ELSEVIER

Journal of Hepatology 38 (2003) 364–371

Journal of Hepatology

www.elsevier.com/locate/jhep

Special article

Budd–Chiari syndrome: a review by an expert panel

Harry L.A. Janssen[1,*], Juan-Carlos Garcia-Pagan[2], Elwyn Elias[3], Gilles Mentha[4], Antoine Hadengue[4], Dominique-Charles Valla[5], for the European Group for the Study of Vascular Disorders of the Liver

[1]*Department of Gastroenterology and Hepatology, University Hospital Rotterdam, P.O. Box 2040, 3000 CA, Rotterdam, The Netherlands*
[2]*Hepatic Hemodynamic Laboratory, Liver Unit, Hospital Clinic, Barcelona, Spain*
[3]*Liver Unit, Queen Eilzabeth Hospital, Birmingham, UK*
[4]*Division of Hepatology and Transplantation Unit, University Hospital of Geneva, Geneva, Switzerland*
[5]*Service d'Hépatologie, Hôpital Beaujon, Clichy, France*

1. Introduction

Budd–Chiari syndrome is a rare disease with a potentially dismal outcome if not treated optimally. So far, diagnostic and intervention studies on Budd–Chiari syndrome have been small and difficult to interpret. Various definitions have been proposed for Budd–Chiari syndrome [1–3], but agreement on a uniform nomenclature is lacking and will constitute an essential requirement for future collaborative studies. Moreover, events that represent failure of management, and hence should become end-points for therapeutic studies, need to be defined.

In order to review the current status of the diagnosis and treatment of Budd–Chiari syndrome, a group of European investigators with special interest in vascular liver disease recently formed the European Group for the Study of Hepatic Vascular Diseases. The objectives of this group for the study of Budd–Chiari syndrome are threefold: (1) to establish a uniform definition and classification of the disease; (2) to contribute to the management of Budd–Chiari syndrome by identifying areas of consensus and areas where further research is needed and (3) to stimulate research through collaborative studies.

On the occasion of the 36th meeting of the European Association for the Study of the Liver in Prague, an open workshop was held to discuss disease terminology, diagnostic work-up, therapeutic interventions and future collaborative studies. This workshop was organized by the European Group for the Study of Hepatic Vascular Diseases. During the workshop, it became apparent that in the absence of reliable data on prognostic factors and management of the disease, it is not yet possible to reach a consensus on strict diagnostic and therapeutic algorithms. The nomenclature and guidelines presented in this paper is based on available scientific data and a joint effort by experts in the field who organized existing criteria for clinical use and future studies. The nomenclature is based on the following assumptions: (a) in order to be widely accepted, it must be close to that in current use; (b) it must encompass entities that, although heterogeneous in some respects, have common pathogenesis and manifestations; (c) it must provide clear boundaries; and (d) it must be easy to adhere to, irrespective of institutional differences in available techniques.

2. Definition

Several authors who have challenged the term Budd–Chiari syndrome as being ambiguous, have attempted to introduce other nomenclatures, such as hepatic venous outflow obstruction and obliterative hepatocavopathy [2,3]. Although important for our understanding of Budd–Chiari syndrome, most of these nomenclatures have not been used in clinical practice. Although the cause, the mechanism and the nature of the vascular obstruction are not given, the term Budd–Chiari syndrome should be retained for two reasons: (a) it has stood the passage of time; and (b) it is more concise than any other terminology proposed to designate the whole spectrum of disorders encompassed by the present definition. Budd–Chiari syndrome is defined as hepatic venous outflow obstruction at any level from the small hepatic veins to the junction of the inferior vena cava and the right atrium, regardless of the cause of obstruction. Outflow obstruction caused by hepatic veno-occlusive disease and cardiac disorders is excluded from this definition.

Veno-occlusive disease, also referred to as sinusoidal obstruction syndrome, is defined as a non-thrombotic obstruction of sinusoids or central hepatic veins due to injury of the sinusoidal wall [4]. Veno-occlusive disease

* Corresponding author. Tel.: +31-10-463-3793; fax: +31-10-436-5916.
E-mail address: janssen@mdl.azr.nl (H.L.A. Janssen).

doi:10.1016/S0168-8278(02)00434-8

Table 1
Classification of Budd–Chiari syndrome according to etiology

Designation	Definition
Primary	Hepatic venous outflow obstruction originating from endoluminal venous lesion (thrombosis, webs, endophlebitis)
Secondary	Hepatic venous outflow obstruction originating from a lesion outside the venous system (tumor, abscess, cysts). The lesion can obstruct outflow by invading the lumen or by extrinsic compression.

occurs following administration of toxic agents and is, at present, encountered almost exclusively in association with bone marrow transplantation [5]. The epidemiology, pathophysiology, treatment and prognosis of veno-occlusive disease are so distinct from other forms of hepatic venous outflow obstruction that its inclusion in future clinical studies on Budd–Chiari syndrome would introduce an unacceptable source of heterogeneity [6]. Obstruction of the small hepatic veins without involvement of the large veins is included in the definition of Budd–Chiari syndrome, while the specific entity of veno-occlusive disease is excluded. The rationale for this distinction has been much debated but is justified by several arguments. Except for veno-occlusive disease as defined above, the obstruction limited to the small veins are generally due to thrombosis, allergic phlebitis or granulomatous involvement, all reported causes of large hepatic vein obstruction [7]. Although the manifestations are sometimes difficult to distinguish from those of veno-occlusive disease, the context is usually outside the setting of bone marrow transplantation. A differentiation between isolated small vein thrombosis and veno-occlusive disease can be achieved by means of liver biopsy.

