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Small Contributions: Stepping Stones in Search of Knowledge

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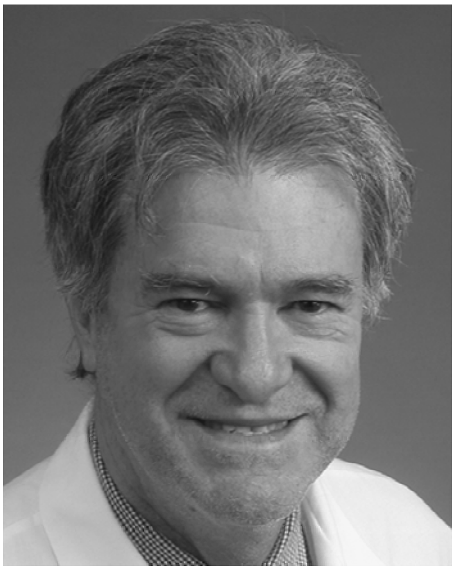

Dr. Sergio Salles-Cunha is the 2004 Pioneer Award Winner for the Society for Vascular Ultrasound and presented the David Phillips Memorial Lecture at the 27th Society for Vascular Ultrasound Annual Conference, Anaheim, California, June 5, 2004

Introduction

A major contribution such as Steve Talbot's development of the duplex ultrasound examination for deep venous thrombosis is not a prerequisite to be recognized as a pioneer in the field.[1] This is a story of many small contributions in search of a better understanding of the vascular system in health and disease. A work that extended for 4 decades is only possible with the collaboration of many individuals. The David Phillips Memorial Lecture and this manuscript focus on teamwork. David Phillips worked with vascular laboratory, vascular surgery, vascular medicine, biomedical engineering, physiology, biophysics, and medical industry personnel. He was a member of a team that received half of the Pioneer Awards. Several Society for Vascular Ultrasound (SVU) members, led by Jean Primozich, contributed effectively as David Phillips' teammates. We all benefited from the heritage of Dr. D. Eugene Strandness Jr. Their influence inspired this piece in recognition of many co-workers. The following is a summary of experiences and small contributions, selected as curious information, controversial topics, or simple provocations. They will challenge the reader into an insightful analysis of the human vasculature from the perspective of noninvasive examination.

Educational Background

American professors greatly influenced the creation of the Instituto Tecnologico de Aeronautica in 1947. For the first time in Brazilian history, a semester-based curriculum replaced the usual 1-year structure of education. Quick changes in course structures were possible to take advantage of visiting professors and to adapt to the fast evolution occurring in the fields of aeronautics, mechanics, and electronics.

Bioengineering became an option under the guidance of Jose Carlos Borges and his contacts with a cardiac research team led by Dr. Adib Jatene. This famous cardiac surgeon has operations named after him, was president of the International Cardiovascular Society, and served as minister of health. At the time, in 1969, this team was developing heart valves. Majoring in electronics, however, my graduation project was to build an electrocardioscope. Matching transistors to balance noise out and to clean the biological signal was time consuming and turned me away from electronics and into biomathematics.

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Systems engineering, an endeavor in applied mathematics, became the focus of my studies at the largest postgraduate program of engineering in Latin America, at the Federal University of Rio de Janeiro. If a plan for a master's thesis had succeeded, this manuscript would not have been conceived. The proposal was to analyze electrocardiograms automatically using a new, exciting, mathematical algorithm called fast Fourier transform (FFT). In 1970, FFT was only 3 years old, as a mathematical theorem in search of practical applications. I found no adviser, no examiners, and no help for such a project. As a consequence, I got well acquainted with Ipanema beach during the 2 months preceding a trip to study in the United States.

Anthony Sances Jr., PhD, a Marquette University professor, created one of the pioneering programs in biomedical engineering. His greatest support came from Sanford J. Larson, MD, presently professor emeritus of neurosurgery at the Medical College of Wisconsin. A fundamental change from theory to practice was forced upon me. The project proposed initially to the U.S. Agency for International Development, my sponsors, was on mathematical modeling of brain behavior. Instead, I learned practical, experimental, biomedical engineering in a program famous for the development of evoked potentials, spinal and cerebellar stimulation, and intracranial pressure monitoring. My master's thesis was on noninvasive measurement of transcranial bioelectrical impedance.

A requisite of this scholarship was the return to the native country for at least 2 years. By this time, in 1972, the Federal University of Rio de Janeiro had started a program in biomedical engineering. Ignoring strong political battles at the university, I advised four of the first five master's theses of this new, young, pioneering program. One, a continuation of the transcranial impedance project, demonstrated that comatose patients with abnormally high or low transcranial impedance were at high risk due to intra- or extracellular intracranial edema. Another, more closely related to the work of the SVU membership, demonstrated that high correlation between the electroencephalogram and electromyogram upon voice command to move the hand had favorable prognosis in stroke recovery.

Exposure to the vascular laboratory occurred in 1974, a product of the joint efforts of Dr. Sances and Victor Bernhard, MD, chief of vascular surgery at the Medical College of Wisconsin. As a new adventure in a new field, my PhD dissertation was a potpourri of noninvasive techniques to evaluate the vascular system.[2] Activities varied from venous impedance plethysmography to periorbital Doppler, and included electromagnetic and nuclear magnetic resonance (NMR) blood flowmetry. Joseph Battocletti, PhD, and Richard Halbach, PhD, were instrumental in the development of NMR flowmetry.[3,4] This team worked with one of the first superconducting magnets ever built, before NMR images were ever published. Again, fate dictated a stronger personal interest in physiology and flow rather than anatomy and imaging.

