CARDIOLOGY Rounds®

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Refractory Angina Pectoris: A Therapeutic Challenge

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Since the advent of coronary artery bypass graft (CABG) surgery in 1966 and percutaneous transluminal coronary angioplasty (PTCA) in 1977, there has been significant progress in the field of coronary revascularization. However, an increasing number of patients remain severely disabled by refractory angina pectoris (RAP) despite optimal conventional medical and invasive management. In addition, as the life expectancy of patients with coronary artery disease increases, there are more patients with RAP and many have already undergone multiple percutaneous coronary interventions (PCIs) or surgical revascularizations. At present, there are various novel treatment modalities available for the management of chronic stable or RAP. Some approaches that have been studied extensively include enhanced external counterpulsation (EECP), neuromodulation, gene therapy, and transmyocardial laser revascularization (TMLR). Other therapeutic approaches (eg, fatty acid oxidation inhibitors and potassium channel activators) are still at an early stage of development. Innovative and experimental surgical techniques have also been developed including percutaneous *in situ* coronary venous arterialization (PICVA) and percutaneous *in situ* coronary artery bypass (PICAB). This issue of *Cardiology Rounds* will define the clinical problem of refractory angina pectoris, review its epidemiology, and discuss the clinical utility of a number of alternate treatment modalities such as EECP, neuromodulation, TMLR, and gene therapy.

Defining refractory angina pectoris (RAP)

Patients with RAP often have marked limitations in ordinary physical activity or are unable to perform any ordinary physical activity without discomfort (Canadian Cardiovascular Society [CCS] functional class III, IV). Four criteria must be met before a patient is considered to have RAP:[1,2]

- angina present for ≥3 months
- angina symptoms produced by objective ischemia and documented by exercise stress testing, stress imaging studies, or coronary physiologic studies
- continuing angina symptoms despite maximally-tolerated medical therapy and with the consensus that coronary revascularization by PCI or CABG is no longer feasible
- secondary causes of angina, such as anemia, thyrotoxicosis, or uncontrolled hypertension are excluded.

The most common reasons why further revascularization procedures are not feasible include:[2]

- unsuitable anatomy, such as diffuse coronary sclerosis, often with well-preserved left ventricular (LV) function; sometimes called end-stage angina
- one or several previous CABGs and/or PTCAs that exclude further benefit or the possibility of further revascularization.
- lack of graft material
- impaired LV function in a patient with previous CABG and/or PTCA.
- extracardiac diseases that increase perioperative/postoperative morbidity or mortality, (eg, general arteriosclerotic disease, renal insufficiency, carotid stenosis, and pulmonary disease)
- age, often in combination with the above factors.

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Table 1: Therapeutic options for refractory angina pectoris

- Pharmacological therapy – eg, low-molecular-weight heparins, partial fatty acid oxidation inhibitors
- Enhanced extracorporeal counterpulsation (EECP)
- Neurostimulation
- Transmyocardial revascularization (TMR)
- Therapeutic angiogenesis (gene therapy)
- Percutaneous *in situ* coronary venous arterialization (PICVA)
- Chelation therapy
- Heart transplantation

Epidemiology

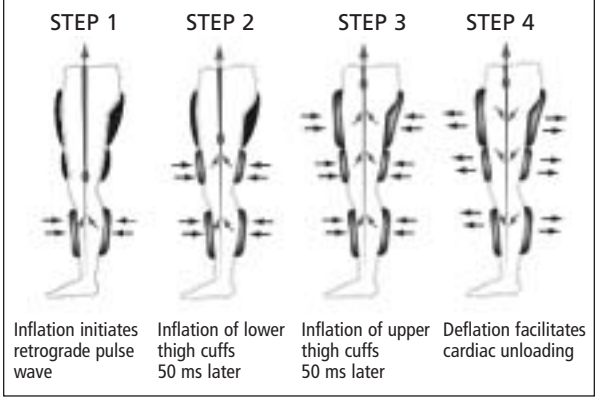
There are no accurate figures on the incidence or prevalence of RAP in the community. All the data available at present represent estimations. For example, even with the success of mechanical revascularization, the population of patients with RAP is estimated to be >100,000 per year in North America.[3] A report published in 1999 on a Spanish population (n= 10,248), aged 45-75 years, gave an overall angina prevalence of 7.3% in men and 7.7% in women. Approximately 5%-10% of these patients go on to develop refractory angina, or 3-7/1000 in these age groups.[4] In 1994-1995, a Swedish survey of patients referred for coronary angiogram because of stable angina pectoris revealed that 9.6% of the referred patients were rejected for revascularization despite severe symptoms.[5] Therefore, there is a need for a national, as well as an international data registry, to obtain more accurate figures for the prevalence and incidence of this condition.

