Original Article

Prophylactic surgery in non-cirrhotic portal fibrosis: is it worthwhile?

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Background*:* In cirrhotic patients with portal hypertension prophylactic portasystemic shunts have been found to be ineffective as deaths from post-shunt liver failure exceed those from bleeding. However, in patients with non-cirrhotic portal hypertension, variceal bleeding rather than liver failure is the common cause of death. In developing countries shortage of tertiary health-care facilities and blood banks further increases mortality due to variceal bleed. **Aim:** To study the results of prophylactic operations to prevent variceal bleeding in patients with portal hypertension due to non-cirrhotic portal fibrosis (NCPF). **Methods:** Between 1976 and 2001, we performed 45 prophylactic operations in patients with NCPF, if the patients had high-risk esophagogastric varices or symptomatic splenomegaly and hypersplenism. Proximal lienorenal shunt was done in 41 patients and the remaining underwent splenectomy with (2 patients) or without (2 patients) devascularization. **Results:** There was no operative mortality. Thirty-eight patients were followed up for a mean 49 (range, 12-236) months. Three patients bled – one was variceal and two due to duodenal ulcers; none died of bleeding. There were 2 late deaths (6 weeks and 10 years after surgery), one from an unknown cause and one due to chronic renal failure. The delayed morbidity was 47%. This included 7 patients who developed portasystemic encephalopathy, 4 glomerulonephritis, 2 pulmonary arteriovenous fistulae and 5 ascites requiring treatment with diuretics. Thus only 20 (53%) patients were symptom-free on follow up. **Conclusions:** Prophylactic surgery is safe and effective in preventing variceal bleeding in NCPF but at the cost of high delayed morbidity. [*Indian J Gastroenterol* 2005;24:239-242]

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In cirrhotic patients the mortality rate from the first episode of variceal bleeding has been reported to range from 30% to 70%.[1,2,3] However, measures to prevent the first bleed, such as endoscopic sclerotherapy or portasystemic shunts, have not been effective. In three of the four early trials[3-6] of prophylactic portasystemic shunts, patients who underwent operation did worse than those who did not, with deaths from post-shunt liver failure exceeding those from bleeding.

Non-cirrhotic portal hypertension is common in India and the causes include extrahepatic portal venous obstruction and non-cirrhotic portal fibrosis (NCPF). This disease usually affects poor patients, who live in rural areas far from medical centers and have little or no access to facilities for blood transfusion. In the West, patients with non-cirrhotic etiologies have mortality ranging from 7% to 31% for a single bleeding episode.[7] In a Japanese national survey (1979-1988) of 671 cases of idiopathic portal hypertension, 24 were managed conservatively. On long-term follow up, the mortality was higher in the non-operated group and the majority of deaths were because of variceal hemorrhage.[8]

Patients with NCPF generally have good liver function and a lower incidence of post-shunt encephalopathy.[9,10] For elective therapeutic splenorenal shunt procedures (to forestall a second or subsequent bleed) the reported mortality rates are also much lower than in cirrhotics.[11,12] We have performed 285 elective proximal lienorenal shunt (PLRS) operations in patients with NCPF with a low mortality rate (0.8%), low variceal re-bleeding rate (8%) and low post-shunt encephalopathy rate (13%).[12] We therefore reckoned, that in spite of their ineffectiveness in cirrhosis, it would be justifiable to perform prophylactic operations on a selected group of NCPF patients with high-risk varices and/or hypersplenism who came from rural areas of the country.

Methods

Between January 1976 and December 2001, 1180 patients with portal hypertension (extrahepatic portal venous obstruction: 720, NCPF: 323, cirrhosis: 94, hepatic venous outflow tract obstruction: 43) were operated on at the Department of Gastrointestinal Surgery, All India Institute of Medical Sciences. Of these, 45 patients (age range 12-45 years, median 23;

Table: Indications for prophylactic surgery and types of surgery done

Indication	Total No. (No. with painful spleen)	Proximal lienorenal shunt	Splenectomy and devascularization	Splenectomy
High-risk varices with/ without hypersplenism	28 (9)	27	1	-
Hypersplenism alone	17 (2)	14	1	2
Total	45 (11)	41	2	2

23 males) with NCPF underwent prophylactic surgery. The criteria for selection of patients for surgery were normal liver function tests, high-risk varices (grade III-IV with red color signs) with/without hypersplenism and who came from a rural area (Table).

