EECP® Newsletter
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Summarizing Results of Randomized Controlled Studies In Enhanced External Counterpulsation (EECP®) Therapy

By John CK Hui and Tom Riedman

Since 1992, there have been more than 150 articles published in various medical journals, most of them peer-reviewed, documenting the clinical outcomes and mechanisms of action of Enhanced External Counterpulsation (EECP®) therapy. The most well- known randomized controlled trials (RCTs) were the Multicenter Study of Enhanced External Counterpulsation (MUST-EECP): Effect of EECP on Exercise-Induced Myocardial Ischemia and Anginal Episodes in the treatment of patients with angina pectoris and the Prospective Evaluation of Enhanced External Counterpulsation in Congestive Heart Failure (PEECH) Trial. There also have been a number of lesser known RCTs demonstrating the mechanisms of action of EECP® Therapy, some with correlation to clinical outcomes. Even though most of these smaller studies had limited numbers of patients, these RCTs illustrated the effects of EECP® Therapy were sufficiently different from the control group and that their measured endpoints did not have to rely on a large number of patients to demonstrate clinical significance. The eight RCTs listed below not only provided clinical evidence on the effectiveness of EECP® Therapy in improving the functions and Quality of life of patients suffering from coronary artery disease (CAD), they also formed our basic understanding on the mechanisms of action of EECP® Therapy in promoting coronary collateral circulation through angiogenesis, reducing inflammatory reactivity and improving endothelial function in controlling vascular tone and neurohormonal activities.

Continued Inside

Vasomedical Releases iPhone Application for EECP® Therapy

Available for free at the iPhone App Store, the Vasomedical EECP® Therapy iPhone App allows patients, physicians and therapists to easily obtain information on patient selection, clinical guidelines for treatment and user tools to optimize treatment. Current and potential patients can access information to learn about EECP® Therapy and its benefits as well as to identify symptoms that they can discuss with their physicians to see if EECP® Therapy could eliminate or reduce their symptoms and improve their quality of life. In addition, the iPhone application includes a Treatment Locator which, based on the iPhone user's current location or an inputted ZIP code, pinpoints on the map the locations of the closest EECP® treatment centers throughout the United States. The app is available for download in the App Store on the iPhone or in iTunes and can be found by searching "EECP" or "Vasomedical."

HIGHLIGHTS

Current Issue

Next Issue

The Results Of Randomized Controlled Studies In Enhanced External Counterpulsation (EECP®) Therapy

