PORTAL VEIN THROMBOSIS IN LIVER TRANSPLANTATION

Trombose de veia porta no transplante hepático

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ABSTRACT – *Background* - Portal vein thrombosis was considered a contraindication for liver transplantation in the past because of the high morbidity and mortality rates. Many advances made the results better. *Aim* - Review the advances and surgical strategies for liver transplantation in presence of portal vein thrombosis. *Method* - Survey of publications in Medline, Scielo and Lilacs databases. Headings crossed: portal vein thrombosis, liver transplantation, vascular complications, jump graft, graft failure, multivisceral transplant. Data analyzed were epidemiology, risk factors, classification, diagnosis, surgical strategies and outcomes. *Conclusion* - Portal vein thrombosis is not a contraindication for liver transplantation anymore. There are many strategies to perform the liver transplantation in this condition, depending on portal vein thrombosis grade. Regardless higher morbidity and re-trhombosis rates, the outcomes of liver transplantation in portal vein thrombosis are similar to series without portal vein thrombosis.

RESUMO – *Introdução* - A trombose de veia porta foi considerada contraindicação ao transplante de fígado no passado em razão da elevada morbi-mortalidade. Diversos avanços permitiram melhora dos resultados. *Objetivo* - Revisão dos avanços e das estratégias cirúrgicas utilizadas para realização do transplante de fígado na vigência de trombose de veia porta. *Método* - Revisão da literatura nas bases de dados Medline, Scielo, Lilacs cruzando os descritores: portal vein thrombosis, liver transplantation, vascular complications, jump graft, graft failure, multivisceral transplant. Foram estudados a epidemiologia, fatores de risco, classificação, diagnóstico, estratégias cirúrgicas e resultados. *Conclusão* - A trombose de veia porta deixou de ser contraindicação para o transplante hepático. O cirurgião dispõe atualmente de uma série de estratégias para realização do transplante, variando conforme o grau da trombose. Apesar de implicar em maior morbidade e taxas de re-trombose, os resultados do transplante na presença de trombose portal são semelhantes aos observados nas séries habituais.

INTRODUCTION

The portal vein thrombosis (PVT) in candidates for liver transplantation, until the recent past, was considered an absolute contraindication to transplantation because of technical difficulties and high mortalidade[34]. It was only in 1985 that Shaw et al. reported the first successful case[27].

Nowadays, with the development of strategies for vascularization of the portal graft portal and refinement of surgical techniques, liver transplantation in patients with PVT is part of the routine in major transplant centers. Despite the improved results, this group of patients should still be considered high risk and should be referred to centers with experience in this type of complication.

The purpose of the review is to assess progress and surgical strategies used to perform the transplantation in this condition.

METHOD

Bibliographic search on Medline, Lilacs and SciELO databases from period 1960 to 2010. The headings were: portal vein thrombosis, liver transplantation, jump graft, graft failure, multivisceral transplant.

Epidemiology and risk factors

In the context of liver cirrhosis, PVT is found in 10-15% of patients[32]. The risk factors are advanced age, male, cryptogenic cirrhosis, alcoholic cirrhosis, autoimmune hepatitis, Child-Pugh C, prior portosystemic shunt, prior variceal bleeding, thrombocytopenia, low concentration of natural anti-coagulants, portal speed flow <15 cm/s and prior splenectomy. In series published related to liver transplantation, its prevalence ranges from 6% to 11% of patients[18,20,31,37]. Ravaioli et al23 diagnosed intraoperatively 91 cases (10.2%) of 889 transplants in 10 years, being 56% partial and 44% total.

Classification

In general context, PVT can be divided into acute or chronic, and classified into four categories: 1) confined to the portal vein, 2) extension to the superior mesenteric vein, but with patent mesenteric vessels, 3) extension to the whole venous splanchnic system, but with large side, 4) with small colaterals[9].

However, in regard to liver transplantation, the most widely used classification for surgical planning is the Yerdel[37] (Figure 1).

