Cellular and Molecular Biology
E-ISSN : 1165-158X / P-ISSN : 0145-5680
www.cellmolbiol.org

Analyses on clinical efficacy of TIPS in the treatment of cirrhotic portal hypertension and relevant influencing factors

Zhihui Liang, liang Li, Liming Cao, Jianyu Liu, Jinglei Liu*

Radiology Department, the 980 Hospital of PLA logistic Force, Hebei, 050082, China

ARTICLE INFO

Original paper

Article history:
Received: March 14, 2022
Accepted: July 05, 2022
Published: July 31, 2022

Keywords:

TIPS, cirrhosis, portal hypertension, efficacy, complications.

ABSTRACT

The study aimed to explore the clinical efficacy of transjugular intrahepatic portosystemic shunt (TIPS) in treating cirrhotic portal hypertension and relevant influencing factors. 100 patients with cirrhotic portal hypertension receiving TIPS in the 980 Hospital of PLA logistic force from January 2015 to January 2018 were enrolled. Blood was collected from patients to detect liver function indicators [aspartate aminotransferase (AST) and alanine aminotransferase (ALT)], renal function indicators [blood urea nitrogen (BUN) and creatinine (Cr)], glucose metabolism indicators [insulin and glucose (GLU)] and inflammatory factors [interleukin-6 (IL-6), IL-8 and CXCL9] before surgery and at1 and 6 month(s) after surgery. Surgical efficacy was evaluated. The physique of patients was examined. The portal venous pressure, diameter and hemorheological indicators of patients were measured. Additionally, postoperative complications and nursing satisfaction were observed. At 1 and 6 month(s) after an operation, the levels of AST, ALT, BUN, Cr, insulin, GLU and inflammatory factors IL-6, IL-8 and CXCL9 and the portal venous pressure were overtly reduced ($p<0.05$), the postoperative dry weight was increased ($p<0.05$), the postoperative nursing satisfaction was 97%, the patients with higher satisfaction had fewer complications ($p<0.05$), the diameter of the portal vein was notably lowered ($p<0.05$), while the blood flow rate was remarkably raised ($p<0.05$). After the application of TIPS in the treatment of cirrhotic portal hypertension, the liver function, renal function, glucose metabolism and portal venous pressure and flow rate of patients return to normal, and postoperative complications are clearly reduced after postoperative nursing, proving the overall efficacy. Hence, TIPS is worthy of popularization and application.

Doi: http://dx.doi.org/10.14715/cmb/2022.68.7.21

Introduction

Cirrhosis, the end stage of chronic liver injury, is correlated with portal hypertension, which is the leading driver limiting the survival of patients and complications (1, 2). Portal hypertension caused by different stimuli is able to lead to inflammation, fibrosis and abnormal angiogenesis in the liver. Transjugular intrahepatic portosystemic shunt (TIPS), which is an increasingly important participant in the management and treatment of portal hypertension complications including variceal hemorrhage and refractory ascites since the 1980s, is a hemodynamically equivalent small-diameter portal shunt. After TIPS, the incidence rates of mortality and stent dysfunction are very high in the early stage due to the use of bare metal stents (3, 4). Therefore, the role of TIPS in the long-term management of complications of portal hypertension has been questioned. However, the procedure of TIPS has revolutionary changes due to the introduction of covered stents, subsequently significantly improving the long-term shunt patency. Besides, some practical guidelines for the application of TIPS in the management of portal hypertension and new studies detailing the progress of TIPS technology have been published (5, 6). At present, the safety and efficacy of TIPS are improved via clinical trials, and the risk of short-term death of patients undergoing TIPS, which is assessed through the model for end-stage liver disease scoring system, is reduced (7). Undeniably, liver transplantation is a major hope for patients with portal hypertension, but limited organ supply is still a limiting factor (8). As a result, TIPS, a bridge for liver transplantation, has become the best option for the treatment of portal hypertension. However, its clinical efficacy and relevant influencing factors remain unclear and need to be further studied.

