
Caring for Patients With Multiple Sclerosis Who Have Undergone Endoluminal Vein Dilation

Based on a report submitted to the Minister of Health and Long-Term Care

By the Ontario MS Expert Advisory Group

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1) PURPOSE STATEMENT

Some research has suggested a relationship between narrowed veins in the neck and chest and the development of MS, although this relationship has not been proven. It has also been suggested, but not proven, that endoluminal vein dilation procedures can improve the symptoms of MS. This procedure is frequently referred to as the Zamboni procedure, after the Italian doctor who first suggested it. While there is not yet sufficient evidence to begin offering this procedure in Canada, some patients have chosen to undergo endoluminal vein dilation procedures outside the country. Typically, follow up of these patients after endoluminal vein dilation procedures is not done by the physician who carried out the procedure, and becomes the responsibility of health providers in their home province. Guidelines were developed by The Ontario Multiple Sclerosis (MS) Expert Advisory Group (see Appendix A for Membership List) to provide guidance to health care practitioners (i.e., family physicians/general practitioners, specialists, nurse practitioners) in the province of Ontario who are providing post-operative and ongoing follow-up care to patients with MS who have had an endoluminal vein dilation procedure for the treatment of MS in another country and have returned to Ontario.

The Expert Advisory Group developed these guidelines at the request of the Minister of Health and Long-Term Care of Ontario. They represent a consensus opinion based on the expertise of the members of the group, as well as the available literature on this subject, which is acknowledged to be of limited scope and quality. The guidelines presented in this report are intended to be read by any interested Ontarian. The companion guideline for primary care providers, *Guidelines for the Management of Patients Following Endoluminal Vein Dilation Procedures for the Treatment of Multiple Sclerosis*, is available in the publications section of on the Ministry of Health and Long-Term Care's professional website, at <http://www.health.gov.on.ca/en/pro/>.

There are currently no evidence-based clinical guidelines for the treatment of complications of vein dilation procedures involving the azygous or jugular veins. Practitioners should tell their patients that they will inform them if and when new information about treatment options becomes available, and that they will make referrals to other health care practitioners as appropriate.

It must be emphasized that the opinion an individual practitioner might have regarding the still controversial endoluminal vein dilation procedure for the treatment of MS should have no bearing on his or her willingness to provide care for patients returning to Ontario after having received the procedure. By the same token, their opinion regarding the procedure should not affect their willingness to refer such patients to other practitioners, their willingness to accept such a referral in a timely manner, or their willingness to accept such patients as new patients (see Appendix B for applicable legislation, regulations, policies, standards, and guidelines).

2) GUIDELINES FOR CARE

2.1) Regular, Ongoing Care for the Management of MS

- a. Patients returning to Ontario after endoluminal vein dilation procedures should have ongoing, routine assessment by their health care practitioners as part of their regular care for the management of MS.
- b. Practitioners should encourage patients to attempt to find out as much information as possible about the out-of-country endoluminal vein dilation procedure that they received, including whether stents were inserted into veins, and whether complications arose during or after the procedure.

2.2) Potential Complications of Endoluminal Vein Dilation Procedures

There are a number of complications that may develop post-procedure. These include:

- a. **Local complications:** may include deep vein thrombosis, bleeding from the vein that was cannulated to do the endoluminal procedure (femoral vein, brachial vein), infection at the site of cannulation, direct trauma to arteries or nerves adjacent to the vein that was cannulated (femoral artery or nerve, brachial artery or median nerve), skin necrosis, distal embolism and arterio-venous fistula formation.
- b. **Complications related to endoluminal vein dilation or dilation plus stenting of the internal jugular or azygous vein:** may include thrombosis of the azygous or internal jugular vein after vein dilation or following vein dilation plus stenting, extension of thrombus into adjacent intra-cranial or intra-thoracic veins, vein laceration or rupture, pulmonary embolism, stent migration, stent fracture or deformation, or compression of adjacent local structures, including cranial nerves and the common or internal carotid arteries.
- c. **Complications related to drugs or medications administered during the course of or after the endoluminal vein dilation procedure:** may include an allergic reaction to the radiographic contrast agent or anaesthetic, renal dysfunction that may result in kidney failure secondary to contrast induced nephropathy, and problems related to anti-platelet agents or anti-coagulant medications, such as gastrointestinal bleeding or cerebral haemorrhage.
- d. **Infection with pathogens:** including those that may be common in the country where the patient underwent the endoluminal vein dilation procedure, but which are uncommon in Ontario.

