A Closer Look at Venous Disease Stratification

Will continued reinvention result in a better wheel?

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Outcome reporting and disease stratification have become the venous therapy equivalent of the sun-dried tomato's presence in recent culinary trends. Assessment methods abound, and each new month brings journal articles discussing the merits of outcome assessment or touting a new method of data collection and analysis. Although some of these instruments will continue to be beneficial in a results comparison, many seem to have been implemented to make a specific statement about the offerings at hand.

Our group alone has been asked to author no fewer than six articles and chapters in the past 2 years on the topic of choosing and applying assessment instruments. Excessive? Possibly. Can we be accused of attempting to reinvent the wheel of data mining? Probably. Is the wheel in dire need of proper reinvention? Definitely. For as the sun-dried tomato gave way to goat cheese and organic fair-trade coffee, the days of assessment surveys delivered via shotgun are being replaced with achingly precise and specific instruments devised to measure fewer variables in greater detail.

VALID, RELIABLE, AND PRACTICAL ASSESSMENTS

Many areas of medicine have been transformed by new approaches and minimally invasive techniques, and venous disease is certainly counted among them. These advances bring new information and opportunities for compilation, analysis, and data reporting, which inevitably requires validation. In an ideal world, the outcome of a study would be reported via the results of analysis of the assessment instrument that best fits the study objective and the type of data collected. However, in the current climate of outcome assessment, practicality is in danger of being lost in the data glut that can result from using multiple survey types and instruments in an attempt to maximize the reportable results from each study.

Not all tests for validity will necessarily lead to validation, and in a time of increased clinical, scientific, and third-party focus on meaningful outcome reporting, the quality of the information presented must match the fervor with which it is collected. In the United States, scientists and clinicians have adapted to a cautious regulatory environment that requires specificity of rationale, documentation of process, and reproducibility of results. Broad use of outcome assessment should support the regulatory process, but only if the instruments used and the parameters studied are valid, reliable, and practical. Reliability ensures consistency in survey responses; patients with similar conditions should respond similarly. Validity relates to consistent measurement of each parameter by the survey questions.[1] Practicality is the relationship between the study at hand and the information that can reasonably be collected to provide the necessary data.[2]

The less malleable an instrument is to selective, cut-and-paste–type data analysis, the more reproducible the results are and the more meaningful the conclusions will be. Instruments that are less open to interpretation, whether patient- or physician-generated, should provide relevant data that will go a long way toward constructing reliable outcome assessments.

TABLE 1. RELIABILITY, VALIDITY, AND PRACTICALITY ATTRIBUTES OF CEAP, VCSS, AND VEINES

Instrument	Reliability	Validity	Practicality
CEAP	Clinical category refined in 2003 to address interobserver variation[14]	Revision is an ongoing process with all changes supported by evidence-based research[6]	Objective, four categories to generate scores, recent revision to improve practicality, especially at lower disease levels[6,14]
VCSS	2010 revision addressed reported ambiguous language[10]	Original instrument validated in studies,[4,15] revision designed to retain validity of original[10]	Good correlation with CEAP,[15] designed to include elements that change over time,[15] revision designed to simplify application to data[10]
VEINES	Tested in huge patient population in four languages and statistically verified[2,12]	Validated in four languages in large patient population using standard psychometric testing[12]	Patient-reported survey available in four languages consists of 35 questions,[2,12] not scored by summary but by response scales, computer scoring program available[12]

TYPES OF ASSESSMENT INSTRUMENTS

What is actually being measured in outcome assessment? In the case of venous disease, the focus has been on patient quality of life and the parameters that affect it. Physician-generated instruments, such as CEAP (clinical, etiologic, anatomic, pathophysiologic) and the Venous Clinical Severity Score (VCSS), can be objective—identification and stratification of the condition and its direct physical manifestation for the patient in the case of CEAP or subjectively objective in the case of the VCSS—and expository in nature, but with more flexibility to consider patient perceptions of the physical manifestations. When considering patient-reported instruments, a survey such as the Venous Insufficiency Epidemiological and Economic Study (VEINES) instrument splits its symptom and quality-of-life questionnaires into two discrete categories, allowing specific reporting of the individual elements of venous disease, as well as the overall impact of their existence (Table 1).

