

Theses of Ph.D. dissertation

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**TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT IN  
THE TREATMENT OF PORTAL HYPERTENSION.**

**Dr. Lázár István**

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Szent-Györgyi Albert Orvostudományi Egyetem

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## **Introduction**

The mortality of chronic liver diseases increased to more than twice in Hungary in the last couple of years. More than 8000 peoples die in every year due to the symptoms of portal hypertension<sup>1</sup> like variceal bleeding, hepatorenal syndrome or spontaneous bacterial peritonitis. Less life threatening but also severe sequels are refractory ascites and/or hydrothorax, hepatic encephalopathy and hepatopulmonary syndrome<sup>2</sup>. The decrease of the hepatocytes and the vascular failure of the liver induce a chain of deterioration regardless of the cause of the cirrhosis. The symptoms of the patients are independently divided between the vascular and parenchymal impairment of the liver. Insufficient hepatic function is exclusively treatable with liver transplantation meanwhile in the treatment of portal hypertension we have multiple alternatives,<sup>3</sup> like selective beta-blockers surgical portocaval shunt procedures and transjugular intrahepatic portosystemic shunt (TIPS).

TIPS was introduced in the nineties and up to now more than 130000 TIPS were performed all over the world<sup>4</sup>. This procedure extremely efficiently decreases portal pressure and bleeding varices can also be treated at the same time.

Procedural morbidity is lower compared to surgical shunts. TIPS is more efficient to prevent variceal bleeding compared to endoscopic methods<sup>5</sup> and to treat refractory ascites compared to diuretics combined with paracentesis<sup>6,7</sup>. TIPS presents a significant procedural challenge and needs technical skills and experiences, as well as good collaboration with internists and anesthesiologists and a well equipped angio suit. Since 1999 TIPS is successfully performed in Miskolc and the results are extensively published and presented both in abroad and Hungary<sup>8,9,10,11,12</sup>.

## **Purposes**

1. To figure out the place of TIPS in the treatment of patients with portal hypertension and to show its advantages compared to endoscopic and surgical methods.
2. To present the technical and clinical results of TIPS in large and consecutive patient cohort.
3. To describe the rare procedural complication like the dissection of the portal vein firstly published by us and other technical difficulties and complications of TIPS.
4. To present the results with rare indications like TIPS in children, TIPS in Budd-Chiari sy. or the treatment of occlusion of the portal vein. All these were firstly performed in Hungary.
5. To describe our technical inventions performed during TIPS revisions.

6. To remind on the radiation exposure of the patients and the staff during TIPS.
7. To present our unique Hungarian 4-year-experiences with stent-grafts for TIPS.

### **Patients and methods**

The first TIPS was performed in September 1999 at the Borsod County Teaching Hospital in Miskolc. Indications for TIPS were raised by gastroenterologists and transplant surgeons. 60% of our patients were admitted from outside of the recruitment area of the hospital. TIPS was performed in 114 patients. The gender of patients was: 66 male, 48 female (58 and 42 %). Age distribution of the patients: between 10-34 years - 7 patients, 36-44 years - 17 patients, 45-54 years - 44 patients, 55-64 years - 34 patients, >65 years – 12 patients.

Distribution of the patients according to the **Child-Pugh score**:

A: 24 patients (21%) B: 62 patients (54,4%) C: 28 patients (24,6%).

Child-Pugh classification is based on 5 parameters (serum total bilirubin, total protein, INR, the severity of ascites and hepatic encephalopathy) each of them rated 1-3 points. Scores are divided like Child-A 5-6 points Child-B 7-9 points and Child-C >10 points.

149 TIPS procedure (including revisions) were performed.

#### Indications of TIPS procedures:

Refractory ascites /hydrothorax	58 patients	36 %
Recurrent variceal bleeding	47 patients	29,2 %
Acute variceal bleeding	9 patients	5,6 %
Thrombosis of the portal vein	4 patients	2,5 %
Budd-Chiari syndrome	1 patients	0,6 %
TIPS revisions	42 procedures in 31 patients	26,1 %

Primary TIPS were performed according to the description of American and German interventionists<sup>15,31</sup>. Invasive pressure measurements were done in 72 patients TIPS (63,2 %). Systemic venous pressure was measured in the right atrium. Portal pressures (all in Hgmm) were determined in the splenic vein and the portosystemic pressure gradients were calculated. In more than 90% of the cases TIPS-200 (Rösch-Uchida) set produced by Cook, in less than 10% other sets (TJL-100 - Colapinto) were used. 25 patients underwent TIPS with Viatorr stent-grafts. Wallstents were deployed in 97 patients. Nitinol or other peripheral stents were implanted in 8 cases.

Patients were followed up every 3 months in the first year after TIPS, than every 6 months. They underwent clinical tests and Doppler ultrasonography. Total time of fluoroscopy was documented in 69 TIPS, meanwhile DAP (dose area product) datas were worked up in 48 procedures.

## **Results and practical use of the results**

### 1. TIPS compared to endoscopic and surgical methods in the treatment of portal hypertension

- Despite their proven results in abroad, TIPS was not recognized in Hungary until the end of nineties. Firstly, Péter M. presented cases with short description of the method<sup>32</sup> but wide recognition of the technique had to wait for our published results and the proof of clinical success in large patient cohort<sup>33</sup>. Due to our results TIPS became the second line therapy of patients with portal hypertension in northern Hungary.
- The majority of Hungarian patients undergo TIPS in our cath-lab. I assisted or trained interventionists to perform the procedure in other three centers.
- TIPS served as a bridge to successful liver transplantation in 5 of our patients. In other 4 patients TIPS made such an important clinical improvement that these patients did not need transplantation, and could be cancelled from waiting list.
- TIPS became the treatment of choice in patients with acute subcardial variceal bleeding or those who had recurrent variceal bleeding after more then 3 sclerotherapy. All the acutely treated patients improved clinically. This needs to be emphasized, as we lost 5 patients in the waiting list for TIPS!
- TIPS also became the method of choice in the treatment of patients with refractory ascites for 4-9 months despite maximal diuretic therapy. Our results are so convincing that 50,9% of TIPS patients were admitted with this indication.

