Classification of Non-malignant Portal Vein Thrombosis

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Abstract

When thrombosis of the portal vein occurs, a wide range of symptoms and clinical consequences can be seen. Management decisions can be especially challenging, as much of the research on portal vein thrombosis (PVT) has been performed on heterogeneous populations of patients, often with varying degrees of underlying liver dysfunction, portal hypertension, and clot burden. In this setting, a standardized classification of PVT is especially appealing. While no universally accepted classification system currently exists, multiple systems have been proposed over the years.

Keywords

Portal vein thrombosis · Thrombosis · Portal vein · Classification · Yerdel

5.1 Introduction

Non-malignant thrombosis of the portal vein can lead to a wide range of presentations and clinical consequences. While some individuals may be completely asymptomatic, others may develop severe abdominal pain in the setting of intestinal ischemia or symptoms related to worsening portal hypertension and synthetic liver dysfunction. When occurring in liver transplant candidates, management strategies range from routine monitoring with serial imaging to performing medical

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interventions in hopes of maintaining portal vein patency, with additional considerations for significant adjustments to surgical technique.

There are multiple potential reasons for this heterogeneity in presentations and clinical implications, as both patient and thrombus characteristics play important roles. Portal vein thrombosis (PVT) can vary in regard to the actual location of thrombus (including if there is extension into the splenic vein and superior mesenteric vein), as well as the overall degree of lumen obstruction and whether or not features of chronicity are present. In addition, patients may have different symptoms and complications of portal hypertension. Given that prognosis and treatment response likely depends on the site, extent, rapidity of development, duration of thrombosis, and stage of liver disease, the "one-size-fits-all" approach for PVT is not appropriate, as the risks and benefits of treatment and transplantation likely vary widely between individuals.

Classically, clinicians classify PVT simply as acute or chronic, which may be an important consideration as more recently developing PVTs likely have higher rates of recanalization with anticoagulant therapy [1]. However, determining the time course in the absence of prior imaging can be very difficult. While cavernous transformation of the portal vein is commonly considered a sign of chronicity, duration from thrombus formation to cavernous transformation can be as little as 6 days [2]. In addition, symptoms often do not correspond to the duration of thrombosis, as the thrombus may occur long before symptoms develop.

In this setting, there is a clear need for classification systems to guide clinicians and researchers in determining the best therapeutic approach for any given patient. Over the last 30 years, multiple attempts to develop such systems have been made, each with relative strengths and limitations (see Table 5.1).

5.2 Classification Systems for PVT

PVT was previously considered a contraindication to transplantation due to concerns regarding appropriate portal inflow [3]. As experiences with transplantation grew, a variety of surgical techniques were described based on the anatomical location of the thrombosis and, in this setting, early classification systems were largely anatomical. Over time, however, attempts were made to incorporate signs of chronicity and functional components in hopes of guiding therapies and understanding prognoses.

5.2.1 Stieber Classification (1991)

In 1991, while PVT was a major technical hurdle to transplantation, Stieber and colleagues published a series of 34 subjects with PVT who were successfully transplanted between April of 1986 and October of 1989 [4]. These individuals underwent intraoperative cannulation of either the ileocolic or the inferior mesenteric vein and a venogram was performed to determine the extent of thrombosis. The thrombosis was then classified as follows:

Table 5.1 Overview of classification systems for portal vein thrombosis

	Stieber (1991)	Nonami (1992)	Gayowski (1996)	Yerdel (2000)	Jamieson (2000)	Charco (2005)	Bauer (2006)	Ma (2014)	Sarin (2016)
Description	*Type A:* segmental involvement of main PV *Type B:* main PV and SMV *Type C*: more extensive, including SV and IMV	*Grade 1*: Intrahepatic PV *Grade 2*: right or left portal branches or bifurcation *Grade 3*: partial obstruction of PV trunk *Grade 4*: complete obstruction of PV trunk	*Grade 1*: partial thrombosis of main PV trunk, residual flow *Grade 2*: complete thrombosis of main PV trunk, not extending to confluence *Grade 3*: complete thrombosis, extending to confluence *Grade 4*: complete thrombosis of main PV trunk, extending below confluence	*Grade 1*: main PV affecting < 50% of lumen, with or without minimal extension to SMV *Grade 2*: main PV affecting > 50% of lumen, with or without minimal extension to SMV *Grade 3*: complete PVT plus extension to proximal SMV *Grade 4*: complete PVT plus complete thrombosis of SMV	*1*: confined to PV beyond confluence (partial or complete) *2*: extending to proximal SMV (with patent vessel in mesentery) *3*: diffuse thrombosis of splanchnic venous system, with large accessible collaterals *4*: Extensive thrombosis of splanchnic venous system, with only fine collaterals	*1*: confined to PV (partial or complete) *2*: extending to proximal SMV (with permeability of confluence) *3*: diffuse thrombosis of splanchnic system, presence of dilated collateral veins *4*: diffuse thrombosis, presence of fine collateral veins	Thrombosis was graded as follows for the portal, mesenteric, and splenic veins separately: *Grade 1*: <25% of lumen occluded *Grade 2*: 26–50% of lumen occluded *Grade 3*: 51–75% of lumen occluded *Grade 4*: 76–100% of lumen occluded	*Type 1*: partial, without cavernoma *Type 2*: partial, with cavernoma *Type 3*: complete, without cavernoma *Type 4*: complete, with cavernoma	*Site*: Type 1: trunk Type 2a: one branch Type 2b: two branches Type 3: trunk and branch *Grade*: O: occlusive NO: non-occlusive *Duration and Presentation*: R: recent Ch: chronic As: asymptomatic S: symptomatic *Extent*: S: SV M: Mesenteric vein SM: both

