# 43 THE MEM-NET PROGRAM FOR CHRONIC CEREBRO-SPINAL VENOUS INSUFFICIENCY COLOR FLOW DOPPLER IMAGING ASSESSMENT

S. MANDOLESI, A. D'ALESSANDRO

Chronic venous insufficiency (CVI) is the condition in which one or more veins become unable to fulfill their three specific functions:[1]
– drainage from the tissues of toxic substances;
– filling of the heart cavities;
– thermoregulation of tissues;
in any physical activity or position of the subject.

*What is the event that causes the CVI*?

Any condition that poses an obstacle to the drainage of one or more veins it is the cause that in time will determine the appearance of clinical disorders manifested as CVI.

The CVI has been studied mainly for its effects on the circulation of the lower limbs. Specifically, lower limb varicose veins are characterized first by the dilation of the veins and gradually, over the years, from the serious adverse effects on the skin of the lower limbs. Varicose veins if not treated in time with elastic-compression stockings, sclerotherapy, surgical, laser or a conservative hemodynamic method they will progress.

*How does the varicose disease evolve over time*?
– They first appear as dilated and tortuous veins;
– after a while the skin pigment becomes darker due to leakage of blood into the tissues (hemosiderin deposits);
– then there is chronic inflammation of the skin which becomes red and painful (ekzema) and hardened (lipodermatosclerosis);
– finally, tissue necrosis results in a destructive and painful deep wound of the skin, the varicose ulcer, which is followed by very slow healing with repair scar tissue.

Superficial vein thrombosis of the veins of the lower extremities is a frequent event which is painful and disabling, but with low risk of major complications such as pulmonary embolism. Thrombosis that affects the deep veins of the legs or pelvis (DVT) is at high risk of pulmonary embolism and should be promptly recognized and treated.

*How to recognize the presence of a varicose vein or thrombosis of a vein of the lower limbs*?

The fastest and accurate non-invasive method of investigation is the color Doppler ultrasound imaging (CDUI)). For more proximal vessels such as those of the pelvis magnetic resonance imaging (MRI) is very reliable for the detection of thrombosis.

In 1988 with the birth of the conservative hemodynamic ambulatory treatment of varicose veins, Claude Franceschi has realized the first cartographic maps of venous hemodynamics of the lower limbs.[1] In 1992, the authors showed for the first time the venous compression syndrome (VCS) of the lower limbs [2] and in 2011 that of the veins draining cerebral spinal flow.[3] The VCS has widened the field of interest of the phlebologists and lead to static and dynamic biomechanic studies. Phlebological treatments have been performed by dermatologists, general surgeons, vascular surgeons, angiologists, cardiologists or radiologists, but how can we define a phlebologist today?

"Phlebologist is an expert in venous system diseases who is able to realize and interpret a CFDI venous hemodynamic map".[4]

Why is it so important that a phlebologist is able to realize and interpret a venous CFDI map? The hemodynamic venous map today is the lowest common denominator of venous investigation for understanding the pathological condition of the subject's vein.

## CHRONIC CEREBRO-SPINAL VENOUS INSUFFICIENCY (CCSVI)

In recent years, the CVI has been recognized to be present in many parts of the body. It is now well-defined also at the level of the venous system draining the cerebro-spinal blood and is called chronic cerebro-spinal venous insufficiency (CCSVI). It is a CVI that determines its effects in the brain and spinal cord and it is linked to blocked drainage or venous stasis in the territory of the derivation of the internal jugular and vertebral veins.

The CCSVI is characterized by multiple stenosis/obstructions affecting the principal extracranial outflow pathways of the cerebrospinal ve-

nous system, the internal jugular veins (IJVs), the vertebral veins (VVs) and the azygos vein (AZY). It is distributed in four main hemodynamic patterns.[5] Furthermore, CCSVI determines significant changes in cerebral venous hemodynamic, with a very high incidence of reflux in both intra- and extra-cranial venous segments as well as loss of the postural regulation of cerebral venous outflow.[5] Zamboni and his team in 2011 suggested a protocol including five CFDI venous criteria that characterize this syndrome as follows:

- *criterion 1*: reflux in the IJV and/or VV; a) bidirectional flow in one or both of the IJVs in both postures or bidirectional flow in one position with absence of flow in the other position. These findings suggest IJV stenosis; b) reversal or bidirectional flow in one or both of VVs in both positions. These findings suggest stenosis in the azygos vein, based on reports controlling the Doppler parameter in comparison with catheter venography;
- *criterion 2*: intracranial reflux;
- *criterion 3*: IJV stenosis a) severe reduction of the cross sectional area (CSA) of the IJV in the supine position <0.3 cm $^2$ which does not increase with a Valsalva maneuver, performed at the end of the examination; b) intraluminal defects such as webs, septa or malformed valves combined with hemodynamic changes like increased velocity, absence of flow, reflux/ bidirectional flow etc. An M-mode investigation of the leaflets may clarify if they are mobile or not;
- *criterion 4*: absence of detectable flow in the IJV and/or VVs. Outflow obstruction in the cervical veins indicated by: a) absence of Doppler signal in the IJV and/or the VVs, even after deep inspiration, in both sitting and supine positions or b) in one posture but with bidirectional flow detected in the other position. These findings are associated with stenosis proximal to the point of assessment;
- *criterion 5*: negative difference of the CSA of the IJVs measured at the J2 point, that is a change in the area between the supine and orthostatic hypotension. The presence of two of them is enough to diagnose CCSVI.[6]

It is well known the compressive venous syndrome affecting the veins of the lower limbs.[2]

Similarly in CCSVI it has been shown with CFDI that venous compression can be detected in approximately 48% of the subjects.[7] The most important biomechanical factors involved are dislocation of the first and the other distal cervical vertebrae. They cause venous compression due to traction of muscle bands or dislocation of the cervical muscles.

