Section: Biochemistry

Original Research Article

SHORT-TERM AND LONG-TERM OUTCOMES OF PATIENTS UNDERGOING PROXIMAL SPLENORENAL SHUNT SURGERY: A CLINICAL ANALYSIS.

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ABSTRACT

Background: Two diseases, which are very common in developing countries and almost always present only with features of Non Cirrhotic Portal Hypertension (NCPH), include Non-Cirrhotic Portal Fibrosis (NCPF) and Extra-Hepatic Portal Vein Obstruction (EHPVO).[3] Proximal Spleno Renal Shunt (PSRS) is the most commonly performed shunt surgery for these patients.[5] Present study was aimed to clinically analyse the short-term and long-term outcomes of patients undergoing proximal splenorenal shunt surgery at a superspecialty hospital.

Material and Methods: Present study was Retrospective observational study from prospectively maintained database, conducted in patients who underwent proximal splenorenal shunt surgery (PSRS) done for EHPVO, NCPF, portal biliopathy.

Results: In the present study, a total of 30 patients with NCPH were studied. All the 30 patients (100%) had hematemesis in the pre-operative period. After surgery, none of the patients reported to have hematemesis. Preoperatively, 26 (86.7%) of patients had complained of Melena. After PSRS, all the 30 patients reported symptomatic relief from melena. This improvement was found to be highly statistically significant. (p - <0.0001). Pre-operatively, none of the patients revealed any history of hepatic encephalopathy. Post-operatively, in all the patients, there was improvement of anemia and normalization of leucocyte count and majority showed normal platelet count. There was no statistically significant difference between the pre – operative and post – operative liver function statuses except for total and conjugated bilirubin, which showed improvement after shunt surgery. Post-operatively, most of the patients had disappearance of varices and few patients had persistent varices, but reduced to grade I.

Conclusion: For patients of NCPH with recurrent GI bleeding and symptoms of hypersplenism and with dilated shuntable splenic vein, PSRS is a safe and effective single time solution with good shunt patency and no further episodes of GI bleeding with low mortality rate and favourable long term outcomes and improved quality of life.

Keywords: Non Cirrhotic Portal hypertension (NCPH), Non-Cirrhotic Portal Fibrosis (NCPF), Extra-Hepatic Portal Vein Obstruction (EHPVO), Proximal Spleno Renal Shunt (PSRS)

INTRODUCTION

Portal hypertension (PHT) is a clinical syndrome defined by a portal venous pressure gradient between the portal vein (PV) and inferior vena cava exceeding 5 mmHg.[1] Cirrhosis is the most common cause of portal hypertension but portal hypertension

can also be present in the absence of cirrhosis, a condition referred to as "Non Cirrhotic Portal Hypertension" (NCPH).[2] Two diseases, which are very common in developing countries and almost always present only with features of PHT, include Non-Cirrhotic Portal Fibrosis (NCPF) and Extra-Hepatic Portal Vein Obstruction (EHPVO).[3]

NCPH presents with upper gastrointestinal bleeding, splenomegaly, transient ascites after gastrointestinal bleeding, features of hypersplenism, growth retardation, and jaundice due to portal hypertensive biliopathy. Other sequelae include hyperdynamic circulation, pulmonary complications, and other effects of portosystemic collateral circulation like portosystemic encephalopathy.[3]

Lowering the portal pressure by portosystemic shunts in these patients provides good control of variceal bleeding without the adverse effects of hepatocellular decompensation. Shunt surgeries still has an important place in the management of patients with noncirrhotic portal hypertension. Many of these patients have symptomatic splenomegaly and hypersplenism.[4] Proximal Spleno Renal Shunt (PSRS) is the most commonly performed shunt surgery for these patients.[5] A proximal lienorenal shunt removes the spleen in addition to effectively preventing variceal bleeding and is the most common portosystemic shunt procedure in India.[4] Present study was aimed to clinically analyse the short-term and long-term outcomes of patients undergoing proximal splenorenal shunt surgery at a super-specialty hospital.

