Procalcitonin as a Biomarker for Early Trans-jugular Intrahepatic Porto-Systemic Shunt (TIPS) Stent Occlusion Prediction in Patients with Budd Chiari Syndrome

Mohamed A Sakr[1], Eman M El Gindy[1], Nadia A Abdelkader[1], Mohamed S Ghazy[2], Hany M Dabbous[1], Marwa M Shabban[3], Ahmed F Sherief[1], Ahmed S Abdelmoaty[1]

[1]*Department of Tropical Medicine, Faculty of Medicine, Ain Shams University. Cairo, Abbasia, Egypt*

[2]*Department of Radiodiagnosis and Interventional Radiology, Ain Shams University. Cairo, Abbasia, Egypt*

[3]*Department of Medical Microbiology and Immunology, Ain Shams University. Cairo, Abbasia, Egypt*

Corresponding Author
Ahmed S Abdelmoaty
ORCID 0000-0002-2646-9646
Mobile:
(+2) 01002873845
Email:
drahmedsamir@med.asu.edu.eg

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Background and study aim: One of the serious complications infrequently reported with trans jugular intrahepatic portosystemic shunt (TIPS) stent endovascular infection is bacteremia in up to 35% of patients. White blood cells (WBCs), procalcitonin (PCT), and C-reactive protein (CRP) could be used with ease for those infections' diagnosis and follow-up. In this study, we sought to investigate the potential biomarkers of infection and early TIPS stent occlusion in BCS patients by looking at the relationship between bacteremia and aberrant serum procalcitonin (PCT) levels before and after TIPS.

Patients and Methods: Thirty BCS patients with TIPS participated in this pilot exploratory investigation. For every patient, the following data were collected: procalcitonin (PCT) levels pre-TIPS, two days post-TIPS, two weeks post-TIPS, or at the time of stent occlusion; erythrocyte sedimentation rates (ESRs), blood cultures; and C-reactive protein levels.

Results: With a sensitivity of 100% and a specificity of 95.6%, there was a statistically significant increase in PC levels in blood culture-positive patients before and two weeks after TIPS or at the time of stent occlusion.

Additionally, in patients with obstructed stents, there was a correlation between positive blood culture results before and two weeks after TIPS. Regardless of the blood culture results, PCT levels were also higher in patients with occluded stents two days and two weeks after TIPS or at the time of stent occlusion.

Conclusion: PCT is a valuable infection biomarker, and its levels are elevated post-TIPS in Budd Chiari patients with occluded stents.

INTRODUCTION

Budd-Chiari syndrome (BCS) can happen if the small hepatic veins or the point where the inferior vena cava and the right atrium meet are blocked in any way [1]. For BCS, there are various treatment options, such as surgical, radiological, and medical treatments [2]. Trans-jugular intrahepatic portosystemic shunting (TIPS) is an image-guided technique that attempts to lower portal venous pressure by decompressing the portal system [3].

TIPS dysfunction is a common occurrence that needs to be diagnosed and treated right away. To maximize the clinical results for patients with complex portal hypertension, a comprehensive understanding of the many reasons for shunt failure and the methods for reestablishing shunt patency is required [4].

Patients undergoing TIPS procedures may have up to 35% of cases of bacteremia linked to endovascular TIPS stent infections. a dangerous consequence that was easily identified and monitored by taking measurements of inflammatory indicators such as procalcitonin (PCT), C-reactive protein (CRP), and white blood cells (WBCs) [5, 6].

The thyroid glands' C cells typically produce procalcitonin, a 116-amino acid prohormone of calcitonin. Liver and inflammatory cells are further sources of PCT [7]. In this study,

we sought to assess the association between serum procalcitonin (PCT) levels pre- and post-TIPS as a biomarker of infection, early TIPS stent occlusion in BCS patients, and the occurrence of bacteremia.

PATIENTS/MATERIALS AND METHODS

A pilot exploratory prospective interventional study was conducted on thirty individuals diagnosed with Budd Chiari syndrome who had hepatic decompression using the TIPS procedure. Patients were chosen among those referred to the Tropical Medicine Department of Ain Shams University Hospitals and the Egyptian Association for Studying of Vascular Liver Diseases.