3. Classification

Budd–Chiari syndrome can be classified according to etiology, site of obstruction, manifestations and duration of the disease.

3.1. Etiology

Budd–Chiari syndrome is considered primary when obstruction of the hepatic venous outflow tract is the result of an endoluminal venous lesion (thrombosis or web) (Table 1). It is considered secondary when the obstruction results from the presence in the lumen of material not originating from the venous system (malignant tumor or a parasitic mass invading the lumen) or from extrinsic compression by a neighboring tumor (abscesses, cysts, benign or malignant solid tumors) [3]. In practice, Budd–Chiari syndrome is regarded as primary when no causes of secondary obstruction are found. Modern imaging techniques allow easy recognition of these associated lesions. Venous compression can be complicated by thrombosis, particularly when prothrombotic factors are present by chance (inherited thrombophilia) or by association (inflammatory response secondary to an adjacent abscess).

3.2. Site of obstruction

Obstruction of the hepatic venous outflow tract is classified according to its location: small hepatic veins, large hepatic veins, inferior vena cava and combined obstruction of large hepatic veins and inferior vena cava (Table 2) [2]. The term thrombosis should be used only when there is pathological evidence for this lesion. This classification can be used in the absence of pathological examination of the venous outflow tract, which should be preferred in future clinical investigations [8]. The site of obstruction is in general easily determined through non-invasive imaging (Doppler-ultrasound, magnetic resonance (MRI), computed tomography) or conventional venography.

3.3. Manifestations and duration of disease

It is important to recognize that Budd–Chiari syndrome is not always a severe disease requiring aggressive treatment. Lack of long-term prognostic studies of unselected patients

Table 2
Classification of Budd–Chiari syndrome according to site of obstruction [2]

Designation	Definition
Small hepatic veins	Veins that cannot be shown clearly on hepatic venograms or by ultrasound studies; they include terminal hepatic veins (central veins), intercalated veins and interlobular veins.
Large hepatic veins	Veins that are regularly demonstrable on hepatic venograms and ultrasound studies; segmental branches of hepatic veins are generally included
Inferior vena cava (IVC)	A segment of the IVC which extends from the entry level of the right, middle and left hepatic veins to the junction between the IVC and the right atrium
Combined obstruction	Combination of obstruction in the large hepatic veins and IVC

has limited our knowledge about the real prevalence of the different clinical forms of the syndrome. Budd–Chiari syndrome is considered asymptomatic when there are no signs of abdominal pain, ascites, hepatomegaly, edema, encephalopathy and gastrointestinal bleeding, or a history of any of them [9]. The diagnosis of asymptomatic Budd–Chiari syndrome in these patients is often made in the course of a routine examination, e.g. in patients with myeloproliferative syndrome.

There is currently no consensus on the classification of disease severity (fulminant vs. non-fulminant) and disease duration (acute, subacute and chronic). To be clinically useful, such a classification should be based on factors influencing prognosis and factors, which guide physicians in their management of the disease. These factors should be extracted from future studies based on large retrospective or prospective data sets. A purely descriptive stratification for disease severity should be used in clinical studies until such a prognostic classification is validated. In previous classifications, duration of symptoms, rate of disease progression, severity of manifestations and the age of venous or hepatic lesions have been variously used to differentiate among fulminant, acute, subacute or chronic disease [1,7,10–14]. The prognostic value of these categories has not been assessed. It is well known that the disease can have a long insidious course or a rapid downhill course. Furthermore, the apparent age of the macroscopic and microscopic damage to the liver may differ from the apparent duration of symptoms. Several cases with a recent clinical onset have been associated with marked liver fibrosis, suggesting a long preclinical course [15]. Recent thrombosis superimposed on older lesions probably explains the acute clinical onset in these patients.

4. Diagnostic investigations

The aims of diagnostic work-up in Budd–Chiari syndrome are threefold: assessment of the diagnosis, liver injury and etiology.

4.1. Assessment of diagnosis

Since the disease can deteriorate rapidly, the need to obtain the correct diagnosis is usually urgent. The diagnosis of Budd–Chiari syndrome should be suspected under the following circumstances: (a) whenever ascites, liver enlargement and upper abdominal pain are present simultaneously; (b) for patients with signs of chronic liver disease, whenever intractable ascites contrasts with mildly altered liver function tests; (c) whenever liver disease is documented in a patient known to have a prothrombotic disorder; (d) whenever fulminant hepatic failure is associated with liver enlargement and ascites; (e) whenever chronic liver disease remains unexplained after alcoholism, chronic viral hepatitis B or C, autoimmunity, iron overload, Wilson's disease and alpha-1 antitrypsin deficiency have been excluded. These circumstances, although suggestive, are not sufficient to make a diagnosis of Budd–Chiari syndrome. This is established only upon demonstration of an obstructed hepatic venous outflow tract. Obviously, histopathological assessment of an explanted liver or of a necropsy specimen is the ultimate method to firmly establish the diagnosis [15,16]. However, in the clinical setting, various imaging modalities are available for investigating the gross hepatic vascular anatomy: ultrasound, MRI, computed tomography and X-ray venography (Fig. 1A). Ultrasound combined with Doppler imaging has a diagnostic sensitivity of more than 75% and should be the first line of investigation [17,18]. Hepatic veins devoid of flow signal, collateral hepatic venous circulation, a spider-web appearance usually located in the vicinity of the hepatic vein ostia and stagnant, reversed or turbulent flow can all be indicative of Budd–Chiari syndrome [19,20]. Lack of visualization or tortuosity of the hepatic veins at real-time ultrasonography is common but not specific for Budd–Chiari syndrome because such features can be seen in advanced cirrhosis.