### 2. The success rates of TIPS

- Intrahepatic punctation was successful in 97,4%. TIPS could be performed in 95,7. (The difference is coming from the cases when extrahepatic portal vein occlusion was recognized only after the punctation of the portal vein). These are the best Hungarian results and also fulfill north-American requirements.
- We achieved the demanded portosystemic pressure gradient in 94,7% of patients. The mean gradient decreased from 19,6 to 8,9 mmHg.
- Clinical success was achieved in 88,6% of patients.

- We added 4 new indications for TIPS in Hungary: Budd-Chiari syndrome, TIPS in a child, subacute portal vein thrombosis, TIPS in transplanted liver.

### 3. Complications of TIPS

- Our rate of serious complications is within the ranges of recommendation according to the Society of Cardiovascular and Interventional Radiology of North America<sup>33</sup> (1. table):

<b>Early complications</b>	SCVIR recommended (%)	Own results (%)
Intraperitoneal bleeding	7	4,4
Gallbladder puncture	2	1,7
Stent malposition	2	1,7
Haemobilia	2	0,8
Radiation skin injury	0,1	0
Infection	2	2,6
Hepatic artery injury	1-5	0,8
Haemolysis	10	-
Jugular hematoma	5	3,5
Contrast nephropathy	5	2,6
Worsened encephalopathy	20-30	17
Pulmonary edema	1	0
Procedural mortality	<1	1,7
<b>Late complications</b>		
Persisting ascites	10-30	10,5
Recurrent variceal bleeding	15-25	7
TIPS stenosis (with bare stents)	50 (in the first year)	23,7

**1. table:** TIPS complications as recommended and our results

- We firstly ever published a procedural complication in the literature. We observed the dissection of the portal vein in 1% in our practice and published three cases<sup>S7</sup>.

### 4. TIPS procedures firstly ever performed in Hungary

- The first child who underwent TIPS was a 10 years old boy with liver and renal failure of unknown etiology. He presented gastro-esophageal variceal bleedings and waited for transplantation. I performed TIPS for him in acute settings. At that time living

donor transplantation was not yet performed in Hungary, but TIPS successfully served as a bridge for transplantation. Beside the size of kid (he weighted 28 kg) technical difficulties came from the preazotemic state of the patient. We injected only 30 ml of iodinated contrast medium during the procedure. No more bleeding occurred until the transplantation of both the liver and the kidneys 5 months later.

- I performed TIPS for the first time in Hungary in patient with Budd-Chiari syndrome. The patient presented with severe vascular failure of the liver and waited for transplantation. As there was no patent hepatic vein I started the puncture from the intrahepatic portion of the inferior vena cava. The one year ultrasonographic control of the patient showed normal flow through the shunt. He has no symptoms at all and is not a transplant candidate anymore.
- The third newly performed procedure was a TIPS in a 41-year-old male with thrombosis of the portal vein due to protein C deficiency. He presented with refractory ascites. During the procedure we also had to perform the angioplasty of the recanalized spleno-mesenteric venous confluent in order to normalize the portosystemic pressure gradient. TIPS was technically successful but unfortunately the patient died 6 weeks later due to progressive parenchymal liver failure.

#### 5. My technical inventions performed during TIPS revisions

- To decrease the symptoms of worsened hepatic encephalopathy due to TIPS I used a non-published method of narrowing the shunt. In two cases a self-expandable stent was deployed through the non-covered portion of the previously implanted stent-graft. Distal portion of this narrowing stent was placed outside of the previous. The proximal part of the stent remained inside and finally showed an hour-glass shape. So, the stent was perpendicularly deployed and decreased the inflow of the TIPS and consequently increased the portosystemic pressure gradient.
- The other invention helped to recanalize an occluded shunt. For anatomic reasons there was no chance to get into the lumen of the TIPS from the proximal part. Finally I made a puncture with a liver biopsy needle through the sidewall of the TIPS and got into the portal vein. The new TIPS performed through the meshes of the previous stent kept normal flow for two years. The patient is free of symptoms and is not a candidate for liver transplantation anymore.

## 6. The radiation exposure of the patients and the staff during TIPS

- The mean DAP was 6181 (546-17999) Gy/cm<sup>2</sup>, the mean skin dose was found to be 583 (66-2151) mGy. Total fluoroscopy mean time was 24,5 minutes (6,8-83 min.). According to these data TIPS is one of the procedures with the highest radiation exposure for the patients. However, we did not experience skin erythema or other skin reaction.
- We regularly use all of the available radiation protection devices and none of the film dosimetric studies of the staff showed significant elevation of irradiation. My own body exposure data from the last years are:  
2002: 0,23 mSv 2003: 0,14 mSv 2004: 0,18 mSv 2005: 0,25 mSv,  
2006: under noticeable (These data were accumulated during all of angiographic workload – more than 1000/year - not only TIPS.)

## 7. Experiences with stent-grafts for TIPS

- We used stent-grafts for TIPS in a uniquely large number of cases in Hungary, which is also in international comparison a significant number. The reason was to improve long-term results and to prevent or treat procedural complications. Since July 2002 TIPS was performed in 80 patients. 25 of them (31,25%) underwent TIPS or revision with PTFE-covered stent-graft.

