About 5.8 million people in the United States have heart failure, with 670,000 new diagnoses each year. Heart failure is associated with both a high level of mortality and cost burden on the health care system.\(^1\) Left ventricular ejection fraction (LVEF) is one of the most important predictors of prognosis, with a substantial increase in mortality when \(<40\%\).\(^2\)

Rahimtoola\(^3\) was the first to show that many patients with left ventricular dysfunction exhibit improvement of ventricular function after revascularization. To explain the improvement in function, the concept of dysfunctional but viable myocardium with the potential to recover function after revascularization was introduced. Viable myocardium has different characteristics, and these form the basis for the different imaging modalities that are most frequently used for the assessment of myocardial viability.\(^4\) Cell membrane integrity and mitochondrial function is evaluated by \(^{201}\)Tl and \(^{99m}\)Tc-labeled tracer single photon emission computed tomography (SPECT), respectively, preserved glucose metabolism with \(^{18}\)F-FDG positron emission tomography, and contractile reserve with dobutamine stress echocardiography. To date, there is no agreement for indication of surgical revascularization in patients with viable myocardium and heart failure.\(^5\) Despite possible symptomatic relief and cardiac function improvement, surgical treatment is limited in heart failure patients due to a high incidence of major adverse events.\(^6\) Extracorporeal shock wave therapy (ESWT) is a new, noninvasive, angiogenesis-based option in patients with refractory angina pectoris.\(^7\)\(^-\)\(^9\) Shock wave therapy has been used for decades in urology for lithotripsy. In the 1990s, the regenerative potential of shock waves was discovered.\(^10\)\(^-\)\(^12\) Despite that exact mechanism of shock wave–induced angiogenesis is unknown, it is thought to be mediated through increased production of vascular endothelial growth factor and eNOS activation.\(^13\)\(^,\)\(^14\) Taking into account a previous experimental study, we suggest a beneficial effect of ESWT in patients with ischemic heart failure.\(^15\)

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 evaluated at baseline and at 3 and 6 months after ESWT. \(^{99m}\)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\pm0.8 to 1.7\pm0.7 at 3 months (\(P<.01\)) and 6 months after ESWT (1.7\pm0.7). Six-minute walk test improved from 414\pm141 to 509\pm141 and 538\pm116 (\(P<.01\)) at 3 and 6 months, respectively. A steady decrease of Canadian Cardiovascular Society angina class from 2.6\pm0.7 to 2.1\pm0.8 and 1.9\pm0.7 (\(P<.01\)) 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\pm6.0 to 34.8\pm9.6 and 37.7\pm9.5, \(P=.03\), respectively) was noted. Summed rest score (from 23.9\pm8.1 to 21.4\pm7.1, \(P=.03\)) and stress score improvement (from 28.2\pm8.4 to 24.6\pm6.4, \(P=.04\)) 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. Congest Heart Fail. ****;***;**;*.

Yury A. Vasyuk, MD; Alla B. Hadzegova, MD; Evgeny L. Shkolnik, MD; Maya V. Kopeleva, MD; Olga V. Krikunova, MD; Elena N. Iouchtcchouk, MD; Elena M. Aronova, MD; Svetlana V. Ivanova, MD

From the Department of Functional Methods in Internal Medicine, Moscow State University of Medicine and Dentistry, Moscow; and the Nuclear Medicine Department, Prof. A.A. Ostroumov City Hospital 33, Moscow, Russian Federation

Address for correspondence:
Evgeny L. Shkolnik, MD, Moscow State University of Medicine and Dentistry, Department of Functional Methods in Internal Medicine, ul. Delegatskaya 20/1, 127473, Moscow, Russian Federation
E-mail: eshkolnik@mail.ru

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Methods
The ethics committee of Moscow State University of Medicine and Dentistry approved the study protocol and an informed consent form was signed by the patients.