Jonathan Towne, MD, joined the vascular surgery service in the 1970s. He was the primary author of two papers deserving citation to exemplify two extremes. One, a technique that has been abandoned;[5] another, an unexpected observation that deserves additional investigation.[6] The work with periorbital Doppler suggested that a technique with an accuracy not much better than 60% had a place in screening patients at risk of stroke. The other investigation demonstrated progression of atherosclerosis in peripheral arteries with increased blood flow. To this date, the deleterious effects of continuous flow through an artery have not received appropriate attention. The following paragraphs describe a few challenging ideas that may be right, wrong, and/or irrelevant. The objective is to create a mentality of frequent and continuous analysis of vascular laboratory activities.

Vascular Evaluation

Topics on peripheral arterial, carotid, and venous evaluation were selected based on a present perception that differentiates protocols for (1) screening, (2) definitive diagnosis, (3) preoperative mapping, (4) intraoperative imaging, and (5) patient follow-up. Venous evaluation focuses primarily on chronic valvular insufficiency in general and mapping/treatment of saphenous veins in particular. The latter is probably the fastest growing vascular field in the United States today.

Peripheral Arterial Evaluation

This section describes basic protocols, emphasizes the importance of a few technical details, and discusses philosophies linked to implementation of innovative arterial mapping of the lower extremities.

Screening

Ankle pressure. A simple means to screen for blockage of the arteries in the lower extremity is to measure ankle and brachial systolic pressures and calculate the ankle/brachial systolic pressure ratio or ankle/brachial index (ABI). An ABI greater than 1 is normal at rest, and an ABI less than 0.5 suggests severe arterial obstruction. Concomitant analysis of the Doppler waveform obtained at the distal tibial arteries complements the ABI. Triphasic waveforms are normal, and monophasic waveforms suggest severe obstruction proximal to the site of Doppler observation. Some prefer to use pulse volume recording (PVR), a technique that is less dependent than Doppler on the ability and experience of the operator.

Toe pressures. Toe pressures may be used to screen disease of the leg and foot arteries. Toe systolic pressure is often detected with a photoplethysmograph that senses toe pulsations. A toe/brachial index (TBI) greater than 0.8 is normal, and a TBI less than 0.4 suggests severe arterial obstruction.

Besides the evaluation of foot arteries, TBI measurement may be needed in the evaluation of patients with unreliable ankle pressure measurements. Papers by Katie Vollrath, Terry Sondgeroth, and Dennis Vincent described frequently forgotten advantages and/or inadequacies of protocols for toe pressure measurements:[7–9]

(1) Pressures must be measured at heart level. Measuring toe pressures with the foot sticking up results in lower pressures affecting significantly the calculation of a TBI, particularly in the patient with severe obstructions.
(2) The foot must be rotated to place the toe at heart level.
(3) Foot and toe temperatures affect toe pressures. Measuring toe pressures in an air-conditioned room, optimized for a completely dressed technologist and to avoid instrument overheating, but not for a quasi-naked patient, results in falsely decreased toe pressures. Room and patient should be warm enough to cause toe temperatures to be as close as possible to 28°C. Only under reproducible, controlled temperatures can toe pressures be compared adequately.
(4) Toe pressures should be measured on inflation. Actually, Doppler pressures should also be measured on inflation (and deflation too, for confirmation).
(5) The toe/ankle systolic pressure index (TAI) may be used for evaluation of the arterial segments in the foot.
(6) TBI may replace ABI in the presence of arterial incompressibility.
(7) A condition of partial arterial incompressibility precedes total or complete incompressibility. ABI can be abnormally low and yet be falsely elevated. TBI and/or tibial waveforms may alert about abnormal but falsely elevated ABIs.
(8) Partial or complete arterial incompressibility is more common in diabetic than nondiabetic patients. In particular, the long-term, insulin-treated diabetic is prone to have partial or complete incompressibility of the leg arteries.
(9) Variable ankle pressures along time are another characteristic of partial arterial incompressibility. For example, a patient had 9 ankle pressure measurements in a period of 1 year. Chronologically, the posterior tibial pressures were 120, 135, 70, 145, 85, 115, 60, 120, and 145 mmHg, respectively. Probably, the closest to reality was 60 mmHg. All pressures had to be considered falsely elevated. Toe pressures and/or tibial waveforms may elucidate this quandary.

Oscillometry. The oscillometric technique allows for noninvasive, air plethysmographic measurements of systolic, mean, and diastolic pressures based on alterations of pulse amplitudes with externally applied pressures. For example, maximum amplitude is obtained when mean pressure is applied to the cuff wrapped around the measurement location. Although the technique was primarily designed to monitor arm pressure, ankle, toe, and penile pressures may be successfully measured by oscillometry.[10] As a consequence, ABIs can be measured for systolic, mean and/or diastolic pressures. Systolic pressure is decreased first in the presence of disease. Therefore, systolic ABI should be lower than mean or diastolic ABI. Systolic ABI may fall to as low as 0.7 before significant drops in mean or diastolic ABIs are noted.

An advantage of oscillometry is that mean and diastolic pressures may be measured in incompressible vessels. Partial arterial incompressibility is suspected if the mean ABI decreases below systolic ABI.

Pressure/flow rate relation. Traditionally, one expects leg blood flow rate to remain constant at rest until a significant stenosis is present. It is also expected that claudicants have normal leg blood flow rate at rest. Only during claudication is blood flow rate inferior to the demands of exercise. Also, it is often stated that ischemia causes a decrease in the peripheral resistance. Our experience with pressure and blood flow rates in thousands of extremities revealed alternate interpretations for the pathophysiology of the peripheral arterial circulation.

