Cardiac schockwave therapy in the treatment of ischemic heart disease patiens with refractive angina pectoris

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Summary

Objective: To evaluate of the effectiveness of cardiac shockwave therapy in the treatment of ischemic heart disease with refractive angina pectoris. *Subject and method:* A prospective, cross-sectional study with comparison and follow-up for 6 months on 50 patients with refractive angina pectoris from January 2017 to January 2020. The protocol application of 100 shocks/spot at 0.09mJ/mm^2 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. *Result:* The average age was 71.32 ± 10.5 years, men accounted for 78%. The symptoms of angina improved significantly (amount of chest pain 5.87 ± 2.7 to 0.28 ± 0.45 times; Nitrat consumed per week from 6.3 ± 3.5 to 0.3 ± 0.5 tablets/week). The 6-minute walking test all improved (278.1 ± 71m compared with 390.5 ± 42.3m). CCS angina class improved significant. NYHA grade improved significantly (NYHA III from 40.7% to 11.1%, NYHA II from 51.9% to 33.3%). Pro-BNP decreased (994.99 ± 1708.9 to 429.0 ± 453.9 pg/ml). WSMI decreased from 1.49 ± 0.22 to 1.24 ± 0.12, GLS improved from -9.79 ± 2.68 to -12.7 ± 2.42. Average score of SSS, SRS, SDS markedly improved with $p<0.05$ by SPECT. The degree of severe perfusion defect and the wide perfusion defect area decreased significantly after treatment by 52% to 12% and 58% to 28%, respectively. *Conclusion:* Cardiac shockwave therapy improved clinical symptoms and increased myocardial perfusion in ischemic heart disease with refractive angina pectoris.

Keywords: Ischemic heart disease (IHD), cardiac shockwave therapy (CSWT), refractive angina pectoris (RAP).

1. Background

Worldwide, approximately 17.9 million/year people died from cardiovascular disease, accounting for 31% of the total number of deaths, of which up to 85% died from coronary heart disease or stroke. The current management of ischemic heart disease (IHD) relies on three major therapeutic options, namely medication, percutanuos coronary intervention (PCI), and coronary artery bypass grafting (CABG). The purpose of these methods is to restore circulation of the damaged coronary artery due to refractory angina or blockage, thereby improving symptoms and preserving the cardiac function and reducing mortality. However, there is still a large proportion of patients with refractive angina pectoris symptoms despite of revascularization of coronary artery by PCI or CABG.

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In Europe, the percentage of patients who still have chest pain after PCI is about 26% and after CABG about 30% [5]. Besides, there are cases where coronary artery can not be revascularizated (due to patient refusal, old age, weak co-morbidities, small coronary arteries twisting, many calcifications not suitable for revascularization, etc.) who have been treated by optimal medical therapy but still refractive angina pectoris. In 2006, cardiac shockwave therapy (CSWT) reported on human for the first time. Therefore, the introduction of the cardiac shockwave therapy has helped treat this group of patients.

Cardiac shockwave therapy is a non-invasive intervention. Shockwave is radiofrequency waveforms similar to energetic ultrasound wave. They have high pressure amplitude, small pulse and short pulse rise time. When the shockwave irradiated to the anemia areas, it immediately causes vasodilatation and pain relief through promotion of endothelial cell to release NO from L-arginine by NO synthases enzyme. NO works to reduce adhesion of leukocyte to artery wall, decrease proliferation of smooth muscle cells and vascular restructuring, inhibit platelet aggregation and thrombus formation in artery wall. Then NO goes from endothelial cells to smooth muscle cells of blood vessels causing vasodilatation and at the same time causing increase in generation of vascular endothelial growth factors (VEGF) from endothelial cells, inhibiting vascular contraction through minimizing pathological interactions between actin and myosin fibers, promoting the regeneration of collagen in vascular endothelium [5]. The main purpose of this study was to evaluate the effectiveness and safety of cardiac shockwave therapy in the treatment of ischemic heart disease with refractive angina pectoris.

2. Subject and method

2.1. Subject

50 patients diagnosed ischemic heart disease with refractive angina pectoris treated at 108 Military Central Hospital from January 2017 to January 2020.

Inclusion criteria

Patients with ischemic heart disease are not suitable for PCI or CABG who despite optimal medical therapy still have chest pain.

Patients still had refractive chest pain despite of PCI or CABG revascularization.

There is evidence of at least moderate myocardial ischemia on SPECT.