2.3) Recommendations Regarding Care

- a. Patients should be advised that the decision to discontinue any MS disease-modifying therapies they might previously have been prescribed after endoluminal vein dilation procedures needs to be discussed with their practitioner.
- b. Many patients who undergo an endoluminal vein dilation procedure for reasons other than the potential treatment of MS are routinely placed on anti-platelet agents, and these agents are often continued after the procedure, unless there is a specific reasons not to. The decision to treat asymptomatic patients with anti-platelet agents after an endoluminal vein dilation procedure should be made on a case-by-case basis, and physicians should carefully evaluate patients for the risks associated with anti-platelet therapy.
- c. It is unknown if anti-platelet agents such as aspirin help keep veins unobstructed after venoplasty or venoplasty with simultaneous stent placement in patients with MS. Based on the overall health benefit of taking low-dose aspirin, however, it is not unreasonable for asymptomatic patients with or without MS to take low-dose aspirin indefinitely, as long as there is no reason not to.

2.4) Indications for Diagnostic Imaging

- a. Unless the patient has symptoms and signs of complication following the vein dilation procedure, follow-up imaging studies such as Duplex Doppler ultrasound or magnetic resonance (MR) venography are not indicated. This is because the findings of such imaging studies are of uncertain significance in a patient without symptoms related to the vein dilation procedure, and because the results of such studies would not change the ongoing management of the patient.

- b. Stents are designed to be placed in arteries to help keep them open. They are not designed to be placed in veins, and are not approved by Health Canada for use in that way. However, stents are occasionally placed in veins to manage patients with recurrent central vein stenosis secondary to central venous or hemodialysis catheters. MS patients who have undergone vein stent placement should be considered for imaging studies if they exhibit symptoms that may be directly related to stent thrombosis, or if a complication of vein dilation and stent placement is suspected. Imaging studies of the internal jugular or azygous veins are not indicated in asymptomatic patients after endoluminal vein dilation or stenting procedures.
- c. Worsening or recurrence of MS symptoms (including MS relapse) after a vein dilation procedure does not currently constitute an indication for venous imaging studies.
- d. In situations where stents have been placed in the azygous vein, computed tomography (CT) or MR venography are required to assess those stents if thrombosis or other complications are suspected.

2.5) Symptoms and Treatment of Stent Thrombosis

- a. The symptoms associated with stent thrombosis in the neck are not completely known at the present time, but may include (but not be restricted to) pain and/or swelling in the head and neck. Embolization of thrombus within a stent to the pulmonary circulation may cause chest pain, shortness of breath, hemoptysis and/or pleuritic chest pain. The symptoms related to stent migration are likely to depend on the direction the stent migrates. For example, stent migration to the right side of the heart may cause arrhythmia, incompetence of the tricuspid or pulmonary valves, or sudden cardiac decompensation.
- b. If stent thrombosis is identified, the patient should be referred to a thrombosis expert such as a haematologist and/or vascular surgeon for ongoing management. If a pulmonary embolus is identified, patients should be told that this is a potentially life-threatening condition that will require emergency assessment and treatment.
- c. There is currently little or no evidence specific to the management of thrombosis of the internal jugular or azygous veins. Consequently, the management of thrombosis of these veins should be based upon the evidence-based management of deep vein thrombosis (DVT) in more common locations, such as the lower extremities. For further information on management of venous thrombosis, and to start treatment while waiting for a specialist referral, please refer to guidelines for DVT management at: http://chestjournal.chestpubs.org/content/133/6_suppl/454S.full.html.
- d. Thrombolysis (breaking up blood clots) is not indicated and is not approved by Health Canada for patients with stent thrombosis, because of the significant and potentially life-threatening bleeding risks associated with this therapy. In addition, the benefits of this therapy in a thrombosed internal jugular or azygous vein of a patient with MS, regardless of whether there is a stent, has not been established. Therefore, at this time, the risks likely outweighs the potential benefits of this therapy in patients with MS.

2.6) Risks Associated with Repeat Endoluminal Vein Dilation Procedures

Repeat endoluminal vein dilation procedures carry the risk of vein damage, including re-stenosis, thrombosis or vein rupture, and are associated with increasing exposure to ionizing radiation.