Criteria for inclusion and exclusion

We included patients with Budd Chiari syndrome who were fit for the TIPS operation and had total blockage of all hepatic veins as shown by duplex ultrasound. According to the 2010 modifications to the AASLD recommendations, any patient exhibiting pre-procedure infection symptoms, such as fever, dysuria, coughing, expectoration, leukocytosis TLC > 11000 m/mm3, fever, abdominal tenderness, and rebound tenderness, was excluded. Additionally, patients with congestive heart failure, multiple hepatic cysts, unresolved biliary obstruction, severe pulmonary hypertension, hepatocellular carcinoma, particularly if central, portal vein thrombosis, severe coagulopathy (INR >5), or thrombocytopenia of 20,000/cm3 were not included in the TIPS procedure pool [8].

Every patient featured was exposed to:

Before the intervention, we performed a thorough medical history, a clinical examination, and laboratory tests such as prothrombin time INR, complete blood counts, and thrombophilia workup (including anti-DNA, lupus anticoagulant, anticardiolipin Ab, JACK 2 mutation, protein C, S, and antithrombin III levels).

Before TIPS, two days to two weeks after TIPS, and/or at the time of stent occlusion (if it happened), patients had duplex ultrasounds for the IVC, portal vein, and hepatic veins (0, 2, 7, 14) to assess the patency of the shunt. The samples also yielded results for serum procalcitonin levels, blood culture and sensitivity, ESR, CRP, and CBC. The RayBio Human Procalcitonin ELISA Kit (Raybiotec Company, United States of America) is an in vitro enzyme-linked immunosorbent assay for the quantitative measurement of human procalcitonin in serum, plasma, cell culture supernatants, and urine. It was used to measure the level of procalcitonin in the serum.

Before the treatment, all patients had taken a course of prophylactic antibiotics, which they continued to take for five days while they were in the hospital.

Statistical analysis

We gathered, edited, coded, and entered the data into IBM SPSS, a statistical package for social science, version 20. Quantitative data having a parametric distribution were shown as means, standard deviations, and ranges; non-parametric data were shown as the median and interquartile range (IQR); and qualitative data were presented as numbers and percentages. When comparing two groups with qualitative data, the Chi-square test or the Fisher exact test was utilized in place of the Chi-square test if any cell's predicted count was less than five. The independent t-test was used to compare two independent groups' quantitative data with a parametric distribution, and the Mann-Whitney test was used to compare two separate groups' non-parametric data. When comparing two paired groups' quantitative data with parametric distribution, the paired t-test was utilized; however, the Wilcoxon rank test was employed when comparing two paired groups' non-parametric data. The optimal cut-off point was determined using the receiver operating characteristic curve's area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The allowable margin of error was set at 5%, while the confidence interval was set at 95%.

RESULTS

Thirty Egyptian BCS patients participated in the current prospective interventional trial. They were chosen from the presentations made to the Tropical Medicine Department of Ain Shams University Hospitals and the Egyptian Association of Study of Vascular Liver Diseases.

These are suitable candidates for TIPS as a form of treatment.

The cohort under study had a mean age of 30.27 ± 6.03 years. In the study population, there were more women than men (63.3%).

The Child-Pugh score mean was 7.3 ± 1.56 and the mean MELD was 12.10 ± 3.43 before the TIPS surgery, with child B accounting for 43.3 percent of the cases.

The current study included thirty BCS patients who received the TIPS treatment. The patients were monitored for one day before, two days following TIPS, two weeks following the intervention, or at the onset of TIPS stent occlusion, if that happened.

An evaluation of the procedure's results was conducted, taking into account the survival rate, stent patency, and procedure-related problems like intraperitoneal hemorrhage or infection.

Of the thirty patients, seven experienced stent occlusions. Of these, 23 patients were able to maintain primary stent patency.

In terms of overall survival, three patients (10%) passed away throughout the follow-up period. Following the intervention, one patient developed sepsis, while the other two patients experienced severe intraperitoneal bleeding necessitating surgical exploration (Figure 1).

Hepatic encephalopathy, chest infection, and stent occlusion complicated the cases for those two patients following surgery. One of them became critically ill. They both declined and passed away from chest infections and septic shock.

Three of the thirty individuals had intraperitoneal bleeding. As previously said, two of them passed away, while the other one lived to see the follow-up period following surgical surgery with a patent stent.

Two of the thirty patients in the study had positive blood culture results, and twelve of them had a fever two days after TIPS.

