ESMR

Extracorporeal Shockwave Myocardial Revascularization

Compendium of selected clinical trials based on ESMR therapy

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Extracorporeal shockwave myocardial revascularization improves clinical symptoms and left ventricular function in patients with refractory angina

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Abstract

Background: Medical therapy for refractory angina is limited and the prognosis is poor. Experimental data suggest that the use of extracorporeal shockwave myocardial revascularization (ESMR) can contribute to angiogenesis and improve symptoms of angina and left ventricular (LV) function. The objective of this study was to examine the effects of ESMR on clinical symptoms as well as LV function as assessed by cardiac MRI in patients with refractory angina.

Methods: Patients with Canadian Cardiovascular Society (CCS) class III–IV angina despite medical therapy and ischemia documented on thallium or echo-dobutamine were eligible for the study. ESMR therapy was applied with a commercially available cardiac shockwave generator system under echocardiographic guidance. LV function was assessed before and 6 months after therapy by cardiac MRI.

Results: Twenty patients (four women, 16 men; mean age 64 years, range 45–83) were included in the study. The CCS class after treatment improved in all patients (16 patients angina pectoris CCS from III to II and four patients from IV to III). The use of sublingual nitroglycerin was significantly reduced as well. There was a significant improvement in LV ejection fraction as assessed by blinded MRI following therapy in the overall population (51 vs. 59%, \( P < 0.05 \)).

Conclusion: This study demonstrates the potential efficacy of ESMR for the treatment of refractory angina pectoris. The patients showed both a significant clinical response as well as improved LV ejection fraction on serial MRI imaging. Larger studies are needed to adequately define the clinical utility of this novel therapy.

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Initial Clinical Experience with Extracorporeal Shock Wave Therapy in Treatment of Ischemic Heart Failure

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Previous experimental studies have suggested a beneficial effect of extracorporeal shock wave therapy (ESWT) in patients with ischemic heart failure. Twenty-four patients with ischemic heart failure and left ventricular ejection fraction (LVEF) <40% received ESWT in addition to their stable treatment. ESWT was performed in 9 sessions with 100 shocks per spot in viable segments detected by dobutamine stress echocardiography. Patients were evaluated at baseline and at 3 and 6 months after ESWT. Tc-99m MIBI single photon emission computed tomography was performed on inclusion and at 6 months. ESWT significantly decreased New York Heart Association class from 2.2±0.8 to 1.7±0.7 at 3 months (P<.01) and 6 months after ESWT (1.7±0.7). Six-minute walk test improved from 414±141 to 509±141 and 538±116 (P<.01) at 3 and 6 months, respectively. A steady decrease of Canadian Cardiovascular Society angina class from 2.6±0.7 to 2.1±0.8 and 1.9±0.7 (P<.01) at 3 and 6 months, respectively, was observed. A significant increase in LVEF at rest at 3 and 6 months after ESWT (from 32.2±6.0 to 34.8±9.6 and 37.7±9.5, P=.03, respectively) was noted. Summed rest score (from 23.9±8.1 to 21.4±7.1, P=.03) and stress score improvement (from 28.2±8.4 to 24.6±6.4, P=.04) by single photon emission computed tomography was registered. Significant clinical improvement accompanied by beneficial changes of LVEF and rest/stress perfusion was found after ESWT.

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O280 - Extracorporeal shockwave myocardial revascularization (ESMR) therapy: a novel therapy for refractory angina

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Introduction: With improvement in cardiovascular care, there is a rapidly growing group of patients who remain severely disabled by symptoms of myocardial ischaemia but yet not amenable to conventional revascularization therapy. ESMR is a shockwave therapy given to the area of ischaemic myocardium which theoretically induces angiogenesis and hence improvement in myocardial perfusion and clinical symptoms.

Objectives: To analyse the effect of ESMR in patients with refractory angina in improving angina symptoms and myocardial perfusion.

Methods: Sixteen patients (81% with three vessels disease and 19% with two vessels disease) who fulfill these inclusion criteria:
1. Patient with refractory angina
2. Presence of angina which cannot be controlled by medical therapy, percutaneous coronary intervention or coronary artery bypass graft surgery
3. Patients with Canadian Cardiovascular Society angina class II to IV
4. Proven reversible myocardial ischaemia as shown by SPECT
5. Patient was declined PCI or CABG by the attending cardiologist or surgeon were recruited and treated with ESMR 3 sessions per week for 3 cycles at intervals of three weeks. Each patient had total of nine sessions with 500 shocks in each session. They were assessed clinically using CCS angina class, Seattle Angina Questionnaire, exercise tolerance test and myocardial perfusion.

