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DISTAL SPLENORENAL SHUNT IN SURGICAL TREATMENT OF PORTAL HYPERTENSION IN CHILDREN

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Background. Management of pediatric patients with portal hypertension (PH) has evolved considerably in recent years. Physiologic shunts and successful liver transplant has changed the paradigm of portal hypertension surgery. However, pediatric patients with noncirrhotic causes of PH and unfavorable anatomy, and patients with cirrhotic causes require other radical surgical approaches. There is a lack of publications on pediatric cohorts in which other surgical procedures, including DSRS, was performed.

Aim: to analyze effectiveness of DSRS in treatment of most dangerous PH symptoms: esophageal varices grade and bleeding episodes recurrence, splenomegaly, thrombocytopenia and anemia, and to assess DSRD survival in different groups of patients.

Materials and methods. A single-center retrospective study was performed. In 37 children underwent distal splenorenal shunt (DSRS) was performed in the period from January 2011 to January 2022. The mean follow-up period was 55.4±6.1 months.

Results. Patients of the study group (n=37,100%) were divided into two groups according to etiological factor, that caused PH: 29 (78.3%) were diagnosed EHPVO, and 8 (21.7%) – HPH. Comparison showed difference in spleen volume (p=0.009) and follow-up duration (p=0.001). DSRS resolved thrombocytopenia, anemia and decreased the spleen size in all the patients, platelets count increase in patients of both EHPVO (p=0.009) and HPH patients (p=0.021) and hemoglobin level increase in EHPVO patients (p=0.037). Varices grade comparison showed involution in both groups (p<0,001). However, DSRS dysfunction was observed in 8 (28.5%) patients from EHPVO group and in 1(12.5%) in HPH group. DSRS survival in EHPVO patients was assessed 0.309 (95%CI 0.0186-0.708) with no difference in overall shunt survival between groups.

Conclusion. DSRS showed good results in resolving dangerous symptoms of PH in both study groups with non-cirrhotic (EHPVO) and cirrhotic (HPH) causes of PH, with significant thrombocyte count increase and varices grade involution. However, despite no difference was found in DSRS survival between study groups, DSRS survival in patients with EHPVO reached median survival by 136 months.

Key words: portal hypertension, distal splenorenal shunt, shunt dysfunction, recurrent variceal bleeding, children.

Background. Management of pediatric patients with portal hypertension (PH) has evolved considerably in recent years. Development of physiologic shunts (meso-Rex bypass) and successful liver transplant has changed the paradigm of portal hypertension surgery. [1]. Surgical treatment is typically reserved for those patients who have failed medical and endoscopic measures, or who have significant sequela of portal venous hypertension, including significant splenomegaly [2]. While it is world-wide accepted, that children with extrahepatic portal vein obstruction (EHPVO) and PH that results from it are to be investigated and, if suitable, offered the mesenteric-to-left portal vein bypass [3,4], for children with hepatic form of portal hypertension (HPH), other words it is in the setting of decompensated liver disease it is mostly offered to manage medically (via endoscopy) or radiologically (via transjugular intrahepatic portosystemic shunt) with the aim to offer liver transplant after this initial treatment [1,2,5]. There is a lack of publications on pediatric cohorts in which other surgical procedures, including DSRS, was performed.

Aim: to analyze effectiveness of DSRS in treatment of most dangerous PH symptoms: esophageal varices grade and bleeding episodes recurrence, splenomegaly, thrombocytopenia and anemia, and to assess DSRD survival in different groups of patients.

MATERIALS AND METHODS

Patients data were collected from case-records retrospectively. 308 case histories of children diagnosed portal hypertension were analyzed, in the period from January 2011 to January 2022, 226 (73.3%) out of which underwent surgical treatment. In 37 (16.4%) children distal splenorenal shunt (DSRS) was performed. The mean follow-up period was 55.4±6.1 months.