MATERIAL AND METHODS

Present study was Retrospective observational study from prospectively maintained database, conducted in Department of Surgical Gastroenterology at Nizam's Institute of Medical Sciences(NIMS), Hyderabad, India. Study duration was of 10 years (January 2011 to December 2020). Study was approved by institutional ethical committee.

Inclusion Criteria

- Patients who underwent proximal splenorenal shunt surgery (PSRS) done for EHPVO, NCPF, portal biliopathy.

Exclusion Criteria

- Patients with documented chronic liver disease.
- Patients with mesocaval shunts & distal spleno renal shunt.

A detailed written informed consent was taken from all the study participants prior to enrollment into the study. Patient demographics, detailed history including symptoms of GI bleeding such as hematemesis, melena, symptoms and signs of hypersplenism such as petechiae, menorrhagia, epistaxis, gum bleeding, pallor etc. was noted. Standard clinical examination including neurological assessment for hepatic encephalopathy such as orientation with time, place and person, ability to write their own name (signature) and ability to perform number connection test properly, was performed.

All patients underwent investigations such as Complete blood picture, Renal Function tests, Liver function tests including Prothrombin time – INR (International Normalised Ratio), Ultrasound (USG) whole abdomen with colour doppler study & Upper GI endoscopy (UGIE)

Liver status was assessed in individual patients by evaluating Child – Turcotte – Pugh score as given below - by evaluating LFT reports (raised liver enzymes, total and conjugated bilirubin and Alkaline phosphatase [ALP] levels) and USG whole abdomen reports (echotexture of liver, dilatation of common bile duct with or without intra hepatic biliary radicle dilatation and ascites). Quality of life was assessed using SF-36 questionnaire.

Other relevant blood tests and consultations, as needed, was done for the patients with comorbidities like Hypertension, Diabetes, Coronary Artery Disease, Hypothyroidism etc. Contrast Enhanced Computerized Tomography (CECT) abdomen was done to check for patency of the shunts, if needed, when ultrasound whole abdomen gave equivocal or inconclusive reporting.

The outcomes are classified as short term and long term outcomes.

- Immediate short-term outcomes – (within 1 month of surgery): Includes post operative infection / fever, post splenectomy thrombocytosis and leucocytosis.
- Late short-term outcomes- (1 month to six months after surgery) - Recurrence of hematemesis or melena, shunt stenosis, shunt thrombosis and improvement in parameters related to hypersplenism (hemoglobin, total leucocyte count and Platelet count), quality of life after procedure.
- Long term outcomes (more than 6 months after surgery) – Recurrence of hematemesis or melena, shunt stenosis, shunt thrombosis, growth spurt in children, nephropathy, hepatic encephalopathy, quality of life after procedure.

All patients were evaluated with a doppler ultrasound to document the patency of the shunt. Visualization of the shunt and good flow through it was considered as direct evidence of patency. In cases where bowel gas obscured the shunt, dilated left renal vein, hepatopetal blood flow in splenic vein and absence of left upper quadrant collaterals, were also taken to be indirect evidences of shunt patency. If none of these findings were present, the shunt was labeled non-patent. If the findings of the ultrasound were equivocal, CECT was done to look for shunt patency. Routinely UGIE was done to see whether varices have decreased in size from the previous grade. If the varices have disappeared or decreased in size, it implies that the shunt is patent. However, in patients with a similar grade of varices

or equivocal colour doppler study, a CT portogram was planned to confirm the shunt patency.

Statistical analysis was performed using Graph pad prism version 9.1.2 (226) and Microsoft Excel. Continuous variables were presented as mean ± standard deviation for normally distributed data and median with interquartile range for non-parametric data and categorical variables were presented as absolute numbers and percentages. At first, univariate analysis was performed using unpaired t-test for normal data and Mann-Whitney test for nonparametric data for all the continuous variables and Chi square test for the categorical variables. $P < 0.05$ considered as statistically significant. Wilcoxon signed rank test was used to compare the variceal grades before and after surgery.