Portal hypertension has associations with complications that are severe and often life-threatening. Increased intrahepatic resistance causes the increase of splanchnic blood flow, the development of varicose veins that may lead to bleeding, and splenomegaly. Increased cardiac output and reduced systemic vascular resistance result in the formation of a high dynamic cycle. Visceral blood stagnation may lead to systemic hypovolemia, thereby triggering the activation of the vasoactive agents, mainly vasoconstrictors, which may further result in sodium retention, ascites and ultimately hepatorenal syndrome (9). It is found in a study that inflammation factors and chemokines have abnormal increases in the case of cirrhotic portal hypertension, especially CXCL9 which is increased in liver

* Corresponding author. Email: liujinglei81@sina.com

diseases (10), which is functionally associated with liver damage, inflammation, fibrosis (11), angiogenesis and cirrhosis complications (12). Liver-resident cells, including hepatocytes and hepatic stellate cells, are found to be the major sources of CXCL9 ligands in the liver (13, 14). As mentioned above, in addition to hepatocyte proliferation, circulating inflammatory cells may participate in the synthesis and secretion of pro-inflammatory factors in other cells (15). Further promotion of the over-activation of neutrophils and endothelial cells leads to the upregulation of cell surface adhesion molecules, including selectins and integrins, and the adhesion of neutrophils to the inflammatory endothelium, thus resulting in the extravasation of neutrophils into important organs and then the degranulation, release of proteases, other hydrolases and reactive oxygen species, and synthesis of inflammatory cytokines including IL-8 (16). The progression of portal hypertension during chronic liver disease parallels the increases in intrahepatic and circulating levels of these chemokines, and their specific effects and prognostic value in portal hypertension are well studied. Elevated levels of these chemokines indicate an inflammatory syndrome known to be related to the poor prognosis of patients with cirrhosis. In patients with end-stage liver disease, the complications of chronic liver disease have a direct relation to the CXCL9 level (17). However, its specific mechanism of action remains unclear.

In this study, therefore, patients with cirrhotic portal hypertension receiving TIPS were followed up, the liver function, renal function and glucose metabolism indicators as well as inflammatory factor levels were detected, the physique of patients was examined, the patient's portal venous pressure, diameter and blood hemorheological indicators were measured, and postoperative complications and nursing satisfaction were observed, so as to comprehensively evaluate the advantages of TIPS.

Materials and Methods

General data

A total of 100 patients with cirrhotic portal hypertension undergoing TIPS for the first time in the 980 Hospital of the PLA logistic force from January 2015 to January 2018 were selected. Subsequent research was performed only after the patients enrolled signed the informed consent. There were 58 males and 42 females, aged 30-85 years old, with a mean of (44±11) years old and weighing 42-80kg with an average of (55±11.5) kg. Inclusion criteria: Patients were diagnosed with cirrhosis via ultrasound and CT, without other severe complications before surgery, not allergic to drugs used in this research, and not received TIPS previously. Exclusion criteria: Patients with acute heart failure, nervous system diseases, severe cardiovascular or cerebrovascular diseases such as coronary heart disease or heart valve disease, or severe secondary infections complicated with severely abnormal liver or renal function, or pregnant or lactating women. This clinical study protocol, including all detection programs in assays, was carried out with approval from the Ethics Committee of the 980 Hospital of the PLA logistic force.

Surgical methods

The right internal jugular vein was punctured to insert the puncture system (Cook) slowly. After the successful entrance into the portal vein by puncturing via the hepatic vein, portal vein angiography was performed, and portal venous pressure was measured. Next, the catheter was replaced, and the varicose coronary gastric vein was embolized using materials including a steel ring (Cook), gelatin sponge particles and tissue glue via the catheter. Then, stents were placed on establishing shunt ways. After that, the pigtail catheter was introduced again to perform splenic and portal vein angiography, and portal venous pressure was detected. Upon the completion of the surgery, the vagina vasorum was pulled out, and the puncture site was pressed to stop bleeding and bandaged. After surgery, conventional sign observation and therapy were performed, and the condition of patients was observed at any time for various subsequent experimental studies.

Evaluation of surgical outcomes

The outcomes were assessed in accordance with internationally accepted standards. Successful surgery: The shunt between the hepatic vein and the portal vein is successfully established. Based on the Baveno V international consensus standard, re-bleeding after TIPS is clinically manifested as hematemesis, vomiting of coffee-like liquid and melena, accompanied by a decrease of >30 g/L in hemoglobin, or transfusion therapy. Shunt way failure: The direction of blood flow changes, and the blood flow velocity of the shunt is <50 cm/s. The results were recorded in detail and analyzed by a specially-assigned person.

