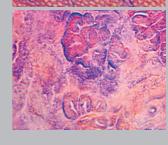
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P0011 EVALUATION OF BONE MARROW DERIVED MESENCHYMAL STEM CELLS INJECTION IN EGYPTIAN PATIENTS WITH LIVER **CIRRHOSIS**

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INTRODUCTION: Liver transplantation has become a procedure with a relatively good 5-year survival. Yet, organ donation has not kept up with the demand because of many problems, including relative lack of donors, operative complication, risk of rejection and high cost. Owing to the ability of stem cells to repopulate and differentiate at the engrafted site, stem cell-based therapy has received attention as a possible alternative to organ transplantation.

AIMS & METHODS: was to evaluate the effect of transplantation of autologous

bone marrow derived mesenchymal stem cells into cirrhotic patients in improving

liver function tests as a possible alternative to organ transplantation

Patients and methods: After approval of ethical committee, twenty patients with end stage liver cirrhosis were selected from the outpatients of internal medicine department in Kaser Al-Aini hospitals. 30–40 ml bone marrow was aspirated from iliac crest under complete aseptic condition and after local anesthesia. Human BM-derived MSCs were Isolated, propagated, and identified. Under complete aseptic conditions, a mean of $10{\times}106$ of the isolated DM-derived MSCs in 5 ml normal saline were injected intrasplenic to the patients under sonographic guidance, and without anesthesia, as

Monthly Follow up for 6 months by clinical assessment and laboratory investigations including serum total bilirubin, serum albumin, aspartate amino transferase, alanine amino transferase, prothrombin time, prothrombin concentration, INR, and abdominal ultrasonography were done.

RESULTS: Statistical comparison between the clinical and laboratory data before and 6 months after MSCs injections showed a highly significant decrease in the main total bilirubin level from 2.55 ± 1.11 to 1.91 ± 1.0 (P value <0.01), a significant increase in the main albumin level from 2.83 ± 0.44 to 3.26 ± 0.33 (P value <0.05), hat a highly significant decrease in the mean AST from 78.00±25.35 to 43.50±18.74 (P value <0.01) a highly significant decrease in the mean ALT from 50.50±11.26 to 36.83±10.78 (P value <0.01), a significant decrease in the mean prothrombin time from 18.44±2.0 to 18.00±2.68 (P value <0.05), a significant increase in the mean prothrombin concentration from 47.05±11.47 to 57.25±14.47 (P value <0.05), in figure decrease in the mean prothrombin concentration from 47.05±11.47 to 57.25±14.47 (P value <0.05). a significant decrease in the mean INR from 1.71 ± 0.26 to 1.65 ± 0.38 (P value <0.05) CONCLUSION: Our study suggested the safety, feasibility and efficacy of the intrasplenic injection of autologous bone marrow-derived mesenchymal stem cells in improving liver functions in cirrhotic patients

Disclosure of Interest: None Declared Gut 2012; 61 (Suppl 3) A107

P0012 DEPRESSION AND ANXIETY IN PATIENTS WITH CHRONIC LIVER DISEASE

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INTRODUCTION: In previous years mental health of the patients including those with chronic liver disease (CLD) raze interest because their presence leads to reduced quality of life and it is associated worsening of clinical evolution, reduced compliance and increased mortality. The most frequently described are depression and anxiety. The aim of our study was to describe depression and anxiety in patients with CLD, and assessment impact of socio-demographic characteristics, etiology and disease severity and on the occurrence of these disorders.

AIMS & METHODS: We performed a cross sectional study. Disease's severity was determined by the Child-Pough classification. Assessment of depression and anxiety were performed by Hamilton depression rating scale (HDRS) and Hamilton anxiety rating scale (HARS). Clinically significant depression was marked for the value of HDRS >10. Clinically significant anxiety was marked for the value of HARS >17. For statistical analyzes we used Kolmogorov-Smirnov test, one-way ANOVA and post-

