

ROUNDTABLE DISCUSSION

Making Sense of Chaos: Formalizing an Approach to Female Pelvic Venous Disorder and Setting a Research Agenda

An update from the International Pelvic Venous Disorders in Women Work Group.

With Kathleen Gibson, MD; Neil Khilnani, MD, FSIR, FAVLS; and Mark H. Meissner, MD



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In October 2017, a Society of Interventional Radiology Foundation (SIRF) research consensus panel identified several tools that are necessary to develop in order to execute high-quality clinical studies to strengthen the evidence base related to treatment of pelvic venous disorders (PeVDs).¹ Since that time, many of the panelists have been working to accomplish these recommendations. We are joined by three members of the International PeVD in Women Work Group, Drs. Kathleen Gibson, Neil Khilnani, and Mark Meissner, to discuss the group's progress.

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Dr. Khilnani, can you tell us about the PeVD work group?

Dr. Khilnani: The work group is composed of physicians and researchers from multiple disciplines interested in advancing the evidence base related to PeVD. It developed as an extension of the SIRF consensus panel and includes physicians from gynecology, interventional radiology, and vascular surgery, representing many of their larger specialty societies. Also contributing to our work are scientists in patient-centered outcomes research and study methodology.

The most recent accomplishment of our work group has been the development of an instrument called SVP (symptoms, varices, pathophysiology), which can precisely classify all clinical, anatomic, and pathophysiologic variations of PeVD.^{2,3}

Dr. Gibson, how would you explain the SVP tool? Can you share some examples of how it works?

Dr. Gibson: Much like the CEAP classification (clinical, etiology, anatomy, pathophysiology), the SVP instrument was designed as a discriminative tool to place patients in homogeneous groups based on their symptoms, the location of their varices, and their pathophysiology. It is not meant to be a tool that measures disease severity or be responsive to change with treatment. It will allow us to speak a “common language” in clinical practice and research when discussing or writing about patients with PeVD. There are three domains. “S” describes the location of symptoms in different anatomic zones: the left renal venous reservoir (S1, flank pain/hematuria), pelvis (S2, chronic pelvic pain [CPP]), genital pain (S3a, vulvar or scrotal), pain in the extrapelvic pelvic-origin escape point–derived varicose veins of the perineum and upper thighs (S3b), and venous claudication (S3c). “V” refers to location of varices: V1 (left renal hilum), V2 (pelvic venous plexus), V3a (vulva, scrotum), and V3b (extrapelvic pelvic-origin lower extremity veins varicose veins). The “P” refers to pathophysiology and has three subdomains: anatomy (A), hemodynamics (H), and etiology (E). Anatomy refers to the vein(s) involved using easy-to-remember abbreviations. Hemodynamics are designated as either reflux (R) or obstruction (O), and etiology is defined as nonthrombotic (NT), thrombotic (T), or congenital (C).

To give examples of how the instrument works, let’s classify three different patients with CPP. The first patient is a woman in her early 40s. She is a P3G3 with symptoms of pelvic aching, heaviness, and dyspareunia; nonpainful vulvar varices on exam; and imaging

that shows left ovarian vein reflux, left internal iliac vein reflux, and pelvic and left vulvar varicose veins. Her SVP classification would be S₂ (symptoms in the pelvis), V_{2,3a} (varices in the pelvis and vulva), and P_{LOV,R,NT;LIIV,R,NT;LPELV,R,NT} (left ovarian vein reflux, nonthrombotic; left internal iliac vein reflux, nonthrombotic; and pelvic escape point vein, reflux, nonthrombotic). The second patient is a woman in her mid-30s with CPP and left leg bursting pain with exercise. On duplex ultrasound, she has nonthrombotic extrinsic compression of her left common iliac vein, reflux in her left internal iliac vein, and large parauterine veins. Her SVP classification would be S_{2,3c} (symptoms in the pelvis and venous claudication), V₂ (varices in the pelvis), and P_{LCIV,O,NT;LIIV,R,NT} (left common iliac vein, obstruction, nonthrombotic; left internal iliac vein, reflux, nonthrombotic). The final patient is a woman in her late 20s, who is nulliparous with CPP and has no visible lower extremity varicose veins, with left renal vein compression, left ovarian vein reflux, and dilated pelvic veins. Her SVP classification would be S₂ (symptoms in the pelvis), V₂ (varices in the pelvis), and P_{LRV,O,NT;LOV,R,NT} (left renal vein, obstruction, nonthrombotic; left ovarian vein, reflux, nonthrombotic). Although this seems complex, this classification scheme becomes straightforward with practice.

