, results from
previous studies have been conflicting regarding this point (Torregrosa et al., 2005).

Portal hypertension is an important and common complication of liver cirrhosis. The pathophysiology of portal hypertension includes two important factors, vascular resistance and blood flow. Endothelin, angiotensin 2 and alpha adrenergic stimulus increase hepatic vascular resistance (Theodorakis et al., 2009).

Cirrhotic cardiomyopathy presents mainly by:
1- High output failure (with normal EF% measured by echocardiography) but with blunted response to stress.
2- Diastolic dysfunction as evaluated by Doppler examination of the mitral flow and presenting by reversed E/A ratio and prolonged deceleration time (>200ms).
3- Elevated serum BNP level (Moller and Henriksen, 2009).

Brain natriuretic peptide (BNP) is a biologically active peptide of 32 amino acids and has vasodilator and natriuretic properties. BNP is cleaved from the 108 amino acids pro-brain natriuretic peptide released from cardiac ventricles in response to stretching chambers. Release of BNP appears to be indirect proportion to ventricular volume expansion and pressure overload. BNP decreases after effective treatment of heart failure. It is used in routine assessment for differentiating acute heart failure from other causes of dyspnea such as respiratory failure (Hobbs et al., 2002).

Cardiac natriuretic peptides, namely atrial natriuretic peptide and BNP, have long been known to be elevated in cirrhotic patients as a consequence of increased cardiac release and not because of impaired hepatic extraction (Gines et al., 1988 & La Villa et al., 1992).

BNP levels increase markedly in left ventricular dysfunction and the level in heart failure is correlated with symptoms severity (Jankowski, 2008). Serum BNP levels of ≥ 100 pg /ml have a greater than 95% specificity and greater than 98% sensitivity in patient with congestive heart failure (CHF) (Hobbs et al., 2002).

Causes of increase of BNP could be cardiac such as heart failure, diastolic dysfunction, acute coronary syndrome, hypertension with left ventricular hypertrophy, valvular heart disease, atrial fibrillation, myocarditis and cardiac allograft rejection or non cardiac such as acute pulmonary embolism, pulmonary hypertension, sepsis, chronic obstructive pulmonary disease (COPD) with cor-pulmonale or respiratory failure, hyperthyroidism and renal failure (Felker et al., 2006).

Percutaneous radiofrequency ablation (RFA) is an exciting approach to destroying inoperable primary or metastatic tumors in the liver. In the treatment of hepatocellular carcinoma (HCC), less than 40% of patients are candidates for surgery, and the rate of recurrence after curative surgery is high. Percutaneous techniques like RFA are, therefore, very important. RFA is widely used for metastatic and small primary tumors. RFA serves as a bridge for transplant candidates, especially in relation to small primary lesions (Buell et al., 2008).

2. Patients and Methods

This study was conducted on 30 patients with chronic liver disease selected from El Demerdash hospital and Ain Shams University Specialized hospital (Internal Medicine and Interventional radiology units) in the period from October 2011 to June 2012. They were divided into 2 groups:

**Group I:** Included 20 Patients with liver cirrhosis and hepatocellular carcinoma candidate for radiofrequency ablation as patient group.

**Group II:** Included 10 patients with liver cirrhosis (child A) according to child pugh score as control group (Child et al., 1964).

All patients were subjected to the following:

**I - Full history taking and clinical examination.**

**II - Laboratory investigations including:**

1. **Liver function tests:**
   - Serum albumin (S.Alb).
   - Serum alanine aminotransferase (S.ALT).
   - Serum aspartate aminotransferase (S.AST).
   - Serum alkaline phosphatase (S.ALP).
   - Serum total and direct bilirubin.
   - Gamma glutamyl transpeptidase (GGT).
   - Serum total protein.

2. **Tumor markers as serum alpha fetoprotein and carcinoembryonic antigen (CEA).**

3. **Prothrombin time (PT) and international normalized ratio (INR).**

4. **Kidney function tests:**
   - Serum blood urea nitrogen (BUN), serum creatinine and urine analysis.

