ORIGINAL ARTICLE

Treatment of severe coronary artery calcification with intravascular lithotripsy: Initial experience of a prospective single centre registry

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ABSTRACT

Introduction: Coronary artery calcification can lead to suboptimal results when performing coronary angioplasty with conventional techniques. Shockwave intravascular lithotripsy (IVL) has recently been introduced as a new modality to treat heavily calcified coronary arteries. The purpose of this study was to determine the procedural success and safety of IVL in calcified lesions.

Materials and Methods: This was a prospective single-centre study regarding the utility of IVL in treatment of calcified coronary arteries. Intravascular ultrasound (IVUS) was used in all cases to characterise the lesions pre procedure and to assess procedural success post procedure. The primary end point was procedural success, defined by IVL treatment and successful stent implantation. The secondary end point was in-hospital and 30-day major adverse cardiovascular event (MACE).

Results: Five patients with severely calcified lesions were successfully treated with IVL. The primary end point was achieved in all patients. All of the lesions were severely calcified with concentric calcium. Multiple calcium fractures were identified on IVUS after IVL in all cases. None of the patients suffered in-hospital or 30-day MACE. The average diameter stenosis at baseline was 1.8±0.4mm and the post PCI diameter stenosis was 2.9±0.1mm, with significant acute luminal gain of 1.2±0.3mm (p<0.01). There were no complications of coronary dissection, slow or no reflow, stent thrombosis, or vessel perforation.

Conclusion: Our initial experience demonstrates the feasibility and safety of IVL in the management of calcified coronary stenosis. The shockwave IVL is an effective treatment approach to disrupt coronary calcification, facilitating stent implantation with optimal results. It is a safe procedure with a good success rate and low rate of complications.

KEYWORDS:
Intravascular lithotripsy, Intravascular ultrasound, Coronary atherectomy

INTRODUCTION

Coronary artery calcification is due to deposited calcium in the intimal and medial layers of the arterial wall, commonly due to increasing age and co-morbidities.[1] Heavily calcified plaques in coronary arteries are a risk factor for major adverse cardiac events and mortality.[2] Percutaneous coronary intervention (PCI) in calcified coronary arteries is challenging as it may be resistant to dilatation of the calcified segment with angioplasty balloons.[3] During angioplasty, inadequate stent expansion may lead to malapposition of stent struts[4] and subsequently stent thrombosis and early stent restenosis.[5] Coronary calcium can often be treated successfully with different therapeutic calcium debulking techniques, including orbital or rotational atherectomy, excimer lasers as well as cutting and scoring balloons.[6] Non-compliant (NC) balloons may require high pressure for vessel dilation, and the use of cutting balloons in severely calcified lesions can be associated with serious complications such as coronary artery dissection and perforation.[7] There has thus been a need for alternative treatment modalities, especially those which are associated with a minimal degree of complications.

Shockwave intravascular lithotripsy (IVL), a technique similar to the one used in nephrolithiasis, has evolved as a new modality to treat heavily calcified coronary arteries. IVL involves using a percutaneous device to produce acoustic pressure waves resulting in the delivery of sufficient energy to break up superficial and deep calcium deposits.[8] Early studies showed that IVL has been used successfully to treat coronary calcific plaques with minimal vascular complications.[9] Intravascular ultrasound (IVUS) or optical coherent tomography (OCT) are often performed pre-IVL treatment to evaluate the extent of calcification and post procedure as well as to demonstrate calcium fractures and evaluate procedural success.

In this study, we describe the data of a prospective registry in a single centre for the use of IVL to treat severely calcified coronary artery lesions.