Therapeutic options for refractory angina pectoris

Patients with milder angina (CCS class I/II) can be managed with traditional medical therapy (eg, beta-blockers, calcium channel blockers, nitrates, antiplatelet agents, angiotensin-converting enzyme (ACE) inhibitors, and statins). For those patients who are inadequately managed medically, revascularization strategies such as PCI or CABG are widely available in North America. However, there remains a large group of RAP patients whose quality of life is significantly affected despite traditional medical therapy and whose anatomy is not suitable for any revascularization strategy. The therapeutic options available for these RAP patients who have failed traditional management are listed in Table 1.

It should be noted that not all of these therapies are of proven value. This review will focus the discussion on EECP, neurostimulation, therapeutic angiogenesis, chelation therapy, transmyocardial revascularization, PICVA, and heart transplantation.

Figure 1: Sequential compression of the lower limb by EECP



Enhanced external counterpulsation (EECP)

EECP is a non-invasive approach to RAP that results in enhancement of coronary blood flow in the ischemic area. The concept of counterpulsation was known for almost half a century and subsequently, these ideas found a strong base in clinical practice. In 1953, Kantrowitz and Kantrowitz described diastolic augmentation as a means of improving coronary blood flow. In 1969, Soroff used the term "counterpulsation" for the first time, and then Zheng introduced sequential 3-cuff external counterpulsation. This procedure works by using 3 sets of inflatable cuffs that are wrapped around the calves, and the lower and upper thighs. The inflation and deflation are timed to the patient's electrocardiogram (ECG). During diastole, the cuffs are inflated sequentially from the calves proximally, resulting in the initiation of a retrograde pulse wave (Figure 1). This results in an augmentation of coronary perfusion pressure. In addition, there is an overall increase in venous return and cardiac output resulting from compression of the vascular bed. During systole, the cuffs are deflated simultaneously, resulting in systolic unloading and reduction in the cardiac workload (Table 2).

The mechanisms behind the benefits of EECP in patients with RAP are not entirely clear. Animal studies have demon-

Table 2: Hemodynamic effects of EECP

- Increases stroke volume per unit of work leading to increased efficiency of the left ventricle
- Increases diastolic perfusion pressure and increases the ratio of mean diastolic pressure to mean systolic pressure
- Increases coronary blood flow
- Increases coronary collateral flow to ischemic regions
- Increases mean arterial pressure (MAP)

EECP = enhanced external counterpulsation

strated that EECP increases the collateral circulation. It has also been found that EECP increases sheer stress in the coronary circulation that subsequently activates multiple biochemical signaling pathways and leads to angiogenesis or the opening of previously dormant vessels, or both.[6] Masuda et al reported a 66% increase in human growth factor and fibroblast growth factor, and a 33% increase in vascular endothelial growth factor (VEGF) and monocyte chemoattractant protein 1.[7] Urano et al reported a decrease in the serum level of brain natriuretic peptide after EECP treatment.[8] The International EECP Patient Registry revealed an improvement of at least 1 angina class in 81% of patients with CCS class III and IV.[9]

The first controlled clinical study examining the safety and efficacy of EECP was the MUST-EECP trial.[10] In this study, 139 outpatients with angina, documented coronary artery disease (CAD), and positive exercise tolerance were randomized to 35 hours of active EECP using a cuff pressure of 300 mm Hg or inactive counterpulsation using a cuff pressure of 75 mm Hg over 4 to 7 weeks. The study found an increase in exercise duration for both groups; however, the patients undergoing active EECP had a significant increase in the time to ≥1 mm ST-segment depression and a decrease in anginal episodes. In most patients, the treatment was relatively well tolerated and free of limiting side effects.

