In the first two parts of this five-part series, we talked about the anatomy of the lower extremity and the pelvic and abdominal venous systems. In the second part we have explained the concept of post ambulatory venous hypertension (PAVH) and how that leads to the signs and symptoms of chronic venous insufficiency in patients with class C1-C6 disease. In this installment, we will discuss the various pathologic conditions that lead to PAVH and consequently the sequelae of PAVH in the lower extremity.

**Causes of Increased Venous Pressure in the Pelvis and Lower Extremity**

- **Increased Venous Pressure**
  - Pelvic Venous Hypertension
  - Outflow Obstruction (MTS/NCS/PTS)
  - Enhanced Inflow Ovarian Vein Reflux
  - Insufficiency of the Lower Extremity Veins
  - Ovarian vein reflux in the Pelvic Venous Hypertension Column
  - Calf Muscle Pump Dysfunction
  - Outflow Obstruction (Secondary to Post Thrombotic Changes)
  - Enhanced Pelvic Venous Pressure escaping into the leg through escape veins - non saphenous varicosities

**Pelvic venous hypertension secondary to outflow obstruction:**

May Thurner Syndrome (MTS) and Nutcracker Syndrome (NCS) are the two common conditions that lead to Pelvic Venous Hypertension secondary to venous outflow obstruction.¹ MTS was first described in 1957 when it was noted that 22% of 430 cadavers on autopsy possessed an anatomical variant in which an overriding right common iliac artery caused compression of the left common iliac vein against the lumbar spine. More recently, a similar prevalence (22%–24%) of MTS was reported in a retrospective analysis of computed tomography scans.²

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Most typical nutcracker morphologic features imply compression of the Left Renal Vein (LRV) between the aorta and the Superior Mesenteric Artery (SMA).

Pathogenesis of Secondary Pelvic Congestion Syndrome (PCS):

There are several disease entities that obstruct venous flow out of the pelvis. The most common cause for venous outflow obstruction in the pelvis is May-Thurner Syndrome. Typically, an obstructive lesion forms where the right common iliac artery crosses the left common iliac vein. It is hypothesized that this normal physiologic site of compression, in some patients, leads to the development of obstructive lesions like intimal hyperplasia, vein wall fibrosis and webs. The decrease in venous flow increases the risk for development of an acute ilio-femoral deep vein thrombosis and subsequent post-thrombotic outflow obstruction.

The second most common pelvic venous outflow lesion is the Nutcracker Syndrome. Nutcracker Syndrome is compression of the left renal vein (LRV) by the superior mesenteric artery. It can also be observed in patients with retro-aortic renal veins. The left ovarian vein drains via the LRV (see discussion below). Obstruction of the LRV causes ovarian vein hypertension with reflux into the uterine veins and internal iliac veins via the pampiniform plexus. Reflux into the pelvic veins causes venous hypertension and the feeling of bloating, heaviness, dyspareunia and post-coital pain symptoms observed in patients with pelvic congestion syndrome. In a recent investigation conducted by the Center for Vascular Medicine, we observed that iliac vein obstruction either with or without ovarian vein reflux is the most common etiology for pelvic congestion syndrome. These findings have been submitted to the American Venous Forum for presentation at the 2017 meeting in New Orleans, Louisiana.

Pelvic Venous Hypertension Secondary to Enhanced Inflow:

Ovarian Vein Reflux

Anatomy of the Ovarian Vein: The Ovarian Vein Provides drainage to the Parametrium, cervix, mesosalpinx and the pampiniform plexus. It forms a rich anastomotic venous plexus with the Paraovarian, uterine, vesical, rectal and vulvar venous plexus.

Two to three trunks form a single ovarian vein at the L4 interspace. The Left Ovarian vein drains into the Left Renal Vein while the Right Ovarian vein drains directly into the IVC in 90% of patients. In 10% of patients the right ovarian vein drains into the right renal vein. The average diameter of the ovarian vein ranges between 3 and 5 millimeters. Ovarian veins greater than or equal to 6 millimeters have a high incidence of reflux. Women with three or more pregnancies are at risk for developing ovarian vein reflux. Valves are present mainly in the distal third of the ovarian veins. Valves are absent in the left and right ovarian veins in 15% and 6% of patients respectively.

Two anatomic findings define PCS: Ovarian vein reflux and pelvic varicosities. Each may be seen without the other or both can be present in asymptomatic patients.