Recently the authors are working on a biomechanical test that will indicate the best manipulative treatment. Also what exercises could have an effect to decompress these vessels. Initially one should aim with only spinal manipulation and postural exercises to obtain sufficient resolution of the venous compression that causes the hemodynamical disturbance. If failed and only then a surgical option to resect the bands should be offered.

The CCSVI is a condition found in many neurological diseases, as we have seen with varying incidence in Alzheimer's disease (AD), in the pseudo-tumor cerebri, in Meniere's disease, macular degeneration of the retina, in the Arnold-Chiari syndrome and multiple sclerosis (MS).

Its possible correlation with these diseases needs several years of scientific longitudinal studies to be verified. What we can extrapolate from our current knowledge from CVI in the lower limbs is that similar hemodynamic, morphological and clinical situations can be applied to CCSVI.

In the literature there evidence of the following:

- formation of plaques in the cerebral spinal tissue that is inflamed and becomes active causing a so-called contrastographic enhancement;
- dilated veins in the center of the plates and the surface regions of the brain;
- iron deposits around cerebral veins and in cerebral plaques;
- there gliosis zones representing scarring of the brain tissue.

The presence of contributing factors such as metabolic, genetic or biomechanical could lead to different clinical presentation of CCSVI in patients with the same venous abnormalities. To identify these contributing factors may explain the different clinical manifestations; some patients have long periods of well being while in others there is rapid transition to progression of the disease.

Many subjects without any symptoms may have CCSVI, therefore, it is prudent to be diagnosed early with a CFDI assessment.

The CFDI examination to assess CCSVI is a very difficult and tedious test that needs about an hour's work by an expert ultrasonographer.

It involves venous CFDI assessment of the main veins draining the brain in the supine and upright position, the Manconi breathing test, the neck rotation test, a Valsalva maneuver, transcranical deep veins assessment and 3 rd ventricle measurements. The main problem of the assessment is to remember the CCSVI five Criteria that may frequently be misinterpreted.

The CFDI written reports at present are either too simple and repetitive or very complex and only comprehensible to an expert; sometimes they are shown on complex diagrams that are difficult to understand.

The last but not the least problem currently is the presence in the literature, of two groups of criteria for the CFDI diagnosis of CCSVI.

The first list of five criteria is the original one proposed by Zamboni in 2009.

The second list was approved in 2011 by a consensus of experts of the international vascular scientific societies. This last list of criteria is extensive.

## MAP HISTORY

Since 1988 the authors have reported, by hemodynamic and morphological criteria, the CFDI as-