Currently, the primary indication for EECP treatment is chronic stable angina. There are a number of private clinics across North America offering this service. Patients who are accepted for such treatment must be prepared to undergo 35 hours of EECP therapy. Treatment is administered for 1 or 2 hours, at least 5 days per week. The service is not currently covered by the Ontario provincial health insurance.

Neurostimulation

Neurostimulation was developed in response to the gate theory of pain transmission to provide a nonpharmacological means of pain relief.[11] The mechanisms behind beneficial effects in angina are thought to be related to a reduction in transmission of nociceptive impulses via the spinothalamic tract due to increased levels of gamma-aminobutyric acid (GABA) during myocardial ischemia. Another theory states that neurostimulation facilitates the redistribution of myocardial blood flow from nonischemic to ischemic regions.[12] Two methods were found to be useful in the treatment of refractory angina, transcutaneous electrical nerve stimulation (TENS) and spinal cord stimulation (SCS).

TENS: The first description of the beneficial effects of TENS was by Mannheimer in the early 1980s.[13] TENS involves the use of 2 electrodes of silicone-conducted rubber that are applied over the chest (1 on the dermatome with the highest intensity of pain and the other on the contralateral dermatome). The patient can apply stimulation for 1-3 minutes during an anginal attack or as a prophylaxis. The main drawback of this treatment modality is the skin irritation that results from high-frequency direct current, which limits its use as a long-term therapy.

SCS: SCS was first described in Australia in 1987. Implantation of the device is a surgical procedure that is performed under local anesthesia. The electrodes are introduced at the level of the first or second thoracic vertebra. A subcutaneous wire connects these electrodes to a pulse generator that is implanted subcutaneously in the left side of the abdomen. The role of SCS was evaluated in the Electrical Stimulation versus Coronary Artery Bypass surgery (ESBY) trial.[14] The trial was a randomized prospective study that compared SCS with CABG in 104 patients at high risk for CABG or not expected to benefit from CABG. After 6-months follow-up, it was clear that both techniques reduced anginal episodes to a similar degree. However, the CABG group had a greater increase in exercise capacity and less ST-segment depression when compared to the SCS group. On the other hand, SCS patients had a lower 6-month mortality rate and fewer cerebrovascular events compared to the CABG group. Greco et al found that SCS resulted in a significant decrease in NYHA functional class with no adverse outcomes on mortality in patients with RAP.[15]

Therapeutic angiogenesis

In the last few years, there has been tremendous progress in the field of gene therapy as a treatment modality for CAD. The concept of therapeutic angiogenesis is based on stimulating blood vessel growth in the adult heart with the aim of restoring myocardial blood flow and function.[16] In this process, endothelial cells produce metalloproteinases that digest the basement membrane, which through several steps, leads to the formation of a network of endothelial tubes. Subsequently, the blood vessels will be covered by a muscular coat in a process called "arteriogenesis." Several angiogenic growth factors have been shown to stimulate blood vessel growth, including fibroblast growth factor (FGF), VEGF, platelet-derived growth factor (PDGF), and master switch genes (eg, hypoxia-inducible factor 1 alpha). The optimal approach to deliver these agents is still being defined.