Grade I	<50% of light, with no or minimal obstruction of the superior mesenteric vein
Grade II	Grade I with obstruction > 50%, including total obstruction
Grade III	Complete obstruction of the portal vein and proximal superior mesenteric vein
Grade IV	Complete obstruction of the portal vein and superior mesenteric vein

FIGURE 1 - Yerdel classification for portal vein thrombosis

Diagnosis

The portal involvement before transplantation is required in planning the surgical strategy. Despite the preoperative radiological evaluation, 12% to 63.7% of cases are diagnosed intraoperatively[6,24]. This happens due to clinical consequences in the long waiting list for transplantation and/or failure in the interpretation of diagnostic methods.

The Doppler abdominal ultrasound is the initial method of evaluation. The sensitivity, specificity, positive and negative predictive values of the tests were reported by Yerdel[37] as 73%, 99%, 86% and 98% respectively. The sensitivity increased with the degree of thrombosis: 48% grade I, grade II in 82% and 100% in grades III and IV. False negatives occur only in partial cases, being significantly higher in grade I. However,

the ultrasound was not able to differentiate between grade III and IV. In the literature, the sensitivity and specificity ranging from 60 to 100% [4].

In the presence or suspicion of PVT on ultrasound, further evaluation is mandatory and can be through angiography with venous phase (indirect portography), computed tomography or magnetic resonance[18,20,37]. The choice of method will depend on availability, experience, clinical condition of the patient, the possibility of patient cooperation, adverse effects of contrast media and associated complications.

Angiography can identify 13% of false positive cases evaluated by ultrasound, and differentiate between different degrees of thrombosis. However, it is invasive procedure, wherein the contrast medium used is nephrotoxic and does not allow evaluation of other abdominal structures, such as liver parenchyma[37].

Resonance and tomography allows 3-D reconstruction with optimal evaluation of the venous system, having high accuracy for detecting venous anomalies[8]. They also enable the identification and evaluation of cavernomatous transformation of hepatic parenchyma and surrounding structures, being the resonance superior in the characterization of hepatic mass[2, 8,10,22].

Strategies for surgical transplantation

The first successful liver transplant in a patient with portal vein thrombosis was reported by Shaw et al.[27] in 1985. Proper planning involves not only the surgical team, but also the organ capture team, who must withdraw venous grafts appropriately, anesthetic and blood bank, that should be alerted to major blood loss.

The surgical strategies are: resection of the affected segment and primary anastomosis, thrombectomy, grafting to superior mesenteric vein, to the splenic vein or varix, and portal arterialization, hemitransposition cavoportal, renoportal anastomosis and multivisceral transplant[3,16,18,20,21,23,25,26,31,35,36,37].

The initial strategy for PVT grades I and II is the removal of the thrombus[16,20,23,31,37]. It can be accomplished through various ways and may involve not only the removal of the thrombus, but also the innermost layer of the vessel (thromboendovenectomy)[16,20,29]. In the presence of short-affected segment, its resection and primary anastomosis can also be tried[37].

In the strategy described by Stieber[29], the edges of the portal vein are repaired with sutures. The thrombus is separated from the wall of the portal vein using an endarterectomy spatula, simultaneously with the protrusion of the vessel wall. Vascular clamps are used to pull gently until the thrombus is removed. The effectiveness of the procedure is confirmed by intense portal blood flow after removal of the thrombus.

In the technique described by Molmenti16, the edges of the veins are tensioned with vascular clamps. The thrombus is detached from the wall of the

portal vein through the apprehension with vascular clamps and performing circular motions towards the splenomensenteric junction. After release of the vessel wall, the thrombus is pulled and removed. Some authors describe techniques with minor differences, maintaining however the same principles[20].

For thrombi that extend beyond the splenomesenteric junction, removing the thrombus can not be efficiently. For PVT grade III where no thrombus was removed, the use of grafts for superior mesenteric vein tributary or others (left gastric, splenic veins) is the primary alternative[18,20,23,31,37].