Appendix A - Ontario MS Expert Advisory Group Membership List

Name	Title and Organization
Dr. Barry Rubin (Co-Chair)	Program Medical Director, Peter Munk Cardiac Centre, University Network Hospital (UHN)
Dr. Paul O'Connor (Co-Chair)	Director, MS Clinic and MS Research and the Evoked Potentials Laboratory, St. Michael's Hospital
Dr. Marcelo Kremenchutzky	Director, Multiple Sclerosis Clinic, London Health Sciences Centre
Dr. Julian Spears	Co-Director, Neurovascular Program, St. Michael's Hospital
Dr. Liesly Lee	Consultant Neurologist, Sunnybrook Health Sciences Centre and Director, Sunnybrook MS Clinic
Dr. David Henry	President and CEO, Institute for Clinical Evaluative Sciences (ICES)
Dr. Andreas Laupacis	Executive Director, Li Ka Shing Knowledge Institute of St. Michael's Hospital
Dr. Phil Wells	Professor, Chief and Chair, Department of Medicine, The Ottawa Hospital and University of Ottawa
Two patients living with MS	

Appendix B - Applicable Legislation, Regulations, Policies, Standards, and Guidelines

Physicians must act in accordance with applicable legislation, including the **Regulated Health Professions Act, 1991** and the **Medicine Act, 1991**, and regulations made under such Acts, as well as policies of the College of Physicians and Surgeons of Ontario (CPSO), including policies regarding accepting new patients and ending the physician-patient relationship.

Relevant CPSO policies can be accessed and viewed through the following links:

Accepting New Patients - http://www.cpso.on.ca/uploadedFiles/policies/policies/policyitems/Accepting_patients.pdf

Ending the Physician Patient Relationship - http://www.cpso.on.ca/uploadedFiles/policies/policies/policyitems/ending_rel.pdf

Physicians and the Ontario Human Rights Code - http://www.cpso.on.ca/uploadedFiles/downloads/cpsodocuments/policies/policies/human_rights.pdf

Non-allopathic (Non-conventional) Therapies in Medical Practice (*Note: a revised draft of this policy is currently out for public consultation*) - <http://www.cpso.on.ca/policies/consultations/default.aspx?id=4310>

The Practice Guide: Medical Professionalism and College Policies - <http://www.cpso.on.ca/policies/guide/default.aspx?id=1696>

Nurse practitioners must act in accordance with applicable legislation, including the **Regulated Health Professions Act, 1991** and the **Nursing Act, 1991**, and regulations made under such Acts, as well as standards and guidelines of the College of Nurses of Ontario (CNO).

Relevant CNO standards and guidelines can be accessed and viewed through the following links:

Professional Standards (*currently undergoing revision*) - http://www.cno.org/Global/docs/prac/41006_ProfStds.pdf

Nurse Practitioners Practice Standard - http://www.cno.org/Global/docs/prac/41038_StrdRnec.pdf

Refusing Assignments and Discontinuing Nursing Services - http://www.cno.org/Global/docs/prac/41070_refusing.pdf