Isner et al[17] was the first to provide evidence for the efficacy of angiogenesis in a patient with an ischemic leg. After intra-arterial infusion of VEGF, he noted an improvement in the blood supply to the ischemic leg. Udelson et al[18] studied the use of intracoronary and intravenous recombinant fibroblast growth factor (rFGF) in 59 patients with refractory angina. After 180 days, he noted an improvement in both stress and rest myocardial perfusion abnormalities. The safety and efficacy of intracoronary injections of adenoviral-encoded FGF-4 was examined in the AGENT trial.[19] It demonstrated that patients receiving gene therapy exhibited a trend towards a greater increase in exercise time at 4 weeks compared to patients in the placebo group. The use of granulocyte-macrophage colony-stimulating factor (GM-CSF) was tested in 21 patients with inoperable CAD who were randomized to receive placebo or intracoronary recombinant GM-CSF, followed by 2 weeks of subcutaneous administration.[20] Compared to placebo, GM-CSF improved collateral flow.

Table 3: Complications of therapeutic angiogenesis

- Abnormal vascular proliferation in nontargeted tissues
- Hazards from the viral vectors
- Paradoxical worsening of atherosclerosis
- Stimulation of neoplasm growth or the development of *de novo* tumours
- Hazards associated with direct myocardial delivery of these agents

Despite the potential benefits of gene therapy, it is not entirely free from possible complications (Table 3); however, thus far clinical trials have reported only a few significant ones.[21]

Chelation therapy

Chelation therapy was first described in 1950 as a potential treatment for atherosclerosis when patients treated for lead poisoning reported relief from their anginal symptoms after undergoing ethylenediaminetetracetic acid (EDTA) therapy. There is no strong scientific basis behind the potential benefits of chelation therapy; however, EDTA is thought to extract calcium from atherosclerotic plaques. Based on a number of trials, it is thought that this treatment modality is not effective. The most recent randomized study of this therapy is the Program to assess Alternative Treatment strategy to achieve Cardiac Health (PATCH) trial,[22] in which 84 patients with stable angina were randomized to receive either EDTA treatment or placebo. After 6 months, there was no difference in exercise tolerance or hospital readmission rates. Based on current published data, the American Heart Association concluded that there was no scientific evidence to support this form of therapy.[23] Furthermore, there are real concerns regarding the potentially lethal side effects of EDTA treatment.

Transmyocardial revascularization (TMR)

The TMR technique uses laser ablation to create transmural channels in the ischemic myocardium to restore myocardial perfusion. Reptilian heart physiology provided the basis for modern laser revascularization. Reptiles do not have a significant epicardial coronary circulation. Instead, 90% of the heart blood supply is delivered directly to the heart muscle from the ventricle through a network of channels.

There are 2 modalities for creating myocardial channels: surgical and percutaneous.

TMLR: With the surgical approach (transmyocardial laser revascularization [TMLR]), the left pleural space is entered through a limited thoracotomy incision, usually via the fifth intercostal space. Subsequently, the laser arm (mostly CO_2 or holmium:yttrium-aluminum-garnet [YAG] laser) is aimed at the epicardium in the area of reversible ischemia, which has been assessed prior to the procedure. TMLR is not effective in acute myocardial ischemia and patients with poor LV function are not good candidates for this procedure. The mechanism behind the benefit is not known, but there are a number of theories that might explain the favourable role of TMLR in patients with RAP (Table 4).

Table 4: Mechanisms of TMLR effects

- Myocardial angiogenesis resulting from the upregulation and release of vascular endothelial growth factors and inflammatory mediators
- Myocardial sympathetic denervation
- Myocardial fibrosis that results in a tethering action to improve myocardial function and promote favourable remodeling

Several clinical trials have reported encouraging results following TMLR. Frazier et al[24] randomized 192 patients with predominately CCS class IV angina to receive either TMLR or medical treatment. After 12 months of follow-up, the TMLR group had a significant improvement in angina class and quality of life. Furthermore, only 2% of patients treated with TMLR were hospitalized with unstable angina over 12 months compared to a 69% hospitalization rate in the medically-treated patients. Similar findings were noted in a trial by Allen et al in 275 patients with RAP.[25] At ≥1 year, the patients undergoing TMLR had an improvement in angina, a higher rate of survival, higher exercise tolerance, and a better quality of life. In a long-term follow-up of a Norwegian trial in 100 patients, anginal symptoms and hospitalizations for RAP were still significantly reduced at 43 months.[26] The complications of TMLR are almost exclusively cardiac related and include myocardial infarction (MI), LV hypertrophy, atrial fibrillation, and ventricular arrhythmias.