hoc Turkey's test. Statistical significance was set for p < 0.05. **RESULTS:** We include 54 male and 43 female patients, mean age 53.5 ± 12.8 yrs. The average value of the HDRS score was 13.4 ± 9.4 The average value of the HARS score was 10.0 ± 6.4 . Depression was present in 55.7%, and anxiety in 13.4% patients. Men had significantly lower HARS score than women $(8.6\pm6.0 \text{ vs. } 11.5\pm6.7)$. (t = 2.332, p=0.022). Patients with different employment status were significantly different in the HDRS (F=3.652, p=0.029) and HARS scores (F=3.998, p=0.021). In comparison with patients who are retired, employed patients had significantly lower HDRS $(10.5\pm8.9~\text{ys}.~15.8\pm9.2)$ and HARS scores $(7.5\pm5.0~\text{ys}.~11.6\pm6.9)$. There were HDRS (10.5 \pm 8.9 vs. 15.8 \pm 9.2) and HARS scores (7.5 \pm 5.0 vs. 11.6 \pm 6.9). There were no significant differences in HDRS scores of patients with different: gender (p=0.107), age (p=0.119), level of education (p=0.730), occupation (p=0.807), marital status (p=0.054), children status (p=0.189), alcohol consumption (p=0.380), smoking status (p=0.619), etiology (p=0.209) and severity of CLD (p=0.662). Patients with different: age (p=0.128), marital status (p=0.187), level of education (p=0.848), occupation (p=0.465), children status (p=0.175), alcohol consumption (p=0.075), smoking status (p=0.824), etiology (p=0.074) and severity of CLD (p=0.772) did not differ in the HARS scores not differ in the HARS scores.

CONCLUSION: Men have lower anxiety scores than women. Patients who are employed have lower scores of depression and anxiety in relation to the retired. For the other socio-demographic characteristics, etiology and severity of CLD, there was no difference in scores of depression and anxiety.

Disclosure of Interest: None Declared

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P0013 ASSESMENT OF ADRENAL FUNCTION IN HCV PATIENTS WITH LIVER CIRRHOSIS AFTER VARICEAL BLEEDING

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INTRODUCTION: Patients with liver cirrhosis commonly have abnormalities in adrenal function. Adrenal insufficiency is common in critically ill patients with liver cirrhosis, these abnormalities have been described in the absence of clinical sepsis raising the possibility that the adrenal insufficiency arising in liver cirrhosis may be a different entity to that observed in septic shock.

AIMS & METHODS: The aim of this study is to assess adrenal function in cirrhotic patients after variceal bleeding and if there is relationship between the severity of liver disease and adrenal insufficiency.it included 60 hepatic patients (30 with history of bleeding and 30 non bleeder)basal and subsequent cortisol levela were measured.

RESULTS: Our results showed a clear relationship between the severity of liver disease

and adrenal insufficiency as follow: The serum basal cortisol level "sample I" in child A was normal in both groups wether none bleeders or bleeders.

- The serum basal cortisol level "sample I" in child B was subnormal in 20% of group without bleeding and 10% of group with bleeding, and in child C it was also subnormal in 60% of group without bleeding and 30% of group with bleeding, The response to synecthen injection (LDSST) was relatively good in all groups without bleeding (A, B and C) and all groups with bleeding, and the maximum
- cortisol response was after one hour from synecthen injection, but inspite of these results, the response was much lower in group C than group B than group A respectively in all groups none bleeders and bleeders. The responses to synecthen injection (LDSST) were significantly low in groups with bleeding than those groups

without bleeding.

CONCLUSION: It is concluded from this study that; Adrenal dysfunction is common in patients with advanced liver cirrhosis. Adrenal insufficiency is progressively increased with worsening severity of liver disease described by modified Child-Pugh classification. Adrenal insufficiency was found many frequently in cirrhotic patients during variceal bleeding. Morning basal cortisol could be useful to identify cirrhotics with high risk of adrenal insufficiency.

