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BRIEF COMMUNICATION

Increases in Cardiac Output and Oxygen Consumption During Enhanced External Counterpulsation

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Background Regular enhanced external counterpulsation (EECP) improves exercise capacity possibly through a training effect, but the roles of oxygen consumption (VO_2) vs. direct EECP effects (diastolic augmentation, DA-ratio), and their relation to cardiac index (CI) during EECP are unknown.

Methods We studied eight patients with angina pectoris (median [range] age 72 [53-85], 25% women), who underwent EECP for 35 daily sessions. Before, during and after the first and last sessions, we assessed VO_2, DA-ratio and CI.

Results At first EECP, CI increased from 2.2 (1.7-2.9) L/min/m^2 prior to EECP to 3.0 (2.2-3.8) during EECP (p=0.011), and returned to 2.4 (0.8-3.0). Similarly, VO_2 increased during EECP and returned to baseline after EECP. These patterns were reproduced at the last EECP session. Absolute values of CI and VO_2 correlated with each other during but not prior to or after EECP. The increase in CI correlated with the increase in VO_2 by trend: (first session, r 0.52, p=0.19; second session r 0.69, p=0.09), but not with DA-ratio.

Conclusions Acutely during EECP, there is an increase in cardiac output that is unrelated to direct EECP effects but related to, and may be secondary to, an increase in peripheral O_2 demand. This may represent a training effect.

Keywords Angina pectoris • Heart failure • Enhanced external counterpulsation • Diastolic augmentation • Cardiac output • Oxygen consumption

Background

Enhanced external counterpulsation (EECP) is a noninvasive ECG-gated diastolic arterial pressure augmentation system. Cuffs are wrapped around calves and thighs and during early diastole sequentially inflated to 300 mm Hg using compressed air, increasing arterial blood pressure and retrograde aortic flow during diastole (diastolic augmentation, DA) and reducing systolic afterload (systolic unloading, SU), analogously to the intra-aortic balloon pump. Enhanced external counterpulsation is given for one hour daily over 35 sessions. In angina and heart failure, EECP may improve symptoms and exercise duration [1–3]. The mechanisms underlying the long-term benefits of EECP are unclear. During EECP, cardiac output (CO) may increase [4]. The mechanism may be direct EECP effects or indirect through increased peripheral

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O_2 demand. Increased oxygen consumption (VO_2) during EECP suggests a training effect [5], but it is unknown whether this increase in VO_2 is related to increases in CO. Therefore we assessed the roles of VO_2 and direct EECP effects and their relation to CO and stroke volume during EECP administration.

Methods

Eight patients underwent a standard 35-day EECP protocol for angina. The study conformed to the Declaration of Helsinki, received ethics approval, and patients provided written informed consent. Prior to the first EECP session, we collected clinical data and non-invasive resting pulmonary blood flow and VO_2 in duplicate (Innocor®, Innovision, Odense, Denmark). The Innocor is a non-invasive device that measures pulmonary blood flow using an inert gas rebreathing technique, and measures VO_2 directly. It has been validated for CO and VO_2 at rest and exercise [6,7]. The coefficient of variance is low (VO_2 < 2%; CO 5-7%) [7], similar to gold standard Fick [8] and superior to other non-invasive methods [8]. In the absence of a significant intrapulmonary shunt, pulmonary blood flow as calculated by inert gas rebreathing measured by the Innocor® has been shown to provide a reliable estimate of cardiac output [7] and is reported as cardiac output or cardiac index here. The pulmonary blood flow may underestimate CO somewhat and the re-breathing VO_2 may underestimate VO_2, but for the purposes of our analyses, the main outcome was per cent change in cardiac output and VO_2, which is not affected. The heart rate (HR) was measured and the stroke volume index (SVI) calculated as $CO/HR/m^2$. Cardiac output and VO_2 were measured in duplicate again 15 minutes after starting EECP (i.e. during EECP) and 10 minutes after stopping EECP. During EECP, the EECP effectiveness ratio or DA-ratio (the ratio of peak diastolic blood pressure, which is increased during EECP, to the peak systolic blood pressure, which is reduced during EECP) was assessed by the EECP software. This protocol was repeated during one of the last (of total 35) EECP sessions. Statistics were performed in IBM SPSS version 22 (Armonk, New York, USA). Variable differences were analysed using Wilcoxon Signed Ranks test. Data are expressed as median (range). Correlations were analysed using Spearman's r.

Results

Median age (range) was 72 (53-85) years, two patients (25%) were women and all had angina. Additional baseline data are presented in Table 1. At both EECP sessions, CI and VO_2 increased significantly during EECP and returned to baseline after EECP. There was no difference between the first and last session with regard to CI or VO_2 (baseline, during EECP, increase from baseline, or after EECP) or DA-ratio. All four parameters increased significantly during EECP at, at least one session. Figure 1A shows CI, VO_2, stroke volume index (SVI) and HR before, during and after EECP for the first session. Cardiac index, VO_2 and HR increased significantly. Figure 1B shows the same for session 2. CI, VO_2 and SV increased significantly. For absolute values, the correlations between CI and VO_2 were significant during the first EECP session (r 0.81, p = 0.01) but not the second. There were no correlations prior to or after EECP. Similarly, SVI correlated

Table 1 Patient Baseline characteristics

Patient baseline characteristics	
n	8(100%)
Demographics	
Age, years	72(53-85)
Ischaemic heart disease	8(100%)
Angina	8(100%)
Hypertension	5(62.5%)
Diabetes	2(25%)
EF≤ 35%	4(50%)
NYHA class I	1(12.5%)
NYHA class II	3(37.5%)
NYHA class III	4(50%)
CCS class I	-
CCS class II	5(62.5%)
CCS class III	2(25%)
CCS not classifiable (variant angina)	1(12.5%)
Physical exam	
Weight, kg	79(60-80)
Height, m	1.71(1.63-1.79)
BMI, kg/m2	27(24-35)
Blood pressure systolic, mm Hg	135 (120-165)
Blood pressure diastolic, mm Hg	75 (60-80)
Heartrate, beats per minute	60 (54-68)
Laboratory	
Creatinine, µmol/L	100 (76-161)
Haemoglobin, g/dl	14.0 (12.8-15.7)
NT-proBNP, ng/L	551 (98-3180)
Medications	
Aspirin	7(87.5%)
Beta blockers	7(87.5%)
Insulin	1(12.5%)
Statins	7(87.5%)
ACE-inhibitors/ARBs	7(87.5%)
Diuretics	4(50%)
Nitrates	8(100%)
Metformin	1(12.5%)
Calcium channel blockers	2(25%)
Platelet aggregation inhibitors	3(37.5%)

Data are median (range)
ACE inhibitors, Angiotensin-converting-enzyme inhibitor
ARBs, Angiotensin receptor blockers
BMI, Body mass index
CCS class, Canadian Cardiovascular Society grading of angina pectoris
EF, Ejection fraction
NYHA class, New York Heart Association (NYHA) Functional Classification
NT-proBNP, N-terminal pro-brain natriuretic peptide

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