RESULTS

In the present study, a total of 30 patients with NCPH were studied. The mean age of the study population was 28 ± 10.5 years. There were 11 males and 19 females included in the study. There was a female preponderance (female: male = 1.7: 1). The mean BMI of the study population was in the range of 18.7 ± 2.7 kg/m^2. Out of the 30 patients included, 15 were diagnosed with NCPF and the rest 15 were having EHPVO. The median duration from diagnosis of the disease to surgery was found to be 3 years. The median duration of post shunt surgery follow up in this study is 5 years (60 months). The elective surgeries accounted for the majority.

Table 1: Baseline demographic profile of the study population

Parameter	Mean ± standard deviation / median (interquartile range)
Age (years)	28 ± 10.5
Gender	
Male,	11 (36.6)
Female	19 (63.3)
Height (cms)	154 (143, 160)
Weight (kg)	43 ± 12.3
BMI (kg/m^2)	18.7 ± 2.7
Diagnosis –	
NCPF	15 (50)
EHPVO	15 (50)
Duration of symptoms before surgery (years)	3 (2,4)
Duration from shunt surgery (months)	60 ± 22.2
Elective PSRS	28 (93.3%)
Emergency PSRS	2 (6.67%)

28 out of 30 cases (93.3%). Emergency surgeries accounted only for 2 cases (6.67%) which were indicated for massive uncontrollable gastrointestinal bleeding.

All the 30 patients (100%) had hematemesis in the pre-operative period. After surgery, none of the patients reported to have hematemesis. Preoperatively, 26 (86.7%) of patients had complained of Melena. After PSRS, all the 30 patients reported relief from melena. This improvement was found to be highly statistically significant. (p - <0.0001). Pre-operatively, none of the patients revealed any history of hepatic encephalopathy.

Post-operatively, none of the 30 patients presented with any obvious signs and symptoms indicating shunt stenosis and shunt thrombosis. Even on Colour Doppler study of Splenoportal axis, which was done as follow up investigation as per protocol, none of them demonstrated any evidence of shunt thrombosis or shunt stenosis.

Before surgery, half of patients had massive splenomegaly and the other half had moderate splenomegaly and all had one or the other symptoms or signs of hypersplenism namely, recurrent epistaxis, gum bleeding, menorrhagia, pallor etc. These symptoms improved drastically in all patients following splenectomy, which is performed as a part of PSRS.

In the pre-operative period, all the 30 patients had pain due to moderate to massive splenomegaly. After PSRS, all the patients reported relief of pain.

Pre-operatively majority of the patients were having severe anemia, leucopenia and thrombocytopenia. Post-operatively, in all the patients, there was improvement of anemia and normalization of leucocyte count and majority showed normal platelet count. There was highly significant improvement in hemoglobin, total leucocyte count and platelet count, post shunt surgery (p <0.0001).

Table 2: Comparison of pre- operative and post operative hemogram

Parameter	Values expressed as mean ± standard deviation / median (interquartile range)		P value
	Pre operative values	Post operative values	
Haemoglobin (g/dl)	6.7 (6.4,7.5)	11.3 (10.4,12.4)	<0.0001*
Total leucocyte count (per cumm)	1850 (1375, 3425)	6500 (5600, 7625)	<0.0001*
Platelet count (lakhs per cumm)	30000 (20000, 40000)	185000 (150000, 232500)	<0.0001*

Pre-operatively, Urea and Creatinine were found to be within normal limits for all the patients. During post – operative follow up visits, urea and creatinine were repeated and were found to be within normal limits, which indicated absence of nephropathy in all the study patients after shunt surgery.

Table 3: Comparison of pre- operative and post operative renal status

Parameter	Expressed as mean ± standard deviation / median (interquartile range)		P value
	Pre operative values	Post operative values	
Urea (mg/dl)	26.5 (24, 29.25)	25 (18, 28)	0.07
Creatinine (mg/dl)	0.71 ± 0.24	0.7 ± 0.23	0.87

There was no statistically significant difference between the pre – operative and post – operative liver statuses except for total and conjugated bilirubin, which showed improvement after shunt surgery.

