Intrahepatic portal venous systems in children with noncirrhotic prehepatic portal hypertension: Anatomy and clinical relevance

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Abstract

Background: Children with extrahepatic portal hypertension typically present with cavernomatous transformation of the portal vein and a poorly defined intrahepatic portal vein system on conventional imaging. With the Meso-Rex Bypass becoming the gold-standard intervention for a cure, a precise assessment of the intrahepatic portal vein system provides helpful data for deciding whether a Meso-Rex Bypass is feasible or not.

Methods: All children with extrahepatic portal hypertension were prospectively assessed by wedged hepatic venous portography. Venous anatomy was categorized into five subtypes (A to E), depending on the presence of thrombosis in the Rex recessus, or not, and its extension within the intrahepatic portal venous system.

Results: Eighty-nine children entered the study. Previous umbilical vein catheterization is usually associated with Rex thrombosis, while the Rex recessus and the intrahepatic portal venous system are patent in idiopathic cases, thus allowing for the performance of a Meso-Rex Bypass with a good outcome.

Conclusions: Wedged hepatic venous portography is a very effective tool for detailed preoperative assessment and identification of children being considered for Meso-Rex Bypass surgery. An anatomic–radiological classification is useful in selecting patients for Meso-Rex Bypass with anticipation of a high rate of success.

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Extrahepatic portal vein thrombosis (PVT) is a common cause of prehepatic (noncirrhotic) portal hypertension in children. Most cases are "idiopathic" in the absence of a congenital hypercoagulable state, a systemic disease, or locoregional favoring causes [1,2]. PVT can be limited to the trunk of the portal vein only, or extend into either, the intrahepatic portal system, or the splanchic venous system (splenic and mesenteric veins), or both [3–5]. There is no previous detailed anatomic–radiological study, or published classification, of the intrahepatic portal venous system (IHPS) in patients with PVT.

First proposed two decades ago, the Meso-Rex Bypass (MRB) is an original technique for the decompression of portal hypertension caused by PVT [6–8]. This operation restores the splanchic venous blood circulation to—and through—the IHPS, by creating a bypass between the superior mesenteric vein and the left portal system (the bypass is anastomosed onto the Rex recessus (RexR)) [9–11]. The MRB has been implemented with success in children. It is now considered to be the gold-standard strategy when feasible, and is even proposed as an elective preemptive strategy by some surgeons (meaning it is proposed to patients with such clinical symptoms—i.e. splenomegaly, esophageal varices—even in the absence of active complications of portal hypertension) [12–14].

Since MRB surgery is not feasible when the recessus of the Rex and the IHPS are thrombosed, Wedged hepatic venous (retrograde) portography (WHVP) became part of our routine preoperative assessment. This study is conducted to identify patients who are good candidates for an MRB, (thus avoiding unnecessary surgical exploration for those with a thrombosed Rex recessus) [8,15,16]. WHVP is in fact not a new technique [17,18] and interventional radiologists use retrograde portal imaging for various purposes, including portal hypertension assessments [18–20] and during TIPPS procedures. However, a detailed analysis of the intrahepatic venous portal system (IHPS) anatomical patterns in children with cavernous transformation of the portal vein has never been proposed or described in the literature.

The aim of this study was to employ wedged hepatic venous (retrograde) portography (WHVP), to prospectively assess, all children with extrahepatic portal hypertension (EHPH) caused by extrahepatic portal vein thrombosis (PVT). WHVP radiological findings were then categorized into five specific different imaging patterns—with this new classification being proposed for further studies.
1. Patients and methods

The institutional scientific board approved this study. All children (<18 years of age) referred to, or in care at our center, between January 2007 and December 2010, with a diagnosis of noncirrhotic prehepatic portal hypertension caused by extrahepatic portal vein thrombosis, were assessed by WHVP and enrolled in the study. Noncirrhotic prehepatic portal hypertension caused by extrahepatic portal vein thrombosis was defined by a clinical presentation associating classical symptoms of portal hypertension (oesophageal varices, splenomegaly and hypersplenism, with or without hyperammonemia, coagulopathy or ascites); the absence of any evidence of associated liver disease (normal liver function tests, with a normal appearance, and sonoelastography of the parenchyma on ultrasonographic imaging—a biopsy of the liver not being part of the standard assessment); an association at imaging with the absence of a normal portal vein trunk; and the presence of cavernomatous venous collaterals at the porta hepatis. WHVP was performed by the interventional radiology team (three radiologists) and all procedures were performed by the senior radiologist (author—P.F.) or under his direct supervision. All patients and parents were informed of their diagnosis and the procedure, and informed consent was then obtained prior to the procedure.