Ethics Practice Standard - http://www.cno.org/Global/docs/prac/41034_Ethics.pdf

Glossary

Term	Definition
<i>Allopathic</i>	Relating to treatment of illnesses/diseases using conventional techniques or medicines to help alleviate or suppress the symptoms
<i>Anaesthetic</i>	A substance used to reduce pain or sensation either in the whole body by causing unconsciousness (general anaesthetic) or in part of the body while conscious (local anaesthetic)
<i>Anaesthetic agent</i>	A drug that causes a temporary loss of feeling or sensation in the body
<i>Anticoagulant medications</i>	Medicine that prevents the clotting of blood
<i>Anti-platelet agents</i>	A substance in the body that prevents blood from clotting
<i>Arrhythmia</i>	An irregular heartbeat; the irregularity exists in the rhythm or force of the beat
<i>Arterio-venous fistula</i>	An abnormal channel or passage between an artery and a vein
<i>Artery</i>	A (tube-like) vessel that directs oxygen-carrying blood away from the heart to the rest of the body
<i>Asymptomatic</i>	Showing no symptoms or signs of a disease, disorder, condition, or complication
<i>Axillary vein</i>	The large blood vessel that conveys blood from the axilla (armpit) and upper arm toward the heart
<i>Azygous vein</i>	A vein located along the right side of the spinal column that carries blood from the chest and abdomen to the heart
<i>Brachial artery</i>	The main artery of the upper arm
<i>Brachial vein</i>	Two veins, one in either arm, that accompany the brachial artery and empty blood into the axillary vein
<i>Cannula</i>	A flexible tube inserted into the body to help guide/channel fluid
<i>Cannulated / Cannulation</i>	To insert a cannula or tube/catheter into (a bodily cavity, duct, or vessel), to drain fluid or to deliver medication, or to allow for a procedure
<i>Cardiac decompensation</i>	Failure of the heart to maintain sufficient blood circulation to the body
<i>Carotid arteries</i>	The principal artery of the neck on each side of the head which divides into two main branches (internal and external)
<i>Catheters</i>	Small tube-like, flexible surgical instruments that are inserted into the body to extract or introduce fluid(s)
<i>Central vein stenosis</i>	A narrowing or contraction of the central vein (e.g., jugular vein in the neck or in the femoral vein in the thigh) that is not normal
<i>Cerebral haemorrhage</i>	Bleeding from a ruptured/broken blood vessel in the brain
<i>Clot</i>	A soft, semi-solid mass that forms when blood gels
<i>Common carotid artery</i>	One of the major arteries that runs upwards from the heart, supplying blood to the head and neck (and divides into the external and internal carotid arteries)
<i>Computed tomography (CT)</i>	A method of examining body organs by scanning them with X-rays and using a computer to construct a series of cross-sectional scans (or slice-like scans)
<i>Contraindication</i>	A condition or factor which causes a particular line of treatment (medication or procedure) to be considered improper or undesirable
<i>Cranial nerves</i>	The twelve pairs of nerves that are connected from the brain outwards through openings in the skull
<i>Deep vein thrombosis (DVT)</i>	A blood clot in a major vein
<i>Dilated / Dilatation</i>	The widening or stretching of an opening or a hollow structure in the body

<i>Distal embolism</i>	When a blood clot gets stuck in a blood vessel, causing an obstruction
<i>Duplex Doppler Ultrasound</i>	A test to see how blood moves through the arteries and veins
<i>Embolism</i>	When a blood clot travelling through the blood stream gets stuck in a blood vessel causing an obstruction
<i>Endemic</i>	Relating to a disease or pathogen that is usually confined to or found in a particular location, region, or people (see pathogen)
<i>Endoluminal</i>	The inner portion of a tubular organ, a blood vessel or an intestine
<i>Endoluminal vein dilation procedure</i>	A procedure in which a tube-like device (catheter), capped by a deflated balloon, is inserted into a vein and advanced to where the vein is narrowed or blocked (usually in the head or neck region as it relates to this document). The balloon is then inflated to open the vein, deflated and removed. This procedure may also involve stents, which are intended to keep the vein open
<i>Erythema</i>	Redness of the skin caused by the widening and abnormal accumulation of blood in the smallest blood vessels, often a sign of inflammation or infection
<i>Femoral</i>	Pertaining to the femur or the thigh
<i>Femoral artery</i>	The main artery of the thigh
<i>Femoral nerve</i>	One of a pair of nerves that originate from the spine and supply the muscles and skin at the back of the thigh with signals/impulses of feeling
<i>Femoral vein</i>	The vein that accompanies the femoral artery (see femoral artery)
<i>Fistula</i>	A permanent abnormal passageway between two organs in the body or between an organ and the exterior of the body
<i>Gastrointestinal bleeding</i>	Any bleeding in the organs from the stomach to the intestines
<i>Haematology / Haematologist</i>	The branch of medical science dealing with the blood and blood-forming tissues. A Haematologist is a specialist in this area of medicine
<i>Hematoma</i>	The abnormal build up of blood in an organ, or other tissue of the body, caused by a rupture in a blood vessel
<i>Hemodialysis catheter</i>	A tube-like, flexible instrument that carries blood from the body to a machine that can mechanically clean the blood in order to remove various substances that would normally be cleaned by the kidneys
<i>Haemorrhage</i>	The escape of blood from an injured vessel (e.g., internal bleeding)
<i>Hemoptysis</i>	The coughing up of blood from the lungs or airway
<i>Hypertension</i>	High blood pressure
<i>Incompetence of the pulmonary valves</i>	The defective functioning of the pulmonary valve (see pulmonary valve). Incomplete closure of this valve can cause pulmonic regurgitation – the backflow of blood from the artery to the right atrium chamber
<i>Incompetence of the tricuspid valves</i>	The defective functioning of the tricuspid valve (see tricuspid valve). Incomplete closure of this valve can cause tricuspid regurgitation – the backflow of blood from the right ventricle into the right atrium
<i>Internal carotid artery</i>	Either of the two major arteries, one on each side of the neck, that supplies blood to the brain and eyes and internal parts of the head
<i>Intra-cranial</i>	Occurring within the skull
<i>Intra-thoracic veins</i>	Veins within the thorax (the division between the head and abdomen); situated on the inside of the rib cage