Table 4: Comparison of pre- operative and post operative liver statuses

Parameter	Values expressed as mean ± standard deviation / median (interquartile range)		P value
	Pre operative values	Post operative values	
AST (U/L)	77.9 ± 18.4	73.8 ± 21.6	0.44
ALT (U/L)	77.9 ± 17.2	73.8 ± 22.6	0.43
ALP (U/L)	124.9 ± 30	121.2 ± 34.1	0.65
Total bilirubin (mg/dL)	0.9 (0.8, 1.1)	0.8 (0.58, 0.9)	0.028*
Conjugated Bilirubin (mg/dl)	0.5 (0.4, 0.8)	0.4 (0.3, 0.5)	0.0085*
Total protein (g/dl)	7.2 (6.4, 7.3)	7.4 (6.8, 7.5)	0.08
Albumin (g/dl)	3.6 (3.2, 4.2)	3.7 (3.4, 4.2)	0.36
INR	1.05 (0.9, 1.1)	0.9 (0.8, 1.13)	0.65
Child-Turcotte- Pugh score	6 (5,6), Child A	5 (5,6), Child A	0.44

Post-operatively, most of the patients had disappearance of varices and few patients had persistent varices, but reduced to grade I. UGIE showed highly significant improvement in the variceal grades post – operatively, compared to pre-operative variceal grades (p – 0.000) by Wilcoxon signed rank test. Post – operative UGIE showed evidence of portal hypertensive gastropathy in 6 patients.

Table 5: Comparison of pre- operative and post operative UGIE findings

	Variceal grades	Proportion of patients, n (%)
PRE-OPERATIVE UGIE	Grade III	30 (100%)
	Grade II	11 (36.7%)
Esophageal varices (EV)	EV	18 (60%)
	Grade III	13 43.3%)
	1 column	6
	2 columns	7
	Grade II - 3 column	5 (16.6%)
Gastroesophageal varices (GOV)	GOV	9 (30%)
	GOV – 1 Grade III – 2 columns	8
	GOV – 2 Grade III - 2 column	1
Isolated gastric varices (IGV)	IGV	21 (70%)
	IGV 1 Grade III	17
	IGV 2 Grade II	4
POST-OPERATIVE UGIE	No varices	25 (83.3%)
	Grade I	5 (16.6 %)
Esophageal varices (EV)	EV Grade I – 1 column	3 (10%)
Isolated gastric varices (IGV)	IGV 2 Grade 1	2 (6.7%)

Pre-operatively, all patients had splenomegaly and peri-portal collaterals. Half of patients had portal cavernoma and dilatation of portal vein and one third of the patients had peripheral pruning of portal vein branches. Post operatively, in all the patients, hepato-petal flow was documented.

Table 6: Comparison of pre- operative and post operative USG & Doppler

PRE-OPERATIVE USG & DOPPLER FINDINGS	Proportion of patients, n (%)
Normal echotexture of Liver	30 (100%)
Moderate splenomegaly	15 (50%)
Massive splenomegaly	15 (50%)
Presence of periportal collaterals	30 (100%)
Presence of portal cavernoma	15 (50%)

Dilatation of main portal vein	15 (50%)
Peripheral pruning of portal vein branches	10 (33.33 %)
POST - OPERATIVE USG & DOPPLER	Proportion of patients, n (%)
Normal echotexture of Liver	30 (100%)
Hepato-petal flow	30 (100%)
Patent shunt with patent splenic vein and left renal vein	30 (100%)

The growth parameters were assessed separately in a subgroup of 8 patients who were below 16 years of age at the time of shunt surgery. There was significant improvement in height, weight and BMI post operatively compared to pre-operative status. Although we analysed weight and BMI before and after shunt surgery, height is considered as the sole parameter, indicative of growth spurt. All patients had improvement in height, however, it is difficult to distinguish between growth spurt and regular growth retrospectively.