Investigations performed included complete blood count, liver function tests, upper gastrointestinal endoscopy (barium swallow prior to 1980), Doppler ultrasound to evaluate portal venous system (splenoportovenogram prior to 1984), and liver biopsy during the operation. Patients underwent PLRS or splenectomy with/without devascularization. The technique for PLRS has been described earlier.[11,13] Hassab's technique for splenectomy and devascularization was followed where PLRS was not feasible (splenic vein damaged irreparably) or was considered inappropriate (splenic vein >2.5 cm and in the patient with microcephaly and mental retardation).[14]

Patients were followed up every three months for one year, every 6 months for the second, and yearly thereafter. Those who defaulted were sent postal questionnaires to ascertain their clinical status. They were asked regarding their current status, history of upper gastrointestinal bleeding, encephalopathy, pedal edema, ascites or any other complaints.

For this study all complications occurring within 30 days of the operation or during the same hospital admission (whichever was later) were regarded as early. All complications (including death) occurring beyond this period were considered as delayed.

Results

Forty-one patients underwent splenectomy and PLRS, 2 underwent splenectomy and devascularization and 2 underwent splenectomy alone (Table).

Liver biopsy in all patients was consistent with NCPF. The median operating time was 5 (range, 2 to 7) hours. Estimated median blood loss was 800 (range, 200 to 3500) mL. The median postoperative stay was 7 (range, 5 to 20) days. There was no operative mortality and none of the patients developed subphrenic collections or overwhelming post-splenectomy sepsis. There was no significant postoperative respiratory or wound-related morbidity.

Thirty-eight (84.4%) patients were followed up for 12-236 (median, 24) months. Of these, 18 developed delayed complications (detailed below); 20 (52.6%) were completely free of symptoms.

Upper gastrointestinal bleeding

Three patients developed upper gastrointestinal hemorrhage requiring hospitalization for management, at 3-10 years. In two patients the bleeding was from chronic duodenal ulcer, and in the third it was variceal. In the patients with duodenal ulcer the varices had disappeared in one and were present but not bleeding in the other. The latter patient had undergone splenectomy and devascularization. The patient with variceal bleeding had had a PLRS. Therefore, of 41 patients who had prophylactic PLRS only one bled from varices.

Late deaths

There were 2 late deaths (at 6 weeks and 10 years postoperatively). One of these was due to unknown cause. The other occurred in a patient who developed chronic renal failure due to membranoproliferative glomerulonephritis.

Post-shunt encephalopathy

Seven patients developed encephalopathy, of whom 3 also had myelopathy. Encephalopathy was mild in 4 patients and settled with oral lactulose, avoiding animal protein in diet, and taking 5-10 g of sodium benzoate daily. Among patients with myelopathy, 2 required shunt ligation and one underwent angiographic shunt embolization to ameliorate the debilitating symptoms. These patients have not had variceal bleeding and are on regular follow up.

Nephropathy

Three patients developed membranoproliferative glomerulonephritis. One died at 1 year of follow up from chronic renal failure. One other patient who was a known diabetic had both encephalopathy and nephropathy, the latter due to diabetic glomerulosclerosis.

Other morbidities

Two patients developed pulmonary arteriovenous fistulae with cyanosis and digital clubbing. Five patients developed ascites that needed treatment with diuretics. All these patients had patent shunts.

Effect on hypersplenism

The mean splenic weight was 1744 (range, 950-3500)

g. Hypersplenism, present in 41 (90%) patients, was reversed by surgery in all patients. Blood counts improved significantly with mean hemoglobin level rising from 8.7 (SD 2.6) g/dL to 12.2 (3.7) g/dL, leukocyte count from 3230 (1780) cells/ mm^3 to 8630 (1850) cells/mm^3, and platelet count from 117,000 (74400) cells /mm^3 to 177,600 (53300) cells/mm^3.

Discussion

During the period of this study, 272 patients with NCPF underwent elective PLRS for secondary prophylaxis of variceal bleeding. In this group, the elective operative mortality was <1%, rebleeding rate was 8%, and post-shunt encephalopathy rate was 13%. Kaplan-Meier analysis showed 15-year cumulative survival of 80% and median survival of 230 months.[12] Therefore we consider the lienorenal shunt an effective operation for secondary prophylaxis of variceal bleeding in NCPF, with acceptable long-term morbidity.

In this series, there was no operative mortality following either PLRS or splenectomy and devascularization operations. This is in accordance with our overall experience. We also achieved our primary objective by documenting a low rate of variceal bleeding (1/38; 2.9%) and preventing long-term deaths due to variceal bleeding. However this was achieved at a cost of high shunt-related morbidity (18/38; 47%) in the long term and two late deaths.