Our indications for the use of stent-graft were:

1. Longer life expectancy according to liver function (Child-Pugh A,B)
  2. Younger age - 44,7 years (33-59) – mean age of our other patients 52,7 years
  3. Complicated procedure makes early shunt failure likely (i.e. biliary puncture)
  4. Budd-Chiari sy.
  5. Recurrent revisions
- Only two of the 25 implanted grafts failed. One patient developed portal thrombosis 5 months later so the lack of inflow was the cause of TIPS failure. The other patient developed hepatocellular carcinoma and subsequent portal vein thrombosis 4 months after TIPS. For this reason we did not try to recanalize the shunt.
  - The rate of encephalopathy which necessitated narrowing of the shunt was not higher (8%) than in TIPS cases with bare stents.
  - Revisions were indicated far less frequently than in TIPS with bare stents. They were necessary only in false positive follow up diagnostic results. (One early control when

ultrasound could not penetrate the grafts due to captured air bubbles. The other was due to a misinterpreted CT in an inexperienced institution.)

- Two stent-graft patients were transplanted since. Both of them developed progressive liver failure (primary biliary cirrhosis and persisting B-virus hepatitis). The transplantation was not complicated by the TIPS stent-graft in any of them<sup>34</sup>. Consequently, it seems to be clear that using stent-graft for proper indications can significantly decrease the expenses of health care system and increase life-chances of cirrhotic patients.

## Conclusions

### 1. The place of TIPS in the treatment of patients with portal hypertension.

- TIPS is proved to be the most effective method to decrease portal hypertension<sup>35,36</sup>. It is more invasive and more expensive than endoscopic methods, therefore only in case of clinical failure of the latter is indicated<sup>37,38</sup>.
- The advantage of TIPS is being more efficient to prevent recurrent variceal bleeding than endoscopic ligation or sclerotherapy or non-selective  $\beta$ -blockers like propranolol<sup>37,38</sup>. The likelihood of recurrent variceal bleeding is found to be 19% after TIPS while 47% with endoscopic treatment<sup>5</sup>. Recent improvements result in less than 30% recurrence rate but using stent-grafts for TIPS can improve the results even more, below 10%<sup>22-24</sup>. Nevertheless, TIPS with bare stent do not improve the survival of patients<sup>39</sup>. The preliminary results of the use of stent-grafts seem to strongly suggest that this is going to be changed.
- In the treatment of refractory ascites TIPS has 79% efficacy after 6 months, while repeated paracentesis only 24%<sup>40</sup>. TIPS procedural morbidity is so much lower than the morbidity of surgical shunts (i.e. Denver) that the latter are less and less practiced.

### 2. Technical results of TIPS

- TIPS procedure has lot of technical difficulties. For the expected results we have to (a) carefully select patients (b) carry out the procedure in a controlled and standardized way (c) to monitorize patients during TIPS and the next 6 hours.
- The interventionist who has carried out the TIPS procedure has to follow the clinical course of the patients as well. Technical and clinical success, as well as the rate of complications have to be continuously checked. Significant prolongation of hospital



stay, the need of intensive care, definitive failure of any organ or death in 30 day has to be concerned as major complication. They altogether must not exceed 5%.

Expected rates of success<sup>33</sup>:

<u>Technical success:</u> (Patent intrahepatic shunt)	<b>95%</b>
<u>Hemodynamical success:</u> (Expected decrease of the portosystemic pressure gradient)	<b>95%</b>
<u>Clinical success:</u> (Significant decrease of symptoms.)	<b>90%</b>

### 3. Intraoperative complications of TIPS

We have to face numerous difficulties during this challenging procedure<sup>41</sup>.

- During jugular vein puncture nerve injury, pneumothorax, neck hematoma, pseudaneurysm of the carotid arteries can occur. Most of them can be prevented with ultrasonographic guidance, placing the patient into Trendelenburg position and asking him to perform Valsalva maneuver.
- During catheterization of the hepatic vein arrhythmia (guidewire or introducer in the right atrium) can occur. Guidewire can buckle in the atrium and devices intended to push through can even perforate the heart.
- Left liver lobe or segment I. hypertrophy can raise anatomic difficulties. Hepatic veins run almost horizontal in cases of tense ascites as well. Left jugular vein approach and paracentesis can ease these situations.
- Localization of portal branch as a target of intrahepatic puncture can be made by iodinated contrast material or CO<sub>2</sub> injection into the wedged hepatic vein catheter. During this step of the procedure subcapsular haematoma or even severe liver laceration can occur. The bleeding site has to be promptly embolized and stent-graft deployment can also decrease the bleeding.
- The most critical moment of TIPS creation is intrahepatic puncture. We can observe extrahepatic puncture, biliary puncture, extrahepatic portal puncture or hepatic artery puncture. The most important is to recognize them and alert the anesthesiologist. At the same time we have different tools to deal with the complication (embolization, balloon tamponade, stent-graft deployment, blood transfusion). The most dangerous complication is the puncture of an extrahepatic portal branch because the next step is the dilatation of the punctured branch. If it is not tamponaded by the liver this carries

a real risk of bleeding to death. The extrahepatic puncture itself can be clinically silent if treated with stent-graft placement<sup>42</sup>.

- We published firstly ever in the literature the rare complication of portal vein dissection during TIPS<sup>S7</sup>. Our explanation is that portal pressure in our patients was measured 32-44 mmHg instead of the physiologic 10-12 mmHg and this can produce significant change in the wall of large veins, like portal vein. This extreme pressure makes the thin internal elastic membrane surrounded by smooth muscular fibers less compliant because of fibrosis. According to our experiences it may develop – similarly to the arteries – a dissection along this layer during puncture or more likely due to the direct perpendicular force applied on the guidewire at the end of the needle. Dissection can result in exactly the same consequences like in the arteries. We have, for instance, a well documented case of pseudoaneurysm formation.
- During stent placement migration or malposition can occur. It is very important to let the proximal part of the stent free for a subsequent catheterization because the need for TIPS revision is quite high later on. We have to keep in mind also an eventual liver transplantation. That is why the stent must not encroach on the lumen of inferior vena cava and must not reach the confluent of superior mesenteric vein and splenic vein in order not to interfere with a future clamping by transplantation. Using stent-grafts we have to make correct measurements not to obstruct the blood flow with the covered part of the graft in the main portal branch or in the inferior vena cava.
- Dilating a TIPS stent: overdilation should be avoided not to provoke hepatic encephalopathy. Wallstent has known ability to selfdilate over 24 hours. Using stent-grafts we don't have to count on late restenosis. There will not be anything to decrease the flow through an over dilated shunt.
- Variceal embolization is routinely part of TIPS in case of the treatment of acutely bleeding patients. Embolizing agents can be moved to pulmonary circulation through the varices<sup>41</sup>. When using acrilates, solidified glue may attach to the end of the delivery catheter and by pulling back the catheter, the glue can be detached and obstructs splenic vein or even the TIPS channel.