Disclosure of Interest: None Declared

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P0014 THE INHIBITORY EFFECT OF NUCLEAR RECEPTORS LIGANDS ON HEPATIC STELLATE CELLS (HSC) ACTIVATION AND PROLIFERATION IS MEDIATED BY DOWNREGULATION OF CELL CYCLE PROTEINS

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INTRODUCTION: Peroxisome proliferator activator receptors (PPAR) ligands have

INTRODUCTION: Peroxisome proliferator activator receptors (PPAR) figands have been shown to inhibit development of liver fibrosis. AIMS & METHODS: In this study, we investigated the effects of the combination of ligands of peroxisome proliferator activator receptor γ (PPAR γ) and retinoic acid receptor (ATRA, 9-cis and PPAR γ ligand 15-deoxy- Δ 12,14-prostaglandinJ(2)[PJ(2)]) on activation and proliferation of primary hepatic stellate cells, and on PPARg, α SMA gene and protein expression in these cells. We also determined the effects of the combination of ligands on cell cycle proteins involved in HSC proliferation. combination of ligands on cell cycle proteins involved in HSC proliferation.

Methods: We assessed proliferation of primary hepatic stellate cells by BrdU and

crystal violet. Cell cycle was determined by FACS analysis. Cyclin D1, P21, P27, mTOR, p70^{S6K}. Collagen Ia1, and α SMA proteins were determined by western blot analysis. Collagen Ia1, and α SMAmRNA expression were determined by real time

RESULTS: Proliferation of primary HSC was inhibited by the combination of 9-Cis, ATRA and PJ and the effect of the 3 ligands was additive. As demonstrated by FACS analysis, the inhibition of proliferation was due to cell cycle arrest. Studies using western blot analysis demonstrated reduced expression of cyclin D1 and increased expression of P21 and P27 by the above combination. When examining proteins leading to HSC proliferation, we found that the 3 ligands down regulated the phosphorylation of mTOR and p70^{S6K}. Using Oil red-O staining, we demonstrated that the combined treatment led to inhibition of release of vitamin A droplets from cultured HSC. Studies using real time PCR and western blot analysis showed marked inhibition of collagen $I\alpha 1$ and αSMA in the presence of the combination of the 3 ligands.

CONCLUSION: Our studies demonstrate that the combination of these 3 ligands inhibited the mTOR pathway which leads to inhibition of HSC proliferation, G_0/G_1 arrest and affect cell cycle proteins. Furthermore, the inhibition of collagen $I\alpha I$ and aSMA by the 3 ligands combination indicates an antifibrotic effect.

Disclosure of Interest: None Declared

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P0015 BREATH ANALYSIS BY PROTON TRANSFER REACTION TIME OF FLIGHT MASS SPECTROMETRY IN CIRRHOTIC PATIENTS

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INTRODUCTION: Being rapid and non-invasive, breath analysis is a promising diagnostic tool although difficulties related to data interpretation, reproducibility and sensibility have limited its application.

AIMS & METHODS: The aim of the present work was to investigate whether a recently realized direct injection mass spectrometric technique (Proton Transfer Reaction Time of Flight Mass Spectrometry, PTR-ToF-MS) allows the direct and noninvasive diagnosis of cirrhosis as well as the assessment of the disease severity by direct analysis of exhaled breath.

Twelve patients (M/F 8/4, mean age 70.5, range 42–80 years) with liver cirrhosis of different etiologies and status and 14 healthy subjects (M/F 5/9, mean age 52.3, range 35-77 years) were enrolled in the study. The etiology of cirrhosis was viral in 9 (8 HCV and 1 HBV) and metabolic in 3. The Child-Pugh class was A in 6 patients, B in 3, and C in the remaining 3 patients.

Real time breath analysis was performed using a buffered end-tidal on-line sampler directly coupled to a PTR-ToF-MS. Spectra were acquired using the data acquisition software TOF-DAQ (Tofwerk AG, Switzerland) with a mass/charge range of 10-400 Th. The data were analyzed by non-parametric ANOVA (Kruskal-Wallis test) using

the Statistica 9.1 (StatSoft, USA) software.

RESULTS: Eight peaks resulted significantly different in cirrhotic patients compared to healthy controls: two related to ketones, (2-pentanone, C8-ketone), two to terpenes and four to sulfur compounds. Three peaks resulted significantly different between Child-Pugh A cirrhotic patients and Child-Pugh B+C cirrhotic patients and precisely:

C8-ketone, a monoterpene and a NS-compound.
CONCLUSION: In conclusion: real time analysis of breath allows to distinguish cirrhotic from healthy subjects and well compensated liver disease from more advanced liver stage. The proposed method can be used to identify the stage and severity of liver disease in real time with a safe and non-invasive procedure.