When reviewing the patient notes and collecting general and demographic data, care was taken to search for the cause of the portal vein thrombosis. All patients were screened for thrombophilia— including testing for a mutation of prothrombin (PTTHR); factor V Leiden (FVL) or methylenetetrahydrofolate reductase (MTHFR) genes; or a deficiency of factors 2, 5 or 7; or a deficiency of one of the natural anticoagulant proteins C and S; or antithrombin III.

The rate of success or failure of the WHVP procedure and any related morbidity was recorded. In all cases, the duration of fluoroscopy, the dose of contrast administered, and the total irradiation dose, were measured automatically and recorded. The impact on patient care (the continuation of conservative management or the proposal for MRB surgery), the outcome of the operation (shunt patency or not), survival and follow-up, were analyzed (minimum follow-up after surgery: 1 year).

1.1. Technique for transjugular wedged hepatic venous (retrograde) portography (WHVP)

Although WHVP can be performed under sedation/local anesthesia in cooperative patients >12 years of age, this procedure was carried out under general anesthesia for all patients, because most were less than 12 years old, and it is our routine practice. A 5F sheath (4F sheath in small patients) is inserted into the right internal jugular vein (ultrasound-guided puncture). Using a multipurpose single hand-hole, or a Vertebral Terumo® catheter, selective catheterization of the left hepatic vein is performed under fluoroscopy. Once the tip of the catheter is wedged, venous portography is obtained by a hand-forced retrograde contrast injection. An iodinated contrast medium (iodine concentration of 300 mg/ml— Iomeron® Bracco) is used and injected by hand using a 20-ml syringe. The maximum allowed contrast dose is 6 ml/kg. All angiograms are performed by conventional nonsubstracting angio- graphy, using a Siemens® Artis zee biplane system, in apnea. The viewing field is chosen to cover the entire hepatic area, with standardized projections, to optimally image the anatomy of the portal system (Fig. 1): A: posteroanterior craniocaudal right-to-left oblique position; B: caudocranial right-to-left oblique position; C: craniocaudal left-to-right oblique position and D: caudocranial left-to-right oblique position. The procedure is relatively rapid, and care is taken to reduce radiation doses, with four to eight angiographic runs, each around 10 seconds long, performed at two frames per second.

Free (right atrium) and wedged hepatic venous pressures are measured at the end of the procedure to calculate the transhepatic pressure gradient.

1.2. Study of the imaging and categorization of the results

The images obtained by WHVP were viewed by the radiologist and the surgeon together, and analyzed with other imaging types to determine the patency (or not) of the main intrahepatic and segmental portal branches (Figs. 2 and 3). Subsequently, the occlusion pattern was defined and possible indications for MRB surgery were deliberated. The anatomy of the IHPS was categorized into five subtypes:

Type A: A complete opacification of the IHPS, with all segmental portal branches: characteristic findings were the smooth and regular aspect of the vein walls; the branching of the main veins with a typical anatomical distribution in the various segments (including a connection between the left and the right liver through a well identified venous central confluence, and of the progressive change in diameter from the central to distal areas).

Type B: A patent IHPS with abnormal imaging of the Rex R (partial thrombosis, hypoplastic or re-canalized aspect): characteristic findings were the slightly irregular aspect of the vein walls, or an incomplete venogram when compared to a standard anatomy; also a diameter smaller than expected of the main venous trunks, with irregular branching, or sudden changes in diameter of the veins from the central to distal areas.

