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• BASIC RESEARCH •

Direct intrahepatic portacaval shunt: an experimental study

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Abstract

AIM: To determine the feasibility of creating direct intrahepatic portacaval shunt (DIPS) in swine with puncture under sonographic guidance.

METHODS: DIPS was created in 10 domestic swine under sonographic guidance. Liver function, blood ammonia level and portosystemic gradient (PSG) were compared before and after the procedure. Patency of shunt was followed by portography every 7 days after DIPS.

RESULTS: DIPS was successfully established in all 10 swine without any complications. One day after procedure the alanine aminotransferase (ALT), aspartate aminotransferase (AST), and blood ammonia level (BAL) of swine rose from 5.40±0.69, 16.00±0.79 and 35.66±4.10 to 34.20±3.46, 59.70±2.22 and 66.94±3.44 respectively. (P<0.05). The PSG decreased from 0.59±0.20 kPa to 0.24±0.11 kPa after DIPS (P<0.05). The shunt of 10 swine was kept patent from 7-28 days (median patency time was 14 days).

CONCLUSION: This initial experience demonstrated that creating intrahepatic portacaval shunt from retrohepatic segment of IVC to portal vein with puncture under sonographic guidance in swine is safe and feasible. Further studies are necessary to perform DIPS in cirrhosis patients.

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INTRODUCTION

Since Röschl successfully created an intrahepatic shunt from hepatic vein to portal vein in a canine model in 1969, the transjugular intraheptic portosystemic shunt (TIPS) procedure has been used increasingly in the management of portal hypertension and its complications[1-12]. One of the main limitations of TIPS has been the high incidence of shunt malfunction. There is a wide range of shunt malfunction rates reported in the literature from 17-50 % within six months to 23-87 % within the first year[11-21]. Many experimental and clinical studies[4,15,23,26] demonstrated that stenosis of the outflow hepatic vein (HV) is the main problem to limit the long-term patency of TIPS and development of HV stenosis after TIPS placement will be minimized by the use of the largest HV (RHV or MHV). The inferior vane cava (IVC) is the largest vein in human being, whose diameter is far wider than that of HV. Therefore, using IVC as the outflow vein might improve the patency of intrahepatic portosystemic shunt theoretically[24-28]. To determine the feasibility and safety of creating DIPS in swine under a sonographic guidance, we carried out this study to provide a new route for clinical intrahepatic portosystemic shunt.

MATERIALS AND METHODS

Animals

10 domestic swine, 6-8 weeks old, each weighing 22-25 kg, were used for this study. All animals had a normal liver without portal hypertension.

Pre-procedural preparation

Before procedure, each animal underwent abdominal enhanced CT scan by bolus injection of 80 ml Iopamidol intravenously. The length, diameter and the extent of RHSIVC invested by hepatic parenchyma were measured. The anatomical relationship of the intrahepatic portal vein and RHSIVC was also carefully studied. Liver function and blood ammonia level were checked before procedure to serve as a baseline for further evaluating the damage to swine' s liver function after DIPS.