Two days after TIPS and before the intervention, thirty patients were enrolled. Five patients failed to show up for the two-week follow-up after TIPS. Four of the five patients experienced stent occlusion two days after TIPS, while the fifth patient passed away from sepsis and DIC on the seventh day following TIPS. We chose angioplasty for those individuals with occluded stents.

The goal of this study was to find out if there was a link between early TIPS shunt occlusion in people with Budd Chiari syndrome and their pre-TIPS serum procalcitonin level, which is a sign of infection. Additionally, the study aimed to ascertain the relationship between post-TIPS serum procalcitonin level, blood culture results, and early TIPS shunt occlusion.

Twenty-seven patients remained alive after two weeks of treatment, and 23 patients (76.6%) had a patent TIPS stent two weeks following the intervention. Out of all patients, only three (10%) experienced post-interventional bleeding.

A big statistical difference was seen in the levels of TLC, AST, ALT, total bilirubin, INR, CRP, ESR, and procalcitonin that went up between the tests done before and two days after TIPS. However, between the pre- and two days after TIPS findings, there was a statistically significant difference in the form of decreasing serum albumin and hemoglobin levels. When comparing the procalcitonin serum levels two days after TIPS to the pre-TIPS findings, there was an increase (Table 1).

Regarding an increase in INR and ESR levels in two weeks post-TIPS or at the time of stent occlusion in comparison to the pre-interventional result, there was a significant statistical difference between laboratory investigations pre-TIPS and two weeks post-TIPS or at the time of stent occlusion. Additionally, there was a statistically significant drop in hemoglobin levels at the time of stent occlusion or between the pre- and two-week post-TIPS. Additionally, there was a statistically significant difference in the CRP, ESR, AST, ESR, and ALT laboratory data at the time of stent occlusion compared to two weeks after TIPS or two days later. These differences showed decreasing values. When compared to two days after TIPS findings, serum albumin and INR values increased statistically significantly two weeks after TIPS or at the time of occlusion (Table 1).

Four, two, and two patients' blood cultures were positive prior to, two days after, and two weeks after the procedure, or at the time of stent occlusion, respectively.

One of the four patients whose blood culture was positive prior to the TIPS result developed sepsis during the intervention, persisted in declining

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even with a patent stent, and passed away on the seventh day following TIPS. In another case, the TIPS stent became occluded on the second post-TIPS day. One patient suffered post-interventional intraperitoneal hemorrhage, necessitating surgical intervention. Two weeks after TIPS, this patient was one of the two with a positive blood culture. The patient lived and attained stent patency in spite of these difficulties.

Only one patient had positive blood culture results prior to TIPS and did not experience any post-interventional complications.

Two days after TIPS, two patients with positive blood cultures experienced a fever that quickly subsided without any complications. Both patients also had patent stents.

In addition to the patient who was previously addressed, at the third point of the research, there was another patient who had a positive blood culture four days following TIPS, at which point the stent was blocked. After undergoing surgical exploration for post-TIPS intraperitoneal hemorrhage, the patient experienced fever, hepatic encephalopathy, stent occlusion, and a positive blood culture result. The patient's death brought the disease to an end.

Prior to the TIPS operation, procalcitonin levels significantly increased in blood culture-positive patients. Two days after the TIPS surgery, procalcitonin levels in blood culture-positive patients showed negligible change. Procalcitonin levels significantly increased in patients with positive blood cultures at the time of occlusion or two weeks after TIPS (Table 2).

In Figure 2, the pre-TIPS procalcitonin levels ROC curve is shown as a predictor of positive blood culture results. At the cutoff value of 0.11 ng/ml, the curve is 100% sensitive and 96.15% specific, meaning that it can find 80% of positive blood culture results and 100% of negative blood culture results.

The procalcitonin ROC curve as a predictor of positive blood culture two days after TIPS results demonstrates (at a cutoff value of 0.2 ng/ml) 50% sensitivity and 75% specificity, with a positive predictive value of 12.5% and a negative predictive value of 95.5% (Figure 3).

Procalcitonin's ROC curve as a predictor of positive blood culture results two weeks after TIPS or at the time of stent occlusion demonstrates 100% sensitivity and 95.6% specificity (at a cutoff value of 0.11 ng/ml), with 66.7% positive predictive value and 100% negative predictive value in identifying blood culture positive results (Figure 4).