#### 4. TIPS procedures firstly ever performed in Hungary

- TIPS can be safely performed even in high-risk situations in the hand of experienced interventionist, who treats a reasonable number of patients yearly. The angio suit has to possess all the materials potentially needed and the operator has to check up the

results time to time for quality improvements. It is clearly demonstrated with the case of a 19-year-old girl who presented with Budd-Chiari syndrome a couple of years ago. She could not be transplanted soon after and 3 months later bled to death from her subcardial varices. 3 years later – as we possessed stent-graft and had more experiences – a successful TIPS was performed in the same clinical scenario. This fortunate patient is not even a transplant candidate anymore<sup>48</sup>.

#### 5. My technical inventions performed during TIPS revisions

I firstly described two technical points make TIPS revisions possible or more successful in difficult situations. Both of them have proved midterm results already.

- Inner PTFE covering of stent-grafts result in an extremely smooth surface. Thus, stents used for narrowing to reverse hepatic encephalopathy can easily migrate. Stent migration towards the heart is practically impossible with my method. Beside, there is a potential disadvantage because theoretically the blood which is flowing through the mesh of the stent may hemolyse. Erythrocytes already damaged by the impaired liver function can be crushed at the metal mesh of the stent and finally eliminated by the spleen<sup>49</sup>. This type of hemolysis is not severe and self-limited in most of the cases.
- My second invention for revision of a thrombosed TIPS has obviously alternatives. The parallel TIPS between the left hepatic vein and the left portal branch is a known tool as a supplement for the previously performed TIPS if the function of the former was not sufficient to decrease the portosystemic pressure gradient<sup>50</sup>. We also had such a case performed to replace the right sided TIPS which had been occluded several times due to unfavorable anatomy. Despite this successful case – having known the technical difficulties of that – I am convinced that it is reasonable to try firstly my new method to regain the patency of the thrombosed TIPS. Procedural risk seems to be lower and at the same time we can reserve the chance for the patient to undergo an eventual left sided TIPS if it was going to be inevitable.

#### 6. The radiation exposure of the patients and the staff during TIPS

- There are few datas in the literature concerning radiation doses of patients and staff during TIPS. Our measures for patients proved no higher entry skin dose than 3 Gy (limit of depilation). The results of an American study covering 135 TIPS procedure found 38,7 min. average fluoroscopy time and 2039 mGy cumulative skin dose<sup>51</sup>. Comparing our result (24,5 min. fluoroscopy and 583 mGy) with these there is no reason to be unsatisfied.

## 7. Experiences with stent-grafts for TIPS

- TIPS performed with bare stents during the first 10 years after the introduction of the procedure resulted in disappointment with the long-term results<sup>7,29,35</sup>. Reintervention rate and additional cost with that was very high<sup>44</sup>. The average one-year patency without revision was found to be no more than 69%<sup>53</sup>. Stent-grafts raised that number up to 85-90% and the secondary one-year patency from 85% up to 98%<sup>22-24, 54</sup>. Only the bile impermeable ePTFE-covered grafts achieved such a favorable result. Others, like PET-covered grafts developed not specifically for TIPS did not improve the patency rate<sup>54</sup>.
- Control ultrasonography after TIPS with stent-graft is indicated only in case of recurrent clinical signs or no more frequently than every 6 months according to my results.
- The rate of worsened hepatic encephalopathy was not higher with stent-grafts than with bare stents. It can be explained by the fact that grafts are dilated to a smaller diameter having known that they are significantly less prone to in-stent restenosis.
- Our 90% primary one-year patency rate with grafts suggests that stent-grafts significantly decrease the reintervention rate and the cost of the treatment. At the same time long term success makes gastroenterologist and transplant surgeons more confident with this method.

**We can conclude**, that TIPS is safe method to treat portal hypertension with lower morbidity and higher efficacy than surgical or endoscopic methods. Proper indications, experience-based patient choice, technical developments like stent-grafts improved long-term patency and widened the acceptance of TIPS. We have to prove the economical efficacy and make the method better known and available all over in Hungary. These are the key points to better treat hundreds of patients with impaired liver function and make their life expectancy longer.

### **Literature**

1. Altörjay I. A portális hypertensio patogenezise és a gyógyszeres befolyásolás lehetőségei. MOTESZ Magazin 2004. 17. szám
2. McGuire B, Bloomer J. A máj-cirrhosis szövödményei. Orvostovábbképző Szemle 2000.VII/3. p81.
3. Papp J, Kupcsulik P. A portális hypertensio és kezelése. 1995. Jegyzet. Bp. Pharma Press Kiadó
4. Haskal Z. Lessons learned. Special session. Annual meeting and postgraduate Course of the Cardiovascular and Interventional Radiological Society of Europe. Nice, 2005.