The encephalopathy rate (18.4%) was less than that reported following prophylactic shunt surgery in cirrhotics (~30%) but somewhat higher than that reported previously by our group in patients with NCPF (13%).[3-6,12] In a previous cohort study from our center we documented subclinical encephalopathy in 35% of patients with NCPF undergoing non-selective shunt surgery.[15] In the present series, in a majority of patients who developed clinically overt encephalopathy (5/7), the severity was mild. The encephalopathy could be managed on an outpatient basis with dietary modifications, use of sodium benzoate[16,17] and lactulose. Reoperation, at a later date, for shunt ligation was required in 2 patients who also had debilitating myelopathy. The relatively high rate of encephalopathy may reflect the damaging effect of diverting the portal blood flow from a liver that presumably has little functional reserve.

The occurrence of nephropathy (4 patients) is unpredictable and irreversible. In three cases renal biopsy showed membranoproliferative glomerulonephritis as the cause of the nephropathy. This was responsible for one of the late deaths noted in this series. Two patients have required long-term hemodialysis. Whether nephropathy is a consequence of the shunt or a result of the underlying etiology of NCPF remains unresolved. It has been previously shown that immune complex deposits are present in the glomeruli of NCPF patients even before a shunt has been constructed.[18]

If hypersplenism is associated with significant clinical sequelae, non-shunt procedures such as splenectomy and devascularization may be a viable option. In this regard, the Japanese multi-center study in cirrhotics, the only randomized controlled study so far that evaluated prophylactic esophagogastric devascularization, showed that the cumulative 5-year survival rate for the operated group was significantly higher (72%) than that of the non-operated group (45%), and the cumulative 5-year variceal bleeding rate was significantly lower in the operated group (7%) than the untreated controls (46%).[19] However, results obtained in cirrhotics cannot be entirely extrapolated to an NCPF population. Further, the number of patients who underwent devascularization in the present series is too small to draw any meaningful conclusion regarding its efficacy.

Regarding the use of a selective shunt, there is evidence that the distal lienorenal shunt loses selectivity after a year when collaterals form between the high-pressure greater splanchnic and low-pressure lesser splanchnic systems, and the ultimate incidence of encephalopathy after non-selective and selective shunts is almost the same.[20] Moreover, the very large spleens in patients with NCPF make the difficult selective shunt procedure more formidable. Warren *et al*[21] studied the effect of distal splenorenal shunt on hypersplenism and spleen size in 6 patients over 4.5 years. They found that spleen size reduced significantly and platelet count increased. However, Lodge *et al*[22] provide a contrary view to this. They found that the Warren shunt improved leukocyte and platelet counts in the short term but in the long term hypersplenism was not relieved, whereas PLRS was associated with a return to normal hematological values. This has been our experience as well.

The long-term outcome in this series and the above considerations have prompted us to change our policy with regard to prophylactic management of NCPF patients. There is evidence from the literature that endoscopic sclerotherapy and endoscopic variceal ligation may benefit non-cirrhotic patients (including NCPF) with bleeding varices. In one study from our institute, involving 60 NCPF patients, successful variceal obliteration by endoscopic sclero-

therapy was achieved in 88%, with a complication rate of 12%, variceal recurrence rate of 15% and mortality (due to variceal hemorrhage and encephalopathy) of 6.7% over a mean follow up of 19 months.[23] A recently published prospective randomized study by Sarin *et al*[24] showed that endoscopic variceal ligation was better than drug therapy alone (propranolol and isosorbide mononitrate) in preventing variceal rebleeding in patients with non-cirrhotic portal hypertension, albeit with a recurrence rate of 25% over a mean follow-up period of 24 months. But the number of patients with non-cirrhotic portal hypertension in this study was small and the rebleeding rate was higher than what we achieved following shunt surgery in NCPF. We believe that NCPF patients with high-risk varices, who have not bled, should be primarily offered endoscopic variceal ligation or sclerotherapy with or without propranolol for variceal eradication.[25] Since the natural history of varices in NCPF patients has not been well delineated, it is difficult to predict the clinical value and cost-effectiveness of such treatment in preventing deaths from variceal bleeding.

Despite the efficacy of surgery in preventing variceal bleeding, the high incidence of post-shunt morbidity does not justify its routine use in the prophylactic setting in patients with NCPF.

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