Only individuals with a patent stent compared to those with stent occlusion showed a statistically significant difference in procalcitonin levels at two days, two weeks, or at the time of stent occlusion. Regardless of positive blood cultures, patients with occluded stents had somewhat higher procalcitonin levels than those with patent stents. There was no statistically significant difference between TIPS stent occlusion and the pre-TIPS procalcitonin values.

In the two days and two weeks following TIPS or at the time of stent occlusion, procalcitonin levels were higher in the occluded TIPS stent group than in the patent group (Table 3).

Blood culture results before TIPS, two weeks after TIPS, and the period of stent occlusion differed statistically significantly in the patent stent group when compared to the occluded stent patients (P-values of 0.027 and 0.001, respectively). When comparing the pre-TIPS CRP levels of the deceased group to those of the survivors, there was a statistically significant difference (Table 4).

Two days after TIPS, the deceased patient group had significantly higher levels of procalcitonin. Results of blood cultures, procalcitonin, and CRP at two weeks after TIPS or during stent occlusion were significantly correlated with survival. They were all at the top of the list of patients who passed away.

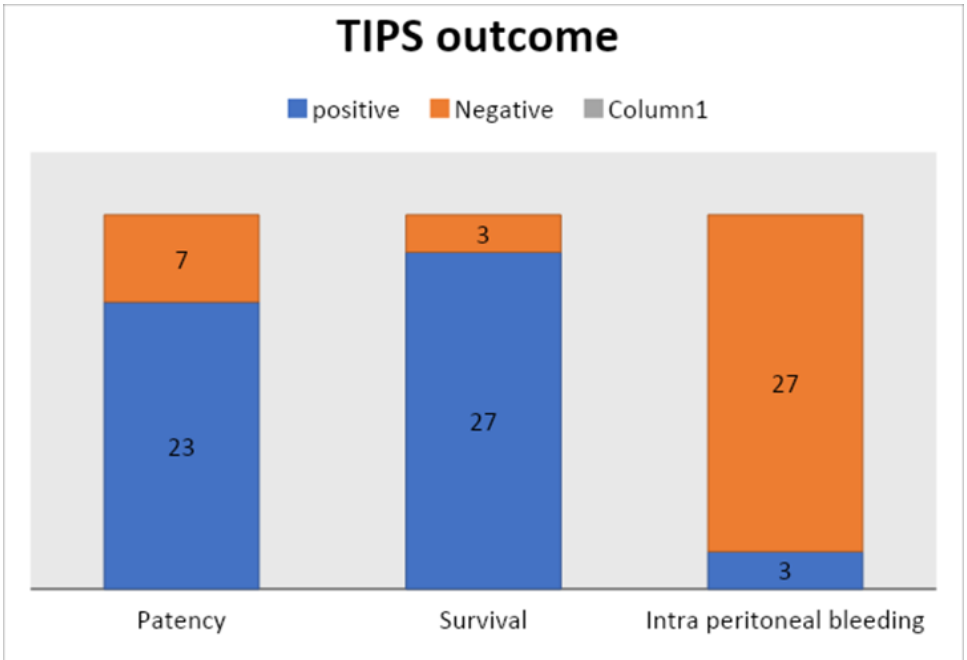

Figure 1. TIPS outcome regarding stent patency, survival and intra peritoneal bleeding post TIPS.

Table 1. Comparison between laboratory investigations pre and 2 days Post and two weeks Post TIPS or at time of stent occlusion TIPS (n=30):