MATERIALS AND METHODS

Patients and study design

The Prospective Registry of Calcified Coronary Artery lesions

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Table I: Baseline characteristics

Male, n (%)	5 (100)
Age (mean±SD %)	60±12
Hypertension, n (%)	3 (60)
Hypercholesterolaemia, n (%)	4 (80)
Smoking, n (%)	1 (20)
Family history of cardiac disease, n (%)	3 (60)
Diabetes mellitus, n (%)	1 (20)
LVEF (mean±SD %)	61±1.6
eGFR (ml/min/1.73 m2)	81±25.5
Stable angina / positive stress test	3 (60)
Unstable angina	2 (40)
Male, n (%)	5 (100)

Table II: Procedural characteristics and Clinical Outcomes

Vessel treated	
LAD, n (%)	4 (80)
LCX, n (%)	1 (20)
RCA, n (%)	0 (0)
Lesion characteristics	
Proximal, n (%)	5 (100)
Mid, n (%)	2 (40)
Length (mean±SD), mm	20.6±3.7
Severe calcification, n (%)	5 (100)
Procedural characteristics	
Procedural time (mean±SD)	135.2±13.9
Fluoroscopy time (mean±SD)	28.6±6.5
Femoral vascular access, n (%)	4 (80)
Radial vascular access, n (%)	1 (20)
Number of lithotripsy pulses applied (median, range)	50 (30-60)
Diameter of lithotripsy balloon (2.5 mm), n	3 (60)
Diameter of lithotripsy balloon (3.0 mm), n	2 (40)
Largest diameter of predilatation balloon, mm (median, range)	3.0 (2.5-3.0)
Mean pressure of predilatation, atm (mean±SD)	11.2±1.8
Largest diameter of postdilatation balloon, mm (median, range)	3.0 (2.75-3.25)
Mean pressure, of postdilatation, atm (mean±SD)	14.8±4.6
2 stents/lesion, n (%)	3 (60)
1 stent /lesion, n (%)	2 (4)
IVUS Characteristics	
Baseline MLD (mm±SD)	1.8±0.4
Post PCI MLD (mm ±SD)	2.9±0.1
Baseline MLA (mm2 ±SD)	3.3±0.9
Post PCI MLA (mm2 ±SD)	6.7±0.5
Post PCI Luminal Gain (mm±SD)	1.2±0.3
Angiographic and clinical outcomes	
Procedure success with facilitated stent delivery	5 (100)
Perforation, dissection, slow flow, stent thrombosis	0 (0)
In-hospital MACE (MI/TVR/Death)	0 (0)
30-day MACE (MI/TVR/Death)	0 (0)

is a single-centre study. Approval for the study was granted by Independent Ethics Committee of Ramsay Sime Darby Healthcare. Anonymised data were collected by medical record review and all patients gave written informed consent for inclusion into the registry. Baseline characteristics of patients including age, cardiac risk factors, and clinical presentation were documented from clinical records. Left ventricular ejection fraction (LVEF) and baseline renal function (eGFR) were documented.

Percutaneous coronary intervention

All patients were given dual-antiplatelet therapy and received intra-arterial heparin for anticoagulation during the PCI procedure. Patients underwent IVL with the Shockwave C2 lithotripsy (Shockwave Medical, Santa Clara, CA, USA). IVUS was used in all cases to characterise the lesions pre procedure, and calcium was defined as a (hyperechoic) lesion with a brighter shadow than reference adventitia.10 Measurements of pre and post-PCI mean luminal diameter (MLD) and mean luminal area (MLA) were recorded. The angioplasty balloon size was selected based on vessel diameter measured by IVUS at a 1:1 ratio. The balloon catheter was inflated to 4 atm and up to 10 impulses were delivered at 1 pulse/second. A maximum of up to 80 impulses could be delivered with a single IVL catheter. IVUS was used after IVL to assess procedural success and document procedural complications post procedure. Post-IVL calcium fracture was identified on IVUS as the presence of a new disruption or discontinuity in the calcium arc. Following PCI, all patients were given dual antiplatelet therapy with either