Ionization	The gain or loss of electrons of an atom or molecule to create a positive or negative charge. Ionization of cells in the body could cause cell death or mutation
Ionizing radiation	Electromagnetic radiation capable of producing ionization (see: Ionization), directly or indirectly, in its passage through body tissue or other matter. Ionization can also cause cell death or mutation
Jugular vein	Any of several large veins of the neck that drain blood from the head
Laceration	The process or act of tearing tissue
Lower extremities	Body parts from the waist down (e.g., legs, feet, toes, etc.)
Lumen	The inner open space or cavity of a tubular organ, like that of a blood vessel or an intestine
Lysing	The destruction of a cell by a chemical substance damaging its membrane
Magnetic resonance (MR) venography	The process of using a contrast dye injected into the blood stream to help image the veins and identify different absorption rates of fluids in the body
Median nerve	One of the nerves that extend along the inside portion of the forearm and the hand and supplies various muscles and the skin with feeling
Necrosis	The death of cells or tissues through injury or disease, especially in a specific area of the body
Nerve	A cordlike structure that conveys signals between one part of the body and another part of the body (e.g., from the arm to the spine or brain)
Non-allopathic	Non-conventional medical treatment of disease symptoms that uses substances or techniques to suppress the disease's symptoms
Patency	The state of a bodily passage (e.g., vein, artery, etc.) being open or unobstructed
Pathogens	An agent that causes disease (e.g., a living micro-organism like bacteria or fungus)
Pleuritic chest pain	Sharp chest pain caused by the inflammation of the membrane that surrounds and protects the lungs (the pleura). Inflammation occurs when an infection or damaging agent irritates the pleural surface
Pulmonary embolism	An obstruction of a blood vessel in the lungs, usually due to a blood clot
Pulmonary hypertension	A rare lung disorder characterized by increased pressure in the pulmonary artery (the vessel that takes blood from the heart to the lungs)
Pulmonary valve	A valve in the heart that prevents blood from re-entering the heart once it has entered the artery that takes the blood away from the heart to the lungs
Radiographic contrast agent	A radioactive dye that allows imaging technology distinguish features of the body in pictures
Renal dysfunction	A reduction in kidney function, resulting in waste accumulation in the kidneys
Re-stenosis	The re-blockage of an artery, vein or lumen after otherwise adequate therapy, which may occur after stenting
Right heart failure	The inability of the right side of the heart to adequately pump blood from the veins into the circulatory system (to the lungs to get oxygen). This causes a back-up of fluid in the body, resulting in swelling
Stenosis	An abnormal narrowing or contraction of a tube-like vessel in the body (e.g., duct, canal, artery, vein, lumen)
Stent	A slender rod-like device used to provide support for tube-like structures that are trying to be kept open
Stent migration	The movement of a stent away from its required or originally inserted location
Stent thrombosis	Formation of a clot in the blood that either blocks, or partially blocks a stent used to open a blood vessel

<i>Stenting</i>	The surgical procedure of inserting a stent into a vein, artery or tube-like vessel in the body
<i>Sudden cardiac decompensation</i>	Sudden failure of the heart to maintain adequate blood circulation
<i>Thrombolysis</i>	The process of breaking up and dissolving blood clots
<i>Thrombosis</i>	The formation or presence of a clot of coagulated (hardened or hardening) blood attached on the inside of a blood vessel
<i>Tricuspid valve</i>	A heart valve that is situated between the right atrium (upper right chamber) and the right ventricle (lower right chamber). This allows blood to pass from the atrium to the ventricle and then closes to prevent backflow when the ventricle contracts to push blood throughout the body
<i>Vascular</i>	Relating to the tube-like vessels that carry or circulate fluids, such as blood, through the body
<i>Vein</i>	Any of the tubes that form a branching system and carry deoxygenated blood to the heart
<i>Venography</i>	Venography is an x-ray test that provides an image of the veins in a particular part of the body after a contrast dye is injected into a vein
<i>Venoplasty</i>	The repair of a vein
<i>Venous imaging studies</i>	Research reports relating to the outcomes or findings of pictures (images) of veins before and after a medical procedure or in patients with or without a particular medical condition

References

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