Fig. 1. Standardized projections to optimally image the anatomy of the portal system. Comparison, in a single patient, between the frontal standard view (left), posteroanterior cranio-caudal right-to-left oblique view (middle) and posteroanterior caudocranial left-to-right oblique view (right). The latter two projections optimally delineate the anatomy of the intrahepatic portal venous system and the Rex Recessus (arrow) in patients with cavernoma.
seen in many patients, and as reported previously, as a secondary coagulopathy to a portal cavernoma [21].

All WHVP, but one, was accessed through the right internal jugular vein, with a 4F or 5F catheter (in 20 and 69 patients, respectively). None were associated with perioperative complications. In 88 patients, the catheter was first inserted into the LHV, while this was not possible in one patient (the median hepatic vein was catheterized instead). In 64 cases, in a second instance, the right hepatic vein was also catheterized, to be able to complete the anatomical assessment, because the hepatic venography from the LHV was incomplete or abnormal. The duration of fluoroscopy (median = 10’ [range: 2’ to 37’]), with a total median irradiation dose of 2252μGy m2 (range: 239 to 10,750 μGy m²), and a maximum allowed dose of contrast of 6 ml/kg were optimal. Measurements of the atrial pressure (median: 11 mm Hg [range: range 3–19 mm Hg]) and wedged hepatic pressure (median: 18 mm Hg [range: 11–31 mm Hg]) allowed for the calculation of a pressure gradient (med: 6 mm Hg [range: 1–20 mm Hg]), and subsequently, with only 5 patients (1 type B, 1 type C, and 3 type E) having a gradient > 10 mm Hg. Interestingly, in two of these patients (1 type B, 1 type C) a Meso-Rex Bypass was attempted and failed, because very poor flow was achieved; histology retrospectively confirmed obliterator portal venopathy [22].

The anatomy of the intrahepatic portal system was assessed, categorizing each examination within one of the five types as previously defined. Results were as follows: type A = 26 cases, type B = 12 cases, type C = 3 cases, type D = 12 cases, and Type E = 36 cases. Overall, a RexR was anatomically identified in 37 patients (41.57 %) (26 type A, 9 type B, 2 type C), with the venogram findings favoring performance of a preemptive Meso-Rex Bypass intervention in 31 patients (26 type A, 4 type B, 1 type C). In these 31 patients, the RexR median diameter was 2.9 mm [range: 1.4 to 7.8 mm]). Interestingly, of 49 patients, with a history of neonatal UC, 26 (53.1 %) presented with a type E pattern (complete thrombosis), while type A, B or D was observed in 6 (12.2%), 5 (10.2%) and 12 (24.5%), respectively. Two patients with a history of omphalitis were type E. Conversely, of 38 children with an idiopathic cavernoma, 20 patients (52.6 %) had complete patency of the intrahepatic portal tree (type A), 7 patients (18.4 %) had a B pattern, and only 11 patients were found to have a C (3; 7.9 %) or E (8; 21.1 %) pattern.

Overall, 26 patients (group A) were considered excellent candidates for an MRB. The patency of the Rex was confirmed upon surgical exploration in all, with a successful outcome (all alive and well—follow-up >2 years for all, up to 5 years for the longest).

Of group B, five patients were proposed for the intervention. Although the bypass was successful in one case, the Rex was found abnormal in two (in that the vascular lumen was small in caliber and most irregular, with no possibility of envisaging a satisfactory Anastomosis), and the procedure was abandoned. In the remaining two patients, although a patent vascular lumen was found at exploration, no flow could be established through the bypass; surgical revision failed, and both were converted successfully to a Meso-Caval shunt. In group C, one patient was operated upon; although a patent Rex was found, and the flow had been established initially, a progressive reduction of flow velocity was observed over time, followed by a recurrence of severe episodes of variceal hemorrhage, related to obliterator portal venopathy (biopsy proven) [22]: the patient was proposed for a liver transplantation. Interestingly, two of the three patients with a failed MRB had a pressure gradient at WHVP of 15 and 20 mm Hg respectively, and the biopsy of the liver (done at surgery) showed diffuse hepatoportal sclerosis.