Twenty-four stable patients (20 men; mean age, 63.3\pm6.1 years) with ischemic heart failure due to documented acute myocardial infarction (at least 6 months before inclusion) and systolic dysfunction (LVEF \(<40\%\) calculated by...
echocardiography blipane Simpson method) and no planned revascularization in 6 months were included in the study. Twelve patients (50.0%) had recurrent myocardial infarction in history. Two patients had previously undergone percutaneous coronary intervention. The mean duration of heart failure was 6.0 years (interquartile range, 3.0–12.0). Three patients were in New York Heart Association (NYHA) class I, 13 in class II, 7 in class III, and 1 in class IV. The mean duration of angina was 7.0 years (interquartile range, 4.0–12.0). One patient had no angina, one was in Canadian Cardiovascular Society (CCS) class I, 8 in class II, 11 in class III, and 3 in class IV. All patients received optimal stable treatment for heart failure including angiotensin-converting enzyme inhibitors (24; 100%), β-blockers (23; 95.8%), aspirin (22; 91.7%), statins (13; 54.2%), prolonged nitrates (15; 62.5%), and diuretics (14; 58.3%) for at least 3 months.

The patients were evaluated at baseline and at 3 and 6 months with a clinical examination, quality of life assessment (Minnesota Living With Heart Failure [MLHF]), 6-minute walk test, and echocardiography.

Echocardiography was performed on a Vivid 7 (GE Vingmed, Horten, Norway). The images were stored digitally and analyzed offline by a single experienced observer. For the assessment of ejection fraction by blipane Simpson method, all images were anonymized and were evaluated in a random order by an independent blinded reviewer. To measure intraobserver variability, 10 randomly selected studies were evaluated twice.

Low-dose dobutamine stress echocardiography was performed at an initial dobutamine dose of 5 mcg/kg/min for 3 minutes, with increases to 10, 15, and 20 mcg/kg/min for 3 minutes each under continuous electrocardiographic and echocardiographic monitoring. β-Blockers were withdrawn 24 hours before the test. Hibernation was judged to be present if dysfunctional segments showed any improvement on 10 mcg/kg/min stage. In 14 patients (58%), there was evidence of viability. Others showed only ischemic response.

To assess myocardial perfusion, 99mTc-MIBI SPECT was performed at baseline and 6 months after the last ESWT treatment. The same camera (eNTEGRA, General Electric, Milwauke, WI) was used. Two-day rest-stress protocol was used with modified Bruce treadmill protocol with tracer injection on peak exercise (370 mBq). Summed stress score (SSS) and summed rest score (SRS) were calculated semi-quantitatively using a 20-segment model by a blinded observer.

ESWT was performed with Cardiospec (Medispec, Germantown, MD) in a standardized protocol of 9 sessions (with 3 sessions every other day in 1, 5, and 9 weeks) with 100 shocks per spot per session at 0.09 mj/mm² energy level in hibernated or ischemic segments detected by low-dose dobutamine stress echocardiography (ECHO). CHF indicates congestive heart failure; MLHF, Minnesota Living With Heart Failure; SPECT, single photon emission computed tomography.

**Results**

Four patients (16.6%) died during follow-up (one of recurrent myocardial infarction 4 months after the first treatment, one of recurrent myocardial infarction 5 months after the first treatment, one of sudden death 8 months after the first treatment, and one of pulmonary embolism 8 months after the
first treatment). One patient withdrew the study after the first treatment week due to the long distance to the hospital. Finally, 19 patients were examined 6 months after the last treatment.

Treatment with ESWT significantly decreased NYHA class, from 2.2±0.8 to 1.7±0.7 at 3 months (P<.01) without any worsening to 6 months after ESWT (1.7±0.7) (Figure 2a). Clinical improvement was associated with significant improvement in 6-minute walk test, from 414±14 to 509±50 and 538±14 (P<.01) at 3 and 6 months after ESWT, respectively (Figure 2b).

ESWT resulted in a steady decrease of CCS angina class from 2.6±0.7 to 2.1±0.8 and 1.9±0.7 (P<.01) at 3 and 6 months after ESWT, respectively. Significant decrease of nitroglycerin use per week was observed from 2.0 (1.0–5.0) to 1.0 (0.0–3.0) at 3 months after ESWT (P<.01). Antianginal effects lasted up to 6 months after ESWT (1.0 [0.0–2.0]).

