

**ISNVD**

International Society for  
Neurovascular Disease

**ISNVD 2013 ANNUAL MEETING - SUMMARY**



## 24th February

### **Key note lecture by Seshadri Raju (USA): Hemodynamics and treatment response in vein stenosis: Lessons from iliac stent experience**



Iliac vein stenosis is a relatively well recognized indication for endovascular management, including balloon angioplasty and stenting. Professor Raju has an enormous experience in this particular vascular territory, thus his remarks were very helpful for those who perform interventions in the patients presenting with CCSVI. In this key note lecture it was emphasized how little is actually known about venous pathology and hemodynamics, that veins in different parts of the body behave very differently, especially in the settings of disease, and that the rules governing the treatment for arterial disease are not valid in a case of venous pathology. Much more basic research is needed to understand what happens in a case of impaired cerebrospinal drainage, what should be regarded as a pathology (especially in terms of significant degree of stenosis) and which therapeutic strategy should be preferred. In addition, Professor Raju stressed on the fact that quite often venous abnormalities represent a permissive pathology, i.e. they are silent in most of the cases and become symptomatic when secondary insults are superimposed. Such secondary insults cannot evoke the disease if permissive lesion is absent. A general principle is to treat the permissive lesion first in symptomatic patients, which is often curative. It is likely that CCSVI is also such a permissive pathology.

## Sessions on acute stroke management



Two educational sessions on acute stroke management presented state-of-the-art in this emerging topic of vascular medicine. Management of acute stroke requires coordinated efforts of different specialists: neurologists, radiologists, emergency medicine specialists, vascular interventionalists and neurosurgeons. Such a team work could be a pattern for those involved in the research on CCSVI, and treatment of venous abnormalities in cerebrovascular territory.



**Timothy Duong** (USA) presented the results of animal experiments in acute stroke, with focus on neuroprotective agents trials.



**Adnan Siddiqui** (USA) summarized current clinical trials on arterial thrombolysis and mechanical thrombectomy for the treatment of acute cerebral stroke.



**Nikolaos Liasis** (Greece) presented the results of research on evaluation of the risk of cerebral ischemic stroke depending on carotid plaque characteristics.



**Krzysztof Bartu** (Poland) discussed the role of percutaneous left atrial appendage closure for stroke prophylaxis.



**Iris Grunwald** (UK) told how to set up an acute stroke service. Also, she gave a characteristics of different devices used for mechanical thrombectomy. **Adnan Siddiqui** (USA) presented review of CT and MR imaging for the assessment of acute stroke patients and the role of this diagnostics in decision making. Finally, **Du an Ku era** (Czech Republic) shared his experience in the management of acute stroke.

## Session on CCSVI - Current status of the research



**Robert Zivadinov** (USA) summarized the research presented at last ECTRIMS conference (Lyon, France, September 2012). In brief, CCSVI hypothesis still provokes great controversy and debate in the MS community. A number of papers presented in Lyon revealed negative results (very low prevalence of CCSVI, the same prevalence in healthy controls and in patients, no clinical benefit from the treatment for CCSVI).



**Jaap Valk** (the Netherlands) presented the results of prospective study on the patients with chronic intractable headache and other concurrent symptoms, such as vertigo, dizziness, tinnitus, and visual disturbances. The patients were examined by means of MR venography. Very often the patients were diagnosed with intracranial venous abnormalities (for example, persistent occipital sinus with “loop” formation) or even with thrombosed intracranial sinuses. He concluded that venous intracranial pathology is prevalent in patients presenting with neurological symptoms and that MR venography should be a part of diagnostic protocol in these patients.



**Paolo Zamboni** (Italy) told about different results of sonographic studies. In his opinion good training is necessary to conduct such a research on CCSVI. Studies performed by non-experienced sonographers are doomed to fail and to reveal incorrect results.



