Expandable Intrahepatic Portacaval Shunt Stents in Dogs with Chronic Portal Hypertension

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A canine experimental model was used to investigate the feasibility of using balloon-expandable portacaval shunts in humans with chronic portal hypertension. Intrahepatic portacaval shunts were created in nine dogs with stable portal hypertension previously induced by intraportal injections of polyvinyl alcohol (Ivalon). Embolic material was injected periodically through a subcutaneous port that allowed repeated access to the portal system. Shunts were placed 14 weeks after the last embolization. A shunt patency rate of 100% was observed up to 48 weeks. Low portacaval pressure gradient and high shunt flow accounted for the good results.

In a previous report [1] we described a method of creating intrahepatic portacaval shunts in experimental animals. The technique, modified from that of Rosch et al. [2], involved placement of a balloon-expandable metal stent within a liver-tissue track previously formed by a transjugular needle puncture. Unlike previously described intrahepatic shunts [2–7], ours directly connected the inferior vena cava with the portal bifurcation in a side-to-side fashion. Most of our reported shunts remained patent for as long as they were under study; nevertheless, more than half required recanalization of the lumen by balloon angioplasty after early thrombosis. Although these initial failures were associated with technical errors that resulted in obstruction of shunt flow, the lack of sustained portal hypertension and high flow in the shunt must have contributed substantially to the occlusions.

To evaluate the performance of balloon-expandable portacaval shunts with sustained elevation of the portal pressure, we injected several doses of polyvinyl alcohol (Ivalon) into the portal circulation of large, adult dogs before placing percutaneous transjugular portacaval shunts. The objective of this study was to investigate further the feasibility of human application of the technique by studying the short- and long-term performance of intrahepatic shunt stents in experimentally created chronic portal hypertension.

Materials and Methods

Induction of Experimental Chronic Portal Hypertension

Nine dogs had injection ports placed subcutaneously as vascular access to the portal system for repeated particle embolization (Fig. 1). The ports (Norfolk Medical Products, Inc., Skokie, IL) consisted of a diaphragm placed subcutaneously in the right abdominal flank and connected to a silicone rubber 7-French tube that was introduced into the superior mesenteric vein through a mesenteric vein branch. An 18-gauge Huberd deflected-point needle (Norfolk) was used to gain access to the subcutaneous diaphragm, measure pressures, inject contrast material, and create embolisms in the portal system. Barium-impregnated Ivalon powder (Unipoint Industries, High Point, NC) with a particle size of 250–400 μm was suspended in saline and injected at a dosage of 0.5 g/week for a maximum of four doses. Embolization was avoided if the preembolization portal pressure was 20 cm of saline or higher. Before each embolization, a portogram was obtained by injecting 76% contrast material through the

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port (Fig. 2). Four weeks after initial placement, the port was removed through a small skin incision. Biochemical liver profiles were assessed by SMA-12 (SMA = sequential multichannel autoanalyzer) analysis every week during the embolization period and every other week thereafter. A percutaneous liver biopsy was performed with a 14.5 gauge Tru-Cut needle (Travenol, Inc., Deerfield, IL) immediately before shunt placement.

Placement of Percutaneous Portacaval Shunt

Each dog was given general gaseous anesthesia, and a valved 12-French introducer sheath (Cook, Inc., Bloomington, IN) was placed percutaneously in the right jugular vein while the animal was lying on its left side. A 12-French Teflon dilator mounted on an 8-French Teflon catheter was advanced in the inferior vena cava to the level of the hepatic veins. The inner catheter was removed, and an 18-gauge cannula with a diamond-tipped mandril [1] was introduced. The needle tip was oriented toward the portal vein bifurcation by using (as a "road map") a previously obtained portogram of the dog in an identical position. After the needle penetrated the portal vein, which was perceived as a sudden give to the operator's hand, the trocar was removed, and portal blood was aspirated. A guidewire 260 cm long and 0.09 cm (0.035-in.) in diameter was advanced into the superior mesenteric vein. After the needle was removed, the 8-French Teflon dilator and 12-French sheath were advanced across the needle track with a rotary motion. The dilators were then exchanged for an 8 mm × 4 cm balloon angioplasty catheter, and the balloon was expanded for 3 min after the injection of 1500 units of heparin into the portal vein. The site where the balloon was indented before full expansion was used as a landmark to position the stent.