Six other patients, with a thrombosed Rex, and complicated portal hypertension, were managed with a splenorenal shunt (three cases), splenic embolization (two patients), or an isolated splenectomy (one patient with extensive splanchic vein thrombosis, including confluence and a splenic vein). At the time of this writing, all six patients are alive and well, with normal Doppler ultrasonography in the three

1.3. Data analysis
Continuous data were expressed as median and range.

2. Results

Eighty-nine children, 55 boys and 34 girls, with a median age of 10.34 years (range: 0.35 to 17.58 years) with EHPT were identified and selected for the WHVP study (Table 1). Previous umbilical catheterization (UC), or omphalitis in the neonatal period, was found in 49 and 2 patients, respectively; in the other 38 cases, a portal cavernoma was considered to be “idiopathic” in the absence of other favoring factors. None of the patients had previous peritonitis or abdominal surgery. No patient was identified as having a genetic prothrombotic status after a detailed assessment of the coagulation profile (although minor variations of the coagulation profile were

Fig. 2. Schematic representation of types of intrahepatic portal system anatomy in patients with portal cavernoma. (A) Patent IHPS (legend of picture: hepatic segments numbered SII to SVIII (according Couinaud) and Rex recessus®). (B) Patent IHPS with parietal abnormalities within the left liver. (C) Partially patent IHPS with thrombosed right liver. (D) Partially patent IHPS with thrombosed left liver. (E) Extensive thrombosis of the main portal vein radicals in the liver.

Type C: Opacification of the left portal branches only (including the RexR) and thrombosis of the right portal system (with or without features of partial thrombosis, hypoplastic or recanalized aspect).

Type D: Thrombosis of the left portal branches (including the RexR) with opacification of the main right portal branches (right trunk or sectorial branches).

Type E: Complete thrombosis of the intrahepatic portal venous system, right and left.

Patients with a patent Rex recessus (type A, B or C) were proposed for MRB surgery, while it was considered contra-indicated in the others for anatomical and technical reasons (types D and E): the latter group of patients were offered continued conservative management (stable patients), or a portosystemic shunt when the complications of portal hypertension were no longer manageable conservatively. All surgical procedures were performed by the senior surgeon (last author) himself, or under his direct supervision (expertise with MRB being gained by performing more than 100 cases in the last 15 years in various centers [6–8,10]).
patients with shunts, and an absence of complications related to portal hypertension in the other three cases.

Of the whole cohort, two patients underwent liver transplantation, with an excellent outcome. The first case, with a failed MRB and obliterative portal venopathy [22], is described above. In this patient, performing a portosystemic shunt at that point would have caused thrombosis of the MRB (and loss of the jugular vein graft used for the MRB), while also adding technical difficulties for a further transplant if needed in the future. It was, therefore, decided to transplant this patient, as the existing jugular bypass was used, simply and successfully, for portal reconstruction at the time of the transplant. The second patient was a teenager with severe growth retardation, massive splenomegaly, and severe hypertensive gastropathy. As he also had a coagulopathy and chronic hyperammonemia, a

Fig. 3. Imaging of intrahepatic portal system (anatomical subtypes) in patients with portal cavernoma. Type A Portogram: complete opacification of a normal intrahepatic portal venous tree, with all segmental portal branches. A2: anatomical drawing of patient A with references to hepatic segments (S II to S VIII, according Couinaud) and Rex recessus (R). Type B Portogram: patent intrahepatic venous system with abnormal imaging of the Rex recessus (partial thrombosis, hypoplastic or recanalized aspect of the vein). Type C Portogram: opacification of the left portal branches only (including the Rex recessus) and thrombosis of right portal system. Type D Portogram: thrombosis of the left portal branches (including the Rex recessus) (left image) with opacification of main right portal branches (right trunk or sectorial branches) (left image). Type E Portogram: complete thrombosis of the right and left main branches of the intrahepatic portal system (right and left images, respectively).
A portosystemic shunt was contraindicated. Liver transplantation resulted in a cure of his condition, including growth catch-up.

4. Discussion

To our knowledge, this is the first report of a detailed anatomic–radiological study, together with a classification of the anatomy of the intrahepatic portal venous system, in patients with portal cavernoma. It is also the largest series to date of cavernoma patients studied by WHVP in the literature [23,24].