**Marian Simka** (Poland) discussed the reliability of current sonographic criteria of CCSVI. He presented the results of a prospective study that was aimed at evaluation of diagnostic value of Doppler sonography of the internal jugular veins. Also, such a diagnostic accuracy was calculated for T2 FatSat and time-of-flight MR imaging. The authors assessed 252 internal jugular veins in 126 MS patients. Findings of Doppler sonography and MR venography were compared to the results of catheter venography. It was found that diagnostic accuracy of Doppler sonography was not high: positive and negative Bayesian likelihood ratios were at the level of 70% and 40%, while these values were higher for MRV assessment (about 75% and 70%).



**Tomasz Urbanek** (Poland) presented a meta-analysis of the studies on the treatment for CCSVI in MS patients. Currently there is no high-level evidence to support or refute the efficacy of endovascular treatment for CCSVI. Well-designed randomized controlled trials should answer the question whether such procedures are effective and safe.



### Session on CCSVI – Sonographic diagnostics

**Marcello Mancini** (Italy) presented results of the study that evaluated cerebral circulation time in MS patients using contrast enhanced ultrasound. Cerebral circulation time was defined as the time difference of ultrasound contrast bolus arrival between the carotid artery and internal jugular vein. The authors found that the longest and average cerebral circulation times were significantly prolonged in MS patients compared to healthy controls. No correlation was found between cerebral circulation times and duration of disease, level of disability (EDSS score) or age - in both group of patients and controls. These results suggest that venous outflow impairment is associated with MS and that cerebral circulation time measurement can be used for the assessment of such circulatory dysfunction in MS patients.

**Adnan Siddiqui** (USA) presented the results of the PREMise with focus at diagnosis value of intravascular ultrasound (IVUS) for the assessment of CCSVI. He evaluated 30 MS patients using catheter venography and IVUS. Catheter venography was considered abnormal when  $\geq 50\%$  restriction of the lumen was detected, IVUS was considered abnormal when  $\geq 50\%$  restriction of the lumen, intraluminal defects or reduced pulsatility were detected. Venous abnormalities detected by IVUS were observed in 85% of azygous veins, 50% of right IJVs and 83.3% of left IJVs, while catheter venography showed stenosis in 50% of azygous veins, 55% of right IJV and 72% of left IJV. In conclusion, IVUS assessment showed higher rate of venous abnormalities compared to catheter venography thus providing diagnostic advantage over "gold standard" in detecting extracranial venous abnormalities indicative of CCSVI.



## Poster sessions



**Tommaso Lupattelli** (Italy) analyzed safety profile of endovascular treatment for CCSVI in a cohort of 1202 MS patients. There was no mortality associated with the procedures. Major complications occurred in 0.6% and minor in 2.5% of the patients. Majority of complications occurred in the first 400 cases performed, thus a “learning curve” applies to these treatments.

**Guillermo Eisele** (Argentina) presented the results of endovascular treatment for CCSVI in 19 MS patients 2 years after the procedure. Clinical status of the patients improved soon after the angioplasty, with maximum effect between 6 and 12 months. One year after the treatment this improvement diminished, however after 24 months clinical benefits were still observed in most of the patients.

**Siamak Salari Sharif** (USA) investigated 20 MS patients using digital subtraction X-ray angiography. The results of this test were compared to those of contrast-enhanced MR venography.

The authors found very good correspondence between these tests. MR venography was more



accurate for the measure of the width and cross-sectional area of the veins, while digital subtraction X-ray angiography was better at visualizing the flow at the confluence of the internal jugular veins and the subclavian vein.

**Marian Simka** (Poland) presented case report of internal jugular vein entrapment in an MS patient. Internal jugular vein compression was caused by aberrant omohyoid muscle. Pathological muscle was transected surgically. Sonographic control 3 weeks after this surgical procedure revealed a decompressed vein with fully restored venous outflow.

### 25th February

#### **Key note lecture by Paolo Zamboni (Italy): 10 years of research on CCSVI: What we know and what we need to know**



In this key note lecture professor Zamboni gave an overview of the research on abnormal venous outflows from the brain and spinal cord, the so-called chronic cerebrospinal venous insufficiency (CCSVI). This discovery is now 10 years old. Now we know much more than some years before. However, most of important questions remain unanswered. More research is needed to understand this clinical entity properly and a good collaboration between different specialists is necessary.