5. Papatheodoridis GV, Goulis J, Leandro G, Patch D, Burroughs AK. Transjugular intrahepatic portosystemic shunt compared with endoscopic treatment for prevention of variceal rebleeding: a meta-analysis. *Hepatology*. 1999;30:612-622
6. Lebrech D, Giuily N, Hadengue A, et al. Transjugular intrahepatic portosystemic shunts: comparison with paracentesis in patients with cirrhosis and refractory ascites: a randomized trial. *J Hepatol* 1996;25:135-144
7. Spencer EB, Cohen DT, Darcy MD. Safety and efficacy of transjugular intrahepatic portosystemic shunt creation for the treatment of hepatic hydrothorax. *J Vasc Interv Radiol* 2002;Apr;13(4):385-90
8. Hanafee W, Weiner M. Transjugular percutaneous cholangiography. *Radiology* 1967;88:35-39
9. Rösch J, Hanafee WN, Snow H. Transjugular portal venography and radiologic portacaval shunt: an experimental study. *Radiology* 1969;92:1112-1114
10. Dotter CT. Cardiac catheterization and angiographic techniques of the future. *Csl Radiol* 1965;19:217-236
11. Rösch J, Hanafee W, Snow H, et al. Transjugular intrahepatic portacaval shunt. *Am J Surg* 1971;121:588-592
12. Gutierrez OH, Burgener FA. Production of nonsurgical portosystemic venous shunts in dogs by transjugular approach. *Radiology* 1979;130:507-509
13. Colapinto RF, Stronell RD, Gildiner M, et al. Formation of intrahepatic portosystemic shunts using a balloon dilation catheter: preliminary clinical experience. *AJR* 1983;140:709-714
14. Palmaz JC, Garcia F, Sibbitt RR, et al. Expandable intra-hepatic portacaval shunt stents in dogs with chronic portal hypertension. *AJR* 1986;147:1251-1254
15. Richter G, Palmaz J, Nöldge G, et al. The transjugular intrahepatic portosystemic stent-shunt (TIPS): a new non-operative, transjugular percutaneous procedure. *Radiologe* 1989;29:406-11
16. Lind CD, Malish TW, Chong WK, et al. Incidence of shunt occlusion or stenosis following transjugular intrahepatic portosystemic shunt placement. *Gastroenterology* 1994;106:1277-83
17. Luca A, D'Amico G, La Galla R, Midiri M, Morabito A, Pagliaro L. TIPS for prevention of recurrent bleeding in patients with cirrhosis: meta-analysis of randomized clinical trials. *Radiology* 1999;212:411-21
18. Sanyal AJ, Contos MJ, Yager D, Zhu YN, Willey A, Graham MF. Development of pseudointima and stenosis after transjugular intrahepatic portosystemic shunts: characterization of cell phenotype and function. *Hepatology* 1998;28:22-32
19. LaBerge JM, Ferrell LD, Ring EJ, Gordon RL. Histopathologic study of stenotic and occluded transjugular intrahepatic portosystemic shunts. *J Vasc Intervent Radiol* 1993;4:779-786
20. Nishimine K, Saxon R, Kichikawa K, et al. Improved TIPS patency using PTFE covered stent-grfts: experimental results in swine. *Radiology* 1995;196:341-347

21. Saxon RR, Timmermans HA, Uchida BT, Petersen BD, Benner KG, Rabkin J, Keller FS. Stent-grafts for revision of TIPS stenoses and occlusions: a clinical pilot study. *J Vasc Intervent Radiol* 1997; 8:539-48
22. Hausegger KA, Karnel F, Georgieva B, et al. Transjugular intrahepatic portosystemic shunt creation with the Viatorr expanded polytetrafluoroethylene-covered stent-graft. *J Vasc Intervent Radiol* 2004;15:239-248
23. Rossi P, Salvatori FM, Fanelli F, et al. Polytetrafluoroethylene-covered nitinol stent-graft for transjugular intrahepatic portosystemic shunt creation: 3-year experience. *Radiology* 2004;231:820-830
24. Maleux G, Nevens F, Wilmer A, et al. Early and long-term clinical and radiological follow-up results of expanded-polytetrafluoroethylene-covered stent-grafts for transjugular intrahepatic portosystemic shunt procedures. *Eur Radiol* 2004;14:1842-50
25. Rees CR, Niblett RL, Lee SP, Diamond NG, Cippin JS. Use of carbon dioxide as a contrast medium for transjugular intrahepatic portosystemic shunt procedures. *J Vasc Intervent Radiol* 1994;5:383-386
26. Uflacker R, Reichert P, D'Albuquerque LC, Silva AO. Liver anatomy applied to the placement of transjugular intrahepatic portosystemic shunts. *Radiology* 1994;191:705-712
27. Wilson MW, Gordon RL, LaBerge JM, et al. Liver transplantation complicated by malpositioned transjugular intrahepatic portosystemic shunts. *J Vasc Intervent Radiol* 1995;6:695-699
28. Garcia-Tsao G, Groszmann RJ, Fisher RL, Conn HO, Atterbury CE, Glickman M. Portal pressure, presence of gastroesophageal varices and variceal bleeding. *Hepatology* 1985;5:419-424
29. Sahagun G, Benner KG, Saxon R, et al. Outcome of 100 patients after transjugular intrahepatic portosystemic shunt for variceal hemorrhage. *Am J Gastroenterol* 1997;92:1444-1452
30. Feldstein VA, Patel MD, LaBerge JM. Transjugular intrahepatic portosystemic shunts: accuracy of Doppler US in determination of patency and detection of stenoses. *Radiology* 1996;201:141-7
31. Haskal ZJ, Rees CR, Ring EJ, Saxon R, Sacks D. Reporting standards for transjugular intrahepatic portosystemic shunts. Technology Assessment Committee of the SCVIR. *J Vasc Intervent Radiol* 1997;8:289-297
32. Péter M. Transjugularis intrahepaticus portosystémás shunt (TIPS). *Magyar Radiol.* 1995;3:79-83
33. Haskal ZJ, Martin L, Cardella JF, et al. Quality improvement guidelines for transjugular intrahepatic portosystemic shunts. SCVIR Standards of Practice Committee. *J Vasc Intervent Radiol* 2001;12:131-136
34. Maleux G, Pirenne J, Vaninbrouckx J, Aerts R, Nevens F. Are TIPS stent-grafts a contraindication for future liver transplantation? *Cardiovasc Intervent Radiol* 2004;27:140-142
35. Rossle M, Haag K, Oches A, et al. The transjugular intrahepatic portosystemic stent-shunt procedure for variceal bleeding. *N Engl J Med* 1994;330:165-171

