International Journal of Medical and Health Research
ISSN: 2454-9142
Received: xx-11-2018; Accepted: 12-12-2018
www.medicalsciencejournal.com
Volume 5; Issue 1; January 2019; Page No. 00-00

Analysis of systemic hemodynamics in Refractory ascites

Dr. Supriya Sharma[1], Dr. Gaurav Pande[2*], Dr. Prabhat[3], Dr. Krishna VP[4], Dr. Alok Kumar[5], Dr. Manjunath[6], Dr. Vivek Anand Saraswat[7]

[1, 3-7] Department of Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Preach, India

[2] Assistant Professor, Department of Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Preach, India

[*]Correspondence Author: Dr. Gaurav Pande

Abstract
A comparative study of radiation characteristics of a polarized switchable microstrip planar array of triangular patch antenna printed on synthesized LiTiMg ferrite substrate with a normal magnetic bias field has been done and reporting here. Radiation patterns and some important characteristics of proposed array antenna have been compared with the same geometry printed on RT duroid and silicon. 61% miniaturization and high quality factor are some advantages of using LiTiMg ferrite compare to RT duroid. With the biasing of external magnetic field perpendicular to the ferrite substrate arise some tunable behavior which has been elaborated by the generation quasi TEM, magnetostatic and spin waves. In this analysis spin wave exchange term (ω_r) which depends upon the static internal field (H_{ex}), has also included in the dispersion formula because the wavelength of microwave approach the inter-atomic distance of ferrite material which is the main cause of generation of spin waves in such types of layered structures.

Keywords: substituted Li ferrite, magnetostatic and spin waves, microstrip array antenna, X-band frequency range

Introduction
Systemic circulation in cirrhotics is characterized by a hyper dynamic circulatory state manifesting as low systemic vascular resistance (SVR) caused by vasodilatation, high cardiac output (CO), low mean arterial pressure (MAP) and a reduced renal blood flow. Splanchnic arterial vasodilatation and the consequent reduction of systemic vascular resistance (SVR) and effective circulating volume are the hallmarks of the circulatory dysfunction in these patients [1, 2]. Characteristic changes also occur in the portal circulation, including increased portal pressure and porto-systemic shunting [3, 4].
This pathophysiology plays a major role in abnormalities play a major role in the pathogenesis of major complications of cirrhosis such as ascites, hyponatremia, and hepatorenal syndrome (HRS).
In decompensated cirrhosis, refractory ascites represents a group of patients characterized by splanchnic and systemic vasodialtion at its extreme with consequent marked renal vasoconstriction [5].
Previous studies on this aspect by Kumar *et al.* [6] showed that the mean arterial pressure (MAP) and systemic vascular resistance (SVR) were lower in the decompensated cirrhotic patients as compared with compensated cirrhotics.
The aim of our study was to assess the peripheral and cardiac hemodynamics in patients with Refractory ascites and compensated cirrhosis and to correlate these with clinical profile of the subjects.

Methods
This was a single center observational study assessing consecutive patients with refractory ascites admitted at department of gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, between April 2017 to July 2017.Consecutive patients with compensated cirrhosis, evaluated at the outpatient clinic during the same period were also assessed.
Refractory ascites was defined as per the International ascites club criteria [7, 8] i.e. patients not showing response(mean weight loss of <0.8 kg over 4 days and urinary sodium output less than the sodium intake) despite intensive diuretic therapy(spironolactone 400 mg/day and furosemide 160 mg/day)for at least 1 week and on a salt-restricted diet of less than 90 mmoles/day or 5.2 g of salt/day. They may be either diuretic resistant or diuretic intractable due to complications(hepatic encephalopathy, hyponatremia, hypo- or hyperkalemia, renalimpairment).
Patients with chronic liver disease, as evidenced by clinical, endoscopic, radiological and/or histological criteria, with no previous or present evidence of decompensating (jaundice, ascites, hepatic encephalopathy, or variceal bleed), were diagnosed to have compensated cirrhotics andincluded in the study.
Patients with active bleeding, severe anaemia (Hb<9gm/dL), known or suspected coronary artery disease (on the basis of symptoms, ECG, and echocardiography), those receiving beta blockers, antihypertensive or other cardio active drugs were excluded. Patients with pregnancy, hepatocellular carcinoma, hepatic encephalopathy deeper than grade 2, and those with severe comorbid conditions such as chronic obstructive pulmonary disease (COPD) or chronic kidney disease (CKD) were also excluded.
Patients with Budd-Chiari syndrome were also excluded from the study as the obstructed outflow tract didn't allowed for assessment of inferior vena cava variability with respiration, in the determination of right atrial mean pressure [9].
Written informed consent was obtained from all patients. The protocol was approved by the institutional ethics committee.

