



IEPR Newsletter

Special Edition

IEPR-1 Clinical Outcomes

In 1998 the International EEC Patient Registry (IEPR), housed at the University of Pittsburgh Epidemiology Data Center, was organized to document patient characteristics, long-term outcomes, safety and efficacy during the EEC treatment period. To date, over 5,000 patients from 80 centers have been enrolled. The IEPR was designed to enroll patients from a wide range of clinical treatment centers, both in the United States and other countries. Each clinical center using EEC as a treatment modality was contacted by the sponsor and invited to join the Registry. Clinical sites include academic and non-academic, hospital-based and free-standing EEC participants.

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Patient enrollment in the IEPR is purely voluntary, and without payment to either the clinical centers or patients. All Registry participants have been approved by their Institutional Review Boards for participation in the Registry (if required) and patients in the Registry must give informed consent. The Registry's goal is to collect data on as broad a range of patients as possible. The only patient entry criteria is that patients give informed consent and have had at least one hour of EEC therapy for the treatment of chronic angina. Every center enrolls all consecutive patients entering treatment for angina with no exclusions due to demographics, clinical status or outcome. Data collected prior to the first hour of treatment include demographics, medical history, disease characteristics, symptoms and medication use. After the final treatment hour, data recorded include the length of treatment, the degree of diastolic augmentation achieved, toward clinical events and current symptoms. At the six month, one-, two-, and three-year follow-up periods, the patient is interviewed and data are recorded concerning interim clinical events, hospitalizations and current symptomatology. The primary outcome is exertional angina as measured by the Canadian Cardiovascular Society (CCS) Classification.

Other outcome measures include frequency of anginal episodes, use of, and frequency of, anti-anginal medications, and patient assessed quality of life.¹

The IEPR database has provided comprehensive information and significant insights on the patient population treated with EEC during the past four years.^{2,3}

1. The overwhelming majority of these patients show a profile of long-standing, end-stage coronary disease with chronic severe angina unrelieved by medical means or conventional revascularization.

2. Most patients experienced improvement in anginal symptoms after a complete course of EEC treatment. Patients reported decreases in the number of anginal episodes and use of nitroglycerin, as well as improved function as measured by CCS class.

3. Because EEC is noninvasive and is provided as an outpatient therapy, despite the required time commitment, most patients complete the 35-hour course of treatment with very low rates of serious adverse events.