Disclosure of Interest: None Declared Gut 2012; 61 (Suppl 3) A107

P0016 RANDOMIZED CONTROLLED TRIAL COMPARING EFFECTS OF SEDATION FOR UPPER GASTROINTESTINAL ENDOSCOPY WITH PROPOFOL VERSUS MIDAZOLAM ON PSYCHOMETRIC TESTS AND CRITICAL FLICKER FREQUENCY IN CIRRHOTICS

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INTRODUCTION: Patients with cirrhosis are at increased risk of development of complications related to sedation

AIMS & METHODS: To compare effects of sedation for upper gastrointestinal

endoscopy (UGIE) with propofol and midazolam on psychometric tests and critical flicker frequency (CFF) in cirrhotics.

Design: Prospective randomized study

Setting: A tertiary-referral university hospital endoscopy unit.

Patients and methods: 148 cirrhotic patients randomized into 3 groups, propofol group (n = 47), midazolam group(n = 49) and no sedation (n = 52). All patients underwent CFF test and combination of psychometry [number connection test-A and B(NCT-A,B); digit symbol test(DST), line tracing test(LTT) and serial dotting test(SDT) at baseline and at 2 hours post endoscopy. CFF done at 30 min and repeated every 30 mins for

Main outcome measurements: Deterioration in psychometry tests and CF **RESULTS:** 92/148 patients(62.2%) had minimal hepatic encephalopathy(MHE) before RESULTS. 29 148 patients (0.2.2%) had minimal nepatic encephalopathy (White) bothometry [NCT-A(55.6±18.7 vs 56.4±19.0 sec), NCT-B(98.2±35.1 vs 97.8±34.6 sec), DST(26.7±5.7 vs 26.3±5.3), LTT(112.9±35.7 vs 113.7±36.6 sec), SDT (94.6±34.1 vs 95.2±34.5 sec)]. Significant deterioration from baseline (39.8±2.9 Hz) was seen in CFF at 30 min (38.8±2.3 Hz) and 1 hr (39.2±2.4 Hz), p=0.01 but no difference the product of the production of the producti In Crr at 30 lmin (38.6±2.5 Hz) and 1 lif (39.2±2.4 Hz), p=0.01 but no different thereafter. In midazolam group significant deterioration was observed on psychometry [NCT-A (56.0±18.5 vs 60.4±19.8 sec), NCT-B(99.9±29.1 vs 105.9.6±30.3 sec), DST(26.1±4.7 vs25.2±4.3), LTT(129.1±34.5 vs132.9±35.4sec), SDT (95.6±34.2 vs midazolam group showed overt HE after sedation. No deterioration observed in psychometry and CFF in cirrhotics without sedation.

CONCLUSION: Propofol sedation for UGIE is associated with earlier recovery in patients with cirrhosis compared to midazolam which causes deterioration of psychometric tests and CFF for a longer time in comparison with propofol Disclosure of Interest: None Declared

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P0017 MELD SCORE AND CTP SCORE IN THE PREDICTION OF SURVIVAL OF PATIENTS WITH CIRRHOSIS AWAITING LIVER TRANSPLANTATION

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INTRODUCTION: Liver transplantation (LT) provides the only curative treatment option for decompensated cirrhosis. The Model for End-Stage Liver Disease (MELD) score is now used for allocation in LT waiting lists, replacing the Child-Turcotte-Pugh (CTP) score. However, the optimal strategy based on scoring systems and/or waiting

AIMS & METHODS: Aim of the present was to compare the CTP scores and MELD score for 3, 6months survival in cirrhotic patients waiting for liver transplant.