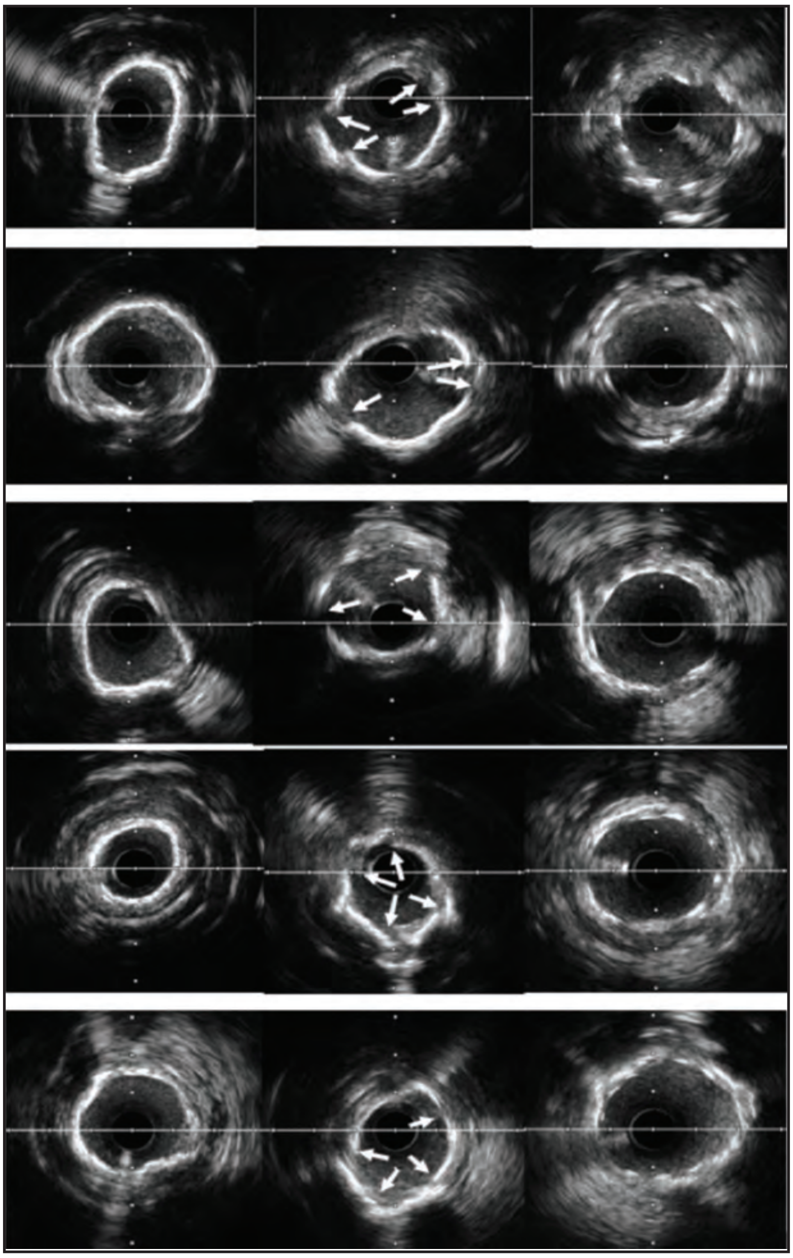

Fig. 1: IVUS images show surrounding severe calcification with concentric arc (left) in all five cases (top to bottom). Corresponding post IVL and calcium fractures (arrows) in the vessel (middle). IVUS images post stenting (right) showing well-apposed stent struts

aspirin 100 mg, clopidogrel 75mg or ticagrelor 180mg/day for 12 months.

Endpoints
The primary end point was procedural success defined as successful IVL treatment and stent implantation with <30% residual stenosis. The secondary endpoint was in-hospital major adverse cardiovascular event (MACE), including cardiac death, myocardial infarction (MI), or target-vessel revascularisation (TVR) and 30-day MACE.[11] Safety outcome was procedural complication, defined as coronary dissection, slow or no reflow, stent thrombus, or vessel perforation.

Statistical analysis
Descriptive statistics, including mean, median, and ranges were used. Categorical variables are presented as counts (%) and continuous variables are presented as mean±standard deviation. The paired t-test was used for comparison of MLD at baseline and after PCI. A $p \leq 0.05$ was considered significant.