Metriflow, Inc., built a few NMR noninvasive flowmeters based on the research performed at the Medical College of Wisconsin. This flowmeter measured the amount of pulsatile blood flow rate through a cross section of the limb. We collected data from a cross section just below the knee, thus representing flow to the calf and foot. Once we related the average pulsatile blood flow rate for intervals of ABI, a straight line was obtained with an amazing, almost perfect, linear correlation approaching 1. Pulsatile flow rates across the upper calf averaged about 60 ml/min for an ABI equal to 1 and 30 ml/min for an ABI equal to 0.5. Although 60 ml/min seems low, it is a value similar to flow rates measured with ultrasound through popliteal bypass grafts implanted in the elderly. In-depth analysis of the literature revealed that pulsatile flow represents primarily the large arteries, whereas continuous, diastolic flow represents primarily the microcirculation and skin flow. The concept of peripheral resistance can be expanded to include pulsatile impedance in addition to resistance relating mean pressure and flow. Pulsatile impedance, or pulsatile resistance, relates pulsatile pressure to pulsatile flow in a complex way. Our work with Gerald Harris demonstrated increased pulsatile impedance in the amputee and decreased pulsatile impedance in the child.[11] Work by Paulo Moraes, MD, an international fellow at the Jobst Vascular Center (JVC), revealed that continuous, diastolic flow varied significantly with room and toe temperature, whereas pulsatile flow and pulsatile dynamics varied little with temperature. In worst-case conditions, pulsatile flow is the only flow feeding the tissue. One may also raise the hypothesis that continuous, diastolic flow rarely feeds the tissue, bypassing tissue via the arteriovenous collateral shunts. Two major reasons to study pulsatile flow rate and pulsatile dynamics are (1) pulsatile dynamics represent the large arteries and their obstructions; these are the arteries repairable by vascular surgeons; and (2) pulsatile flow is the "feeding" flow, at least in worst-case conditions. Based on these considerations, the following analysis evolved.

A linear relation between ABI and pulsatile flow suggests that the large arteries like to maintain a constant resistance. Assuming that this resistance is largely determined by arterial diameters, one extrapolates that large arteries like to maintain constant diameters. This pulsatile impedance is apparently constant as the ABI decreases as a consequence of arterial obstructions. As the distal pressures decrease, the pulsatile flow through the leg also decreases. A corollary of these observations is that claudicants may have normal blood flow at rest if they have normal ABIs. Claudicants with ABIs approaching the critical ischemia level do have decreased blood flow rate at rest.[12]

Another corollary is that ischemia causes the arteries to be vasodilatable but not necessarily vasodilated. Pressure is needed to dilate the arteries. As the pressure falls distal to obstructions, the arterial diameters tend to decrease, and the resistance to increase. In the limit, an occluded artery has infinite resistance to passage of flow. The biochemical reaction, however, makes the arteries vasodilatable. Despite the decreased pressures, the diameters may be the same as normal; the resistance to flow may remain unchanged. The reactive hyperemia response after revascularization is then explained by the sudden increase in pressure. A dilatable vasculature then becomes dilated until a new neuro-biochemical balance is reestablished.

Although the average flow rate passing through the upper calf and the ABIs showed great correlation, many patients do not conform to the expected averages. About 20% of the patients have significantly higher flow and another 20% of the patients have significantly lower flow than expected for their ABIs. This wide variability in flow rates for the same ABI justifies measuring both pressure and flow to determine the hemodynamics of the lower extremity. We demonstrated that balloon dilatation of iliac arteries may increase flow rate significantly without necessarily affecting the ankle pressures.[13]

This comparison between flow rates and ABIs raised another issue. What happens to flow if the posterior and anterior tibial pressures are different? Traditionally, the higher of the two pressures is used for interpretation. Flow rates through the upper calf, however, matched the lower rather than the higher pressure in a majority of cases.[14] These data makes sense because, due to collaterals from the peroneal artery, at least two arteries must be diseased for the posterior or anterior tibial pressures to be significantly decreased. A decreased pressure in one of the tibial arteries may represent that flow is affected not by ½ but by a factor of ⅔. In practice, therefore, the importance of the lower pressure is significant. Both tibial pressures must be considered, not only the highest one, when analyzing the arterial circulation of the leg.

Another question was then investigated: should we also measure peroneal artery pressure? Lucy Mally's research indicated that the interpretation of distal pressures would be affected significantly in about 5% of the patients if the peroneal pressures were considered. For example, lower than expected peroneal pressures suggest more infrapopliteal disease, whereas higher than expected peroneal pressures may be due to lack of distal collaterals. Most of these cases are unusual, and the vascular laboratory can get away without peroneal pressure measurements. Services that focus on peroneal revascularization, however, benefit from measuring pressures in the three infrapopliteal arteries.

Definitive Diagnosis

The screening protocol includes ankle or toe pressures and analysis of tibial Doppler waveforms or PVRs. Definitive diagnosis has a broader objective besides detection of peripheral arterial occlusive disease. Most likely, the objective is to locate the most significant obstruction, be it aortoiliac, femoropopliteal, and/or infrapopliteal. This knowledge may dictate medical treatment or additional preoperative imaging, either ultrasound mapping, x-ray arteriography, or MR angiography.

Steven Gale et al. demonstrated that segmental flow waveforms obtained at the common femoral, popliteal, and tibial arteries together with ABIs can predict the arteriographic site of most severe stenosis with an accuracy varying from 50% to 85%, depending on the experience of the interpreter. Thigh and upper calf pressures measurements did not alter significantly the interpretation obtained with waveforms and ABI alone.[15] Thigh pressure may add valuable information in a few cases but may add confusion in others. The tendency is then to avoid pain (and suffering) of patients by not performing thigh pressure measurements. The waveform protocol has been expanded to include the mid superficial femoral artery and is now being implemented with duplex ultrasound rather than continuous-wave Doppler. This modification allows for training on arterial mapping. A continuous move from the common femoral to the mid femoral artery and then to the popliteal artery is the precursor of femoropopliteal arterial mapping. For example, instead of only analyzing a monophasic waveform at mid thigh, one may find high velocities at a femoral artery stenosis, just above the site of the monophasic flow detection. One may start paying attention to enlarged femoral artery collaterals just prior to an occlusion in a leg with monophasic popliteal artery waveforms.