Observation of postoperative complications and nursing satisfaction

After surgery, patients' complications (including types) and satisfaction to postoperative nursing were recorded in detail. Postoperative complications mainly included mild hepatic coma, abnormal stool, confusion, dizziness and lethargy. A self-made satisfaction rating scale was adopted to rate the satisfaction (satisfied, fair and dissatisfied). Satisfaction = satisfied + fair.

Detection of serum liver function, renal function and glucose metabolism indicators

In the case of cirrhosis, the biochemical indicators such as liver function, renal function and glucose metabolism indexes will be changed, so the development and progression of the disease can be indicated by detecting changes in these indicators. Fasting peripheral venous blood (5 mL) was collected from patients in the morning into Eppendorf (Ep) tubes containing the anticoagulant ethylene diamine tetraacetic acid (EDTA) and centrifuged at 3500 g and room temperature for 10 min. Thereafter, the supernatant was collected for the detection of liver function, renal function and glucose metabolism indicators, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), creatinine (Cr), insulin and glucose (GLU), providing important theoretical references for early treatment.

Measurement of serum inflammatory factors using ELISA

After collecting fasting peripheral venous blood (5 mL) from patients in the morning into Ep tubes containing the anticoagulant EDTA, centrifugation was carried out at room temperature and 3500 g for 10 min, followed by the collection of the supernatant. Next, levels of serum inflam-

matory factors interleukin-6 (IL-6), CXCL9 and IL-8 were measured according to the instructions of an enzyme-linked immunosorbent assay (ELISA) kit (Nanjing SenBeiJia Biological Technology Co., Ltd.). Lastly, the absorbance in each group was read using a microplate reader.

Examination of the physique of patients

A body composition analyzer was employed to measure the body physique of the 100 patients before surgery and at 1 and 6 month(s) after surgery by a specially-assigned person as per the instructions of the analyzer. Body weight and body fat were recorded, and dry weight was calculated as the following formula: dry weight = body weight - total body water - body fat. Experimental data were recorded in detail, and the average value was calculated after repeat measurements.

Determination of patient portal venous pressure, diameter and blood hemorheological indicators

An HDI3500 color Doppler ultrasound system was used, with a probe frequency of 3.5 MHz. After transhepatic portal vein angiography and intubation, the portal venous pressure, portal venous blood flow velocity, vessel diameter and mean velocity were detected and recorded by a specially-assigned person according to the instructions of the instrument. The experimental data were recorded in detail, and the average was calculated after repeat measurements.

Statistical analysis

All raw experimental data recorded were processed by SPSS 20.0 analysis software and subjected to multiple comparisons. χ^2 test was employed for the percentage. The experimental results obtained were expressed as mean ± standard deviation ($\chi \pm SD$), and $p<0.05$ suggested that the difference was statistically significant. Graphpad Prism 6.0 was applied for plotting histograms.

Results

Clinical efficacy of patients

As shown in Table 1, the total response rate of clinical efficacy was 99% and 98% at 1 and 6 month(s) after surgery, respectively, showing no statistically significant difference ($p>0.05$). It implies that the clinical efficacy is sustained in the long term after treatment with TIPS.

Postoperative complications

There were only 8 cases of complications at one month after surgery and only 4 at 6 months after surgery, displaying no statistically significant difference ($p>0.05$) (Table 2). It indicates that TIPS achieves an obvious effect in the treatment of cirrhotic portal hypertension, with fewer adverse reactions and postoperative complications.

Nursing satisfaction

The patients' satisfaction in the two groups shown in Table 3 revealed that the patients' satisfaction was 97% one month after surgery and 94% at 6 months after surgery, and there was no statistically significant difference ($p>0.05$).

Levels of serum liver function, renal function and glucose metabolism indicators

As shown in Table 4, the levels of AST, ALT, Cr, BUN and insulin declined remarkably ($p<0.05$), while the GLU level increased clearly ($p<0.05$) at 1 and 6 month(s) after surgery, indicating that the liver function, renal function and glucose metabolism of patients are evidently improved after application of TIPS in treating cirrhotic portal hypertension.