We investigated 216 consecutive patients listed for single-organ liver transplantation for nonfulminant liver disease between April 2010 and June 2011. To assess the ability of MELD and CTP score predicting the risk of death, the study was performed by

range by using c-statistic for area under the receiver operating characteristic curve. **RESULTS:** 56 patients died during the observation period. The mean CTP score at baseline, 3, 6 months was 7.4, 7.67 and 8.1 respectively for patients in the waiting list 7.63, 8.9 and 9.48 for patients who died on waiting. The Mean MELD at 3, 6 months was 12.2, 13.37 and 16.99 respectively for patients in the waiting. The sensitivity and specificity to identify mortality or severe deterioration for CTP was 83.9% and 89.5%, respectively; for MELD 88.6%, 91%, respectively. In stratified analysis there were significant (<0.001) differences between them with low and intermediate range MELD scores at 3 and no difference in 6 months.

CONCLUSION: MELD has a better performance over the CTP in determination of

priorities for organ allocation. Outcome with lower range MELD cannot be reliably predicted only with their MELD scores, and alternative prognostic markers should be used in conjunction to enhance the predictive accuracy. So, prognostic markers like ascites and hyponatremia should be added with MELD to enhance the predictive

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Disclosure of Interest: None Declared

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P0018 IDIOPATHIC NON-CIRRHOTIC PORTAL HYPERTENSION: A PROSPECTIVE LONG TERM FOLLOW-UP STUDY

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INTRODUCTION: Cirrhosis is the most common cause of portal hypertension but portal hypertension can also be present in the absence of cirrhosis, a condition referred to as Idiopathic Non-Cirrhotic Portal Hypertension (INCPH). NCPH includes Extra Hepatic Portal Vein Obstruction (EHPVO) and Non-Cirrhotic Portal Fibrosis (NCPF). The natural history of INCPH is not clear.

AIMS & METHODS: Aim of the present was to determine prospectively the changes in the portal venous system in patients with NCPH.

Patients with a diagnosis of NCPF and EHPVO registered since 2001 were serially followed at an yearly interval for changes in liver size, its echotexture, and in the intra and extrahepatic portal venous system. Baseline demographic details, LFT, and co-morbid illness including virological profile were noted. Patients with co-morbid illness and those with known etiology of cirrhosis were excluded from the study.

illness and those with known etiology of cirrhosis were excluded from the study.

RESULTS: There were 34 patients with NCPF (M: F 1:1.8) and 30 patients with EHPVO (M: F ratio 1.6:1). The mean age was 24.9 yrs and 41.2 yrs respectively. During follow up, 20 out of 34 and 16 out of 30 patients with NCPF and EHPVO respectively had no progression of disease. 14 patients with NCPF progressed to cirrhosis over a mean period of 5.21 years. Eight patients developed ascites and required diuretics. 14 patients with EHPVO progressed to NCPF over the mean period of 8.6 years, 12 patients further progressed to cirrhosis over a mean period of 5.1 years. Overall 40% of patients with EHPVO progressed to cirrhosis over a mean period of 13.7 years.

CONCLUSION: INCPH is a spectrum wherein EHPVO progresses to NCPF and further to cirrhosis over a period of 13.7 years at least in a proportion of patients.

Disclosure of Interest: None Declared

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P0019 SPLEEN STIFFNESS MEASUREMENT AS A NONINVASIVE SUROGATE MARKER OF CLINICALLY SIGNIFICANT PORTAI HYPERTENSION AND LARGE ESOPHAGEAL VARICES IN CIRRHOTIC PATIENTS

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INTRODUCTION: Identification of novel noninvasive methods for liver cirrhosis(LC) assessment is one of the recommendations of the BavenoV meeting. Spleen stiffness measurement(SSM) using Fibroscan was recently proposed as an estimate of

large esophageal varices(LEV) in cirrhotic patients.

AIMS & METHODS: The aim of this study was to validate SSM as a noninvasive

surrogate marker for LEV and clinically significant portal-hypertension(CSPH). 37 consecutive LC patients (training set – mean age 55.08 years, 68.3% males) were included. All patients underwent HVPG measurement, endoscopy for esophageal varices evaluation, common laboratory tests, liver and spleen stiffness measurements – using the medium probe and the conventional calculation algorithm. The diagnostic performance of SSM was evaluated using the AUROC method. The best cutoff values of the 2 variables were used to estimate the presence of LEV in an independent validation set of 118 cirrhotic patients (55.32 years, 61.8% males). The LEV estimation according to SSM values was compared against endoscopy evaluation using the interclass correlation coefficient.