RESULTS
Baseline clinical and procedural characteristics.
Between March 2021 and February 2022, five patients with severely calcified lesions were treated with IVL. The baseline characteristics of the patients are shown in Table 1. Mean age was 60±12 years, with a high prevalence of risk factors of hypertension, hypercholesterolemia, and family history of cardiac disease. One (20%) patient had diabetes mellitus (commonly associated with coronary artery calcification).[12]

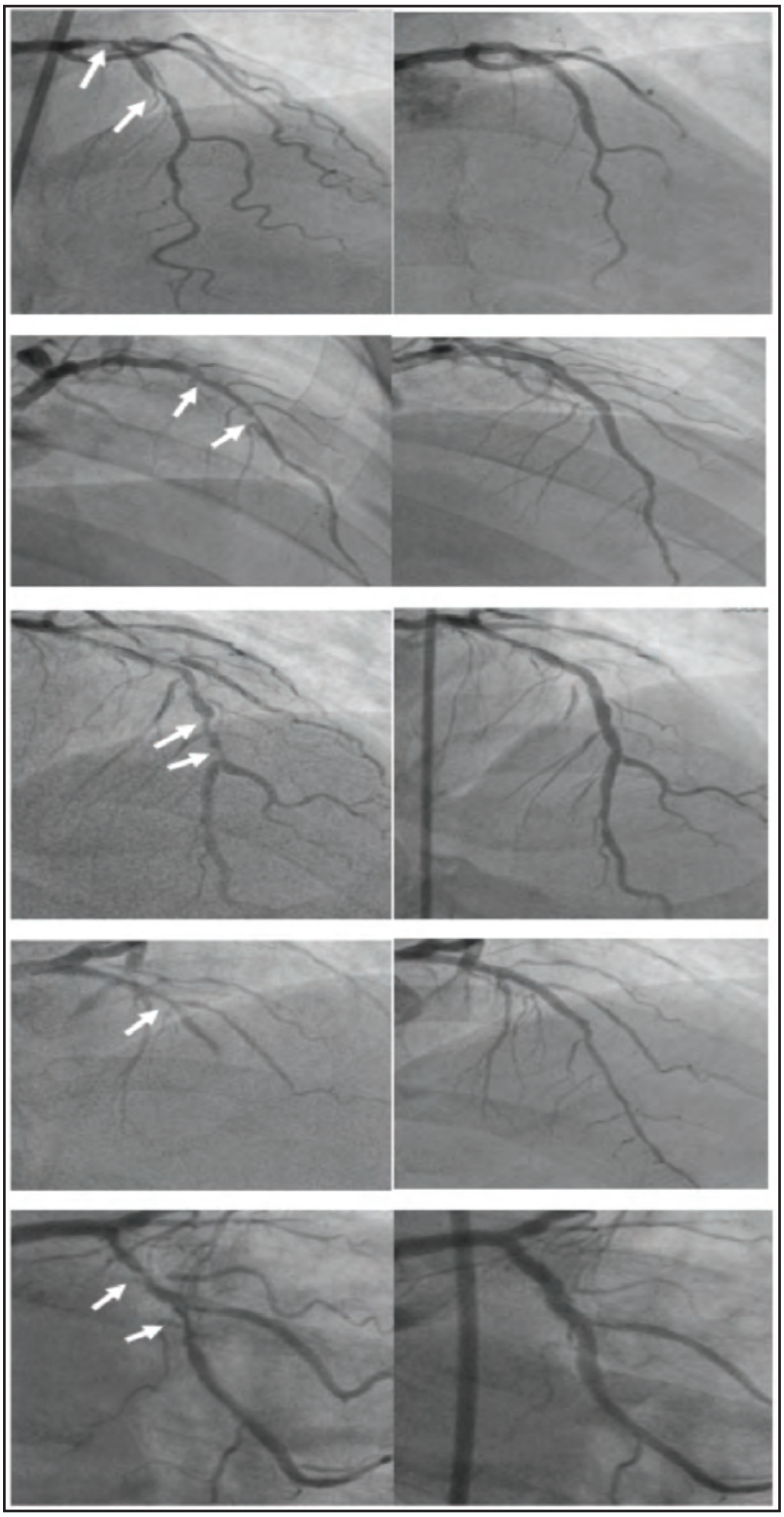

Fig. 2: Pre-procedure angiogram (left) showing areas of calcified stenosis (arrow) for the five patients (top to bottom). Post procedure and corresponding final result after IVL and stenting of the lesion (right)