For all patients, the following criteria were analyzed: gender, age of disease debut, variceal bleeding as initial symptom, underlying pathology, basic laboratory (thrombocytes count and hemoglobin level) and ultrasound results (initial and following spleen volume), endoscopic examination results (initial and following varices grade), recurrent bleeding episodes, shunt dysfunction. Examination was as follows: CBC with thrombocytes count, ultrasonography (US) in gray scale with spleen volume measurement (using the standard prolate ellipsoid formula: length × width × depth × 0.523), color Doppler, and spectral Doppler tracings, using Samsung RS80A-UA, convex transducer (mean frequencies 1–7 MHz). Endoscopy was performed using endoscopes GIF-H185, GIF-Q150, GIF-XQ260, Olympus LTD, Japan. Esophageal varices grade was assessed according to Japanese Research Society for Portal Hypertension [6]. DSRS was performed according to a standard method [7] by the same surgeon.

Statistical analysis was preformed using IBM SPSS for Windows version 24.0 (IBM Corp., Armonk, NY) and EZR Statistical Software, v.1.6 (The R Foundation for Statistical Computing). Data distributions were compared (for different surgical methods) using the paired Student's t-test or Wilcoxon criteria. Kaplan-Meier estimator was used to assess shunt survival. Scheffe's test, Kruskal-Wallis and dispersion analysis were used for multiple comparisons, and Dunn test were used to compare the endoscopic follow-up results. Chi-square test was used to assess nonparametric data analysis for varices regression assessment. A P-value <0.05 was considered statistically significant.

The Committee on Clinical Investigation of Bogomolets National Medical University approved this study (Protocol №141 27.01.2021). All the studies were conducted according to implemented guidelines in consideration of GCP-ICH, Declaration of Helsinki and declaration of Istanbul. The written informed consent of all participants' parents/guardians was achieved.

RESULTS

Patients of the study group (n=37,100%) were divided into two groups according to etiological factor, that caused PH: 29 (78.3%) were diagnosed EHPVO, and 8 (21.7%) – HPH. The EHPVO was confirmed in all patients by ultrasound with a sonographic Doppler study of the portal system and computed tomography. Underlying liver disease when suspected was confirmed by liver biopsy before the surgery.

In EHPVO group 13(35.1%) had umbilical catheter in anamnesis because of complicated labor and delivery, that required following treatment within neonatal intensive care unit. In 24(64.9%) patients EHPVO was considered idiopathic.

In PH group biopsy showed idiopathic fibrosis in 4(50%) patients. Other diagnoses included Polycystic kidney disease accompanied by liver fibrosis (n=2; 25%), cystic fibrosis (n=1; 12.5%), and autoimmune hepatitis (n=1; 12.5%).

Comparison of the study groups' homogeneity according to the primary clinical, ultrasound, laboratory and endoscopic examination at initial admission are represented in Table 1.

As it is seen, no significant difference revealed between groups except the spleen volume which was greater in PHP patients (p=0.009) and the general follow-up of the EHPVO patients is longer (p=0.001). In general, most patients of both groups presented symptoms of OH, such as splenomegaly, hypersplenism (here - thrombocytopenia), anemia, high grade varices and variceal bleeding episodes.

The indications to operation were high grade (II-III), manifestation of preoperative recurrent bleeding episodes, significant splenomegaly with thrombocytopenia progression. All the patients from PHP group were additionally assessed by standard scales for end stage liver diseases [8,9] to

Table 1

Comparison of the study groups' homogeneity according to the primary clinical, ultrasound, laboratory and endoscopic data

Variable	Patients with EHPVO	Patients with HPH	P value
Sex (%) Male Female	19 (67.8%) / 9 (32.2%)	4 (50%) / 4 (50%)	0.620[1]
Age at diagnosis (median (Q1÷Q3))	5 (3÷9)	11 (7÷16)	0.250[2]
Platelets count per mm3 (median (Q1÷Q3))	81 (65÷121)	56 (48÷86)	0.052[2]
Hemoglobin level g/l (median (Q1÷Q3))	93.5 (82÷110)	97 (85÷106)	0.924[2]
Spleen volume (cm3) (median (Q1÷Q3))	384 (276÷420)	863 (420÷1104)	0,009[2]
Esophageal varices grade II-III (%)	25 (89.2%) / 3 (10.8%)	6 (75%) / 2 (25%)	0.670[3]
Variceal bleeding as a debute sign(%) YesNo	19 (67.8%) / 9 (32.2%)	3 (37.5%) / 5 (62.5%)	0,266[1]
Preoperative recurrent bleeding episodes (%) YesNo	6 (21.4%) / 22 (78.6%)	2 (25%) / 6 (75%)	0.789[1]
DSRS dysfunction (%) YesNo	8 (28.5%) / 20 (71.5%)	1 (12.5) / 7 (87.5%)	0.634[1]
Follow up, months (mean±SD)	61.79±7.4	30.38±4.95	0,001[4]

