VILNIUS UNIVERSITY

Gitana Zuozienė

EVALUATION OF MYOCARDIUM REVASCULARISATION BY CARDIAC SHOCK WAVE THERAPY APPLYING MULTIMODAL IMAGE ANALYSIS

Summary of the Doctoral Dissertation

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VILNIAUS UNIVERSITETAS

Gitana Zuozienė

MIOKARDO REVASKULIARIZACIJOS, TAIKANT SMŪGINĖS BANGOS TERAPIJĄ, EFEKTYVUMO VERTINIMAS DAUGIALYPĖS (MULTIMODALIOS) VAIZDINĖS DIAGNOSTIKOS METODAIS

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CONTENTS

LIST OF ABBREVIATIONS

ACC	American College of Cardiology
AHA	American Heart Association
CABG	coronary artery bypass graft surgery
CCS	Canadian Cardiovascular Society
CSWT	cardiac shock wave therapy
CVD	cardiovascular disease
DST	dobutamine stress test
ECG	electrocardiography
EF	ejection fraction
EDV	end-diastolic volume
ESV	end-systolic volume
HMRI	heart magnetic resonance imaging
IHD	ischemic heart disease
LV	left ventricle
LVEF	left ventricular ejection fraction
MPRCT	myocardium perfusion radionuclide computer tomography
MI	myocardial infarction
NYHA	New York Heart Association
PCI	percutaneous coronary intervention
SV	stroke volume
TID	transient ischemic dilation
WMSI	wall motion score index

INTRODUCTION

Relevance of the issue being studied

Ischemic heart disease (IHD) is one of the leading causes of morbidity and mortality worldwide.

The structure of the causes of mortality among Lithuanian citizens tends to stay unchanged for many years. Three main causes of mortality are cardiovascular diseases (CVD), malignant tumours and external causes of death. More than half of deaths, i.e. 56.1%, were caused by IHD in 2010, in the same year malignancies accounted for 19.3%, and external causes of death – 9.6% of all deaths. Cardiovascular diseases were and still remain the main cause of death among people in Lithuania and other EU countries. The standardised IHD mortality rate in Lithuania in 2009 was one of the highest in the EU (the situation was worse in Romania and Bulgaria only). Based on data from the Statistics Department, 23627 cardiovascular deaths were reported in Lithuania in 2010 (56.1% of all deaths).

Such a situation encourages the seeking of expedient treatment for IHD.

Along with medical treatment currently there are two main methods of coronary revascularisation – percutaneous coronary intervention (PCI) and aortocoronary bypass surgery (ACBS).

New heart revascularisation methods are under development, which are to be applied for routine practice in the future. One of the methods stimulating angiogenesis is cardiac shock wave therapy (CSWT).

CSWT is a new reconstructive/regeneration treatment method offering an alternative to revascularisation, as the use of steam cells for such purposes is still at the trial stage. Low frequency mechanical waves are used for CSWT. Their effect results in improved heart perfusion and the development of blood vessels' network. Such waves were first applied in medicine about 20 years ago for renal stones fragmentation.

This treatment method has been recently applied in clinics worldwide with only a few of them obtaining some experience in this area.

CSWT, along with medical and invasive treatment methods for patients with severely advanced ischemic heart disease, was introduced in the Santariškių Clinics of Vilnius University Hospital in 2008.

STUDY OBJECTIVE

Optimisation of protocol for myocardium revascularisation by cardiac shock wave therapy, an evaluation of the efficacy and safety of the method, justified both by clinical and objective criteria of multimodal image analysis for the patients with severely advanced ischemic heart disease and frequent angina pectoris.

STUDY TASKS

1. To evaluate the characteristics of clinical stable angina pectoris before and after treatment.
2. Applying heart magnetic resonance imaging to evaluate injection fraction of the left ventricle, volumes of the left ventricle, and outspread and thickness of scar before and after treatment.
3. To evaluate myocardium viability before and after treatment, applying dobutamine echocardiographic examination.
4. To evaluate myocardial reserve before and after treatment, applying myocardium perfusion examination by radionuclide computer tomography imaging.
5. To evaluate the efficacy of cardiac shock wave therapy in patients of different age groups as well as the correlation with the severity of underlying pathology before treatment.
6. To evaluate the effect of cardiac shock wave therapy on arterial blood pressure.
7. To carry out complex evaluations of the informativeness of new heart image diagnostic methods applied to establish the efficacy of regeneration therapy by cardiac shock wave therapy.

RESEARCH SIGNIFICANCE AND NOVELTY

1. The cardiac shock wave therapy method has been introduced and studied in the Santariškių Clinics of Vilnius University Hospital for the first time not only in Lithuania, but also in the Baltic States, and earlier than in many European countries.
2. Data about small groups of patients (8-25 persons) have been reported in international medical publications. It has been constantly emphasised in the authors' conclusions that further studies involving larger study populations should be carried out to confirm the results of the available studies. We have examined 40 patients. This was one of biggest study population with the highest reliability of data.
3. Heart magnetic resonance imaging, currently considered as a golden standard for heart muscle alteration evaluation, was applied for the first time to evaluate the condition before and after CSWT. Our data are presented together with data of heart magnetic resonance imaging.
4. This was the biggest study group examined by echocardiographic dobutamine stress test before and after CSWT.
5. Optimal algorithm for patients' evaluation before and after cardiac shock wave therapy and its efficacy was developed on the bases of study results and justified by multimodal image analysis; this algorithm has already been introduced in the Santariškių Clinics of Vilnius University Hospital. Patients to whom this treatment method is most beneficial were defined applying this algorithm.
6. New opportunities to expand indications for this treatment have been enclosed.

DEFENSIVE STATEMENTS

1. Cardiac shock wave therapy is a new non-invasive method of regeneration therapy controlled by visual diagnostic means for the treatment of end-stage ischemic heart disease.
2. Cardiac shock wave therapy is an effective and safe treatment method for end-stage ischemic heart disease.
3. The efficacy or this method can be evaluated by the objective criteria of heart image analysis.
4. The efficacy of this method has been justified by the evaluation of complex image analysis criteria.

STUDY POPULATION AND STUDY METHODS

Study population

Cardiac shock wave therapy was applied for the patients diagnosed with end-stage ischemic heart disease, angina pectoris, class III-IV according to the classification of Canadian Cardiovascular Society, with three-vessel coronary disease, in some cases with stenosis of the main trunk of the left coronary artery.

Percutaneous coronary intervention and stent implantation procedures were carried out for the patients being studied along with aortocoronary bypass surgery and maximal tolerated doses of nitrates were prescribed for permanently reoccurring angina pectoris (AP). Episodes of angina pectoris in such circumstances reoccurred several times per day during minimal physical load or even at rest.

Participation in the study was offered to patients who were having their consultations at the Outpatient Cardiology Section of the Santariškių Clinics of Vilnius University Hospital, diagnosed with angina pectoris, III-IV class according to the classification of the Canadian Cardiovascular Society (CCS). Patients above 18 years old of both genders were enrolled into the study after giving consent to participate in the study and signing a Subject's Information and Informed Consent Form.

45 patients were selected for CSWT. Coronarography was carried out for these patients before treatment and based on the results of poor distal segments of coronary arteries, inactive bypasses and also obturated blood vessels with implanted stents were identified. Repeated revascularisation was contraindicated for the screened patients, however ejection fraction of the left ventricle was good or moderately reduced (up to 40%). To evaluate the vitality of myocardium an echocardiographic dobutamine stress test (DST) was carried out for all patients before and after treatment; heart magnetic resonance imaging (HMRI) was carried out to evaluate the thickness of scar and myocardium perfusion radionuclide; computer tomography imaging (MPRCT) with adenosine stress test was performed to discover any myocardial defects.

Course and technique of cardiac shock wave therapy

The study was carried out in the Cardiology and Angiology Centre of Santariškių Clinics of Vilnius University Hospital during the period 2008–2013. This was the first time that CSWT was introduced in the Baltic States.

Study inclusion criteria

1. Males and females patients.
2. Above 18 years old.
3. Patients with coronary artery disease.
4. Angina pectoris, class III-IV.
5. Sufficient ejection fraction of the left ventricle (40% and above).
6. Thickness of scar of the left ventricle based on MRI findings less than 50% of the wall.
7. Sinus rhythm of heart.
8. Medical history of MI and ACBS at least 3 months prior.
9. Angioplasty at least 6 months prior.
10. Weekly attacks of angina pectoris during the previous three months.
11. 3 attacks of angina pectoris per week during the previous 2 weeks.