A 30 × 3.7 mm stainless steel stent was mounted snugly over a 10 mm × 4 cm high-pressure angioplasty balloon catheter. Unlike the stent used in our previous series, the new one was a single piece, a stainless steel tube with parallel staggered slots etched in the wall. On inflation each slot became a diamond-shaped space. The wall thickness of the stent was 0.15 mm (0.006 in.); therefore, the diameter of the collapsed stent-balloon assembly was only slightly wider than the folded balloon and was easily introduced through the sheath's valve. After adequate positioning of the stent, the balloon was inflated and immediately deflated, leaving the expanded stent in place. After balloon withdrawal, pressure measurements in the portal vein, inferior vena cava, and right atrium and a portogram were obtained.

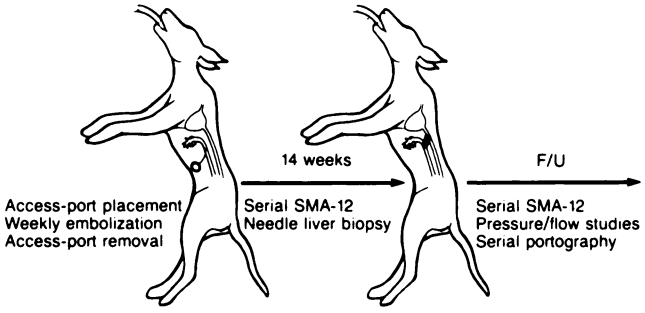

Fig. 1.—Experimental design. SMA = sequential multichannel autoanalyzer; F/U = follow-up.

Postshunt Evaluation

Percutaneous transjugular portograms, serial SMA-12 analysis, and pressure measurements were obtained after shunt placement. Portograms and pressure studies were performed at 1, 3, 6, and 12 weeks after shunt placement and were repeated every 12 weeks thereafter. Occlusive and opening portal pressures were recorded only once by means of a rubber occlusive balloon in the shunt lumen 3 to 6 weeks after shunt placement.

The fraction of portal flow shunted to the systemic circulation was established by injecting ^{99m}Tc-labeled human albumin microspheres into the portal vein and inferior vena cava circulations and then comparing the corresponding radioactivity in a region of interest (ROI)

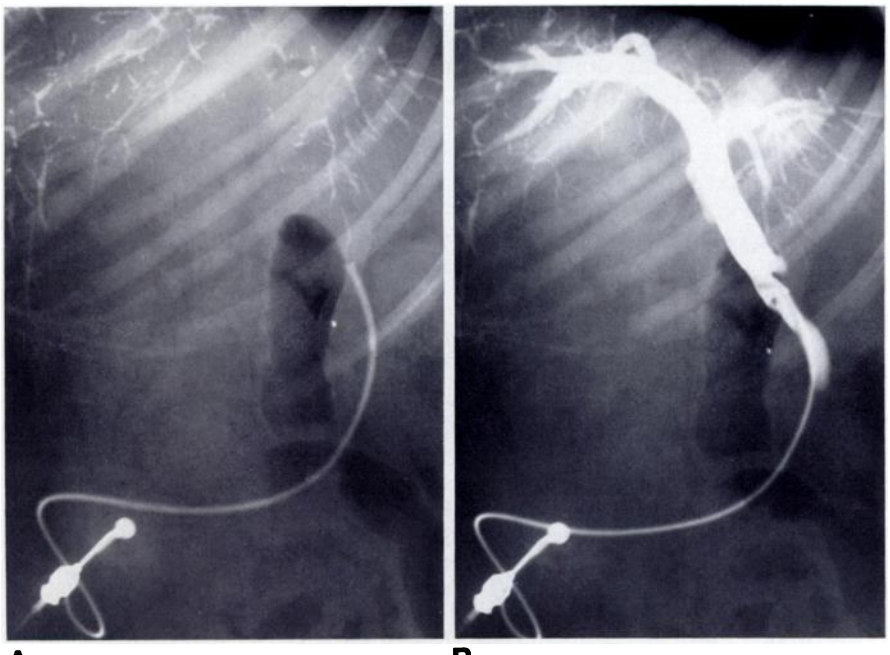

Fig. 2.—*A*, After last embolization portal radicles are extensively filled with opaque embolic material.