Study/ Investigators	Design/Entry	Control	EECP	Endpoints	Results			Ref
					Control	EECP	p	
MUST-EECP Arora	Outcome Study Entry: Angina positive stress test	Sham EECP with ≤ 80 mm Hg inflation pressure in patients with coronary artery disease N=56	1 hour each EECP session for 35 hours over 7 weeks N=56	Exercise duration	Pre: 432±22 sec Post: 464±22 sec Δ 22 sec, p<0.03	Pre: 426±20 sec Post:470±20 sec Δ 44 sec, p<.001	<0.31	1,2
				Time to ST segment	Pre: 326±21 sec Post: 330±18 sec Δ 4 sec, p<0.74	Pre: 337±18 sec Post: 379±18 sec Δ 42 sec, p<.002	=0.01	
				Angina counts	Pre:0.76±0.13 Post: 0.77±0.2 Mean Δ0.13±0.22	Pre:0.75±0.15 Post: 0.55±0.27 Mean Δ-0.11±0.21	<0.09	
				Nitroglycerin use	Pre: 0.51±0.15 Post: 0.45±0.19 Δ -0.10±0.12	Pre:0.47±0.13 Post: 0.19±0.07 Δ -0.32±0.12	>0.1	
PEECH Feldman	Outcome Study Entry: Mild-to-moderate heart failure symptoms	Protocol defined pharma-cologic therapy (PT) N=94	PT+ 35 hours with 1 hour each EECP session N=93	Primary endpoints: % subjects with ≥60 s increase in exercise duration at 6-month; or	25%	35%	=0.016	3
				% subjects with ≥1.25 ml/min increase in pVO_2 at 6-month	24%	23%	=0.698	
				Secondary endpoints % subjects improve in NYHA class	1week:11% 6-month: 14%	1 week: 33% 6-month: 31%	<0.001	
				Change in exercise duration	1 week -6±12 s 6-month -10±13 s	1 week: 26±12 s 6-month 25±15 s	=0.010 =0.013	
	Subgroup Analysis Age ≥ 65 years	PT N=44	PT+ EECP N=41	% subjects with ≥60 s increase in exercise duration at 6-month	25%	35%	=0.008	4
				% subjects with ≥1.25 ml/min increase in pVO_2 at 6-month	11%	30%	=0.017	
				Secondary endpoints % subjects improve in NYHA class	1week:10% 6-month: 16%	1 week: 35% 6-month: 38%	=0.042 NS	
				Change in exercise duration	1 week 3.4 sec 6-month -22 sec	1 week 23 sec 6-month 30 sec	=0.07 =0.001	
				Change in pVO_2 at 6-month ml/kg/min	1 week -0.8 6-month -1.1	1 week -0.1 6-month -0.2	=0.09 <0.001	
Gloekler	Mechanism Coronary collateral Angiogenesis in chronic stable angina patients	Sham with ≤ 80 mm Hg inflation pressure N=10	EECP with =≥300 mmHg pressure 30 hours, 90 min each session, 20 sessions over 4 weeks N=10	Primary endpoint Invasive Collateral Flow Index (CFI)	Pre: 0.129±0.122 Post: 0.111±0.125 Absolute Δ -0.017 p=0.14	Pre: 0.125±0.073 Post: 0.173±0.104 Absolute Δ 0.069 p=0.006	=.0009	5
				Secondary endpoints Myocardial blood flow reserve	Pre:1.26±1.99 Post: 2.11±2.95 p=0.40	Pre: 1.51±0.96 Post: 2.06±1.22 p=0.11		
				Coronary collateral conductance (ml/min/100mm Hg)	Pre: 0.229±0.212 Post: 0.305±0.422 p=0.45	Pre: 0.365±0.268 Post: 0.568±0.585 p=0.072		
				Right brachial artery Flow-mediated dilation (FMD)	Pre: 6.0±3.0% Post: 7.6±3.5% Absolute Δ 0.5±1.0% p=0.10	Pre: 4.3±1.5% Post: 6.9±3.5% Absolute Δ1.8±2.8% p=0.018	=0.07	
Art.Net.-2 Trial Buschmann	Proof-of-concept Prospective controlled study Coronary Collateral arteries Angiogenesis in chronic stable angina patients	Medically treated CAD patients. Catheterization at baseline and after 7 weeks N=7	EECP 35 1-hour sessions over 7 weeks Catheterization at baseline and after 7 weeks N=16	Primary endpoints: Pressure-derived collateral flow index (CFIp); and	Pre: 0.15±0.03 Post: 0.14±0.02 p<0.7	Pre: 0.08±0.01 Post: 0.15±0.02 p<0.001	<0.001	6,7
				Fractional flow reserve (FFR)	Pre: 0.68±0.06 Post: 0.70±0.05 p=0.4	Pre: 0.68±0.03 Post: 0.79±0.03 p=0.001	<0.05	
Casey	Mechanism/ outcomes Circulating inflamma-tory cytokines and adhesion molecules in patients with angina pectoris	Sham EECP 35 1-hour sessions over 7 weeks with ≤75 mm Hg inflation pressure N=9	EECP 35 1-hour sessions over 7 weeks with 300 mm Hg inflation pressure N=12	Plasma tumor necrosis factor-α (TNF-α)	Pre: 6.4±1.9 pg/ml Post: 6.7±1.9 pg/ml p=0.54	Pre: 6.9±2.7 pg/ml Post 4.9±2.5 pg/ml p<0.01		8
				Monocyte chemoattractant protein-1 (MCP-1)	Pre: 270±82 pg/ml Post: 264±66 pg/ml p=0.51	Pre:225±56 pg/ml Post:190±48 pg/ml p<0.01		
				Soluble vascular cell adhesion molecule-1 (sVCAM-1)	Pre: 847±177 ng/ml Post: 859±160 ng/ml p=0.81	Pre: 776±280 ng/ml Post: 726±278 ng/ml p=0.14		
				Change in CCS* angina class	No change	Pre: 3.1±0.5 Post: 1.2±0.4 p<0.01		
				Reduction in angina episodes	No change	Pre: 1.6±1.4 Post: 0.4±0.6 p< 0.05		
				Nitroglycerin use/day	No change	Pre: 0.5±0.7 Post: 0.1±0.2 p< 0.05		