		Pre	2 days Post TIPS	Post (2 weeks or occlusion)	Paired t-test			
					2 days Post TIPS		Post (2 weeks or occlusion)	
					t/Z*	P-value	t/Z*	P-value
TLC (thousands/cmm)	Mean±SD	6.68 ± 2.12	8.41 ± 3.11	7.22 ± 5.60	0.002	0.002	-0.790	0.437
Hb (gm/l)	Mean±SD	12.11 ± 1.70	11.10 ± 1.59	11.03 ± 1.30	0.000	0.000	2.986	0.006
Plat (thousands/cmm)	Mean±SD	184.77 ± 84.58	174.20 ± 82.58	194.88 ± 72.39	0.353	0.353	-0.552	0.586
AST (IU/L)	Mean±SD	48.67 ± 30.77	100.90 ± 68.84	59.16 ± 75.67	0.000	0.000	-0.830	0.415
ALT (IU/L)	Mean±SD	34.40 ± 19.00	104.73 ± 106.32	50.08 ± 62.92	0.001	0.001	-1.287	0.210
ALB (gm/dl)	Mean±SD	3.34 ± 0.68	3.18 ± 0.55	3.35 ± 0.55	0.013	0.013	0.583	0.565
Bil-T (mg/dl)	Mean±SD	1.99 ± 1.45	2.32 ± 1.51	1.73 ± 1.21	0.035	0.035	0.381	0.707
Bil-D (mg/dl)	Mean±SD	0.93 ± 0.78	0.98 ± 0.72	0.78 ± 0.86	0.484	0.484	0.664	0.513
INR	Mean±SD	1.34 ± 0.15	1.43 ± 0.18	1.96 ± 0.49	0.007	0.007	-5.844	0.000
ESR (mm/hr)	Mean±SD	22.67 ± 9.74	37.87 ± 12.08	29.92 ± 12.88	0.000	0.000	-2.690	0.013
CRP	<6 **(mg/l)**	26 (86.7%)	2 (6.7%)	17 (56.70%)	0.000 •	0.000 •	2.786	0.095•
	> 6 **(mg/l)**	4 (13.3%)	28 (93.3%)	8 (26.70%)				
Procalcitonin (ng/ml)	Median (IQR)	0.07 (0.06 – 0.11)	0.08 (0.07–0.25)	0.07 (0.06 –0.08)	0.001 *	0.001 *	-0.327	0.743*

*: Wilcoxon test •: Chi-square test

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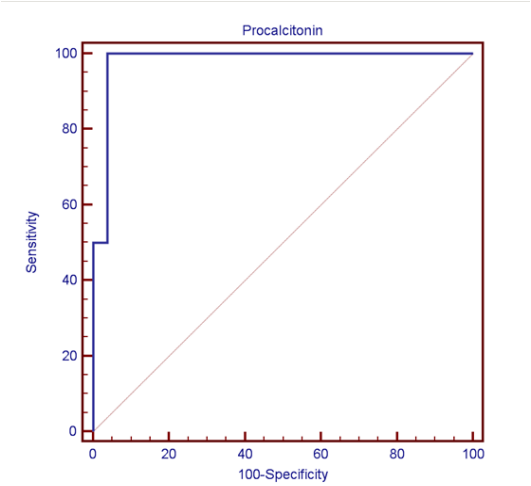

Figure 2. ROC curve of Pre-TIPS procalcitonin as a predictor of positive blood culture.

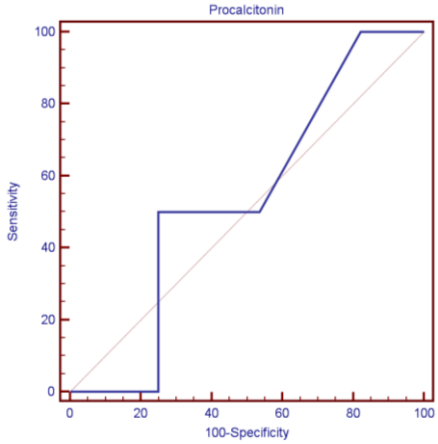

Figure 3. ROC curve of procalcitonin as a predictor of positive blood culture two days Post TIPS.

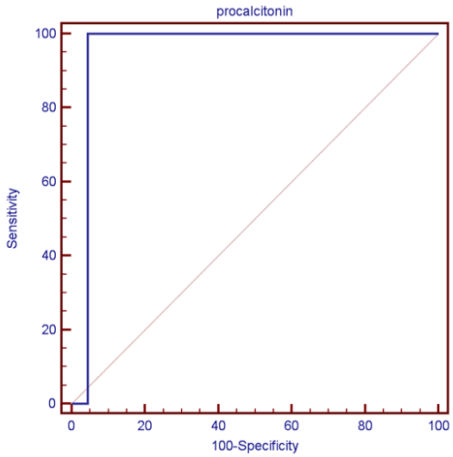

Figure 4. ROC curve of procalcitonin as a predictor of positive blood culture two weeks Post TIPS or at time of stent occlusion

Table 2. Relation between blood culture and procalcitonin levels (pre- TIPS, 2 days, 2 weeks post TIPS)