Table 1. Clinical efficacy.

Group	Successful surgery	Re-bleeding after TIPS	Shunt way failure	Total response rate (%)
1 month after surgery	99	1	0	99
6 months after surgery	98	1	1	98

Note: Comparison of clinical efficacy shows that the total response rate is 99% at 1 month after surgery and 98% at 6 months after surgery, and the difference is not statistically significant ($p>0.05$).

Table 2. Postoperative complications.

Group	Confusion	Dizziness	Lethargy	Mild hepatic coma	Stool abnormality	Total complication (%)
1 month after surgery	2	1	2	1	2	8
6 months after surgery	1	1	1	0	1	4

Note: There was no statistically significant difference in complications between 1 month after surgery and 6 months after surgery (8 cases vs. 4 cases, $p>0.05$).

Table 3. Nursing satisfaction.

Group	Satisfied	Fair	Dissatisfied	Satisfaction (%)
1 month after surgery	90	7	3	97
6 months after surgery	89	5	6	94

Note: The patients' satisfaction is 97% and 94% at 1 and 6 month(s) after surgery, respectively, showing no statistically significant difference ($p>0.05$).

Table 4. Levels of serum liver function, renal function and glucose metabolism indexes.

Group	AST (U/L)	ALT (U/L)	Cr (umol/L)	BUN (mmol/L)	Insulin (mU/L)	GLU (mmol/L)
Before surgery	80.4±2.1	65.8±2.1	100.7±5.2	10.5±1.8	20.5±1.6	5.3±0.5
1 month after surgery	40.8±2.8[a]	50.7±1.7[a]	78.9±4.2[a]	6.3±1.7[a]	14.3±1.3[a]	7.5±0.8[a]
6 months after surgery	32.4±2.1[a]	42.7±3.1[a]	69.5±5.2[a]	5.1±1.0[a]	13.0±1.2[a]	8.4±0.2[a]

Note: The levels of AST, ALT, Cr, BUN and insulin are lowered markedly (p<0.05), while the GLU level is elevated overtly (p<0.05) at 1 and 6 month(s) after surgery. [a]p<0.05 vs. before surgery.

Table 5. Results of physique examination (kg).

Group	Body weight	Body fat	Dry weight
Before surgery	49.1±1.2	14.4±1.0	14.2±2.1
1 month after surgery	53.5±1.8[a]	15.0±2.4	16.3±2.5[a]
6 months after surgery	57.7±1.9[a]	15.4±1.6	18.8±1.9[a]

Note: Compared with those before surgery, the body weight and body fat were increased at both 1 and 6 month(s) after surgery (p<0.05, p<0.05). [a]p<0.05 vs. before surgery.

Table 6. Intrahepatic venous pressure and blood flow.

Group	Venous pressure (cm H_2O)	Internal diameter (cm)	Velocity (cm/s)
Before surgery	48.6±2.9	1.5±0.2	13.5±1.3
1 month after surgery	26.4±1.8[a]	1.15±0.3[a]	34.9±1.9[a]
6 months after surgery	25.8±2.4[a]	1.02±0.1[a]	36.7±2.2[a]

Note: Compared with those before surgery, the pressure and diameter of the portal vein were markedly reduced after surgery, while the velocity was raised (p<0.05). [a]p<0.05 vs. before surgery.

Levels of serum inflammatory factors measured through ELISA

According to Figure 1, the levels of IL-6, IL-8 and CXCL9, inflammatory factors, were decreased obviously at 1 and 6 month(s) after surgery (p<0.05), suggesting that the application of TIPS in the treatment of cirrhotic portal hypertension clearly inhibits the subsequent production of inflammatory factors in patients.

Results of physique examination

The body weight was evidently greater at both1 and 6 month(s) after surgery than that before surgery (p<0.05), the body fat at 1 and 6 month(s) after surgery was returned to that before surgery, and the dry weight was raised at both 1 and 6 month(s) after surgery compared with that before surgery (p<0.05) (Table 5).