PTMLR: Percutaneous transmyocardial laser revascularization (PTMLR) is a less invasive approach that can be carried out in the catheterization laboratory using a holmium:YAG laser that can channel energy through a fiberoptic system, which is introduced via the femoral artery. The PACIFIC trial randomly assigned 221 patients with refractory angina (CCS class III or IV) to PTMLR or conventional medical therapy.[27] At 12 months, those undergoing PTMLR had a greater median increase in exercise tolerance with an improvement in angina class; however, there was no difference in survival. Another trial evaluated 141 patients with class III or IV angina.[28] Patients were randomized to maximal medical therapy with or without PTMLR. At 6 months, there was no

difference between the 2 groups in improvement of anginal class, exercise duration, rates of death, or MI.

Despite these trials, whether laser channels remain patent for any significant amount of time is still debatable. Randomized clinical trials without a placebo-control group have produced consistent improvements in anginal symptoms, exercise duration, and quality of life; however, improvement in myocardial perfusion has not been validated by this technique. Some of the improvements in anginal symptoms could potentially come from placebo effects of the treatment.

Percutaneous in situ coronary venous arterialization (PICVA)

Newer surgical techniques are being developed as an alternative to CABG. In PICVA, arterial blood flow is directed from the occluded artery to the adjacent coronary vein, thereby arterializing the vein and providing retroperfusion to the ischemic myocardium. In another experimental procedure, the percutaneous *in situ* coronary artery bypass (PICAB), arterial blood flow is redirected from the occluded artery to the adjacent coronary vein and then rerouted back to the artery after the occlusion. In other words, the vein acts as a coronary bypass conduit.[29] It is too early to make any conclusions regarding the benefits of these procedures, but this innovative area remains an active area of investigation with significant potential benefits.

Heart transplantation

Heart transplantations have been performed in patients with RAP in some centres after all conventional or nonconventional treatments have been exhausted. However, due to the limited number of donors, only approximately 3000 transplantations are being performed worldwide, annually.[2] Furthermore, cardiac transplantation patients may not necessarily have a better survival when compared with conventional medical treatment.

Conclusions

Refractory angina pectoris is a definite challenge in contemporary clinical practice. There are increasing numbers of patients who remain severely disabled by angina despite optimal medical and revascularization procedures. Fortunately, there are a variety of emerging novel medical and surgical options to treat RAP, the majority of which are still at various stages of investigation. Enhanced external counterpulsation is probably the most attractive option, given its noninvasive nature, particularly for patients who have exhausted the conventional modalities of angina management, but remain symptomatic. Transcutaneous electric nerve stimulation and spinal cord stimulation are also effective methods for treating RAP. These techniques have been widely studied and have a good safety profile, but are not easily accessible. Therapeutic angiogenesis represents an exciting avenue of research in the treatment of ischemic vascular disease. The various methods for angiogenesis still need further study and validation to document their safety and efficacy. The potential efficacy of percutaneous *in situ* coronary venous arterialization and percutaneous *in situ* coronary artery bypass as an alternative to CABG in those with poor coronary anatomy needs to be evaluated further in future clinical trials. Given the lack of placebo-controlled trials for transmyocardial revascularization, the placebo effect cannot be ruled out as an important component of improvement for all the options mentioned. Further research into RAP epidemiology and treatment is needed, as well as comparative studies between the different treatment modalities, to ascertain the relative risks and benefits of these procedures.