The functional improvement of ESWT-treated patients was associated with 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=0.03], respectively) (Figure 3). Intra-observer variability was 5%.

Small but significant improvement of SRS by SPECT was observed (from 23.9±8.1 to 21.4±7.1 at 6 months after the last treatment; P=.03) (Figure 4). In patients able to exercise (modified Bruce protocol, n=12) significant improvement of SSS was registered (from 28.2±8.4 to 24.6±6.4 at 6 months after the last treatment, P=.04) despite increased exercise tolerance from 4.0±2.2 to 4.7±2.4 metabolic equivalents (P=.05).

ESWT was safe in our patients with ischemic heart failure. No adverse events were registered. Troponin T level was always negative (<0.1 ng/mL) in all patients.

**Discussion**

A high prevalence of hibernated myocardium in patients with ischemic heart failure and limited revascularization options in this population lead to unfavorable prognosis. Four patients (16.7%) died during follow-up, which is consistent with mortality in heart failure patients with viability on medical treatment (16%). Negative troponin T values during the treatment of these patients combined with clinical improvement of angina and prolonged time between start of treatment and death make the association of ESWT with death doubtful. The present study demonstrates that ESWT noninvasively improves left ventricular function and perfusion in patients with ischemic heart failure. An associated increase in LVEF and clinical improvement was observed soon after the treatment and persisted for 6 months' follow-up. To our knowledge, this is the first clinical study of ESWT in a heart failure population. A recently published experimental study of direct epicardial shock wave therapy showed marked improvement of LVEF and decline of N-terminal prohormone B-type natriuretic peptide in a rat model of chronic heart failure. Authors were able to confirm up-regulation of vascular endothelial growth factor and ESWT-induced angiogenesis in heart failure, similar to previous clinical and animal studies in stable angina. However, direct epicardial shock wave therapy can be used only in combination with coronary artery bypass grafting due to low penetration depth of unfocused shock wave therapy in treatment of ischemic heart failure

![Figure 2](https://via.placeholder.com/150)

**Figure 2.** Clinical improvement: Extracorporeal shock wave therapy significantly improved New York Heart Association class (A) and 6-minute walk test distance (B). *P<.01 vs baseline.

![Figure 3](https://via.placeholder.com/150)

**Figure 3.** Left ventricular function: Extracorporeal shock wave therapy was associated with a significant and stable increase in left ventricular ejection fraction (LVEF). *P=.03 vs baseline.
Baseline: SSS = 27; SRS = 24

6 months: SSS = 19; SRS = 16

Figure 4. Typical single photon emission computed polar maps of the patient M: Marked improvement of summed stress score (SSS) and summed rest score (SRS) was observed despite increase of exercise tolerance from 2.0 to 3.4 metabolic equivalents. Treated area is shown with red line.

shock waves. The higher energies of shock waves used in this study require additional safety confirmation. Energy levels used in our study were safe and did not produce any damage to myocardium (confirmed by negative troponin T). Similar to other studies in refractory angina, our shock wave therapy produced marked improvement in 6-minute walk test and treadmill exercise tolerance. Significant improvement of SPECT stress and rest perfusion confirms an angiogenesis-based mechanism of ESWT in chronic heart failure, as it was shown in several clinical studies before.7,8

Limitations
This study included a limited number of patients. Due to its exploratory nature, this study did not have a placebo arm and was not designed for assessment of the long-term safety of ESWT. Early clinical and functional improvement confirmed objectively by echocardiography and SPECT was stable for 6 months after ESWT. However, a properly powered randomized controlled trial is needed to confirm beneficial effects of ESWT in ischemic heart failure.

Conclusions
Significant clinical improvement, accompanied by beneficial changes of LVEF and rest/stress perfusion, was found after ESWT. In this small trial, ESWT was effective in patients with ischemic heart failure and systolic dysfunction. If safety and efficacy are confirmed in a larger randomized controlled trial, ESWT may become effective addition to traditional treatment of ischemic heart failure.

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