Procedure

Each swine was anaesthetized with ketamine (20 mg/kg) and diazepam (5 mg/kg) intramusculary. After right femoral vein cut down and dilated, a 10-F-diamter, 41-cm-long sheath (Cook Bloomington, U.S.A) was introduced into swine' s IVC and pressure measurement was made. Then, RUPS-100 portal access set modified by increasing the primary curve was passed through the 10-F sheath and placed into swine' s RHSIVC. Under songraphic guidance, the tip of modified RUPS set was wedged against the right anterior-lateral wall of the IVC just beneath the level of the portal vein (Figure 1). RUPS-100 set was advanced slightly and orientation of the tip was adjusted ceaselessly. When the posterior-lateral wall of intrahepatic portal vein became "pushed" on songraphy the 0.038-inch metal needle and 5-F teflon catheter of modified RUPS set was thrust toward portal vein. After metal needle removed the 5-F teflon catheter was pulled back slowly with intermittent aspiration. When blood can be freely aspirated 5 ml contrast medium was infused as test injection. If portal vein' s access was confirmed a 0.035-inch guide wire was passed through the 5-F teflon catheter into the portal vein. Subsequently, a 5-F pigtail catheter was advanced over the guide wire into the portal vein. Then, portography was performed and the pressure of portal vein was measured. After 500 U/kg heparin was intravenously infused a 0.035-inch Amplatz super stiff guide wire was introduced into the portal vein and 5-F pigtail catheter was removed. A 6-mm-diameter, 8-cm-long angioplasty balloon catheter was advanced over the Amplatz guide wire and positioned in the tract between the RHSIVC and portal vein. The balloon was partially inflated and a spot radiography of the partially inflated balloon catheter was used as a road map guide for stent placement. The distal "waist" of the balloon served to mark the portal vein wall and the proximal "waist" marked the wall of the RHSIVC. The distance between the two "waists" is the length of the hepatic parenchymal tract between the portal vein and RHSIVC and is the minimum

length of the stent required to connecting these two structures. The balloon catheter was then fully inflated to predilate the tract. As the balloon was being deflated, the 10-F sheath was advanced over the balloon catheter into the portal vein. With use of the road map image as a guide, the shunt was lined by one or two home-made metal bare stents. Portography was performed immediately after stent placement and pressure measurements were also made. Finally, a 5-F pigtail catheter was retained in animal' s IVC for follow-up portography and right femoral vein incision was sutured. No anticoagulant, antibiotics or antiplatelet therapy was administered after procedure. At termination of the study, the animals were sacrificed by overdose ketamine intravenously for pathological examination.

Fellow-up

Cross-sectional abdominal contrast-enhanced CT scan was performed 3 days after DIPS to detect any puncture-related complications. Liver function and blood ammonia level were rechecked at 1, 7 and 14 days after procedure. Portography was performed through the 5-F pigtail catheter previously retained in animal' s IVC every 7 days after DIPS to evaluate the patency of shunt till the shunt complete occlusion.

Statistical analysis

All measured values were expressed as mean ±SD. Laboratory values and portosystemic gradient (PSG) before and after DIPS was compared using paired-samples *t* test. The patency of DIPS shunt was evaluated by Kaplan-Meier analysis. If *P* values <0.05 the difference was considered significant.

RESULTS

CT scan

On pre-procedure CT imaging the mean length and diameter of swine' s RHSIVC was 47.28±3.65 mm and 19.00±2.24 mm respectively. About 85.83-100 % of swine' s RHSIVC was completely invested by hepatic parenchyma (Figure 2). On the CT imaging obtained 3 days after DIPS no hematoma beneath the hepatic integument or intraperitoneal bleeding was revealed. All stents were accurately deployed in the shunt connecting the intrahepatic portal vein and RHSIVC. No thrombosis could be detected in the portal vein or IVC (Figure 3).

Portal vein puncture and stent deployment

The direct RHSIVC to portal vein puncture visualized with real-time ultrasound was successfully made in all 10 swine. 1-5 (mean 2.2) passes were required to complete the puncture. Mean length of the intraparenchymal tract from RHIVC to portal vein was 15.43±3.36 mm. In 8 swine, the shunt linked right branch of portal vein and RHSIVC, in the remaining 2 animals the left branch of portal vein was connected. Mean angles between the axial of shunt and RHSIVC was 29.42±2.31°. Totally 14 stents were deployed in 10 animals' shunts. In No. 1 and 6 swine, first stent was deployed too far into the portal vein and a second stent was required to fully cover the tract. In No.2 and 8 swine, the first stent dislodged into animals' RHSIVC and a second stent was necessitated. All stents were dilated to 8 mm in diameter without any contraction. After stents deployment, immediate portography demonstrated rapid flow from portal vein to IVC through widely patent DIPS shunt and no obvious contrast-medium extravasation was observed. The post-procedure PSG was significantly lower than that of before (Table 1) (Figure 4, 5).