Preoperative Mapping

Carlos Engelhorn, a vascular surgeon from Curitiba, Brazil, may have been the catalyst of modern interest in duplex ultrasound arterial mapping. He described 15 revascularizations of the lower extremity following ultrasound arteriography that he performed himself.[16] A couple of institutions in New York started work in this area soon after, and Sidney Hollec/William Schroeder then publicized their experience, already significant at the time. At Maimonides Medical Center, arterial mapping took off with another trained vascular surgeon from Brazil, Fernanda Mazzariol.[17] This group, now led by Natalia Markevich, MD, as the chief vascular sonographer, has provided imaging for close to 1,000 leg revascularizations performed solely based on ultrasound preoperative mapping.

Several implementation protocols were considered. Ultrasound had already been compared with arteriography with mixed results. Later, Engelhorn provided data in his PhD dissertation demonstrating why this approach may be unsuccessful in justifying ultrasound preoperative mapping.[18] Although correlation in the femoropopliteal segment was near perfect, ultrasound failed to demonstrate segments patent by x-ray arteriography in 15% of the infrapopliteal arteries, and x-ray arteriography failed to demonstrate segments that were patent by ultrasound in 30% of the tibioperoneal arteries.

Analysis of virtual decision-making was apparently the next step in this process. Two different approaches were considered. A surgeon would design a revascularization based on ultrasound, another based on x-ray. The virtual decisions would then be compared. This approach also did not work. Why? Engelhorn's data and the paper of Kohler et al. may explain why.[18,19] If the patient has more than one arterial segment open as potential sites for a distal anastomosis, one of these segments may have been imaged by ultrasound but not by arteriography or vice versa, or one surgeon may have preferred one segment while the second surgeon preferred another. Indeed, given the same information about a patient on different occasions, the same surgeon may opt for a different revascularization procedure in close to 30% of the cases! Therefore, distinct anatomic and treatment options make this type of virtual decision-making study quite variable. A second approach was successful at the Maimonides Medical Center to convince Enrico Ascher, MD, to start performing leg revascularizations based on ultrasound mapping. He analyzed Mazzariol's ultrasound-based suggestions of revascularization while looking at the corresponding x-ray arteriogram. He would then accept or reject the proposed revascularization. A few lessons became evident during this procedure. A minimal number of exams, in this case about 15, were necessary as a "learning-curve." This learning period included not only improvements in ultrasound scanning but also learning the surgical preferences of the vascular surgeon in charge of the case. Different focuses are needed if the surgeon prefers the anterior tibial or the peroneal as a target artery. Vein length may be the difference between a proximal superficial femoral to dorsal pedal bypass or a balloon dilatation followed by a popliteal to dorsal pedal bypass, for example. Finally, one must learn how to give up on ultrasound arterial mapping in the difficult or uncooperative patient.

Actual decision-making then becomes the next real step. This process may have several options also: (1) take the patient to the operating room based on ultrasound mapping and then perform a preprocedure x-ray arteriogram, (2) measure inflow pressures before distal revascularization, (3) perform a completion arteriogram, (4) measure inflow pressures after distal revascularization, and/or (5) perform a completion ultrasound arteriogram. Currently, the team at the Maimonides Medical Center prefers preoperative ultrasound mapping, post distal revascularization inflow pressures, and ultrasound completion arteriography. Increased flow after revascularization of the distal limb exacerbates the hemodynamics of iliac stenosis, increasing the sensibility of inflow pressures. Iliac artery dilatation, as a secondary procedure post distal bypasses, has occurred in less than 10% of the cases.

Additional protocol changes occurred to shorten ultrasound scanning time. Protocols are different for claudicators than for patients with critical ischemia. A short protocol may start proximally at the aorta and stop at the site of the proximal anastomosis, before a significant obstruction. Then, the next scanning starts distally at the foot arteries and stops at the site or sites of a distal anastomosis, just after a significant obstruction. The prolonged waist of time caused by scanning occluded or severely diseased arteries is avoided.

Venous mapping. Venous mapping is part of preoperative arterial mapping. The length and quality of vein available may alter the type of revascularization performed. Our original contribution was primarily on imaging of arm veins.[20] Of interest, cephalic veins that are 2 mm in diameter will dilate to become 4 mm bypass grafts once under arterial pressure in the leg.

Bypass Graft Surveillance

Our experience started early on in Burbank as described by Roma Mofford et al. in a paper that made the cover of Bruit.[21] The DAHOS group (Dulawa, Andros, Harris, Oblath, Schneider) performed a wide variety of bypasses and revascularizations, including large series of cephalic and distal bypasses, jump and composite grafts, and some of the earliest balloon dilatations. Many of these bypasses did not conform to the classical Milwaukee criterion of 45 cm/sec as a velocity threshold for graft failure. We then focused on two philosophical teachings of Dennis Bandyk's group.[22] Two distinct findings may be indicative of graft failure: (1) low flow as indicated by low velocity, regardless of the best threshold for that particular type of graft, and (2) significant drop in flow, usually greater than 20–30% from a previous study. As demonstrated by their data, bypasses that were supposed to have velocities above 70 cm/sec were at risk if that velocity fell to below 45 cm/sec.

We also changed the focus from velocity to flow rate.[23,24] One practical reason was that velocity measurement is location dependent, whereas flow rate is exactly the same regardless where it is measured along the graft. Therefore, thanks to the extraordinary work of Robert Scissons, we determined that popliteal, tibial, and paramalleolar bypass grafts with flow rates less than 50, 40, and 30 ml/min should be considered at risk.[24] Furthermore, a decrease of 20–30% in flow rate between studies is also a significant event. Graft surveillance can thus be simplified by having a duplex ultrasound study in the first postoperative month and then by monitoring flow rate. Once a significant change or an unacceptably low flow rate was detected, then another full duplex scanning is indicated. Work by Samuel Bentes, an international fellow at JVC, suggested that low flow rates result from graft defects or inflow or outflow arterial obstructions. Indeed, low flow rates may be caused by poor cardiac performance, and 1-year mortality after detection of a low flow state in a bypass graft can be extremely high.

