

# A regional network to assist patients with portal hypertension

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## **Q. Why is there a need for a regional network to assist patients with portal hypertension in the era of successful etiologic treatments for chronic viral hepatitis?**

Improving population health and citizens' well-being is the mission of the Regions for Health Network (RHN) promoted by the World Health Organization (WHO) starting in 1992. To date, the high efficacy demonstrated by direct-antiviral agents (DAA) to achieve HCV-clearance together with the prophylactic strategies for HBV infection have fostered the WHO ambition of eliminating viral hepatitis which is the most common cause of cirrhosis and portal hypertension. This has been translated into the action plan for the elimination of viral hepatitis health threat by 2030. There is no doubt that such a well-hatched plan of action will achieve the result of reducing the number of patients developing virus-related cirrhosis and complications due to portal hypertension, however this positive perspective should be counterbalanced by some important concrete facts.

It has been estimated that up to 69% of patients with cirrhosis are totally unaware that they are suffering from an advanced liver disease.<sup>1</sup> Therefore, in the coming years, a non-negligible proportion of patients with chronic hepatitis would receive the antiviral treatment when cirrhosis has already developed. This renders the possibility of cure more challenging. Indeed, the elimination/control of the etiologic factor(s), is excellent to avoid the evolution from chronic hepatitis to cirrhosis, but, when cirrhosis has already developed, a definitive cure is achieved only if our intervention interrupts the individual risk of a compensated patient to develop a decompensation or if our intervention makes the life-expectancy of the patient with decompensated cirrhosis similar to that of the same aged-population with no need for transplantation. Unfortunately, the more advanced the stage of cirrhosis, the lower the possibility of achieving these goals. This has been well documented for HCV-cirrhosis. As a matter of fact, only few patients reduce HVPg below the threshold of risk for clinical decompensation after achieving a sustained virological response (SVR) and only 20-30% of patients achieving SVR while on the waiting-list for liver transplant are de-listed.<sup>2-3</sup> Altogether, these observations demonstrate that the life-threatening evolution of cirrhosis may persist even after SVR is achieved.

Furthermore, even if we eliminated virus-related chronic hepatitis, other highly prevalent etiologies, such as obesity, diabetes, alcohol would account for progression of chronic hepatitis to a symptomatic cirrhosis. More specifically, the WHO observed that Europe has one of the highest levels of alcohol consumption in the world, particularly in central and eastern regions.<sup>4</sup> The most alarming data is that alcohol abuse occurs even among young people. On average, up to 31% of 15-19 year old European individuals are heavy episodic drinkers representing, in the near future, an important category of risk for developing a symptomatic liver disease.<sup>5</sup> In addition, non-alcoholic fatty liver disease (NAFLD), which is the liver's manifestation of obesity, diabetes and, more in general, of metabolic syndrome is progressively increasing also among the paediatric population with a dramatic rise of cirrhosis already detectable at that age and/or the consequent increase of subjects who will be adult chronic liver diseases potentially evolving to cirrhosis.<sup>6</sup>

Lastly, although cirrhosis represents the main cause of a symptomatic syndrome due to portal hypertension in recent years the interest in non-cirrhotic portal hypertension has increased and vascular diseases of the liver account for the largest proportion of this clinical condition. The course of non-cirrhotic portal hypertension, which is heterogeneous in terms of etiology, often resembles the clinical presentation and evolution of patients with cirrhosis. The correct management of patients suffering from non-cirrhotic portal hypertension requires highly experienced centres for early diagnosis and treatment. Therefore, all these epidemiological observations make portal hypertension still a timely topic for the creation of a RHN.

### **Q. What are the objectives to be pursued by a Regional Health Network for portal hypertension and how should it be organized?**

Over the years, many randomized controlled trials and observational studies targeted patients with cirrhotic and non-cirrhotic portal hypertension and studies have been performed and, today, practice guidelines exist that outline standards of care in this clinical setting. Nevertheless, the adherence to these recommendations can be suboptimal. Indeed, at least in the context of cirrhosis, it was calculated that as few as 6% to 22% of patients with high-risk varices received primary prophylaxis with non-selective beta-blockers, and only 33% of patients with ascites were addressed to receive the recommended treatment.<sup>7</sup>

More recent data demonstrate that the adherence to international recommendations can be even worse if we consider more complex interventions such as the early TIPS approach proposed for the management of patients with acute variceal bleeding who are at high risk of medical and endoscopic therapy failure.<sup>8</sup> Altogether, these observations demonstrate the access for patients to the best options of treatment could be difficult even in tertiary care hospitals. This calls for an effort of coordination that promotes the existence of centres of excellence where doctors, nurses, any health professional highly skilled for the management of patients with portal hypertension work with competence inside a regional health network. Ideal candidates to host these kind of centres are research hospitals equipped with interventional radiology, intensive care units and liver transplant facilities. The multidisciplinary approach should be mandatory as the severity of portal hypertension can cause clinical complications to the gastro-intestinal tract as well as other organs such as the kidney, brain, lung, cardio-vascular system, hemostasis.

Furthermore, acute infections are frequently observed in patients with a decompensated disease, as the experience on patients with cirrhosis has largely demonstrated. Consequently, infectious disease specialists would be essential to increase the chances of survival using prompt and appropriate antibiotic therapy. These centres should offer behavioural education and counselling, nutritional status evaluation and should be perfectly integrated inside their own territory. This could be achieved only if local administrations and health-institutions facilitate the communication among generalists and specialists.

Another key-point would be the inclusion of family doctors in these programs in order to make the centre of excellence closer to people and guarantee an easy access to the standard of cure. Finally, this network should be adequately prepared to support patients who need periodical evaluation and routine manoeuvres like paracentesis and endoscopic band ligation of varices.

As of today, little has been done to experiment new models of care for the management of portal hypertension. An interesting experience was published by Morando et al. who demonstrated that a caregiving support based on several diagnostic facilities performed in real time and integrating consultant hepatologists, dedicated nurses, physicians in training and primary physicians is efficacious and financially sustainable.<sup>9</sup> Along this line, Tandon et al. demonstrated that a specialized nurse-run titration is a valid option of care to increase the compliance to non-selective beta-blockade close to 80%.<sup>10</sup> These experiences suggest that there is room to improve our care of patients with portal hypertension and RHN could be a great occasion to offer universal and equal access to cure, make the scientific community go more in depth of the pathogenic mechanisms of disease, ameliorate protocols of diagnosis and treatment.

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