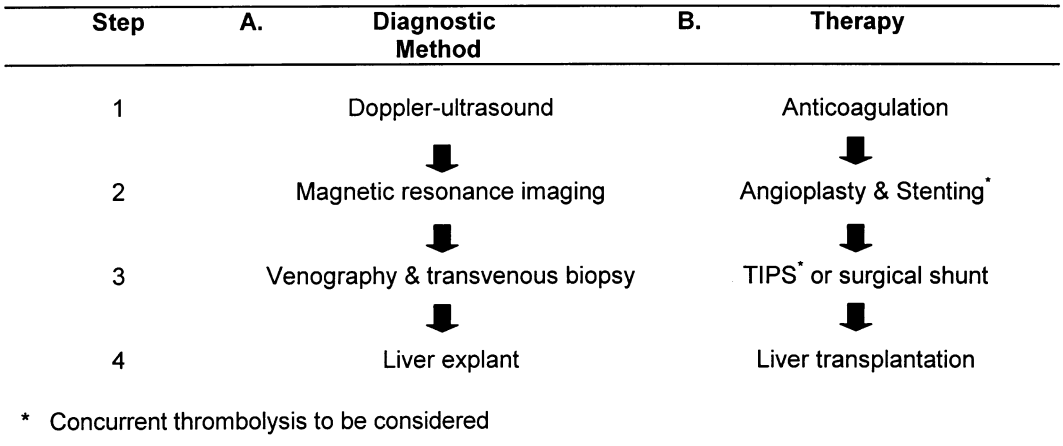

Fig. 1. Successive diagnostic (A) and therapeutic (B) steps to be considered for patients with Budd–Chiari syndrome.

A distinctive feature of Budd–Chiari syndrome, however, is the association with intrahepatic or subcapsular hepatic venous collaterals. When it is technically difficult to obtain an adequate sonographic evaluation or when the diagnostic features cannot be demonstrated, computed tomography or, preferably, MRI should be performed as a second line of investigation [19,21]. With the combination of these imaging procedures, the diagnosis will remain uncertain only in a small minority of cases. Uncertainty is likely to occur mainly in patients with cirrhosis. The third line of investigation should be retrograde cannulation of the hepatic veins for venography and liver biopsy [22]. Venography is useful in the assessment of the extent of outflow obstruction and also allows for pressure measurements, while the concurrent liver biopsy yields data that is useful not only for confirming the diagnosis of Budd–Chiari syndrome but also for ruling out other processes such as veno-occlusive disease and cirrhosis of other etiologies [23]. The disadvantage of venography is that it is often impossible to cannulate the hepatic veins and that the procedure usually requires the use of considerable amounts of iodine-containing contrast medium.

4.2. Assessment of disease severity

Liver injury and the extent of venous obstruction should be assessed to clarify prognosis and treatment of the disease. Although a liver biopsy can help in the diagnosis of Budd–Chiari syndrome, its value in the assessment of disease severity and prognosis has been shown to be of limited value [8,24]. This is probably due to sample variation, which is caused by the inhomogeneous distribution of disease in the liver. Liver histology, therefore, should not be considered essential to assess liver injury in patients with an established diagnosis of Budd–Chiari syndrome. Laboratory and radiological investigations, in addition to being safer, are probably better in providing prognostic information and in guiding therapy. Child–Pugh score and renal function are important determinants of prognosis [8,24]. The combination of Doppler-ultrasound and MRI allow optimal delineation of venous obstruction for therapeutic decisions. Venography with pressure measurements, in particular, should be performed when percutaneous or surgical shunting is considered. A major, as yet, unanswered issue is how to take the degree of liver dysfunction into account when choosing the type of medical or surgical therapy. The uncontrolled non-randomized studies performed thus far do not allow this issue to be addressed [14,25,26].

4.3. Assessment of etiology

The cause of Budd–Chiari syndrome should be investigated systematically. Liver imaging allows recognition of the lesions causing secondary Budd–Chiari syndrome. In primary Budd–Chiari syndrome, the search for an underlying thrombogenic condition can be carried out using the following investigations: hemogram, determination of plasma levels of coagulation factors and inhibitors, determination of genetic defects in the factor V and prothrombin gene, determination of antiphospholipid antibodies and lupus anticoagulant, and flow cytometry testing for paroxysmal nocturnal hemoglobinuria [27–33]. Primary Budd–Chiari syndrome is associated with one or more underlying thrombogenic conditions in at least 75% of the patients [28,34–36]. Several forms of hypercoagulability are inherited, a fact, which can be used to trace affected family members. Several systemic disorders, such as myeloproliferative disorders, may necessitate specific therapy, in addition to anticoagulation. Careful evaluation of the peripheral blood pattern for evidence of a primary myeloproliferative disorder may be followed by bone marrow biopsy, determination of total red cell mass and serum erythropoietin determination. Alternatively, culture of bone marrow or peripheral blood progenitors for assessment of spontaneous erythroid colony formation, when available, may support the diagnosis of a primary myeloproliferative disorder [37–39].