*CCS angina classification: Canadian Cardiovascular Society angina classification;
** Distension = (maximum artery diameter – minimum diameter)
❤ß stiffness Index in the carotid artery is = ln(central systolic / central diastolic central blood pressure)/distension

Reference:
1. J Am Coll Cardiol.1999;33(7):1833-1840.
2. J Investigative Med 2002;50(1):25-32.
3. J Am Coll Cardiol. 2006;48(6):1199-1206.
4. Congestive Heart Failure. 2006;12(6):307-311.
5. Heart 2010;96:202-207
6. Int J Cardiol 2009;
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8. Am J Cardiol 2008;101(3):300-302
9. Cardiology. 2007;108(2):104-110
10. Am J Hypertension. 2006;19(8):867-872.
11. Circulation 2010;122:1612-1620

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The Results Of Randomized Controlled Studies In Enhanced External Counterpulsation (EECP®) Therapy (Continued)

Study/ Investigators	Design/Entry	Control	EECP	Endpoints	Results			Ref
					Control	EECP	p	
Levenson	Mechanisms Arterial stiffness and resistance in patients with stable coronary artery disease	Sham EECP, 35 1-hour sessions with 75 mm Hg cuff inflation pressure N=15	Active EECP 35 1-hour sessions with 300 mm Hg cuff inflation pressure N=15	Arterial distension in the carotid artery (x10^3)**	Absolute change Δ from baseline -4.4±6.5	Absolute change Δ from baseline 9.5±6.3	<0.05	9
				ß stiffness Index in the carotid artery ❤	Absolute change Δ from baseline 2.2±2.1	Absolute change Δ from baseline -3.3±0.9	<0.05	
				Mean carotid blood flow (ml/min)	Absolute change Δ from baseline -18±37	Absolute change Δ from baseline 164±35	<0.001	
				Carotid vascular resistance (mm Hg/ml/s)	Absolute change Δ from baseline 1.8±1.1	Absolute change Δ from baseline -3.9±1.1	<0.001	
Levenson	Mechanism Plasma and platelet cGMP production in asymptomatic subjects with high cardiovascular risk (HCVR) N=25 and subjects with stable coronary artery disease (CAD) N=30	Sham EECP, 1 hour session with 75 mm Hg cuff inflation pressure CAD patients N=15, and HCVR subjects N=13 Total N=28	Active EECP 1 hour session with 300 mm Hg cuff inflation pressure CAD patients N=15, and HCVR subjects N=12 Total N=27	Plasma Cyclic Guanosine Monophos-phate (cGMP) Baseline: All CAD patients 3.03±1.51nmol/L All HCVR subjects 2.54±1.39 nmol/L	Baseline overall: 2.7±1.3 nmol/L Increase from baseline Post-Sham: CAD: 0.7±0.4 Increase 23%±28% HCVR: 1.2±0.3 Increase 46%±38% Overall: 1.0±0.3 Increase 36%±34%	Baseline overall: 2.9±1.6 nmol/L Increase from baseline Post-EECP: CAD: 2.8±0.7, increase 58%±70% HCVR: 1.0±0.3 increase 43%±48% Overall: 2.0±0.6 increase 52%±66%	CAD: <0.01 HCVR: NS Overall <0.05	10
Braith	Mechanism / Outcomes CCS class; angina episodes, nitroglycerin use; Exercise duration and peak oxygen consumption; Flow-Mediated Dilation (FMD); Endothelial-Derived Vasoactive agents; and inflammatory cytokines, redox balance	Sham EECP, 35 1-hour sessions with 70 mm Hg cuff inflation pressure N=14	Active EECP 35 1-hour sessions with 300 mm Hg cuff inflation pressure N=28	CCS Classification	Before 3.0±0.3 After 3.0±0.3	Before 3.16±0.5 After 1.2±0.4	<0.001	11