Study exclusion criteria

1. Unstable angina pectoris.

2. Thrombi in heart cameras.

3. Significant pathological alteration of valves, mechanical valve endoprosthesis.

4. Severely advanced lung disease (emphysema).

5. Cardiopathy of non-ischemic origin.

6. Severe arterial hypertension.

7. Severe condition of the patient (cardiogenic shock or uncontrolled heart failure [HF]).

8. Arrhythmias

9. Malignancy

10. Heart transplantation

11. Pregnancy

12. Poorly controlled diabetic retinopathy

13. General contraindications to carry out dobutamine and MRI studies

14. Use of anticoagulants (warfarin)

15. Patients not able/not willing to sign the consent form

16. Patients not complying with study requirements

17. Breast implants (silicone).

CARDIAC SHOCK WAVE SYSTEM DESCRIPTION

The generation of the shock wave is based on the electrohydraulic principle. An external source of waves generates a high acoustic wave which is transferred through a rubber membrane is placed on the patient's chest and focused to the predetermined heart areas. As a result of the acoustic shock wave action, a therapeutic effect occurs in predetermined zones of myocardium, however the surrounding tissues remain intact. The system "Cardiospec" enables the exact targeting of the wave to predetermined ischemic zones of myocardium. Shock wave therapy stimulates the production of angiogenesis factors, also known as "therapeutic angiogenesis", which stimulate the growth of new myocardial blood vessels.

The wave is directed to the required cardiac zone by means of a two-dimensional echoscope and cardiac sensor. Impulses of the shock wave are synchronised with the R wave of the patient's electrocardiogram.

Description of procedure

First the patient stripped to the waist, then he (she) laid down on his (her) back and electrodes of standard ECG leads were attached.

Zones, the targets for the CSWT, were visible by echoscope. A square of a single zone was 1 square centimetre. Not more than 5 such zones were allowed in the left ventricle. 100 impulses were allowed to be applied to one zone during a single session. 500 impulses were sent to a patient during a single procedure.

Treatment schedule: CSWT procedures during the first week were carried every second day (on Monday, Wednesday and Friday). 5 zones were selected for the first procedure and 100 impulses for a 1 cm^2 zone were applied. An ECG was recorded before the start of the first procedure. A three week treatment-free interval was required after the first week of treatment. During Week 5, procedures were carried out every second week (5 zones, 100 impulses for each). The three week treatment-free interval was applied and procedures were repeated on Week 9 following the same schedule. A heart electrocardiogram was recorded during the last procedure.

To evaluate the effect of CSWT after a 6 month treatment period all tests were carried out again: dobutamine stress test, echocardiography, heart magnetic resonance imaging and myocardial perfusion radionuclide computer tomography test. Results of laboratory tests were also evaluated.

Statistical methods applied

The statistical software package SPSS 17.0 (*version for Windows*) was used for the data analysis. Descriptive statistics were presented in frequency tables for qualitative variables, with mean values and standard deviations for quantitative variables.

Chi-square or Fisher's exact criterion was applied to compare groups based on qualitative variable. When two groups were compared based on quantitative variable, t-criterion for independent samples or non-parametric Man-Whitney criterion was used.

When more than two groups were compared based on quantitative variable, non-parametric Kruskal-Wallis criterion was applied. Correlation of two quantitative variables was tested by calculation of Kendall rank (τ) correlation coefficients. The t-

criterion for dependent samples or the non-parametric Wilcoxon signed rank test was applied to compare quantitative variables before and after each procedure.

All p values in this study were used to check the two-sided hypotheses. The significance level was predefined as equal to 0.05.

STUDY RESULTS

To evaluate the efficacy of cardiac shock wave therapy, multimodal image analysis was chosen.

For the assessment of heart systolic function (volumes of the left ventricle, ejection fraction, stroke volume, and scar tissue transmurality) MRI was used. Echocardiographic examination with dobutamine was used to evaluate the vitality of myocardium (wall motion score index – WMSI). Total defect of myocardial perfusion was assessed using the myocardial perfusion radionuclide computer tomography method. Such complex diagnostic method of multimodal image analysis was selected based on the algorithms used in the Santariškių Clinics of Vilnius University and published data.

Demographic characteristics of the study subjects

40 patients with the disease of 3 coronary arteries with dyslipidemia being treated with cardiac shock wave therapy (CSWT) were enrolled onto the study. The age of the patients varied from 44 to 83 years (mean ± SD; 67.73 ± 9.45). 75% of the study population were males (30 patients). 30% of patients did not have clear myocardial infarction previously. 70% of study subjects had one or more myocardial infarctions (1 MI – 60%, 2 MI – 7.5%, 3 MI – 2.5%). The majority of females (90%) had a history of myocardial infarction, however MI was diagnosed in only 63.3% of males. Patients without aortocoronary bypass surgery made up 22.5% of all the population, those with one surgical intervention – 60% and with two surgeries – 17.5%. 55% of the patients were percutaneous intervention naive, those who had experienced 1 intervention – 30% and 2 – 12.5%. There was one patient with a medical history of 17 PCIs. A cardiac pacemaker was implanted in 7.5% of patients (an MRI examination for these patients was not carried out due to presence of the cardiac pacemaker). 22.5% of patients had diabetes and 95% of the study population had arterial hypertension. CCS class 3 or class

4 angina pectoris (67.5% and 32.5% respectively) was diagnosed for the patients before the CSWT.

The derivative indicator – mean arterial blood pressure (ABP) – was calculated using the following formula for a detailed analysis of the correlation between arterial blood pressure and other variables:

mean ABP = 1/3 systolic ABP + 2/3 diastolic ABP

The patients' characteristics before treatment were compared in three age groups: 64 years old and younger, 65-73 years old and 74 years old and above (Table 3).

Before the treatment the lowest amount of nitrates was consumed in the group of the youngest patients (30 tablets per week, on average), patients in the oldest age group used, on average, 3.83 tablets more and those of middle age – by 7 tablets more when compared with the younger patients. A significant statistical difference of WMSI at rest was discovered (p=0.004). Value of index was higher among older patients. WMSImax was also higher among the older patients, however a statistically significant difference was not reached. The fact that groups were more homogeneous based on this indicator could probably be explained by the inability to discover all damaged segments by WMSI at rest. The highest LV EF measured by HMRI and TID measured by MPRCT and the lowest LV EDV, LV ES, LV SV and LV SV measured by HMRI were found among patients of the middle age group. The mean ABP was highest in the group of youngest patients and decreased in the older patients. As the majority of patients were diagnosed with arterial hypertension (AH), such a decrease could be related to the longer duration of antihypertensive treatment in the older patients compared with those of a younger age and the decrease of ABP was a result of the effect of medicines.

Table 1. Characteristics of patients before CSWT in age groups

	Age <= 64 (n = 14)	Age 65-73 (n = 14)	Age >= 74 (n = 12)	p value
Age	**57.21 ± 6.6**	**69.86 ± 2.18**	**77.5 ± 2.94**	**0.001**
Nitrates tab. x week before treatment	30 ± 12.1	37 ± 9.28	33.83 ± 8.35	0.252
WMSI at rest before treatment*	**1.23 ± 0.34**	**1.58 ± 0.46**	**1.77 ± 0.39**	**0.004**
WMSI max. *	1.35 ± 0.31	1.54 ± 0.47	1.63 ± 0.45	0.352
LV EF before treatment***	52.98 ± 13.65	54.38 ± 8.59	45.4 ± 11.3	0.119
LV EDV before treatment***	137.73 ± 50.23	119.92 ± 33.87	163.3 ± 83.25	0.505
LV ESV before treatment***	74.43 ± 47.36	49.62 ± 23.6	94.5 ± 71.15	0.163
LV SV before treatment***	70.43 ± 22.61	65.31 ± 17.67	72.5 ± 31.14	0.782
TID before treatment**	1.12 ± 0.11	1.16 ± 0.13	1.15 ± 0.1	0.579
Systolic ABP before treatment	137.14 ± 13.26	135.71 ± 16.04	130.83 ± 20.21	0.670
Diastolic ABP before treatment	84.64 ± 7.96	81.07 ± 9.64	78.75 ± 8.01	0.234
Mean ABP before treatment	102.14 ± 9.21	99.29 ± 10.47	96.11 ± 11.53	0.420

Sample size in groups (respectively): *- n = 13, 14, 12; ***- n = 14, 13, 10; **- n = 12, 14, 12.