The diagnosis of inherited deficiencies in protein C, protein S and antithrombin in patients with Budd–Chiari syndrome is difficult because acquired deficiencies can develop in the event of liver failure, acute thrombosis and anticoagulant therapy. Therefore, decreased levels of coagulation inhibitors are of significance only when associated with normal or slightly reduced levels of coagulation factors. Otherwise, correction for the effect of liver insufficiency must be performed using e.g. the factor II or X plasma levels [28]. Family studies can provide useful information. Testing for methylene tetrahydrofolate reductase gene is not yet considered an essential part of the etiological work-up. Investigation of other recently documented thrombogenic factors (homocystein, factor XI, factor VIII) may prove useful but the sensitivity and specificity of the findings in the presence of chronic liver disease have to be assessed.

Since a combined etiology is found in at least 25% of the patients, identification of a single cause should not preclude investigation of other etiological factors [35]. Hormonal supplementation, for oral contraception, may enhance preexisting prothrombotic tendency and be implicated in the pathogenesis of Budd–Chiari syndrome [28].

5. Therapeutic interventions

The therapeutic approach to Budd–Chiari syndrome is diverse and should be adapted to disease severity. Asymptomatic patients should receive treatment for the potential underlying disease. Although based on circumstantial evidence, additional therapy with anticoagulation should be considered in these patients because (a) underlying prothrombotic states are often present, (b) recent improvement in the prognosis of Budd–Chiari syndrome has coincided with the generalized use of anticoagulation [24], (c)

there are no reports of severe bleeding in patients with the syndrome who received anticoagulation and (d) there is proven efficacy of anticoagulation in other forms of thrombosis. For symptomatic patients, anticoagulation should be combined with diuretics or paracentesis for ascites and with pharmacological or endoscopic therapy when there is a history of bleeding due to portal hypertension. Patients with ascites, variceal bleeding or signs of liver failure should be followed closely. Those who do not improve or develop severe or recurrent complications despite medical treatment should be considered for stenting, placement of transjugular intrahepatic portosystemic shunt (TIPS) or surgical portosystemic shunting. Liver transplantation should be considered when there is progression of liver dysfunction [40]. A stepwise approach to therapeutic interventions for Budd–Chiari patients is shown in Fig. 1B. Clearly, the eventual therapeutic choice may be influenced by local expertise in specific intervention techniques. At present, there are no clear end-points for defining failure of a given treatment and thus the need for more definitive intervention. Many studies of therapeutic interventions, particularly surgical shunts, have been published [14,25,41]. However, the scientific value of the published data is unsatisfactory. Data on selection criteria, proportion of patients not suitable for the studied procedures and long-term follow-up are often not mentioned. Therefore, conclusive information obtained from such studies is limited. Nevertheless, these studies provide important information that can be used in the design of future studies.

In patients with short segment stenosis [42] or occlusion of the hepatic veins with significant patent segments, it is desirable to overcome the obstruction between hepatic vein remnants and the inferior vena cava by means of balloon angioplasty with or without stenting [43–46]. This approach will reestablish hepatic venous outflow via the physiological route. Use of thrombolysis may enhance the success rate of these procedures [46–49]. If the veins cannot be entered via the transjugular route, then transhepatic puncture of hepatic vein remnants can be considered. The predictive factors for restenosis are still unknown. Therefore, the indications for stenting – at the time of initial angioplasty or after recurrence – remain unclear. After failure of angioplasy or stenting a surgical portosystemic shunt or TIPS should be considered (Fig. 1B).

The rationale for surgical portosystemic shunting is to convert the portal vein into an outflow tract of the liver [50]. There is controversy as to the superiority of a side-to-side portocaval vs. a mesocaval shunt in the management of Budd–Chiari syndrome. The latter was introduced because of the difficulty to perform a portocaval shunt in the presence of a hypertrophied caudate lobe [51]. In addition, mesocaval shunting can be achieved at some distance from the portal vein, thereby increasing the feasibility of a subsequent liver transplantation. Complete obstruction of the inferior vena cava or its compression by the caudate lobe adds to the difficulty of deciding to perform a surgical portosystemic shunt [52]. Patients with severe forms of Budd–Chiari syndrome have the potential to benefit from decompression of the liver by means of a surgical shunt. However, the surgical mortality of such high-risk patients may surpass the benefit of the shunt. The only study assessing the impact of surgical shunts on survival after adjustment of prognostic factors could not demonstrate a favorable effect [24]. The technique of TIPS has been described extensively but requires refinement for those with Budd–Chiari syndrome because the hepatic vein obstruction makes the procedure more difficult [53–55]. In most patients, it is possible to cannulate the remaining hepatic vein stump and to direct a needle through the liver parenchyma towards the right intrahepatic branch of the portal vein. When no hepatic vein remnants are found, ultrasound-guided puncture in the liver can be performed directly through the intrahepatic portion of the inferior vena cava. Orthotopic liver transplantation should be considered as effective treatment for rapidly progressive Budd–Chiari syndrome after failure of conventional treatment or portosystemic shunting [25,56]. Early mortality is related mainly to infections and late mortality to recurrent Budd–Chiari syndrome or thrombosis of the vena cava or portal vein, despite anticoagulation. Morbidity is related mainly to portal and arterial thrombosis, and hemorrhage under anticoagulant therapy. Since most patients with Budd–Chiari syndrome exhibit important risk factors for thrombosis, anticoagulation is probably best continued after transplantation. How long to continue anticoagulation is at present unclear. The European Liver Transplant Association (ELTA) collected the results for Budd–Chiari syndrome patients transplanted from 1998 using the European Liver Transplantation Registry. These data show a 5-year survival rate of 76%. There was no impact on survival of recipient age or whether transplantation was emergency vs. elective. The results, however, were negatively influenced by renal failure pre-transplantation and by the interval between diagnosis and transplantation.