				Angina episodes/day	Before 1.7±1.4 After 1.6±1.2	Before 1.8±1.5 After 0.5±0.7	<0.01	
				Daily nitrate use	Before 1.0±1.1 After 0.9±1.1	Before 1.1±1.4 After 0.2±0.4	<0.01	
				Peak exercise duration (sec)	Before 597.1±181.6 After 612.1±175.6 p=NS	Before 586.0±193.5 After 773.6±263.2 p<0.01	<0.001	
				Peak VO_2 (ml/kg/min)	Before 16.5±4.7 After 16.6±5.2, p=NS	Before 17.0±6.0 After 19.4±6.9, p<0.01	=0.002	
				Peak time to angina during exercise (sec)	Before 449.4±202.9 After 471.3±197.4 p=NS	Before 406.1±184.6 After 645.1±297.8 p<0.001	=0.003	
				Brachial flow-mediated dilation (FMD): absolute change (mm) % change (%)	Before 2.2±0.3 After 2.3±0.4, p=NS Before 4.3±0.3% After 4.2±0.4%, p=NS	Before 2.1±0.1 After 3.3±0.3, p<0.01 Before 3.9±0.1% After 6.1±0.3% p<0.01	<0.01	
				Femoral flow-mediated dilation (FMD): absolute change (mm) % change (%)	Before 2.2±0.2 After 2.3±0.3, p=NS Before 2.9±0.3% After 3.1±0.4%, p=NS	Before 2.2±0.2 After 2.7±0.3, p<0.01 Before 2.8±0.2% After 3.7±0.3% p<0.01	<0.01	
				Plasma levels of nitrate and nitrite NOx (µmol/L)	Before 23.9±16.1 After 24.3±14.5 Increased 2%	Before 22.8±9.8 After 31.9±11.1 Increased 36%		
				Plasma levels of endothelin-1 (ET-1) (pg/mL)	Before 2.1±0.9 After 2.1±0.9 Increased 5%	Before 2.2±0.8 After 1.5±1.3 Decreased 25%	<0.05	
				Vasodilatory prostaglandin 6-keto-$PGF_{1\alpha}$ (pg/mL)	Before118±60 After 120±94 Increased 1%	Before 108±71 After 185±111 Increased 71%	<0.05	
				Tumor necrosis factor-α (TNF-α) (pg/mL)	Before 6.2±1.2 After 6.4±1.5 Increased 12%	Before 6.1±2.2 After 5.0±1.7 Decreased 16%	<0.01	
				High-sensitivity C-reactive protein (hs-CRP) (mg/mL)	Before 3.4±0.9 After 3.5±1.1 Increased 5%	Before 3.4±2.17 After 2.3±1.8 Decreased 32%	<0.05	
				Monocyte chemoattractant protein-1 (pg/mL)	Before 230±92 After 231±75 Increased 0.2%	Before 227±74 After 171±43 Decreased 13%	<0.05	
				Soluble vascular cell adhesion molecule-1 (sVCAM-1)(ng/mL)	Before 955±256 After 967±230 Increased 1%	Before 917±406 After 821±317 Decreased 6%	<0.05	
				Lipid peroxidation marker 8-isoprostane (pg/mL)	Before 1720±674 After 1696±472 Increased 1.3%	Before 1709±594 After 1356±411 Decreased 21%	<0.01	
				Asymmetrical dimethylarginine (ADMA)(µmol/L)	Before 0.66±0.11 After 0.66±0.22 Increased 0.2%	Before 0.64±0.18 After 0.46±0.18 Decreased 28%	<0.001	

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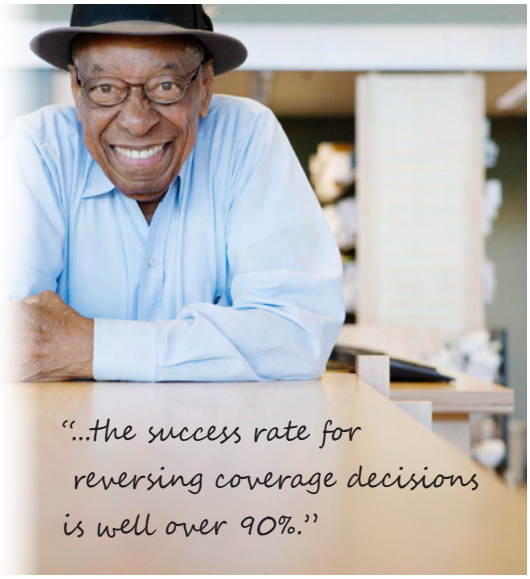
11. Circulation 2010;122:1612-1620

EECP® Therapy Reimbursement Update

Decreasing Your Claim Denial Rates and Increasing Reimbursement Opportunities

While Vasomedical continues working towards the improvement of reimbursement rates and the coverage environment for EECP® Therapy, carriers are only influenced by the providing physician or the actual companies and people who buy their coverage policies. We hear constantly from providers and others in the healthcare industry that when providers/centers implement a strategy for handling denials and other challenges to reimbursement, the success rate for reversing coverage decisions is well over 90%.



