

Dear reviewer (02537403),

Thank you very much for your comments about our paper submitted to World Journal of Clinical Cases (54949). We are very appreciated for your careful reading, and we quite agree with your opinion that our findings about the potential protective factors which lead to good prognosis in patients without treatment need further study and multicentric trials will help clinicians to discover better options for management.

Thanks again for your valuable comments.

Best regards,

Zhang Wei

Dear reviewer (01490498),

Thank you very much for your comments about our paper submitted to World Journal of Clinical Cases (54949). We would like to answer your questions and revised our manuscript according to your comments.

1. I am intrigued by the large number of patients that refused. They agreed to have the diagnostic investigation but did not want the problem to be fixed? I cannot imagine most patients would refuse treatment, and certainly not up to 50% of them. What were they told? What is the exact reason for refusal? Was it due to financial aspects?

Response : In our study, patients after recanalization procedure are regularly followed, and the main diagnostic investigation is color Doppler ultrasonography which is very cheap in China (120RMB). However, as for the cost of treatment, it's very expensive (About 20000+RMB). Our previous study which explored the epidemiological features based on the Chinese literature survey (Gastroenterol Res Pract 2015; 2015: 738548 [PMID: 26504461 PMCID: PMC4609452 DOI: 10.1155/2015/738548]) demonstrated that most of Chinese BCS patients lived in relatively poor areas. All patients who had restenosis were told the importance of treatment in detail, and most of the patients who refuse further treatment were due to financial difficulties.

2. Much details of the procedures is missing with regards to types of stent, pressures etc.

Response : The detailed information of technical aspects (such as balloon and stent specifications, pressures before and after treatment) were not presented because the focus of our study was treatment strategy of BCS patients with restenosis. So, we didn't pay much attention to this.

3. It is really not surprising that patients who have interventions do better so not sure what this study add to the literature?

Response : We agree that that patients who have interventions do better than those who refused further treatment, and our study also confirms that. However, we find more important things are that it is extremely valuable due to the very long follow-up period of these patients that will give a clear overview about the outcome of the BCS patients developing restenosis after recanalization intervention. Moreover, we highlight the strengths and the limits of this retrospective study and strongly suggest the need of studying potential protective factors which lead to good prognosis in patients without treatment. The further multicentric trials will help us to discover better options for management.

4. Were patients on long term anticoagulation? Surely patients would have consented to simple tablets and follow up?

Response : All patients received intravenous heparin for 5-7 days during hospitalization and were advised to continue with warfarin for 6-12 months after discharge to maintain an international normalized ratio of 2-3.

Thanks again for your valuable comments.

Best regards,

Zhang Wei

Dear reviewer (05060622),

Thank you very much for your comments about our paper submitted to World Journal of Clinical Cases (54949). We are very appreciated for your valuable corrections and careful reading. The manuscript has been revised according to your correction, and the corresponding revisions were highlighted in the revised manuscript.

1. A limited and very heterogeneous group of patients in terms of clinical characteristics as well as the pattern of involvement.

Response : As a retrospective study, some biases may have been introduced in the case selection and data collection, and the clinical characteristics and the pattern involved were heterogeneous.

2. The term groups (PTA and PTA+stenting) are not comparable. In fact, the analysis of Table 1 shows that 40% patients in the PTA+stent group had stenosis>5 cm which is not an ideal candidate for recanalisation.

Response : The patients were grouped retrospectively according to the treatment method, and the baseline results were not homogenous, which made the comparison infeasible. In present study, 8 patients in PTA+stent group (which accounting for 40% of the group) with long-segmental (more than 5 cm) obstruction of IVC had encountered restenosis. We believe that long-segmental obstruction of IVC is not the contraindication for recanalization, and in our department, the technical success rate is high (seen our previous study: World J Gastroenterol 2018; 24(10): 1134-1143 [PMID: 29563757 PMID: PMC5850132 DOI: 10.3748/wjg.v24.i10.1134]). However, the prevention of restenosis after recanalization is a great challenge. As we known, restenosis commonly occurs due to thrombosis of the IVC, membranous obstructive lesion regeneration, or elastic recoiling of segmental obstructive lesions. Because the etiology of Chinese BCS patients with membranous or segmental obstruction is not clear, the prevention is hard to

deal.

3. The study period spans over 30 years and one can expect changes in the technique as well as expertise of the interventional radiologists.

Response : We agree that our study spanned 30 years, and in a few cases, the treatment strategies of the early stage were not quite consistent with those of the later stage, and the technique as well as expertise were also constantly updated. This is a potential defect of our study.

4. There is no mention of the technical details-including the size of balloon, size of stent, criteria for initial selection of patients for PTA vs stenting, definition of technical success during recanalisation.

Response : The detailed information of technical aspects (such as balloon and stent specifications, pressures before and after treatment) were not presented because the focus of our study was treatment strategy of BCS patients with restenosis. The criteria for initial selection of patients for recanalization were reported in our previous study (seen World J Gastroenterol 2018; 24(10): 1134-1143 [PMID: 29563757 PMID: PMC5850132 DOI: 10.3748/wjg.v24.i10.1134]), and the selection criteria were not described in present study.

5. The management strategy for the combined type of BCS which was the most common type in this study is not clear. Did the authors recanalised both IVC as well as hepatic veins and where stenting or PTA was done.

Response : Thank you very much for your reminder. For the treatment strategy of combined type of BCS, the IVC recanalization was performed initially, and a “wait-and-see” attitude was adopted and the response to the treatment was observed subsequently. In cases of clinical failure of IVC recanalization alone, HV recanalization or TIPS placement was performed. The management of restenosis of combined type of BCS were follow the above principles, and IVC

recanalization was performed prior to HV recanalization. PTA was always used first for recanalization, and stenting was considered only if PTA treatment fails.