Assessment of patients

All patients underwent baseline testing to evaluate liver and kidney function tests, hemogram, ascitic fluid examination, timed urine collections for electrolytes, abdominal ultrasound, endoscopy for varices and tests to establish etiology of underlying chronic liver disease within initial 24 hours of admission. Severity of the liver disease was assessed by Child-Turcotte-Pugh score(CTP) and model for end-stage liver disease (MELD) score.

All patients underwent echocardiographic examination to assess

- Left ventricular outflow tract (LVOT) diameter
- LVOT velocity- time integral (VTI)
- Right atrial (RA)mean pressure
- Wall motion abnormalities

These values were then used to calculate the following hemodynamic parameters as summarized in table 1.

Table 1: Computation of hemodynamic parameters

Variable	Derivation	Normal range
Stroke Volume (SV)	LVOT area x LVOT VTI	60 – 100 mL/beat
Stroke Volume Index (SVI)	Stroke Volume/BSA	33-47 mL/m^2/beat
Cardiac output (CO)	Heart Rate * SV	4.0 - 8.0 L/min
Cardiac Index (CI)	Cardiac output/BSA	2.5 - 4.0 L/min/m^2
Systemic Vascular Resistance (SVR)	(MAP-RA mean pressure/CO) * 80	800 - 1200 dynes - sec/cm^{-5}
Systemic Vascular Resistance Index (SVRI)	SVR * BSA	1970 - 2390 dynes - sec/cm^{-5}/m^2
Stroke Work (SW)	SV* Systolic blood pressure(SBP) * 0.0014	8 – 10 g/beat
Arterial compliance (AC)	SV/Pulse pressure	1.7- 2 ml/mmHg

Statistical analysis

Descriptive statistics are expressed as mean unless otherwise stated. For inter-group comparisons, one-way ANOVA test was used. For post-hoc comparisons within the groups, either Bonferroni test or Games Howell test was used, based on homogeneity of variance. P value less than 0.05 was considered significant.

Results

A total thirty five with Refractory ascites were enrolled in the study over a period of four months. Their baseline characteristics are summarized in table 2.

Table 2

Parameter	Refractory ascites(B)
Age(years)	47.24 ± 12.15
Sex (M/F)	23/12
Etiology (alcohol/ other)	15/20
Ascites n(%)	35(100%)
Hepatic encephalopathy ≤grade 2 n(%)	21(60%)
Albumin(g/dL)	2.800 ±.5000
Bilirubin(mg/dL)	2.76 ± 2.55
INR	1.96 ±. 61
Creatinine(mg/dL)	1.80 ± 0.87
24 hour UNa (mmol/L)	39.52 ± 17.43
CTP score	10.32 ± 1.62
MELD score	20.96 ± 6.84

Table 3

Etiology	Refractory ascites
Cryptogenic	9(26%)
HBV	4(11%)
HCV	5(14%)
Alcohol	13(37%)
NAFLD	2(6%)
AIH	2(6%)
Celiac disease	-

All data as n, (%) HBV, Hepatitis B virus; HCV, Hepatitis C virus; NAFLD, Non alcoholic fatty liver disease; AIH, Autoimmune hepatitis

The systemic hemodynamic parameters of patients are summarized in table 5.