Follow-up

On follow-up, no procedure-related death occurred, every animal grew well and no signs or symptoms of infection could be observed. The patency time of DIPS shunt varied from 7 days to 28 days (median patency time was 14 days) after procedure (Figure 6).

Table 1 Portosystemic Gradient before and after DIPS (kPa)

	Pressure of IVC		Pressure of Portal vein		PSG	
	Before	After	Before	After	Before	After
	1.28±0.28	1.41±0.28	1.86±0.21	1.57±0.17	0.59±0.20	0.24±0.11
P values	0.034		0.001		0.007	

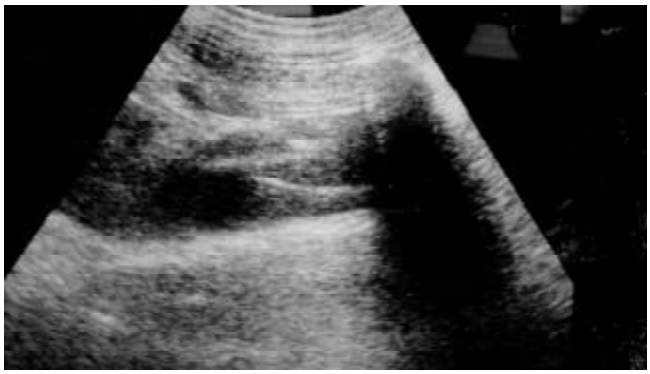

Figure 1 Intrahepatic portal vein, RHSIVC of swine and the modified RUPS-100 set wedging against the anterior-lateral wall of RHSIVC are clearly demonstrated on sonography.

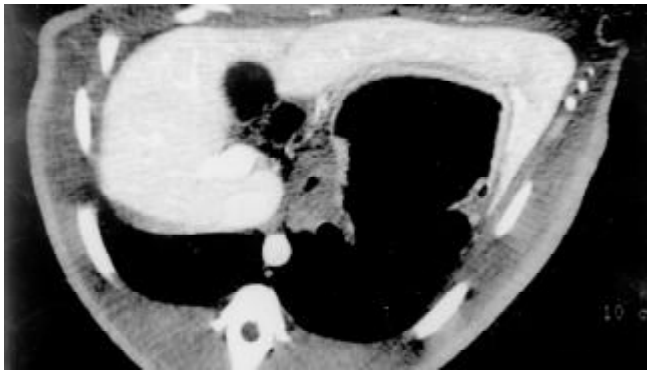

Figure 2 Sectional abdominal enhanced CT scan of swine before DIPS demonstrates the swine's intrahepatic portal vein and retrohepatic segment of IVC clearly.

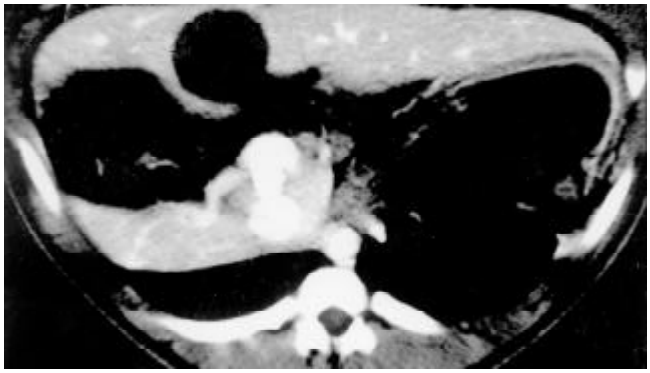

Figure 3 No hematoma beneath the hepatic integument or intraperitoneal bleeding is dectected on sectional abdominal enhanced CT imaging of swine after DIPS. The self-expandable home-made stent is accurately deployed in the shunt connecting the intrahepatic portal vein and RHSIVC.