Results: There were significant improvement in CCS angina class (p-value = 0.001), angina symptoms based on SAQ (p-value = 0.023) and decreased in nitroglycerin usage (p-value = 0.024). An increased in the duration of exercise stress test was demonstrated (7.47 vs 9.85 minutes, p-value < 0.0001) and correlated with an improvement in METS (4.88 vs 6.12, p-value < 0.0001). There was also improvement in mean defect extent score at stress on SPECT, pre and 3 months post ESMR treatment, 29.36 ± 9.75% and 24.63 ± 11.26% (p-value = 0.021) respectively.

Conclusion: We observed an overall improvement in both clinical symptoms and myocardial perfusion after ESMR therapy. This exciting novel therapy offers new hope in symptomatic CAD patients not amenable to conventional therapy.

References:

Disclosure of Interest: None Declared
P025 - Extracorporeal shockwave myocardial reperfusion (ESMR) therapy improves left ventricular dyssynchrony

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Introduction: Left ventricular (LV) dyssynchrony is frequently observed in patients with ischaemic myocardium and is recognized as an adverse predictor of clinical outcome. ESMR on the other hand, is a novel therapy for refractory angina in patients with severe coronary artery disease not amenable for conventional revascularization therapy (CABG or PCI). ESMR induces angiogenesis in the area of ischaemic myocardium which later translates into improvement in clinical angina symptoms.

Objectives: The objective of this study is to analyse the impact of ESMR on LV dyssynchrony in patients with severe coronary artery disease.

Methods: We examined 20 consecutive patients with refractory angina due to severe coronary artery disease which is deemed unsuitable for conventional revascularization. Echocardiography with tissue Doppler study was performed for all patients before undergoing ESMR therapy of 9 weeks duration and was repeated again 3 months after completion of ESMR therapy. The degree of left ventricular dyssynchrony was expressed as Yu index. Comparison of pre and post ESMR LV dyssynchrony was then compared using paired t-test.

Results: Pre and post ESMR LV dyssynchrony in all 20 patients was 30.9 +/- 19 (pre) vs 26.9 +/- 11.5 (post), P-value = 0.385. However, comparative analysis of patients with initial (pre-ESMR) LV dyssynchrony with Yu index of 32 or more revealed pre and post ESMR mean values of 42.8 +/- 15.6 (pre) vs 26.4 +/- 8.6 (post), P value = 0.008.

Conclusion: Our study suggests a potential beneficial effect of ESMR therapy in improving LV dyssynchrony in a sub-set of patients (Yu index of more than 32) with severe coronary artery disease not amenable for conventional revascularisation. Further study is warranted to gather more evidence in supporting this finding.


Disclosure of Interest: None Declared
A new treatment for patients with refractory angina: extracorporeal shockwave myocardial revascularization (ESMR)

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Citation:
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Purpose: For treating the coronary artery disease (CAD) we have three options so far: coronary angioplasty (PCI), surgery (CABG) and antianginal drugs. The Extracorporeal Shockwave Myocardial Revascularization (ESMR) can be a reliable toll to treat those hopeless patients.

Methods: We treated 15 patients with severe symptomatic CAD, rejected by the PCI and/or CABG treatments, mean age (71±5.6), 3 female (20%) and 12 male (80%) by ESMR (3 times a week at intervals of four weeks for a total of 3 months, nine treatments patient in total). Before this treatment we have carefully localized ischemic or hibernating segments responsible for the symptoms of patients. After six months of treatment we have carefully analyzed the segmental perfusion by myocardial scintigraphy (SPECT) and segmental and global systolic function by echo. The perfusion was assessed by SPECT, analyzing the global perfusion at rest (SSS; summed stress score;) and stress (SRS; summed rest score;) before and after treatment. At 1,3,6,12 months after we evaluated the presence of angina (CCS class) and the use of nitroglycerin (NP).

Results: The ESMR therapy has led to an improvement of symptoms to Canadian Cardiovascular Society (CCS), average from 2.8 to 1.27 at 12 months, P<0.0001) and reduced the use of nitroglycerin and hospitalization (p<0.001). Number of of akinetic segments was reduced from 11.5% to 6%
(p=0.03). The perfusion evaluated by SPECT has improved statistically significant: SRS average was reduced from 14.4 to 6.55 (p=0.0045), while SSS was reduced from 21.1 to 12 (p=0.006). None patients had any damage or discomfort.

**Conclusions:** Our data, even if preliminary and limited, document a definite improvement in term of perfusion, function and clinical benefit, in a very difficult subset of patients.
Extracorporeal shock wave therapy reverses ischemia-related left ventricular dysfunction and remodeling: molecular-cellular and functional assessment

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European Heart Journal ( 2011 ) 32 ( Abstract Supplement ), 455

Objectives: An optimal treatment for patients with diffuse obstructive arterial disease unsuitable for catheter-based or surgical intervention is still pending. This study tested the hypothesis that extracorporeal shock wave (ECSW) therapy may be a therapeutic alternative under such clinical situation.