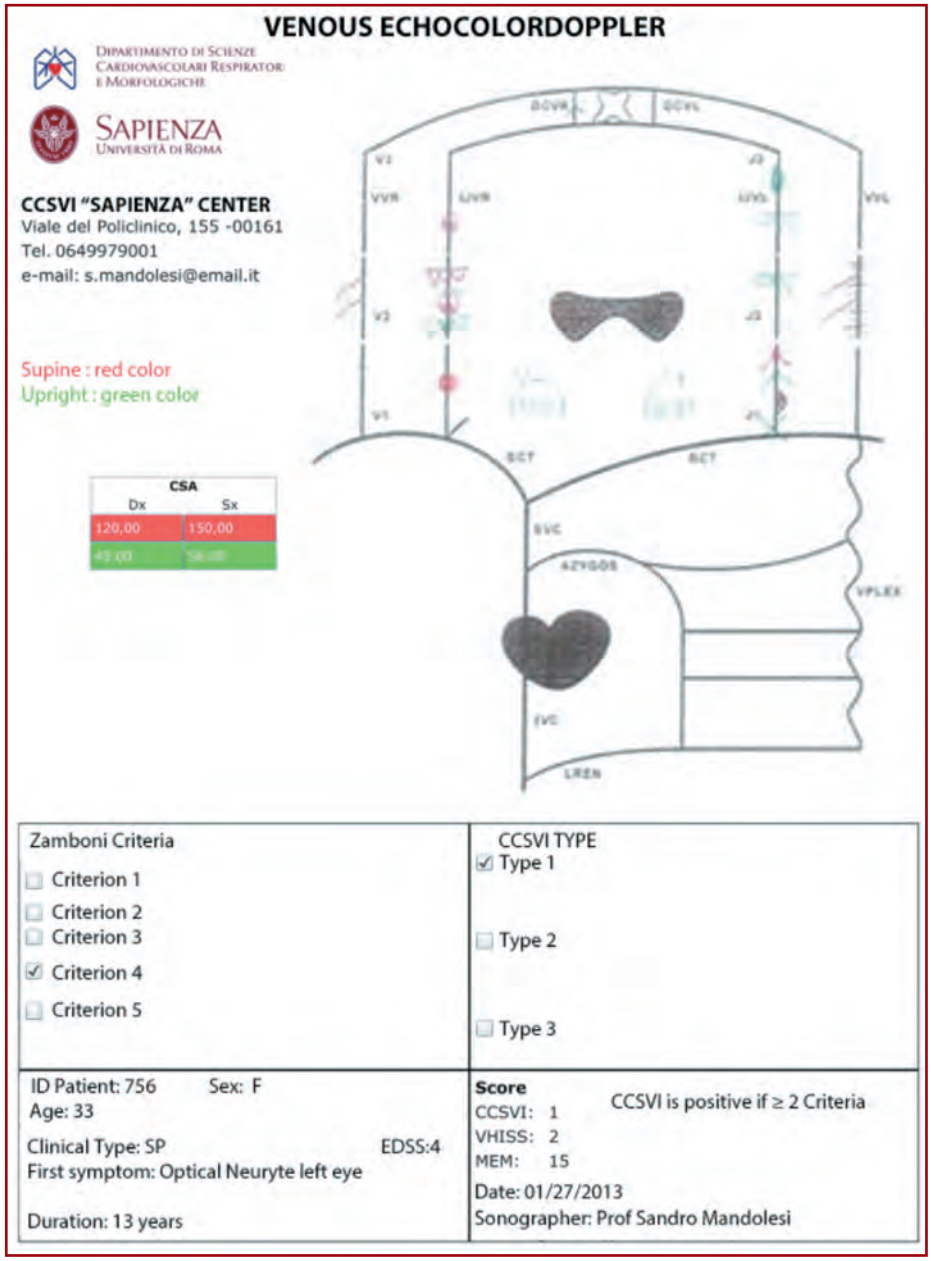


**Figure 43.I** – Map on paper of CFDI with morphological and hemodynamic symbols.

sessment of the veins of the lower limbs first on a paper map and then in 1992 on a computed map.[8] In 2005 the authors realized the MEV-net software and in 2009 the Flebo-map program.[4] It is for this reason that they have reported on map also the CFDI assessment of the veins draining the brain. The first maps they used were on paper (Figure 43.1). Using paper map the possibility of mistakes in the final assessment of CFDI report was lower but always possible for the human error.

After two years of work in 2012 the MEM-net program www.mem-net.it was completed. The authors created this software to collect morphological venous anomalies and hemodynamic CFDI data on a morphological hemodynamic map. They designed an algorithm for data analysis of patients with CCSVI, following Zamboni's ultrasound criteria.[6] First in 2011 they identified in patients with CCSVI, by using this hemodynamic morphological map (MEM-net), the venous compression syndrome (VCS) of IJVs and VVs and they classified CCSVI in three types. Type-1 with intravenous block, type-2 with venous compression syndrome and type-3 with both conditions.[3]

## THE NATIONAL EPIDEMIOLOGICAL OBSERVATORY ON CCSVI

The department of cardiovascular and respiratory sciences at the University of Sapienza Umberto primo in Rome, directed by Professor Francesco Fedele sponsored in 2010 the national epidemiological observatory on CCSVI and in 2011 developed the digitalized platform CCSVI-database for gathering the data.

This program is accessible via the internet and it is possible to enter the patient's history, the neurological presentation at the visit, the CFDI assess-

Table 43-I – Symbols and terminology of venous anatomical anomalies.

| | | |
|---|---|---|
|  | Membrane | hyperechoic area endovascular |
|  | Septum | abnormal valve leaflet |
|  | Thickening | valvular thickening |
|  | Twist | twisting of the vessel |
|  | Ectasia | Vein diameter more than 20 mm |
|  | Confluence | Thickening of the confluence of jugular to subclavian |
|  | Thickening-dyspasia | Thickening (dysplasia) of the vessel wall |
|  | Thyroidectomy | |
|  | Nodules | |
|  | Hypoplasia | Vein with diameter of less than 6 mm |
|  | Net | Reticular image into vessel lumen |
|  | Anatomical stenosis | Organic stenosis <3 mm$^2$ |
|  | Calcification | Endo or extra vascular |
| D | Double channel | CFDI anechoic area |
|  | Thrombosis | Thrombosed segment |
|  | Recanalization | Recanalization with parietal residues |

ment of the brain veins, the MRI, the venography examination, the angioplasty procedure, the physical therapy and any surgical procedures. The website is run by a powerful program for data analysis and statistics in real time.

The national epidemiological observatory on CCSVI www.osservatorioccsvi.org uses the program MEM-net for CFDI data collection in its computerized platform that works on the internet. In 2013 it organized a consensus conference with national vascular scientific societies in order to disseminate the symbols and terminology to be used in its MEM-net mapping (Table 43-I).

## THE VENOUS MAP OF CCSVI

The CFDI map scheme is a stylized diagram of the veins draining the brain and spinal cord (Figure 43.2). The internal jugular and the vertebral veins, on the map, are divided into three segments. The proximal segments are J1-V1, the medium segments are J2-V2 and the distal are J3-V3. The J1 segment goes from the confluence into subclavian vein to the inferior level of the thyroid (Figure 43.3). The J2 segment goes from the inferior level of the thyroid to the jugular point; this point is when the vein crosses the bifurcation of the carotid arteries. The J3 segment goes from the jugular point to the higher point that is detectable by CFDI. The V1 segment goes from the confluence into the subclavian vein to the point in which the vertebral vein goes up from the vertebral canal. The V2 segment goes from this last point to the 3 rd cervical vertebra (C3) (Figure 43.4). The V3 segment is above this level.