## Session on venous disorders in non-MS neurologic disorders

**Mark Haacke** (USA) showed the results of MR venography in Parkinson patients. These patients present with very high rate of severe venous abnormalities, even more often than MS patients. This suggests that venous outflow abnormalities are much more prevalent in neurological patients than it was previously thought.



**Robert Zivadinov** (USA) presented the results of sonographic study on prevalence of CCSVI in pediatric MS patients and the patients with non-MS neurologic disorders. Sonographic diagnosis of CCSVI (Zamboni's criteria) was positive in 30% of healthy adults and healthy children, in 54% of adult non-MS neurologic patients, 40% of pediatric non-MS neurologic patients and 44% of pediatric MS. The authors concluded that their finding point against CCSVI having a primary causative role in the development of MS or other neurologic diseases.



**Steven Fry** (USA) presented preliminary data on the discovery of biofilm-forming protozoan, called *Protomyxzoa rheumatica* that has been found in the blood of patients presenting with chronic fatigue syndrome, multiple sclerosis, lateral amyotrophic sclerosis and other chronic neurologic disorders. He emphasized the fact that this protozoan is very difficult to diagnose. Special staining of blood smears is required to see these parasites using traditional microbiologic technique. The best way to diagnose it is to use novel diagnostics, such as polymerase chain reaction (PCR) assays and multiplex molecular technology. However, specific tests are not yet available. For the time being pathological role of this newly discovered microorganism remains elusive. Still, it is tempting to speculate that some chronic neurological diseases may be linked to this unicellular parasite.

## Session on CCSVI – CT and MR imaging



**Robert Zivadinov** (USA) presented the results of multimodal approach for the diagnosis of CCSVI. Two invasive diagnostic modalities (catheter venography and IVUS) and 3 non-invasive techniques (Doppler sonography, MR venography and CT venography) were used in the Prospective Randomized Endovascular Treatment in Multiple Sclerosis (PREMiSe) study. The results of this study suggest that such a multimodal diagnostics should be preferred, since it is more accurate in comparison with diagnosis given with one or two tests. Multimodal diagnostics should also be applied in future studies, especially in healthy controls.



**Mark Haacke** (USA) summarized their studies on quantitative MR in MS patients. His team performed such a research in 468 MS subjects who were compared with a group of 33 healthy controls. Internal jugular veins were assessed for stenosis, atresia, and aplasia using a combination of 2D time-of-flight MR venography and 3D contrast enhanced MR angiography and venography. Two dimensional phase contrast flow quantification was used to quantify the flow through the vessels of the neck. Venous flow was normalized to the total arterial input. About 30% of MS patients who presented with stenoses of jugular veins could be demonstrated severely decreased venous outflow, while such a flow pattern was very rare in non-stenotic MS patients and healthy controls. The authors concluded that quantifying the flow for studying CCSVI in MS is a critical part of evaluating what is abnormal in an MS patient.



**Efrosini Papadaki** (Greece) investigated MR hemodynamic parameters (cerebral blood volume, cerebral blood flow and mean transit time) in clinically isolated syndrome (CIS), relapsing-remitting MS patients and healthy controls. This study showed that patients with CIS were characterized by increased cerebral blood volume and mean transit time values if compared to controls and relapsing-remitting MS patients. Although the mechanism(s) responsible for the globally increased cerebral blood volume values in CIS patients remain unclear, inflammation-induced vasodilatation at the very early stages of MS may play a role.



**Pascal Niggemann** (Germany) presented the results of upright MR venography for the assessment of neck veins. Almost all currently applied MR machines enable such an assessment only in the supine position. Still, it is well known that venous hemodynamics in the jugular and vertebral veins changes dramatically depending on position of the body. Assessing these veins only in the supine position means that a substantial body of information is lacking. German doctors have shown that upright MR venography is technically feasible. Yet, currently available machines that can examine a patient in the upright position are of low resolution, consequently MR venographies are of poor

quality. Thus, higher resolution MR units with a possibility of performing the scans both in supine and in upright positions are needed.