The use of nitrates has equalized after treatment in all patient groups (Table 2), although usage of nitrates remained slightly bigger ir the middle age patient group. The oldest patient group was using the lowest amount of medicines. Both WMSI at rest and maximal WMSI (dobutamine echocardiography) values remained higher for older patients. The diferrence between age groups for WMSI values at rest has reduced and difference between age groups for maximal WMSI values has increased. The best LV EF and largest LV EDV were reported in the youngest patients group and the largest LV ESV was found among the oldest patients, the highest TID remained among the patients of the middle age group. The lowest mean ABP was found among the older patients.

Table 2. Characteristics of patients after CSWT in age groups

	Age <= 64 (n = 14)	Age 65-73 (n = 14)	Age >= 74 (n = 12)	p value
Nitrates tab. x week after treatment	4.86 ± 5.25	5.29 ± 4.43	4.25 ± 3.14	0.735
WMSI at rest after treatment*	1.23 ± 0.26	1.41 ± 0.45	1.57 ± 0.39	0.098
WMSI max after treatment*	1.18 ± 0.24	1.36 ± 0.5	1.48 ± 0.36	0.067
LV EF after treatment***	59.21 ± 14.69	58.38 ± 8.88	50.6 ± 10.37	0.085
LV EDV after treatment***	166.69 ± 73.81	123.69 ± 52.25	154.8 ± 62.94	0.212
LV ESV after treatment***	79.29 ± 74.53	55 ± 34.01	84.6 ± 57.48	0.348
LV SV after treatment* **	**87.79 ± 18.74**	**65.38 ± 18.25**	**75.8 ± 25.45**	**0.019**
TID after treatment**	1.04 ± 0.1	1.12 ± 0.12	1.06 ± 0.1	0.179
Systolic ABP after treatment	133.57 ± 14.99	131.07 ± 13.89	127.5 ± 16.03	0.530
Diastolic ABP after treatment	80.71 ± 7.3	80 ± 8.77	79.17 ± 6.69	0.833
Average ABP after treatment	98.33 ± 8.84	97.02 ± 8.92	95.28 ± 8.93	0.667

Sample size in groups (respectively): *- n = 13, 14, 12; ***- n = 14, 13, 10; **- n = 12, 14, 12.

Comparison of patient data (clinical and multimodal image analysis) before and after CSWT

Aiming to discover effect of treatment, the results of the tests carried out before and after the CSWT of each age group were compared. A statistically significant difference was detected for the majority of test results (Table 3). Nitrate consumption decreased by 28.77 tablets, on average, per week ($p < 0.001$). WMSI, calculated on the basis of the echocardiographic dobutamine stress test, used to assess myocardium vitality decreased by 0.12 and WMSImax decreased by 0.16, while LV EF, assessed by heart magnetic resonance imaging increased by 5.17% and LV SV increased by 7.49 ml.

Myocardium perfusion radionuclide computer tomography study revealed a reduction of TID by 0.07 and mean ABP reduced by 2.37 mmHg.

Based on the findings of heart magnetic resonance imaging LV EDV increased by 9.99 ml and LV ESV increased by 1.05 ml, however changes of these data did not reach statistical significance.

Table 3. Comparison of patient data before and after treatment

	n	Before treatment	After treatment	p value
Nitrates tablets x per week	**40**	**33.6 ± 10.3**	**4.83 ± 4.32**	**< 0.001**
WMSI at rest	**39**	**1.52 ± 0.45**	**1.4 ± 0.39**	**< 0.001**
WMSI max.	**39**	**1.5 ± 0.42**	**1.34 ± 0.39**	**< 0.001**
LV EF	**37**	**51.42 ± 11.75**	**56.59 ± 12.04**	**< 0.001**
LV EDV	37	138.38 ± 57.64	148.37 ± 65.04	0.334
LV ESV	37	71.14 ± 50.84	72.19 ± 58.19	0.555
LV SV	**37**	**69.19 ± 23.24**	**76.68 ± 22.22**	**0.040**
TID	**38**	**1.14 ± 0.11**	**1.07 ± 0.11**	**< 0.001**
Systolic ABP	**40**	**134.75 ± 16.33**	**130.88 ± 14.76**	**0.021**
Diastolic ABP	40	81.63 ± 8.73	80 ± 7.51	0.062
Mean ABP	**40**	**99.33 ± 10.41**	**96.96 ± 8.75**	**0.012**

The use of nitrates significantly decreased in all groups. Image analysis (echocardiographic dobutamine stress test to assess vitality of myocardium) findings revealed that WMSI at rest did not reach statistical significance only in the group of the youngest patients, however mean WMSI at rest before treatment was also lowest in this group. WMSImax values changes were reported in all age groups: after treatment it was 0.15 lower, on average, among the oldest patients, and by 0.18 and 0.17 lower in the groups of middle and youngest age, respectively. Statistically significant changes of LV EF from baseline values were reported in all age groups. The LV EF increased, on average, by 4% (in the middle age group) up to 6.23% (in the group of the youngest patients). Statistically significant changes of LV EDV as well as LV SV were found in the group of youngest patients only, however statistically significant changes of LV ESV were not reached in any study group. Significant changes of arterial blood pressure were detected in the group of the youngest patients.

Correlation between WMSI and established changes in ABP

A statistically significant change in systolic ABP was reported in all groups, as well as diastolic APB in some groups. We raised the question as to whether ABP is related to the treatment effect, i.e. is there a statistically significant linear link between the change of WMSI from the baseline and change of ABP from the baseline (Figure 13). Kendal τ correlation coefficient was calculated to verify whether blood pressure before the treatment procedure could have had an effect on the changes of WMSI.

Weak but statistically significant correlation was discovered for WMSI at rest change with all three tested ABP parameters (Figure 1): systolic ABP (r =-0.291, p = 0.019), diastolic ABP (r =-0.286, p = 0.026), and mean ABP (r =-0.292, p = 0.015). These findings proved that higher ABP before treatment leads to less improvement (or even a worsening) after treatment (Figure 2). Correlation between ABP after treatment and change in WMSI at rest: systolic ABP (r =-0.340, p = 0.006), diastolic ABP (r =-373, p = 0.026), mean ABP (r =-0.374, p = 0.015). This result demonstrated that higher ABP after procedure resulted in a less positive result of WMSI at rest.

Figure 1. Change of WMSI at rest and mean ABP before treatment dispersion chart

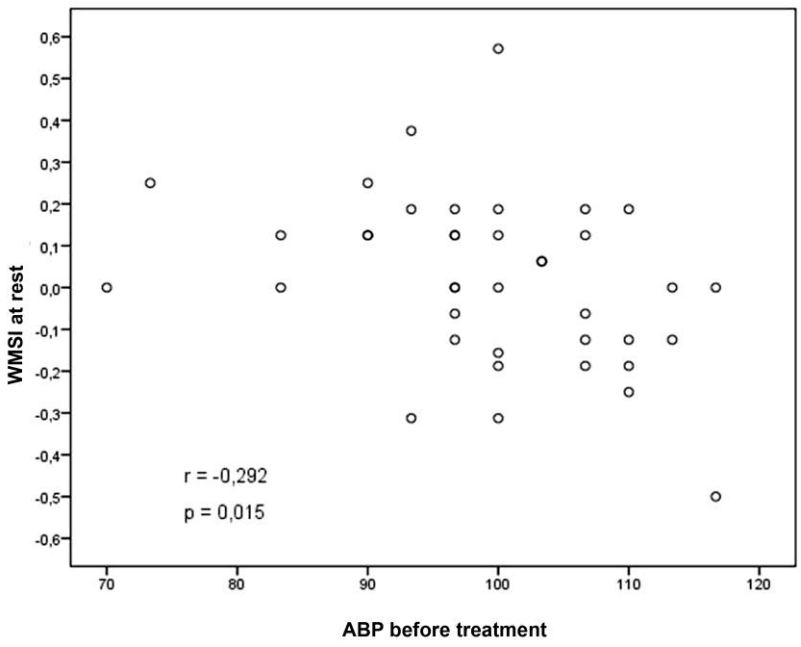
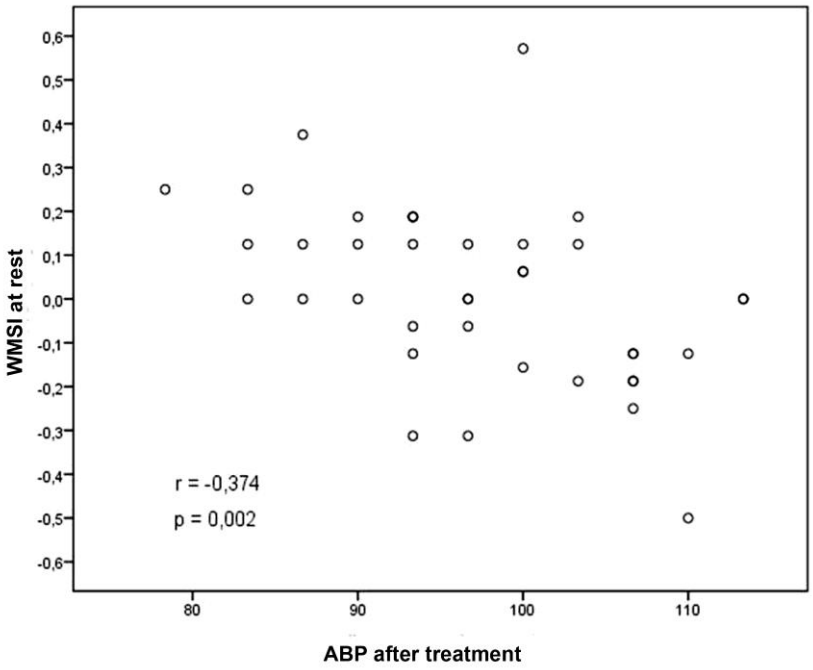