Blood culture pre-TIPS	**Procalcitonin (n=30)**		**Mann-Whitney test**	
	Median (IQR)	**Range**	**Z**	**P-value**
Negative (n=26)	**0.07 (0.06 – 0.09)**	**0.04 – 0.4**	**-3.090**	**0.002**
Positive (n=4)	**0.4 (0.3 – 0.55)**	**0.3 – 0.6**		
Blood culture two days post TIPS	**Procalcitonin (n=30)**		**Mann-Whitney test**	
	Median (IQR)	**Range**	**Z**	**P-value**
Negative (n=28)	**0.08 (0.07 – 0.25)**	**0.04 – 2.3**	**-0.169**	**0.866**
Positive (n=2)	**0.16 (0.07 – 0.25)**	**0.07 – 0.25**		
Blood culture Post (two weeks post	**Procalcitonin (n=25)**		**Mann-Whitney test**	
TIPS or occlusion)	**Median (IQR)**	**Range**	**Z**	**P-value**
Negative (n=23)	**0.07 (0.06 – 0.07)**	**0.05 – 1.9**	**-2.215**	**0.027**
Positive (n=2)	**0.55 (0.3 – 0.8)**	**0.3 – 0.8**		

Table 3: Relation between procalcitonin levels at different time points with the TIPS stent patency

		Patent	**Occluded**	**Mann-Whitney test**	
				Z	**P-value**
Procalcitonin Pre n= 30	**Median**	0.06	0.09	-1.341	0.180
	(IQR)	(0.06 – 0.11)	(0.08 – 0.11)		
Procalcitonin two days post TIPS n= 30	**Median**	0.07	0.2	-2.416	0.016
	(IQR)	(0.07 – 0.2)	(0.11 – 0.35)		
Procalcitonin two weeks post TIPS or occlusion n= 25	**Median**	0.07	0.8	-2.818	0.005
	(IQR)	(0.06 – 0.07)	(0.11 – 1.9)		

Table 4: The relation between CRP, blood culture results and Procalcitonin and two-week survival post TIPS

			Died	**Lived**	**Chi-square test**	
					X^2/Z*	**P-value**
Pre TIPS (n=30)	**CRP**	<6	1 (33.3%)	25 (92.6%)	8.205	0.004
		>6	2 (66.7%)	2 (7.4%)		
	Blood culture	Negative	2 (66.7%)	24 (88.9%)	1.154	0.283
		Positive	1 (33.3%)	3 (11.1%)		
	PCT	Median(IQR)	0.1	0.07	-1.645	0.100*
Two days post TIPS (n=30)	**CRP**	<6	0 (0.0%)	2 (7.4%)	0.238	0.626
		>6	3 (100.0%)	25 (92.6%)		
	Blood culture	Negative	3 (100.0%)	25 (92.6%)	0.238	0.626
		Positive	0 (0.0%)	2 (7.4%)		
	PCT	Median(IQR)	0.6	0.07	-2.563	0.010*
Two weeks post TIPS or occlusion (n=25)	**CRP**	<6	0 (0.0%)	17 (73.9%)	4.620	0.032
		>6	2 (100.0%)	6 (26.1%)		
	Blood culture	Negative	1 (50.0%)	22 (95.7%)	5.210	0.022
		Positive	1 (50.0%)	1 (4.3%)		
	PCT	Median(IQR)	1.35	0.07	-2.426	0.015*

*: Mann-Whitney test

DISCUSSION

Budd Chiari syndrome is an uncommon illness that can be fatal, particularly if treatment is not received right away. Hence, favorable outcomes arise from adhering to conventional guidelines for medicinal, interventional, or surgical therapy [9].

Thirty Egyptian patients with Budd Chiari syndrome who were seen between January 2014 and December 2015 at the Ain Shams University Hospitals' Tropical Medicine Department and the Egyptian Society for Studying of Vascular Liver Disorders were included in this study.

TIPS have a decompressive effect on the enlarged liver, slowing the advancement of cirrhosis and liver fibrosis [10]. Nowadays, people view TIPS as a long-term therapeutic option, not just a temporary measure before liver transplantation [11].

Many studies were conducted to assess its efficacy, prognostic indicators, and outcome predictors to establish stringent guidelines for case selection and the avoidance of maneuver problems.

Our study's primary goal was to compare and correlate the TIPS outcome after 14 days with other parameters, primarily the amount of procalcitonin and other factors.