Table 7: Comparison of pre- operative and post operative growth parameters

Parameter	Values expressed as mean ± standard deviation / median (interquartile range)		P value
	Pre operative values	Post operative values	
Mean age	15.75 ± 4.3	11.63 ±3.4	0.05
Height	135.5 (130.8, 141)	158 (145.8,159.8)	0.012*
Weight	28.1 ± 8.3	45 ± 8.7	0.001*
BMI	16.1 ± 1.67	19.8 ± 1.9	0.0009*

Comparison of the quality of life scores before and after PSRS assessed by SF- 36 questionnaire. It demonstrated highly significant improvement in the scores (p - <0.0001*) post-surgery in each of the domains namely physical functioning, role limitation due to physical health and emotional problems, energy/ fatigue, emotional wellbeing, social functioning, pain and general health. This indicated that the quality of life of patients who underwent shunt surgery improved significantly compared to their pre – operative status.

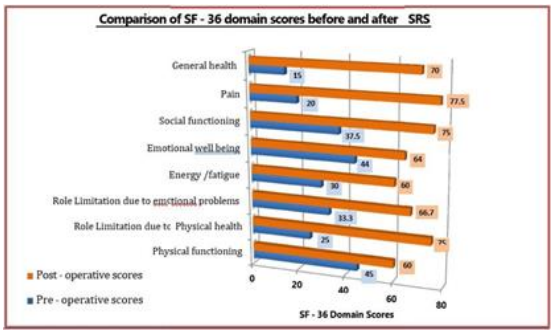

Figure 1: Comparison of SF-36 domain scores before and after PSRS

Figure 2: Ultrasound showing the left Renal vein, shunt and splenic vein

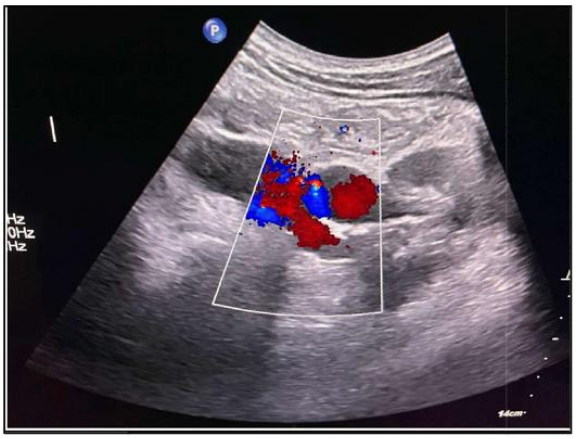

Figure 3: Dopler showing flow in the shunt

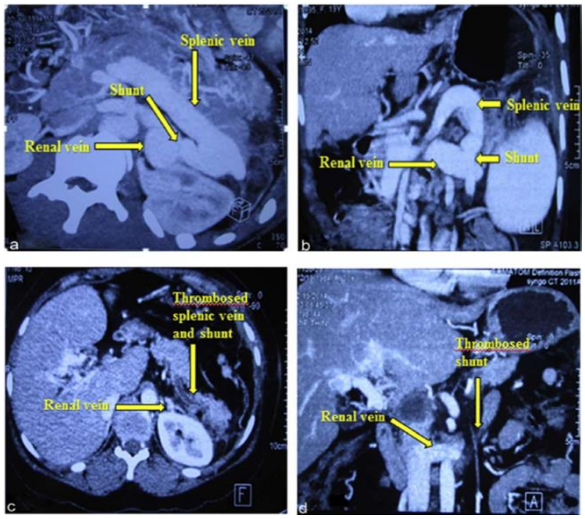

Figure 4: Dynamic CT portography images of proximal splenorenal shunt: a) axial view of patent shunt b) coronal view of patent shunt, c) axial view of blocked shunt, d) coronal view of blocked shunt.