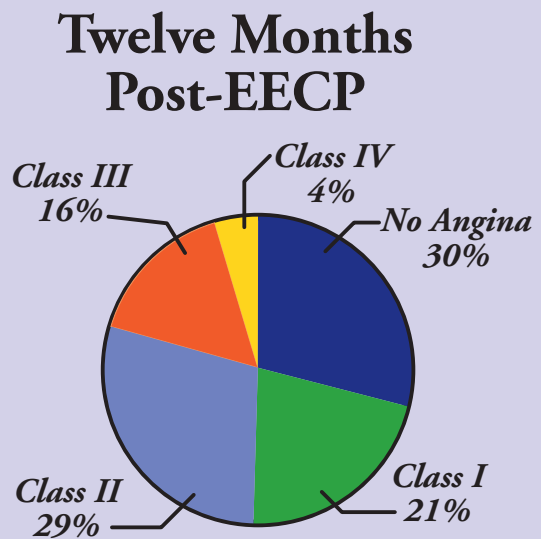
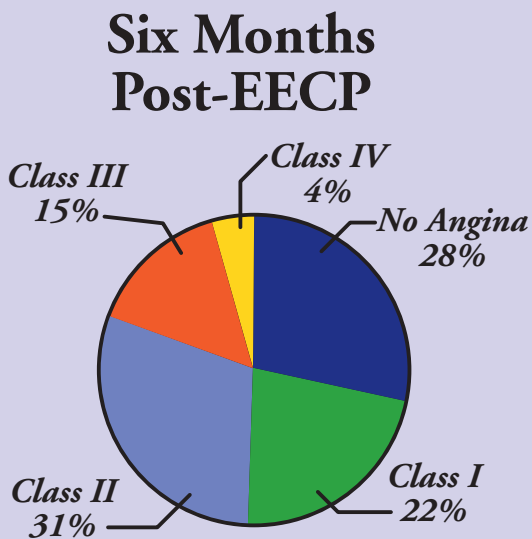
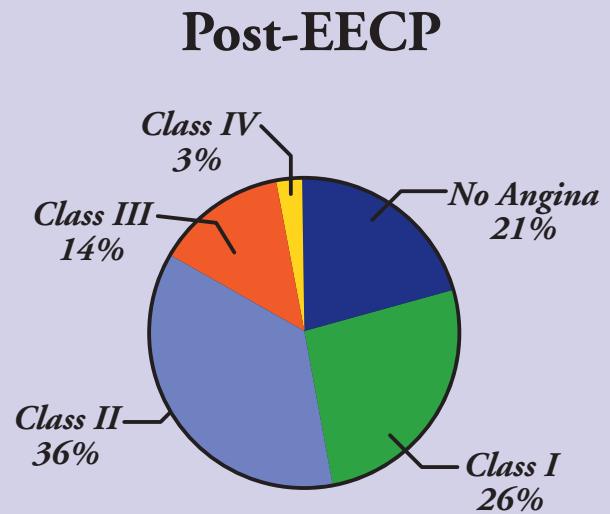
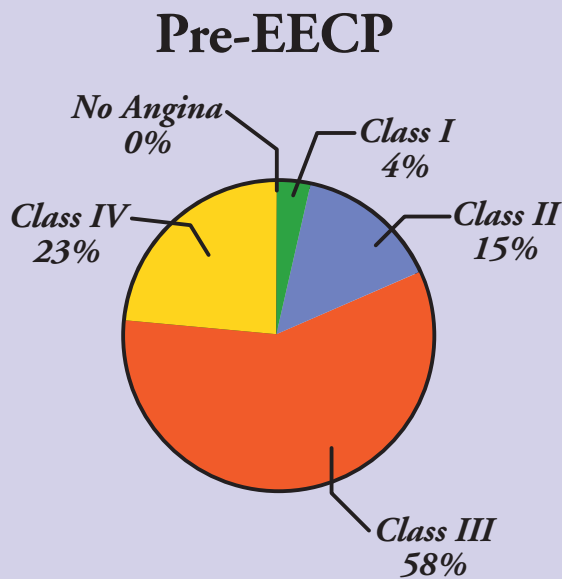
4. Whether the benefits of EEC persist after treatment is completed and for how long, is crucial. As the follow-up period continues to lengthen, the durability of benefit has been confirmed.

Although most registry patients have severe coronary artery disease in common, they present for treatment with a wide range of characteristics and co-morbidities.

1. Congestive Heart Failure (CHF) 32% of Registry patients reported a history of CHF (mean EF 39%). The heart failure cohort was older, with more females and more prior infarcts. Although fewer heart failure patients were able to complete a course of EEC (77% vs. 86%), and exacerbation of heart failure was more frequent during the treatment period (4.6% vs. 0.4%), angina class improved in 70% with

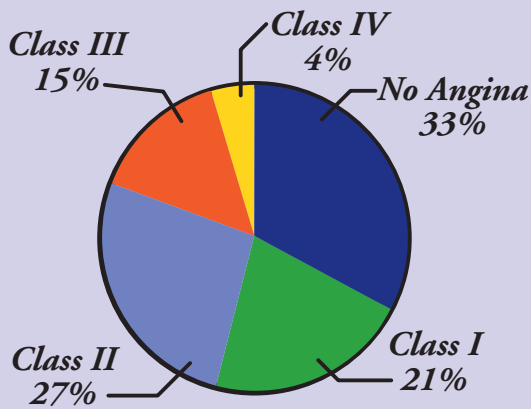
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EECP Therapy: Duration of Clinical Benefit