The radiological anatomy of the cavernoma itself (extrahepatic portion) has been generally described in the literature. Conventional imaging (superior mesenteric artery angiography, splenopertography, ultrasound, angio-CT and, more recently, spiral CT and angio-MR) gives a precise picture of the vascular pattern of the larger extrahepatic vessels, the location of the cavernoma, and how much it extends down into the splanchnic venous system (splenic and mesenteric veins) [4–6]. The Rex recessus is observed only when both the vein is large enough in caliber and in the absence of perivenous vascular changes [23,24]. In contrast, intrahepatic cavernomatous changes make it very difficult—or impossible—to differentiate the left portal vein and the Rex recessus, from the venous collaterals with conventional imaging (Figs. 4 and 5) [22,24,25]. This is related to both the small diameter of the portal radicals, and the presence of cavernomatous collateral venous channels and dilated arterial trunks, within the hepatic hilum and the intrahepatic portal sheet. As a result, it creates a complex vascular pattern at the porta hepatitis, extending into the liver, and masks the main portal veins and the RexR (Figs. 4 and 5) [24–26]. With wedged hepatic retrograde portography, the contrast injection flows directly through the hepatic sinusoids, and into the portal venous system, providing a very detailed specific image. In our and others’ experience, the implementation of this technique for diagnostic and therapeutic purposes has contributed to the development of Meso-Rex Bypass surgery (Figs. 6) [8,15,16,24–26]. Both Chaves et al. [24] and Kwan et al. [25] report a >90% accuracy for identifying a patent Rex recessus with portography.

Overall, 31 patients (26 type A, 4 type B, and 1 type C) were selected prospectively for an MRB on the basis that the Rex was patent at WHVP. In three patients, the procedure was abandoned intraoperatively, with one converted to a Meso-Caval shunt. Of 28 MRBs, 1 failed during the first 48 hours and was converted to a Meso-Caval shunt as well, and a second failed in the long-term and was managed by liver transplantation. The overall success rate of performing MRB surgery was 26/28 (93%)—and that is in line with other series [7,8,11].

An important message is that children with a idiopathic portal vein cavernomatous transformation, do not present (as thought in the table below). Two other patients planned but still waiting for surgery.

**Table 1**

<table>
<thead>
<tr>
<th>Type</th>
<th>No.</th>
<th>Gender</th>
<th>Age</th>
<th>Etiology</th>
<th>Primary surgery</th>
<th>Outcomes</th>
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<tr>
<td>M</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td>MRB Other</td>
<td></td>
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<tr>
<td>A</td>
<td>13</td>
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<td>8.08</td>
<td>ID 20</td>
<td>26</td>
<td>26/26</td>
</tr>
<tr>
<td>B</td>
<td>9</td>
<td>3</td>
<td>9.66</td>
<td>UC 7</td>
<td>4   LAP 1/4</td>
<td>2 MCS; 1 SRS</td>
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<tr>
<td>C</td>
<td>2</td>
<td>10.49</td>
<td>3</td>
<td>OM 1</td>
<td>4 ES</td>
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<td>D</td>
<td>8</td>
<td>11</td>
<td>10.45</td>
<td>26 2</td>
<td>3 SRS; 1 SPL; 1 LTX</td>
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| E    | 25  | 3       | 9.60| ES 8     | 2 ES; 1 SPL; 1 LTX | 0        |

Two other patients planned but still waiting for surgery.

Abbreviations: ID, idiopathic; UC, umbilical catheterization; OM, omphalitis; MRB, Meso-Rex Bypass; LAP, explorative laparotomy only; MCS, mesocaval shunt; SRS, splenorenal shunt; SE, splenic embolization; SPL, splenectomy; LTX, liver transplantation.

