

EECP® Newsletter

Updating our clinical knowledge on an evidence-based therapy

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The Expanding Horizon of Potential EECP® Therapy Candidates—Part I

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Since EECP® therapy was FDA-cleared for marketing in February 1995 the broadening clinical experience and substantive clinical data have continually expanded the subsets of patients with coronary artery disease (CAD) now considered candidates for EECP therapy. The early adopters followed the FDA guidelines in their patient selection criteria, participating in the International EECP Patient Registry (IEPR) to document patient demographics, medical history, anginal status (Canadian Cardiovascular Society Classification [CCSC] pre and post therapy), adverse clinical events, comorbidities, outcomes data, duration of benefit, repeat and extended courses of EECP therapy, and quality of life.

Over 8,000 patients were enrolled in the IEPR between 1998 and 2001. Subsequent publications derived from the IEPR data and randomized, controlled, clinical trials data, have served to substantiate the effectiveness of EECP therapy and the durability of the treatment outcomes. Concomitantly the broadening clinical experience has enhanced the visibility of EECP therapy as a widely applicable treatment for CAD, significantly expanding the eligible patient base.

Cardiac Syndrome X (CSX) Compelling among those now being considered are the patients suffering with microvascular angina, Cardiac Syndrome X (CSX) i.e., typical chest pain, electrocardiographic changes and documented ischemia despite normal coronary arteriograms. Described in literature since 1982, CSX remains “a diagnostic and therapeutic riddle...treatment is a challenging and often a frustrating exercise for both patients and physicians.”¹ “More than half of women with chest pain undergoing coronary angiography in the U.S. are found to have normal or near-normal coronaries, compared with only 15% of men. This high “false positive” rate for severe coronary artery stenosis among symptomatic women has not declined since it was first reported.”² Approximately 50% of women discharged with a finding of “normal coronaries” (and atypical, non-specific chest pain) continue to experience disabling symptoms that are often unresponsive to conventional anti-ischemic therapy.² These patients often find themselves in a revolving-door experience of hospitalization for acute cardiac events and unsuccessful treatment, resulting

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HIGHLIGHTS

Current Issue

- CARDIAC SYNDROME X PATIENTS MAY BENEFIT FROM EECP THERAPY

Next Issue

- REPEAT TREATMENT WITH EECP THERAPY

NEWS & EVENTS

- VASOMEDICAL LAUNCHES REDESIGNED WEBSITE
- VASOMEDICAL EXPANDS PRODUCT LINE TO INCLUDE:
 - HOLTER MONITORING SYSTEMS
 - ULTRASOUND SCANNERS
- AHA Scientific Session NOVEMBER 9-11, 2008 NEW ORLEANS, LA BOOTH No.: 603 - TWO PRESENTATIONS

in a significantly negative impact on quality of life. While earlier reports indicated that the prognosis for survival and preserved left ventricular function was good,¹ recent findings in the NIH-NHLBI WISE study demonstrate that some of these patients may be at increased risk of myocardial infarction and death.³

The pathology of microvascular angina (reduced coronary microvascular dilatory responses and increased coronary resistance) has been consistently found in CSX patients and suggested as a cause for regional myocardial blood flow abnormalities and heterogenous myocardial perfusion. Endothelial dysfunction, with reduced nitric oxide (NO) and increased plasma levels of endothelin (ET-1), may explain the abnormal behavior of the coronary microvasculature in CSX.¹

In 2003, Bonetti, *et al* at the Mayo Clinic reported that EECP therapy increases NO and reduces ET-1.⁴ Michaels, *et al* at the university of San Francisco demonstrated that EECP therapy increases coronary perfusion pressure and flow.⁵ Both these studies served to substantiate the potential for EECP therapy to address the identified pathologies of CSX, alleviate the symptoms of this challenging and often frustrating syndrome, and provide symptomatic relief and enhanced quality of life to CSX patients.