Methods: Myocardial ischemia was induced in male mini-pigs through applying an ameroid constrictor over mid-left anterior descending artery (LAD). Twelve mini-pigs were equally randomized into group 1 (Constrictor over LAD only) and group 2 [Constrictor over LAD plus ECSW (800 impulses at 0.09 mJ/mm²) once 3 months after the procedure].

Results: The parameters measured by echocardiography did not differ between two groups on days 0 and 90. However, echocardiography and left ventricular (LV) angiography showed higher LV ejection fraction and lower LV end-systolic dimension and volume in group 2 on day 180 (p<0.035). Besides, mRNA and protein expressions of CXCR4 and SDF-1α were increased in group 2 (p<0.04). Immunofluorescence staining also showed higher number of vWF-, CD31-, SDF-1α, and CXCR4-positive cells in group 2 (all p<0.04). Moreover, immunohistochemical staining showed notably higher vessel density but lower mean fibrosis area, number of CD40-positive cells and apoptotic nuclei in group 2 (all p<0.045). Mitochondrial protein expression of oxidative stress was lower, whereas cytochrome-C was higher in group 2 (all p<0.03). Furthermore, mRNA expressions of MMP-9, Bax and caspase-3 were lower, whereas Bcl-2, eNOS, VEGF and PGC-1α were higher in group 2 (all p<0.01).

Conclusion: ECSW therapy effectively reversed ischemia-elicited LV dysfunction and remodeling through enhancing angiogenesis and attenuating inflammation and oxidative stress.
Extracorporeal cardiac shockwave therapy in severe coronary artery disease unsuitable for percutaneous coronary intervention (PCI) and coronary artery bypass surgery (CABG): A single center experience.

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Materials of the 13th International Congress of the ISMST, June 24th-26th, 2010

Introduction: To test the effectiveness and feasibility of extracorporeal cardiac shockwave(SW) therapy in patients(pts) with severe coronary artery disease (CAD) unsuitable for revascularization.

Methods: Extracorporeal SW is performed with the application of 100 shocks/spot at 0.09mJ/mm2 energy flux density for 3-6 spots each time, with three times per week at each series for three series at 1, 5, 9 weeks. The location and depth of SW application are based on thallium scan findings guided by echocardiography. The following parameters will be evaluated including symptoms of angina and needs of nitroglycerine use. The exercise tolerance and dipyridamole thallium 201 myocardial perfusion scan and echocardiography will be followed up after 6 months of initial therapy.

Results: This study included 27 pts, 18 males and 9 females with mean age of 70 + 9 (50-89) yrs old. 14 pts had DM, 7 had CVA, 7 had previous CABG, 15 had old MI. 25 pts had triple vessel disease and 2 had two vessel disease. Each patient received 1200 to 5200 shocks (3881 + 935) respectively during the whole course of therapy. One patient did not complete the study due to recurrent CVA. Among the remaining 26 pts, 11 pts could perform treadmill exercise test, the maximal exercise duration increased from 248 to 319 second (P=0.007). 21 of 26 (80%) pts showed improvement of reversible ischemia by follow up thallium scan. Two patients received coronary angiography and coronary artery showed new neovascularization after SW therapy.

Discussion: Extracorporeal cardiac SW therapy can ameliorate myocardial ischemia detected by thallium 201 myocardial perfusion scan and improve symptoms of angina.
Conclusion: Extracorporeal cardiac SW is feasible and effective in patients with CAD unsuitable for PCI and CABG.
ECHO-GUIDED EXTRACORPOREAL SHOCK WAVE THERAPY FOR REFRACTORY ANGINA IMPROVES REGIONAL MYOCARDIAL BLOOD FLOW AS ASSESSED BY PET IMAGING

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Background: Low-intensity shock wave (SW) therapy (SWT) has been shown to improve symptoms and exercise tolerance in patients (pts.) with coronary artery disease (CAD). Induction of neovascularization and improvement of myocardial perfusion are mechanisms suspected in this context.

Methods: 16 pts. with advanced CAD (mean age 66±10 years) not suitable for revascularization who were suffering from severe chronic angina pectoris (CCS class III or IV) refractory to individually optimized medical treatment underwent a series of 9 echocardiography-targeted SW applications (3 sessions per week; weeks 1, 5, and 9). The antero-septal wall (LAD territory) was targeted in 9, the lateral wall (RCX territory) in 5, and the inferior wall (RCA territory) in 2 patients. A series of 300-500 shocks was applied per session. Anti-anginal medication (combination of 2 or 3 drugs) was kept unchanged. Regional myocardial blood flow (MBF) and coronary flow reserve was measured quantitatively by NH3-PET at baseline and 4 weeks after completion of SWT.