assess the stage pf pathogenic process in dynamics, and surgery was considered only when the patients was assessed, as stable, with scores not more than 10 in both scales. Early postoperative period was uneventful in all patients.

DSRS dysfunction was observed in 8 (28.5%) patients from EHPVO group; shunt thrombosis, accompanied by a recurrent bleeding and splenomegaly with thrombocytopenia progression occurred in a period from 1 week to 136 months after surgery. All patients with DSRS dysfunction underwent repeated surgeries, among which . In HPH group (n=1,12.5%) patient manifested recurrent bleeding 24 months after initial shunting procedure. DSRS thrombosis was diagnosed and splenectomy with complete portoazygos disconnection.

Kaplan-Meyer survival analysis was performed to estimate and compare DSRS survival in both groups of patients (Fig. 1).

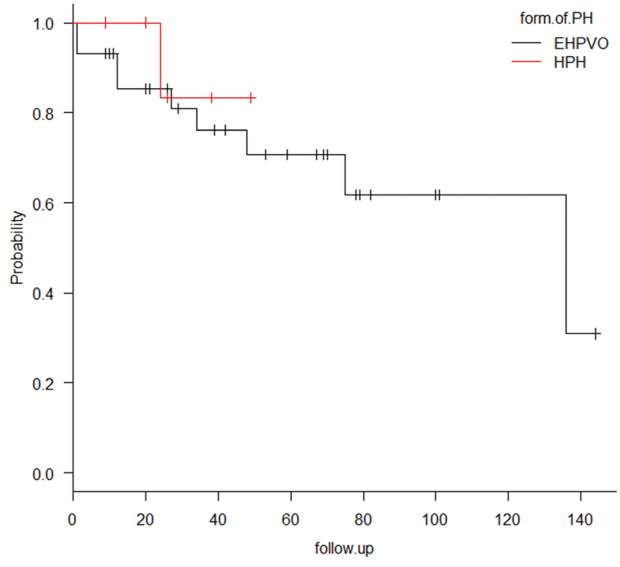

Fig. 1. Shunt survival (Kaplan-Meier curve) for DSRS in patients with HPH (red uniform line) 0.833 95%CI(0.237-0.975), versus DSRS in patients with EHPVO (black uniform line) 0.309 95%CI(0.0186-0.708)

Median overall shunt survival was not reached by the patients of the HPH group. No difference was found in the survival between two groups (p=0.631).

The dynamics in laboratory tests, spleen volume, between initial admission, the first postoperative month after DSRS and the end of study period (long-term follow up) is shown in Table 2. The results were compared in pure DSRS (n=20 in EHPVO group and n=7 in HPH group), patients after repeated surgical interventions are excluded from the comparison.

Notes: 1 Kruskal-Wallis test; 2 multiple comparison, dispersion analysis; 3 Scheffe test.

DSRS resolved thrombocytopenia, anemia and decreased the spleen size in all the patients, with significant difference achieved in platelets count increase in patients of both EHPVO and HPH groups (p=0.009 and p=0.021 correspondingly) and in hemoglobin level increase in EHPVO patients (p=0.037)

As the first endoscopy is performed not earlier than 6 months after the surgery, endoscopy results were not included into the Table 2. By the time the study was completed, the decrease in varices grade was observed in most patients, grade I varices were registered in 14(65,5%) patients of EHPVO group and in 7(100%) in HPH group. Chi-square test was used to analyze the varices involution and revealed the difference p<0,001 between initial and long-term endoscopic results in both EHPVO and HPH patients.

There was zero mortality in both study groups.

