

RELATIONSHIP BETWEEN THE VALUES OF NT-PRO-BNP AND INSERTION OF TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT

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Abstract: I studied the cardiovascular impairment reflected by NT-pro-BNP values in a group of patients with liver cirrhosis. The frequency of positive values of NT-pro-BNP in those who had a medical history of TIPS insertion compared to those without TIPS insertion was quantified and expressed statistically. All patients with TIPS insertion were on the liver transplantation waiting list of the clinic where the study was conducted. In this study, the natriuretic peptide NT-pro-BNP in the blood of patients with cirrhosis was not influenced by the presence of portocaval shunt (TIPS).

Cuvinte cheie: NT-pro-BNP, ciroză hepatică, TIPS

Rezumat: Am studiat afectarea cardiovasculară reflectată prin valorile NT-pro-BNP la un lot de pacienți cu ciroză hepatică. Frecvența de apariție a valorilor NT-pro-BNP pozitive la cei care au avut în antecedente inserție de TIPS, față de cei fără TIPS, a fost cuantificată și exprimată statistic. Toți pacienții cu inserție TIPS erau înscriși pe lista de transplant hepatic a clinicii unde s-a desfășurat studiul. În acest studiu, valoarea peptidului natriuretic NT-pro-BNP în sângele bolnavilor cu ciroză nu a fost influențată de prezența șuntului porto-cav (TIPS).

INTRODUCTION

The transjugular intrahepatic portosystemic shunt (TIPS) has become increasingly popular over the past decade, as a non-surgical approach to treat resistant ascites or variceal bleeding in patients with cirrhosis.(1) It has also been used successfully in some rare and severe cases as Budd-Chiari syndrome and cirrhotic hydrothorax. TIPS insertion has a significant effect on systemic hemodynamics.(2) It is a cardiovascular challenge, as it suddenly shifts a significant amount of splanchnic venous blood to the systemic veins, that is, it increases preload. Not surprisingly, this procedure, almost invariably performed in patients with advanced liver dysfunction, is associated with high mortality.(1)

The normal heart should easily accommodate the mild-to-moderate increase in preload induced by a TIPS insertion. This inability to accommodate an increased preload is an evidence of the existence of cirrhotic cardiomyopathy.(3,4,5)

This cardiomyopathy may also help determining the final outcome after liver transplantation. Before the syndrome was widely recognized, transplant physicians were often surprised by the apparently inexplicable appearance of severe cardiac dysfunction in the postoperative period in patients with no previous history or risk factors for cardiovascular disease.(1)

Several recent studies have shown that patients with liver cirrhosis have increased plasma concentrations of BNP and NT-pro-BNP, representing in fact, markers of early ventricular dysfunction.(6,7) Henriksen et al (7) showed that these markers are correlated with both the severity of liver cirrhosis and that of cardiac dysfunction.

Given that natriuretic peptides are secreted in response to the extent of myocytes and overload, we expect that after TIPS insertion, which leads to an increase in preload, values of NT-pro-BNP be higher than in those without insertion of TIPS.

PURPOSE

Considering all these data, we aimed to study whether NT-pro-BNP values of patients in the group were influenced by the presence of transjugular intrahepatic portosystemic shunt; or whether there were notable differences in the values of NT-pro-BNP in patients with TIPS insertion, as compared to those without TIPS insertion.

METHODS

The study group consisted of 54 patients with liver cirrhosis admitted to the Liver Transplant Clinic in Hamburg, Germany, in February-April 2011. Most patients (45) were on the liver transplantation waiting list of the clinic.

Patients were evaluated in terms of hepatology and cardiology, and NT-pro-BNP was determined in all patients on the day of admission to the clinic. NT-pro-BNP concentration was determined by Electrochemiluminescent Immunoassay "ECLIA" method using a Cobas system.

NT-pro-BNP values obtained in patients that we studied were laid out on a great range from 15 to 2342 pg/ml. Values less than 250 pg/ml were considered negative and values greater than or equal to 250 pg/ml were considered positive, in order to study the relationship between NT-pro-BNP and cardiac impairment from liver cirrhosis on the basis of positive values.

We drafted a patient monitoring record in each patient and we collected all data in a nominal table and inserted them into a database that allows statistical analysis. We used the "Epi Info" program for creating and managing the database. The relationship between TIPS insertion and NT-pro-BNP values was analyzed by us using the "Chi-squared" statistical significance test, about alternative qualitative characteristics – we have demonstrated the presence or absence of significant differences between patients who were subjected to a specific treatment, compared with those who did not receive this treatment. The results we presented in tables that allow a

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detailed analysis of the phenomenon, and graphics that suggestively highlight this phenomenon.

Selection of patients:

The inclusion criteria for participation in the study were represented by: patients with clearly established diagnosis of liver cirrhosis (clinical and paraclinical) and the symptoms attributed to this disease.