Decreased flow rates with time of follow-up were detected during graft surveillance, as presented at the annual meeting organized by Montefiore Hospital in New York in 1997. Another unusual finding related to changes in pressure with time. Ankle or toe pressures did not decrease as significantly as flow rates. Indeed, ankle pressures actually increased with time in the subgroup of tibial bypass grafts, most likely due to worsening of partial arterial incompressibility in diabetic patients.

Abdominal Evaluation

A few developments are worth mentioning related to abdominal aortic aneurysms. Andrew Kriegel, also an international fellow at JVC, demonstrated the feasibility of imaging the aorta with an intravascular ultrasound (IVUS) probe placed in the inferior vena cava.[25] In addition, color-flow duplex-doppler IVUS was performed during aortic or renal revascularization experiments in the sheep by using a pediatric transesophageal probe inserted via the jugular vein.[26]

The advantages of following aortic aneurysms based on volume rather than diameter measurements are demanding attention, investigation, and practice. Khalil Dajani related that volume measurement of aortic aneurysms by ultrasound is feasible, with a variability approaching 10%.[27] Volume changes greater than 10% as measured by ultrasound should be considered significant.

Carotid Evaluation

Most carotid studies currently performed are normal or show minimal disease. Noncertified personnel in unaccredited laboratories are performing many of these tests. They may eventually be considered screening tests, and reimbursement may decrease accordingly. In contrast, carotid studies have been performed with such a high quality that arteriography or magnetic resonance angiography (MRA) have become unnecessary. Reimbursement for an ultrasound test that precludes more expensive angiographic tests should increase and become competitive. For an accredited vascular laboratory to be solvent, effective screening protocols should be created to adjust for predicted "screening" payments, and definitive diagnostic testing should be differentiated from preoperative mapping, with distinct, increased reimbursement fees. The Angiolab group from Vitoria, ES, Brazil, already negotiated payment for two distinct pre-endarterectomy exams performed by different examiners. Although these statements are applicable for carotid studies, they are valid even more so for peripheral arterial and venous mapping.

Screening

Extracranial carotid stenosis can be effectively screened by performing transverse and longitudinal imaging scans and by recording blood velocity at the site of maximum stenosis. Minimal documentation should include a transverse image and measurements of peak-systolic and end-diastolic velocities with a longitudinal image at the site of maximum stenosis.

Transverse Imaging

The following statements exemplify the values of transverse carotid imaging:

(1) A transverse image showing a circular lumen of a carotid artery explains why only a single arteriographic projection is needed to estimate the degree of stenosis. Any projection, in any direction, will show the same lumen.
(2) A transverse image showing an elliptical lumen of a carotid artery explains why multiple arteriographic projections are needed to estimate the short axis of the elliptical lumen. In such circumstances, most likely, biplane arteriography will underestimate the degree of stenosis as compared with rotational angiography with multiple projections.
(3) A transverse image showing a crescent moon-shaped lumen of a carotid artery explains why not even multiple arteriographic projections will ever estimate properly the degree of stenosis.
(4) A transverse image explains the direction of an arteriographic projection that overlaps both the internal and external carotid arteries on top of each other.

Definitive Diagnosis

Extracranial carotid stenosis can be effectively diagnosed by performing transverse and longitudinal imaging scans and by recording blood velocities at the proximal and distal common carotid, proximal external carotid, and proximal and distal internal carotid arteries. If a stenosis is noted, then demonstration that maximum velocities were detected while sweeping the entire area of stenosis can be documented by recording velocities proximal to, at, and distal to the stenosis.

Currently, we prefer the following priorities in the interpretation of carotid ultrasound data:

(1) Transverse image measurements based on minimal diameter of a circular lumen or minimal axis of an elliptical lumen. The later is based on the assumption that occlusion may occur following compression of this minimal lumen dimension.
(2) Longitudinal images to confirm transverse image measurements.
(3) Velocity measurements to confirm image measurements.
(4) If the velocity measurements confirm the image

measurements, then we have two sets of correlating measurements enhancing the results of the ultrasound test.

(5) An explanation should be given to explain why the velocity measurements failed to match the imaging determinations. Usually, one of the following reasons is the cause of mismatch:
   (a) very low velocities in the presence of a critical, preocclusive stenosis;
   (b) high velocities in curvatures or kinks, representing a physiological but not an anatomical stricture of the flow channel;
   (c) high velocities as increased collateral flow compensates for contralateral severe obstruction;
   (d) high velocities in young subjects with bruits due to strong cardiac dynamics;
   (e) low velocities in the elderly with poor cardiac dynamics;
   (f) low velocities in long stenosis;
   (g) velocities may be gender dependent, as recently described by Anthony Comerota, MD.[28] Additional investigation is need to determine if such differences predominate in women with small arteries or men with large arteries.

Most carotid studies are not performed in surgical candidates. There are strong reasons to prefer measurements at the locale of stenosis rather than comparison with distal internal carotid diameter as recommended by NASCET/ACAS:

(1) No one in his right mind is going to report a negative stenosis, a common NASCET/ACAS finding in patients with minimal or even mild stenosis.
(2) The NASCET/ACAS criterion underestimates the degree of mild or moderate stenosis treated medically, precluding proper follow-up of plaque development.
(3) Even for severe stenosis, a local 80% stenosis is a very good predictor of a NASCET/ACAS 70% stenosis.[29] So, the NASCET/ACAS criterion has been relegated to be a limited, confirmatory measurement in surgical candidates.