Figure 2. Change of WMSI at rest and mean ABP after treatment dispersion chart



The correlation of values of the patient data before and after treatment were statistically significant for each them. Study subjects with higher values before the treatment procedure tended to have higher values of the same indicators after the procedure too. The strongest correlation was established for ABP (systolic, diastolic and calculated mean ABP) and WMSI at rest ($r = 0.734$; $p < 0.001$).

Changes in left ventricle characteristics compared with normal values

Table 4. Changes in left ventricle characteristics compared with normal values

Indica-tor	Norm -> Norm (no changes)	Norm -> No (worsened)	No -> Norm (improved)	No -> No (no changes)	p value
LV EDV	25	3	3	6	1
LV ESV	22	2	4	9	0.687
LV SV	27	3	4	3	1
LV EF	**13**	**1**	**10**	**13**	**0.012**

Changes in ejection fraction of the left ventricle with regards to normal values were statistically significant: ejection fraction came back to normal in 10 subjects

out of 23, abnormal values were reported in 1 patient who had normal value before treatment.

Changes of indicators before and after CSWT in groups

Statistically significant differences for females were reported in the use of nitrates, LV IF and TID; in males these indicators were replenished with WMSI at rest, WMSImax as well as systolic and mean ABP (Tables 5 and 6).

Table 5. Changes of indicators before and after CSWT in females (N 10)

	n	Before treatment	After treatment	p value
Nitrates tablets x per week	**10**	**38.5 ± 8.89**	**7.4 ± 5.76**	**0.005**
WMSI at rest	10	1.41 ± 0.38	1.31 ± 0.33	0.345
WMSImax.	10	1.28 ± 0.3	1.23 ± 0.3	0.395
LV EF	**9**	**52.89 ± 9.88**	**57.56 ± 8.2**	**0.015**
LV EDV	9	109.44 ± 37.15	128.44 ± 47.99	0.325
LV ESV	9	46.67 ± 19.67	54.67 ± 25.58	0.089
LV SV	9	66 ± 29.93	77.22 ± 29.01	0.778
TID	**9**	**1.13 ± 0.11**	**1.05 ± 0.11**	**0.012**
Systolic ABP	10	133 ± 17.67	129.5 ± 14.62	0.336
Diastolic ABP	10	80.5 ± 8.96	76 ± 9.66	0.066
Mean ABP	10	98 ± 11.67	93.83 ± 10.89	0.074

Table 6. Changes of indicators before and after CSWT in males (N 30)

	n	Before treatment	After treatment	p value
Nitrates tablets x per week	**30**	**31.97 ± 10.35**	**3.97 ± 3.43**	**< 0.001**
WMSI at rest	**29**	**1.56 ± 0.47**	**1.43 ± 0.41**	**< 0.001**
WMSImax.	**29**	**1.58 ± 0.43**	**1.37 ± 0.42**	**< 0.001**
LV EF	**28**	**50.95 ± 12.41**	**56.29 ± 13.15**	**< 0.001**
LV EDV	28	147.69 ± 60.43	154.78 ± 69.16	0.580
LV ESV	28	79 ± 55.38	77.82 ± 64.7	0.186
LV SV	28	70.21 ± 21.22	76.5 ± 20.23	0.139
TID	**29**	**1.15 ± 0.12**	**1.08 ± 0.11**	**< 0.001**
Systolic ABP	**30**	**135.33 ± 16.13**	**131.33 ± 15.02**	**0.030**
Diastolic ABP	30	82 ± 8.77	81.33 ± 6.29	0.339
Mean ABP	**30**	**99.78 ± 10.13**	**98 ± 7.86**	**0.003**

Nitrate use or number of tablets, TID and mean ABP reduced and LV EF increased among MI naive patients (Table 7). Nitrate use or number of tablets, WMSI at rest and WMSImax, TID as well as systolic and mean ABP reduced and LV EF increased among patients with a history of MI (Table 8).

Table 7. MI naive patients

	n	Before treatment	After treatment	p value
Nitrates tablets x per week	**12**	**30.33 ± 11.3**	**2.42 ± 1.88**	**0.002**
WMSI at rest	12	1.31 ± 0.43	1.27 ± 0.39	0.345
WMSI max.	12	1.44 ± 0.38	1.34 ± 0.48	0.196
LV EF	**10**	**55.17 ± 6.2**	**61.3 ± 8.08**	**0.016**
LV EDV	10	126.42 ± 28.65	138.97 ± 40.05	0.202
LV ESV	10	62.8 ± 22.49	53 ± 19.8	0.203
LV SV	10	73.3 ± 19.8	87.2 ± 22.67	0.167
TID	**10**	**1.14 ± 0.11**	**1.07 ± 0.11**	**0.005**
Systolic ABP	12	139.17 ± 16.21	138.33 ± 15.86	0.705
Diastolic ABP	12	85.83 ± 8.75	83.33 ± 6.51	0.063
Mean ABP	**12**	**103.61 ± 9.69**	**101.67 ± 8.1**	**0.035**

Table 8. Patients after MI

	n	Before treatment	After treatment	p value
Nitrates tablets x per week	**28**	**35 ± 9.71**	**5.86 ± 4.67**	**< 0.001**
WMSI at rest	**27**	**1.61 ± 0.43**	**1.45 ± 0.38**	**< 0.001**
WMSI max.	**27**	**1.53 ± 0.44**	**1.33 ± 0.36**	**< 0.001**
LV EF	**27**	**50.04 ± 13.05**	**54.85 ± 12.9**	**< 0.001**
LV EDV	27	142.81 ± 65.11	151.85 ± 72.49	0.686
LV ESV	27	74.22 ± 58.02	79.3 ± 66.02	0.840
LV SV	27	67.67 ± 24.56	72.78 ± 21.16	0.381
TID	**28**	**1.15 ± 0.12**	**1.08 ± 0.11**	**< 0.001**
Systolic ABP	**28**	**132.86 ± 16.3**	**127.68 ± 13.3**	**0.020**
Diastolic ABP	28	79.82 ± 8.22	78.57 ± 7.56	0.288
Mean ABP	**28**	**97.5 ± 10.33**	**94.94 ± 8.36**	**0.011**

LV EF values before and after treatment were also compared in the groups (LV EF before treatment > 52% (group of better LV EF) and LV EF before treatment <= 52% (worse LV EF group). A statistically significant difference in the worse LV EF

group was not reached for LV ESV as well as systolic and diastolic ABP, all other indicators improved.

A statistically significant difference in the better LV EF was reported for nitrate use, WMSImax, LV EF, TID, diastolic and mean ABP; these values after treatment, on average, improved when compared with baseline values. However, mean LV EDV, LV ESV and LV SV values were lower in this group compared with baseline values.