5. **Complete blood picture (CBC).**

6. **Fasting blood sugar, postprandial sugar and glycosylated hemoglobin (HbA1c).**

7. **Lipid profile:**
   - Serum Low-density lipoprotein (S.LDL).
   - Serum high-density lipoprotein (S.HDL).
   - Serum cholesterol.
   - Serum Triglycerides (S.TG).
8. Viral markers for HBV, HCV, CMV and EBV (HCV Ab, HBsAg, HBsAb, HBcoreAb IgM, CMV Ab IgM, EBV Ab IgM).

**III - Radiological investigations:**
2. Abdominal ultrasound and portal vein Doppler.
   To evaluate hepatomegaly, splenomegaly, portal vein dilatation, thrombosis and focal lesion in liver.
3. Upper and lower GIT endoscopy.
4. Echocardiography to evaluate:
   a- Left ventricular (LV) systolic function, LV ejection fraction was measured using the modified Simpson technique (Folland et al., 1979).
   b- Assessment of diastolic function:
      Transmirtal flow profile was assessed by 2-D guided pulsed wave Doppler from the apical 4-chamber view by positioning a 3 - mm - sized sample volume between the tips of the mitral leaflets in diastole and recording at a sweep velocity of 100 mm/s. Mitral flow parameters included peak velocities during early diastole (E) and late diastole (A), their ratio (E/A ratio), as well as the deceleration time (DT) of the early filling wave (E-wave). This echocardiographic evaluation was done before and one week after radiofrequency ablation (Rakowski et al., 1996).
   - **Ejection fraction:** is a measurement of the percentage of end-diastolic volume that is ejected from the left ventricle in systole.
   - **E/A ratio:** is the ratio between early (E) and late (atrial - A) ventricular filling velocity. In diastolic dysfunction, a greater portion of end-diastolic volume results from late filling rather than early filling. Therefore, the E/A ratio is reduced in diastolic dysfunction. The late phase is dependent upon atrial contraction and is therefore absent in patients with atrial fibrillation, making the E/A ratio very large (Abdul Latif et al., 2004).
     The normal transmirtal flow profile has two peaks - an E and an A wave.
     The E peak arises due to early diastolic filling. Most filling (70-75%) of the ventricle occurs during this phase.
     The A peak arises due to atrial contraction, forcing approximately 20-25% of stroke volume into the ventricle.
   - **The deceleration time (DT):** is the time taken from the maximum E (early) point to baseline. Normally in adults it is less than 220 milliseconds.

5. Triphasic abdominal CT scan:
   To evaluate the abdominal organomegaly, portal vein dilatation, focal lesion size and their enhancement in which rapid enhancement in arterial phase with delayed venous washout confirms hepatocellular carcinoma.

**IV- ECG**

**V- Liver biopsy**
   Ultrasound guided liver biopsy under local anaesthesia by semiautomated needle for patients not confirmed to have hepatocellular carcinoma (HCC) by alpha fetoprotein or triphasic abdominal CT scan (it was done after patient consent) with satisfactory bleeding profile (PT, INR, platelet count).

**VI- Measurement of serum BNP**
   Brain natriuretic peptide (BNP) concentration by ELISA was done immediately before radiofrequency ablation and one week after the procedure, in patient group and was done also for the control group only once.

**Methods**

**Blood Samples**
   15 ml was sampled from peripheral veins from both patients and controls, that was collected into two tubes ; 5 ml of heparinized blood for separation of mononuclear cells for detection of virus B by real time PCR and another 10ml of plain tubes for serum separation for BNP detection and for other laboratory investigation.

**Isolation of peripheral blood mononuclear layer:**
   Peripheral blood mononuclear cells(PBMCs) were isolated from blood by density gradient centrifugation using ficoll-hypaque 1077 ml in separation of serum to detect BNP , virus C by real laboratory investigation of peripheral blood mononuclear cells (PBMCs) were isolated from blood by density gradient centrifugation 07 (Sigma, USA ) at 1200 g for 30 minutes at 4°C. The interface cells were removed, washed twice with 25 ml of sterile PBS (pH 7.3), pelleted, and resuspended in 1ml of PBS. The cells were pelleted again at 1200 g for 2 minutes. The cell pellets were kept at -80°C until nucleic acid extraction.