Several recent publications have confirmed Beebe's report on the effectiveness of ultrasound imaging measurements.[29] A local ultrasound imaging stenosis of 80% or greater or of less than 50% predicts a severe stenosis or lack of hemodynamic significant stenosis (<50%) by arteriography with positive and negative predictive values approaching or superior to 95%. Local stenosis in the 70–80% range with high velocities also predicts severe stenosis by arteriography accurately. The variability of results in the 50–70% stenosis range has little to do with the imaging modality and a lot to do with the variable being calculated. Measurement variability is directly related to the calculation of percent diameter reduction. To exemplify this fact, three correct calculations, based on arteriographic resolution of 0.2 mm, are described below for a 60% stenosis:

(1) 3.0 mm obstruction / 5.0 mm lumen = 60% stenosis
(2) 2.8 mm obstruction / 5.2 mm lumen = 54% stenosis
(3) 3.2 mm obstruction / 4.8 mm lumen = 67% stenosis

All these measurements are correct based on potential deviations due to the image resolution. The dilemma for the surgeon is stronger in the 55–65% range than in the 80–90% range. Furthermore, percent stenosis may differ by 5% between systole and diastole, even as much as 30% in some patients that are probably hypovolemic or have large pulsatile arterial changes. These data imply that decision-making is dependent on medical factors beyond imaging measurements much more so in the moderate than in the severe stenosis range.

Preoperative Mapping

If another, more expensive imaging modality is to be avoided, reimbursement should value an ultrasonographic preoperative mapping accordingly. Preoperative carotid protocols identify the beginning and the end of the plaque on the neck skin. Thickening of the common carotid artery is accessed. Patency, diameter, and thickness of the distal internal carotid are determined. As a consequence, a very short, effective skin incision over the skin mark would be enough to eradicate most plaques. Such detailed evaluation is not needed during a definitive diagnostic test, should distinguish among these types of exams, and should be enough for additional reimbursement. Otherwise, economical survival will force the medical community away from insolvent carotid or arterial preoperative mapping exams, toward additional, sophisticated, complex, expensive, well-paid imaging modalities such as x-ray, MR, and CT angiography. The Angiolab service of Vitoria, ES, Brazil, already convinced insurance carriers to pay for a separate, preoperative mapping performed by a second examiner.

Venous Evaluation

Most of this section deals with valvular insufficiency of the saphenous veins. Only a few comments are made about deep venous thrombosis and deep venous insufficiency of the lower extremities.

DEEP VENOUS THROMBOSIS

Screening of symptomatic or high-risk patients is not recommended. The noninvasive ultrasound examination, however, has opened the doors for testing of many asymptomatic patients at low risk for deep venous thrombosis.

Screening

A femoropopliteal evaluation should be considered a screening procedure. It could be enough for definitive diagnosis, however, if the test is positive and continuation of the exam is contraindicated or unnecessary. In addition, this limited procedure could be considered screening for patients hospitalized with other serious conditions and that would be treated only in the event of thrombosis beyond the calf veins.

Definitive Diagnosis

The protocol for definitive diagnosis includes evaluation of proximal common femoral and iliac veins, femoropopliteal veins, calf veins, and superficial veins. At a time when venography was still available on a routine basis, Christine Muller et al. described some advantages of ultrasound over venography, better exemplified by citing a few examples:[30]

(1) Over half of the calf veins not visualized by venography were patent by ultrasonography.
(2) Venography failed to confirm nonocclusive thrombus in the common femoral vein with an interpretation of blood-dye mixing.
(3) Venography failed to provide enough anatomical information for identification of deep versus superficial calf veins.

Most importantly in modern days is that more than 50% of exams requested for deep venous thrombosis can be positive, yet less than 10% are positive for acute deep venous thrombosis. Venous or nonvenous positive findings can be asserted by ultrasonography. Robert Scissons noted gender differences in vascular laboratory use.[31] More women were being tested; yet men had a higher percentage of positive tests for deep vein thrombosis. Later, it was corroborated that many of the women being tested for thrombosis actually had venous valvular insufficiency. Besides chronic venous obstruction and valvular incompetence, findings of popliteal aneurysms, false aneurysms, arteriovenous fistulas, popliteal cysts, sinovial cysts, masses such as hematomas, seromas, enlarged lymph nodes, suspicion of lymphedema, all can be reported as positive findings during a “venous” examination. This approach, focusing on venous and nonvenous pathology, eliminates unnecessary testing and investigation in the majority of patients coming to the vascular laboratory.[32]

VALVULAR INSUFFICIENCY

Although we have worked in the selection and follow-up of patients with deep venous insufficiency, the fastest growing specialty in vascular disease is treatment of saphenous insufficiency. Radio-frequency ablation and endovascular laser treatment have been widely accepted by many physicians due to the easiness of treatment and apparent lack of complications. At present, it seems irrelevant that we still lack long-term follow-up data. These minimally invasive procedures please both the treatment physician and the patient. This section raises several questions about appropriate diagnosis, preoperative mapping, needed research on types of treatment, and patient follow-up.

CEAP classification. Disease classification must be reinforced at all times. In the past, critics of the venous literature emphasized the confusion created due to the lack of proper description and characterization of patients. Different patient populations seemed to be a good reason for contrasting results obtained with apparently the same treatment performed at different institutions. A classical phrase in the field was and still is “I don’t have varicose vein recurrence but I see recurrence from everybody else.” Apparently, patients with varicose veins change doctors a lot. The CEAP classification was created to avoid this confusion.

The C, clinical classification, includes normal legs, telangiectasias (i.e., spider veins), varicose veins, edema, pigmentation and lipodermatosclerosis, and ulcers, healed or not. The etiologic (E) classification includes primary, secondary, or congenital etiology. The A, anatomic classification, describes findings in the deep, superficial, and/or perforating veins. The P, pathophysiologic classification, looks at obstruction and/or reflux.

Modern practice, however, still creates confusion. Now the patients are properly described using the CEAP classification. We then know that mixed populations are commonly included in the analysis of different types of treatment. This mix still creates confusion regarding results of treatment. We now emphasize that venous studies must be limited to very specific populations. Two papers were presented at the 2004 American Venous Forum using data collected at the Angiolab of Curitiba, Brazil. They described the patterns of saphenous vein reflux separately for women with telangiectasias (C1) and varicose veins (C2) alone.[33–34] Subclassification of patients should be narrowed even further. For example, patterns of saphenous vein reflux are not only different in patients with edema versus varicose veins alone (C3 vs. C2), they are different in women with varicose veins depending on having been pregnant or not.