Table 9. LV EF <= 52%

	n	Before treatment	After treatment	p value
Nitrates tablets x per week	**19**	**33.89 ± 8.81**	**4.47 ± 3.55**	**< 0.001**
WMSI at rest	**18**	**1.76 ± 0.43**	**1.6 ± 0.39**	**0.007**
WMSI max.	**18**	**1.73 ± 0.42**	**1.49 ± 0.35**	**0.002**
LV EF	**19**	**42.77 ± 9.46**	**49.74 ± 12.8**	**< 0.001**
LV EDV	**19**	**154.38 ± 68.73**	**178.41 ± 72.39**	**0.031**
LV ESV	19	91.47 ± 61.13	99.47 ± 70.36	0.702
LV SV	**19**	**62.68 ± 23.94**	**79.37 ± 21.98**	**0.008**
TID	**17**	**1.17 ± 0.11**	**1.07 ± 0.1**	**< 0.001**
Systolic ABP	19	136.32 ± 17.39	132.11 ± 14.37	0.078
Diastolic ABP	19	81.32 ± 7.79	80.53 ± 6.21	0.581
Mean ABP	**19**	**99.65 ± 10.48**	**97.72 ± 7.7**	**0.046**

Table 10. LV EF > 52%

	n	Before treatment	After treatment	p value
Nitrates tablets x per week	**18**	**33.06 ± 11.96**	**5.44 ± 5.23**	**< 0.001**
WMSI at rest	18	1.24 ± 0.28	1.19 ± 0.2	0.080
WMSI max.	**18**	**1.27 ± 0.24**	**1.13 ± 0.18**	**0.005**
LV EF	**18**	**60.56 ± 5.06**	**63.83 ± 5.03**	**0.008**
LV EDV	18	121.5 ± 38.02	116.67 ± 36.56	0.276
LV ESV	18	49.67 ± 23.77	43.39 ± 14.83	0.133
LV SV	18	76.06 ± 20.96	73.83 ± 22.76	0.225
TID	**18**	**1.13 ± 0.13**	**1.09 ± 0.12**	**0.007**
Systolic ABP	18	136.11 ± 15.01	132.5 ± 14.78	0.163
Diastolic ABP	**18**	**82.5 ± 10.33**	**80 ± 9.07**	**0.034**
Mean ABP	**18**	**100.37 ± 9.87**	**97.5 ± 9.87**	**0.015**

The group of better WMSI at rest (WMSI <= 1.5) was characterised by reduced nitrate use, reduction of mean WMSImax by 0.12, an increase of LV EF by 4.66%, on average, and TID reduction by 0.04, on average. ABP values also reduced. It should be noted that systolic blood pressure reduced by 6 mmHg and diastolic – by 3 mmHg, on average, coming close to normal arterial blood pressure.

The same statistically significant changes as in the group of better WMSI at rest group were reported in the group of worse WMSI at rest group (WMSI > 1.5), accompanied by the indicator WMSI at rest; however changes in ABP parameters did not reach a statistically significant level. WMSI at rest decreased by 0.24, WMSImax – by 0.23, LV EF increased by 6.12% and TID reduced by 0.1.

Table 11. WMSI <= 1.5

	n	Before treatment	After treatment	p value
Nitrates tablets x per week	**21**	**32.33 ± 11.17**	**4.33 ± 4.59**	**< 0.001**
WMSI at rest	21	1.18 ± 0.18	1.16 ± 0.13	0.438
WMSI max.	**21**	**1.25 ± 0.22**	**1.13 ± 0.17**	**0.013**
LV EF	**20**	**58.64 ± 7.04**	**63.3 ± 7.43**	**0.001**
LV EDV	20	126.01 ± 33.64	128.59 ± 40.39	0.952
LV ESV	20	54.4 ± 23.21	47.7 ± 18.47	0.102
LV SV	20	74.75 ± 19.75	79 ± 22.01	0.840
TID	**19**	**1.11 ± 0.1**	**1.07 ± 0.12**	**0.005**
Systolic ABP	**21**	**138.1 ± 12.89**	**132.86 ± 14.19**	**0.012**
Diastolic ABP	**21**	**85.24 ± 7.98**	**82.86 ± 7.17**	**0.023**
Mean ABP	**21**	**102.86 ± 8.52**	**99.52 ± 8.52**	**0.001**

Table 12. WMSI > 1.5

	n	Before treatment	After treatment	p value
Nitrates tablets x per week	**18**	**36.17 ± 8.05**	**5.61 ± 4.03**	**< 0.001**
WMSI at rest	**18**	**1.92 ± 0.32**	**1.68 ± 0.4**	**< 0.001**
WMSI max.	**18**	**1.8 ± 0.41**	**1.57 ± 0.45**	**0.004**
LV EF	**16**	**43.13 ± 10.81**	**49.25 ± 11.92**	**0.001**
LV EDV	16	147 ± 73.85	157.81 ± 58.98	0.211
LV ESV	16	86.31 ± 65.87	88.63 ± 56.37	0.698
LV SV	16	61.25 ± 26.02	72.69 ± 22.97	0.074
TID	**18**	**1.18 ± 0.12**	**1.08 ± 0.11**	**< 0.001**
Systolic ABP	18	131.11 ± 19.67	129.17 ± 15.74	0.537
Diastolic ABP	18	77.5 ± 8.09	76.67 ± 6.86	0.581
Mean ABP	18	95.37 ± 8.56	94.17 ± 8.56	0.282

Use of nitrates, WMSI at rest, WMSI max decreased in both higher and lower TID groups; LV EF was higher by 5.53%, on average, in the group of lower TID and by 3.72% in the group of higher TID. Changes in TID value were statistically significant in both groups: it was 0.05 lower, on average, in the group of lower TID and by 0.10 lower in the group of higher TID.

Table 13. TID <= 1.12

	n	Before treatment	After treatment	p value
Nitrates tablets x per week	**20**	**32.20 ± 10.26**	**3.85 ± 3.94**	**< 0.001**
WMSI at rest	**20**	**1.42 ± 0.35**	**1.28 ± 0.33**	**0.009**
WMSI max.	**20**	**1.39 ± 0.36**	**1.27 ± 0.41**	**0.014**
LV EF	**17**	**54.65 ± 7.78**	**60.18 ± 6.66**	**0.001**
LV EDV	17	129.29 ± 41.34	132.88 ± 32.67	0.849
LV ESV	17	54.47 ± 22.71	54.24 ± 18.75	0.776
LV SV	17	76.29 ± 26.86	80.53 ± 20.44	0.831
TID	**20**	**1.06 ± 0.06**	**1.01 ± 0.1**	**0.003**
Systolic ABP	**20**	**134.00 ± 15.36**	**132.00 ± 16.73**	**0.008**
Diastolic ABP	20	83.00 ± 8.49	80.50 ± 8.26	0.206
Mean ABP	**20**	**100.00 ± 10.09**	**97.67 ± 10.27**	**0.023**

Table 13. TID <= 1.12

	n	Before treatment	After treatment	p value
Nitrates tablets x per week	**20**	**32.20 ± 10.26**	**3.85 ± 3.94**	**< 0.001**
WMSI at rest	**20**	**1.42 ± 0.35**	**1.28 ± 0.33**	**0.009**
WMSI max.	**20**	**1.39 ± 0.36**	**1.27 ± 0.41**	**0.014**
LV EF	**17**	**54.65 ± 7.78**	**60.18 ± 6.66**	**0.001**
LV EDV	17	129.29 ± 41.34	132.88 ± 32.67	0.849
LV ESV	17	54.47 ± 22.71	54.24 ± 18.75	0.776
LV SV	17	76.29 ± 26.86	80.53 ± 20.44	0.831
TID	**20**	**1.06 ± 0.06**	**1.01 ± 0.1**	**0.003**
Systolic ABP	**20**	**134.00 ± 15.36**	**132.00 ± 16.73**	**0.008**
Diastolic ABP	20	83.00 ± 8.49	80.50 ± 8.26	0.206
Mean ABP	**20**	**100.00 ± 10.09**	**97.67 ± 10.27**	**0.023**

Table 14. TID > 1.12

	n	Before treatment	After treatment	p value
Nitrates tablets x per week	**18**	**35.00 ± 10.74**	**6.17 ± 4.67**	**< 0.001**
WMSI at rest	**17**	**1.70 ± 0.5**	**1.56 ± 0.42**	**0.003**
WMSI max.	**17**	**1.66 ± 0.47**	**1.42 ± 0.38**	**0.001**
LV EF	**18**	**48.67 ± 14.66**	**52.39 ± 14.28**	**0.002**
LV EDV	18	149.44 ± 71.80	160.33 ± 85.38	0.569
LV ESV	18	88.22 ± 66.20	90.39 ± 77.62	0.619
LV SV	18	62.72 ± 18.61	69.22 ± 20.76	0.236
TID	**18**	**1.24 ± 0.07**	**1.14 ± 0.07**	**< 0.001**
Systolic ABP	18	134.44 ± 18.22	129.17 ± 13.31	0.088
Diastolic ABP	18	79.72 ± 9.15	78.89 ± 6.76	0.105
Mean ABP	18	97.96 ± 11.21	95.65 ± 7.07	0.581

Comparison of data in the groups by median LV EF

Study subjects were divided into two groups based on median LV EF (median = 52%). Study subjects with LV EF above 52% were younger by about 4 years, they had lower values of WMSI at rest and WMSI max, their LV EF was also about 17.79% higher and LV ESV was by 41.8 ml lower compared with study subjects with a

baseline LV EF level equal or under 52%. The tendency of reduced LV EDV by 32.88 ml, on average, and reduced LV SV by 13.38 ml was detected in the group of study subjects with LV EF above 52%. Changes in the use of nitrates (tablets), TID, systolic diastolic and mean ABP in both groups were insignificant.