Portal venous pressure, diameter and blood hemorheological index

As shown in Table 6, portal venous pressure and internal diameter were substantially lower after surgery than those before surgery, with statistically significant differences (p<0.05), while the velocity was increased significantly (p<0.05).

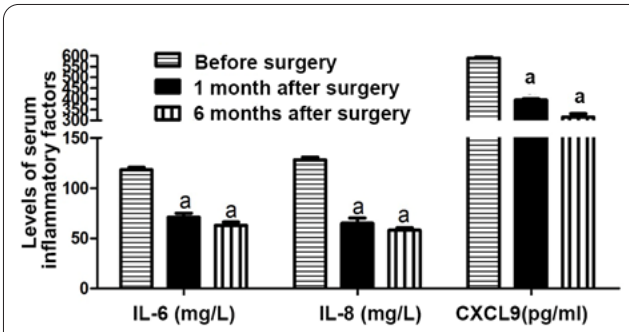

Figure 1. Levels of serum inflammatory factors. At 1 and 6 month(s) after surgery, the levels of serum inflammatory factors IL-6, IL-8 and CXCL9 decline markedly (p<0.05). ap<0.05 vs. before surgery.

Discussion

TIPS has been used for the treatment of complications of portal hypertension for over 30 years and has been established in thousands of patients with liver disease (18). In 2005, the American Association for the Study of Liver Diseases (AASLD) published the practical guidelines for the use of TIPS in the management of portal hypertension (19). In addition, recommendations on its use are further discussed in the practical guidelines for the prevention and management of variceal bleeding. Since then, technological progress and new research on TIPS have rapid development (20). This study aims to investigate the clinical efficacy of TIPS in the treatment of cirrhotic portal hypertension and the influencing factors. The results showed that the total response rate of clinical efficacy was 99% and 98% at 1 and 6 month(s) after surgery, respectively, and exhibited no statistically significant difference, indicating that the clinical efficacy of patients treated with TIPS is lasting. Such complications as neck hematoma, confusion, dizziness, drowsiness, mild hepatic coma, stool abnormity and shunt thrombosis may occur within a few days or months after surgery. Moreover, arrhythmia will occur if the distal end of the guidewire is removed from the right atrium, which is self-limited. The above-mentioned complications can be controlled through subsequent therapy (21). After embolization, only 8 cases of complications were observed at 1 month after surgery, and only

4 cases at 6 months after surgery, showing no statistically significant difference between the two groups. Besides, there were fewer adverse reactions and postoperative complications. In addition, the comparison of patients' satisfaction between the two groups revealed that there was no statistically significant difference in patients' satisfaction between 1 month after surgery and 6 months after surgery (97% vs. 94%). It suggests that postoperative nursing plays an evident role in the outcome and development of the disease and is capable of enhancing the efficacy of TIPS in the treatment of such a disease.