**Nucleic acid extraction**
   - Viral RNA extraction for virus C was done using viral RNA extraction kit supplied by (Qiagen) according to the manufacturer instruction .
   - Viral DNA extraction for virus B was done using the QIAamp DSP virus DNA extraction
kit supplied by (Qiagen) according to the manufacturer instruction.
- All DNA and RNA preparation and handling took place in a biosafety level 2 laminar flow hood.
- The isolated DNA and RNA were resuspended in molecular grade water and stored at \( -80 \, ^{\circ}C \) until assay. Both the RNA and the DNA concentrations were assessed by absorbance reading at 260 nm with UV spectrophotometry (Beckman ; Du series 650, INC USA ).

Real time PCR

In real-time PCR the amplified product is detected via fluorescent dyes. These are usually linked to oligonucleotide probes which bind specifically to the amplified product. Monitoring the fluorescence intensities during the PCR run (i.e in real-time) allows the detection and quantitation of the accumulating product without having to re-open the reaction tubes after the PCR run.

The artus HBV TM PCR Kit and the artus HCV RT-PCR kit supplied by QIAGen were used for the detection of HBV and HCV. Programming of the applied biosystems apparatus (ABI PRISM 7500 FAST) was done according to the manufacturer instruction.

Immuonassay for detection of BNP

Circulating BNP was determined by commercially available ELISA and STANDARDS. The BNP ELISA kit allows for the in vitro quantitative determination of BNP concentrations in serum. The microtitre plate provided has been precoated with an antibody specific to BNP. Standards and samples were added to microtitre plate wells with a biotin-conjugated polyclonal antibody preparation specific for BNP. Next avidin conjugated to horseradish peroxidase (HRP) was added to each well and incubated ,then a substrate solution was added to each well. Only those wells that contained BNP, biotin- conjugated antibody and enzyme-conjugated avidin will exhibit a change in colour. The colour change was measured spectrophotometrically at a wavelength of 450 nm. The concentration of BNP in samples was determined by comparing the O.D of the samples to the standard curve.

VII – Percutaneous radiofrequency ablation (RFA)

Was done using cool tip RF operating system used with cluster needle for up to 5 cm lesions. (After patient consent)

Anesthesia:

Percutaneous ablation was performed with the patient under conscious sedation using a combination of intravenous midazolam and Propofol (Diprivan) (Low et al., 2006).

Exclusion Criteria:

I - Patients with diseases affecting BNP level such as:

1. Congestive Heart Failure.
2. Left Ventricular Hypertrophy.
4. Primary Pulmonary Hypertension.
5. Renal Failure.
6. Thyrotoxicosis.
7. Medications (Digoxin, Beta Blocker).

II – Patients with chronic liver disease and hepatic focal lesion not fulfilling criteria for RFA such as:

1. Large focal lesion > 5 cm.
2. Child B or C.
3. Focal lesion near large blood vessel or common bile duct (CBD).
4. HCC with vascular invasion or extrahepatic extension.
5. Benign focal lesion or metastasizing hepatic focal lesions.

Inclusion Criteria for patient group:

Patients with chronic liver disease and hepatic focal lesion that was diagnosed to be hepatocellular carcinoma by either increased alpha fetoprotein > 400 ng % and / or triphasic abdominal CT scan that showed rapid arterial enhancement of the hepatic focal lesion with delayed venous phase.

Criteria needed for radiofrequency ablation (RFA):

1. 3-5 lesions each < 3 cm or one focal lesion ≤ 5 cm.
2. Child A score of chronic liver disease.
3. Tumor lesion not near large blood vessel, intestinal loop or common bile duct.
4. No vascular invasion or extrahepatic extension.