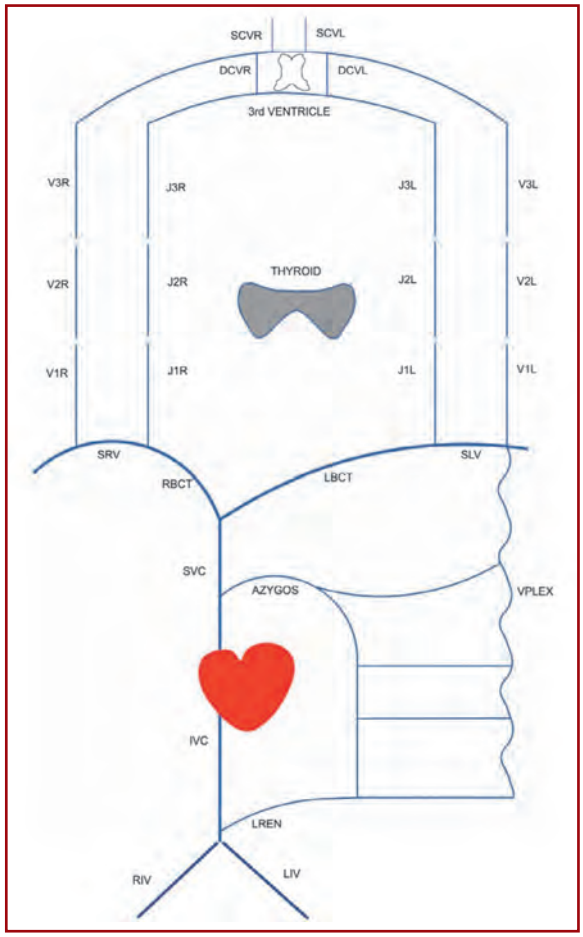


**Figure 43.2** – Map scheme for CFDI report.

The veins are represented by blue lines and on them are reported the morphological and the hemodynamic symbols that correspond to the assessment with CFDI. With color red are reported the symbols of the CFDI assessment done in supine position and with green color the symbols of the up-right assessment.

When the sonographer finds an anomaly or a hemodynamic pathological flow he/she immediately puts the equivalent symbol on the corresponding point on the map. A legend with all the symbols are close to the map and you can pick which you need to put on the map by using the mouse (Figure 43.5).

## THE MEM-NET PROGRAM

To enter in the MEM-net program which is part of the platform of the national epidemiological observatory on CCSVI, one must register using a personal ID and password to have access to the program. One can insert a new patient in the archive and automatically the program creates an ID number for privacy. Once entering into the program one can enter all the clinical data of the patient. Then one can access the hemodynamic page where the symbols and the MEM-net map for the CFDI report are found (Figure 43.5). After saving the map of the CFDI assessment this can be printed on its own or with a written report. One can also use the statistics area for general or clinical data analysis of the patients (Figure 43.6). The report on the map, by the MEM-net, shortens the time of CFDI written reporting since is done automatically.

The MEM-net program allows to collect all the data of a long and difficult CFDI examination and, by its algorithm, makes the reports uniform. The MEM-net program contols the reports blindly and allows to use them for scientific research.

