Selection of patients and operations for bleeding esophageal varices

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Portosystemic shunts were first introduced in 1945.[1] That a high level of interest in this subject persists is attested to by the more than 300 reports that have been published in the past few years. This interest has developed because of high morbidity and mortality in cirrhotic patients with bleeding esophageal varices. Some studies have indicated that less than one third of patients who sustain a major variceal hemorrhage survive 1 or more years after bleeding.[2]

The theoretical objective of portacaval shunts is reduction of the incidence of variceal hemorrhage and extension of long-term survival of cirrhotic patients beyond that of a nonoperated group. Presumably these operations should be accompanied by minimal morbidity, mortality, and metabolic side effects.

Although it has taken nearly 30 years to establish what shunting operations do and do not accomplish, several recent reports have shed light on this subject.[3-6] All shunting operations are unphysiologic because they deprive the liver of variable quantities of portal blood flow and reroute ammonia-rich colonic blood into the systemic circulation.

How do we evaluate published reports on shunts?

There are limitations and criticisms of all retrospective and prospective studies on shunting operations. These limitations include study design,

patient selection, and manner and type of follow-up. Results of most retrospective studies have shown that shunts were inherently "protective," and that the absence of randomization and control patients is a serious drawback. The limitation of most of the randomized studies is that the patients are of the lower socioeconomic groups and, although the conclusions are valid, they may not apply to all cirrhotic patients. Many of these patients have better liver function than the study patients.

Five randomized studies examining prophylactic and therapeutic shunts have been published,[3, 5, 7-9] four in the United States and one in France. The studies comprised 268 patients who underwent prophylactic shunting operation (varices, no hemorrhage) and 398 patients who had shunts for therapeutic reasons (varices and hemorrhage).

Prophylactic shunts

The results of most prophylactic shunt studies (cirrhotic patients with varices but no major hemorrhage) have shown that (1) the 5-year survival was no better, and perhaps worse in shunted patients when compared with controls, and (2) the incidence of variceal hemorrhage is significantly less in shunted patients.

For example, in one report only 1 of 33 patients who underwent shunting operations experienced recurrent bleeding from varices, whereas 12 of 45 control patients had recurrent bleeding during the same follow-up period. In 5 of 12 patients bleeding proved fatal. There were no specific factors identified that helped predict the group at higher risk for bleeding. In one study an impression that ascitic patients were at greater risk from hemorrhage was not borne out in a subsequent, prospective, randomized trial.[3] Most investigators have shown that the incidence of portal systemic encephalopathy is higher in shunted than in control patients. The increased incidence of this complication may not be significant, although it is more severe in shunted patients.[10]

Therapeutic shunts

Four groups have conducted randomized, controlled studies on 398 patients who bled from varices (therapeutic shunt). It was concluded that at 5 years there was no significant difference in survival between shunted and nonshunted patients. However, in two studies there was a trend, although short of statistical significance, toward a longer survival of patients who underwent an end-to-side portacaval shunt than in controls and patients who underwent side-to-side portacaval shunt.[5, 9] In Mikkelsen's[9] study, not yet statistically analyzed (all A risk patients), end-to-side shunt patients survived longer than the controls; this conclusion may reach statistical significance. Shunted patients had a lower incidence of recurrent bleeding and a higher incidence of liver failure. Of interest was the observation that the type of bleeding (minor or major) helped determine survival in control patients. In one report, control patients with minor hemorrhages had a 46%, 3-year survival rate, and control patients with multiple small hemorrhages had a 72%, 3-year survival rate.[5] This was in contrast to those patients with one major hemorrhage where only 22% of control patients

lived 3 years as opposed to 53% in the shunted group. In study patients in whom major bleeding occurred once, the survival rate was 42% in the nonoperated group compared with 70% of the shunted patients.

A surprising fact in some studies was good survival in those patients whose liver function was sufficient to allow their inclusion in the study, who were randomized to surgery, but who then refused operation. As Conn[7] has concluded, "It is thus reassuring to know that an operation done for 30 years does protect against recurrent variceal hemorrhage although it may not extend life beyond that of control patients."

Prognostic factors

Further confusing the results of retrospective published reports are a number of factors that may directly influence the end result of a shunting operation.[1]

Age. All else being equal, younger patients (less than 55 years) may survive and tolerate shunts better than older patients.[11]

Emergency versus elective shunts. The mortality following emergency shunts is five to nine times higher than when done electively.[12] Therefore, for most patients with acute variceal bleeding, nonoperative measures should be first attempted to control hemorrhage. The presence of a large liver and macronodular cirrhosis and the absence of hyaline necrosis may indicate a better immediate and subsequent survival.[11]

Type of cirrhosis. Although cirrhosis secondary to alcohol ingestion has implied a poorer prognosis than postnecrotic cirrhosis, this issue is controversial. Nearly all studies show better survival rates in patients with good liver function than in those with poor function.[11, 13]

Surgical experience. As the experience of surgeons increases, mortality decreases. This may reflect better technical expertise or better selection of patients, but is probably a combination of both.

Hemodynamic studies. Much has been written both pro and con about preoperative, hemodynamic studies.[14-16] The theoretical reasons for these studies have been based on the supposition that patients with the greatest preoperative hepatic flows who have shunts will experience the greatest deprivation of flow and the highest incidence of encephalopathy. The hemodynamic studies include splenoportography, hepatic blood flow, hepatic occluded maximum perfusion pressure, and portal perfusion pressure.