Fig. 4. Comparison of various conventional imaging and retrograde portography in two patients. Satisfactory imaging of the intrahepatic portal veins is obtained only at retrograde portograms (images on the right). Patient 1 (upper): Ultrasound and venous phase at angiography. Patient 2 (lower): angio-CT reconstruction and venous phase at angiography.
past) with extensive thrombosis of the IHPS, and most, in fact, are
good candidates for a cure by MRB relatively early in life [8,11,24–26].
Importantly, WHVP helps to accurately identify those patients with
RexR thrombosis; this in turn avoids unnecessary explorative
laparotomy, or proceeding intraoperatively to perform a portosys-
temic shunt, when it might not be formally indicated. In the series by
Chaves et al. [24], 92 patients were surgically explored, with only
69 benefiting from a successful MRB: thus the “intent to treat success
rate” was 75%. Selecting patients with WHVP in our series achieved
an 87% success rate [27/31].

WHVP is an important tool in selecting patients for MRB surgery:
this is especially true in a population of patients where the prevalence
of intrahepatic thrombosis is high, as we found in association with
patients that had a history of UC [27–29]. Although the contribution of
UC as a cause of PVT remains controversial in the literature, Kim et al.
[30] highlighted the importance of minimizing the duration of
catheter placement, and of an US monitoring as a guide to catheter
removal. What is clear is the fact that the catheter passes through the
Rex recessus, and this portion of the vein is likely to be involved
in the thrombotic process if it happens. In another group of Italian
children, Alberti et al. [31] also observed a 55% prevalence of
patients with a history of UC (36 cases out of a cohort of 65 EHPH
children); and confirmed a high prevalence of thrombosis of the
Rex recessus (58% in their series) in the former group, and a highly
significant association between obstructed Rex recessus and history
of umbilical catheter placement (Pearson correlation $p = 0.01$).
Similarly, Gibelli et al. [32] observed that it was not possible to
perform an MRB in eight of nine cases who had neonatal umbilical
catheterization and concluded that the role of the MRB surgery is
yet to be evaluated in this particular group of children.

Having experienced difficulties and failure when operating on
patients classified as type B or type C, we conclude that type A patients

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**Fig. 5.** Comparison of conventional mesenteric angiography and retrograde portography in three patients. Portogram are shown on the left of each angiogram (Both imaging obtained in same patients A, B and C).
can be proposed for a preemptive MRB procedure without reservation, while type B and type C should be carefully considered: WHVP provides a detailed enough picture of the whole IHPS in order to select these cases. It is retrospectively clear that today patients classified as group B and group C would not initially be proposed for an MRB at least not without a detailed complementary assessment (i.e. biopsy). This is another important lesson we learned. Together with WHVP, other procedures, such as measuring the portohepatic pressure gradient, or performing a liver biopsy, can help to improve the diagnostic accuracy and consequently aid in selecting patients for surgery. Our current strategy for these children, with a less than optimal RexR (type B and type C), is to continue conservative treatment, and to perform a liver biopsy (to rule out obliterator portal venopathy). The result is to delay surgery, until clinical conditions make it necessary to perform surgical decompression. Then, later at laparotomy, the RexR can be explored and assessed, and either an MRB, or a splenorenal shunt, can be performed, according to the intraoperative findings.

With percutaneous transjugular access currently being a standard procedure for many interventional radiological procedures, and because inserting a catheter within the hepatic venous system is relatively simple to achieve, WHVP is not a challenging or difficult procedure, even for radiologists who are not familiar with retrograde portography. Some useful and important observations were made during the learning phase (before this study). They were pointed out in the Methods section, being that:

1. The best results can only be achieved routinely by transjugular access (straight line for maneuvers, and the best “blocking” of the catheter tip).
2. Using a standard catheter (not a balloon catheter—see below), and
3. A contrast injection through segments II or III (left lateral segment) for achieving an optimal imaging of the Rex recessus, and the connection between left and right portal venous systems (personal observation).

Importantly, using a different incidence for imaging is crucial in obtaining a precise assessment of the venous anatomy (Fig. 1).

Transjugular WHVP is an effective tool to identify children with cavernomatous transformation of the portal vein who are good candidates for a successful Meso-Rex Bypass surgery (Figs. 4, 5 and 6). An anatomic–radiological classification is proposed for the selection of patients, and in particular, for those who are considered in the absence of nonmanageable portal hypertension complications (pre-emptive indication). WHVP has the advantage that it can also be associated with wedged hepatic pressure measurements, and/or the addition of a transvenous liver biopsy, for refining the diagnosis, when necessary.

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