In a study of 30 CSX patients (22 women, 8 men – 73% female), Dr. Kenneth Kronhaus and I concluded that EECP has broad utility in treating angina refractory to medical therapy, including both patients with large epicardial vessel disease and those with microvascular coronary disease.⁶



Cardiac Syndrome X patients with microvascular angina demonstrate subjective and objective sustained improvement after treatment with EECP therapy.

CAD and microvascular angina may coexist in the same patient and cause refractory angina, or microvascular angina may present as a unique and difficult to manage clinical entity.⁷ By increasing sheer stress, EECP therapy has been shown to promote angiogenesis and collateral recruitment, and normalize endovascular tone and function, thereby addressing the underlying pathology of CSX and offering a realistic, effective option for the treatment of microvascular angina. CSX patients with microvascular angina demonstrate subjective and objective sustained improvement after treatment with EECP.⁸ CCS improved from a baseline of 3.57 ± 0.50 to a CCS class of 1.43 ± 0.57 ($p < 0.001$) early post treatment. All treated patients demonstrated an initial improvement in CCS angina class, 27% improved one angina class, 33% improved two angina classes, and 40% improved three classes. An imaging stress test obtained at an average of 2.2 months post-EECP therapy showed no ischemic defects in 93% of cases ($p < 0.001$). With an average follow-up period of 11.9 ± 9.8 months, 87% of patients were without MACE and demonstrated sustained improvement in CCS angina class. Recurrent, worsening angina and ischemic defects occurred in four patients. All four patients responded positively to repeat EECP treatments.⁶

EECP therapy directly addresses the pathology of CSX and ameliorates its symptomatology, offering a demonstrably effective therapy for

these patients. CMS coverage for EECp therapy is provided for “patients who have been diagnosed with disabling angina (Class III or Class IV, Canadian Cardiovascular Society Classification or equivalent classification) who, in the opinion of a cardiologist or cardiothoracic surgeon, are not readily amenable to surgical intervention, such as PTCA or cardiac bypass, because:

1. Their condition is inoperable, or at high risk of operative complications or post-operative failure;
2. Their coronary anatomy is not readily amenable to such procedures; or
3. They have co-morbid states that create excessive risk.”⁹

The CSX patient often suffers chronic Class III or IV anginal symptoms, has demonstrable regional ischemia, often does not respond to conventional medical therapies, and cannot be treated with PTCA and coronary artery bypass grafting (CABG) as these interventions cannot address the underlying pathology of CSX. By definition, and with proper documentation, the CSX patient may be considered a reimbursable candidate for EECp therapy.

In the NIH-NHLBI WISE study, the “Symptom driven care for women is costly and accounts for the majority of cardiovascular care costs. On the basis of WISE estimates, the societal economic burden for CAD care for women with angina is expansive and could be responsible for a sizeable portion of U.S. health-care costs. For women undergoing coronary angiography, a lack of identifiable obstructive CAD lesions does not portend a low risk for persistent and refractory symptoms precipitating high lifetime costs of care.”¹⁰

Syndrome X is effectively treated with EECp therapy. There is significant reduction after treatment in CCS angina class and in inducible ischemia. The effect is durable with a low incidence of recurrent angina following treatment. The efficacy of EECp therapy in treating CSX patients supports improvement in endothelial function as a potential mechanism of action. Due to its multiple modes of action, EECp therapy may have broad utility in treating angina refractory to usual medical therapy, whether due to epicardial or microvascular coronary disease. The improvement in severe chronic angina would be expected to decrease disability and reduce health care costs due to recurrent hospitalizations and catheterizations.⁶

EECP therapy enhances quality-of-life by its very nature, a non-invasive, outpatient treatment virtually free of the need for a post-treatment recovery period. Patients can go on with their daily lives while deriving its therapeutic benefits. When repeat treatment is indicated it is not coupled with increased morbidity or mortality. Optimal therapeutic levels are not the harbingers of debilitating side effects, and side effects do not necessitate sub-therapeutic treatment levels.