***B*, Contrast injection through percutaneous needle shows patency of portal system.**

in the upper lungs. Counts within the ROI were assumed to be proportional to the amount of radioactivity injected directly into the inferior vena cava (A_{ivc}) or indirectly through the portal shunt (A_{ps}). Attempts were made to inject for each dog similar amounts of radioactive material into the inferior vena cava and into the portal vein. Average radioactivity was 1.1 mCi (40.7 MBq) per injection (range, 0.63–2.3 mCi [23.3–85.1 MBq]). It was assumed that the distribution in the lungs was the same for material entering the vena cava directly or indirectly, that the small number of microspheres per dose (20,000) would not alter pulmonary flow distribution, and that mixing of the labeled microspheres with blood was adequately accomplished by giving injections through side-hole catheters. Given these assumptions, the following relationship applies:

$$ROIcts_{ivc}/ROIcts_{pv} = A_{ivc}/A_{ps} = A_{ivc}/(A_{pv} \times f)$$

where $ROIcts_{ivc}$ and $ROIcts_{pv}$ represent the net counts within the lung ROI for the inferior vena cava and portal vein injections, respectively. The fraction (f) of flow from the portal vein to the inferior vena cava is given then by

$$f = (ROIcts_{pv}/A_{pv})/(ROIcts_{ivc}/A_{ivc})$$

This implies that the fraction of flow to the lungs via the portacaval shunt is equal to the ratio of the observed net counts over the lung ROI, with the observed count weighted for the amount of radioactivity injected. The possibility of passage of microspheres through spontaneous portosystemic collaterals was ruled out by observing the absence of such collateral flow in a portogram performed before the microspheres were injected. The catheter position was identical in both studies.

Results

Eight animals completed the embolization schedule and had a percutaneous transjugular shunt. One dog had thrombosis of the portal vein at the time of portacaval shunt placement. Before shunt placement, one dog received two embolizations of Ivalon and two received three because the portal pressure was higher than 20 cm of saline at the time of embolization. The rest of the dogs received four embolizations (2 g of embolic material). The portal pressure rose immediately after each embolization and dropped before the next one (Fig. 3). The mean postembolization pressure peak reached maximal values after the second embolization and was lower in the last two. The mean portal pressure of 11 ± 5.3 cm of saline before embolization steadily increased and reached the highest value of 20 ± 4.9 cm of saline ($p < .02$) before shunt placement. Serial measurements of serum transaminases (SGOT, SGPT) and lactic dehydrogenase showed an expected transient elevation immediately after placement of the subcutaneous port and then a decline to normal levels. After shunt placement there was a transient second elevation of the enzymes that leveled off, but at higher levels than those found before the shunt was placed. Serum bilirubin also showed this bimodal elevation. Serum albumin was lowered substantially after placement of the shunt, probably reflecting the lower protein concentration of the postshunt diet. The results of percutaneous liver biopsy showed that most of the portal areas were normal, with occasional mild periportal fibrosis and proliferation of the bile ducts. Ivalon filled up portal veins as small as 0.045 mm in diameter. The portal veins that remained patent appeared distended and were surrounded by prominent perivenous capillaries. The hepatic sinusoids were distended. No liver-cell necrosis or cirrhosis was present.