CEAP

The CEAP classification is a physician-generated descriptive diagnostic reporting platform for use in patients with chronic venous disease.[3] The C clinical component is scored from 0 to 6 to indicate increasing disease severity, ranging from none to active ulcers. The E etiologic component defines the venous disease as congenital, primary, or secondary. The A anatomic classification identifies the veins involved as superficial, deep, or perforating. The P pathophysiologic component defines reflux and outflow obstruction in the superficial, communicating, or deep systems. The main issue in using CEAP as a standalone assessment instrument is its responsiveness to changes over time. The measurements are relatively static, especially in disease C4 and upward, with little flexibility in tracking changes in response to therapy.[4]

To address this insensitivity and to encourage its use as a clinical assessment instrument, CEAP was revised in 2004. Several categories were refined and expanded,[5] including a division of the C4 class into a and b categories that are predictive of ulcer risk based on observed skin changes and revision of the E, A, and P classifications with the descriptor n to indicate a lack of venous abnormality. To make CEAP easier to use in a clinical setting, a basic system was introduced that used the highest-level descriptive element in clinical classification. An advanced CEAP that includes all parameters is available for research and reporting (Table 2).[6]

VCSS

The VCSS is a measurement tool that provides additional information about disease severity and longitudinal changes in patient conditions during treatment.[7] It was designed to supplement CEAP and provide a method for serial assessment.[8] The VCSS includes nine common manifestations of venous disease, scored on a severity scale from 0 to 3. The VCSS categories are presented elementally to add emphasis to the most severe sequelae of venous disease that are likely to show the

TABLE 2. SUMMARY OF THE REVISIONS TO CEAP[6]

Clinical classification
- C0: no visible or palpable signs of venous disease
- C1: telangiectasies or reticular veins
- C2: varicose veins
- C3: edema
- C4a: pigmentation or eczema
- C4b: lipodermatosclerosis or atrophie blanche
- C5: healed venous ulcer
- C6: active venous ulcer
- S: symptomatic, including ache, pain, tightness, skin irritation, heaviness, and muscle cramps, and other complaints attributable to venous dysfunction
- A: asymptomatic

Etiologic classification
- Ec: congenital
- Ep: primary
- Es: secondary (postthrombotic)
- En: no venous cause identified

Anatomic classification
- As: superficial veins
- Ap: perforator veins
- Ad: deep veins
- An: no venous location identified

Pathophysiologic classification

Basic CEAP
- Pr: reflux
- Po: obstruction
- Pr,o: reflux and obstruction
- Pn: no venous pathophysiology identifiable

Advanced CEAP (same as basic CEAP, with the addition that any of the 18 named venous segments can be used as locators for venous pathology)

Superficial veins
- Telangiectasies or reticular veins
- Great saphenous vein above knee
- Great saphenous vein below knee
- Small saphenous vein
- Nonsaphenous veins

Deep veins
- Inferior vena cava
- Common iliac vein
- Internal iliac vein
- External iliac vein
- Pelvic: gonadal, broad ligament veins, other
- Common femoral vein
- Deep femoral vein
- Femoral vein
- Popliteal vein
- Crural: anterior tibial, posterior tibial, peroneal veins (all paired)
- Muscular: gastrocnemial, soleal veins, other

Perforating veins
- Thigh
- Calf

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greatest change in response to therapy. These include skin changes, inflammation, induration, and ulcers.[9]

The VCSS is easy to administer and score, rendering it useful as a standalone scoring instrument in the clinical setting for longitudinal surveillance after treatment. The individual components of the VCSS add flexibility to CEAP to adjust for changing physician and patient perceptions during treatment.[8] The VCSS is close to being a hybrid of physician- and patient-generated surveys; it is administered by a physician, but subjective components such as pain are scored based on patient responses.

The main criticisms of the VCSS involve specificity of the language and terminology, most notably with skin complications at the C3 and C4 levels. In addition, ease of use and relevance to patients in the C1 and C2 categories were frequently discussed.[10] During the past several years, the VCSS has been revised to address these concerns, mainly by the use of language from other patient-reported quality-of-life instruments to expand on the descriptions of complicating factors and to clarify relevant findings for scoring each level of venous disease (Table 3).[10]

VEINES

Patient-reported surveys add another layer of data in assessing the outcomes of treatment for venous disease. These disease-specific surveys can provide a targeted patient perspective to the particular venous sequelae. The VEINES instrument comprises 35 items in two cat-