6. Future studies

6.1. Aims for future studies

The implementation of a uniform terminology for Budd–Chiari syndrome will facilitate our understanding of future intervention studies and prognostic evaluations. Large multicenter studies are required to gain the information that will help us choose the best diagnostic and therapeutic options. As far as diagnostic work-up is concerned, it is necessary to further investigate the possibility of establishing the diagnosis by means of non-invasive imaging and of assessing liver injury by means of histological examination. Furthermore, it is necessary to determine whether an extensive work-up for prothrombotic disorders is justifiable. For all therapeutic interventions, the indications need to be

established. For angioplasty and thrombolysis, technical aspects need to be refined. For portosystemic shunting, it is important that factors that influence the results be identified and that the respective contributions of TIPS and surgical portosystemic shunting be determined. For liver transplantation, we need to assess the results after adjustment for severity of the liver disease.

6.2. End-points

The main complications of Budd–Chiari syndrome have been described in various patient series and case reports [1,3,9,12,24,57–61]. The rarity of the syndrome hinders extensive studies on prognostic factors. Survival is the main end-point of clinical studies to assess the management of Budd–Chiari syndrome. Portosystemic shunting and liver transplantation could also be used as an end-point (Table 3). However, as yet, indications for therapeutic modalities vary widely for Budd–Chiari syndrome [14,25,41,62]. Clearly, there is a need to find good secondary end-points for therapeutic decisions (e.g. early indications to proceed with portal decompression after unsuccessful medical therapy). In order to be used in clinical studies, the criteria indicating treatment failure are, at present, best defined by consensus definitions of the complications of other acute and chronic liver diseases. As a rule, such definitions have been established by interest groups. It is assumed that these definitions can apply to the complications of Budd–Chiari syndrome. Depending on the aim of the study, several of these secondary end-points can be used for future investigations (Table 3).

7. Conclusion

Budd–Chiari syndrome is an uncommon disorder. Outcome is poor in many cases. Therefore, a successful diagnostic and therapeutic approach is of vital importance. At present many definitions of Budd–Chiari syndrome are used and the distinction between acute and chronic Budd–Chiari syndrome, terms commonly used in clinical practice, is ambiguous. Many diagnostic and therapeutic algorithms applied today are based on personal experience or data from a limited number of patients. Furthermore, it is still uncertain whether portosystemic shunting, which is considered the primary therapy for this disease, in fact improves the clinical outcome. What can help us to overcome these dilemmas? In our opinion, two goals need to be achieved. Firstly, uniform definitions and a standardized classification system are of major importance not only to enhance our understanding of the disease but also to facilitate future studies and disease management. We hope that implementation of the nomenclature described in this paper will bring this goal closer. Secondly, prospective multicenter studies are needed to acquire the solid results needed to determine the best interventions for this challenging disorder.

Table 3
End-points for future studies in Budd–Chiari syndrome

(A) Primary end-points
Survival
Portosystemic shunting
Liver transplantation
(B) Secondary end-points
Quality of life by non-specific and liver specific scales [63,64]
General performance status according to the Karnovski scale
Nutritional status by classical anthropomorphic measurements [65]
Severity of liver disease by the Child–Pugh score [24,66]
Ascites, refractory ascites, renal failure and hepatorenal syndrome [67]
Pleural effusion
Gastrointestinal bleeding [68]
Hepatic encephalopathy [69]
Spontaneous bacterial peritonitis
Other severe infections [70]
Portal vein thrombosis
Thrombosis at extrasplanchnic sites
Complications of the underlying (prothrombotic) disorder

Acknowledgements

The European Group for the Study of Vascular Disorders of the Liver is supported by the European Commission of Community Research (Thematic Network, 5th Framework). Dr Janssen is a Clinical Fellow of the Netherlands Organisation for Scientific Research (NWO).