The largest and most thoroughly studied group hemodynamically has been recently reported by Burchell et al,[16] who studied 145 patients undergoing shunt surgery. They concluded that (1) the extent of preshunt flow is unrelated to the incidence of portal systemic encephalopathy, (2) since direct measurement of portal blood cannot predict the clinical course or survival rates of patients there is no reason to keep searching for better indirect methods, and (3) there is no correlation between pressure differences, total flow, splenoportographic findings, and clinical results.

Therefore, the present value of hemodynamic studies may be investigative only. One measurement that should be done, however, is preopera-

tive caval pressure, since encroachment of the caudate lobe of the liver on the cava may preclude a conventional shunting operation.[17]

Type of shunt

The type of shunt is also controversial. Ten years ago the commonly performed operations were few and included an end-to-side portacaval shunt, a side-to-side portacaval shunt, and a splenorenal shunt with splenectomy. Today there are several options that include side-to-side interposition mesocaval shunt,[18] end-to-side portacaval shunt with arterialization of the ligated portal stump or of the open ligamentum teres,[19] and the distal splenorenal shunt (Warren-Zeppa).[20]

Representative figures culled from the surgical literature show few significant differences between the various operations except for a possible higher incidence of encephalopathy after a portacaval shunt. Whether the distal splenorenal shunt or arterialization of the portal stump will lower the incidence of encephalopathy remains to be proved in control studies. One preliminary report does indicate that the distal splenorenal shunt may be associated with a lower incidence of encephalopathy when compared to the interposition mesocaval shunt.[21]

Morbidity after shunts

Four complications have been reported to occur more frequently following standard portacaval shunts. These are portal systemic encephalopathy (PSE), hemosiderosis, diabetes mellitus, and peptic ulcer.[10]

PSE. PSE is the most common disabling complication following portacaval shunt surgery. That it occurs in significant incidence in the nonshunted population has been shown by several of the randomized and control studies. Whether the greater incidence in shunted patients reaches statistical significance has not been conclusively shown, although it does occur more frequently and in greater severity in shunted than in control patients.

The exact cause of PSE remains unknown. Despite the claim that the diminished portal flow of varying quantities following shunts is responsible for encephalopathy, enough shortcomings in flow studies have already been cited. Increased and normal levels of blood ammonia have been reported in shunted patients with encephalopathy. Arterial and cerebrospinal fluid levels correlate more closely than venous levels. Normal levels in many patients may reflect an intracellular ammonia shift if the encephalopathy is accompanied by alkalosis.[22] Fisher et al[23] have indicated that increased levels of false neurotransmitters are present in patients with encephalopathy.

It may be that decreased blood flow and functional reserve of the liver after a shunt are responsible for the induction of PSE; current investigation is directed toward this end. Warren and Harmon[21] have reported changes in the maximum rate of urea synthesis following shunt surgery. They have suggested that this changes minimally after a distal splenorenal shunt, and that this factor correlates well with the lower incidence of encephalopathy after this operation.

Hemosiderosis has been reported at least 25 times following portacaval shunts.[24] When hepatic iron deposi-

tion was investigated prospectively in control and shunted patients, the incidence increased in the latter group (36% preshunt, 56% postshunt).[10] This increased incidence was suggestive but not statistically significant between the groups.

Peptic ulcer. It has been estimated that 5% of noncirrhotic patients, 5% to 15% of cirrhotic patients, and 15% to 20% of cirrhotic patients with a portacaval anastomosis have duodenal ulcers. An increase in gastric acid secretion due to a humoral mediator that is released following shunting may not necessarily be followed by an increased incidence of peptic ulcer disease, since the prospective studies[25] show little difference in ulcer incidence in control and shunted patients.[10]

Diabetes mellitus. Diabetes mellitus has been reported to occur more frequently after portacaval shunts. The pathogenesis is unclear, since the increase in portal venous glucose into the systemic circulation, which theoretically would cause hyperglycemia in shunted patients should be neutralized by increased levels of circulating insulin. Again the control clinical studies show no differences in shunted and in control patients.[10]

Comment

It is likely that the increased incidence of PSE, diabetes mellitus, hemosiderosis, and peptic ulcer reflect progressive, coexisting problems in cirrhotic patients whose disease is progressive but who do not succumb earlier to variceal hemorrhage.

It may be that selective shunts which allow continued portal hepatic perfusion and theoretically should decompress esophageal varices may decrease the serious complication of portal systemic encephalopathy and liver failure in shunted patients. If these operations can be done with an acceptable mortality, a controlled trial would be of interest.

Conclusions

Portosystemic shunts effectively decompress esophageal varices and reduce the incidence of variceal hemorrhage at an acceptable mortality level when done electively.

There is no increase in survival when shunts are done prophylactically, but there may be a significant trend toward survival in some groups after therapeutic end-to-side portacaval shunts are done in patients who have sustained one major hemorrhage.

A higher incidence of PSE and liver failure are probably due to a decrease in hepatic function, and in the future biochemical tests may identify a susceptible group.

Diabetes mellitus, hemosiderosis, and peptic ulcer disease do not occur with increased frequency after shunting.

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