As the leading driving factor limiting patients' survival and complications, portal hypertension is able to result in liver inflammation and fibrosis, abnormal serum liver function, renal function and glucose metabolism indexes and abnormal angiogenesis. As to the treatment of portal hypertension, TIPS has become the best option. In the present study, liver function, renal function and glucose metabolism indexes were detected, and the results showed that the levels of AST, ALT, Cr, BUN and insulin were remarkably lowered at 1 and 6 month(s) after surgery, while the level of GLU significantly rose, indicating that the application of TIPS in the treatment of cirrhotic portal hypertension obviously improves the liver function, renal function and sugar metabolism of patients. A study manifested that inflammatory chemokines are abnormally increased in the case of cirrhotic portal hypertension, especially CXCL9 that is raised in liver diseases (22), which is functionally associated with liver injury, inflammation and complications. The over-activation of neutrophils and endothelial cells and the adhesion of neutrophils to the inflammatory endothelium are further promoted, thus resulting in the extravasation of neutrophils into important organs to synthesize inflammatory cytokines like IL-8 (23). A study pointed out that the level of CXCL9 is relatively high in patients with alcoholic cirrhosis, especially in the portal vein, andTIPS applied in patients with portal hypertension increases the effective blood volume and improves renal perfusion (24). CXCL9 level is strongly related to renal function parameters. Ascites and renal function are improved in patients treated with TIPS, which is correlated with a decreased level of CXCL9 in the portal vein. Furthermore, the level of CXCL9 in venous blood accurately reflects liver function (22,25). In this study, it was found that the levels of inflammatory factors IL-6, IL-8 and CXCL9 were reduced significantly at 1 and 6 month(s) after surgery, suggesting that the subsequent production of inflammatory factors in patients is notably repressed, and the liver and renal functions are overtly improved after treating cirrhotic portal hypertension with TIPS. This suggests that liver function, renal function and glucose metabolism indicators and the levels of inflammatory factors are largely correlated with clinical efficacy, which can significantly affect the prognosis of patients. Moreover, the body weight and dry weight were evidently higher at 1 and 6 month(s) after surgery than those before surgery, and the physical condition of the patient had recovered, which is similar to the findings of the above studies. Research has discovered that the portal venous flow of patients with cirrhotic portal hypertension undergoing TIPS is converted to hepatic venous flow with increased rate and volume, and esophageal venous bleeding is stopped (26). It was observed in this study that the postoperative portal venous pressure and internal diameter were markedly lower than those before surgery, and the flow rate was obviously increased, which is in line with the findings of previous studies. The above studies demonstrate that TIPS has better clinical efficacy in the treatment of cirrhotic portal hypertension, with fewer complications, and the efficacy is clearly affected by liver function, renal function, glucose metabolism, postoperative nursing and inflammatory factor levels. Subsequently, the efficacy can be verified through more cases or patients from different countries from multiple levels and perspectives to provide important theoretical and experimental bases for relevant subsequent research.

In conclusion, TIPS applied in the treatment of cirrhotic portal hypertension is effective, with distinctly improved physical condition and liver and renal functions of patients, reduced serum inflammatory factor levels and postoperative complications and normal postoperative portal venous hemorheological index. This study provides a basis for the treatment of patients with cirrhotic portal hypertension and new ideas for subsequent in-depth research.

Acknowledgments
Not applicable.

Funding
No funding was received

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Authors' contributions
ZLwrote the manuscript. ZL and LL collected and analyzed general data of patients. JLL and LC performed ELISA. JYL and JH were responsible for statistical analysis. All authors read and approved the final manuscript.

Ethics approval and consent to participate
The study was approved by the ethics committee of the 980 Hospital of PLA logistic forceand written informed consents were signed by the patients and/or guardians.

Consent for publication
Not applicable.

Interest conflict
The authors declare that they have no conflict of interest.

References

1. Lee UE, Friedman SL. Mechanisms of hepatic fibrogenesis. Best Pract Res Clin Gastroenterol. 2011 Apr;25(2):195-206. doi: 10.1016/j.bpg.2011.02.005. PMID: 21497738; PMCID: PMC3079877.
2. Bosch J, García-Pagán JC. Complications of cirrhosis. I. Portal hypertension. J Hepatol 2000 Jan 1;32:141-156.
3. Mezawa S, Homma H, Ohta H, Masuko E, Doi T, Miyanishi K, Takada K, Kukitsu T, Sato T, Niitsu Y. Effect of transjugular intrahepatic portosystemic shunt formation on portal hypertensive gastropathy and gastric circulation. Am J Gastroenterol. 2001 Apr;96(4):1155-1159. doi: 10.1111/j.1572-0241.2001.03694.x. PMID: 11316163.
4. Blokzijl H, de Knegt RJ. Long-term effect of treatment of acute Budd-Chiari syndrome with a transjugular intrahepatic portosyte-