DISCUSSION

Symptomatic PH in pediatric patients manifests with life-threatening symptoms, such as variceal, and others, such as such as splenomegaly, hypersplenism, anemia, ascites [2,3,6,10]. bleeding EHPVO in pediatric patients is the main cause of portal hypertension [1,9]. Despite the successful development of endoscopic treatment methods, where band ligation showed its effectiveness in primary bleeding prophylaxis in pediatric patients [6], the method is temporal and does not influence the portal pressure as is [1,6,11,12], while the mortality from variceal bleeding in pediatric population remains high, assessed up to 19% [12]. Against the background of the lack of worldwide standardized surgical approaches to the PH treatment in children, all prominent clinics and authors agreed Rex(mesoportal) shunt to be the golden standard of PH surgical treatment [1-4,13,14], though since its first description it was clear favorable anatomy is required for Rex-shunt to be feasible [2,4,14].

Table 2

Comparison of the experimental groups' primary, postoperative and final US and laboratory results

Variable		Primary results	Postoperative	Final results	p-value
Spleen volume	EHPVO	540 (275÷689)	401 (330÷481)	386 (228÷545)	0.250[1]
(cm3) (median (Q1÷Q3))	PHP	774.4 (420.4÷1128)	494.1 (274.7÷713.5)	436.7 (256.5÷616.9)	0.084[1]
Platelets count per mm3 (median (Q1÷Q3)) (mean±SD)	EHPVO	79.5 (55÷102)	93.5 (78÷156)	122 (96÷168)	0,009[1]
	PHP	67±9.8	142.1±24.4	158±27..7	0.021[2] 0.03[3]
Hemoglobin g/l (mean±SD)	EHPVO	94.8±5.4	99.25±3.7	110.1±3.08	0.037[2] 0.04[3]
	PHP	97.0±4.3	115.7±8.6	116.3±9.8	0.161[2]

Moreover, the so called "golden standard" of PH surgical treatment cannot be used in patient with HPH, as their portal vein is safe, and the shunting would not influence the resistance of liver parenchyma, and therefore, would not decrease the portal pressure [2,5,6,15]. Other surgical options are to be thought of in EHPVO patients with unfavorable anatomy and for HPH patients. In one of the earliest publications, in 1978 Maksoud et. al. described the group of 7 pediatric patients with cirrhosis and symptomatic PH, in which DSRS, end-to-side anastomosis, was considered safe and effective for leaving the intestinal portal inflow into the liver without changes [16].

Nevertheless, two of seven described shunts developed thrombosis. In later publication by Moon et. al. [17] we find a group of 10 EHPVO and 5 cirrhotic pediatric patients, in which indication to DSRS was severe thrombocytopenia, successfully treated by the shunting procedure. In general, most described groups are relatively small, with relatively short follow up period. The indications for DSRS in EHPVO patients of our study were based on peculiarities of vascular anatomy and vessels patency. As for HPH patients, DSRS is called the "bridge" to transplantation by some authors [17,18], not causing the major changes in vascular anatomy and having more positive results regarding encephalopathy in comparison to TIPS. In our study the HPH patients were selected for DSRS considering mentioned details, and their continuous liver function stability according to accepted liver end stage diseases scales. The results of current study confirmed the results of previous smaller groups regarding the ability of DSRS to resolve varices, and signs of cytopenia.

Moreover, in both groups insignificant spleen volume decrease was observed, and hemoglobin level increase, significant in EHPVO patients. At the same time, DSRS survival is to be discussed separately: in EHPVO group it was assessed 0.309 95%CI 0.0186-0.708, with 9(32.2%) cases of shunt thrombosis occurred. Authors hypothesis is – the surgical approach results into the division of the portal system into the "left" (splenic) and "right" (splanchnic), with following portal pressure increasement within the left one, and new collaterals around spleen and pancreas appearance to compensate the high portal pressure again.

Thus it might reduce the flow within DSRS, the shunt becomes deserted and thrombosis develops. As a PH treatment option, DSRS must be considered effective in thrombocytopenia resolving and varices involution.