References

[1] Dilawari JB, Bambery P, Chawla Y, Kaur U, Bhusnurmath SR, Malhotra HS, et al. Hepatic outflow obstruction (Budd–Chiari syndrome). Experience with 177 patients and a review of the literature. Medicine (Baltimore) 1994;73(1):21–36.
[2] Ludwig J, Hashimoto E, McGill DB, van Heerden JA. Classification of hepatic venous outflow obstruction: ambiguous terminology of the Budd–Chiari syndrome. Mayo Clin Proc 1990;65(1):51–55.
[3] Okuda K, Kage M, Shrestha SM. Proposal of a new nomenclature for Budd–Chiari syndrome: hepatic vein thrombosis versus thrombosis of the inferior vena cava at its hepatic portion. Hepatology 1998;28(5):1191–1198.
[4] Deleve L, Shulman H, McDonald G. Toxic injury to hepatic sinusoids: sinusoidal obstruction syndrome. Sem Liv Dis 2002;22:27–41.
[5] Shulman HM, Fisher LB, Schoch HG, Henne KW, McDonald GB. Veno-occlusive disease of the liver after marrow transplantation: histological correlates of clinical signs and symptoms. Hepatology 1994;19(5):1171–1181.
[6] Stuart K, Bras G. Veno-occlusive disease of the liver. Q J Med 1957;26:291–314.
[7] Valla D, Benhamou J. Obstruction of the hepatic venous system. In: Bircher J, Benhamou J, McIntyre N, Rizzetto M, Rodes J, editors. Oxford textbook of clinical hepatology, 2nd ed. Oxford: Oxford Medical Publication, 1999. pp. 1469–1478.
[8] Tang T, Batts K, de Groen P, van Hoek B, Haagsma E, Hop W, et al. The prognostic value of histology in the assessment of patients with Budd–Chiari syndrome. J Hepatol 2001;35:338–343.
[9] Hadengue A, Poliquin M, Vilgrain V, Belghiti J, Degott C, Erlinger S, et al. The changing scene of hepatic vein thrombosis: recognition of asymptomatic cases. Gastroenterology 1994;106(4):1042–1047.
[10] Reynolds T, Peters R. Budd–Chiari syndrome. In: Schiff L, editor.