TABLE 3. REVISED VENOUS CLINICAL SEVERITY SCORE[10]				
Pain (or other discomfort [ie, aching, heaviness, fatigue, soreness, burning], presumes venous origin)	None: 0	Mild: 1 Occasional pain or other discomfort (ie, not restricting regular daily activity)	Moderate: 2 Daily pain or other discomfort (ie, interfering with but not preventing regular daily activities)	Severe: 3 Daily pain or discomfort (ie, limits most regular daily activities)
Varicose veins ("varicose" veins must be ≥ 3 mm in diameter to qualify)	None: 0	Mild: 1 Few/scattered (ie, isolated branch varicosities or clusters), also includes corona phlebectatica (ankle flare)	Moderate: 2 Confined to calf or thigh	Severe: 3 Involves calf and thigh
Venous edema (presumes venous origin)	None: 0	Mild: 1 Limited to foot and ankle area	Moderate: 2 Extends above ankle but below knee	Severe: 3 Extends to knee and above
Skin pigmentation (presumes venous origin, does not include focal pigmentation over varicose veins or pigmentation due to other chronic diseases [ie, vasculitis purpura])	None: 0 None or focal	Mild: 1 Limited to perimalleolar area	Moderate: 2 Diffuse over lower third of calf	Severe: 3 Wider distribution above lower third of calf
Inflammation (more than just recent pigmentation [ie, erythema, cellulitis, venous eczema, dermatitis])	None: 0	Mild: 1 Limited to perimalleolar area	Moderate: 2 Diffuse over lower third of calf	Severe: 3 Wider distribution above lower third of calf
Induration (presumes venous origin of secondary skin and subcutaneous changes [ie, chronic edema with fibrosis, hypodermitis], includes white atrophy and lipodermatosclerosis)	None: 0	Mild: 1 Limited to perimalleolar area	Moderate: 2 Diffuse over lower third of calf	Severe: 3 Wider distribution above lower third of calf
Active ulcer number	0	1	2	≥ 3
Active ulcer duration (longest active)	N/A	< 3 mo	> 3 mo but < 1 y	Not healed for > 1 y
Active ulcer size (largest active)	N/A	Diameter < 2 cm	Diameter 2–6 cm	Diameter > 6 cm
Use of compression therapy	0 Not used	1 Intermittent use of stockings	2 Wears stockings most days	3 Full compliance with stockings

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egories. The VEINES-QOL (quality-of-life) questionnaire has 25 questions that assess disease impact on quality of life, whereas the VEINES-Sym (symptom) questionnaire has 10 items that specifically measure clinical symptoms. This division of summary scores into discrete categories increases the applicability of the VEINES instrument to clinical outcome and quality-of-life studies.[11]

In a study on treatment outcomes and the patient perspective of quality of life, Lamping et al[12] administered the VEINES survey along with routine clinical assessment during 12 months after patients' vein treatment. Patients underwent various treatments for several types and degrees of venous disease, with the VEINES questionnaire being the only common element in the evaluation. VEINES proved valid throughout the investigation, regardless of the clinical manifestation or degree of disease.[12] Padberg commented on this article, voicing concern about VEINES, specifically whether the VEINES scores could be accurately scaled and whether their presentation actually indicated clinical significance and longitudinal change.[13]

DISCUSSION

This limited discussion of venous disease stratification methods is intended to stimulate specific and general inquiry that these three instruments are valid within themselves and are practical for various study types. Generally, the larger issue regarding the use of these types of assessments, including the decision to use them and then the choice of instrument, is the bigger concern. The future of venous disease stratification does not specifically hinge on whether the right revisions were made to CEAP and VCSS at the right time. The future of venous disease stratification may hinge on whether researchers and clinicians can effectively pair their desired application with the best-fit instrument, not whether they can manipulate an instrument to give them their desired results.

If the revisions to CEAP and VCSS have been made to improve the ability to sort relevant data, then we will see them used with increasing frequency and honest, valid results. If the revisions were done to appeal to those who have not seen the need to invest the time and energy to track outcomes, then we may have spent a lot of time simply polishing something to put back on the shelf. What have we lost if these instruments exist, but no one uses them in a way that generates meaningful, valid, practical data? The answer to this larger question may lie in the future of assessment methods in clinical trials, especially trials performed for the National Institutes of Health or the US Food and Drug Administration in America. Data from these assessments used in large-scale clinical trials may serve to validate the validity of the instrument, so to speak, and may provide a framework for the best application of the best instrument in a given study or clinical application.

The time to examine outcomes, whether for research, clinical standards, or in a protocol-driven third-party payer scenario, has come. The evolution of available instruments and their corresponding appropriate applications continues. ■

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