Statistical Analysis

Data was analyzed on IBM personal computer, using Statistical Package for Special Science (SPSS) software computer program version 15. The following tests were used as mean ± standard deviation (SD), frequency & percentage Independent Student t test, Paired t test Chi-square test, Pearson correlation coefficient, Significance level \( (P) \) value:

- \( P < 0.05 \) is significant (S).
- \( P < 0.01 \) is highly significant (HS).
- \( P > 0.05 \) is insignificant (NS).

3. Results

This study included 30 patients with liver cirrhosis. They were divided into 20 with liver cirrhosis (child A) with hepatocellular carcinoma candidates for radiofrequency ablation as a patient group and 10 patients with liver cirrhosis (child A) as a control group. The patient group were 17 males (85%) and 3 females (15%) while the control group...
were 9 males (90%) and 1 female (10%) with no significant difference as regard sex. As regard age patient group had mean ±SD 56.8±6.2 years while control group had mean ±SD 50.30±7.70 years and there was no significant difference as regard age.

Table (1): Comparison between both groups as regard serum BNP level before radiofrequency ablation:

<table>
<thead>
<tr>
<th>BNP – Before (pg/mL)</th>
<th>Group</th>
<th>N</th>
<th>Mean ± SD</th>
<th>t</th>
<th>P</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients</td>
<td>20</td>
<td>894.79 ± 101.05</td>
<td>-0.166</td>
<td>0.869</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>10</td>
<td>901.18 ± 95.03</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There was no significant difference between patient and control groups as regard serum BNP level before radiofrequency ablation.

Table (2): Comparison between both groups as regard EF% before radiofrequency ablation.

<table>
<thead>
<tr>
<th>EF% Before</th>
<th>Group</th>
<th>N</th>
<th>Mean ± SD</th>
<th>t</th>
<th>P</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients</td>
<td>20</td>
<td>65.3500 ± 15.50645</td>
<td>0.368</td>
<td>0.715</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>10</td>
<td>63.5000 ± 3.89444</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There was no significant difference between patient and control groups as regard the EF% before radiofrequency ablation.

Table (3): Correlation between BNP level and EF % before radiofrequency ablation in patient group.

<table>
<thead>
<tr>
<th>BNP – Before (pg/mL)</th>
<th>EF% - Before</th>
<th>Pearson Correlation</th>
<th>P value</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pearson Correlation</td>
<td>-0.002</td>
<td>0.995</td>
<td>NS</td>
</tr>
</tbody>
</table>

There was no significant difference between BNP level and EF % before radiofrequency ablation in patient group.

Table (4): Correlation between BNP level, E/A ratio and Decleration time before radiofrequency ablation in patient group.

<table>
<thead>
<tr>
<th>E/A ratio - Before</th>
<th>BNP -Before (pg/mL)</th>
<th>N</th>
<th>Mean ± SD</th>
<th>P value</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td></td>
<td>11</td>
<td>927.94 ± 105.4</td>
<td>0.117</td>
<td>NS</td>
</tr>
<tr>
<td>&lt;1</td>
<td></td>
<td>9</td>
<td>855.36 ± 84.698</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prolonged</td>
<td></td>
<td>17</td>
<td>887.64 ± 103.47</td>
<td>0.466</td>
<td>NS</td>
</tr>
</tbody>
</table>

There was no statistically significant difference between BNP level with E/A ratio and deceleration time before radiofrequency ablation in patient group.

Table (5): Comparison between levels of serum BNP before and after radiofrequency ablation in patient group.

<table>
<thead>
<tr>
<th>BNP – Before (pg/mL)</th>
<th>N</th>
<th>Mean ± SD</th>
<th>t</th>
<th>P</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>BNP – Before (pg/mL)</td>
<td>20</td>
<td>894.79 ± 101.05</td>
<td>-0.450</td>
<td>0.658</td>
<td>NS</td>
</tr>
<tr>
<td>BNP – After (pg/mL)</td>
<td>20</td>
<td>909.73 ± 143.05</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There was no statistically significant difference between levels of serum BNP before and after radiofrequency ablation in patient group.