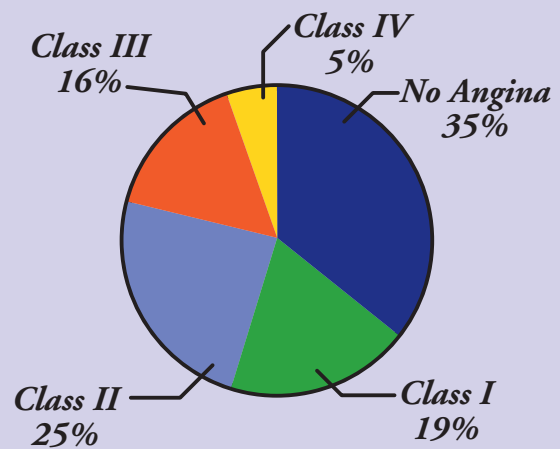


EECP Therapy: Duration of Clinical Benefit

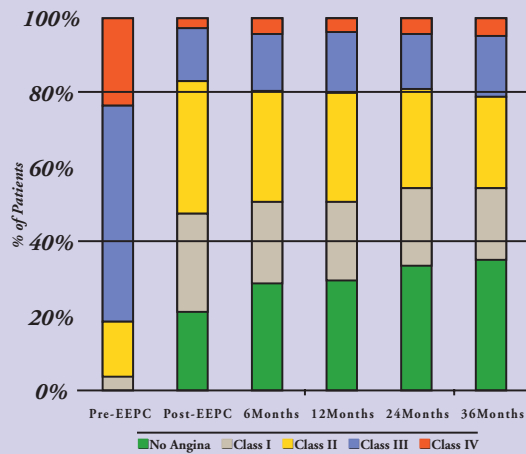
Twenty-four Months Post-EECP



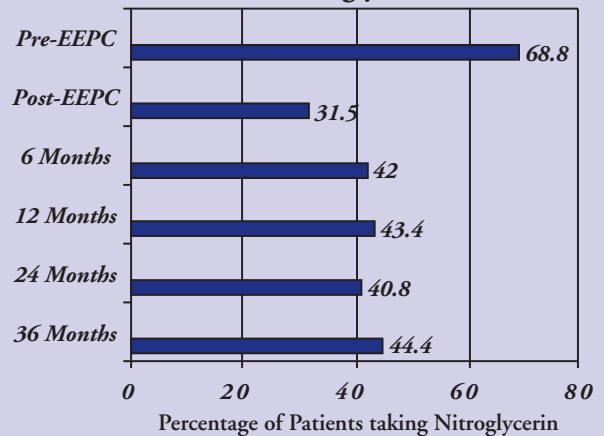
Thirty-six Months Post-EECP



Changes in Angina Class Through 36 Months



PRN Nitroglycerin Use



comparable quality of life benefit in the heart failure cohort. At six months, patients with CHF maintained their reduction in angina, but were significantly more likely to have experienced CHF or a major adverse cardiac event in proportion to the severity of left ventricular dysfunction. The relative rarity of cases of significant pulmonary congestion in this high-risk group suggests that EECP, with appropriate monitoring, may be safely applied to this group of patients. However, because of the increased risk of CHF during treatment, there is a continued need to take an interim history and to examine the patient prior to treatment for peripheral edema or pulmonary congestion. Routine use of oximetry and hemodynamic monitoring, as well as performing EECP in an appropriate clinical setting with immediate availability of personnel trained to recognize and treat pulmonary edema, are crucial to safely and effectively providing EECP to this patient population.²

2. Diabetes 41% of Registry patients have a physician diagnosis of diabetes. Patients with diabetes reported more CHF and were more often female. Treatment completion rates were similar to non-diabetic patients. Skin breakdown (3.2% vs. 1.7%), CHF (2.9% vs. 0.8%), and myocardial infarction (1.3% vs. 0.4%) were infrequent, but higher in the diabetic group during the treatment period. Immediately following EECP, 69% of diabetic patients demonstrated a reduction in angina of greater than or equal to one CCS class. After one year, maintenance of angina reduction was reported in 72% of diabetic patients. Quality of life was significantly improved. Despite a high-risk profile among the diabetic group in this study, one-year mortality was relatively low compared to similar patient registry populations.⁶