Exclusion criteria

Patients have a thrombus in the chambers of the heart.

Patients have coronary vasculititis disease.

Patients with acute myocardial infarction within a month.

Patients with malignancy in the application area.

Patients cannot get the appropriate echocardiogram view.

Patients did not consent to participate in the study.

2.2. Method

This is a prospective, cross-sectional study with comparison between pre-post treatment and follow-up for 6 months.

Procedure: Application of shocks to the area to be treated with doses (100 shocks/spot at 0.09mJ/mm^2 energy flux density for 3 - 6 spots each time). The treatment process is repeated 3 times per week within the first week of each month for 3 months [5].

The following parameters will be evaluated including symptoms of angina and the exercise tolerance, echocardiography and myocardial perfusion imaging by single- photon emission computed tomography (SPECT) after 6 months.

Monitoring adverse effects.

2.3. Statistical analysis

The study data are processed with SPSS 20.0 software.

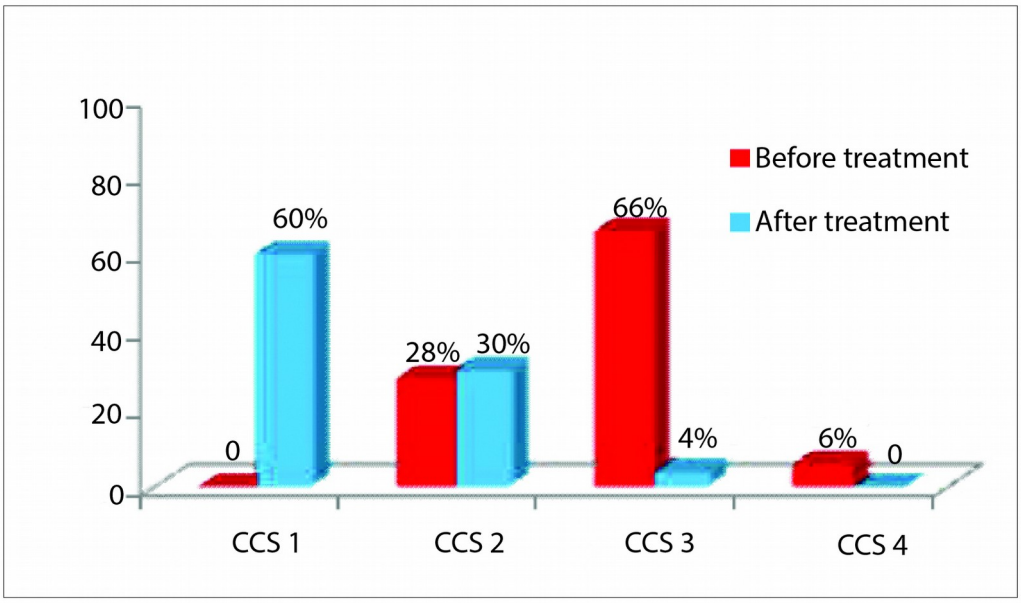
3. Result

3.1. Some common characteristics

Table 1. Some characteristics of the objects and risk factors

Characteristics			Percentage (n, %)
Gender	Male		39 (78%)
	Female		11 (22%)
Average age (year)			71.3 ± 10.5
Revascularization	No		15 (30%)
	Yes	PCI	28 (54%)
		CABG	6 (12%)
		PCI + CABG	1 (2%)
BMI (kg/m^2) ≥ 25			12 (24%)
Age ≥ 65			42 (84%)
Diabetes			19 (38%)
Hypertension			50 (100%)
Smokers			38 (76%)
Dyslipidemia			48 (96%)
Coronary artery lesions	Single vessel		2 (4%)
	Double vessels		19 (38%)
	Three vessels		29 (58%)

The average age of the objects of the study was 71.3 ± 10.5 years. The majority were male (78%). Patients with revascularization accounted for 85%.