(continued)

Table 5.1 (continued)

	Stieber (1991)	Nonami (1992)	Gayowski (1996)	Yerdel (2000)	Jamieson (2000)	Charco (2005)	Bauer (2006)	Ma (2014)	Sarin (2016)
Site[a]	X	X	X	X	X	X	X		X
Grade[b]		X	X	X	X	X	X	X	X
Extent[c]	X		X	X	X	X	X		X
Duration[d]								X	X
Symptoms[e]									X
Quantitative Assessment[f]							X		

PV portal vein, *SMV* superior mesenteric vein, *IMV* inferior mesenteric vein, *SV* splenic vein

[a]Site refers to venous segment which is involved by thrombosis

[b]Grade refers to whether the thrombosis is occlusive or non-occlusive

[c]Extent refers to the overall length of the portal venous system affected

[d]Duration refers to if features of chronicity on imaging or by history are accounted for

[e]Symptoms refer to the presence of associated symptoms which may include features associated with portal hypertension

[f]Quantitative assessment refers to if the classification system allowed for a means to quantitatively assess clot burden to potentially allow for monitoring response to interventions

1. Type A: segmental involvement of the main portal vein
2. Type B: involvement of the main portal vein and superior mesenteric vein
3. Type C: more extensive involvement including the splenic vein and inferior mesenteric vein

The authors described various techniques used to treat the different forms of thrombosis encountered and provided an algorithm for surgically managing these patients, including suggestions for when to perform a direct dissection and anastomosis, when to perform a jump graft, and when to manage with declotting and anticoagulation. Given the focus on surgical implications, this classification system was primarily anatomic and only accounted for the site (which venous segment was involved) and extent (the length affected) of thrombosis. It did not account for the grade of thrombosis (i.e., if it was occlusive), the duration of thrombosis, the presence of associated symptoms, or a quantitative measurement of clot burden.

Importantly, this was the first proposed classification system for PVT and the authors of the study provided evidence that individuals with thrombosis in the portal system could be technically transplanted, as their overall survival rate was 67.6% (23 of 34 subjects). Survival did vary by the extent of thrombosis, as those with thrombosis of the portal vein only had a survival rate of 73.9% (17/23), compared to 54.5% (6/11) with more extensive thrombosis.

5.2.2 Nonami Classification (1992)

In an attempt to describe the incidence of PVT in liver transplant recipients (as well as potential risk factors), Nonami and colleagues examined their experiences transplanting 885 patients with end-stage liver disease between 1989 and 1990 [5]. Of these 885 patients, they described 14 patients (1.4%) who had thrombosis of the intrahepatic portal vein branches (defined as grade 1 thrombosis), 27 patients (3.2%) who had thrombosis of the right or left portal branches or at the bifurcation (defined as grade 2 thrombosis), 27 patients (3.2%) who had partial obstruction of the portal vein trunk (defined as grade 3 thrombosis), and 49 patients (5.8%) who had complete obstruction of the portal vein trunk (defined as grade 4 thrombosis). In this large cohort, they showed that a significant proportion of those undergoing transplantation had some degree of PVT (13.8%) and described higher incidences of PVT in those with primary hepatic malignancy, chronic encephalopathy, and refractory ascites.

Similar to its predecessor, this scoring system was primarily anatomic with a focus on surgical implications—specifically if a standard end-to-end portal vein anastomosis was feasible or if additional methods, such as a vein graft (specifically a jump graft or interpositional graft) or thromboembolectomy, may be required. There were no considerations for underlying liver disease, associated symptoms, features of chronicity, or quantitative measurements to assess treatment response. An additional limitation was its focus only on the portal vein without considerations for extension into the splenic vein or superior mesenteric vein.