Table 4

Variable	Refractory ascites
Heart rate (beats/min)	99.72 ± 9.89
Stroke Volume (mL/beat)	83.08 ± 36.52
Stroke Volume Index (mL/m^2/beat)	49.20 ± 20.12
Cardiac output (L/min)	8.28 ± 3.60
Cardiac index (L/min/m^2)	4.88 ± 1.87
Stroke work (g/beat)	12.16 ± 5.62
Arterial compliance (ml/mm Hg)	2.20 ± 0.86
Systemic vascular resistance (dynes - sec/cm^{-5})	748.92 ± 303.16
Systemic vascular resistance index (dynes - sec/cm^{-5}/m^2)	1259.40 ± 515.05
Systolic blood pressure(mm Hg)	104 ± 7.25
Mean arterial pressure (mmHg)	78.40 ± 8.15

Discussion

The perturbation of hemodynamics, leading to "hyperdynamic circulation", characterized by increased cardiac output, decreased systemic vascular resistance and mean arterial pressure, is thought to lead to third spacing of fluids, resulting in ascites; congestion of bowel, resulting in increased translocation of gut microbiota. Sustained activation of innate host immunity brought about by abnormal gut translocation of bacteria and bacterial products (known as pathogen-associated molecular patterns(PAMPs) and damage associated molecular patterns(DAMPs)) is responsible for persistent activation of innate pattern recognition receptors (e.g., Toll-like receptors) and subsequent inflammation. Pro-inflammatory cytokines and oxidative/nitrosative stress impair effective hypovolemia by enhancing arterial vasodilation (mainly mediated by NO) and preventing cardiac output to fulfill the needs of peripheral circulation. Moreover, direct effects on kidney and other organs worsen their dysfunction and ultimately failure of cardiac compensation and organ failure(s), particularly HRS [10, 16]. This has been adequately demonstrated in multiple

studies with increasing mortality as the hemodynamics worsen [17-19]. Angeli *et al.* [17] have elaborately shown that there is progressive deterioration in systolic function with worsening liver disease from compensated cirrhosis through diuretic responsive ascites to refractory ascites. All these available data suggest,that, with progressive deterioration of hemodynamics, there is increased risk of developing HRS [18] SBP [19] and consequent increased mortality. The underlying pathophysiologic mechanism is believed to be progressive splanchnic and systemic vasodilation with consequent renal vasoconstriction [11-15]. This in turn leads to renal salt and water retention and ascites. Additionally, it also leads to further aggravation of the active intrahepatic vascular resistance and the development of multi organ failure [20]. The time-frame of the development of decompensating in ACLF is rapid (within weeks), which is in contrast to the slow decompensating in cirrhotics (over months to years). Our results provide evidence that at least the degree of hemodynamic derangements in patients with ACLF and decompensated cirrhosis is the same.

Our study showed that the peripheral and cardiac hemodynamics could be easily derived through widely available 2D echocardiographic variables, which would help in day to day clinical application, as compared to invasive monitoring via cardiac catheterization. Echocardiographic ally derived hemodynamic parameters have been shown to correlate well with invasive methods[20].Therapeutic interventions, specifically, targeted towards, correction of peripheral and systemic hemodynamics, may significantly improve survival in decompensated cirrhosis.

This could possibly reflect the 'rebalanced' state of systemic hemodynamics in advanced decompensated cirrhosis, such as refractory ascites. Or possibly, the hemodynamics are at their extreme in the state of refractory ascites, and any insult,hepatic or extra-hepatic, leads to organ failure(s), rather than attempting to rebalance.

Barring the limitations of unavailability of HVPG data, our study shows the worse systemic and peripheral hemodynamics in refractory ascites.. Future studies, on this aspect might better reflect the prognostic values of these parameters and help in designing strategies to improve the outcome of this sick group of patients.