mic shunt. Hepatology. 2002 Jun;35(6):1551-1552. doi: 10.1053/jhep.2002.33199. PMID: 12029648.
5. Boyer TD, Haskal ZJ. The role of transjugular intrahepatic portosystemic shunt in the management of portal hypertension. Hepatology. 2005 Feb;41(2):386-400.
6. Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W; Practice Guidelines Committee of the American Association for the Study of Liver Diseases; Practice Parameters Committee of the American College of Gastroenterology. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Hepatology. 2007 Sep;46(3):922-938. doi: 10.1002/hep.21907. Erratum in: Hepatology. 2007 Dec;46(6):2052. PMID: 17879356.
7. Toomey PG, Ross SB, Golkar FC, Hernandez JM, Clark WC, Luberice K, Alsina AE, Rosemurgy AS. Outcomes after transjugular intrahepatic portosystemic stent shunt: a "bridge" to nowhere. Am J Surg. 2013 Apr;205(4):441-446. doi: 10.1016/j.amjsurg.2012.06.005. Epub 2013 Jan 30. PMID: 23375760.
8. García-Pagán JC, Caca K, Bureau C, Laleman W, Appenrodt B, Luca A, Abraldes JG, Nevens F, Vinel JP, Mössner J, Bosch J; Early TIPS (Transjugular Intrahepatic Portosystemic Shunt) Cooperative Study Group. Early use of TIPS in patients with cirrhosis and variceal bleeding. N Engl J Med. 2010 Jun 24;362(25):2370-2379. doi: 10.1056/NEJMoa0910102. PMID: 20573925.
9. Blei AT. Portal hypertension and its complications. Curr Opin Gastroenterol. 2007 May;23(3):275-282. doi: 10.1097/MOG.0b013e3280b0841f. PMID: 17414843.
10. Manousou P, Kolios G, Drygiannakis I, Koulentaki M, Pyrovolaki K, Voumvouraki A, Notas G, Bourikas L, Papadaki HA, Kouroumalis E. CXCR3 axis in patients with primary biliary cirrhosis: a possible novel mechanism of the effect of ursodeoxycholic acid. Clin Exp Immunol. 2013 Apr;172(1):9-15. doi: 10.1111/cei.12032. PMID: 23480180; PMCID: PMC3719926.
11. Larrubia JR, Benito-Martínez S, Calvino M, Sanz-de-Villalobos E, Parra-Cid T. Role of chemokines and their receptors in viral persistence and liver damage during chronic hepatitis C virus infection. World J Gastroenterol. 2008 Dec 21;14(47):7149-7159. doi: 10.3748/wjg.14.7149. PMID: 19084927; PMCID: PMC2776871.
12. Tacke F, Zimmermann HW, Berres ML, Trautwein C, Wasmuth HE. Serum chemokine receptor CXCR3 ligands are associated with progression, organ dysfunction and complications of chronic liver diseases. Liver Int. 2011 Jul;31(6):840-849. doi: 10.1111/j.1478-3231.2011.02504.x. Epub 2011 Mar 10. PMID: 21645215.
13. Hintermann E, Bayer M, Pfeilschifter JM, Luster AD, Christen U. CXCL10 promotes liver fibrosis by prevention of NK cell mediated hepatic stellate cell inactivation. J Autoimmun. 2010 Dec;35(4):424-435. doi: 10.1016/j.jaut.2010.09.003. Epub 2010 Oct 6. PMID: 20932719; PMCID: PMC3855675.
14. Harvey CE, Post JJ, Palladinetti P, Freeman AJ, Ffrench RA, Kumar RK, Marinos G, Lloyd AR. Expression of the chemokine IP-10 (CXCL10) by hepatocytes in chronic hepatitis C virus infection correlates with histological severity and lobular inflammation. J Leukoc Biol. 2003 Sep;74(3):360-369. doi: 10.1189/jlb.0303093. PMID: 12949239.
15. Wasmuth HE, Lammert F, Zaldivar MM, Weiskirchen R, Hellerbrand C, Scholten D, Berres ML, Zimmermann H, Streetz KL, Tacke F, Hillebrandt S, Schmitz P, Keppeler H, Berg T, Dahl E, Gassler N, Friedman SL, Trautwein C. Antifibrotic effects of CXCL9 and its receptor CXCR3 in livers of mice and humans. Gastroenterology. 2009 Jul;137(1):309-319, 319.e1-3. doi: 10.1053/j.gastro.2009.03.053. Epub 2009 Apr 1. PMID: 19344719; PMCID: PMC2892869.