### Session on CCSVI – free communications

**Aldo Bruno** (Italy) presented his experience of 144 endovascular treatments for CCSVI (balloon angioplasty of internal jugular vein and/or azygous vein) in MS patients. No major complications were observed, in 2 cases minor complication occurred (groin hematoma), which resolved without further sequelae. The authors reported good clinical results in about 55% of the patients. In 25% of patients they observed a recurrence of clinical symptoms. No clinical benefit from the treatment was found in 20% of patients. Restenosis after 6 months was found in 31% of the patients.



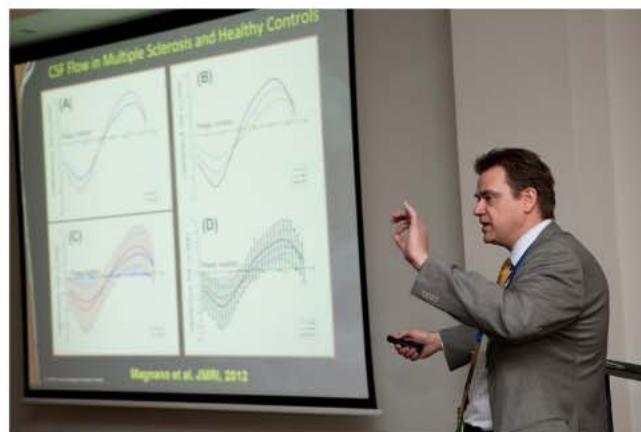
**Tomasz Ludyga** (Poland) presented the report on feasibility and safety of cutting balloon angioplasty for the management of malformed internal jugular veins. Cutting balloons were used during 70 procedures in 65 MS patients presenting with CCSVI in jugular territory, primarily at the level of jugular valves. These devices were used only in selected cases, following unsuccessful standard balloon angioplasty. Immediate technical success rate was 94.3%, primary, assisted primary and secondary patency rates after 6 months were: 88.1%, 94.1% and 98.5%, respectively. The authors concluded that cutting balloons can be safely used for the management of stenotic internal jugular veins. However, clinical efficacy of such procedures should be assessed by randomized trials.



**Tommaso Lupattelli** (Italy) performed catheter venography of the veins draining the central nervous system in a cohort of 1202 MS patients. He observed an external compression of internal jugular veins in about 7% of the patients, in most of the cases on the left side. These compressions were localized either in the middle part of jugular veins or at the level of jugular vein's ostium. These lesions were shown to be unresponsive to balloon dilatations. However, in most of the cases outflow improved with the patient's head turned to the opposite site. In addition, 0.5% of the patients presented with narrowing of brachiocephalic vein, which cannot be improved by balloon angioplasty or change of head position.



**Robert Zivadinov** (USA) investigated cerebrospinal fluid flow in MS patients before and after endovascular treatment for CCSVI in a MR-blinded 12 months cross-over study. The authors used cine phase contrast-calculated cerebrospinal fluid flow and velocity measurements. They found significant increase of cerebrospinal fluid flow in the patients who underwent immediate treatment and decreased flow in the patients from delayed treatment group. Altered cerebrospinal fluid flow and velocity measures were associated with worsening of clinical and MRI outcomes in delayed treatment arm.



**Clive Beggs** (UK) analyzed the results of cervical plethysmography in 40 healthy controls and 44 CCSVI patients. The rate at which venous blood discharged in the vertical position was significantly faster in the controls compared with CCSVI patients. Also, the mean hydraulic resistance of the extracranial venous system was significantly smaller in the healthy controls than in the patients. In conclusion, cerebral venous return hemodynamics of the patients with CCSVI were markedly different from those of the controls, with the hydraulic resistance of the CCSVI patients being on average 63.5% greater than in the controls.