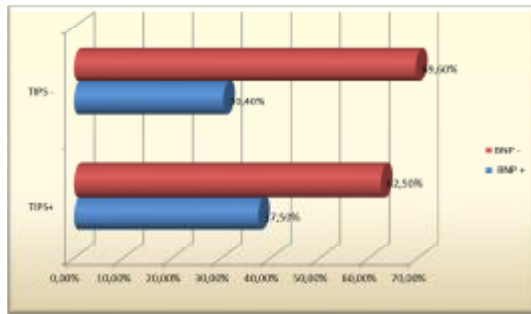
Patients with secondary cirrhosis were not included: cardiac cirrhosis, Budd-Chiari syndrome etc.

RESULTS

8 out of 54 patients involved in the research study had a history of TIPS insertion.

Regarding the NT-pro-BNP values in patients undergoing intrahepatic shunt (TIPS), compared to NT-pro-BNP values in patients who did not practice this operation, 3 out of the 8 patients with TIPS insertion had positive values of NT-pro-BNP (above 250 pg/ml), i.e. 37,5%, and 14 out of the 46 patients without TIPS insertion had positive values of NT-pro-BNP, i.e. 30,4%. It is noted that the frequency of NT-pro-BNP positive values is 7% higher among patients with TIPS insertion, than among those without TIPS insertion.

Figure no. 1. The relationship between TIPS and NT-pro-BNP



The analysis of NT-pro-BNP values according to TIPS and gender shows that 4 out of the 8 human subjects with TIPS insertion are female and 4 are male. 2 out of the four female human subjects have NT-pro-BNP positive values, and 1 out of the 4 male human subjects has NT-pro-BNP positive values, with no significant values between the two genders.

Regarding the human subjects without TIPS insertion, 30 out of the 46 are male and between these 8 have NT-pro-BNP positive values (26,6%), and 16 are female and between these 6 have NT-pro-BNP positive values (37,5%). Therefore, NT-pro-BNP positive values are 11% more common in women.

Table no. 1. NT-pro-BNP values according to TIPS and GENDER

Gender	TIPS+		TIPS -		TOTAL	
	B-	B+	B-	B+	B-	B+
F	2	2	10	6	12	8
M	3	1	22	8	25	9
TOTAL	5	3	32	14	37	17
%	13,5	17,6	86,5	82,5	100	100

The analysis of NT-pro-BNP values according to TIPS and age groups shows that 2 out of the 8 human subjects with TIPS insertion are under 50 years old and they have normal value of NT-pro-BNP, 3 human subjects are between 50 and 59 years old, where only 1 has NT-pro-BNP positive values and 3

human subjects are above 60 years old, where 2 have NT-pro-BNP positive values as shown in the following table:

Table no. 2. NT-pro-BNP values according to TIPS and age groups

Age group	TIPS +		TIPS -		TOTAL	
	B -	B +	B -	B +	B -	B +
<50 years old	2	0	7	2	9	2
50 - 59 years old	2	1	17	9	19	10
60 years old	1	2	8	3	9	5
TOTAL	5	3	32	14	37	17
%					100	100

There is an increasing trend in the number of human subjects with positive values of NT-pro-BNP in patients over 60 years old among those with TIPS insertion. Regarding the human subjects without TIPS insertion, 9 out of 46 are human subjects below 50 years old, 2 out of these have positive NT-pro-BNP, 16 are human subjects between 50 and 59 years old, 9 out of these subjects have positive NT-pro-BNP, and 11 are human subjects over 60 years old, and here only 3 have positive NT-pro-BNP. In conclusion, there are no significant differences for the three age groups.

DISCUSSIONS

Symptomatic heart failure is rare due to peripheral vasodilatation of cirrhosis, which results in a "self treatment" of ventricle, the systemic vasodilatation reduces the postload and it decreases inhibitory influences in a compensatory manner, as the cardiac muscarinic system.(4,8)

Patients with diastolic dysfunction are particularly sensitive to changes in volume that occur, for example, in connection with a TIPS insertion. Portal decompression with TIPS may lead to a further increase in the diameter of the left atrium and of the blocked pulmonary capillary pressure, this indicating that the cirrhotic heart is unable to adequately receive an increased preload.(9,10,11)

We could not confirm a systolic dysfunction in the patients studied herein, and 3 patients in the group who presented signs of diastolic dysfunction had negative values of NT-pro-BNP.

The results obtained in the present study look like this because of the time elapsed between TIPS insertion and the NT-pro-BNP determination (over 1 year), time which probably allowed NT-pro-BNP values to normalize, and also because of the small number of patients with TIPS insertion studied.

CONCLUSIONS

In this study, the natriuretic peptide NT-pro-BNP in the blood of patients with cirrhosis was not influenced by the presence of portocaval shunt (TIPS).

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