Table 15. LV EF before treatment

	n	LV EF <= 52	n	LV EF > 52	p value
Age	19	69.21 ± 10.10	18	65.11 ± 8.84	0.176
Nitrates tab. x week before treatment	19	33.89 ± 8.81	18	33.06 ± 11.96	0.876
WMSI at rest before treatment	**18**	**1.76 ± 0.43**	**18**	**1.24 ± 0.28**	**< 0.001**
WMSI max. before treatment	**18**	**1.73 ± 0.42**	**18**	**1.27 ± 0.24**	**0.001**
LV EF before treatment	**19**	**42.77 ± 9.46**	**18**	**60.56 ± 5.06**	**< 0.001**
LV EDV before treatment	19	154.38 ± 68.73	18	121.5 ± 38.02	0.186
LV ESV before treatment	**19**	**91.47 ± 61.13**	**18**	**49.67 ± 23.77**	**0.009**
LV SV before treatment	19	62.68 ± 23.94	18	76.06 ± 20.96	0.078
TID before treatment	17	1.17 ± 0.11	18	1.13 ± 0.13	0.297
Systolic ABP before treatment	19	136.32 ± 17.39	18	136.11 ± 15.01	0.988
Diastolic ABP before treatment	19	81.32 ± 7.79	18	82.5 ± 10.33	0.641
Mean ABP before treatment	19	99.65 ± 10.48	18	100.37 ± 9.87	0.866

Values of WMSI at rest and WMSI maximal after treatment were less by 0.41 and 0.36 respectively in the group of LV EF above 52%. The value of LV EF in this group was, on average, higher by 14.09% and LV EDV by 61.74 ml and LV ESV lower by 56.08 ml, compared with the study subjects with baseline LV EF level equal to or under 52%. It should be noted that mean LV EDV and mean LV ESV values increased compared with mean baseline value, but these indicators decreased in the group of LV EF above 52%. Significant differences in the use of nitrates, LV SV, TID, systolic, diastolic and mean ABP were not detected.

Table 16. LV EF after treatment

	n	LV EF <= 52	n	LV EF > 52	p value
Nitrates tab. x week after treatment	19	4.47 ± 3.55	18	5.44 ± 5.23	0.926
WMSI at rest after treatment	**18**	**1.6 ± 0.39**	**18**	**1.19 ± 0.2**	**0.001**
WMSI max after treatment	**18**	**1.49 ± 0.35**	**18**	**1.13 ± 0.18**	**0.001**
LV EF after treatment	**19**	**49.74 ± 12.8**	**18**	**63.83 ± 5.03**	**< 0.001**
LV EDV after treatment	**19**	**178.41 ± 72.39**	**18**	**116.67 ± 36.56**	**0.003**
LV ESV after treatment	**19**	**99.47 ± 70.36**	**18**	**43.39 ± 14.83**	**< 0.001**
LV SV after treatment	19	79.37 ± 21.98	18	73.83 ± 22.76	0.403
TID after treatment	17	1.07 ± 0.1	18	1.09 ± 0.12	0.715
Systolic ABP after treatment	19	132.11 ± 14.37	18	132.5 ± 14.78	1.000
Diastolic ABP after treatment	19	80.53 ± 6.21	18	80.00 ± 9.07	1.000
Mean ABP after treatment	19	97.72 ± 7.7	18	97.5 ± 9.87	0.988

Patients with an established WMSI at rest (n = 39) were subdivided into two groups based on the median value (1.5).

Patients with WMSI smaller than median WMSI value were 8.21 years younger. Differences in the mean WMSI at rest value before and after treatment were statistically significant, similar differences were also discovered for LV EF. The difference in baseline LV ESV was not statistically significant, however a trend of lower LV ESV in the group of lower WMSI was established. The difference in LV ESV after treatment reached a statistical significance level ($p < 0.010$) and was almost two-fold higher in the group of higher WMSI, when compared with the group of lower WMSI. A significant difference was also established for diastolic blood pressure; the mean difference was 9.74 mmHg at baseline and by 6.19 mmHg after treatment.

A statistically significant difference of age was not detected between the group of TID equal to or under 1.12 (n = 38) and that of TID above 1.12 (patients in the group of TID <= 1.12 were younger by 2 years, on average). A statistically significant difference was established for TID value only – it was 0.18 higher in the group of TID > 1.12. A tendency of higher WMSI at rest and WMSImax and lower LV SV was noticed in the group characterised by inferior characteristics.

Statistically significant differences in mean WMSI at rest and TID values were reported after treatment. The use of nitrates and WMSImax tended to be higher in the group of TID > 1.12, however LV EF and LV SV values in this group were lower.

CONCLUSIONS

1. Based on the assessment of stable angina pectoris characteristics at baseline and after treatment, a lower angina pectoris class was established in all patients.
2. Based on heart magnetic resonance imaging findings for the assessment of left ventricle ejection fraction, LV EF after treatment increased. Assessment of left ventricle volumes revealed an increase of LV SV after treatment and insignificant changes of LV EDV and LV ESV after treatment from baseline levels.
3. An assessment of myocardium vitality, based on the dobutamine echocardiography test, demonstrated a reduction of WMSI and improved LV EF.
4. Results of myocardium perfusion radionuclide computer tomography imaging designed to assess myocardium reserve at baseline and after treatment demonstrated reduced transcendent ischemic dilation and improved myocardial perfusion.
5. Assessment of the efficacy of cardiac shock wave therapy for patients of different age groups and depending on the severity of underlying pathology before treatment proved better toleration of physical load, reduction in nitrate use, improved parameters of left ventricle systolic and diastolic function, myocardium perfusion and vitality indicators.
6. Assessment effect of cardiac shock wave therapy on arterial blood pressure showed a decrease in mean ABP.
7. The importance of multimodal image analysis indicators was disclosed for the first time for the assessment of cardiac shock wave therapy efficacy, when the most informative parameters of heart left ventricle were selected from each method.
8. This study enabled the development of the cardiac shock wave therapy method and its application for the treatment of less advanced ischemic heart disease.

CLINICAL IMPLICATIONS

Cardiac shock wave therapy is a safe and effective treatment method for end-stage ischemic heart disease. CSWT improves patients' condition and may be applied as a treatment method at clinic and recommended to patients. It was demonstrated that cardiac shock wave therapy is relatively more effective for the patients with more severe clinical condition.

SUMMARY IN LITHUANIAN

ĮVADAS

Širdies ir kraujagyslių ligos buvo ir tebėra pagrindinė Lietuvos ir kitų ES šalių žmonių mirčių priežastis. Standartizuoto mirtingumo nuo ŠKL rodiklis 2009 m. Lietuvoje buvo vienas iš blogiausių ES (blogesnė padėtis tik Rumunijoje ir Bulgarijoje). Remiantis Statistikos departamento duomenimis, 2010 m. Lietuvoje nuo ŠKL mirė 23 627 asmenys (56,1 proc. visų mirusiųjų)

Dabar kuriami nauji širdies kraujotakos atkūrimo metodai, kuriuos ateityje ketinama pritaikyti kasdienėje praktikoje. Vienas iš angiogenezę skatinančių metodų yra miokardo smūginės bangos terapija (MSBT).