36. Coldwell DM, Ring EJ, Rees CR, et al. Multicenter investigation of the role of transjugular intrahepatic portosystemic shunt in management of portal hypertension. *Radiology* 1995;196:335-340
37. Rossle M, Deibert P, Haag K, et al. TIPS vs.sclerotherapy and B-blockade: Preliminary results of a randomized study in patients with recurrent variceal hemorrhage. *Lancet* 1997;349:1043-1049
38. Pomier-Layrargues G, Villeneuve JP, Deschenes M, et al. Transjugular intrahepatic portosystemic shunt (TIPS) versus endoscopic variceal ligation in the prevention of variceal rebleeding inpatients with cirrhosis: a randomised trial. *Gut* 2001;48:390-6
39. Albillos A, Banares R, Gonzalez M, Catalina MV, Molinero LM. A meta-analysis of transjugular intrahepatic portosystemic shunt versus paracentesis for refractory ascites. *J Hepatol* 2005;43:990-6
40. Rössle M, Ochs A, Gülberg V, et al. A comparison of paracentesis and transjugular intrahepatic portosystemic shunting in patients with ascites. *N Engl J Med* 2000;342:1701-1707
41. Freedman AM, Sanyal AJ. Complications of transjugular intrahepatic portosystemic shunts. *Sem Interv Radiol* 1994;11:161-177
42. Krajina A, Hulek P, Ferko A, Nozicka J. Extrahepatic portal venous laceration in TIPS treated with stent graft placement. *Hepato-Gastroenterol* 1997;44:667-670
43. Lehr S, Haskal ZJ, Furth EE, Gannon F. Histopathologic analysis of the biologic response to transjugular intrahepatic portosystemic shunts (TIPS) and proposal of a pathogenetic model. *J Vasc Intervent Radiol* 1997;8:180
44. Saxon RS, Ross PL, Mendel-Hartvig J, et al. Transjugular intrahepatic portosystemic shunt patency and the importance of stenosis location in the development of recurrent symptoms. *Radiology* 1998;207:683-693
45. Ferral H, Banks B, Wholey M, et al. Techniques for transjugular intrahepatic portosystemic shunt revision. *Am J Roentgenol* 1998;171:1041-1047
46. Nazarian G, Ferral H, Bjarnason H, et al. Effect of transjugular intrahepatic portosystemic shunt on quality of life. *Am J Roentgenol* 1996;167:963-969
47. Zuckerman D, Darcy M, Bocchini T, Hildebolt C. Encephalopathy after transjugular intrahepatic portosystemic shunting : analysis of incidence and potential risk factors. *Am J Roentgenol* 1997;169:1727-1731
48. Peltzer MY, Ring EJ, LaBerge JM, Haskal ZJ, Radosevich PM, Gordon RL. Treatment of Budd-Chiari syndrome with a transjugular intrahepatic portosystemic shunt. *J Vasc Intervent Radiol* 1993;4:263-267
49. Sanyal A, Freedman A, Purdum P, Shiffman M, Luketic V. The hematologic consequences of transjugular intrahepatic portosystemic shunts. *Hepatology* 1996;23:32-39
50. Haskal ZJ, Ring EJ, LaBerge JM, et al. Role of parallel transjugular intrahepatic portosystemic shunts in patients with persistent portal hypertension. *Radiology* 1992;185:813-817

51. Balter S, Schueler BA, Miller DL, et al. Radiation doses in interventional radiology procedures: the RAD-IR Study. Part III: Dosimetric performance of the interventional fluoroscopy units. *J Vasc Intervent Radiol* 2004;15:919-926
52. Hidajat N, Wust P, Kreuschner M, Felix R, Schroder RJ. Radiation risks for the radiologist performing transjugular intrahepatic portosystemic shunt (TIPS). *Br J Radiol* 2006;79:483-486
53. Haskal ZJ, Pentecost MJ, Soulen MC, Shlansky-Goldberg RD, Baum RA, Cope C. Transjugular intrahepatic portosystemic shunt stenosis and revision: early and midterm results. *Am J Roentgenol* 1994;163:439-444
54. Haskal ZJ. Improved patency of transjugular intrahepatic portosystemic shunts in humans: creation and revision with PTFE stent-grafts. *Radiology* 1999;213:759-766
55. Keussen I, Berqqvist L, Rissler P, Cwikel W. Acute effects of liver vein occlusion by stent-graft placed in transjugular intrahepatic portosystemic shunt channel: an experimental study. *Cardiovasc Intervent Radiol* 2006;29:120-123
56. Salerno F, Merli M, Cazzaniga M, et al. MELD score is better than Child-Pugh score in predicting 3-month survival of patients undergoing transjugular intrahepatic portosystemic shunt. *J Hepatol* 2002;36:494-500
57. Angermayr B, Cejna M, Karnel F, et al. Child-Pugh versus MELD score in predicting survival in patients undergoing transjugular intrahepatic portosystemic shunt. *Gut* 2003;52:879-85
58. Fernandez-Aquilar JL, Bondia Navarro JA, Santoyo Santoyo J, et al. Calibrated portacaval H-graft shunt in variceal hemorrhage. Long-term results. *Hepatogastroenterology* 2003;50:2000-4
59. Nazarian GK, Ferral H, Bjarnason H, Castaneda-Zuniga WR, Rank JM, Bernadas CA, Hunter DW. Effect of transjugular intrahepatic portosystemic shunt on quality of life. *Am J Roentgenol* 1996;167:963-969

## **Our publications.**

1. **Lázár I**, Soós L, Gombos J, Akoto A, Gyarmati J. Imaging features of Gorham-disease. *Osteológiai Közlemények* 1997. V. évf., 4. szám 202-205
2. **Lázár I**. La biopsie hépatique par voie transjugulaire a l'aide du système de Quick-Core: expérience a propos des dix sept premiers patients. Soutenu devant la faculté de médecine de Marseille, le 25 Avril 1998. (Szakvizsga utáni egyetemi *továbbképző diploma dolgozat* (franciául AFSA) egy éves tanulmányok után.
3. **Lázár I**, Bartoli J-M, Moulin G, Baudet J-J. Transjugular intrahepatic portosystemic shunt (TIPS). Indications, contraindications, results. *Lege Artis Medicinae* 8(10):680-687,1998
4. **Lázár I**, Petit P, Moulin G, Bartoli J-M. Transjugular intrahepatic portosystemic shunt and restenosis management in a child with alfa1-antitrypsin deficiency. *Year Book of Pediatric Radiology* Vol.11. 59-63.