In terms of the two-week primary patency without requiring TIPS revision, 23 stents are patent (76.7%) and 7 are occluded (23.3%). These outcomes surpass those of the Eldorry et al. (2011) study, which found that, among sixteen patients who had TIPS, 69% of them still had primary patency two weeks later [13]. Contrary to our findings, Eldorry et al. (2011) reported that the majority of stent occlusions (40%) happened seven days following the intervention. Of the seven patients who experienced stent occlusion, four experienced it most frequently two days after TIPS (57%). Out of the seven occluded TIPS stents, only one (14%) had stent occlusion on day 7, with the other two patients developing stent occlusion on days 4 and 10, respectively [13].

These outcomes fell short of the findings of the Rosenqvist et al. (2016) trial, which saw 100% primary patency of TIPS stents. The use of covered stents and other disease etiologies could be the cause [14]. According to Bachet et al. (2007), 35% of the patients who were included in the study who had surgical portosystemic shunting had shunt malfunctions identified within the first postoperative month [15].

Neumann et al. (2013) and Perarnau et al. (2014), found that the need for revision of TIPS stents during the first year was 0.54 per patient in covered stents, while it was 1.67 per patient in bare stents, with 2 years of patency of 63% and 33% in covered and bare stents, respectively, we used bare metallic stents in our study, which have a higher rate of occlusion than covered stents.

An extremely serious, potentially fatal complication that complicates the TIPS operation is intraperitoneal hemorrhage. Generally, this occurs due to a liver tear or a portal venous puncture. Hemotoperitoneum occurred 10% of the time in the current investigation. These outcomes were superior to those reported by Eldorry et al. (2011) regarding the incidence of intraperitoneal hemorrhage following a maneuver, which happened in two of the sixteen patients with BCS [13]. However, this dispute may stem from the small number of patients (9 patients only) included in the study by Rosenqvist et al. (2016), as no bleeding occurred in the patients they evaluated [14]. 2 patients (6%) out of 35 BCS patients (6%) who underwent TIPS had intra-abdominal hematomas, according to Rössle et al. (2004) [17].

According to Bouza et al. (2004), in several centers, the probability of intraperitoneal hemorrhage complicating TIPS varied from 1% to 33%. Of the three patients who needed to have surgical exploration, two of them experienced stent occlusion, which worsened until they passed away [18]. The other one, which had preserved its stent patency, lived. According to Bachet et al. (2007), this matches.

We observed a sepsis recurrence in two patients (6.6%), both of whom died. One of them had an increased procalcitonin level and a positive pre-TIPS blood culture. This result was better than that reported by Eldorry et al. (2011), who reported that sepsis incidence was 18.75% even when preventive antibiotics, such as cefotaxime and ampicillin-sulbactam, were used, as in our study [13]. Additionally, 13% of the patients in Dravid et al.'s 1998 study experienced sepsis [19].

According to Mizrahi et al. (2010), even with the preventative use of antibiotics, fever and post-TIPS bacteremia may occur in 2–25% of patients following the procedure [20].

Three out of the thirty patients (10%) in the current investigation died as a result of procedural complications. These findings outperform those published by Mancuso et al. (2003). About 26% of the BCS patients the authors treated had mortality [21]. Our findings are comparable to the post-TIPS early survival rates of 10% and 9%, respectively, that were reported by Perelló et al. (2002) and Rossle et al. (2004), with mortality complicating TIPS. [22] [17]. However, compared to Perarnau et al. (2014), who reported a death rate of 6.3%, our results show a higher rate [12].

Before the intervention, 4 out of 30 patients in the study group had a blood culture positive result, with 75% of those bacteria being *Staphylococcus aureus* and 25% being

coagulase-negative *Staphylococcus*. Two patients tested positive following the intervention at two points: two days after the intervention and 14 days after the intervention, or at the time of occlusion. At the two-day mark, the prevalence was 6.6% (2 out of 30 patients), and at the second point, it was 8% (2 out of 25 patients), with 50% of the patients having coagulase-negative staphylococcus and 25% having *staphylococcus aureus* and *Escherichia coli*. These findings were consistent with those of Halpenny and Torreggiani (2011), De Simone et al. (2000), and Mizrahi et al. (2011). And who discovered that post-TIPS bacteremia is caused by the same germs [5] [23] [24]

Compared to what DeSimone et al. (2000) discovered and reported, post-TIPS bacteremia was observed in a very low percentage in the current investigation. The authors reported that even with a preventive antibiotic regimen including cefotaxime and vancomycin, 35% of 99 patients with chronic liver disease who underwent TIPS had positive blood cultures after TIPS [5].