RESULTS: In the training set, SSM correlated well with LSM, HVPG, and with the presence of LEV and CSPH, as showed in the table.

		LSM	HVPG	CSPH	LEV
SSM	r	0.676	0.774	0.692	0.640
	p	<0.0001	<0.0001	<0.0001	<0.0001

SSM mean values were significantly higher in patients with CSPH: 33.11 vs. 65.82kPa (p < 0.0001). The same tendency was observed when LEVs were evaluated: 39.42 vs. (p < 0.0001). The same tendency was observed when LEVs were evaluated. 37.42 vs. 67.48kPa (p < 0.0001).

The AUROC for SSM predicting CSPH was 0.882 (Se=92.9%;Sp=84.2%).

The AUROC for predicting LEV was 0.845 for SSM (Se=100%;Sp=68%).

Interestingly, the cutoff value was the same (>42.7kPa) in predicting both CSPH and

In the validation set, using the above-mentioned SSM cutoff values, we predicted the presence of LEV with moderate accuracy [ICC only 0.402 (p=0.003)].

CONCLUSION: SSM is a novel noninvasive parameter that correlates with the presence of CSPH and LEV in cirrhotic patients, but it is not reliable enough to be used alone for the assessment of LEV, so that endoscopy could be avoided Disclosure of Interest: None Declared Gut 2012; 61 (Suppl 3) A108

P0020 CIRRHOTIC CARDIOMYOPATHY: DO WE NEED MORE THAN **BASELINE EVALUATION?**

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INTRODUCTION: Cirrhotic cardiomyopathy (CC) is an important cause of morbidity and mortality in patients with hepatic cirrhosis, especially when decompensated or in those patients undergoing transjugular intrahepatic portosystemic shunt or hepatic transplantation. In fact, although most cirrhotic patients have normal ventricular function parameters in rest, they frequently reveal an attenuated systolic and diastolic function under stress conditions.

AIMS & METHODS: We aimed to characterize a population of ambulatory cirrhotic patients with determination of the prevalence of clinically silent CC. Patients with hepatic cirrhosis, regardless of the etiology, were included and evaluated regarding clinical, analytical, electrocardiographic and two-dimensional transthoracic doppler echocardiography parameters, both at rest and after pharmacological stress with dobutamine. Patients with cardiac or pulmonary major illness or those with cardiovascular risk factors such as diabetes hypertension or smoking babits were excluded from the risk factors such as diabetes, hypertension or smoking habits were excluded from the study. Diastolic and systolic echocardiographic features were obtained. Left ventricular systolic function (LVSF) was evaluated through the determination of tele-diastolic volume, tele-systolic volume and ejection fraction (EF), in rest and after low dose dobutamine infusion. LVSF was considered insufficient when the EF increase after dobutamine challenge was lower than 10%.

RESULTS: Twenty-six patients were included, 22 (85%) men, with mean age of 55±10 years. The hepatic cirrhosis was mainly of alcoholic etiology (76.9%) and staged Child-Pugh A (n=17), B (n=8) and C (n=1). Natriuretic brain peptide (pro-BNP), an analytical marker of ventricular insufficiency or overload, had a mean value of 110±111pg/ml. In 20 (76.9%) patients, the corrected QT (cQT) electrocardiographic interval was prolonged (mean value 460±23mseg). All patients presented normal baseline echocardiographic LFSV parameters (tele-diastolic volume 94±29.6ml, telesystolic volume 28±9.5ml, EF 69±8.1%). Nine (34.6%) patients presented with diastolic dysfunction under resting conditions. After dobutamine challenge, 10 (38.5%) patients had LVSF impairment, with an EF increase below the threshold of 10%.

CONCLUSION: In our series, a significant proportion (76.9%) of patients had a cQT interval prolongation, and about a third had diastolic cardiac dysfunction. Moreover, dobutamine stress echocardiography revealed a diminished cardiac reserve in more