Entering the hemodynamic and morphological

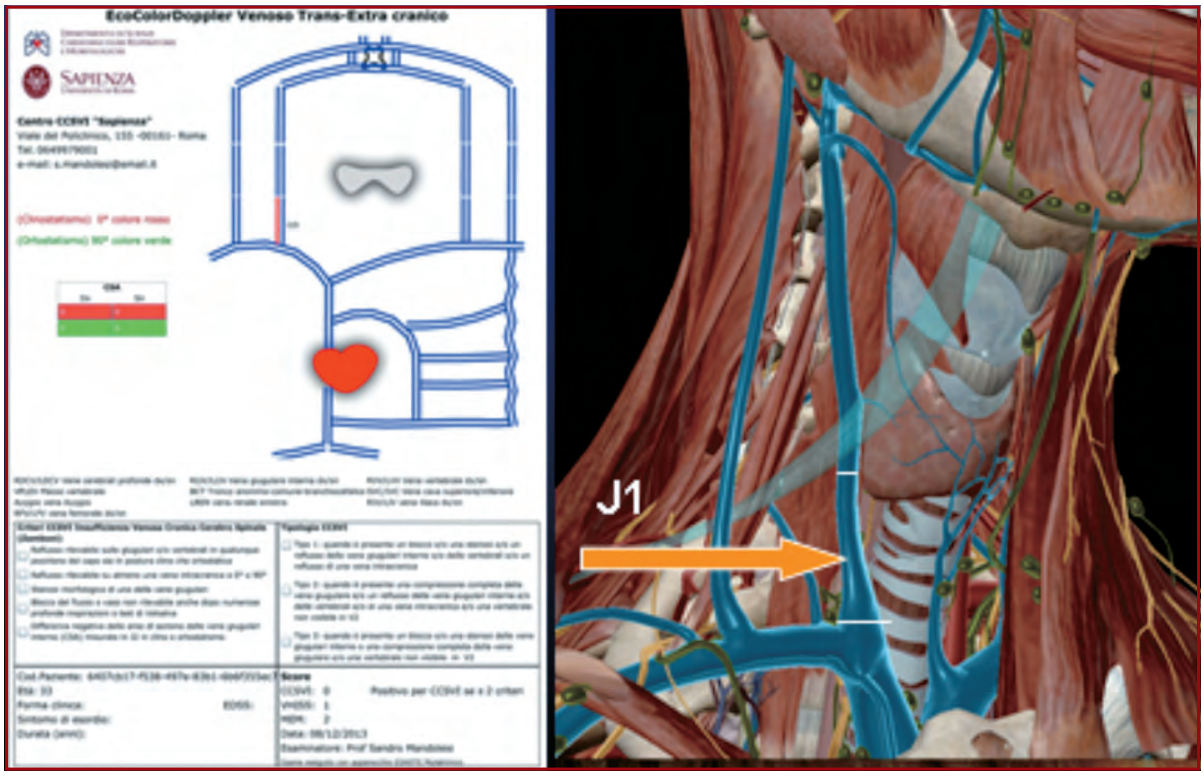


**Figure 43.3** – Internal jugular vein J1 segment.

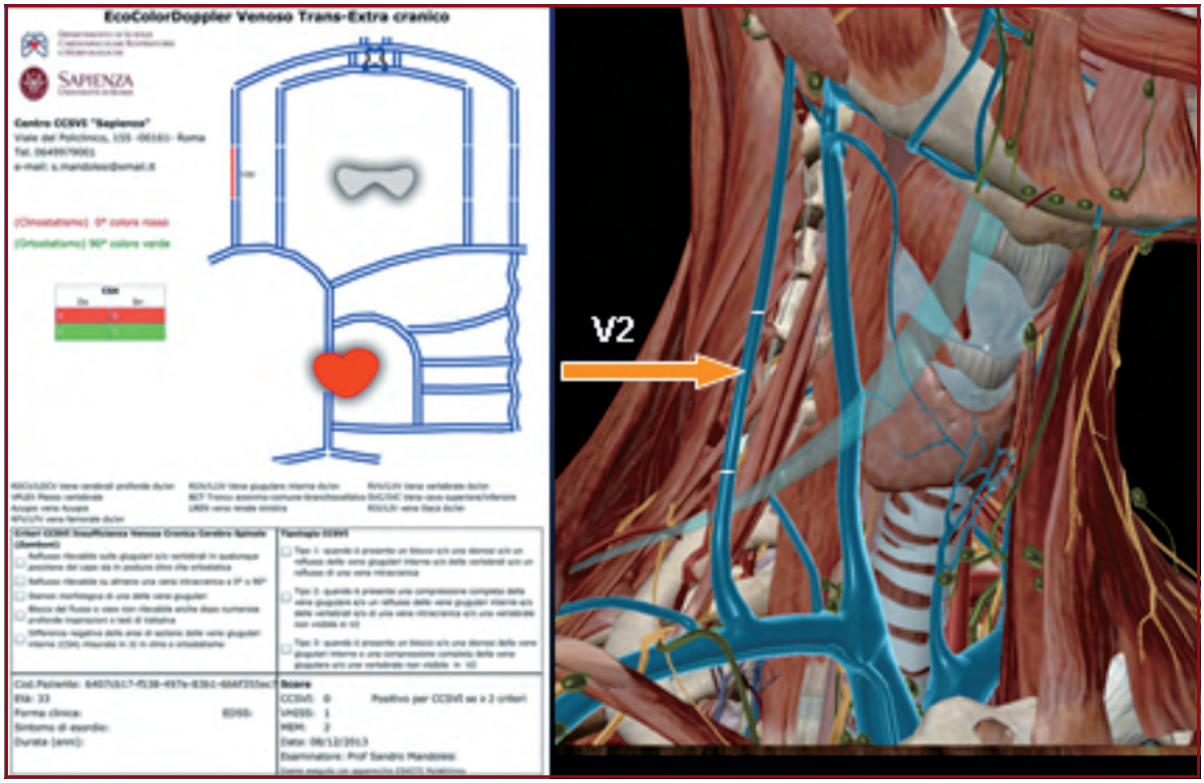


**Figure 43.4** – Vertebral vein V2 segment.

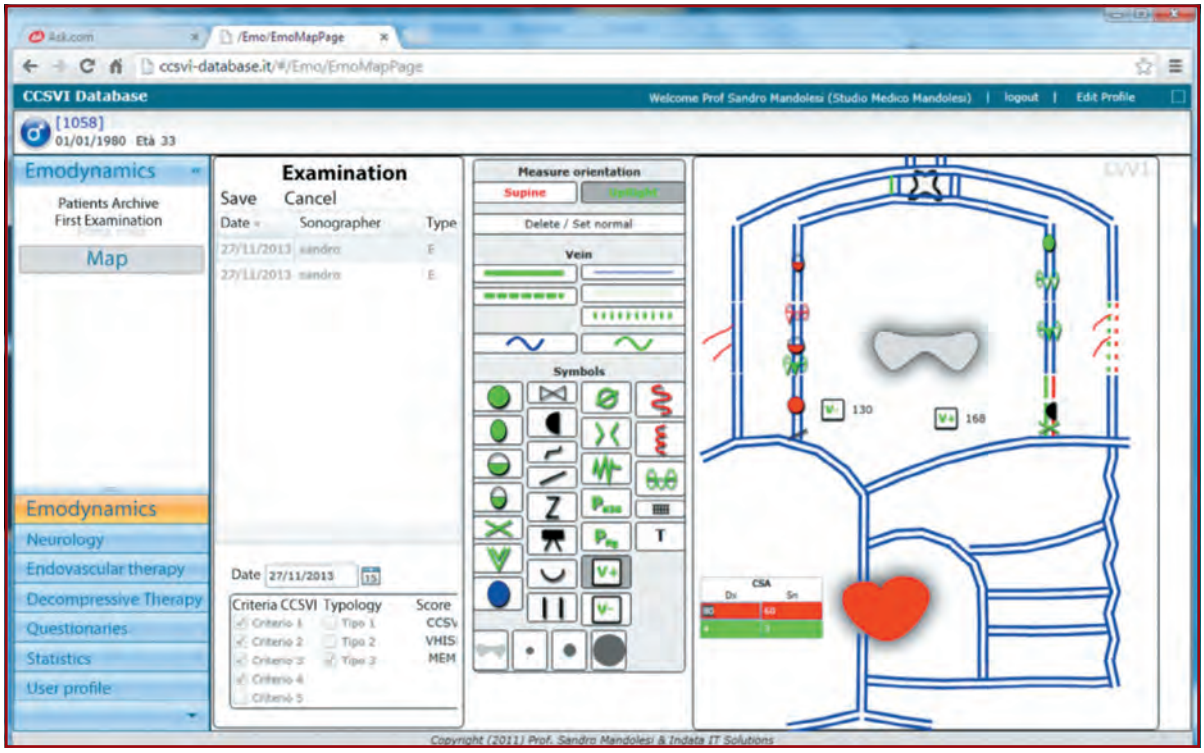


**Figure 43.5** – Page where you create the map.

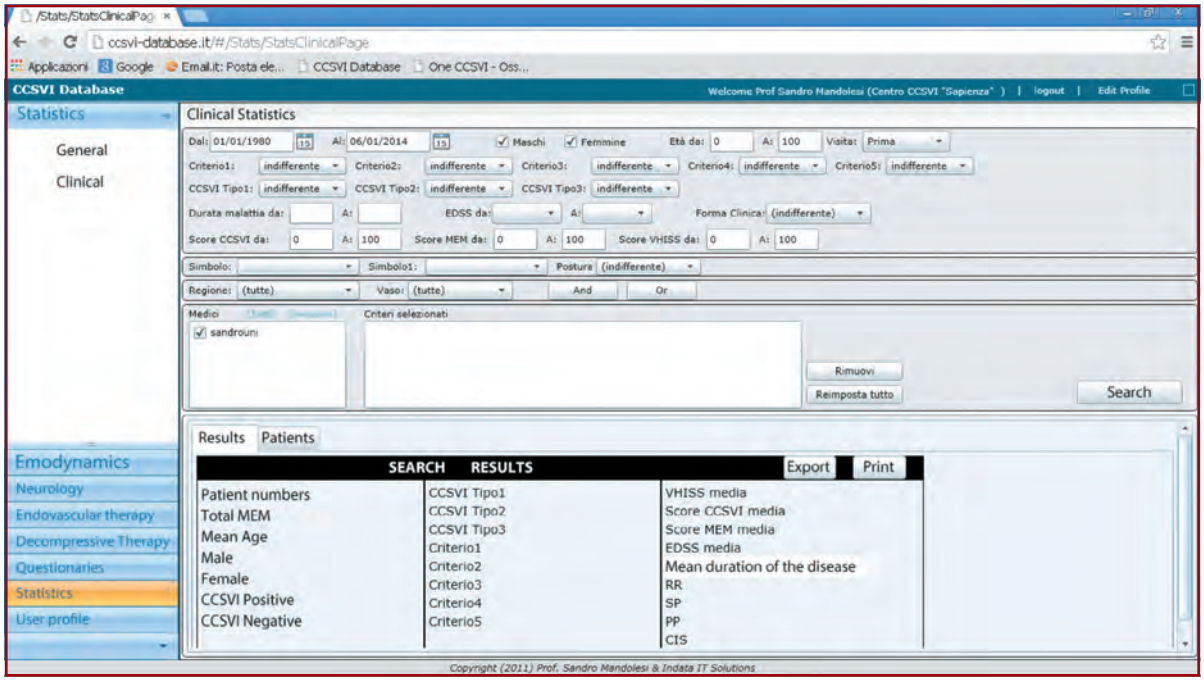


**Figure 43.6** – Page for clinical analysis.

symbols on the MEM-net map automatically allows to print out the following: a CFDI morphological hemodynamic map with the legend of the symbols (Figure 43.5), a written report of the examination, the criteria used for the findings, the CCSVI score, the venous hemodynamic insufficiency severity score (VHISS), the type of CCSVI, type 1, type 2 or type 3, the clinical type such as

relapsing remitting (RR), secondary progressive (SP), primary progressive (PP), clinically isolated syndrome (CIS), the expanded disability status scale (EDSS), the years of disease duration, the first symptom, age and sex, and an identification code for the privacy of the patient.

This software makes:

- faster, easier and appropriate the CFDI report of CCSVI;
- reduces human error;
- standardizes the CFDI report, by the shared symbols of the consensus conference;
- provides a written report of the assessment;
- prints automatically the report (Figure 43.7);
- saves all hemodynamic and morphological results in its data base;
- allows statistical analysis on 90 items of patients' data (Figure 43.6);
- clinical and hemodynamic examinations and follow-up become faster and easier.

The MEM-net algorithm acts as a blind control of the CFDI reports and eliminates possible human errors and subjective interpretation of the examination. The CFDI data are collected by the same standard procedure which is the map report. The MEM-net statistical analysis program allows research on homogeneous samples in a short time.