References

1. Sharma SK, Kim MC, Kini A, Refractory angina pectoris: mechanism and therapeutic options. *J Am Coll Cardiol* 2002;39: 923-934.
2. Mannheimer C, Camici P, Chester MR, et al. The problem of chronic refractory angina. Report from the ESC Joint Study Group on the treatment of refractory angina. *Eur Heart J* 2002; 23:355.
3. Mukherjee D, Bhatt D, Roe MT, et al. Direct myocardial revascularization and angiogenesis: how many patients might be eligible? *Am J Cardiol* 1999;84:598-600.
4. Cosin J, Asin E, Marrugat J, et al. Prevalence of angina pectoris in Spain. PANES study group. *Eur J Epidemiol* 1999;4:323-330.
5. Brorsson B, Persson H, Landelius P, Werko L, Smartor i brostet: *Operation, ballongvidgning, medicinsk behandling*. Stockholm, Sweden: Statens beredning for utvardering av medicinsk metodik; 1998. Report No.:140.
6. Soran O, Crawford LE, Schneider VM, et al. Enhanced external counterpulsation in the management of patients with cardiovascular disease. *Clin Cardiol* 1999;22:173-178.
7. Masuda D, Nohara R, Kataoka K, et al. Enhanced external counterpulsation promotes angiogenesis factors in patients with chronic stable angina. Paper presented at: American Heart Association Scientific Sessions, November 11-14, 2001. Anaheim, California.
8. Urano H, Ikeda H, Ueno T, Matsumoto T, Murohara T, Imaizumi T. Enhanced external counterpulsation in patients with coronary artery disease. *J Am Coll Cardiol* 2001;37:93-99.
9. Barsness G, Feldman AM, Holmes DR Jr, Holubkov R, Kelsey SF, Kennard ED. The internal EECP Patient Registry (IEPR). *Clin Cardiol* 2001;24:435-442.
10. Arora RR, Chou TM, Jain D, et al. The multicenter study of enhanced external counterpulsation (MUST-EECP): effect of EECP on exercise-induced myocardial ischemia and anginal episodes. *J Am Coll Cardiol* 1999;33:1833-40.
11. Shealey CN, Mortimer JT, Reswick JB. Electrical inhibition of pain by stimulation of the dorsal columns. *Anesth Analg* 1967;46:45-47.
12. Murray S, Collins PD, James MA. Neurostimulation treatment for angina pectoris. *Heart* 2000;83:217-220.
13. Mannheimer C, Carlsson CA, Emanuelson H, et al. The effects of transcutaneous electrical stimulation in patients with severe angina pectoris. *Circulation* 1985;71:308-16.
14. Mannheimer C, Eliasson T, Augustinsson LE, et al. Electrical Stimulation versus Coronary Artery Bypass Surgery in severe angina pectoris: the ESBY study. *Circulation* 1998;37:1157-63.
15. Greco S, Auriti A, Fiume D, et al. Spinal cord stimulation for the treatment of refractory angina pectoris: a two-year follow up. *Pacing Clin Electrophysiol* 1999;22:26-32.
16. Tabibiazar R, Rockson SG. Angiogenesis and the ischemic heart. *Eur Heart J* 2001;22:903-918.
17. Isner JM, Pieczek A, Manor O, et al. Clinical evidence of angiogenesis after arterial gene transfer of ph VEGF 165 in patient with ischemic limb. *Lancet* 1996;348:370-374.