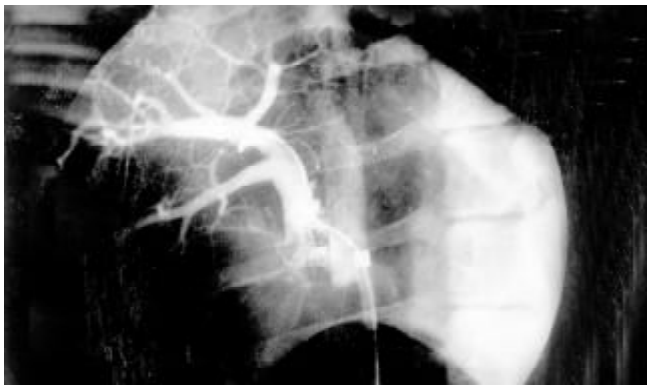

Figure 4 After intrahepatic portal vein successfully accessed via retrohepatic segment of IVC approach, portography was performed with a 5-F pigtail catheter. Swine's anterior and posterior branch of right portal vein is clearly demonstrated.

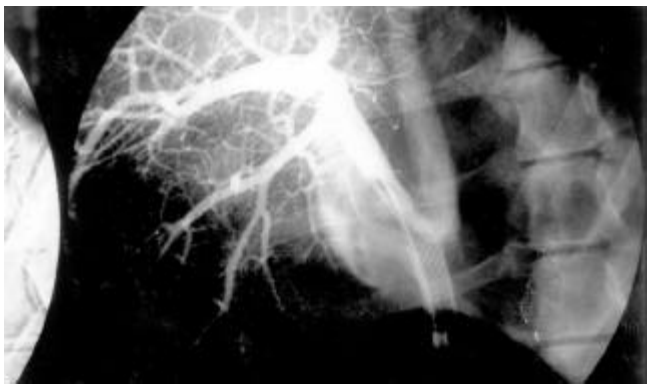

Figure 5 The DIPS shunt is lined by an 8 mm-diamter, 6 cm-long home-made metal bare stent. The stent is fully dilated and accurately connected the swine's RHSIVC and anterior branch of right portal vein. Swine's heptaic perfusion is well and animal's IVC was patent. No extravasation of contrast medium can be detected.

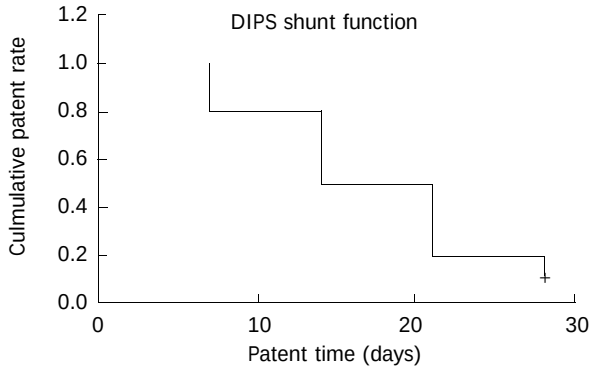

Figure 6 Median patency time of 10 DIPS shunt is 14 days. 7, 14, 21 and 28 days after DIPS procedure the cumulative patency rate of shunt is 100 %, 80 %, 50 % and 20 % respectively.

Laboratory examination

One and 7 days after DIPS, animal' s alanine aminotransferase (ALT) and aspartate aminotransferase (AST) became significantly higher than the pre-DIPS values but the 7 day' s values already became significantly lower than that of the first day after procedure. 14 days after DIPS, ALT and AST of swine returned to their normal pre-DIPS level. Animal' s total bilirubin (TB) and combined bilirubin (CB) remained unchanged before and after DIPS. Swine' s blood ammonia level increased significantly 1 day after procedure and returned to the its baseline value at 7days after DIPS (Table 2).