5.2.3 Gayowski et al. (1996)

In another study, 88 consecutive patients at a Veterans Administration Medical Center were reviewed, 23 of whom had PVT [6]. When comparing those with and without PVT, no association was found between PVT and etiology of underlying liver disease, age, Child–Turcotte–Pugh score, or prior abdominal surgery. The authors did not find differences in patient survival among those with or without PVT, although graft survival was lower (65% vs. 86%) and intraoperative blood loss was higher (median 21 units of PRBCs vs. 14 units) in the cohort with PVT.

PVT was classified according to its surgical implications, as follows:

1. Grade 1—partial thrombosis of the main portal trunk extending to or below the confluence with residual flow
2. Grade 2—complete thrombosis of the main portal trunk, not extending to the confluence of the superior mesenteric and splenic veins
3. Grade 3—complete thrombosis of the main portal trunk extending to the confluence
4. Grade 4—complete thrombosis of the main portal trunk extending below the confluence

This scoring system was used to determine surgical technique, with thrombectomy and standard end-to-end anastomosis in the 10 patients with grades 1 and 2 thrombosis versus reconstruction with jump grafts or interposition grafts in those with grades 3 and 4 PVT. Similar to its predecessors, this classification system did not account for any features of chronicity, the presence of associated symptoms, or a means to quantitatively measure clot burden.

5.2.4 Yerdel Classification (2000)

Of all the classification systems that have been proposed, perhaps the best known and most widely used one is that proposed by Yerdel and colleagues [7]. In their study, they described 63 operatively confirmed PVT in a series of 779 adult liver transplantations from 1987 to 1996. PVTs were retrospectively graded as follows:

1. Grade 1—thrombus at the main portal vein affecting less than half of the lumen (with or without minimal extension into the superior mesenteric vein)
2. Grade 2—thrombus affecting more than half of the portal vein lumen including complete thrombosis (with or without minimal extension into the superior mesenteric vein)
3. Grade 3—complete PVT plus thrombosis extending to the proximal superior mesenteric vein
4. Grade 4—complete PVT plus complete thrombosis of the superior mesenteric vein

They similarly described the surgical approaches taken, including low dissection and/or thrombectomy for grades 1 and 2, using the distal superior mesenteric vein as an inflow vessel (usually via interposition of donor iliac vein) for grade 3, and a splanchnic tributary or a thrombectomy for grade 4. Given that this classification was also designed to guide management decisions in surgical procedures, it was similar to prior classification systems in that it did not account for features of chronicity, the presence of symptoms, or a means to provide a quantitative measurement of clot burden to monitor treatment response.

Notably, this classification system has been shown to have prognostic value in those undergoing liver transplantation. In the initial study, the authors noted that those with grade 1 PVT had similar survival compared to controls (5-year patient survival of 86%), whereas those with grades 2, 3, and 4 PVT had reduced survival. In a subsequent meta-analysis, pooled data from ten studies reported that 30-day mortality was higher in those with grade 4 thrombosis [8].

5.2.5 Jamieson Classification (2000)

In the same year, an additional classification attempted to describe PVT from a practical viewpoint, specifically describing cases based on anatomical locations and their surgical implications [9]. Cases were broken down based on features including thrombosis confined to the portal vein beyond the splenomesenteric confluence, thrombosis extending into the proximal superior mesenteric vein with a patent vessel in the mesentery, diffuse thrombosis of the splanchnic system with large accessible collaterals, and extensive thrombosis with only fine collaterals. The relevant surgical techniques for each were then described, ranging from thrombectomy to jump graft to multivisceral transplantation.

This classification again focused on anatomical considerations and the associated surgical implications. While it did account for the site, grade, and extent of thrombosis, it was similar to prior scoring systems in that it did not consider any features of chronicity, the presence of associated symptoms, or a means to quantitatively measure the clot burden for monitoring treatment response.

5.2.6 Charco et al. (2005)

In a review on PVT in the setting of liver transplantation, authors similarly suggested that PVT could be classified practically to guide surgical management [10]. In it, they proposed a similar PVT classification, as follows:

1. Thrombosis confined to the portal vein (partial or complete)
2. Thrombosis extending to the proximal portion of the superior mesenteric vein with permeability of the mesenteric confluence
3. Diffuse thrombosis of the splanchnic system (with dilated collaterals)
4. Diffuse thrombosis with the presence of fine collateral veins

While accounting for the site, grade, and extent of thrombosis, this classification system was again designed to direct surgical interventions and did not account for features of chronicity, the presence of symptoms, or a means to quantitatively measure clot burden.