MSBT– tai naujas atkuriamojo/ regeneracinio gydymo būdas, galintis tapti revaskuliarizacijos alternatyva, nes kamieninių ląstelių pritaikymas tokiais tikslais tebėra tiriamas. MSBT metu naudojamos žemo dažnio mechaninės bangos, kurioms veikiant, pagerinama širdies perfuzija ir sukuriamas kraujagyslių tinklas. Tokios bangos pirmą kartą medicinoje buvo pritaikytos inkstų akmenims skaldyti maždaug prieš 20 metų [15].

MSBT tyrimai pradėti atlikti su pacientais, kuriems diagnozuota labai pažengusi išeminė širdies liga, lydima III−IV klasės krūtinės anginos(KA) pagal Kanados klasifikaciją (CCS), yra trijų vainikinių arterijų liga, kartais su kairės vainikinės arterijos kamieno stenoze. Šiems pacientams anksčiau atliktos angioplastikos ir stentavimo procedūros arba viena ar kelios aortokoronarinių jungčių suformavimo operacijos, tačiau KA atsinaujino, todėl nuolatos skiriamos maksimalios toleruojamos nitratų dozės. Tačiau krūtinės anginos epizodai kartojasi kelis kartus per dieną minimalaus fizinio krūvio metu ar net ramybėje.

Pasaulyje šis gydymo metodas tik pradedamas taikyti ir pirminės patirties sukaupta tik nedaugelyje klinikų.

TYRIMO TIKSLAS

Optimizuoti miokardo revaskuliarizacijos, taikant smūginės bangos terapiją, protokolą, įvertinti metodo saugumą ir efektyvumą, pagrindžiant ne tik klinikiniais, bet ir objektyviais daugialypės (multimodalinės) vaizdinės diagnostikos kriterijais, pacientams, sergantiems toli pažengusia išemine širdies liga ir dažna krūtinės angina.

TYRIMO UŽDAVINIAI

1. Įvertinti klinikines stabilios krūtinės anginos charakteristikas prieš ir po gydymo.
2. Širdies magnetinio rezonanso tyrimu įvertinti kairiojo skilvelio išstūmimo frakciją, kairiojo skilvelio tūrius, rando išplitimą ir storį prieš ir pogydymo.
3. Dobutaminoechokardiografijos tyrimu vertinti miokardo gyvybingumą prieš ir po gydymo.
4. Miokardo perfuzijos radionuklidinės kompiuterinės tomografijos tyrimu įvertinti miokardo rezervą prieš ir po gydymo.
5. Įvertinti miokardo smūginės bangos terapijos efektyvumą įvairių amžiaus grupių pacientams, o taip pat priklausomai ir nuo prieš gydymą esančios patologijos išreikštumo
6. Įvertinti miokardo smūginės bangos terapijos poveikį arteriniam kraujo spaudimui.
7. Kompleksiškai įvertinti naujų širdies vaizdinės diagnostikos metodų informatyvumą regeneracinės terapijos, taikant miokardo smūginės bangos terapiją, efektyvumui nustatyti.

MOKSLINĖ DARBO REIKŠMĖ IR NAUJUMAS

1. Miokardo smūginės bangos terapijos gydymo metodika Vilniaus universiteto ligoninės Santariškių klinikose pirmą kartą buvo pritaikyta ir tirta ne tik Lietuvoje, bet ir Baltijos šalyse, ir anksčiau nei daugelyje Europos šalių.

2. Tarptautinėje medicinos literatūroje yra skelbta duomenų apie nedideles pacientų grupes (8-25 pacientai). Autorių išvadose nuolat pabrėžiama, jog darbų rezultatai turi būti patikslinti tiriant didesnes pacientų imtis. Mes ištyrėme 40 pacientų. Tai viena iš didžiausių pacientų imčių, o ir duomenų patikimumas didžiausias.

3. Pirmąkart būklei prieš ir po gydymo MSBT įvertinti naudotas širdies magnetinio rezonanso tyrimas, kuris dabar pasaulyje yra auksinis standartas širdies raumens

pokyčiams vertinti. Mūsų duomenys pateikiami su širdies magnetinio rezonanso tyrimo duomenimis.

4. Tai didžiausia grupė, kuriai prieš ir po gydymo MSBT atliktas echokardiografinis dobutamino krūvio testas.
5. Tyrimo pagrindu sukurtas optimalus pacientų tyrimo prieš ir po miokardo smūginės bangos terapijos efektyvumo vertinimo algoritmas, besiremiantis daugialypio vaizdinimo tyrimais, kuris jau taikomas Vilniaus universiteto ligoninės Santariškių klinikose. Šio algoritmo pagrindu nustatyta, kokiems pacientams šis gydymo būdas bus naudingiausias.
6. Atveriamos naujos galimybės išplėsti indikacijas šiam gydymui taikyti.

GINAMIEJI TEIGINIAI

1. Miokardo smūginės bangos terapija yra naujas, vaizdine diagnostika kontroliuojant atliekamas, neinvazinis regeneracinės terapijos būdas toli pažengusiai išeminei širdies ligai gydyti.
2. Miokardo smūginės bangos terapija yra efektyvus ir saugus gydymo būdas toli pažengusiai išeminei širdies ligai gydyti.
3. Objektyvūs daugialypės širdies vaizdinės diagnostikos kriterijai leidžia nustatyti šio gydymo metodo efektyvumą.
4. Kompleksinis daugialypės vaizdinės diagnostikos kriterijų vertinimas pagrindžia šio metodo efektyvumą.

TYRIMO METODIKA

Miokardo smūginės bangos terapija taikyta pacientams, kuriems diagnozuota labai pažengusi išeminė širdies liga, III−IV klasės krūtinės angina pagal Kanados klasifikaciją, trijų vainikinių arterijų liga, kartais su kairės vainikinės arterijos kamieno stenoze.

Prieš procedūrą atliekami tyrimai:

1. Ligoniai apklausiami pagal specialią šiam tyrimui sukurtą anketą, surenkami demografiniai duomenys, informacija apie ligos anamnezę, rizikos veiksnius, įrašomi apžiūros ir instrumentinių tyrimų rezultatai.
2. Atliekama krūvio echokardiografija ir analizuojami deformacijos parametrai.
3. Atliekama echokardiografija.
4. Magnetinio rezonanso tomografija su perfuzijos tyrimu ir vėlyvuoju kontrastavimu.
5. Kompiuterinė angiografija ir širdies tomografija (jei negalima atlikti MRT).
6. Miokardo branduoliniai perfuzijos tyrimai.
7. AKS ir EKG stebėjimas.

Echoskopiškai nustatomos zonos, kuriose taikoma MSBT. Vienos zonos plotas – 1 kvadratinis centimetras. Tokių zonų kairiajame skilvelyje gali būti ne daugiau kaip 5. Į vieną zoną per vieną seansągali būti skiriama 100 impulsų. Iš viso per vieną seansą pacientui siunčiama500 impulsų.

REZULTATAI

Rodikliai prieš gydymą moterų ir vyrų grupėse statistiškai reikšmingai nesiskyrė. Dauguma moterų (90 proc.) buvo patyrusios MI, tuo tarpu tarp vyrų patyrusių MI buvo 63,3 proc.

Pastebėtos tendencijos ($0,05<p<0,1$), kad vyrai vartojo mažiau nitratų, jų DVI maksimalus vidutiniškai 0,30, o KS GST 32,33ml didesnis nei moterų.

Po gydymo išliko ta pati tendencija nitrato suvartojimui, vyrai jų vartojo beveik dvigubai mažiau nei moterys. Nors vyrų DVI maksimalus išliko didesnis nei moterų, tačiau atotrūkis tarp grupių sumažėjo iki 0,14. Atotrūkis tarp grupių KS GST sumažėjo per 11,91 ml.

Amžiaus grupės

Prieš procedūra jauniausi pacientai suvartodavo mažiausiai nitratų (30 per savaitę), vyriausiųjų grupėje suvartodavo vidutiniškai 3,83 daugiau, o vidutinio amžiaus pacientai 7 daugiau nei jauniausieji. Statistiškai reikšmingai (p=0,004) skyrėsi DVI ramybėje. Jis buvo didesnis vyresnėse amžiaus grupėse. DVI max analogiškai buvo didesnis vyresnių pacientų grupėse, tačiau skirtumas nebebuvo statistiškai reikšmingas. Tai, kad grupės buvo glaudesnės šiam rodikliui greičiausiai galima paaiškinti tuo, kad DVI ramybėje „nepasimato“ visi segmentų pažeidimai. Vidutinio amžiaus grupė turėjo didžiausią KS IF ir TID bei mažiausią KS GDT, GS GST, KS ST. Vidutinis AKS didžiausias buvo jauniausių pacientų grupėje ir mažėjo vyresnėms. Kadangi dauguma pacientų serga AH, tai gali būti susiję su tuo, kad vyresniems pacientams kraujospūdį reguliuojantis gydymas galėjo būti taikomas ilgiau nei jaunesniems.