Dr. Meissner, as leader of the SVP project, why is SVP so important to advancing research on PeVD in women? Where can our readers learn more about this instrument and how to use it?

Dr. Meissner: Much of the previous research regarding PeVDs used historical nomenclature such as “pelvic congestion,” “nutcracker syndrome,” and “May-Thurner syndrome” to classify patients. Unfortunately, both the pathophysiology and symptoms associated with these syndromes overlap to a substantial degree, making classification of patients in clinical communication and research studies very imprecise. For example, ovarian vein reflux and left common iliac vein compression can both cause CPP in women. The SVP instrument allows these two different clinical scenarios to be precisely characterized. Identifying homogeneous patient populations is important to developing the outcomes instruments and clinical trials necessary to advance the field. For example, women with pelvic pain secondary to left common iliac vein compression should not be included in trials evaluating the efficacy of ovarian vein embolization.

It is recognized that like pelvic venous disease, the SVP classification is complex. However, when the structure of the classification is understood, it becomes

much more intuitive and should become the standard for clinical communication, research, and publication. Concurrent publication in the *Journal of Vascular Surgery: Venous and Lymphatic Disorders and Phlebology* will ensure the manuscript is widely available,^{2,3} and translation into several languages is also planned. The American Vein & Lymphatic Society has developed several aids to assist in adoption of the classification, including smartphone apps (available at www.myavls.org/svp-classification.html) and a soon-to-be-released educational workbook.⁴

Dr. Khilnani, can you comment on other projects the work group is addressing?

Dr. Khilnani: Nearly all the published evidence related to PeVD in women have been single-arm retrospective case series. In addition, most of the studies related to CPP from a venous source have relied on pain scores as the primary outcome measure. However, we know that the impacts of CPP affect other domains of health, such as social, professional, relationship, and behavioral function. We are currently applying for grant funding to perform qualitative, patient interview research to develop a quality-of-life instrument that can be used as a primary outcome measure in comparative drug and device trials in women with CPP of venous origin. Scientists from Evidera, an outcomes research organization that supports patient-centered research by academia and industry, are collaborating with us to develop the tool. One of the members of our work group from Evidera was involved in developing and validating the Uterine Fibroid Symptom and Quality of Life instrument, the most-used tool for drug and device trials related to uterine fibroids.⁵ We plan to recruit women with CPP and a likely venous cause from CPP gynecologic practices at several academic- and nonacademic-affiliated sites in North America to develop our tool. Then, we'll assess

the differences in how women with CPP of a nonvenous cause are impacted by asking them to comment on the items in the tool we developed in separate qualitative interviews. Finally, we plan to perform preliminary validation of the tool's responsiveness to change in patients before and after endovascular therapy.

Another member of the work group, Dr. Ronald Winokur from Sidney Kimmel Medical College at Thomas Jefferson University Hospital, is in the final stages of preparing a grant application to support a randomized controlled trial to explore the value of ovarian vein embolization. The study will recruit women with ovarian vein reflux and CPP felt to be of a venous origin ($S_2V_2P_{BGV,R,NT}$, $S_2V_2P_{RGV,R,NT}$, or $S_2V_2P_{LGV,R,NT}$). Patients found with clinically significant left renal vein and left common iliac vein compression will not be included. Women will be randomized after venogram/intravascular ultrasound confirmation of their classification to either bilateral ovarian vein and periuterine/ovarian venous plexus embolization or conservative care. The patients will be blinded as to what group they are assigned to. A variety of outcome measures will be used at fixed intervals before and after the procedures, including the novel quality-of-life tool we are currently developing, as well as other generic and women's health-related tools. The study will extend for 6 months before unblinding patients, allowing them to pursue additional therapy as needed. ■

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