All shunts remained open, as shown by contrast examinations, for a maximum follow-up of 48 weeks, and none of them had early thrombosis. The mean lumen of the shunt as measured on the last portogram was 79 ± 12% of the radiopaque graft diameter. Contrast injections in the portal system showed that most of the flow was directed to the shunt, with little or no flow into the portal radicles (Fig. 4). Portograms taken late in the study often showed reversed flow in the portal branches. The mean portal pressure of 26 ± 7.9 cm of saline after inflation of an occlusive rubber balloon in the shunt lumen dropped to 8 ± 3.1 cm of saline after balloon deflation (Fig. 3). The pressure gradients across the shunt remained remarkably stable throughout the postshunt follow-up studies, averaging 2.4 ± 1.9 cm of saline. The estimated fraction of portal flow shunted to the inferior vena cava by ^{99m}Tc-labeled microspheres was 95 ± 11% (range, 76–110%). The percentage in excess of 100% was assumed to be within the margin of error of the method.

Discussion

Creation of stable chronic portal hypertension in dogs by repeated injections of Ivalon was first described by Buergener et al. [8]. This model is well suited to the study of percuta-

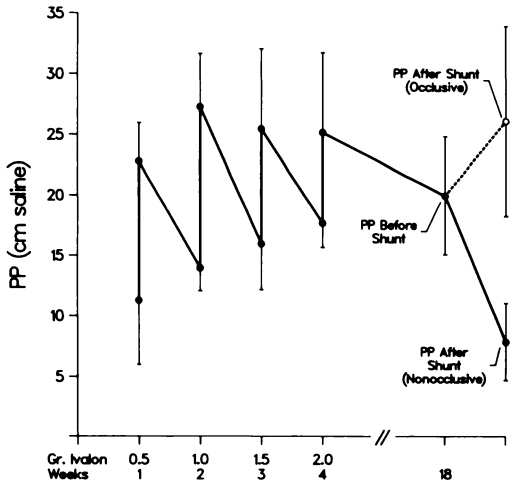

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Fig. 3.—Portal pressure (PP) fluctuations during embolizations and after shunt placement. Each dot represents mean value ± 1 standard deviation (bars). (For clarity, standard deviation values overlapping vertical lines between dots are not indicated.)

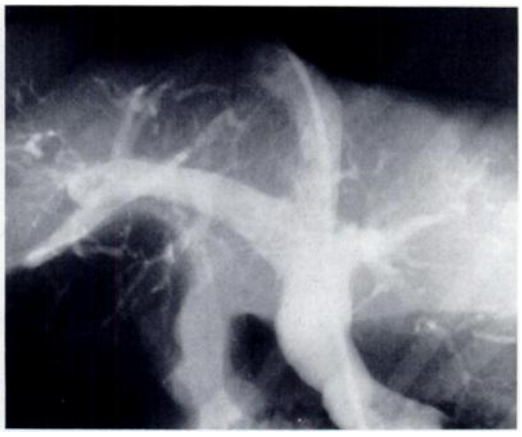

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Fig. 4.—Contrast injection into portal vein through a transjugular catheter introduced across shunt.

neous portosystemic shunts because there is no hepatocellular damage; therefore, the animals remain healthy and in a good nutritional state if they are adequately supported. The portal obstruction is presinusoidal, but the portal vein bifurcation and the major portal branches remain open, allowing the creation of an intrahepatic shunt with the inferior vena cava. We modified the method of Buergener's group by temporarily placing an injection access-port in the portal system and by simplifying the embolization schedule. The benefit of having rapid access to the portal system through an injection port for embolization, pressure measurement, and contrast injection offset the extra cost and time involved in placing and removing the device. With successive embolizations of Ivalon, the portal flow slows, and the possibility of portal thrombosis induced by the presence of the port catheter increases. Therefore, the port must be removed as soon as a total of 2 g of Ivalon have been injected or the portal pressure has been 20 cm of saline or higher for 2 consecutive weeks. With this method, only one animal developed portal thrombosis. The radiopacity provided by the barium mixed with the Ivalon was quite useful because it indicated the degree of filling of the portal radicles, the symmetry of distribution throughout the lobes, and the progressive loss of volume of the liver (Fig. 2A).