References

1. Theocharidou E, Krag A, Bendtsen F, Moller S, Burroughs AK. Cardiac dysfunction in cirrhosis – does adrenal function play a role? A hypothesis. Liver Int. 2012; 32:1327-1332.
2. Moller S, Henriksen JH. Cirrhotic cardiomyopathy. J Hepatol. 2010; 53:179-190.
3. Bosch J, Garcia-Pagan JC. Complications of cirrhosis. I. Portal hypertension. J Hepatol. 2000; 32[Suppl1]:141-156. doi: 10.1016/S0168-8278(00)80422-5
4. Navasa M, Garcia-Pagan JC, Bosch J, Riera JR, Banares R, Mas A, *et al*. Portal hypertension in acute liver failure. Gut. 1992; 33:965-968. doi:10.1136/gut.33.7.965
5. Colle I, Moreau R, Pessione F, Rassiat E, Heller J, Chagneau C, *et al*. Relationships between haemodynamic alterations and the development of ascites or refractory ascites in patients with cirrhosis. Eur J Gastroenterol Hepatol. 2001; 13(3):251-6.
6. Kumar A, Das K, Jain A, *et al*. Hepatic venous pressure gradient, systemic and pulmonary hemodynamics in patients with acute-on-chronic liver failure. Dig. Dis. Sci. 2009; 54:869-78.
7. Moore KP, Wong F, Gines P, *et al*. The management of ascites in cirrhosis: report on the consensus conference of the International Ascites Club. Hepatology. 2003; 38:258-66.
8. Arroyo V, Gines P, Gerbes AL, *et al*. Definition and diagnostic criteria of refractory ascites and hepatorenal syndrome in cirrhosis. International ascites Club. Hepatology. 1996; 23:164-76.
9. Nakao S, Come PC, McKay RG, Ransil BJ. Effects of positional changes on inferior vena caval size and dynamics and correlations with right-sided cardiac pressure.Am J Cardiol. 1987; 59(1):125-32.
10. Arbol LRD, Monescillo A, *et al*. Circulatory function and hepatorenal syndrome in cirrhosis. Hepatology. 2005; 42(2):439-47.
11. Bosch J, Garcia-Pagan JC. Complications of cirrhosis. I. Portal hypertension. J Hepatol. 2000; 32[Suppl 1]:141\-156. doi: 10.1016/S0168-8278(00)80422-5
12. Cardenas A, Gines P. Hepatorenal syndrome. Clin Liver Dis. 2006; 10:371-385. doi:10.1016/j.cld.2006.05.006
13. Groszmann RJ. Vasodilatation and hyperdynamic circulatory state in chronic liver diseases. In: Bosch J, Groszmann RJ (eds) Portal hypertension: pathophysiology and treatment. Blackwell Science, Oxford, 1994, 17-26.
14. Arroyo V, Jimenez W. Complications of cirrhosis. II. Renal and circulatory dysfunction light. and shadows in an important clinical problem. J Hepatol. 2000; 32[Suppl 1]:157-170. doi: 10.1016/S0168-8278(00)80423-7
15. Schrier RW, Arroyo V, Bernardi M, Epstein M, Henriksen JH, Rodes J. Peripheral arterial vasodilation hypothesis: a proposal for the initiation of renal sodium and water retention in cirrhosis. Hepatology./ 1988; 8:1151-1157. doi:10.1002/hep. 1840080532
16. Arroyo V, Moreau R, Jalan R, Gines P. Acute-on-chronic liver failure: A new syndrome that will re-classify cirrhosis. J Hepatol. 2015; 62(1 Suppl):S131-143.
17. Cesari M, Fasolato S, Rosi S, Angeli P. Cardiac dysfunction in patients with cirrhosis: is thesystolic component its main feature? Eur J Gastroenterol Hepatol. 2015; 27(6):660-6.
18. Ruiz-del-Arbol L, Monescillo A, Arocena C, Valer P, Gines P, Moreira V, *et al*. Circulatory function and hepatorenal syndrome in cirrhosis. Hepatology. 2005; 42(2):439-47.
19. Ruiz-del-Arbol L, Urman J, Fernandez J, Gonzalez M, Navasa M, Monescillo A, *et al*. Systemic, renal, and hepatic hemodynamic derangement in cirrhotic patients with spontaneous bacterial peritonitis. Hepatology. 2003; 38(5):1210-8.
20. Porter RT, Sasha KS, *et al*. Guidelines for the Use of Echocardiography as a Monitor for Therapeutic Intervention in Adults: A Report from the American Society of Echocardiography. Journal of the American Society of Echocardiography. 2015; 28(1):40-56.