After her patient was initially denied coverage for EECP® Therapy, Doris Osborn, CET EECP® Supervisor at the EECP® Center of the Ohio Heart and Vascular Center in Cincinnati, appealed the denial by using a combination of materials that she had gathered on her own and that were included in the Vasomedical EECP® Reimbursement Support Folder plus new materials sent to her from Vasomedical. She was successful in getting BCBS of Illinois to cover EECP® Therapy for the first time.

Aaron Hirsch, President of Vascuflo in Cheektowaga, NY used similar tactics along with the expertise of a local attorney to pursue coverage from BCBS of Western NY and was successful in getting them to reverse their coverage decision and reimburse their patient for EECP® Therapy.

I E T A

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Join The IETA!

International ECP Therapists Association

In 1995, there was one EECP center in the United States; today there are almost 700, and close to 200 internationally! In 1995, a therapists' organization was a dream, today it is reality with more than 375 members.

Education and increasing membership continue to be the mandates. Join us! Help us help you achieve professional status & recognition. IETA welcomes you to jump onboard! Become a new member, renew your previous membership and look forward to obtaining your CET this year if you already have not done so. If you have done all these things, then you are truly in support of your IETA and the future of EECP for all those people we touch with heart disease!

Happy Anniversary!

2 years ago, the EECP® Forum was born as a haven for EECP® patients, therapists and physicians to connect and share their knowledge and experiences on EECP Therapy. Today, the forum supports over 2,000 members and going strong!

Connect Today!

EECP® FORUM

www.eecpforum.com

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:
Paul Persaud, Marketing Manager at ppersaud@vasomedical.com

Recent Publications & Presentations

Heart Failure: Device Management
Ed. Arthur Feldman
Ch 13. The Role of Enhanced External Counterpulsation in Heart Failure Management, 151-164 West Sussex, UK: Blackwell Publishing 2010.

Does External Counterpulsation Augment Mean Cerebral Blood Flow in the Healthy Brain? Effects of External Counterpulsation on Middle Cerebral Artery Flow Velocity and Cerebrovascular Regulatory Response in Healthy Subjects
Jungehuelsing GJ, Liman TG, Brunecker P, Ebel A, Endres M, Buschmann I, Pagonas N, Buschmann, EE on behalf of Arteriogenesis Network and the Center for Stroke Research Berlin
Cerebrovascular Diseases 2010;30:612-617

Enhanced External Counterpulsation Improves Peripheral Artery Flow-Mediated Dilation in Patients with Chronic Angina. A Randomized Sham-Controlled Study.
Braith RW, Conti CR, Nichols WW, Choi CY, Khuddus MA, Beck DT, Casey DP
Circulation 2010 [epub October 4, 2010]

Effect of Enhanced External Counterpulsation on Circulating CD34+ Progenitor Cell Subsets.
Kiernan TJ, Boilson BA, Tesmer L, Harbuzariu A, Simari RD, Barsness GW.
Int J Cardiol. 2010 Sep 13. [Epub ahead of print]

Acute Hemodynamic Effects of Enhanced External Counterpulsation
Reddy BT, Michaels AD.
Journal of Geriatric Cardiology June 2010 Vol 7, No. 2, 67-73

The Four Stages of Development: A Historical Perspective of External Counterpulsation
Hui JCK, Zheng ZS
Journal of Geriatric Cardiology June 2010 Vol 7, No. 2, 74-78

EECP in the Treatment of Endothelial Dysfunction: Preventing Progression of Cardiovascular Disease
Hui JCK, Lawson WE, Barsness GW
Journal of Geriatric Cardiology June 2010 Vol 7, No. 2, 79-87

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