DISCUSSION

EHPVO and NCPF constitute 20- 30% of cases of portal hypertension in developing countries like India.[6] EHPVO is the most common cause of PHT in children from the developing world.[7] The majority of patients with these conditions present with variceal bleeding. In addition, significant morbidities arise from hypersplenism, portal biliopathy, growth failure and ectopic varices. Management of these patients is therefore not restricted to treatment of variceal bleeding alone. Shunt surgery is a safe and effective procedure that not only prevents variceal bleeding but also takes care of other morbidities associated with EHPVO/NCPF. It is a good one time treatment option for patients with limited access to blood transfusion facilities and endoscopic therapy.[6]

PSRS has been shown to be effective in not only preventing variceal bleeding but also in managing associated hypersplenism and portal biliopathy.[8,9] But at times, there can be some short term and long term complications reported to manifest after PSRS namely, infections (OPSI – Overwhelming Post Splenectomy Infection), recurrence of GI bleeding presenting as hematemesis and melena, shunt stenosis or thrombosis etc. Hepatic encephalopathy is a long term complication and rarely nephropathy and myelopathy can also occur, both of which are unpredictable and irreversible.[9,10]

In our study, we studied the outcomes of 30 patients who underwent PSRS in NIMS hospital in the past 10 years (2011 – 2020). In our study, there were no episodes of hematemesis or melena after PSRS in any of the patients. According to Pande et al,[11] the rebleeding rates of esophageal varices are low in patients of NCPH treated with proximal splenorenal shunts. In the study by Anand et al,[12] in patients with a mean follow-up period of 3.4 years, the rebleeding rate was only 10% and was successfully managed by endoscopic therapy. It was concluded that, PSRS was effective in controlling gastric variceal hemorrhage in 92% (23 of 25) of patients with preserved liver function.[12]

In a study by Hao Chen et al,[13] it was reported that 98 patients with Child A and B variceal hemorrhage who underwent small diameter (7-10 mm) PSRS, the mean free portal pressure and flow rate of main portal vein decreased significantly compared with that before operation. The rates of peri-operative rebleeding and mortality were 6.12% and 2.04%, respectively. Furthermore, out of 98 patients, 91 patients were followed up for a median period of 48.57 months (7 months to 14 years). It was found that long term rates of rebleeding was 4.4% (4 patients had rebleeding, of which 2 had hematemesis and 2 had melena). Rebleeding rate in the peri-operative period (6.12 %) was reasonable considering that the main cause of bleeding was thrombosis. When compared with the results from other types of small-diameter portacaval shunt, the long-term rebleeding rate was relatively low (4.04%). The 5 year survival rate was 82.12%. From this study, it was confirmed that small-diameter PSRS could effectively prevent variceal rehemorrhage.[13] In conclusion, small-diameter proximal splenorenal shunt surgery can be performed successfully in patients with better liver function.[13]

In our study, there were no reports of shunt stenosis and shunt thrombosis. There was 100% shunt patency till our follow up period. Though our early results of shunt patency are good, we need to follow up these patients for long term to come to a definitive conclusion. Our results are correlating with results of other similar studies. Bismuth et al. has reported shunt patency rates of 96% with PSRS in EHPVO, [14] although the shunt thrombosis occurred in 20% of the patients during the mean follow up period of 3.4 years.[12] According to Mishra et al.,[6] the overall shunt patency rates were 70%, 40% and 60% using clinical parameters, colour Doppler and Dynamic CT portography respectively. Patients with NCPF had a greater shunt patency rate compared to those with EHPVO i.e. 75% vs. 55%, though the difference was not statistically significant (P = 0.430). The shunt patency rates decreased over time. They were 64%, 60% and 43% in the first year, 1 - 5 years and 5 years onwards respectively. Mishra et al,[6] reported that 25% (3/12) of NCPF patients developed the shunt blockage during follow up. In the study by Saluja et al,[8] shunt blockage rate was 1/16 (6.25%).

