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Budd Chiari syndrome

Prognosis in Budd Chiari syndrome after re-establishing hepatic venous drainage

D-C Valla

Treatment of Budd Chiari syndrome by interventional radiology has good medium term survival for patients with all forms of disease severity

Budd Chiari syndrome (BCS), the entity resulting from an obstructed hepatic venous outflow tract,^{1,2} is a so-called ultra rare disease³: the estimated incidence was approximately 1 per 2.5 million per year in France or Japan in the 1990s.⁴ This rarity explains why classical randomised trials could not be performed in the past. Trials cannot be foreseen in the near future either, even though excellent collaborations have been developed in European countries, nationwide, and at an international level (see <http://www.envie-project.org/origin.html>). The report by the Birmingham group⁵ in this issue of *Gut* should be analysed in the context of the rarity of this disease (see page 878).

The authors retrospectively analysed the outcome of patients with primary BCS treated percutaneously with repermeation (hepatic vein or inferior vena cava angioplasty, with or without stenting) or transjugular intrahepatic portosystemic shunting (TIPS). They included 29 patients referred between 1985 and 1999, and 32 patients referred between 1999 and 2004. This is the largest series of BCS patients treated with interventional radiology in a single Western centre. There are several reports on large series from China^{6–8} and India⁹ where, unlike Western countries, there is a

large predominance of inferior vena cava occlusion. Inferior vena cava occlusion differs from pure hepatic vein occlusion in many aspects.¹⁰

The authors made considerable efforts to circumvent the usual limitations in treatment evaluation of rare diseases. Firstly, as above mentioned, they included a remarkably large number of cases, given the ultra rarity of the disease. Secondly, although the study focused on a particular treatment modality, all other modalities were available at this referral centre. Thirdly, they stratified the analyses according to prognostic indices that have been well validated in several Western studies. Fourthly, the findings were placed in the perspective of other contemporary cohorts where interventional radiology had not been as extensively used. Unfortunately, there is no accepted statistical tool to compare survival in small samples of different patient populations, even after adjustment for established prognostic indices.

The results were impressive, as actuarial survival in the entire cohort at one and five years was 94% (95% confidence interval (CI) 88–100%) and 87% (95% CI 78–96%), respectively. These survival rates can be contrasted with those from another British study

dating back to the early 1970s, which illustrates the natural history of BCS: one and five year survival rates were 68% and 10%, respectively.¹¹ These results are even more comforting when one remembers that most BCS patients are young adult females generally not exposed to lifestyle related risk factors except for the contraceptive pill—a demographic group where expected life duration is long. There are several possible reasons for such an improvement: earlier diagnosis, recognition of asymptomatic cases, better general supportive care, or true efficacy of specific treatments for venous obstruction. Whatever the reasons, the authors have to be congratulated for this achievement.

The authors opted for evaluation of a therapeutic modality: “all interventional radiology”. This option is in line with their progressive elaboration of an algorithm for treatment, based on their unique experience.¹² The algorithm was applied to patients seen after 1999. According to this algorithm, patients were treated with angioplasty whenever a short length stenosis on the hepatic veins or inferior vena cava was identified. Such short length stenoses were specifically looked for using ultrasound by world leading experts in hepatic vascular radiology and percutaneous recanalisation. In the other patients, TIPS was performed whenever medical therapy alone failed to control manifestations. Opting for an evaluation of “all interventional radiology” led to pooling of patients treated with percutaneous recanalisation or with TIPS, which is sensible for the purpose of increasing the number of patients. Even with a large number of patients available for enrolment, testing the full strategy in a randomised trial would be difficult as it is unclear what should be the comparator.

There are limitations, however, in evaluating the proposed algorithm. Although 61 patients were analysed, only 32 were deliberately managed according to this algorithm (that is, those referred after 1999). The 29 other

Table 1 Mean survival rates according to baseline prognostic indices in recently reported cohorts of Budd Chiari syndrome patients

	PI ≤ 5.4* (% survival (n))	PI > 5.4 (% survival (n))	Class I** (% survival (n))	Class II (% survival (n))	Class III (% survival (n))
1 y survival					
Eapen ⁵	100 (25)	89 (36)	100 (16)	94 (32)	85 (13)
Zeitoun ²³	100 (60)	77 (60)			
Murad ²⁴			93 (55)	85 (95)	60 (55)
5 y survival					
Eapen ⁵	89 (25)	82 (36)	100 (16)	86 (32)	77 (13)
Zeitoun ²³	95 (60)	62 (60)			
Murad ²⁴			89 (55)	74 (95)	42 (55)

In the study by Eapen *et al*, all patients were treated with interventional radiology. In the studies of Zeitoun *et al* and Murad *et al*, patients were predominantly treated with medical means and/or surgical shunting.

*PI, prognostic index according to Zeitoun and colleagues.²³

**Class according to Murad and colleagues.²⁴

patients were managed with percutaneous repermeation at a time when TIPS was not fully used. As patients undergoing surgical shunt or transplantation after percutaneous recanalisation were excluded, only patients with successful angioplasty or TIPS were included. Overall, 44 patients treated at the centre during the study period were excluded because "all interventional radiology" modality was not applied for unspecified reasons. This option introduces a bias that is attenuated only in part by stratification according to baseline prognostic indices. Moreover, it is not certain that the prognostic indices apply to the populations so selected as these indices were elaborated in unselected patients. An alternative for coping with these limitations would have been to analyse overall survival in the whole cohort of 39 patients referred to the centre since 1999. However, what is gained on the one hand is lost on the other, as sample size and follow up duration would be considerably decreased.