Palyginus rodiklius po gydymo labiau susilygino nitratų vartojimas, daugiausiai jų vartojančia grupe išliko vidutinio amžiaus grupės pacientai, tačiau mažiausiai jų suvartoja vyriausiųjų grupė. Tiek DVI ramybėje, tiek DVI maksimalus išliko didesnis vyresniems pacientams, tačiau atotrūkis tarp amžiaus grupių DVI ramybėje sumažėjo, o DVI maksimalus didėjo. Po gydymo didžiausią KS IF, KS GDT turėjo jauniausieji pacientai, didžiausią KS GST – vyriausieji pacientai, didžiausias TID išliko vidutinio amžiaus pacientams. Vidutinis AKS išliko mažesnis vyresniems pacientams.

Rodikliai prieš ir po

Bendrai grupei

Statistiškai reikšmingas skirtumas nustatytas daugumai rodiklių. Nitratų suvartojimas vidutiniškai sumažėjo 28,77 m.v. per savaitę (p<0,001). DVI sumažėjo 0,12 , o DVI max 0,16 , KS IF padidėjo 5,17 proc., KS GDT padidėjo 9,99ml, KS GST padidėjo 1,05 ml, KS ST padidėjo 7,49 ml, TID sumažėjo 0,07 , vidutinis AKS sumažėjo 2,37 mmHg.

Amžiaus grupėms

Visose grupėse ženkliai mažėjo nitratų suvartojimas. DVI ramybėje statistiškai reikšmingai nesiskyrė tik jauniausių žmonių grupėje, tačiau šių pacientų vidutinis DVI ramybėje ir prieš gydymą buvo mažiausias, tuo tarpu DVI max skyrėsi jau visose amžiaus grupėse ir po gydymo buvo vidutiniškai mažesnis 0,15, vyriausiems, 0,18 vidutinio amžiaus ir 0,17. jauniausiems pacientams. KS IF po gydymo statistškai

reikšmingai skyrėsi nuo prieš gydymą buvusio visose amžiaus grupėse. Ir vidutiniškai padidėjo nuo 4 proc. (vidutinio amžiaus grupėje) iki 6,23 proc. (jauniausiųjų grupėje). KS GDT statistiškai reikšmingas pokytis nustatytas tik jauniausiųjų asmenų grupėje., taip pat ir KS ST, o KS GST nebuvo statistiškai reikšmingas nei vienoje grupėje. Jauniausiųjų grupėje nustatytas ir reikšmingas skirtumas arteriniam kraujo spaudimui.

Bendrai nustatytas statistiškai reikšmingas sistolinio AKS pokytis, o kai kurioms grupėms ir diastolinio AKS pokytis. Kyla klausimas kiek AKS yra susiję su gydymo poveikiu, t.y. ar yra statistiškai reikšmingas tiesinis ryšys tarp rodiklio skirtumo prieš ir po gydymo ir AKS prieš arba po gydymo.

Silpna, statistiškai reikšminga koreliacija nustatyta tik DVI ramybėje visiems trims tirtiems AKS parametrams: sistoliniui AKS (r=-0,291, p=0,019), diastoliniui AKS (r=-0,286, p=0,026), vidutiniam AKS (r=-0,292, p=0,015). Tai rodo, kad kuo didesnis AKS buvo prieš gydymą, tuo mažesnis pagerėjimas (ar net didesnis pablogėjimas) buvo po gydymo. Koreliacija tarp AKS po gydymo ir DVI ramybėje: sistoliniui AKS (r=-0,340, p=0,006), diastoliniui AKS (r=-373, p=0,026), vidutiniam AKS (r=-0,374, p=0,015). Toks rezultatas rodo, kad kuo didesnis buvo AKS po procedūros, tuo mažiau pozityvus DVI ramybėje rezultatas.

Moterims

Moterims statistiškai reikšmingas skirtumas nustatytas nitratų suvartojimui, KS IF ir TID, vyrams be šių rodiklių dar ir DVI ramybėje, DVI maksimaliam ir AKS sistoliniui bei vidutiniui AKS.

MI

MI nepatyrusiems pacientams sumažėjo nitratų skaičius, TID ir vidutinis AKS, padidėjo KS IF. MI patyrusiems sumažėjo nitratų skaičius, DVI ramybėje bei maksimalus, TID ir sistolinis bei vidutinis AKS, padidėjo KS IF.

Rodikliai prieš ir po gydymo palyginti ir KS IF grupėse (KS IF prieš gydymą > 52 (geresnio KS IF grupė) ir KS IF prieš gydymą <= 52 (blogesnio KS IF grupė).

KS IF

Blogesnio KS IF grupėje statistiškai reikšmingai nepasikeitė tik KS GST ir sistolinis bei diastolinis AKS, kitiems rodikliams nustatytas pagerėjimas.

Geresnio KS IF grupėje statistiškai reikšmingai pasikeitė nitratams, DVI maksimumas, KS IF, TID, AKS diastolinis, vidutinis AKS ir šie rodikliai po gydymo vidutiniškai buvo geresni nei pries gydymą. Tačiau šiai grupei nustatytas mažesnis nei pries gydymą vidurkis KS GDT, KS GST, KS ST.

DVI

Geresnio DVI ramybėje (DVI <= 1,5) grupėje sumažėjo nitratų vartojimas, DVI maksimalus vidutiniškai sumažėjo 0,12, KS IF padidėjo vidutiniškai 4,66 proc., TID sumažėjo vidutiniškai 0,04. Taip pat sumažėjo ir AKS parametrai.

Blogesnio DVI ramybėje (DVI > 1,5) grupėje statistiškai reikšmingai skyrėsi tie patys rodikliai kaip ir geresnio atveju, tačiau prisidėjo DVI ramybėje, o AKS parametrų pokyčiai nebuvo statistiškai reikšmingi. DVI ramybėje sumažėjo 0,24, DVI max. 0,23, KS IF padidėjo 6,12 proc., TID sumažėjo 0,10 .

Rezultatai rodo, kad asmenims, kurie turėjo blogesnius rodiklius prieš gydymą, pagerėjimas labiau juntamas nei tiems, kurie turėjo geresnius rodiklius.

IŠVADOS

1. Įvertinus klinikines stabilios krūtinės anginos charakteristikas prieš ir po gydymo visiems pacientams krūtinės anginos klasė sumažėjo.
2. Širdies magnetinio rezonanso tyrimu įvertintinus kairiojo skilvelio išstūmimo frakciją, KS IF po gydymo padidėjo. Įvertinus kairiojo skilvelio tūrius, KS ST po gydymo padidėjo, o KS GDT ir KS GST kito statistikai nereikšmingai palyginus prieš ir po gydymo.
3. Dobutamino echokardiografijos tyrimu įvertinti miokardo gyvybingumą prieš ir po gydymo, DVI sumažėjo, o tuo pačiu pagerėjo KS IF.

4. Miokardo perfuzijos radionuklidinės kompiuterinės tomografijos tyrimu įvertintinus miokardo rezervą prieš ir po gydymo, sumažėjo transciendentinė išeminė dilatacija, pagerėjo miokardo perfuzija.
5. Įvertintinus miokardo smūginės bangos terapijos efektyvumą įvairių amžiaus grupių pacientams, o taip pat priklausomai ir nuo prieš gydymą esančios patologijos išreikštumo, pagerėja pacientų fizinio krūvio tolerancija, sumažėja vartojamų nitratų kiekis, pagerėja kairiojo skilvelio sistolinės ir diastolinės funkcijos parametrai, miokardo perfuzija ir gyvybingumo rodikliai.
6. Įvertintinus miokardo smūginės bangos terapijos poveikį arteriniam kraujo spaudimui, sumažėjo vidutinis AKS.
7. Pirmąkart parodyta daugialypės vaizdinės diagnostikos rodiklių reikšmė, vertinant miokardo smūginės bangos terapijos efektyvumą, iš kiekvieno metodo pasirenkant labiausiai informatyvius širdies kairiojo skilvelio parametrus.
8. Atliktas darbas įgalina plėtoti miokardo smūginės bangos metodą ir taikyti jį mažiau pažengusiai išeminei širdies ligai gydyti.

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