In our study, none of 30 patients developed signs and symptoms of hepatic encephalopathy. This was comparable with other similar study results. Hao Chen et al,[14] reported that, encephalopathy developed in 3 patients (3.30%) on long term follow up after small diameter PSRS. Prasad et al,[15] reported that, out of 160 patients, no patients developed encephalopathy. Saluja et al.,[8] reported about post-shunt encephalopathy in 2 out of 16 patients, who underwent PSRS for NCPF, which was managed with oral lactulose. The overt hepatic encephalopathy rate of 12.5% shown in a study by Saluja et al,[8] was comparable to a previous study done by Pal et al,[16] where cirrhotic patients were included and 13% of patients developed hepatic encephalopathy.

In our study, we studied about hypersplenism parameters before and after surgery. Our results correlate with results of other similar studies. In a study by Saluja et al,[8] where splenectomy was compared with PSRS, the median hemoglobin increased from 8 to 9.5 mg/dl, leucocyte count from 2500 to 8200 / cumm and platelet count from 49000 to 411000 / cumm. In a study by Anand et al,[12] it was demonstrated that, hypersplenism got reversed in all the 25 patients after PSRS. According to Botha et al,[17] 12 patients who presented with hypersplenism as defined by a platelet count less than 200,000/mm^3 and a white cell count 5000/mm^3,

reported reversal in 7 out of 10 patients at a late follow up period.

In our study, we didn't find any nephropathy or myelopathy on follow up. In the study by Saluja et al.,[8] post-PSRS nephropathy or myelopathy was not encountered. In previous study by Pal et al,[16] post-PSRS 4/41 (9.7%) of NCPF patients developed nephropathy, 2 patients needed long-term hemodialysis and one patient died. The cause of nephropathy post PSRS in NCPF is not clear and it may be either due to underlying etiology or consequence of shunt surgery. In study by Prasad et al.,[15] one patient died in the follow-up period due to chronic renal failure. In a study by Anand et al,[12] no patients developed any complications such as post-shunt encephalopathy, myelopathy, and nephropathy until the last follow up.

In our study, 8 out of 30 patients who underwent PSRS at the age below 16 years, had improvement in height. However, it is difficult for us to differentiate regular growth from growth spurt in a retrospective study like ours. In a study by Radhakrishna et al,[7] it was observed that a significant improvement in growth occurred after surgery, as evidenced by increase in the median height z scores increased from -1.7 (-0.5 to -2.8) before surgery to -0.8 (0.6 to -2.6, P = 0.05) after surgery.

In our study, we assessed QOL of 30 patients before shunt surgery and after a median post-surgery follow up of 3 years. To the best of our knowledge, this is first study using SF 36 questionnaire for assessment of QOL among patients undergoing PSRS. In our study, there was highly significant improvement in the SF - 36 scores (p - <0.0001*) after shunt surgery in each of the domains compared to the pre-operative scores. The median scores of the domains were ranging between (15 – 45) pre operatively, which increased significantly to scores ranging between (60 – 77.5) in the post-operative period, which indicates that there is great improvement in quality of life post shunt surgery.

Compared with controls, patients with EHPVO had lower median QOL scores in physical, emotional, social, and school functioning health domains.[7] Children with EHPVO have a poor QOL that is not affected by variceal eradication. We have noticed repeated hospital admissions and multiple endoscopic procedures in these patients before surgical intervention. These patients had low QOL scores pre-operatively, which got improved significantly after PSRS.

On multivariate regression analysis, splenic size and growth retardation were also found to be independent predictors that affect the QOL. After surgery, a trend towards improvement in physical, psychosocial, and total QOL scores was observed, but it was not significant.[7] This could be due to a short time interval (median 1.0 year, range 0.1– 5.5 years) between surgery and QOL assessment, parental anxiety after a major surgery causing voluntary limitation of the child's activities, such as play and school attendance and smaller number of subjects in the post-surgery group. Repeated assessment on a long term follow-up may help to clarify this aspect.[7,18]

CONCLUSION

For patients of NCPH with recurrent GI bleed and symptoms of hypersplenism and with dilated shuntable splenic vein, PSRS is a safe and effective single time solution with good shunt patency and no further episodes of GI bleed with low mortality rate and favourable long –term outcomes and improved quality of life.

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