

March 2011

Managing patients with Multiple Sclerosis after out-of-country endovascular treatment for “CCSVI”

Introduction:

The College been asked for advice regarding the management of multiple sclerosis patients who have traveled outside Canada for medical treatment. There is no official College Standard of Practice on this topic, but the following may be useful regarding the follow-up testing or treatment for any patient who has received medical care outside of the country.

- Alberta physicians have an ethical obligation to provide follow-up care to patients who have had procedures done out of country. However, the details of the follow-up care provided will be determined by the attending Alberta physician using his or her expertise and judgment and acting in the best interests of the patient. That follow-up may not be the same care the patient would have received out of country.
- Alberta physicians are NOT required to order diagnostic tests or medications requested or advised by an out of country physician. Decisions to order any tests must be made by the attending physician using appropriate clinical evidence and judgment.

The following advice on the management of patients with Multiple Sclerosis who’ve undergone the CCSVI treatment was developed by a multidisciplinary group of Alberta physicians including MS neurologists.

It will be updated from time to time and distributed to Alberta physicians as necessary. As noted, the document is not intended to be a substitute for individual clinical judgment.

If you have professional or ethical concerns about this topic, please contact the College and ask to speak to a member of the executive team.

Background:

In the past two years since Dr Paulo Zamboni hypothesized that “chronic cerebrospinal vascular insufficiency” (CCSVI) plays a role in multiple sclerosis (MS), many Albertans with MS have had venous angioplasty with or without stenting outside of Canada. Patients having CCSVI procedures return taking a variety of treatments that have been recommended for variable periods of time (warfarin, ASA, clopidogrel, oral anticoagulants, combinations of these treatments, or nothing). There is generally no follow-up by the out-of-country treating physicians, and a record of the treatment and type of stent may not be provided to the patient. Often recommendations are given to the patient verbally and sometimes there are no recommendations of any kind.

NOTE: A 3-year observational study focusing on the complications and patient reported effects of venous procedures for CCSVI is being developed but cross sectional data is not expected to be available until 2012.

The purpose of this communication is to provide expert opinion to guide management of issues unique to this situation. In addition, we are providing guidance with regard to management of MS related issues. It is important to inform patients of their choices and of the limited data available to guide treatment so they can make their own treatment decisions within the scope of reasonable treatment options. *This document is not intended to be a substitute for individual clinical judgment.*

Information in this document is based on clinical experience managing post-procedure complications, patient reports, and, where possible the medical literature. Actual data about the risks of complications after these procedures, and how to manage them, is extremely limited or non-existent. The consequences of jugular vein thrombosis in the presence of a stent are unknown. Opinions from specialists in neurology (stroke and MS), hematology, vascular surgery and diagnostic imaging have contributed to this guidance document. Evolving evidence may lead to revisions of this document.

In addition to ongoing management of the patients' MS, there appear to be several aspects to follow-up care:

1. Prevention of venous thrombosis.
2. Monitoring for asymptomatic jugular vein thrombosis.
3. Management of jugular vein thrombosis.
4. Management of other complications.

1. With regards to **prevention of thrombosis** it is up to each individual physician to determine if they choose to accept the responsibility of continuing prescribed medications to prevent thrombosis.

Without evidence to support their use however, we cannot recommend off-label prescribing.

2. **Monitoring for asymptomatic jugular vein thrombosis or re-stenosis is not recommended**, just as there is no indication to monitor for deep vein thrombosis in the legs in the absence of sufficient clinical indication of clot. MS relapse, pseudo relapse, and other worsening of MS symptoms are not indications for venous imaging.

3. Management of jugular vein thrombosis, once detected, depends on the clinical situation. Management should be coordinated by the physician who orders the imaging study.