Table 2 Laboratory examination before DIPS, 1, 7 and 14 days after DIPS

Laboratory examination	Pre-DIPS	1d after DIPS	7d after DIPS	14d after DIPS
ALT (U/L)	5.40±0.69	34.20±3.46	18.0±2.11	5.80±0.66
AST(U/L)	16.00±0.79	59.70±2.22	23.90±0.90	17.60±0.75
TB(uoml/L)	1.86±0.20	1.94±023	2.16±0.17	2.10±0.17
CB(uoml/L)	0.66±0.10	0.86±0.14	0.95±0.12	0.88±0.19
BAL(uoml/L)	35.66±4.10	66.94±3.44	36.08±3.93	43.59±3.91

Note: Compared with the value of pre-DIPS the swine's ALT and AST rose significantly 1 and 7 days after DIPS. But 7 days' value had decreased significantly lower than that of first day after procedure. 14 days after DIPS the swine's ALT and AST returned to their baseline value of pre-DIPS. Swine's TB and CB kept no change before and after DIPS. Animal's blood ammonia level elevated significantly first day after DIPS. 7 days after procedure the animal's BAL returned to its baseline value of pre-DIPS and kept no significant change at 14 days after DIPS.

DISCUSSION

Direct intrahepatic portacaval shunt (DIPS) is to establish a low-resistant pathway between the intrahepatic portal vein and RHSIVC by diverting some of portal flow into IVC to achieve the goal of lowering the portal venous pressure. Compared with conventional TIPS, DIPS links RHSIVC rather than the hepatic vein. The diameter of RHSIVC is much wider than that of hepatic vein and the angle of DIPS shunt-to-IVC is more acute than that of TIPS shunt-to-hepatic vein. Thus, after DIPS the local hemodynamic change, a trigger factor of stenosis or occlusion of the outflow vein, may be less than that after TIPS and the patency time of DIPS may be longer than that of TIPS. In some cirrhosis patients, the hepatic vein drained into IVC with an approximate right angle or the level of intrahepatic portal vein might elevate too close to the level of hepatic vein owing to severe fibrosis of the liver. On these clinical situations, the RUPS-100 set can not be favorably introduced into the hepatic vein and puncture into portal vein is too difficult to be made[24]. Moreover, to establish a portosystemic shunt in some portal hypertension patients with Budd-Chiari syndrome or hepatic venoocclusive disease the puncture into portal vein can but be made from IVC[25,29]. Meanwhile, in some patients with previous TIPS shunt occlusion and no suitable hepatic vein could be supported a second parallel TIPS and DIPS seemed to be a rational choice[30].

Local hematoma or pneumothroax resulted from mispunctures of the carotid artery or the trachea was considered as the serious complication of internal jugular vein puncture[4,31,32]. Some authors[31,32] pointed out that a previous TIPS procedure might interfere with the operative management of the subsequent orthotopic liver transplantation by deploying a stent into the suprahepatic portion of IVC, which often occurred at TIPS revision and a second parallel TIPS was established. To completely avoid these puncture-related complications and potential suboptimal stent placement of conventional TIPS we created this DIPS via a femoral vein' s approach.

Anatomic construct of swine' s liver and its post-trauma' s histopathologic response are similar to those of human being[35,36]. So DIPS can be created in pigs using techniques and equipment identical to that used in humans. The key step of successfully established DIPS is to select a suitable puncture site of IVC. In this study, the mean length of swine' s RHSIVC was 47.28±3.65 mm and 85.83-100 % of RHSIVC was completely invested by hepatic parenchyma. These are the anatomic foundation of safely performing DIPS in swine. Mean diameter of swine' s RHSIVC is 19.00±2.24 mm which is far

wider than the 10.10±1.58 mm-diameter of swine' s hepatic vein. These results demonstrated using RHSIVC as the drain vein of DIPS in swine might improve the patency of intrahepatic portosystemic shunt theoretically.