3. Age Although the mean age of Registry patients is 66.8 years, EECP has safely and effectively been administered to patients ranging in age from 31 years to 100 years. 23% of patients were ≥ 75 years, and 60% were over 65 years. Octogenarians, a rapidly growing age group, are frequently female

and have a history of heart failure. A course of EECP therapy is more likely to be interrupted due to a non-cardiac event in this older patient group. Elderly patients, able to complete a course of therapy, reported a decrease in angina episodes and nitroglycerin use while quality of life measures demonstrated significant improvement. Angina relief was sustained at the six-month follow-up period in a population in which a majority of patients are not candidates for coronary revascularization.⁴

4. Sex 24.5% of Registry patients are female. Despite increased diabetes (52% vs. 38%), heart failure (35% vs. 31%), and a higher odds ratio for failure to complete the usual 35 hours, women improved equally and significantly in CCS anginal class and in quality of life measures.⁵

The prevalence of cardiovascular disease is increasing at an unprecedented rate and is expected to grow by 1-2% each year over the next two decades. Given the near epidemic increases in obesity, diabetes and heart failure, the medical community is challenged to implement the latest medical advances, which have the potential of improving patient survival and health status (symptoms, functioning and quality of life).

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¹Barnes G, Feldman A, Holmes D, Holubkov R, Kelsey S, Kennard E, and the IEPR Investigators. "The International EECP Patient Registry (IEPR): Design, Methods, Baseline Characteristics, and Acute Results." Clin. Cardiol. 2001 Jun; 24(6): 435-42.

²Lawson W, Kennard E, Holubkov R, Kelsey S, Strobeck J, Soran O, Feldman A. "Benefit and Safety of Enhanced External Counterpulsation in Treating Coronary Artery Patients with a History of Congestive Heart Failure." Cardiology 2001;96(2):78-84

³Holubkov R, Kennard E, Kelsey S, Soran O. "A Report from the International Enhanced External Counterpulsation Patient Registry (IEPR)." Journal of Coronary Artery Disease 2001 Oct; 4(1): 81.

⁴Linnemeier G, Lawson W, Kennard E. "Enhanced External Counterpulsation for the Treatment of Angina in the Elderly: Safety, Response, and Durability of Benefit." Eur Heart J 2001; 22: (Suppl) 642.

⁵Lawson W, Kennard E, Linnemeier G, Holubkov R, Mehra M. "Do Women With Refractory Angina Respond as Well as Men to Treatment With Enhanced External Counterpulsation?" JACC 2002; 39: (5) 154A.

⁶Linnemeier G, Kennard E, Kelsey S. "Enhanced External Counterpulsation Provides Angina Relief in Diabetic Patients -a One Year Clinical Outcome Study from the International EECP Patient Registry." European Association for the Study of Diabetes, Sept 1-6, 2002, Budapest, Hungary

EECP Therapy: Duration of Clinical Benefit

The International EECP Patient Registry (IEPR) database was frozen on 07/24/02. Post-EECP, 6 month, 12 month, 24 month, and 36 month data reflect patients who completed the prescribed course of EECP treatment and for whom follow-up information was available.

Patient Demographics

Mean age 66.8 years
Age > 65 59.7%
Male gender 75.5%

Medical History

Duration of CAD 10.8 years CHF 31.7%
Prior PCI/CABG 85.8% Diabetes 41.3%
Prior MI 67.6%

	Pre-EECP (N=5019)	Post-EECP (N=3892)	6 months (N=3089)	12 months (N=2374)	24 months (N=1022)	36 months (N=238)
No Angina	-	20.7	28.2	29.1	33.3	34.9
Class I	3.5	26.2	22.4	21.2	20.7	19.3
Class II	14.7	36.4	30.0	29.4	26.7	24.8
Class III	58.4	14.0	15.2	16.2	15.0	16.0
Class IV	23.4	2.6	4.2	4.1	4.3	5.0
		82.3				
Improved by ≥ 2 classes		45.4				
No increase in angina since Post-EECP			79.4	75.5	74.8	74.3
prn Nitro use	68.8	31.5	42.0	43.4	40.8	44.4