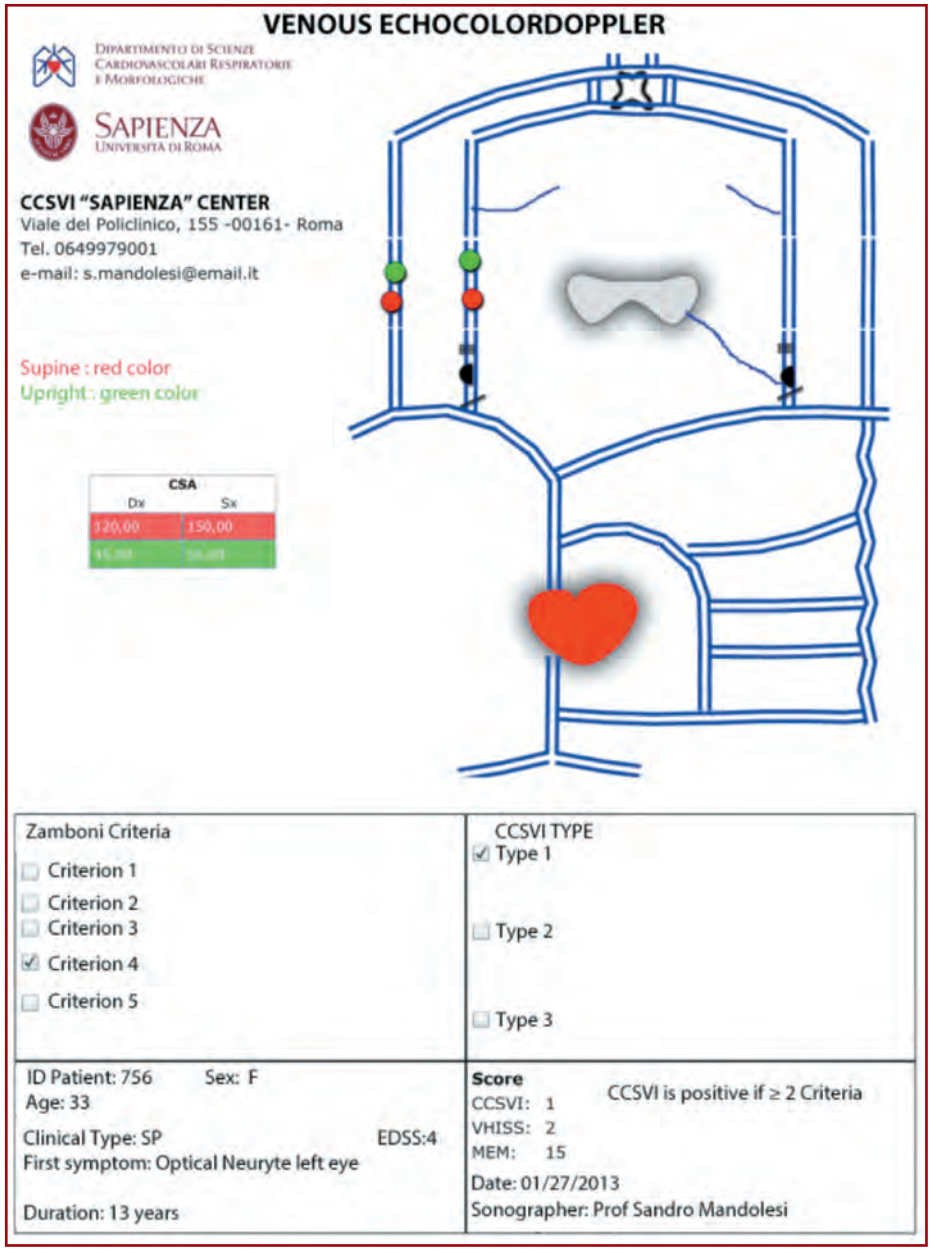


**Figure 43.7** – Report printing of CFDI examination with hemodynamic and morphological symbols.

Table 43-II – Symbols and terminology of venous flow alterations.

| Symbol | Description |
|---|---|
|  Full block | When the block involves one or more segments with caliber ≥ the previous or the following level |
|  Empty block | When the block involves one or more segments with caliber much < the previous or the following level |
|  Semi full block | When the time of the drainage flow detected by pulsed Doppler is longer than the stop flow on one or more segments with caliber ≥ the previous or the following level |
|  Semi empty block | When the time of the drainage flow detected by the Pulsed Doppler is longer than the stop flow on one or more segments of size much smaller than the previous or the following level |
|  Hemodynamic stenosis | Flow velocity >150 cm/s |
|  Vicarious | Flow vicarious >45 cm/s on vertebrals (V2) in clinostatic and >60 cm/s in orthostatic >100 cm/s on the internal jugulars (J2) both in clino and orthostatic position |
| White compression | The compression is defined white when the vein is completely compressed and we cannot detect any flow inside |
|  Frontal | |
|  Right lateral | |
|  Left lateral | |
|  Back protrusion | |
| Black compression | The compression is defined black when the caliber of the vessel is less than 6 mm and shows a flow |
|  Frontal | |
|  Right lateral | |
|  Left lateral | |
|  Antero protrusion | |
| In the upright position the symbols are drawn green. | |
|  Accessory vein | Collateral vessel visible but with physiological flow |
|  Reflux | Reverse, retrograde, anti physiological flow >0.8 s |
|  Semi-reflux | Bidirectional flow |
|  Hypovisibile | CFDI hypovisible flow with PRF* 0.7 |