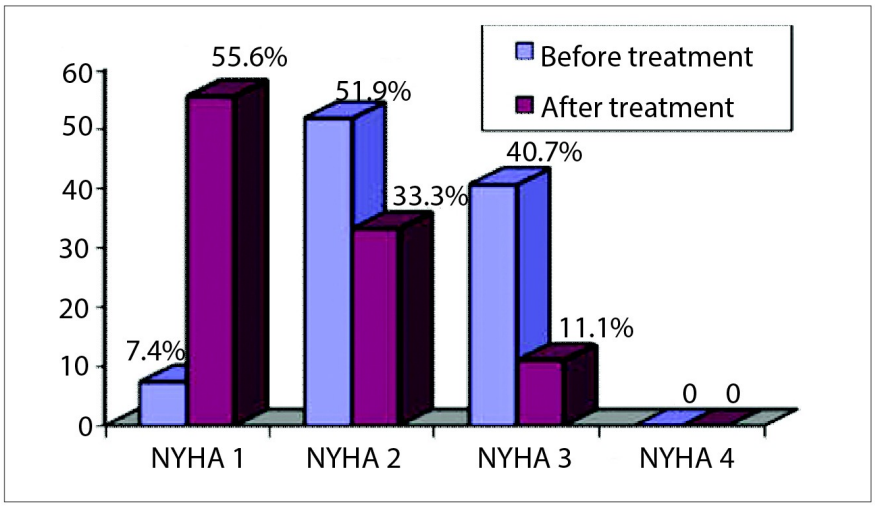


Figures 1. CCS before and after treatment

Table 2. Change of clinical symptoms after treatment

Symptom	Before treatment ($\bar{X}$ ± SD)	After treatment ($\bar{X}$ ± SD)	p
Angina pectoris /week (times)	5.8 ± 2,7	0.28 ± 0.45	<0.001
Nitrate consumed/ week (tablets)	6.3 ± 3,5	0.3 ± 0.46	<0.001
6-minute walk test (m)	278.1 ± 71	390.5 ± 42.3	<0.001

The frequency of chest pain, nitrat consumed reduced in the after treatment group (p<0.05).



Figures 2. Comparison of heart failure rate before and after treatment

Table 3. Comparison of ultrasound parameters before and after treatment

Parameters	Before treatment	After treatment	p

Dd (mm)	50.62 ± 7.87	48.10 ± 5.42	>0.05
Ds (mm)	35.62 ± 9.42	32.46 ± 6.80	>0.05
Simpson's EF (%)	55.70 ± 16.22	59.78 ± 12.74	<0.05
WMSI	1.49 ± 0.22	1.24 ± 0.12	<0.001
GLS (-%)	-9.79 ± 2.68	-12.74 ± 2.42	<0.001

Simpson's EF were significantly increased in the group treated with ESWT. The WMSI, GLS improved after treatment significantly.

Table 4. Comparison of the results of SPECT before and after treatment

Parameters	Before treatment ($\bar{X}$ ± SD)	After treatment ($\bar{X}$ ± SD)	p
Summed stress score of perfusion (SSS)	15.78 ± 9.25	11.54 ± 7.72	<0.05
Summed rest score of perfusion (SRS)	11.0 ± 8.45	8.39 ± 6.77	<0.05
Summed difference score between two phases (SDS)	4.78 ± 2.83	3.02 ± 1.83	<0.05

4. Discussion

Overalls, 50 cases indicated for treatment of chronic myocardial ischemia with refractive angina pectoris by CWST. The average age of the patient was 71.3 ± 10.5 years, most of them were male (78%). 30 percent of patients did not have PCI or CABG. The main risk factors were advanced hypertension (100%), dyslipidemia (96%), age ≥ 65 (84%), smoking prevalence (70%), and diabetes (38%). Cardiovascular disease risk factors are factors that have been shown to be strongly associated with cardiovascular morbidity and mortality. The risk factors often come in clusters and exponentially promote each other leading to worse out come.

The Canadian Heart Association classification of chest pain is a relatively simple tool to help assess the clinical severity of angina and assess the response to treatment of the disease. After 6 months of treatment, there was a marked improvement because the reduction of CCS 3 decreased from 66% to 4%. Thus, patients have a high degree of angina even with normal physical activity or angina significantly affects physical activity after CSWT. The patient's capacity has improved significantly. Conrado et al found that after treatment CCS decreased from 3.2 ± 0.56 to 1.93 ± 0.7 with p<0.05 [1]. After 6 months we found that the symptoms of angina improved significantly (amount of angina 5.87 ± 2.7 to 0.28 ± 0.45 times; using of nitroglycerin reduced per week from 6.3 ± 3.5 to 0.3 ± 0.5 tablets/week). After CSWT, there was a decrease in the amount of angina and duration of angina in the first month and gradually decreased in 3 months after treatment. Especially after 6 months, many patients do not have angina. Since most patients with severe angina pectoris indicate severe myocardial ischemia. CSWT creates immediate local vasodilation through the release of NO at the endothelial cells, thereby helping to dilate the vessels, meet the oxygen demand of the myocardium. Vainer et al studied on 33 patients after 4 months of treatment, the number of angina pectoris decreased from 10 times/week to 2 times/week [9]. Lother Faber et al studied that 88% of patients no longer had chest pain after 3 months of treatment [4].