CONCLUSION

1. DSRS showed appropriate results in resolving dangerous symptoms of PH in both study groups with non-cirrhotic (EHPVO) and cirrhotic (HPH) causes of PH, with significant thrombocyte count increase in both groups (p=0.009 in EHPVO patients and and p=0.021 in HPH patients).
2. Varices grade involution was also significant in both study groups (p<0,001). However, despite no difference was found in DSRS survival between study groups, DSRS survival in patients with EHPVO was 0.309 95%CI 0.0186-0.708, reaching median survival by 136 months, which might result from division of portal system into "left" and "right" with following portal pressure increasement and new collaterals appearance; thus shunt becomes deserted and thrombosis develops. Further studies are required to prove this hypothesis.

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Conflict of interests. The authors of this manuscript claim that there is no conflict of interest during the research and writing of the manuscript.

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Consent to publish and contributions. Author conceived the study, performed experiments and analyzed the data, drafted the manuscript, revised it, critically reviewed and approved the final manuscript.

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ДИСТАЛЬНИЙ СПЛЕНОРЕНАЛЬНИЙ ШУНТ ПРИ ХІРУРГІЧНОМУ ЛІКУВАННІ ПОРТАЛЬНОЇ ГІПЕРТЕНЗІЇ У ДІТЕЙ

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Актуальність. За останні роки лікування дітей із портальною гіпертензією (ПГ) значно вдосконалилося. Фізіологічне шунтування та успіхи в трансплантації печінки змінили парадигму хірургії портальної гіпертензії. Проте діти з нециротичними причинами ПГ і несприятливою анатомією, а також пацієнти з циротичними причинами потребують інших радикальних хірургічних підходів. Публікацій про педіатричні когорти, яким виконувалися інші хірургічні втручання, у тому числі дистальне спленоренальне шунтування (ДСРШ), недостатньо.

Ціль: проаналізувати ефективність ДСРШ у лікуванні найбільш небезпечних симптомів ПГ: рецидивів кровотечі з варикозного розширених вен стравоходу, спленомегалії, тромбоцитопенії та анемії, а також оцінити виживаність при ДСРШ у різних групах пацієнтів.

Матеріали та методи. Проведено одноцентрове ретроспективне дослідження. 37 дітям у період з січня 2011 р. по січень 2022 р. виконано ДСРШ. Період спостереження склав 55,4±6,1 міс.**Conclusion.** Stress echocardiography with strain imaging during intravenous dipyridamole was an effective method for simultaneously detecting violation of the coronary vasodilatation reserve and confirming the myocardial ischemia.

Результати. Пацієнти (n=37100%) були розподілені на дві групи за етіологічним фактором, що спричинив ПГ: у 29 (78,3%) діагностовано допечінкову (ДфПГ), у 8 (21,7%) – печінкову (ПфПГ) форму ПГ. Порівняння груп показало різницю в об'ємі селезінки (p=0,009) і тривалості спостереження (p=0,001). ДСРШ усунула тромбоцитопенію, анемію та зменшила розмір селезінки в усіх пацієнтів, збільшилася кількість тромбоцитів у пацієнтів як з ДфПГ (p=0,009), так і з ПфПГ (p=0,021), а також підвищився рівень гемоглобіну у пацієнтів з ДфПГ (p=0,037). Порівняння ступеня варикозу показало інволюцію в обох групах (p<0,001). Дисфункція ДСРШ спостерігалась у 8 (28,5 %) пацієнтів групи ДфПГ та у 1 (12,5 %) пацієнтів групи ПфПГ. Виживаність ДСРШ у пацієнтів з ДфПГ оцінена як 0,309 (95% ДІ 0,0186-0,708) без різниці в загальній виживаності шунта між групами.

Висновок. ДСРШ продемонструвало добрі результати у розрішенні небезпечних симптомів ЛГ в обох групах дослідження з нециротичною (ДфПГ) і циротичною (ПфПГ) причинами ПГ, зі значним збільшенням кількості тромбоцитів і інволюцією варикозного розширення вен. Однак, незважаючи на відсутність різниці у виживаності ДСРШ між групами дослідження, виживаність ДСРШ у пацієнтів з EHPVO досягла медіани виживання в 136 місяців.

Ключові слова: портальна гіпертензія, дистальне спленоренальне шунтування, дисфункція шунту, рецидив кровотечі з варикозних вен, діти.