Examination of the liver biopsies done before shunt placement showed no significant abnormalities. Periportal fibrosis was seen only occasionally. The lack of histologic abnormalities correlated with the essentially normal liver chemistry profiles before shunt placement. After shunting, the abnormal serum enzyme levels reflected parenchymal liver atrophy caused by the effect of portal flow diversion and high resistance in the hepatic portal circulation.

The mean postembolization elevation of portal pressure was maximal after the second embolization and lower after the following ones. This could have been caused by the development of portosystemic collaterals that dampened the pressure rise of additional embolizations. Those collaterals probably atrophied or decreased in diameter a few weeks after shunt placement as indicated by the high occlusive pressures. Postshunt atrophy of the collaterals caused a "tighter" portal system and, therefore, high occlusive pressures. The portal pressure before each embolization increased steadily, indicating that collateral circulation, just as in human portal hypertension, is insufficient to effectively decompress the portal system. The radiopacity of the metal stent made the follow-up catheterizations simple. The regular, cylindrical lumen permitted measurement of occlusive pressure by means of an occlusive rubber balloon. Although the physiologic value of the test should be further evaluated, the portal pressure measured beyond an occlusive balloon indicated the perfusion pressure of the liver and the degree of atrophy of the portosystemic collaterals.

In contrast to our earlier experience, in which half the shunts thrombosed during the first week [1], all shunts remained open at the latest follow-up study of 48 weeks without the need for recanalization. The shunt lumen averaged 79% of the metal stent diameter as compared with 69% in our first series [1]. The pressure gradient across the shunt was 2.37 cm of saline as compared with 4.9 cm of saline. These findings indicate the beneficial effects of the high shunt flow caused by the portal hypertension. This observation is confirmed by the measurements of shunted portal flow fraction via labeled microsphere, which indicated an almost complete portal flow diversion. The use of a new stent with lower profile and a "learning-curve" effect in the performance of the shunt procedure may have contributed to the improved results. Probably, high shunt flow is necessary to protect against thrombosis before the endothelization of the inner surface of the shunt develops.

Direct intrahepatic portacaval shunting may be hazardous in humans because of the risk of hemorrhage caused by the violation of the peritoneal space. Extensive anatomic studies must be completed before such an approach is considered. Until such time, adequate results may be attained by placing stents between proximal hepatic and portal veins, a modification of the method used by Colapinto et al. [6].

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REFERENCES

1. Palmaz JC, Sibbitt RR, Reuter SR, Garcia F, Tio FO. Expandable intrahepatic portocaval shunt stents: early experience in the dog. *AJR* **1985**;145:821–825
2. Rosch J, Hanafee WN, Snow H. Transjugular portal venography and radiological portocaval shunt: an experimental study. *Radiology* **1969**;92:1112–1114
3. Koch G, Rigler B, Tentzeris M, Schuy S, Sakulin M, Schmidt-Kloiber H. Der intrahepatische porto-cavale Shunt. *Langenbecks Arch Chir* **1973**;333:237–244
4. Reich M, Olumide F, Jorgensen E, Eisenman B. Experimental cryoprobe production of intrahepatic portocaval shunt. *J Surg Res* **1977**;23:14–18
5. Buergener FA, Gutierrez OH. Nonsurgical production of intrahepatic portosystemic shunts in portal hypertension with the double lumen balloon catheter. *ROFO* **1979**;130:686–688
6. Colapinto RF, Stronell RD, Gildiner M, et al. Formation of intrahepatic portosystemic shunts using a balloon dilatation catheter: preliminary clinical experience. *Can Med Assoc J* **1982**;126:267–268
7. Buergener FA, Gutierrez OH. Produktion einer intrahepatischen portokavalen Fistel im Hund mit Leberzirrhose und Pfortaderhonchdruck. *ROFO* **1984**;141:327–332
8. Buergener FA, Gutierrez OH, Logsdon GA. Angiographic, hemodynamic and histologic evaluation of portal hypertension and periportal fibrosis induced in the dog by intraportal polyvinyl alcohol injections. *Radiology* **1982**;143:379–395