The 6-minute walking test all improved (278.1 ± 71m compared with 390.5 ± 42.3m). The patient's exercise capacity was significantly improved after treatment thanks to vasodilation to enhance myocardial perfusion. There are many patients who have improved after 3 months of treatment. However, patients with multiple coronary artery lesions, extensive myocardial ischemia, markedly improved after 6 months of treatment. The 6-minute walking test improved after 3, 6 months of treatment, respectively, from 286.17 ± 34.22m

versus 306.04 ± 33.56m; 304.78 ± 45.05m with p=0.0027 [10].

Through the study, we found that heart failure accounted for 54%. In the heart failure group, NYHA III decreased from 40.7% to 11.1%, NYHA II 51.9% to 33.3%. Thus, almost all the patients in our heart failure group after treatment had an improvement in NYHA level, thanks to vasodilation and neovascular proliferation leading to improved myocardial perfusion, improved contractility of the heart thereby improving the NYHA class of heart failure.

Dd and EF parameters on echocardiogrphy after treatment decreased compared to before treatment. In the study by Wang Yu et al on 25 IHD patients after 6 months, the author found that Dd changed from 63.1 ± 11.36mm to 58.1 ± 4.01mm [10]. Jelena Celutkiene et al studied on 30 patients by CSWT, after 6 months EF improved from 46.5 ± 10.6% to 49.8 ± 8.6% with p<0.05 [3]. Compared with the above studies, the reasons may be the number of small patients in our study, the rate of heart failure in the study group was low, the follow-up time was still no longer enough. When measuring ejection fraction by Teicholz method, it does not accurately reflect cardiac function. Therefore, in clinical practice for patients with ischemic heart disease, cardiac function assessment should be calculated by the Simpson's method.

In order to objectively evaluate and quantify left ventricular function, we conducted both 2D echocardiography and speckle tracking echocardiography. In our study, the wall movement index (WMSI) after treatment (1.49 ± 0.22) was lower than before treatment (1.24 ± 0.12) with statistical significance p<0.001. The left ventricular longitudinal strain (GLS) measured on echocardiography with speckle tracking tissue after treatment improved from -9.8 ± 2.68 to -12.74 ± 2.42 with p<0.001. After treatment with shock waves showed a partial improvement in myocardial perfusion, so there was a change in cardiac function and the degree of heart wall movement after treatment [4].

Our study showed that the SSS score after treatment was 15.78 ± 9.25 significantly reduced compared to before treatment 11.54 ± 7.72. SRS score in the group after shock wave treatment decreased from 11.0 ± 8.45 to 8.39 ± 6.77. SDS score after treatment decreased from 4.78 ± 2.83 to 3.02 ± 1.83 with p<0.05. After treatment with CSWT, myocardial perfusion has improved quite a lot so it improves perfusion defect on SPECT. Megha Prasad et al studied 111 patients of IHD with refractive angina pectoris. The results showed that after treatment SSS decreased from 26.49 ± 19.38 to 23.88 ± 19.9 with p<0.01; SRS after treatment was reduced from 16.62 ± 17.7 compared with 15.82 ± 15.28; SDS after treatment was reduced from 9.53 ± 17.87 to 7.77 ± 11.83 with p<0.01, up to 60% of patients improved SDS index and 60% improved SSS index [6], [8].

5. Conclusion

Our study showed the effectiveness and safety of CSWT as follows:

Angina symptoms improved significantly after CSWT.

The 6-minute walking test all improved (278.1 ± 71m compared with 390.5 ± 42.3m). NYHA grade improved significantly (NYHA III from 40.7% to 11.1%, NYHA II from 51.9% to 33.3%).

WMSI after treatment (1.24 ± 0.12) decreased compared to before treatment (1.49 ± 0.22). GLS improved from -9.79 ± 2.68 to -12.7 ± 2.42.

The average score of SSS (15.78 ± 9.25 versus 11.54 ± 7.7), SRS (11.0 ± 8.45 versus 8.39 ± 6.77), SDS (4.78 ± 2.83 versus 3.02 ± 1.83), much improved compared to before treatment with p<0.05.

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