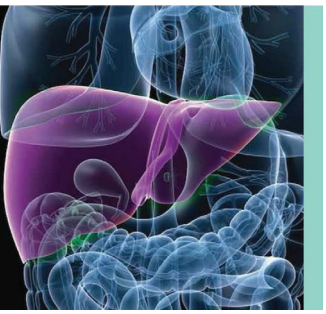

CON: Anticoagulation for Portal Vein Thrombosis in Advanced Cirrhosis

Kevin M. Rank, M.D., and John Lake, M.D.

KEY POINTS

- There is not sufficient quality of evidence to suggest that anticoagulation results in higher rates of complete portal vein thrombosis (PVT) resolution.
- There is evidence to suggest that the presence of PVT does not impact decompensation, rates of transplantation, or mortality.
- There is no reliable manner to assess whether anticoagulation is therapeutic for patients with advanced cirrhosis, and the additional risks of anticoagulation are not clear.
- The presence of PVT in advanced cirrhosis is a surrogate marker for disease severity and decompensation and is not the driver of hepatic decompensation. By the time advanced cirrhosis and PVT develop, the benefits of anticoagulation are likely gone.

CONCEPT 1: DOES ANTICOAGULATION REVERSE PVT MORE THAN NO TREATMENT?

A recent systematic review and meta-analysis by Loffredo et al.[1] examined the available literature regarding the differential effect of anticoagulation for PVT and concluded that anticoagulation did increase rates of complete recanalization, but unfortunately, this finding was influenced by significant publication bias, and overall, the analysis was limited by the quality of evidence included. In addition, a large longitudinal study by Nery et al.[2] in patients with comparable Child-Pugh-Turcotte scores to the meta-analysis found similar rates of spontaneous portal vein recanalization to the anticoagulation cohort examined in Loffredo et al.[1] At this time, it is not clear whether anticoagulation results in differential clearance of PVT.

CONCEPT 2: DOES ANTICOAGULATION INFLUENCE MEANINGFUL OUTCOMES (RATES OF TRANSPLANTATION, DECOMPENSATION, AND DEATH)?

To date, there is no evidence to suggest that anticoagulation for PVT in patients with advanced cirrhosis has any benefit toward improving meaningful outcomes. Although a retrospective study by Englesbe et al.[3] showed a mortality

Abbreviations: PVT, portal vein thrombosis.

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increase in patients with PVT, this has been disproven with more recent studies by Nery et al.[2] and Berry et al.[4] that showed the presence of PVT had no impact on mortality, liver decompensation, or rates of transplantation. Thus, the increased mortality and decreased transplantation rates are likely of historical interest only and were a reflection of issues with donor selection and operative technique, both of which have improved dramatically in recent years.

CONCEPT 3: IS ANTICOAGULATION SAFE—HOW TO MONITOR AND WHEN TO STOP?

In a patient with advanced cirrhosis, the idea of initiating anticoagulation is a daunting one. The majority of data for anticoagulation are in patients with *compensated* cirrhosis,[1] where there does not appear to be an increased risk for bleeding, but there are insufficient data from patients with advanced cirrhosis. Thus, the decision to anticoagulate, which already lacks a clear benefit, becomes even less clearly indicated in the face of unknown risk. In addition, the dosing of anticoagulation and how to monitor for therapeutic effect is uncertain. There are data to suggest unreliability of both the international normalized ratio when using vitamin K antagonists[5,6] and anti-Xa[7] when using low molecular weight heparin. One especially illustrative example of this unreliability is the significantly increased risk for bleeding seen with daily administration of enoxaparin when compared with twice-daily administration, strategies otherwise believed to be equivalent in populations without liver disease.[8] It is also not clear when (or if) to discontinue anticoagulation, because discontinuation likely leads to rapid rethrombosis in a significant portion of patients.[9] In addition, the accepted recommendation is to evaluate and eradicate varices prior to initiation of anticoagulation, which likely adds several months until anticoagulation can be initiated.[10,11] From the standpoint of a clinician, concerns with compliance and appropriate administration of these medications are intuitively present as well.

CONCEPT 4: EARLY INTERVENTION

All of the earlier points represent arguments against routine anticoagulation for nonmalignant PVT in patients with advanced cirrhosis. The lack of efficacy is likely a result of "too little, too late." There is, however, emerging evidence that *prophylactic* anticoagulation in *early* cirrhosis may be of benefit through mechanisms independent of prevention of PVT.[12] The authors argue, and we agree, that PVT and hepatic decompensation are passive surrogates for worsening portal hypertension and not the drivers of worsening liver function, a concept supported by the evidence presented earlier. Thus, anticoagulation may be of benefit early in the development of cirrhosis, but once PVT has formed (especially in advanced cirrhosis), initiation of anticoagulation is treating the symptom and not the disease.

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