5. **Lázár I**, Perreult P, Otal P.  
Embolotherapy of a patient with upper gastrointestinal bleeding.  
*Magyar Radiológia* 1999.73. évf. 1. szám 18-21.
6. **Lázár I**, Charifi A.  
Localization of small pancreatic insulinoma with selective intra-arterial stimulation of  $\beta$ -cells with calcium.  
*Magyar Radiológia* 1999.73. évf. 3. szám 67-72.
7. Petit P, **Lázár I**, Chagnaud C, Moulin G, Castellani P, Bartoli J-M.  
Iatrogenic dissection of the portal vein during TIPS procedure.  
*European Radiology* 10,930-934 (2000)
8. **Lázár I**, Heiner B, Varga E, Gyarmati J.  
Primary stenting: Experiences with 21 patients.  
*Érbetegségek* VII. évf. 2. szám 43-48.
9. **Lázár I**, Pető J, Kristóf T.  
Experiences with transjugular intrahepatic portosystemic shunt (TIPS).  
*Magyar Sebészet* 55, 9-15, 2002
10. Juhász Gy, Mátyás L, **Lázár I**.  
Endovascular treatment of an abdominal aortic aneurysm ruptured to the retroperitoneal cavity.  
*Érbetegségek*, X. évfolyam 3. szám, 2003/3.
11. Juhász Gy, Mátyás L., Simon G, **Lázár I**.  
Endovascular exclusion of aortic aneurysms perforated to the gastrointestinal tract.  
*Érbetegségek*, XI. évf., 1. szám 3-7.
12. Eröss B, Székely Gy, Siket F, **Lázár I**.  
Treatment of a life-threatening esophageal varix rupture resistant to endoscopic sclerotherapy.  
*LAM* 2005;15(11):834-838

### Our in-extenso abstracts

1. **Lázár I**, Chagnaud C, Bartoli J-M, Moulin G, Chamati S.  
Iatrogenic dissection of the portal vein during TIPS.  
CIRSE 1998, Venice *CVIR* 1998 suppl. 1 (21) p-169
2. **Lázár I**, Charifi A-B.  
Selective intraarterial calcium stimulation in the localization of pancreatic insulinoma.  
CIRSE 1999, Prague *CVIR* 1999 suppl.2 (22) p-174
3. **Lázár I**, Vivarrat-Perrin L, Petit P, Moulin G, Bartoli J.M.  
Transjugular Core liver biopsy: preliminary experiences in 9 patients with thrombocytopenia.  
CIRSE 1999, Prague *CVIR* 1999 suppl.2 (22) p-169
4. **Lázár I**, Bartoli J-M, Moulin G, Chamati S.  
Procedural complications of TIPS.  
ESGAR 1999, Tuebingen *Eur. Radiol.* 1999 4 (9)p-838
5. **Lázár I**, Mátyás L, Juhász G, Szarka J, Simon G.  
Initial Hungarian experiences of AAA endovascular grafting.  
CIRSE 2000, Maastricht *CVIR* 2000 (23) suppl. p-145
6. **Lázár I**, Moulin G.  
Intentional blocking of small portosystemic collaterals with stents during TIPS.  
CIRSE 2000, Maastricht *CVIR* 2000 (23) suppl. p-161
7. **Lázár I**.  
Transjugular core liver biopsy: experience with 17 consecutive patients.  
ESGAR 2001, Dublin *Eur. Radiol.* 2001 6 (11) p-C71
8. Mátyás L, Juhász Gy, **Lázár I**.  
Endovascular repair of the para-anastomotic aneurysm of the abdominal aorta.  
ISCVS 2001, Cancun *Card. Surg.* Vol.9 Suppl 2 p-47.
9. **Lázár I**, Bartoli J-M, Moulin G.  
Embolization of different type of portosystemic collaterals during TIPS.

- ESGAR 2001, Dublin *Eur. Radiol.* 2001 6 (11) p-C71
10. **Lázár I**, Sraj Á, Kerekes A, Gyarmati J.  
Life-threatening bleeding from an operated pancreatic pseudocyst: diagnosis and endovascular treatment. A case report.  
CIRSE 2001, Gothemburg *CVIR* Vol 24 Suppl 1 2001. p-195.
  11. **Lázár I**, Mátyás L, Juhász Gy.  
Endovascular treatment of proximal para-anastomotic aneurysms of the abdominal aorta.  
CIRSE 2001, Gothemburg *CVIR* Vol 24 Suppl 1 2001. p-205.
  12. Szentgyörgyi-Ferdinandy R, Vörös E, Barzó P, Mencser, Bodosi , **Lázár I** , Palkó A. Initial experiences with carotid artery stenting.  
ECR, 2002 *Eur. Radiol.* 2002.
  13. Levrier O, **Lázár I**, Manera L, Benali , Bartoli JM, Raybaud C.  
Evaluation of a new method for carotid stenosis quantification using 3D digital subtraction angiography images.  
RSNA, Vol 225 Suppl. to *Radiology* 2002, p-448
  14. **Lázár I**, Vass Z, Soós L, Ludvig Z, Gyarmati J.  
Transjugular intrahepatic porto-systemic shunt interventions: how to proceed further? Our results in comparison with international standards.  
ESGAR 2003, Budapest *Eur Radiol* 2003 suppl 2, Vol 13, p-S115
  15. **Lázár I**, Mátyás L, Juhász G.  
Nitinol stent for carotid artery stenting: a single center's one-year experience with Smart and Precise stents.  
CIRSE 2003, Antalya *CVIR* Vol 26 Suppl 1. p-181.
  16. Mátyás L, **Lázár I**, Juhász G.  
Acute endovascular treatment of ruptured abdominal aortic aneurysma with aorto-uniiliac stent-grafts and subsequent crossover femoro-femoral bypass.  
CIRSE 2003 , Antalya *CVIR* Vol 26 Suppl 1. p-186.
  17. **Lázár I**.  
Interventional radiology in portal hypertension.  
ECR 2005, *Eur Radiol* 2005 suppl 1, Vol 15 p-74.