18. Udelson JE, Dilsizian J, Laham RJ, et al. Therapeutic angiogenesis with recombinant fibroblast growth factor-2 improves stress and rest myocardial perfusion abnormalities in patients with severe symptomatic chronic coronary artery disease. *Circulation* 2000;102:1605-1610.
19. Grines CL, Watkins MW, Helmer G, et al. Angiogenic Gene Therapy (AGENT) trial in patients with stable angina pectoris. *Circulation* 2002;105:1291-1297.
20. Seiler C, Pohl T, Wustmann K, et al. Promotion of collateral growth by granulocyte-macrophage colony-stimulating factor in patients with coronary artery disease: a randomized, double-blind, placebo-controlled study. *Circulation* 2001;104:2012-2017.
21. Simons M, Bonow RO, Chronos NA, et al. Clinical trials in coronary angiogenesis: Issues, problems, consensus: An expert panel summary. *Circulation* 2000;102:E73-86.
22. Knudson ML, Wyse DG, Gailbraith PD, et al. Chelation therapy for ischemic heart disease: A randomized controlled trial. *JAMA* 2002; 287:481-486.
23. American Heart Association. *AHA statement on chelation therapy*. Dallas, TX: Heart & Stroke A-Z Guide, 2000.
24. Frazier OH, March RJ, Horvath KA. Transmyocardial revascularization with a carbon dioxide laser in patients with end-stage coronary artery disease. *N Engl J Med* 1999;341:1021-1028.
25. Allen KB, Dowling RD, Fudge TL, et al. Comparison of transmyocardial revascularization with medical therapy in patients with refractory angina. *N Engl J Med* 1999;341:1029-36.
26. Aaberge L, Rootwelt K, Blomhott S, Saatredt K, Abdelnoor M, Fortang K. A late clinical follow-up of the Norwegian Randomized trial with transmyocardial revascularization. *J Am Coll Cardiol* 2002; 39(10):1588-93.
27. Oesterle SN, Sanborn TA, Ali N, et al. Percutaneous transmyocardial laser revascularisation for severe angina: The PACIFIC randomized trial. Potential Class Improvement from Intramyocardial Channel. *Lancet* 2000;356(9243):1705-10.
28. Stone GW, Teirstein PS, Rubenstein R, et al. Randomized trial of percutaneous transmyocardial laser revascularization. *J Am Coll Cardiol* 2002;39(10):1581-87.
29. Fitzgerald PJ, Hayase M, Yeung AC, et al. New approaches and conduits: in situ venous arterialization and coronary artery bypass. *Curr Interv Cardiol Rep* 1999;1:127-37.

Abstract of Interest

Practicability and limitations of enhanced external counterpulsation as an additional treatment for angina

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BACKGROUND: An increasing number of clinical studies indicates reduction of angina and myocardial ischemia by enhanced external counterpulsation (EECP) therapy. However, given the wide range of contraindications and the long duration of treatment, eligibility and practicality issues have not been addressed systematically.

HYPOTHESIS: Of all candidates for EECP (patients with drug-refractory angina without possibility of revascularization), the majority either have contraindications or have practical problems complying with the time demands that this therapy imposes. In the rest, EECP leads to satisfactory results.

METHODS: During 18 months, every consecutive patient with angina despite medical and interventional therapy was evaluated for EECP at one center. Treated patients underwent a bicycle exercise test and perfusion imaging before and after the standard course of 35 h of EECP. In addition, patients were asked about frequency of angina and nitroglycerin usage before and after EECP, and all patients filled out a final questionnaire 1 year after the end of therapy.

RESULTS: Overall, 48 patients were considered candidates for EECP. Of these, 24 were excluded for medical reasons: poor ejection fraction (4), peripheral artery disease (4), anticoagulation (4), and atrial fibrillation (3). Eight further patients declined EECP for lack of time or accommodation. Another 3 of the 16 remaining patients dropped out because of side effects. In the 13 patients who finished the treatment course, weekly anginal episodes were reduced by 48% ($p < 0.05$), on-demand nitroglycerin puffs were reduced by 51% ($p < 0.05$), work capacity was improved by 22% ($p < 0.05$), and the number of reversible perfusion defects in perfusion scans decreased nonsignificantly (-28%). However, 4 of 13 treated patients determined 1 year later that the detriment of loss of time exceeded the benefits of EECP.

CONCLUSION: Similar to previous reports, our study confirms the reduction of angina and improvement of work capacity after EECP. However, using established contraindications, approximately two-thirds of patients considered to be candidates had to be excluded, and one-third of the treated patients regarded EECP therapy retrospectively as too time consuming.

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