Asymptomatic jugular vein thrombosis is fairly common after jugular vein catheterization but it is not routinely treated with anticoagulation in this clinical situation. However, there is a small risk of pulmonary embolism or clot propagation in the setting of isolated jugular vein thrombosis. The risk of pulmonary embolism is estimated at 2.7% (*Sheikh MA, Topoulos AP, Deitcher SR. Isolated internal jugular vein thrombosis: risk factors and natural history. Vasc Med. 2002 Aug;7 (3):177-9.*) but the literature is limited and some hematologists believe that the risk may be higher. Recent thrombosis and more extensive clot are likely associated with higher risk. The frequency of clot extension is unknown (for example to the axillary vein, intracranial veins or the superior vena cava). It is unclear if confirmatory or follow-up imaging is required; follow-up ultrasound in one week may determine if clot is extending as is useful in the management of calf vein thrombosis.

Therefore, in the absence of specific evidence to guide decision making, “anticoagulation for a minimum of 3 months” and “no treatment” may both be reasonable options. If anticoagulation is planned it should be handled in the same way that anti-coagulation of any venous thrombosis would be in your community. The imaging modality of choice to evaluate jugular vein thrombosis is unclear because studies to compare imaging methods have not been undertaken. Individual patient risks must be considered and clinical follow-up needs to be determined based on each case. Reasonable options should be discussed with patients.

Symptomatic jugular vein thrombosis post-CCSVI procedure should not be managed differently than in any other patient but the presence of a stent may influence treatment options and possibly treatment duration. Patients who have had jugular vein procedures and are suspected to have **intracranial, axillary, or superior vena cava thrombosis or pulmonary embolism should be sent to an emergency department for care whether jugular vein thrombosis is known to be present or not.** If these conditions are confirmed it is likely that these patients will be admitted to a hospital.

Thrombolytics are not approved by Health Canada for venous thrombosis and their safety is unknown. Patients should not be led to believe that thrombolysis or revision of previous CCSVI treatment will be offered.

Venous thrombosis is not a surgical issue. Specialists may choose to *discuss* very unusual situations with a vascular surgeon or an interventional radiologist but referral without prior discussion is not indicated.

4. Other complications should be managed as medically indicated. It is beyond the scope of this communication to discuss all known complications and their management.

MS Follow-up

Some patients who have had CCSVI procedures report subjective improvement in some of their MS symptoms (especially fatigue, cognition, sensation). In many cases this lasts for hours to weeks followed by abrupt or gradual return to their baseline status. This pattern of transient symptom improvement followed by return to baseline is not likely a relapse. However, relapses may also occur. They may be more likely if patients have discontinued MS disease modifying therapy (i.e. Rebif, Betaseron, Avonex, Copaxone, and Tysabri). If you think the patient is relapsing treat as you usually would. One should always rule out an underlying infection. Pulse steroids may be considered for severe attacks, and a referral to a neurologist or MS Clinic may be needed. Patients with later stage MS, typically those with limited ambulation, are much less likely to have relapses but infections or other stressors often cause transient worsening of their symptoms (pseudo relapses). Steroids will not likely be helpful in this situation. Relapse and pseudo relapse are not indications for venous imaging.

MS follow-up after CCSVI procedures should be no different than follow-up for a person who did not have a procedure. Some patients believe that their symptomatic improvement ends if their veins become thrombosed or re-stenosed and, also, that loss of symptomatic improvement is due to thrombosis or re-stenosis of their veins. However, there is no evidence to support this.

Referral of Alberta patients who have had procedures for CCSVI to an MS Clinic is also encouraged. All patients will be triaged based on urgency and will not displace those already on the waitlist. If the patient is followed by a non-MS Clinic neurologist the referral will generally be forwarded to that neurologist unless the referral letter clearly states that the patient wishes transfer of care to an MS Clinic neurologist.

Please include the following information with the MS Clinic referral or advise that the patient will send it separately to allow triage:

- The name of the patients usual MS neurologist
- All imaging reports from outside Alberta
- All documents that the patient received describing their out-of-country procedure and prescribed follow-up
- Your visit record and treatment plan
- A description of any new MS symptoms including the severity, course of the worsening, and time of onset of the worsening and note if they recently discontinued therapy for MS
- Patient contact information

MS Clinics in Alberta:

Calgary MS Clinic
Fax: 403-270-7162

Red Deer MS Clinic
Fax: 403-358-4345

Edmonton MS Clinic
Fax: 780-407-1325