

# **AB0, von Willebrand factor/Factor VIII and portal vein thrombosis in decompensated cirrhosis: too late to unmask the culprit?**

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Dear Editor,

We read with interest the paper from Scheiner et al., who investigated the influence of ABO blood group on the risk of portal vein thrombosis (PVT) in patients with cirrhosis and wish to make comments.<sup>1</sup> In the general population, the venous thrombosis risk is 2-4 fold increased in non-0 individuals, likely because of their higher von Willebrand factor (VWF) and factor VIII (FVIII) levels.<sup>2</sup> In cirrhotics, VWF and FVIII are markedly increased.<sup>3</sup> However, Scheiner et al. could not find association between non-0 group and PVT in 84947 cirrhotics listed for liver transplantation in the USA. In a second independent cohort of 411 cirrhotics (XX/XX Child A/BC), they found that the contribution of non-0 blood group on VWF variation was substantially smaller than in the general population and limited to patients with early stage cirrhosis, without further effect on FVIII, thus justifying the lack of association between non-0 blood group and PVT. To further explore this issue, we evaluated VWF:Ag, FVIII-activity, Protein C and Endogenous Thrombin Potential with/without thrombomodulin ratio (ETPr) in 69 patients with stable cirrhosis (Age 61±12, 70% male, Child A:41%, Child B/C:59%). VWF:Ag increased with cirrhosis severity, without further effect on FVIII. Non-0 vs 0 blood group had higher VWF:Ag (+48%, p<0.05) in Child A patients, but not in Child B/C (+8%, p=486) (Table 1). Interestingly, FVIII/VWF:Ag linear correlation was stronger in non-0 blood-group (Pearson correlation R=0.621, p<0.001) than in 0-blood group (R=0.110, p=0.481). These data confirm that the influence of blood-group on VWF:Ag/FVIII, observed in the general population, is maintained only in the early stages of cirrhosis, and suggests a disease-gradient effect from Child A to Child B/C cirrhosis that overcomes genetics and modifies the correlation VWF/FVIII. FVIII levels, though increased, reached a plateau and did not parallel the further rises of VWF with cirrhosis severity. This notwithstanding, the ETPr increased with cirrhosis severity, as expected, driven by the progressive decrease of protein C.<sup>4</sup> Thus, the FVIII/protein C ratio, rather than the VWF/FVIII levels, better signals the prothrombotic state of advanced cirrhosis.<sup>5</sup> That is why, in our opinion, PVT often occurs in advanced cirrhosis, irrespective of ABO group. Progressive endothelial dysfunction, paralleled by increasing VWF levels, and decreased portal flow velocity, both features of advanced cirrhosis, complete the Virchow triad of pathogenetic factors for PVT. Whether non-0 blood group could be a risk factor for PVT in early cirrhosis needs evaluation in large studies.

## References

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**Table: Hemostatic characteristics of patients by blood group and disease severity - continuous variables are expressed as mean and standard deviation.**

	Overall (n=69)	Child A (n=28)				Child B/C (n=41)			
		Total	0	Non-0	*p	Total	0	Non-0	*p
VWF:Ag (U/dl)	386±167	310±14 4	260±89	386±18 2	0.02 1	438±16 3	413±14 9	451±17 1	0.48 6
FVIII (act%)	159±49	166±37	160±34	175±40	0.295	153±55	149±62	156±53	0.711
Protein C (act%)	47±23	60±20	59±20	62±22	0.66 6	38±21	39±28	37±18	0.80 8
FVIII/Prote in C	437±4.3	3.0±1.1	3.1±1.2	3.0±0.9	0.93 7	5.8±5.4	6.9±8.3	5.2±3.1	0.47 6
ETP Ratio	0.84±0.0 8	0.81±0. 09	0.81±0. 10	0.81±0. 08	0.69 6	0.86±0. 07	0.83±0. 07	0.87±0. 07	0.17 9

\*0 vs non-0 comparison, Student's T-Test