**Table 43-II – Symbols and terminology of venous flow alterations.**

| Symbol | | Description |
|---|---|---|
|  | Invisible | CFDI not visible flow with PRF* 0.7 |
|  | Pathological accessory vein in supine and upright position | Collateral vessel with reverse, retrograde, anti physiological flow |
| Functional stenosis | Equivalent to hemodynamic stenosis | Presence of morphological abnormalities and reflux or two-way flow or block on the same vein |
|  | Valsalva+ | Valsalva test positive |
|  | Valsalva- | Valsalva test negative |

*PRF= pulse repetition frequency

**Table 43-III – Symbols for measures.**

| | | |
|---|---|---|
|  | Caliber | Size in $mm^2$ |
|  | Pressure | Measurement of pressure in cm $H_2O$ |
|  | Pressure | Measurement of pressure in mmHg |
|  | Velocity | Measurement of velocity in cm/s |
|  | Diameter | Measurement in mm |

**Table 43-IV – Respiratory hemodynamic index of Manconi.**

| | |
|---|---|
| CSA in J2 during inspiratory phase | Normally is reduced by at least 30% of expiratory CSA |
| CSA in subclavian inspiratory phase | Normally is reduced by at least 30% of expiratory CSA |
| Speed flow in J2 inspiratory phase | At least doubled compared to the previous inspiration speed flow |
| Speed flow in subclavian inspiratory phase | At least doubled compared to the previous inspiration speed flow |

## TERMINOLOGY

The terminology of CFDI findings for CCSVI has been standardized at the national epidemiological observatory consensus conference. The use of these terms shared by all the executors of ultrasonographic assessments provides a common language and therefore the possibility to compare the results of the CFDI assessments reliably.[9] It is good practice, before any epidemiological research, to establish the language and the procedure for carrying out a CFDI examination.

## MORPHOLOGICAL TERMS

The morphological terms define the anatomical lesions found during the CFDI assessment and they are shown in table 43-I.

## HEMODYNAMIC TERMS

The hemodynamic terms define the modification of the venous flow found during the assessment CFDI and they are shown in table 43-II.

## SYMBOLS

Symbols are graphic signs that correspond to the morphological or hemodynamic lesions found by the CFDI venous assessment (Table 43-III). They are put on the map to indicate the pathological alterations found during the examination. By definition the red color is used for lesions found in the supine position and the green color for lesions found in the upright position. Other symbols for measures are show in table 43-IV. The CFDI map report allows by the MEM-net algorithm to

calculate all the scores, to write the report of the examination, to print the map and to do the statistical analysis of data.

## NECK ROTATION TEST

The test consists of rotation of the head to the outside and inwards, at the same time we check the changes of ultrasound images of the internal jugular veins and vertebral veins to highlight a venous compression syndrome of these vessels.

## THE MANCONI RESPIRATORY TEST

The test consist of a nose breath while the internal jugular and subclavian veins are registered at the J2 level. If the reduction of expiratory versus inspiratory cross sectional area (CSA) is less than 30% and/or the speed flow more than double, the respiratory test is positive. Its receiver operating characteristic (ROC) curve is equal to 97%, the positivity test corresponds to a hindered discharge flow and is four times greater in individuals with MS compared to healthy individuals (Table 43-IV).

## REFERENCES


1. Franceschi C. Théorie et pratique de la cure conservatrice et hemodynamique de l'insuffisance veineuse en ambulatoire. Précy-sous-Thil, France: Editions de l'Armançon; 1988.
2. Mandolesi S, Di Salvo R, Ballo M *et al.* L'attivazione Doppler del circolo venoso superficiale degli arti inferiori (metodiche di studio). Minerva Angiol 1992;17(Suppl 3):159.
3. Mandolesi S, Ciciarello F, Marceca A *et al.* Data analysis of the chronic cerebro-spinal venous insufficiency in patients with multiple sclerosis: new disease classification. 72° Congresso Nazionale della Società Italiana di Cardiologia, Roma, 10-12 Dicembre 2011.
4. Mandolesi S, Flebologia Emodinamica. SUE editor; 2009.
5. Zamboni P, Galeotti R, Menegatti E *et al.* Chronic cerebrospinal venous insufficiency in patients with multiple sclerosis. J Neurol Neurosurg Psychiatry 2009;80:392-9.
6. Zamboni P, Morovic S, Menegatti E *et al.* Screening for chronic cerebrospinal venous insufficiency (CCSVI) using ultrasound - recommendations for a protocol. Int Angiol 2011;30:571-97.
7. Mandolesi S, Manconi E, Niglio T *et al.* Incidence of anatomical compression of the internal jugular veins with full block of their flow in patients with chronic cerebro-spinal venous insufficiency and multiple sclerosis. 21 st Eurochap-IUA 2013. Torino: Edizioni Minerva Medica; 2013.
8. Mandolesi S. C.H.I.V.A. - La mappa emodinamica venosa: sistema computerizzato per la valutazione statistica. Minerva Angiologica 1992;17(Suppl. 4): 3-5.
9. Antignani PL, Gossetti B, Righi D *et al.* Accreditation process for the performance of ultrasound vascular diagnostics procedures. Minerva Cardioangiol 2005;53:485-506.