Diseases of the liver, 4th ed. Philadelphia, PA: JB Lippincott, 1975. pp. 1502–1510.
[11] Bismuth H, Sherlock DJ. Portasystemic shunting versus liver transplantation for the Budd–Chiari syndrome. Ann Surg 1991;214(5):581–589.
[12] Mahmoud AE, Mendoza A, Meshikhes AN, Olliff S, West R, Neuberger J, et al. Clinical spectrum, investigations and treatment of Budd–Chiari syndrome [see comments]. Q J Med 1996;89(1):37–43.
[13] Klein AS, Cameron JL. Diagnostis and management of the Budd–Chiari syndrome [see comments]. Am J Surg 1990;160(1):128–133.
[14] Orloff MJ, Daily PO, Orloff SL, Girard B, Orloff MS. A 27-year experience with surgical treatment of Budd–Chiari syndrome. Ann Surg 2000;232(3):340–352.
[15] Parker P. Occlusion of hepatic veins in man. Medicine 1959;38:369–402.
[16] Miller WJ, Federle MP, Straub WH, Davis PL. Budd–Chiari syndrome: imaging with pathologic correlation. Abdom Imaging 1993;18(4):329–335.
[17] Bolondi L, Gaiani S, Li Bassi S, Zironi G, Bonino F, Brunetto M, et al. Diagnosis of Budd–Chiari syndrome by pulsed Doppler ultrasound. Gastroenterology 1991;100(5 Pt 1):1324–1331.
[18] Chawla Y, Kumar S, Dhiman RK, Suri S, Dilawari JB. Duplex Doppler sonography in patients with Budd–Chiari syndrome. J Gastroenterol Hepatol 1999;14(9):904–907.
[19] Kane R, Eustace S. Diagnosis of Budd–Chiari syndrome: comparison between sonography and MR angiography. Radiology 1995;195(1):117–121.
[20] Millener P, Grant EG, Rose S, Duerinckx A, Schiller VL, Tessler FN, et al. Color Doppler imaging findings in patients with Budd–Chiari syndrome: correlation with venographic findings. AJR Am J Roentgenol 1993;161(2):307–312.
[21] Gupta S, Barter S, Phillips GW, Gibson RN, Hodgson HJ. Comparison of ultrasonography, computed tomography and 99mTc liver scan in diagnosis of Budd–Chiari syndrome. Gut 1987;28(3):242–247.
[22] Kreel L, Freston J, Clain D. Vascular radiology in the Budd–Chiari syndrome. Br J Radiol 1967;40:755–759.
[23] Tanaka M, Wanless IR. Pathology of the liver in Budd–Chiari syndrome: portal vein thrombosis and the histogenesis of veno-centric cirrhosis, veno-portal cirrhosis, and large regenerative nodules. Hepatology 1998;27(2):488–496.
[24] Zeitoun G, Escolano S, Hadengue A, Azar N, El Younsi M, Mallet A, et al. Outcome of Budd–Chiari syndrome: a multivariate analysis of factors related to survival including surgical portosystemic shunting. Hepatology 1999;30(1):84–89.
[25] Ringe B, Lang H, Oldhafer KJ, Gebel M, Flemming P, Georgii A, et al. Which is the best surgery for Budd–Chiari syndrome: venous decompression or liver transplantation? A single-center experience with 50 patients. Hepatology 1995;21(5):1337–1344.
[26] Henderson J, Warren D, Millikan W. Surgical options, hematologic evaluation and pathological changes in Budd–Chiari syndrome. Am J Surg 1990;159:41–50.
[27] Mohanty S, Saxena R, Acharya SK. Activated protein C resistance in Budd–Chiari syndrome. Int J Hematol 2000;72(2):255.
[28] Janssen HL, Meinardi JR, Vleggaar FP, van Uum SH, Haagsma EB, van Der Meer FJ, et al. Factor V Leiden mutation, prothrombin gene mutation, and deficiencies in coagulation inhibitors associated with Budd–Chiari syndrome and portal vein thrombosis: results of a case–control study. Blood 2000;96(7):2364–2368.
[29] Deltenre P, Denninger MH, Hillaire S, Guillin MC, Casadevall N, Briere J, et al. Factor V Leiden related Budd–Chiari syndrome. Gut 2001;48(2):264–268.
[30] Bucciarelli P, Franchi F, Alatri A, Bettini P, Moia M. Budd–Chiari syndrome in a patient heterozygous for the G20210A mutation of the prothrombin gene. Thromb Haemost 1998;79(2):445–446.
[31] Pelletier S, Landi B, Piette JC, Ekert P, Coutellier A, Desmoulins C, et al. Antiphospholipid syndrome as the second cause of non-tumorous Budd–Chiari syndrome. J Hepatol 1994;21(1):76–80.
[32] Aggarwal R, Ravishankar B, Misra R, Aggarwal A, Dwivedi S, Naik SR. Significance of elevated IgG anticardiolipin antibody levels in patients with Budd–Chiari syndrome. Am J Gastroenterol 1998;93(6):954–957.
[33] Valla D, Dhumeaux D, Babany G, Hillon P, Rueff B, Rochant H, et al. Hepatic vein thrombosis in paroxysmal nocturnal hemoglobinuria. A spectrum from asymptomatic occlusion of hepatic venules to fatal Budd–Chiari syndrome. Gastroenterology 1987;93(3):569–575.
[34] Mahmoud AE, Elias E, Beauchamp N, Wilde JT. Prevalence of the factor V Leiden mutation in hepatic and portal vein thrombosis [see comments]. Gut 1997;40(6):798–800.
[35] Denninger MH, Chait Y, Casadevall N, Hillaire S, Guillin MC, Bezeaud A, et al. Cause of portal or hepatic venous thrombosis in adults: the role of multiple concurrent factors. Hepatology 2000;31(3):587–591.
[36] Minnema MC, Janssen HL, Niermeijer P, de Man RA. Budd–Chiari syndrome: combination of genetic defects and the use of oral contraceptives leading to hypercoagulability. J Hepatol 2000;33(3):509–512.
[37] Valla D, Casadevall N, Lacombe C, Varet B, Goldwasser E, Franco D, et al. Primary myeloproliferative disorder and hepatic vein thrombosis. A prospective study of erythroid colony formation in vitro in 20 patients with Budd–Chiari syndrome. Ann Intern Med 1985;103(3):329–334.
[38] Acharya J, Westwood NB, Sawyer BM, Messinezy M, Burroughs AK, Mehta AB, et al. Identification of latent myeloproliferative disease in patients with Budd–Chiari syndrome using X-chromosome inactivation patterns and in vitro erythroid colony formation. Eur J Haematol 1995;55(5):315–321.
[39] Dayal S, Pati HP, Pande GK, Sharma MP, Saraya AK. Multilineage hemopoietic stem cell defects in Budd Chiari syndrome. J Hepatol 1997;26(2):293–297.
[40] Slakey DP, Klein AS, Venbrux AC, Cameron JL. Budd–Chiari syndrome: current management options. Ann Surg 2001;233(4):522–527.
[41] Hemming AW, Langer B, Greig P, Taylor BR, Adams R, Heathcote EJ. Treatment of Budd–Chiari syndrome with portosystemic shunt or liver transplantation. Am J Surg 1996;171(1):176–180 (discussion p. 180–1).
[42] Valla D, Hadengue A, el Younsi M, Azar N, Zeitoun G, Boudet MJ, et al. Hepatic venous outflow block caused by short-length hepatic vein stenoses. Hepatology 1997;25(4):814–819.
[43] Lopez RR, Benner KG, Hall L, Rosch J, Pinson CW. Expandable venous stents for treatment of the Budd–Chiari syndrome. Gastroenterology 1991;100(5 Pt 1):1435–1441.
[44] Baijal SS, Roy S, Phadke RV, Agrawal DK, Kumar S, Choudhuri G. Management of idiopathic Budd–Chiari syndrome with primary stent placement: early results. J Vasc Interv Radiol 1996;7(4):545–553.
[45] Bilbao JI, Pueyo JC, Longo JM, Arias M, Herrero JI, Benito A, et al. Interventional therapeutic techniques in Budd–Chiari syndrome. Cardiovasc Intervent Radiol 1997;20(2):112–119.
[46] Fisher NC, McCafferty I, Dolapci M, Wali M, Buckels JA, Olliff SP, et al. Managing Budd–Chiari syndrome: a retrospective review of percutaneous hepatic vein angioplasty and surgical shunting. Gut 1999;44(4):568–574.
[47] Ishiguchi T, Fukatsu H, Itoh S, Shimamoto K, Sakuma S. Budd–Chiari syndrome with long segmental inferior vena cava obstruction: treatment with thrombolysis, angioplasty, and intravascular stents. J Vasc Interv Radiol 1992;3(2):421–425.
[48] Raju GS, Felver M, Olin JW, Satti SD. Thrombolysis for acute Budd–Chiari syndrome: case report and literature review. Am J Gastroenterol 1996;91(6):1262–1263.
[49] Griffith JF, Mahmoud AE, Cooper S, Elias E, West RJ, Olliff SP. Radiological intervention in Budd–Chiari syndrome: techniques and outcome in 18 patients. Clin Radiol 1996;51(11):775–784.