### **Other oral publications concerning the subject of my dissertation**

1. **Lázár I**, Moulin G, Petit P, Chagnaud C, Bartoli J-M  
Peroperative complications during TIPS.  
*Magyar Radiológus Kongresszus*, Pécs 1998
2. **Lázár I**, Bartoli J-M, Joffre F, Levrier O, Rousseaux H  
Le risque radique en radiologie interventionnelle.  
*Kelet-Európai Frankofón Képzőképző Diagnosztikai Kongresszus*, Budapest 1998
3. **Lázár I**, Petit P, Moulin G, Bartoli J-M  
TIPS in a childhood and restenosis management: case of a girl with mucoviscidosis.  
*MACIRT 1. Kongresszus*, Pécs 1999
4. **Lázár I**, Bartoli J-M, Moulin G, Chamati S  
Dissection iatrogen portal en cours de TIPS.  
*Journées Francaises de Radiologie*, Párizs 1999
5. **Lázár I**, Chagnaud C, Moulin G, Petit P, Bartoli J-M  
Procedural complications of TIPS.  
*5<sup>th</sup> International Congress and Comprehensive Course, Vascular and Non-vascular Intervention in the New Millennium*, Zermatt-Heidelberg 2000
6. **Lázár I**  
Transjugular intrahepatic portosystemic shunt (TIPS): new method to treat portal hypertension.  
*Új évezred, új kihívások. A B.-A.-Z. Megyei Kórház tudományos ülése* 2000
7. **Lázár I**, Bartoli J-M, Moulin G  
Clinical experiences with 58 TIPS.

- A Magyar Gasztroenterológiai Társaság 42. Nagygyűlése, Balatonaliga 2000*
8. **Lázár I**, Bartoli J-M, Moulin G  
Portosystemic collaterals due to portal hypertension and their embolization during TIPS.  
*Az MRT XX. Kongresszusa, Debrecen 2000*
  9. **Lázár I**, Ludvig Zs, Gyarmati J  
Transjugular intrahepatic portosystemic shunt. Single center experiences in Miskolc. *II. Horvát-Magyar Radiológus Symposium, Opatija 2000*
  10. **Lázár I**  
Gastro-oesophageal varices and their embolization during TIPS.  
*Senior Klub és az Ifjúsági Bizottság tudományos ülése, Budapest 2000*
  11. **Lázár I**, Siklósi E, Husonyicza F  
Preliminary experiences with twenty TIPS in Miskolc.  
*MACIRT 2. Kongresszus, Győr 2001*
  12. **Lázár I**  
TIPS. Indications, contraindications, technical difficulties, follow-up.  
*Intervenció tanfolyam, Szeged 2002*
  13. **Lázár I**  
TIPS (Transjugular intrahepatic portosystemic shunt)  
*Máj- és epebetegségek radiológiai diagnosztikája és kezelése, Szombathely 2002*
  14. **Lázár I**, Siklósi E, Kristóf T, Vass Zs, Soós L, Gyarmati J  
Results with 40 TIPS at Miskolc. Comparison with international standards.  
*A Magyar Gasztroenterológiai Társaság 44. Nagygyűlése, Balatonaliga 2002*
  15. **Lázár I**, Vass Zs, Soós L, Ludvig Zs, Gyarmati J  
TIPS interventions. How to proceed further? Our results in comparison with international standards.  
*MRT Kongresszus, Szeged 2002*
  16. **Lázár I**  
New trends in interventional radiology.  
*Korle-Bu University, Accra, Ghana 2003*
  17. **Lázár I**, Vass Zs, Ludvig Zs  
TIPSS in the busiest Hungarian referral center.  
*PannRad 2003, Rust*
  18. **Lázár I**, Mátyás L  
1-year vascular interventional activity in Miskolc.  
*PannRad 2003, Rust*
  19. **Lázár I**  
TIPS.  
*FiRaFo, Debrecen 2003*
  20. **Lázár I**  
TIPS. New trends, pitfalls, clinical results.  
*PIRS, Pécs 2004*
  21. **Lázár I**  
How TIPS results changed with the availability of stent-grafts.  
*Hepatologiai Napok, Bükfürdő 2006*
  22. Eröss B, **Lázár I**, Nemesánszky E, Székely Gy  
Urgent TIPS and the treatment of the subsequent hepatic encephalopathy.  
*Gastroent Kongr. Szeged 2006*
  23. **Lázár I**, Kristóf T, Mátyus Zs, Váczi Zs, Kostyál L, Orosz P  
TIPS. Mid-term results with stent-grafts.  
*Gastroent. Kongr., Szeged 2006*
  24. Orosz P, **Lázár I**  
Acute lower gastrointestinal bleeding.  
*Gastroent. Kongr., Szeged 2006*

## 25. Lázár I

TIPS: actualities.

*MRT 23. Kongr.* Eisenstadt 2006

## 26. Lázár I

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*TRT, Bp.* 2006

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