The venous use was initially described by Shaw[27] for adult patients with PVT or children with sclerosis or hypoplasia of the portal vein. Usually the superior mesenteric vein access is made in the infra-mesocolic portion (Figure 1). A segment of vein is isolated circumferentially to facilitate positioning of vascular clamp. An angled terminolateral anastomosis, between a vein graft (external iliac vein) and superior mesenteric vein, is realized[12,33]. The venous conduit is then passed through the mesocolon and may be placed in position before the pylorus, after the pylorus, but prior to pancreas[18], or in retropancreatic position[12,29] (Figure 2 A and B).
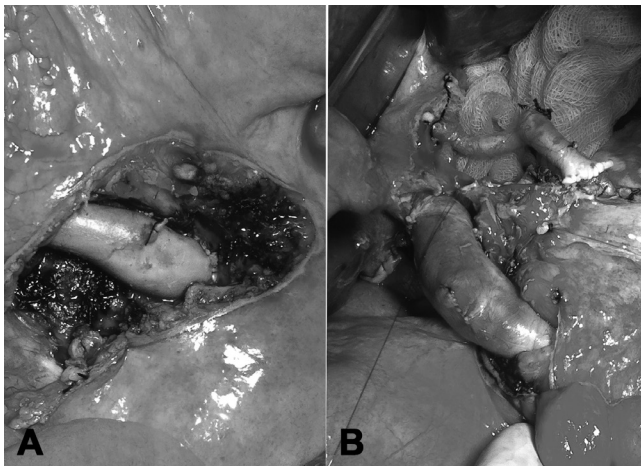

FIGURE 2 - A - Venous anastomosis of the superior mesenteric vein; B - Venous anastomosis in the portal vein graft

More important than access to passage of the venous conduit is its adequate position, avoiding compressions and bendings. In the case of using other tributaries for revascularization (left gastric vein, for example) attention should be directed to the fragility of these dilated vessels that may easily breaks[5,29].

In the presence of complete thrombosis of the venous mesentericoportal system (grade IV) and in the absence of other tributaries for revascularization, hemi-transposition cavoportal, renoportal anastomosis, portal arterialization and multivisceral transplantation are alternatives.

Studies in dogs by Starzl et al. in the late 50s, showed the effects of systemic portal perfusion flow[14]. Both hepatic function and histology remained preserved.

The hemi-cavoportal transposition is an infusion of the portal vein to the systemic circulation through an anastomosis between the portal vein of the liver graft and the recipient inferior vena cava in its suprarenal portion, terminoterminal or terminolateral[26]. To ensure the hepatic perfusion are needed ligation or division of the inferior vena cava in its suprarenal portion[26]. Although allowing perfusion of the hepatic graft, hemi-transposition cavoportal not lead to decompression of mesentericoportal territory; so, patients can maintain ascites, episodes of digestive haemorrhage and edema in the legs.

The portal arterialization may be accomplished through a calibrated anastomosis between the portal vein and splenic artery of the graft or other arterial branch[3,20], or with the proper hepatic artery of the receiver, in which case the arterial blood supply of the graft is made with an arterial conduit[19]. The questions of these methods are the possible hypertension developed in the venous system and liver tropism changes associated with the absence or reduction of portal blood to the graft.

The renoportal anastomosis was first described by Sheil[28], and modified by Kato[11] with interposition of a vein graft. The same discussion regarding the maintenance of hypertension in cavoportal hemi-transposition can be applied. However, this procedure ends up being applied when there spontaneous splenorenal shunts or surgical revascularization allowing portal decompression[15,17,21]. Thus, the renal vein used is always left. This reconstruction has been discussed also in patients with prior splenorenal anastomosis, even in the absence of portal vein thrombosis, since the shunt with or without splenectomy adds significant complexity to transplantation[11].