Pathogenesis of Pain in Pelvic Congestion Syndrome:

Blood pooling in the pelvic and ovarian veins may cause further engorgement, thrombosis, and mass effect on nearby nerves, collectively contributing to pelvic pain. Exacerbation of symptoms with menstruation, sexual activity and ovulation suggests increased arterial flow to the pelvis at these times. This results in pooling of venous blood in pelvic varicosities. The characteristic severe dull aching pain of PCS is thought to be a direct result of the presence of ovarian and pelvic varicosities, much like the leg pain resulting from lower extremity varicose veins. Presence of cross-over veins can cause confusion, leading to increased symptoms on the right side despite a more prominent left ovarian vein.
Lower Extremity Venous Hypertension due to Insufficiency of the Lower Extremity Veins:

Deep Vein Reflux:

The muscles of the lower extremity surround the veins of the deep venous system. Lower extremity muscle contraction acts as a peripheral pump that pushes blood towards the heart. Eighty-five percent of venous return from the legs comes from the deep venous system. The superficial system, the Great and Small Saphenous Veins, accounts for the remaining 15%. Normal functioning venous valves ensure pro-grade flow during muscle relaxation. Valves that become incompetent (unable to close properly), result in retrograde flow of blood known as reflux. Venous reflux leads to pooling of blood in the veins with a subsequent increase in venous pressure. Reflux can be demonstrated visually by performing the Trendelenburg test. In a standing patient with varicose veins place your thumb over the vein and press. With the opposite thumb milk the blood out of the vein up to a point and then release. Rapid filling of the vein from above to the thumb holding pressure is an example of reflux.

Superficial vein reflux:

Dysfunction or incompetence of the valves in the superficial venous system also allows retrograde flow of blood and increased hydrostatic pressures. Valve failure may be primary or secondary. Primary valve failure is caused by a genetic predisposition or the result of preexisting weakness in the vessel wall or valve leaflets. Secondary valve failure is caused by direct injury like superficial thrombophlebitis, or excessive venous distention resulting from hormonal effects or high pressure. Failure of valves located at the junctions of the deep and superficial systems, most notably at the saphenofemoral and saphenopopliteal junctions, allows high pressure to enter the superficial veins. In this situation, venous dilatation and varicose veins form and propagate from the proximal junction site down the extremity. High pressure also can enter the superficial system because of failure of the valves in the communicating perforator veins. Perforator valve incompetence allows blood to flow from deep veins backward into the superficial system and the transmission of the high pressures generated by the calf muscle pump. This local high pressure can produce excessive venous dilatation and secondary failure of superficial vein valves. As a result, a cluster of dilated veins develops at this site and appears to ascend up the leg. Clinically relevant perforator vein incompetence is typically associated with reflux of the deep and/or superficial venous system.

Obstruction of the deep veins:

Obstruction of the deep veins may limit the outflow of blood, causing increased venous pressure with muscle contraction and secondary muscle pump dysfunction. Obstruction may occur because of an intrinsic venous process, such as previous DVT with inadequate recanalization or venous stenosis, or because of extrinsic compression, as in May-Thurner syndrome (compression of the left common iliac vein as it traverses between the right common iliac artery and the lumbosacral region). Venous outflow obstruction appears to play a more significant role in the pathogenesis of CVI and its clinical expression than previously appreciated.

Figure 1. Illustrative ambulatory venous pressure measurements. (A) Normal venous pressure. The resting standing venous pressure is 80 to 90 mm Hg. The pressure drops with calf exercise to 20 to 30 mm Hg, or a 50% decrease. The return in pressure is more gradual, with refill taking 20s. (B) Abnormal venous pressure with deep venous reflux. The drop in pressure with exercise is blunted (50% decrease). The return in venous pressure to the resting level is rapid because of a short refill time (20 s). contration (Figure 1B). Dysfunction of the valves of the deep venous system is most often a consequence of damage from previous deep vein thrombosis (DVT).
Muscle pump dysfunction:
Dysfunction of the calf muscle pumps leads to venous blood not being effectively emptied out of the distal extremity. Calf muscle pump dysfunction is commonly observed in patients with poor ankle range of motion secondary to arthritis or trauma leading to a frozen joint. 

The immediate post ambulatory venous pressure will be nearly as high as the pressure after prolonged standing. Muscle pump dysfunction appears to be a major mechanism for the development of superficial venous incompetence and its complications such as venous ulcers.

The Microscopic level:
Changes in the hemodynamics of the large veins of the lower extremity are transmitted into the microcirculation and eventually result in the development of venous microangiopathy. Features of this microangiopathy include elongation, dilation, and tortuosity of capillary beds, thickening of basement membranes with increased collagen and elastic fibers, endothelial damage with widening of interendothelial spaces, and increased pericapillary edema with “halo” formation. The abnormal capillaries with increased permeability and high venous pressure leads to the accumulation of fluid, macromolecules, and extravasated red blood cells into the interstitial space. In addition to changes in the blood vessels and connective tissue, alteration in the lymphatic network and nervous system may occur. Fragmentation and destruction of microlymphatics may further impair drainage from the extremity, whereas dysfunction of local nerve fibers may alter regulatory mechanisms. The current theory for the development of venous skin damage is the inflammatory theory of chronic venous disease. Extravasation of fluid, macromolecules and red blood cells, secondary to chronic venous hypertension, creates a chronic inflammatory reaction. In response to an injury stimulus, white blood cells enter the interstitial space to remove the offending stimulus. During this process many cytokines and inflammatory mediators are released, leading to an imbalance in tissue remodeling. This imbalance leads to scar tissue formation and the characteristic woody hard dermal fibrosis observed in patients with severe chronic venous insufficiency. Scar tissue development increases the tension in the lower extremity dermis. This loss of skin suppleness and increase in tension is hypothesized to be a cause of venous ulceration. In addition, excess iron deposition has been demonstrated to increase the phenotype of macrophages that prevent wound healing.
Venous hypertension in the pelvis being communicated to the legs:

In patients with pelvic venous outflow obstructive and/or reflux, venous return to the heart occurs through alternate venous pathways. These alternate venous pathways are known as “Escape Veins.” Escape veins re-route veins out of the pelvis to the inferior vena cava. Escape veins often manifest themselves as non-saphenous vein varicosities. Common examples are veins observed in the posterior gluteal folds. These veins arise from the superior gluteal vein. Veins observed in the medial thigh arise from branches of the internal iliac vein. Similarly, vulvar varicosities arise from branches of the internal iliac veins. Finally, ascending lumbar veins are frequently observed on CT scans and venograms, proximal to an iliac vein obstruction.

Conclusion: The venous system of the lower extremities, pelvis and abdomen is inextricably linked through its anatomy physiology and consequently pathology. A complete history and physical examination will guide the physician as to the appropriate imaging studies necessary. All patients require a non-invasive venous ultrasound. Many patients with pelvic venous disease will require either a CT scan, MRI or invasive venogram. After completing a thorough work-up a treatment plan based on the patient’s individual anatomy and physiology will be developed to address their venous pathology.

References for Venous Review Issue 10 Vol. 2

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Our Community Outreach Team Success!

Community Outreach has taken tremendous strides in 2016. Our efforts have allowed us to spread the mission of CVR direct to prospective patients in a plethora of different settings. A new addition to our Community Outreach program are our “Complimentary Physician Visits.” These events are often held after hours in our clinics to give a prospective patient a chance to meet our doctors, raise questions, and be offered a recommendation on next steps. Over the last few months, this model has proven to be a great tool to build with as Community Outreach looks ahead to even more success in 2017.
Center for Vein Restoration & Howard Community College — A New Partnership Has Formed!

In an effort to support our growing practice and the need for vascular technologist with a sound foundation in venous insufficiency testing, CVR has developed a partnership with Howard Community College, Diagnostic Medical Sonography Program. CVR will not only serve as an internship site for their growing vascular program but our collaboration will also provide an avenue for direct access to potential employment opportunities with CVR. In November, CVR will host first year students from HCC DMS program by allowing them to tour our facilities in order to provide them with an early insight into the day to day functions of a Vascular Lab.

Center for Vein Restoration Awarded Venous and Lymphatic Medicine Fellowship Training Program by The American Board of Venous & Lymphatic Medicine (ABVLM)

The Center for Vein Restoration's Venous Fellowship is a 12 month comprehensive program, focused exposure to the entire spectrum of venous disorders. The fellow will rotate in one of three centers in New Jersey and obtain expertise in non-invasive venous imaging, the diagnosis and treatment of superficial and deep venous disorders and skills with the entire spectrum of venous related technologies. Specifically, trainees will gain experience with thermal and non-thermal ablation technologies, ultrasound guided foam sclerotherapy, cosmetic sclerotherapy, diagnostic venography, venous angioplasty and stenting and venous ulcer wound care. Ideal candidates will have graduated from an ACGME accredited residency with preference from one of the following fields: Vascular Surgery, General Surgery, Interventional Radiology, Emergency Medicine, Ob-Gyn, Plastic Surgery, Dermatology, Vascular Medicine and Internal Medicine.

“CVR takes educating the next generation of physicians very seriously and is committed to the highest standards of surgical training,” said Dr. Khanh Nguyen, Chief Medical Officer of the Center for Vein Restoration.

“The cognitive and technological advances in the field of venous disease have expanded exponentially over the past two decades. In order to develop comprehensive knowledge and skills, focused, dedicated training in venous related disorders is needed.” Dr. Pappas continues, “We at the Center for Vein Restoration are pleased that the ABVLM has recognized CVR’s expertise in the field of venous disease. We look forward to training the next generation of venous experts and continuing to deliver comprehensive vein care to the American public.” Dr. Pappas is a past president of the American Venous Forum.
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I would like to take this opportunity to thank Dr. Lakhanpal and the entire staff at the Centers for Vein Restoration for the honor of being the new Editor of the CVR Newsletter.

The Center for Vein Restoration is the largest provider of vein care in the United States. Our physicians and staff provide state of the art venous care to patients suffering from chronic venous disorders and hold themselves to the highest moral, ethical and academic standards. Over the next several months, the newsletter will discuss current technologies and their clinical applications. We will also focus on technologies on the horizon and how they differ to current practices. We will discuss our research activities and how these efforts impact clinical care. We will continue our efforts to integrate ourselves into our communities and become an integral part of your local healthcare network. This is an exciting time for CVR.

I am grateful for the opportunity to share our accomplishments, discuss venous clinical care, educate our community and continue our efforts at improving our patients’ quality of life.

Yours in good health,
Peter Pappas, MD
Associate Editor