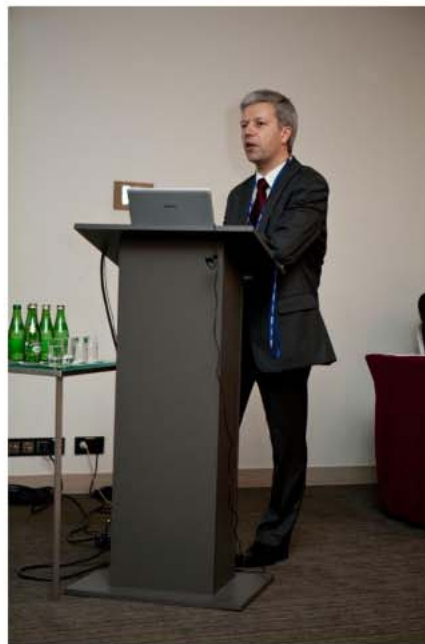


**Clive Beggs** (UK) performed univariate and multivariate statistical analysis of cerebrospinal fluid flow characteristics, T2 lesion number and volume, and MRI parameters of the brain (gray matter volume, white matter volume, lateral ventricle volume and cortical volume). This research was done in 25 CCSVI-negative and 15 CCSVI-positive age- and sex-matched healthy individuals. The study revealed marked differences between the CCSVI-positive and negative groups. He concluded that CCSVI appears to be associated with systemic changes in the intracranial physiology of healthy individuals, which alters the relationship between cerebrospinal fluid flow, enlargement of lateral ventricles and T2 lesion formation.



**Francesco Sisini** (Italy) presented a theoretical hemodynamic model of venous outflow from the brain. A similar work, using mathematical modeling, was presented by **Lucas Omar Mueller** (Italy). It is hoped that such modelings will enable a better understanding physical aspects of CCSVI.

**Marian Simka** (Poland) presented the results of study aimed at exploring a potential role for CCSVI in triggering MS. The authors evaluated severity of CCSVI in 350 MS patients using catheter venography and performed statistical analysis to find correlations between severity of venous lesions and patients' age at onset of MS. They found weak, yet statistically significant, positive correlations between patients' age at onset of MS and severity of CCSVI lesions. The authors concluded that such a positive correlation suggests that venous lesions are not a direct trigger of MS and there should be another factor that initiates pathological processes in the central nervous system.





## Poster sessions



**Rahman Tamizur** (USA) compared a standardized MRI protocol containing 2D time-of-flight MR venography and dynamic 3D contrast enhanced MR venography for the assessment of venous abnormalities in MS patients and healthy controls. He found that although 3D contrast enhanced MR venography depicted the vascular anatomy more completely than 2D time-of-flight imaging, 3D contrast enhanced scans do not provide any information about the flow characteristics, which is indirectly available in the 2D time-of-flight venography.

**Isac Flaishman** (Italy) examined 50 MS patients and 50 controls using Doppler ultrasound (Zamboni's criteria) He found CCSVI (at least 2 positive criteria) in 90% of MS patients and 0% in control subjects.

**Steven Alexander** (USA) examined the relative abundance of adhesion molecules (PECAM-1, CD51<sup>+</sup>/CD61<sup>+</sup> and ICAM) bearing microparticles in the plasma of healthy individuals and patients with relapsing remitting and secondary progressive MS. He also correlated plasma levels of different microparticle species in MS with MR imaging (T1/T2 intensity). This study was aimed at investigating the relationship between these endothelial biomarkers and MS. The authors found that microparticles bearing the above-mentioned adhesion molecules were statistically correlated with conventional MR imaging features of MS. Based on the results of this study the authors concluded that endothelial microparticle profiles in MS may provide mechanistic evidence of microvascular stress.

**Gino Montecinos** (Italy) performed a quantitative assessment of the influence of internal jugular vein stenoses on cerebral hemodynamics, combining a mathematical model of the blood flow with MR imaging and anatomical data This work represents a first step towards a computer-aided understanding of CCSVI hemodynamics.