The multivisceral transplantation is the complete replacement of the abdominal viscera after exenteration[36]. Usually the graft is composed of stomach, duodenum, pancreas, small intestine and liver. It may be indicated for patients with short bowel syndrome associated with liver failure, abdominal catastrophes, unresectable tumors and diffuse portomesenteric thrombosis, even in the absence of liver failure[35]. Can be used as an alternative for patients with thrombosis grade IV. In addition to treating liver failure, is capable to normalize the abdominal vascular flow.

Results of transplantation in PVT

In general manner, PVT can be admitted as unfavorable factor to evolution when present in cirrhotic patients. Englesbe et al.[7] showed that it is independent factor of mortality both in

pretransplant, with risk of 2.62 (IC 95%, 1.97-3.51) from the initial assessment, and 1.99 (IC 95 %, from 1.25 to 2.16) from the moment of inclusion to transplant. Postoperatively, PVT was associated with increased risk of death in 30 days (OR 7.9; IC 95%, 2.9 to 22.83).

In classic study performed by Yerdel et al.[37], the need for transfusion was higher in patients with PVT that in the group without, 10U and 5U respectively (p <0.01). The intrahospital mortality was higher in group with PVT, with 30% versus 12.4% in controls (p <0.01). The presence of postoperative complications, renal insufficiency, not-primary functioning graft and re-thrombosis was higher in group with PVT. The actuarial survival of patients in five years was inferior for the group with PVT in relation to group without PVT (65.6 and 76.3% respectively; p = 0.04). However, patients with PVT grade I presented a survival rate in five years identical to controls (86%); but, patients with degrees II, III and IV had inferior survivals.

In a quite expressive series, Pan et al.[20] showed the experience of a single center with 253 patients submitted to transplantation with PVT. Were: 104 grade I, 114 degree II, 29 degree III and six degree IV. In grades I and II, the thrombectomy with or without eversion of vase was effective, with hospital mortality of 0%. From 29 patients with degree III, the withdrawal the thrombus was possible in 23. In the remaining patients, four had reconstruction with grafts for mesenteric superior vein or to another tributary; two were submitted to portal arterialization. The intrahospital mortality that group was 3.45%. The PVT was done on one of patients submitted to portal arterialization.

For patients with PVT grade IV, in three cases was possible the remove the thrombus successfully, utilizing new technique described by the author. Two other were submitted to anastomosis with the renal vein and one to cavoportal hemi-transposition. The intrahospital mortality was 33.33%, being two associated deaths to hepatic failure. The necessity of transfusion was higher in group with PVT (9.32 ± 3.12 U and 6.02 ± 2.40 U respectively; p <0.01). The actuarial survival of one year was similar for patients with and without PVT (86.56 and 89.40% respectively; p> 0.05).

Other authors reached similar conclusions, showing that PVT adds important difficulties in hepatic transplant, with enlarged operative time, largest need for transfusion, higher incidence of renal insufficiency and re-thrombosis, and need for complex surgical techniques[13,30,31].

There are studies reporting the results relating to thromboendovenectomy. Dumortier[6], evaluating period of 10 years, identified the PVT in 8.1% of patients. In all the portal flow was established through the thromboendovenectomy and primary anastomosis. All patients received heparin of low molecular weight from the 2nd postoperative day until discharge, being started then aspirin. The re-thrombosis occurred in only a patient, that presented extensive splanchnic thrombosis. The actuarial survival of one year was 83.7%, not differing from patients without PVT (86.7%). Molmenti[16] reported the thromboendovenectomy in 5.5% of cases. The survivals of the grafts were of 84.9%, 81.3% and 62.4% respectively for one, three and six years, not differing the group without PVT. The incidence of re-thrombosis was 2.4%, not being also different from control group. Necessity of transfusion, anesthesia time and hospitalization in intensive therapy were similar. The difference occurred only in the portal flow postoperatively that on average was higher in group without PVT (2.11 versus 1.84 l / min). The group used as prophylaxis of re-thrombosis, dextran per 48 h after operation and aspirin by three months.