Table (6): Comparison between the Decleration time before and after radiofrequency ablation in patient group.

<table>
<thead>
<tr>
<th>Deceleration time before (Milliseconds)</th>
<th>Patients with Normal Deceleration</th>
<th>Patients with Abnormal Deceleration</th>
<th>total</th>
<th>P value</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3</td>
<td>17</td>
<td>20</td>
<td>1.00</td>
<td>NS</td>
</tr>
</tbody>
</table>

There was no statistically significant difference between the deceleration time before and after radiofrequency ablation in patient group.
Table (7): Comparison between the E/A ratio before and after radiofrequency ablation in patient group.

<table>
<thead>
<tr>
<th>E/A before</th>
<th>Patients with Normal E/A</th>
<th>Patients with Abnormal E/A (&lt;1)</th>
<th>total</th>
<th>P value</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>E/A before</td>
<td>11</td>
<td>9</td>
<td>20</td>
<td>0.317</td>
<td>NS</td>
</tr>
<tr>
<td>E/A after</td>
<td>10</td>
<td>10</td>
<td>20</td>
<td>0.500</td>
<td>NS</td>
</tr>
</tbody>
</table>

There was no statistically significant difference between E/A ratio before and after radiofrequency ablation in patient group.

Table (8): Comparison between the EF% before and after radiofrequency ablation in patient group.

<table>
<thead>
<tr>
<th>EF% - Before</th>
<th>Pearson Correlation</th>
<th>P value</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF% - After</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td>0.233</td>
<td>0.323</td>
<td>NS</td>
</tr>
<tr>
<td>N</td>
<td>20</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There was no statistically significant difference between the EF% before and after radiofrequency ablation in patient group.

Table (9): Correlation between BNP level and EF % after radiofrequency ablation in patient group.

<table>
<thead>
<tr>
<th>BNP – After (pg/mL)</th>
<th>Pearson Correlation</th>
<th>P value</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF% - After</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td>0.358</td>
<td>0.121</td>
<td>NS</td>
</tr>
<tr>
<td>N</td>
<td>20</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There was no statistically significant difference between BNP level and EF % after radiofrequency ablation in patient group.

Table (10): Correlation between BNP level, E/A ratio and Deceleration time after radiofrequency ablation in patient group.

<table>
<thead>
<tr>
<th>BNP - After pg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>E/A ratio – After</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

There was no statistically significant difference between BNP level, E/A ratio and deceleration time after radiofrequency ablation in patient group.

4. Discussion

Over the last 2 decades, there is accumulating evidence to suggest that the presence of cirrhosis perse is associated with significant cardiovascular abnormalities, irrespective of the cause of cirrhosis. These include resting increased cardiac output; decreased systemic vascular resistance; reduced myocardial contractility or systolic incompetence, especially under conditions of stress, whether physiological, physical, or pharmacological; increased thickness of the left ventricle, associated with diastolic dysfunction; and electrophysiological abnormalities. This constellation of abnormalities has been termed cirrhotic cardiomyopathy (Zambruni et al., 2006).

Cirrhotic cardiomyopathy (CCM) is a chronic cardiac dysfunction in patients with cirrhosis, characterized by blunted contractile responsiveness to stress and/or altered diastolic relaxation with electrophysiological abnormalities, in the absence of any known cardiac disease (Milani et al., 2007). The precise definition and the diagnostic criteria are waiting for a formal publication of the consensus statement. The prevalence of CCM remains unknown at present, mostly because the disease is generally latent and shows itself when the patient is subjected to stress such as exercise, drugs, hemorrhage and surgery (Myers and Lee, 2000). Deaths have occurred following surgery in patients with cirrhosis (Franco et al., 1988 Rayes et al., 1995 & Lebrec et al., 1996), suggesting that better assessment of cardiac function is needed in these patients. CCM has been reported to be a major cause of morbidity and mortality in cirrhotic patients after they have liver transplantation (Therapondos et al., 2004).
However, they have been generally regarded as markers of volume overload rather than markers of cardiac dysfunction. Recently, Wong and colleagues proposed that BNP could be an indicator of cirrhotic cardiomyopathy (Wong et al., 2001).