A major finding of the Birmingham group was the low complication rate for percutaneous repermeation, even though a sophisticated transhepatic approach was used in some patients. It is not certain that similar results can be achieved by any team, as this requires interventional skill and experience in the management of anticoagulation early after percutaneous interventions. What about the efficacy of recanalisation? Four patients were treated with repermeation and TIPS, implying that repermeation was insufficient in these patients. In addition, eight of the 44 patients excluded from the analysis had a surgical shunt after repermeation. Thus among 43 patients treated with repermeation, there appeared to be 12 instances of probable clinical failure (28%). This failure rate seems sufficiently low, and the procedure sufficiently innocuous, to recommend attempting percutaneous recanalisation first. Of greater concern is the fact that

patients with short length stenoses in hepatic veins or the inferior vena cava have a less severe disease and a better outcome than patients with diffuse hepatic vein occlusion.¹³ Moreover, eight of 31 patients treated with recanalisation in Birmingham were possibly asymptomatic (that is, spontaneously compensated) as they were ascribed to Child class A. Asymptomatic BCS patients have a better outcome than symptomatic (that is, decompensated) patients.¹⁴ As symptomatic and asymptomatic patients undergoing recanalisation were pooled, the actual efficacy of repermeation in *symptomatic* cases remains to be clarified. Whether repermeation can be beneficial in *asymptomatic* patients remains conjectural. Recanalisation in asymptomatic patients seems more logical when there are pronounced features of portal hypertension (that is, marked portosystemic collaterals) than when extensive hepatic vein collaterals have developed while portosystemic collaterals are inconspicuous. In any case, even a low risk of serious complications should be kept in mind when making a decision on the management of these asymptomatic patients.¹²

Data on TIPS confirm recent reports from other expert groups¹⁵⁻²² in that TIPS proved feasible, probably efficient, and well tolerated in most patients, and that revision was frequently needed, albeit usually successful. Taken together, the reported experiences in TIPS are sufficiently convincing for medium term outcome that comparison with no treatment or with surgical shunting would be considered unethical by most experts.² However, follow up data are needed in the long term. One of the Birmingham patients died from rapid hepatic failure following TIPS, and this might have also been the case in other centres.¹⁸ Predictive factors for this untoward outcome have to be identified. Where liver graft availability is limited, predictive factors would allow patients at risk to be evaluated for transplantation before TIPS is performed.

Several conclusions can be drawn from the comparison of the Birmingham data with those from centres where contemporary use of interventional radiology has been limited (table 1). Firstly, the indications for interventional radiology are large, as patients did better in Birmingham than those treated mainly with surgical shunting or medical means at other centres. Secondly, interventional radiology appears to prevent patients from requiring liver transplantation in the medium term. Indeed, none of the patients managed through the "all interventional radiology" strategy since 1999 required a liver transplant, while most of them survived (see authors' fig 2).⁵ However, more data with a longer follow up time are needed to confirm this. Finally, can an "all interventional radiology" strategy reduce mortality in BCS patients? Patients with the highest risk scores appeared to benefit the most from the Birmingham approach, based on the data presented in table 1. At five years, differences in survival between the Birmingham and Clichy studies were -6% and +20% in the low risk and high risk groups, respectively²³; similarly, differences between the Birmingham and Rotterdam studies were +11% and +35% in the low risk and high risk groups, respectively.²⁴ Moreover, in Birmingham, differences in survival between high risk and low risk subgroups were halved compared with survival differences between these two subgroups in other centres. As stated above, I recognise that such a comparison is incorrect. Never the less, the most favourable trend in the outcome of severe patients when treated with the "all interventional radiology" strategy cannot be ignored.

Thus an algorithm that is based on the progressive implementation of therapeutic modalities by order of increasing invasiveness, according primarily not to the status of the patient but to the response to previous therapy, is feasible, likely effective, and possibly cost effective. However, it should be kept in mind that the data are from a centre with world renowned experience not only in interventional radiology but also in the general management of Budd Chiari patients. What is true in Birmingham is not necessarily so in every centre.

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EDITOR'S QUIZ: GI SNAPSHOT

An unusual cause and treatment for ascites after liver transplantation

Robin Spiller, Editor

Clinical presentation

Six weeks after orthotopic liver transplantation due to acute Budd-Chiari syndrome, a 48 year old female was admitted for treatment of newly developed ascites and severe cachexia. To rule out recurrence of Budd-Chiari-syndrome, an abdominal ultrasound was performed, showing all hepatic veins with regular flow. The patient had lost 22 kg in weight since surgery (BMI 12.9 kg/m²). The patient was started on enteral and parenteral nutrition and diuretics. However, after a few days she suffered from tense ascites, refractory to increasing doses of diuretics. Serum albumin was 19.1 g/l and the serum-ascites-albumin gradient was >11 g/l. In addition, oesophageal variceal bleeding, requiring rubber band ligation, developed.

Question

What is your diagnosis and what tests would you order?

See page 884 for answer

This case is submitted by:

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