16. Tsukamoto T, Chanthaphavong RS, Pape HC. Current theories on the pathophysiology of multiple organ failure after trauma. Injury. 2010 Jan;41(1):21-26. doi: 10.1016/j.injury.2009.07.010. PMID: 19729158.
17. Zeremski M, Petrovic LM, Chiriboga L, Brown QB, Yee HT, Kinkhabwala M, Jacobson IM, Dimova R, Markatou M, Talal AH. Intrahepatic levels of CXCR3-associated chemokines correlate with liver inflammation and fibrosis in chronic hepatitis C. Hepatology. 2008 Nov;48(5):1440-1450. doi: 10.1002/hep.22500. PMID: 18798334; PMCID: PMC2579317.
18. Shiffman ML, Jeffers L, Hoofnagle JH, Tralka TS. The role of transjugular intrahepatic portosystemic shunt for treatment of portal hypertension and its complications: a conference sponsored by the National Digestive Diseases Advisory Board. Hepatology. 1995 Nov;22(5):1591-1597. PMID: 7590680.
19. Qi X, Han G, Yin Z, He C, Wang J, Guo W, Niu J, Zhang W, Bai M, Fan D. Transjugular intrahepatic portosystemic shunt for portal cavernoma with symptomatic portal hypertension in non-cirrhotic patients. Dig Dis Sci. 2012 Apr;57(4):1072-1082. doi: 10.1007/s10620-011-1975-5. Epub 2011 Dec 7. PMID: 22147244.
20. Xu XY, Li L. [Therapeutic and prevention strategies of gastroesophageal varices and variceal hemorrhage in cirrhosis]. Zhonghua Gan Zang Bing Za Zhi. 2009 Apr;17(4):252-253. Chinese. PMID: 19403019.
21. Pomier-Layrargues G, Bouchard L, Lafortune M, Bissonnette J, Guérette D, Perreault P. The transjugular intrahepatic portosystemic shunt in the treatment of portal hypertension: current status. Int J Hepatol. 2012;2012:167868. doi: 10.1155/2012/167868. Epub 2012 Jul 19. PMID: 22888442; PMCID: PMC3408669.
22. Berres ML, Asmacher S, Lehmann J, Jansen C, Görtzen J, Klein S, Meyer C, Strunk HM, Fimmers R, Tacke F, Strassburg CP, Trautwein C, Sauerbruch T, Wasmuth HE, Trebicka J. CXCL9 is a prognostic marker in patients with liver cirrhosis receiving transjugular intrahepatic portosystemic shunt. J Hepatol. 2015 Feb;62(2):332-339. doi: 10.1016/j.jhep.2014.09.032. Epub 2014 Oct 17. PMID: 25457205.
23. Bissonnette J, Garcia-Pagán JC, Albillos A, Turon F, Ferreira C, Tellez L, Nault JC, Carbonell N, Cervoni JP, Abdel Rehim M, Sibert A, Bouchard L, Perreault P, Trebicka J, Trottier-Tellier F, Rautou PE, Valla DC, Plessier A. Role of the transjugular intrahepatic portosystemic shunt in the management of severe complications of portal hypertension in idiopathic noncirrhotic portal hypertension. Hepatology. 2016 Jul;64(1):224-231. doi: 10.1002/hep.28547. Epub 2016 May 13. PMID: 26990687.
24. Wong F. Recent advances in our understanding of hepatorenal syndrome. Nat Rev Gastroenterol Hepatol. 2012 May 22;9(7):382-391. doi: 10.1038/nrgastro.2012.96. PMID: 22614754.
25. Xia R, Lin L, Yu S, Zhang J, Zheng L, Zhou L, Lin J. A systematic analysis of molecular mechanisms in non-metastatic renal cancer delineates affected regulatory pathways and genes in tumor growth. Cell Mol Biol (Noisy-le-grand). 2022 Feb 4;67(5):427-438. doi: 10.14715/cmb/2021.67.5.55. PMID: 35818225.
26. Kim HK, Kim YJ, Chung WJ, Kim SS, Shim JJ, Choi MS, Kim DY, Jun DW, Um SH, Park SJ, Woo HY, Jung YK, Baik SK, Kim MY, Park SY, Lee JM, Kim YS. Clinical outcomes of transjugular intrahepatic portosystemic shunt for portal hypertension: Korean multicenter real-practice data. Clin Mol Hepatol. 2014 Mar;20(1):18-27. doi: 10.3350/cmh.2014.20.1.18. Epub 2014 Mar 26. PMID: 24757655; PMCID: PMC3992326.