Portal vein can not be precisely targeted under fluoroscopy. Thus, many major even fatal complications of conventional TIPS procedure are related to the "blind puncture" from hepatic vein into portal vein[4,31,32]. Meanwhile, the bile duct injury and subsequent bile leak has been implicated as a cause of shunt thrombosis. Mucus in bile, not bile itself, is thought to be the thrombogenic factor of early shunt malfunction[37,38]. Accordingly, using an effective guiding tool plays a most important role not only in creating DIPS safely but also in achieving a long-term patent shunt owing to improve the accuracy of puncture. We performed DIPS under sonographic guidance because of its free of X-ray and easy to perform. On sonography the location of intrahepatic portal vein and the tip of modified RUPS-100 placed in swine' s RHSIVC can be clearly demonstrated. Only should we do is to adjust the angle of RUPS-100 set-to-IVC and advance the set slightly. When the left posterior-lateral wall of intrahepatic portal vein became "pushed", puncture was made. In our study, only 2.2 passes were required to accomplish the puncture, mean distance of puncture was only 15.43±3.36 mm and no puncture-related complications could be detected after procedure. These findings verified the effectiveness of real-time ultrasound to guide puncture in DIPS procedure. By using sonographic guidance to perform DIPS in cirrhosis patient attention should be paid to the interference brought by regenerated nodules, pneumatosis of bowel and ascites to the clarity of sonography. Portosystemic gradient (PSG) decreasing from 0.59±0.20 kPa to 0.24±0.11 kPa after procedure (P<0.05) verified the effectiveness of DIPS to decompress the portal venous pressure. After DIPS, the swine' s ALT and AST increased significantly for a time but they finally returned to their normal pre-DIPS levels within two weeks after procedure. This exhibited the damage brought by DIPS to swine' s liver function might just be temporary. Animal' s TB and CB remained unchanged before and after DIPS. This implicated the injury of bile duct after DIPS is minor, which might attribute to the less number of passes required to complete the puncture and a short distance of intraparenchymal tract. Animal' s blood ammonia level elevated significantly first day after DIPS. 7 days after procedure the animal' s BAL returned to its baseline value before DIPS. This would be related to the swine used in this study without portal hypertension and portosystemic gradient quickly achieved a dynamic equilibrium after DIPS.

Our DIPS shunt kept patent from 7-28 days (median patency time was 14 days) which were shorter than the results published by Petersen *et al*[26]. Except the breed disparity of animals between two studies some factors may be related to this despondent result. (1) All swine underwent DIPS without intubation and the respiratory movement of animals could not be well controled. 4 stents' unprecisely deployment, 2 deployed far into the portal vein and 2 dislodged into animal' s RHSIVC, were attributed to animal' s irregular respiratory movement. (2) We created this DIPS via a femoral vein' s approach. The direction of flow in shunt is opposite to the flow orientation in IVC. This might form whirlpool or turbulent flow at the outflow venous end of the stent and made it liable to injury from stress of the jet stream of blood. (3) Compared with the Palmaz stents used by Petersen, the high thrombogenicity of home-made stent may lead to early shunt malfunction. Finally, All swine used in this study have a normal liver without portal hypertension. After DIPS, the portosystemic gradient was decreased to 0.24±0.11 kPa which can not maintain the sufficient flow in shunt, using a "bare-stent" that can not effectively prevent the ingrowth of normal liver parenchyma and no anticoagulant being administered were also related to this early stenosis or occlusion of shunt.

Our initial experience demonstrated creating direct intrahepatic portosystemic shunt in swine was safe and feasible. Carefully studying the anatomic relationship of intrahepatic portal vein and RHSIVC in cirrhosis patients and deploying a low-thrombogenic stent-graft in parenchymal track seem to be necessary for safely performing and achieving a long term patent DIPS in human being.

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