5.2.7 Bauer et al. (2006)

In an attempt to study the efficacy and clinical outcomes of transjugular intrahepatic shunt (TIPS) in individuals with PVT and cirrhosis eligible for liver transplantation, nine consecutive patients undergoing elective TIPS to maintain portal vein patency prior to transplantation were described [11]. The authors described successful placement of TIPS in all nine patients without complication, with eight of the nine patients having improvement in thrombosis at follow-up. To determine treatment efficacy, they estimated clot burden in the portal, mesenteric, and splenic veins at the time of their procedure as well as at follow-up, grading thrombosis in each segment as follows:

1. Grade I: less than 25% of lumen occluded
2. Grade II: 26–50% of lumen occluded
3. Grade III: 51–75% of lumen occluded
4. Grade IV: 76–100% of lumen occluded

While this classification system did not consider the presence of underlying symptoms and was limited by difficulties precisely determining the degree of occlusion, it was unique in that it provided a means to quantitatively measure clot burden, allowing for therapeutic monitoring.

5.2.8 Ma et al. (2014)

In a cohort of 60 patients (24 of whom had cirrhosis), researchers from China attempted to classify PVT using contrast-enhanced computed tomography over a 7-year period from 2005 to 2012 [12]. Two radiologists reviewed images to evaluate the location of thrombus and the presence of portal cavernoma and, using an image analysis program, determined the degree of occlusion of the portal vein, superior mesenteric vein, and splenic vein. Thrombosis was defined as complete when it reached 90% of the area of the vein lumen at the point of maximum thrombosis. They then suggested a classification based on the presence of cavernous transformation and complete thrombosis, as follows:

1. Type I—partial PVT without cavernoma
2. Type II—partial PVT with cavernoma
3. Type III—complete PVT without cavernoma
4. Type IV—complete PVT with cavernoma

In it, the authors highlight the rationality of this classification system, including the absence of ambiguous variables (such as pain) and potentially allowing easier treatment considerations based on classification. While the study did consider quantitative measurements for the burden of thrombosis, the final proposed classification system did not include the presence of symptoms, whether the thrombosis extended into other venous segments, or specific parameters quantifying the burden of thrombosis beyond complete or partial.

5.2.9 Sarin et al. (2016)

In the setting of the lack of a universally accepted classification system for PVT in cirrhosis, Sarin and colleagues published an editorial that aimed to provide a classification system assessing both the structural and functional components of thrombosis [13]. They argued for the importance of considering the precise clinical context whenever PVT occurs, including considerations for the anatomical location of the thrombosis as well as the underlying liver disease, the associated symptoms, and the duration of thrombosis.

In this setting, the authors proposed a comprehensive scoring system. They recommended the following classifications regarding the *site* of PVT:

1. Type 1—only the trunk
2. Type 2a—only one branch
3. Type 2b—two branches
4. Type 3—the trunk and branches

Regarding the *degree* of portal venous system occlusion, they recommended the following:

1. O—occlusive
2. NO—non-occlusive with flow visible on imaging

For the *duration* and *presentation*, thrombosis was classified as:

1. R—recent (described as asymptomatic and symptomatic)
2. Ch—chronic (described as asymptomatic and symptomatic)
3. S—symptomatic
4. As—asymptomatic

And regarding the *extent* of portal vein system occlusion, they recommended the following:

1. S—splenic vein
2. M—mesenteric vein
3. SM—both

In addition, they recommended describing the type and presence of underlying liver disease, including individuals with cirrhosis or non-cirrhotic liver disease, those who had previously undergone liver transplantation, and those with hepatocellular carcinoma.

While this proposed classification is likely more burdensome than many of the prior ones described, it is unique in that it accounts for both patient and thrombus characteristics and could potentially allow both clinicians and researchers to classify patients more uniformly. By doing so, it offers the potential for recruiting homogenous groups of patients which could ultimately allow an improved understanding of natural histories and treatment efficacies.

5.3 Conclusion

Over the last 30 years, multiple classification systems for PVT have been proposed, ranging from primarily anatomical systems to guide surgical management (Stieber, Nonami, Gayowski, Yerdel, Jamieson, Charco), to ones quantifying the proportion of lumen obstructed to determine treatment response (Bauer, Ma), to a much more comprehensive system evaluating both functional and anatomical components of thrombosis (Sarin). Given the heterogeneity of presentations and clinical consequences, there is a clear need to determine the natural history of PVT and the risks and benefits of potential therapies in different subpopulations of patients. With improvements in imaging modalities (including computed tomography or magnetic resonance angiography), clinicians and researchers may have opportunities to quantify the volume of PVT (and of the remaining lumen) in specific patients, potentially allowing assessment of treatment response and limiting the need to strictly classify patients. To date, there is no universally accepted classification system or strategy to quantify thrombosis that is widely used in clinical practice.

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