Results: At follow-up, 14 pts. (88%) reported improvement of angina to a tolerable level. CCS angina class decreased from 3.1±0.7 to 2.4±0.6 (p=0.0004). Maximum ergometric workload increased from 80±45 to 90±39 watts (p=0.04), the double product (heart rate x systolic blood pressure) from 14676±4400 to 16460±5006 (p=0.2). MBF in the LV region targeted by SWT improved from 95±30 mL/min/100g at baseline to 114±50 mL/min/100g at follow up (p=0.04), while there was no change in the opposite wall (115±45 vs. 113±48 ml/min/100g; p=0.9).
Conclusions: SWT improves symptoms in patients with chronic refractory angina pectoris. Regional improvement of MBF in the region targeted by SWT was also documented by PET.
Investigation into the effectiveness of shock wave treatment for angina pectoris patients post-bypass surgery

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Citation:

Background: The effectiveness of shock wave based, angiogenesis therapy for patients with ischemic disease has been confirmed in basic experimentation, yet effectiveness in a clinical setting is yet to be fully clarified. Therefore, an investigation was undertaken to determine the effectiveness of shock wave treatment for post-bypass ischemic patients, given that patients that are no longer suitable for coronary intervention or a further bypass procedure.

Method: Target population consisted of 17 patients with ischemia post-bypass surgery. All patients underwent angiography to confirm whether coronary catheter intervention or further bypass procedures were no longer appropriate treatment options. Heart muscle scintigrams were performed in order to focus treatment on ischemic patients with viable blood vessels. The ischemic area was identified by scintigram and with three to five ischemic points selected for treatment a Cardiospec unit was used to deliver 100 shocks per location. Three treatments were performed per week, every four weeks for a total of nine treatments. A scintigram was performed at 1 and 3 month follow-up.

Results: All 17 patients underwent shock wave treatment. No CK, troponin elevations, arrhythmia or other side-effects were observed. Eleven patients had a previous myocardial infarction and 6 other patients presented with angina pectoris. Ten of the 17 patients observed an improvement in symptoms, with no changes in the remaining patients and none observing deterioration in condition. There was no significant change to scintigram
results at 1 month follow-up for the 17 patients. At 3 month follow-up, 3 patients showed significant improvement in myocardium blood flow at rest, however there was no improvement in ischemia during exercise. All ischemic improvements determined by scintigram were exclusive of patients with myocardial infarctions, with no efficacy determined for ischemic area from prior myocardial infarctions. Five patients displayed a significant increase in VEGF one hour post shock wave treatment when measured peripheral blood.

**Conclusion:** Although improvements in symptoms for a number of patients through use of shock wave angiogenesis therapy were observed, it is necessary to exclude patients with myocardial infarction. Furthermore, a number of cases determined an increase in VEGF following shock wave treatment, and this is considered to be one of the mechanisms associated with angiogenesis.
Safety and efficacy of extracorporeal low energy shockwave application for the treatment of refractory angina pectoris and myocardial ischemia in patients with end-stage coronary artery disease

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Presented at European Cardiology Society Congress, September 2008
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Background:

The number of patients with end stage coronary artery disease increases rapidly due to improved techniques in bypass surgery and interventional cardiology. Myocardial ischemia in these patients often leads to refractory angina, a status of disease which can be treated clinically only with limited success so far. Experimental data indicates, that the application of low energy shockwaves may stimulate the release of nitric oxide and induce angionegensis. The following study was conducted to investigate the effects of percutaneous myocardial, low-energy shockwave application in a prospective cohort of patients with end-stage CAD and refractory angina pectoris.

Methods:

24 patients with end stage coronary artery disease, SPECT documented reversible ischemia, and refractory angina were treated using a shock wave generator system (Cardiospec, Medispec, USA) designed to address the clinical-anatomical requirements of the chest cavity under transthoracic echo guidance. About 300 impulses were applied to the ischemic areas using
energy level of 0.09 mJ/mm². This treatment was repeated three times a week on the first week of each month, for three months.

**Results:**

Clinical results showed a significant symptomatic improvement regarding CCS class (3.2 ± 0.8 t baseline vs. 2.2 ± 0.1 at 6-months follow up; p<0.0001), Seattle Angina Questionnaire (mean improvement by 32.6%; p=0.002) and exercise capacity (66.6 ± 6.8 watt at baseline vs. 95.8 ± 5 watt at 6-months follow up; p<0.025). Blinded SPECT analysis demonstrated that myocardial perfusion at stress and at rest was improved significantly at 6-months follow up versus baseline (p<0.001). Therapy was well tolerated by all patients. No side effects and no rise of cardiac enzymes were observed.

**Conclusions:** The present study shows that the extracorporeal application of low intensity shockwaves to the ischemic myocardium in patients with advanced CAD is safe and feasible. In our cohort, low energy shockwaves improved symptoms, delayed ischemic threshold, and increased myocardial perfusion in these end stage patients.