Multiple sclerosis (MS), an acquired inflammatory and neurodegenerative, chronic disorder of the central nervous system (CNS), is the most frequent cause of severe non-traumatic neurologic disability in young adults. It is an immune-mediated disease of unknown etiology, generally accepted as a multifactorial disorder of the CNS that results from the interaction of both genetic and environmental factors. Recently a new vascular hypothesis on the origin of MS was raised based on the concept of the existence of cerebrospinal venous drainage impairment in this disorder. This irregularity was called as “chronic cerebrospinal venous insufficiency (CCSVI)”, and abnormal drainage of the venous blood was claimed to be due to stenosis or malformation of the internal jugular and/or azygos veins. The first publication on this topic claimed 100% specificity and sensitivity of the condition for MS, and a new possible endovascular treatment (“liberation procedure”) of this disorder was suggested by Paolo Zamboni. Until now, numerous studies related to CCSVI have been performed by different groups, which do not replicate consistently original results. Thus, it can be concluded that at present the available data do not support the role of CCSVI as the primary cause of MS. Therefore, prior to considering the impact of endovascular treatment in double-blind placebo controlled trials in MS, the Zamboni’s theory should be further explored in studies with appropriate methodologies in order to clearly elucidate the role of CCSVI in MS.