Screening

The American Venous Forum recommendations for segmental localization of chronic venous disease lists the iliac, femoral, and popliteal veins in detail, groups all three tibial veins into one entry, has one entry for the small saphenous vein, and has two entries for perforating and great saphenous vein. Reflux of the great saphenous vein is located either as above- or below-the-knee. Although this approach is good enough for screening, it is incomplete for diagnosis and too simplistic for preoperative mapping.

A screening protocol includes detection of:

(1) Great saphenous vein reflux/obstruction above and below the knee, most likely evaluated at mid thigh and mid calf.
(2) Small saphenous vein reflux/obstruction, most likely evaluated at mid or lower calf.
(3) Observation of reflux in visible nonsaphenous veins.

This screening protocol is often added to the protocol for deep venous thrombosis in symptomatic patients.

Definitive Diagnosis

Fundamental differences between a screening test and a definitive diagnostic test include more extensive longitudinal evaluation, particularly of the saphenous veins and detection of:

(1) Patency of femoropopliteal veins, most likely evaluated at mid thigh and knee levels. Selection of treatment for superficial venous reflux is affected if the femoropopliteal segments are obstructed.
(2) Femoropopliteal reflux, most likely evaluated at the groin, mid thigh, and knee levels. Deep vein reflux may not affect selection of superficial vein treatment, but the patient and doctor must be aware that treatment may not be as effective.
(3) Reflux at the saphenofemoral junction.
(4) Reflux at the saphenopopliteal junction.
(5) Reflux and diameter of perforating veins in the medial, lateral, posterior, and anterior aspects of the thigh and calf.
(6) Diameters of the great saphenous vein at the junction, proximal, mid and distal thigh, knee, and proximal, mid, and distal calf.
(7) Diameters of the small saphenous vein at the junction, and proximal, mid, and distal calf.
(8) Reflux and anatomy of nonsaphenous veins, particularly those in the proximal thigh that may be associated with a pelvic vein syndrome.

Reflux is closely related to diameter. Engelhorn's group has evaluated diameters of the great saphenous vein, and Joao Luis Sandri and colleagues have investigated the perforating veins.[35–36] For example, saphenofemoral junctions >8 mm, thigh segments >6 mm, and calf segments >4 mm most likely will reflux. This protocol may already be considered the first phase of preoperative saphenous vein mapping described below.

Preoperative Mapping

Preoperative mapping of the saphenous veins must determine patterns of reflux in great detail, with source(s) and drainage of reflux. At early stages of disease, saphenous vein is segmental and the most likely reflux source is a tributary. The junction and the perforators usually become abnormal at late stages of disease. Alberto Sarquis and Engelhorn have expanded the classification of patterns of reflux based on their experience with thousands exams performed yearly.[33–34,37] The following patterns of reflux need to be established for the great saphenous vein:

(1) Diffuse reflux from the saphenofemoral junction to the ankle.
(2) Proximal reflux from the saphenofemoral junction to a tributary or perforator at the thigh or even upper calf.
(3) Single segment reflux from a tributary or perforator to another tributary or perforator.
(4) Double or multiple refluxing segments.
(5) Distal reflux from a tributary or perforator down to the ankle.
(6) Perijunction reflux. Several types exist:
    (a) from the junction to the accessory saphenous or other vein that is not the great saphenous vein;
    (b) from tributaries of the junction to the great saphenous vein;
    (c) from the tributaries of the junction to another vein besides the great saphenous vein.

Reflux of the small saphenous vein follows similar patterns. The small saphenous, however, has a wide anatomical variation at the popliteal fossa with connections to the popliteal, femoral, muscular, and great saphenous vein via the intersaphenous-interconnecting vein (vein of Giacomini).

This detailed mapping is necessary prior to appropriate investigation of the various treatment options. Consensus in treatment matters is nonexistent because appropriate investigation is still lacking. Besides ligation and stripping, options of treatment include:

(1) Simple ligation of the source of reflux. This treatment, performed early on, can reduce diameter of a refluxing vein and may cause the valves to function again.
(2) Banding of the primary refluxing valve.
(3) Ligation, partial or complete, or no ligation of the saphenofemoral junction, in conjunction or not with other saphenous procedures.
(4) Endovascular ablation or obliteration of superficial veins with radio-frequency or laser.
(5) Foam or liquid sclerotherapy performed transcutaneously or by endovascular techniques.
(6) Simple treatment of the refluxing segment.
(7) Ligation or not of perforating veins.
(8) Limiting treatment to the thigh segment without treating calf veins.
(9) Treatment or not of deep venous reflux.
(10) Treatment of deep venous reflux concomitant with treatment of superficial venous reflux.
(11) Complete, preventive treatment versus intermittent, installment treatments as needed.

Only with detailed mapping, selection of very specific populations, and long-term follow-up will the issues of appropriate treatment be clarified.