[50] Tilanus HW. Budd–Chiari syndrome. Br J Surg 1995;82(8):1023–1030.
[51] Mitchell MC, Boitnott JK, Kaufman S, Cameron JL, Maddrey WC. Budd–Chiari syndrome: etiology, diagnosis and management. Medicine (Baltimore) 1982;61(4):199–218.
[52] Emre A, Kalayci G, Ozden I, Bilge O, Acarli K, Kaymakoglu S, et al. Mesoatrial shunt in Budd–Chiari syndrome. Am J Surg 2000;179(4):304–308.
[53] Blum U, Rossle M, Haag K, Ochs A, Blum HE, Hauenstein KH, et al. Budd–Chiari syndrome: technical, hemodynamic, and clinical results of treatment with transjugular intrahepatic portosystemic shunt. Radiology 1995;197(3):805–811.
[54] Ochs A, Sellinger M, Haag K, Noldge G, Herbst EW, Walter E, et al. Transjugular intrahepatic portosystemic stent-shunt (TIPS) in the treatment of Budd–Chiari syndrome. J Hepatol 1993;18(2):217–225.
[55] Ganger DR, Klapman JB, McDonald V, Matalon TA, Kaur S, Rosenblate H, et al. Transjugular intrahepatic portosystemic shunt (TIPS) for Budd–Chiari syndrome or portal vein thrombosis: review of indications and problems. Am J Gastroenterol 1999;94(3):603–608.
[56] Halff G, Todo S, Tzakis A, Gordon R, Starzl T. Liver transplantation for Budd–Chiari syndrome. Ann Surg 1990;211:43–49.
[57] Rector Jr WG, Xu YH, Goldstein L, Peters RL, Reynolds TB. Membranous obstruction of the inferior vena cava in the United States. Medicine (Baltimore) 1985;64(2):134–143.
[58] Wang ZG, Zhu Y, Wang SH, Pu LP, Du YH, Zhang H, et al. Recognition and management of Budd–Chiari syndrome: report of one hundred cases. J Vasc Surg 1989;10(2):149–156.
[59] Simson IW. Membranous obstruction of the inferior vena cava and hepatocellular carcinoma in South Africa. Gastroenterology 1982;82(2):171–178.
[60] Powell-Jackson PR, Ede RJ, Williams R. Budd–Chiari syndrome presenting as fulminant hepatic failure. Gut 1986;27(9):1101–1105.
[61] Mahmoud AE, Helmy AS, Billingham L, Elias E. Poor prognosis and limited therapeutic options in patients with Budd–Chiari syndrome and portal venous system thrombosis. Eur J Gastroenterol Hepatol 1997;9(5):485–489.
[62] Klein AS, Sitzmann JV, Coleman J, Herlong FH, Cameron JL. Current management of the Budd–Chiari syndrome [see comments]. Ann Surg 1990;212(2):144–149.
[63] Essink-Bot ML, Krabbe PF, Bonsel GJ, Aaronson NK. An empirical comparison of four generic health status measures. The Nottingham Health Profile, the Medical Outcomes Study 36-item Short-Form Health Survey, the COOP/WONCA charts, and the EuroQol instrument. Med Care 1997;35(5):522–537.
[64] Gralnek IM, Hays RD, Kilbourne A, Rosen HR, Keeffe EB, Artinian L, et al. Development and evaluation of the Liver Disease Quality of Life instrument in persons with advanced, chronic liver disease – the LDQOL 1.0. Am J Gastroenterol 2000;95(12):3552–3565.
[65] Merli M, Riggio O, Dally L. Does malnutrition affect survival in cirrhosis? PINC (Policentrica Italiana Nutrizione Cirrosi). Hepatology 1996;23(5):1041–1046.
[66] Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. Br J Surg 1973;60(8):646–649.
[67] Arroyo V, Gines P, Gerbes AL, Dudley FJ, Gentilini P, Laffi G, et al. Definition and diagnostic criteria of refractory ascites and hepatorenal syndrome in cirrhosis. International Ascites Club. Hepatology 1996;23(1):164–176.
[68] de Franchis R. Updating consensus in portal hypertension: report of the Baveno III Consensus Workshop on definitions, methodology and therapeutic strategies in portal hypertension. J Hepatol 2000;33(5):846–852.
[69] Blei A. Hepatic encephalopathy. In: Bircher J, Benhamou J, McIntyre N, Rizzetto M, Rodes J, editors. Oxford textbook of clinical hepatology, Oxford: Oxford Medical Publication, 1999. pp. 765–783.
[70] Rimola A, Garcia-Tsao G, Navasa M, Piddock LJ, Planas R, Bernard B, et al. Diagnosis, treatment and prophylaxis of spontaneous bacterial peritonitis: a consensus document. International Ascites Club. J Hepatol 2000;32(1):142–153.