-Methodology: -Study design and case selection: Of the 178 patients, how many underwent PTA or PTA+stenting -Treatment strategy for restenosis: Include details of the technique as described above Results

Response : In our previous study, 178 BCS patients were treated with interventional radiology, among whom 165 were successfully treated by recanalization, including 96 patients with PTA and 69 patients with PTA + stent. For detail information, please refer to our previous research report (seen World J Gastroenterol 2018; 24(10): 1134-1143 [PMID: 29563757 PMID: PMC5850132 DOI: 10.3748/wjg.v24.i10.1134]).

-Follow up: The statements on the death in each group and subgroup (those who underwent treatment and those who refused) are not clear.

Response : In the PTA group, the median time of follow-up was 61.5 (range, 1-313) months. Thirteen patients died during a median survival time of 36 (range, 1-123) months: 7 died of liver or multiple organ failure, 3 died of hepatocellular carcinoma (HCC), and 3 died of variceal bleeding. All these deaths were considered to be related to BCS. The other 3 patients who died of intracranial hemorrhage induced by hypertension, disseminated intravascular coagulation, and traffic accident were considered to be cases not related to BCS. Notably, among the 13 patients who refused active treatment, 7 died (median of 55 months, range of 1 month to 123 months). In the PTA + stent group, the median time of follow-up was 52.5 (range, 2-276) months. Ten patients died, with a median time of 30 (range, 2-239) months: 5 died of liver or multiple organ failure, 2 died of variceal bleeding, 2 died of hepatic encephalopathy, and 1 died of HCC. Notably, all 9 patients who refused further treatment after restenosis died. Detailed information on the follow-up

outcomes is shown in Table 2.

-Discussion -first paragraph: The author describe that in patients who had restenosis after PTA+stenting had more serious condition. This is not clear-are they referring to CTP score?

Response : For the PTA group, the patient condition was relatively mild, while for the PTA + stent group, the condition was more serious (higher Child-Turcotte-Pugh score).

-Additionally authors say that the two groups cannot be compared (contradiction to their initial statement). I believe that the comparison is possible and is important and highlights that the two groups were basically not comparable.

Response :The patients in this study were retrospectively divided into the PTA group and PTA + stent group according to the initial treatment modality, but the baseline characteristics of these two groups were heterogeneous; thus, a comparison cannot be made. It should be noted that the baseline characteristics of patients receiving stent implantation were more serious than those of patients receiving PTA alone, so these two groups can neither directly compare nor deny the role of stent implantation.

-second paragraph: The authors highlight the three issues that can arise with stenting. Unfortunately there are no references for the same and these need to be carefully stated and referenced.

Response : Thank you very much for your reminder. The references of related studies have been added (seen reference 9,10,12,13).

-Please change "lieu" to view"

Response : The manuscript have been revised according to your correction.

-Fifth paragraph The recent RCT on the subject of PTA vs stenting needs more critical analysis and comparison with the current study. The authors have just given a passing reference to this trial. This trial had basically patients with stenosis<4cm compared to this study where significant proportion of patients who has stenosis more than 5 cm. Is this important?

Response : As your comment point out, the recent RCT involved BCS patients with short-length stenosis showed that PTA + stent was superior to PTA alone in terms of the treatment efficacy for preventing restenosis. We acknowledge that the length of the obstructive lesion in BCS patients did influence the treatment selection. However, as for the stent implantation, we payed more attention to the long-term follow-up complications other than the primary obstructive lesion length. For the patients who had stent implantation, the length of stenosis whether it was < 4 cm or > 5 cm may have some influence on the occurrence of restenosis, but we didn't think it was important. What was really of the most importance is the primary etiology of BCS and the cause of restenosis.

-Tables Table 2: needs better format for understanding

Response : The table has been revised according to your suggestion.

Thanks again for your valuable comments.

Best regards,

Zhang Wei

Dear reviewer (03756484),

Thank you very much for your comments about our paper submitted to World Journal of Clinical Cases (54949). We would like to answer your questions as follows.

It is clearly a very large experience about the endovascular treatment of Budd-Chiari syndrome and it is the strong point of this study. Why do you put forward "the follow-up" of these patients since restenosis is always symptomatic ? The results of comparison between patients "retreated" and patients refusing the treatment was predictable

Response : As we known that studies have reported excellent or satisfactory outcomes of recanalization. However, because the long-term outcome of patients with restenosis (the most common complication after recanalization) is unknown, this retrospective study proposes to analyze a case series of BCS patients with restenosis regarding the treatment strategy and long-term survival. Restenosis was defined as the recurrence of symptoms after recanalization.

Our previous study which explored the epidemiological features based on the Chinese literature survey (Gastroenterol Res Pract 2015; 2015: 738548 [PMID: 26504461 PMCID: PMC4609452 DOI: 10.1155/2015/738548]) demonstrated that most of Chinese BCS patients lived in relatively poor areas. All patients who had restenosis were told the importance of treatment in detail, and most of the patients who refuse further treatment were due to financial difficulties.

We agree that that patients who have interventions do better than those who refused further treatment, and our study also confirms that. However, we find more important things are that it is extremely valuable due to the very long follow-up period of these patients that will give a clear overview about the outcome of the BCS patients developing restenosis after recanalization intervention. Moreover, we highlight the strengths and the

limits of this retrospective study and strongly suggest the need of studying potential protective factors which lead to good prognosis in patients without treatment. The further multicentric trials will help us to discover better options for management.

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Zhang Wei