Intraoperative Imaging

Treatment catheter insertion and placement is being performed under ultrasound visualization. Several "tricks" have been developed for prompt and effective venous cannulation. Ultrasound is also used at the end of the endovascular procedures to document closure, ablation, obliteration, or obstruction of blood flow through the treated vein. Injection or foam therapy and ligation have also been performed under ultrasound guidance

Patient follow-up. Our experience on follow-up of patients treated with radio-frequency ablation and/or stripping revealed the following[38]:

(1) Recurrence is a certainty. When, where, and how bad, however, remain to be determined. It may take months, it may take decades. It may need repair, it may be asymptomatic. Different follow-up schedules are recommended based on patient characteristics, results of past studies, and onset of new symptoms.
(2) If a refluxing saphenofemoral junction is not ligated, groin veins may enlarge and become nonvisible, nonpalpable varicose veins.
(3) Complete ligation of all tributaries in the saphenofemoral vein is by intension only and may not be accomplished in practice, particularly in the large patient. Small vessels may dilate and form new "junctions."
(4) Perioperative exsanguination is paramount to avoid thrombosis and inflammation.
(5) The canal of a stripped saphenous vein may reopen.
(6) Segmental recanalization occurs at any level after ablation or obliteration of the saphenous vein.
(7) After ablation, the vein may "disappear," become atretic, or recanalize.
(8) Most recanalizations are related to small vessel networks.
(9) Small vessel networks may be the so-called neovascularization. However, high-resolution ultrasound scanners have demonstrated that these neovascularization networks are formed of veins and arteries.
(10) Patients prone to telangiectasias (spider veins are not really veins) may be prone to small vessel networks and recanalization.
(11) New telangiectasias may appear after treatment of the saphenous vein and may be connected to thrombosed segments of the treated vein or vein channel in case of stripping.
(12) Arterial flow waveforms displaying high diastolic flow (i.e., fistula flow) may be detected adjacent to or in thrombosed and/or recanalizing venous segments.
(13) Distal, untreated venous segments may shrink, thrombose, or continue with severe reflux.

In summary, each patient may have an individual response to treatment, probably dependent on genetics and/or inflammatory processes developed in conjunction with treatment.

Investigational Challenges

This manuscript is concluded with the mention of three topics that have represented significant challenges, both in theoretical and practical aspects.

Plaque Characterization

The Europeans demonstrated that carotid plaque echogenicity might be a better predictor of cerebrovascular symptoms or plaque embolization. Still, the positive predictive value of symptoms or stroke by either percent stenosis or biplane plaque characterization is rather low. Efforts are being made to perform plaque characterization in multiple planes of a plaque. Khalil Dajani, in his PhD dissertation, described a three-dimensional method for plaque characterization[39] and mentioned two types of plaque analysis: one for quantifying heterogeneity and another for echolucency. From a bioengineering observation, not only plaque biological composition is a factor on plaque growth and embolization, but also the architectural distribution of plaques is important as well. The more boundaries between tissues, the higher the probability of breakage. Plaque characterization is a function of the ultrasound frequency and other parameters.[40] We also used satellite programs developed to investigate the surface of the earth to analyze plaque ultrasound data.[41] Vegetation and minerals are evaluated at different frequency bands. Calcium and thrombus should be evaluated at different frequencies. Plaque characterization is a function of the ultrasound frequency. In summary, plaque biology and architecture must be evaluated in 3-D and using multifrequency techniques.

As an addendum to plaque analysis, Dajani also developed methods to measure plaque volume. This approach could simplify monitoring of plaque development of regression in an easier way than plaque characterization.[42]

Shear Rates

It has been hypothesized that shear rate, or shear stress, has a major influence on endothelium behavior, in health and disease. Apparently, just like in a river curve, material is deposited in the vessel wall with low velocities, and the vessel wall is damaged, eroded by the friction of very high blood velocities. Shear rates would be a good indicator of carotid or graft restenosis, of risk for development of plaques and of effect of medication.

We developed a technique to measure shear rate noninvasively in the vascular laboratory.[43,44] Initially, we were able to obtain the velocity profile in a plane across the vessel and determine shear rate in two diametrically opposing points. This does not cover the entire circumference of the vessel. So, in cross section, we were able to determine the velocity profile along the entire area of the vessel. We could then measure shear rate in every point of the vessel circumference (in systole only). Now imagine the size of the problem: to measure shear rate during the entire cardiac cycle in multiple locations around a bifurcation or a graft anastomosis. We need unbelievable computer power or an ingenious way to simplify the measurements on a practical way.

Diastolic Flow

The shear rate introduction leads to the challenge of investigating continuous diastolic flow in the arterial system. The internal carotid arteries have persistent, relatively increased diastolic flow throughout the cardiac cycle. The renal arteries also have persistent, relatively high diastolic flow throughout the cardiac cycle. Diabetic patients with an infected foot also have persistent, high diastolic flow through the tibial arteries. Jaqueline Barreto, another international fellow at JVC, helped demonstrate that flow in the common femoral artery is doubled or tripled after young women smoked one cigarette.[45] The increase in aortic-femoral flow after smoking is similar to the increase in flow with exercise. This one-cigarette effect may last as long as 30 min. One pack a day may be equivalent to a 10-h exercise. That is a deadly load for the endothelium of the aorta, iliac, and femoral arteries. This finding brings us back to Towne's paper mentioned at the beginning of this paper.[6] He demonstrated increased atherosclerosis in the rabbits' iliac arteries in the side with an arteriovenous fistula versus the control side. This finding was in contradiction with the idea that increased flow protected the artery, based on the assumption that exercise is good for you. Perhaps, but for other reasons than increased flow. Properly trained athletes have long cardiac cycles, low heart rates, high systolic flows, short systolic pulses, and NO diastolic flow for most of the day. Perhaps the best effect of exercise is not the increased diastolic flow during exercise but the lack of diastolic flow throughout the nonexercising hours.

Conclusions

I hope that this summary of a lifetime of experiences with great friends and co-workers has stimulated most of the readers. First, in having a critical attitude toward our ingrained ideas and dogmas: These dogmas may be right, may be wrong, and may be important or not. Second, in knowing that even the smallest contribution may lead to progress someday. These contributions may even be recognized during your lifetime. And you may get recognition awards. Finally, at the end of the David Phillips Memorial Lecture in Anaheim, I recalled Luke 12:31. Because I have failed to fulfill the first part of the verse, only the ending was quoted. Awards . . . "And all these things will be added to you." At least Someone has fulfilled His part of the promise. It has been my privilege to work with the members of this society, either the Society of Noninvasive Vascular Technology, the Society of Vascular Technology, or, in its current format, the Society for Vascular Ultrasound. Thank you.

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