Two days after the TIPS findings, the patient group with blocked stents had higher procalcitonin levels. At the third study time point, which occurred 14 days after TIPS or at the moment the TIPS stent was occluded, 25 out of 30 patients were enrolled.

Patients with stent-occluded stents had greater levels of procalcitonin than those with patent stents.

PCT serum levels were higher in the positive blood culture results than in the negative ones, either at the time of stent occlusion or in the pre- and two-weeks following TIPS. At those time points, the PCT cutoff level >0.11 ng/ml had the highest sensitivity and specificity.

The 97% sensitivity at the cutoff level of 2 ng/ml reported by Meynaar et al. (2011) and the 91% specificity of the PCT level in detecting positive blood culture results published by Tsangris et al. (2009) were in line with these results [26] [7]. Conversely, Tsalik et al. (2012) reported 68% and 63% sensitivity and specificity, respectively, with a cutoff PCT of 0.1 ng/ml [27]. According to Kofoed et al. (2007), at the PCT cutoff level of 0.25 ng/ml, the specificity was 58% [28]. Two days after TIPS, the results revealed that the sensitivity and specificity were 50% and 75%, respectively, at the cutoff point of 0.2 ng/ml, with a positive predictive value of 12.5% and a negative predictive value of 95.5%.

This is similar to the findings of Tsalik et al. (2012), who obtained 68% and 63% sensitivity and specificity at the PCT cutoff point of 0.1 ng/ml, respectively [27].

According to Naeini and Montazerolghaem (2006), Tsangris et al. (2009), and Meynaar et al. (2011), the PCT level test had a sensitivity and specificity of about 90% [29], which was different from what this study found.

Two days after TIPS, the test may lose its sensitivity and specificity, which could explain the slight increase in PCT level after abdominal surgery [30] [31].

We determined the pooled sensitivity of the PCT assay in the current study to be approximately 83%, with a corresponding 88% specificity. These results were consistent with those reported by Miglietta et al. (2015) [32].

According to the authors, the test had a sensitivity of 85.75% and a specificity of almost 89%. Additionally, the data gathered from research conducted by Meynaar et al. (2011) revealed that PCT has a 90% sensitivity and specificity [26].

Regarding the relationship between CRP and PCT at the three research periods and with fever, there was no statistically significant difference. This was in line with what Bloos et al. (2011) reported [33].

Results from blood cultures obtained before, two days after, and fourteen days after TIPS, as well as during the period of occlusion, did not show any statistically significant correlation.

This was in line with the findings that Wacker et al. (2013) [34]. CRP rises nonspecifically in other inflammatory illnesses, such as collagen disease, while being utilized as an indicator of infection [35]. In this investigation, PCT outperformed CRP in terms of sensitivity and specificity for identifying positive blood culture results. According to Christ-Crain and Muller (2005), Josselin et al. (2015), and Miglietta et al. (2015) [30] [36] [32], those results were in agreement.

Conversely, Nishikawa et al. (2016) found that there was a substantial correlation between the blood culture results and both CRP and PCT. The lack of surgical or radiological interventions in their study group could explain this [37].

As an early outcome of surgery, pre-TIPS CRP values revealed a statistically significant difference in survival, with more positive

outcomes among the dyed group of patients than the survived one.

CONCLUSION

Pre- and post-TIPS bacteremia increases the rate of TIPS stent occlusion. PCT is a valuable infection biomarker and its levels are elevated post-TIPS in Budd Chiari patients with occluded stents.

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- Research design, or acquisition, analysis or interpretation of data;

- drafting the paper or revising it critically;

- approving the submitted version.

We also declare that no-one who qualifies for authorship has been excluded from the list of authors.

Ethical considerations:

The Ain Shams University Faculty of Medicine's institutional ethics committee authorized the protocol, and the study was carried out in compliance with the 1975 Declaration of Helsinki. Each individual gave their informed consent before the study began.

HIGHLIGHTS

- Patients undergoing transjugular intrahepatic portosystemic shunt (TIPS) procedures may have up to 35% of cases of bacteremia linked to endovascular TIPS stent infections.
- Procalcitonin (PCT) could be used with ease for those infections' diagnosis and follow-up.
- PCT is a valuable infection biomarker and its levels are elevated post-TIPS in Budd Chiari patients with occluded stents.

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