



The Effects of External Counter Pulsation Therapy on Circulating Endothelial Progenitor Cells in Patients with Angina Pectoris

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ABSTRACT

Background: External counter pulsation therapy (ECPT) offers symptomatic relief and improves ischemia in patients with refractory angina pectoris. **Objectives:** We aimed to determine the effects of ECPT on circulating endothelial progenitor cells (EPCs). **Methods:** We prospectively studied 25 patients with angina pectoris treated with ECPT (n=15) or standard care (n=10). The number of EPCs positive for CD34 and kinase insert domain receptor (KDR) was determined by flow cytometry and the number of colony forming units (CFUs) was assessed in a 7-day culture, before ECPT and after 2 months. **Results:** ECPT improved anginal score from a median of 3.0 to 2.0 (p<0.001). Concomitantly, ECPT increased EPC number from a median of 10.2 to 17.8/ 10⁵ mononuclear cells (p<0.05), and CFUs from 3.5 to 11.0 (p=0.01). Flow mediated dilatation (FMD) was improved by ECPT from 7.4 to 12.2% (p<0.001) and was correlated with EPC-CFUs (r= 0.461, p=0.027). The levels of asymmetric dimethylarginine (ADMA) were reduced by ECPT from 0.70 to 0.60 μmol/L (p<0.01). In contrast, the same parameters did not change in the control group, before and after follow-up. **Conclusions:** The present pilot study shows, for the first time, that ECPT increases the number and colony-forming capacity of circulating EPCs.

BACKGROUND

- External counter pulsation therapy (ECPT) has become a viable alternative treatment for patients with refractory angina pectoris unsuitable for coronary artery revascularization procedures.
- The specific mechanism of action of ECPT is not clear.

OBJECTIVE

To explore the effects of ECPT on circulating endothelial progenitor cells (EPCs).

METHODS

We enrolled 25 patients with angina pectoris treated with ECPT (n=15) or standard care (n=10).

The following parameters were measured before ECPT and after 2 months :

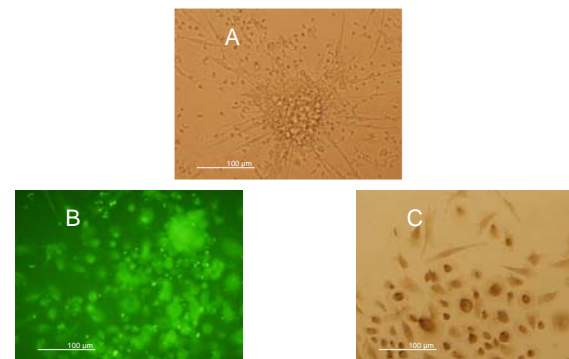
- Angina pectoris severity
 - Number of EPCs determined by flow cytometry.
 - Number of colony forming units (CFUs) assessed in a 7-day culture.
 - Endothelial function assessed by brachial artery flow mediated dilatation (FMD).
 - Other laboratory measurements

RESULTS

Table 1. Patient characteristics

	ECPT group (n=15)	Control group (n=10)
Age (mean±SD)	69.8±11.2	69.3±9.6
Gender (male)	12 (80%)	8 (80%)
CCS angina class IV	6 (40%)	3 (30%)
LVEF (mean±SD)	51.3±10.8%	49.3±10.9%
Three-vessel disease	11 (73.3%)	7 (70%)
Previous revascularization	14 (93.3%)	10 (100%)
Diabetes mellitus	4 (26.6%)	2 (20%)
Hypertension	13 (86.6%)	7 (70%)
Hyperlipidemia	14 (93.3%)	9 (90%)
CRP levels [median (IQR), mg/L]	2.0 (0.9-2.9)	2.0 (1.3-5.3)

Figure 1. An EPC colony as viewed by phase-contrast microscope and EPC phenotyping



An EPC colony as viewed by phase-contrast microscope (A). Confirmation of EPC phenotype by positive immunofluorescence staining for von Willebrand Factor (B) and by positive immunohistochemical staining for BS-1 Lectin (C).

Figure 2. ECPT is associated with improvement in angina symptoms

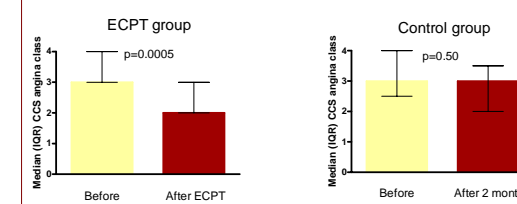
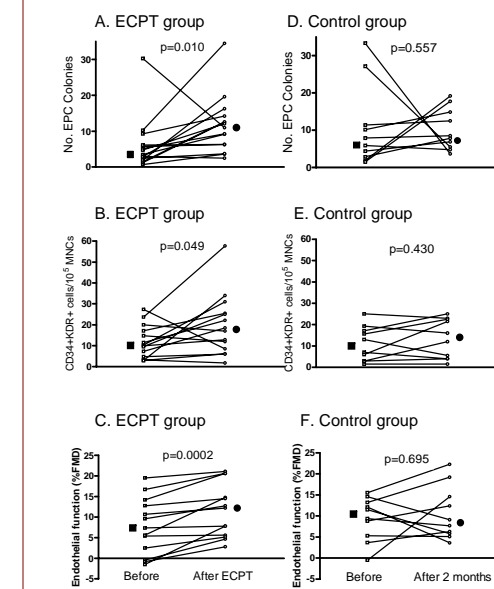
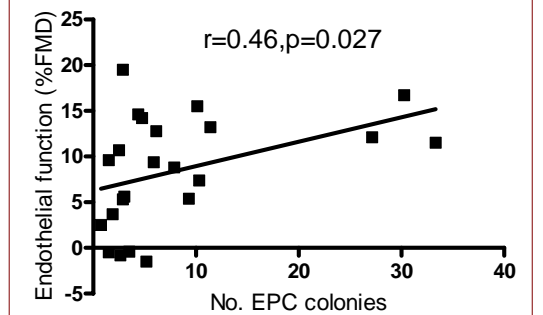


Figure 3. ECPT increases the number and function of EPCs and improves endothelial function



White squares and circles = individual values
Black squares and circles = median values

Figure 4. The number of EPC colonies is correlated with brachial artery endothelial function



CONCLUSIONS

- External counter pulsation therapy (ECPT) increases the number and colony-forming capacity of circulating endothelial progenitor cells.
- This new observation supports the potential role of ECPT in vascular health and suggests another mechanism by which ECPT improves endothelial function and ameliorates symptoms in patients with refractory angina pectoris.