Nikitin et al.[18] evaluated the results in long term of venous conduits for the superior mesenteric vein. Graft survival in five years was 65% in group conduit versus 66% in control; 58% versus 51% in 10 years and 48% versus 35% in 20 years. There was largest incidence of PVT in post-transplantation in group with venous duct (8.6% versus 1.4%), being more important in the three first months. In the initial group's experience, no prophylactic measure for re-thrombosis was used. In the most recent series, was initiated dextran and aspirin in the end of operation, keeping dextran for three days and aspirin for six weeks.

The study also included comparison between the group where were utilized venous conduits and where were made thrombectomies. The cold ischemia time was higher in group with conduits (11 versus 9 h; p = 0.0008). The surgical time also was bigger in this group. However, there was largest need for transfusion in group thrombectomy. As regards to survival of patients and grafts, and major complications, there was no difference between groups.

In metanalysis, Paskonis[21] evaluated 15 publications reporting clinical experience with hemi-transposition cavoportal or renoportal anastomosis. The main complications observed were ascites, renal dysfunction and digestive hemorrhage, being observed in 41.5%, 34% and 24.5% respectively. PVT applicant occurred in 11.3% of patients, 11.3% developed thrombosis of hepatic artery, 9.4% presented deep venous thrombosis and 32% edema of lower limbs or dorsum. The period of follow-up ranged from two to 48 months, with 74% of patients alive during the period. Fourteen died in the period, 11 submitted to hemi-transposition and three to renoportal anastomosis. In a series of 23 cases published by Selvaggi et al.[26] of cavoportal hemi-transposition, the global survival was 60%

in a year and 38% in three years, being the more prolonged survival of 9.3 years. Seven patients presented gastrointestinal bleeding postoperatively, six developed thrombosis of cava vein. Ascites was observed in almost all patients and renal dysfunction was common event after the first month of transplant.

The series reporting portal arterialization are small, being many case reports. In an old series, Stieber[29] reported the realization of portal arterialization in one case, with satisfactory evolution in following of ten months. Nivatvongs[19] reported one case of portal arterialization in one year, maintaining normal hepatic function. Bonnet[3] reported the portal arterialization in a patient after attempt unsuccessfully done of thromboendovenectomy. With follow-up of six years, no manifestations of hypertension portal and liver function exist. However, one aneurysmatic dilatation of the portal branches has developed. Pan[20] reported two cases of portal arterialization in his series of 253 thromboses, occurring portal re-thrombosis in one of cases and death.

Do not exist comparative series between the strategies used for treating diffuse thromboses (splenoportomesenteric). The series of renoportal anastomosis and arterialization are small to allow clear comparison with multivisceral transplantation. Currently, global survival of multivisceral transplantation overcomes the cavoportal hemi-transposition reported by Selvaggi[26] in 60% in a year. Series report survival for one year around 70% to 80% for the multivisceral transplant[1,36]. However, is more complex procedure and of largest cost, with higher incidence of complications, as opportunistic infections, proliferative diseases and rejection episodes. Do not exist specific series reporting the results of multivisceral transplantation for PVT, but is likely that the results surpass those related to alternatives for complex thromboses.

CONCLUSION

PVT is no longer a contraindication for liver transplantation. The surgeon now has a number of strategies for performing the transplant, varying according to the degree of PVT. Although result in increased morbidity and rates of re-thrombosis, the results of the transplant in the presence of PVT are similar to those observed in usual series, especially regarding the levels I, II and III. To diffuse thrombosis (grade IV) the best strategy is still to be established, but multivisceral transplantation appears to be superior alternative to those described. A careful preoperative evaluation, preparation of the anesthesia team, knowledge of different strategies, the best situation to apply and meticulous surgical technique are critical to the success of liver transplantation in the presence of PVT.

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