*Syndrome X is
effectively treated with
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Clinical experience continues to demonstrate and the data continue to support the timeliness, broad therapeutic applicability, and durable benefit of EECp therapy. Outpatient, non-invasive, no appreciable post-treatment recovery time, economic and personnel resource sparing — EECp treatment is ideally suited to today's cost-conscious, time-conscious medical environment.

1. Kaski JC. Physiology and management of patients with chest pain and normal coronary arteriograms (cardiac syndrome X). *Circulation*. 2004;109:578-572.
2. Johnson DB et al. Persistent chest pain predicts cardiovascular events in women without obstructive coronary artery disease: results from the NIH-NHLBI-sponsored Women's Ischemia Syndrome Evaluation (WISE) study. *European Heart Journal*. 2006;27:1408-1415.
3. Bugiardini R. Women, 'non-specific' chest pain, and normal or near-normal coronary angiograms are not synonymous with favourable outcome. *European Heart Journal*. 2006;27:1387-1389.
4. Bonetti PO, et al. Enhanced external counterpulsation improves endothelial function in patients with symptomatic coronary artery disease. *Journal of the American College of Cardiology*. 2003;41(10):1761-1768.
5. Michaels AD, et al. Left ventricular systolic unloading and augmentation of intracoronary pressure and doppler flow during enhanced external counterpulsation. *Circulation*. 2002;106:1237-1242.
6. Kronhaus KD, Lawson WE. Enhanced external counterpulsation is an effective treatment for syndrome X. *International Journal of Cardiology*. 2008 Jun 28. [Epub ahead of print].
7. Kronhaus KD, Lawson WE. Is enhanced external counterpulsation the treatment of choice for microvascular angina? *Journal of Investigative Medicine*. 2003 Mar;51(S2);S386(170).
8. Kronhaus KD, Lawson WE. Enhanced external counterpulsation improves microvascular angina in coronary artery disease patients. *Journal of Investigative Medicine*. 2005 Mar;53(2);S399(71).
9. CMS, <http://www.cms.hhs.gov/Transmittals/Downloads/R50NCD.pdf>
10. Shaw LJ, et al. The economic burden of angina in women with suspected ischemic heart disease: results from the National Institutes of Health-National Heart, Lung, and Blood Institute-sponsored Women's Ischemia Syndrome Evaluation. *Circulation*. 2006;114:894-904.

If you have a story idea or would like to share the results of your experience with other clinicians, please e-mail your idea/story to: [Kasia Smigielska, Marketing Manager at ksmig@vasomedical.com](mailto:Kasia.Smigielska@vasomedical.com).

Recent Publications

Long-term Effect of Enhanced External Counterpulsation on Endothelial Function in the Patients With Intractable Angina

Hashemi M, Hoseinbalam M, Khazaei M.

Heart Lung Circulation. 2008 Oct;17(5):383-7. Epub 2008 Aug 15.

Passive Tobacco Exposure May Impair Symptomatic Improvement in Patients With Chronic Angina Undergoing Enhanced External Counterpulsation

Efstratiadis S, Kennard ED, Kelsey SF, Michaels AD, IEPR-2 IE.

BMC Cardiovascular Disorders. 2008 Sep 17;8(1):23. [Epub ahead of print]

Enhanced External Counterpulsation is an Effective Treatment for Syndrome X

Kronhaus KD, Lawson WE.

International Journal of Cardiology. 2008 Jun 28. [Epub ahead of print].

Expanding the Understanding of the Treatment of Chronic Angina: A 21st Century Approach – Part 1

Conti CR.

Clinical Cardiology. 2008 Jun;31(6):239-240.

Enhanced External Counterpulsation in the Treatment of Chronic Refractory Angina: A Long-term Follow-up Outcome from the International Enhanced External Counterpulsation Patient Registry

Loh PH, Cleland JG, Louis AA, Kennard ED, Cook JF, Caplin JL, Barsness GW, Lawson WE, Soran OZ, Michaels AD.

Clinical Cardiology. 2008 Apr 10;31(4):159-164.