RFA is a localized thermal treatment technique designed to induce tumor destruction by heating the tumor tissue to temperatures that exceed 60°C (McGahan et al., 1992)

The alternating current of radiofrequency waves passing down from an uninsulated electrode tip into the surrounding tissues generates changes in the direction of ions and creates ionic agitation and frictional heating. This tissue heating then drives extracellular and intracellular water out of the tissue, resulting in tissue destruction by coagulative necrosis (Goldberg et al., 1996)

As regard gender and age both groups showed a non significant difference. Some studies had shown that increased age can increase BNP levels. Henriksen et al. (2003) studied the relation between plasma concentrations of cardiac peptides reflecting early ventricular dysfunction (pro-brain natriuretic peptide (pro-BNP), brain natriuretic peptide (BNP)) and markers of severity of liver disease, cardiac dysfunction, and hyperdynamic circulation in 51 patients with cirrhosis. Henriksen et al. (2003) found that circulating pro-BNP and BNP concentrations may increase with age. The increase was weak in subjects less than 70 years but in elderly subjects beyond this age, BNP increased substantially. This may in part reflect unmasked heart failure, but in elderly healthy individuals with a normal exercise test and echocardiography, circulating values of pro-BNP seem higher than in younger subjects.

There was no statistically significant difference between the two groups regarding BNP levels in patient group before RFA and also non significant statistical correlation between BNP (before RFA) and laboratory data in patient group.

Yilmaz et al. (2010) investigated the relation of increased brain natriuretic peptide level with hepatic failure and portal hypertension. He found that BNP levels were positively correlated with the stage of cirrhosis according to Child Pugh classification indicating that BNP was related to severity of liver cell failure. This discrepancy between the two studies can be explained by the fact that the patient group in our study was HCC patients candidates for radiofrequency ablation which mostly indicates Child A patient.

Comparison between patients and controls as regard the EF% before radiofrequency ablation showed non-significant statistical difference.

Zardi et al. (2010) explained in his review article that systolic dysfunction (EF%) worsens with increasing liver cell failure and not related to the presence of ascites and therapeutic paracentesis.

This study showed non significant statistical correlation between BNP & (EF%, E/A ratio, deceleration time) in patient group before RFA which goes with the study of Wong et al. (2001) who evaluated the levels of N-terminal pro-atrial natriuretic peptide and brain natriuretic peptide and their relationship with cardiac structure and function in 19 cirrhotics with ascites and 17 cirrhotics without ascites. Wong found that increased BNP didn’t correlate significantly with EF%, but he found significant statistical correlation with E/A ratio & deceleration time (parameters of diastolic dysfunction). Also Zardi et al. (2010) explained that ascites is known to affect E/A ratio & deceleration time and that both of these parameters improved after paracentesis.

So both studies were conducted on patients with ascites most probably child score B and C which were different from our child A score patients.

As regard the effect of radio frequency ablation on parameters of cirrhotic cardiomyopathy, showed a non significant statistical changes in BNP levels, deceleration time, E/A ratio and EF % respectively (before and after radio frequency ablation).

After radio frequency ablation, BNP did not correlate statistically with any parameter of cirrhotic cardiomyopathy (EF%, E/A ratio & deceleration time) respectively.

From this study, RFA might be a mild stressful maneuver that may not unmask any cardiac dysfunction in cirrhotic child A patients with localized hepatocellular carcinoma.

As regard the serum BNP level or echocardiographic parameters in child A cirrhotic patients with hepatocellular carcinoma candidates for RFA, serial monitoring of these parameters on longer terms may lead to better assessment.

Conclusion

Serum BNP and echocardiography might not be conclusive or diagnostic for unmasking mild cardiac dysfunction in (child A) cirrhotic patients after RFA.

References