Procedural characteristics
The procedural characteristics are shown in Table II. Femoral vascular access was preferred in majority of cases. The target artery was the left anterior descending coronary artery in four patients and the left circumflex coronary artery in one patient. All of the lesions were severely calcified, with a mean length of 20.6±3.7 mm, and concentric calcium was present in all lesions. Three IVL balloons of 2.5 mm diameter and two balloons of 3.0 diameter were used. Multiple (≥2) calcium fractures were identified in all five cases after IVL treatment. Pre and Post PCI IVUS images for all cases are shown in Figure 1. In one case, the IVL balloon ruptured during the

Fig. 3: An illustration of the IVL balloon emitting sonic pressure waves.[17]

procedure (after delivery of 30 Shockwave pulses) with no adverse complications. The pre-procedure angiographic images and post-procedure images for all cases are highlighted in Figure 2.

Clinical outcomes
The primary endpoint of procedural success was achieved in all patients. There were no in-hospital MACE and 30-day MACE events (Table 2). The average diameter stenosis at baseline was 1.8±0.4 mm and the post PCI diameter stenosis was 2.9±0.1 mm, with a significant acute luminal gain of 1.2±0.3 mm ($p<0.01$). There were no cases of coronary dissection, slow or no reflow, stent thrombus, or vessel perforation.

DISCUSSION

This study is the first IVL registry to be published from Malaysia. The main findings of our study are as follows: IVL was performed with successful stent delivery in all cases. IVL was safe, with no major angiographic complications and none of the patients had in-hospital and 30-day follow-up MACE.

IVL was first used in Malaysia in Mar 2021.[13] It is a semi-compliant balloon-catheter system integrated with multiple lithotripsy emitters (Figure 3), which transduces electric pulses into sonic pressure waves.[14] The catheter is compatible with 0.014" coronary guidewires and is available in 2.5, 3.0, 3.5, and 4.0mm diameters with a balloon length of 12mm. The treatment is delivered by placing the balloon catheter within the coronary artery at the site of stenosis and inflating it up to 4 atm pressure.[15] The presence of saline and contrast within the IVL balloon facilitates the transfer of pressure waves through the soft tissue into the calcium deposits. The mechanism of calcific plaque modification by IVL includes splitting of calcific plaque by the impact of compressive circumferential forces which are induced by shock waves. There is also the development of microfractures and also macrofractures following cumulative impact of repetitive shock wave pulses.[16]

During delivery of shockwave cycles, electric signals that mimic pacing spikes may be seen on the electrocardiogram trace, possibly due to piezoelectricity (electric charge that accumulates in soft tissue in response to sonic pressure waves).18 Since severe calcification is an important predictor of restenosis after PCI, treatment with IVL can potentially increase the vessel diameter and ensure better stent placement. This reduces the risk of stent under expansion which in turn reduces the risk of stent thrombosis and restenosis.[19] The system also offers potential benefits to treat both superficial and deep calcium with less risk of atheromatous embolisation and reduced vessel trauma with lower balloon pressures. The rare procedural complications of IVL may include slow coronary blood flow, lack of reflow, distal embolisation, coronary artery perforation, and arterial dissection.

Trial Evidence for IVL
The Disrupt Coronary Artery Disease (Disrupt CAD) I and II trials demonstrated the initial safety and feasibility of IVL in calcified coronary lesions.[9,20] The first multicentre prospective study, Disrupt CAD I, enrolled 60 patients with severely calcified vessels and demonstrated successful stent implantation following IVL in all patients. The second trial, Disrupt CAD II, studied 120 cases with extensive coronary artery calcification and showed similarly successful delivery and use of the IVL catheter in all patients. The trial reported no complications of abrupt vessel closure, slow flow/no-reflow, or coronary perforation.

The largest study so far was the Disrupt CAD III study, which was a prospective, single-arm multicentre study including 431 patients with calcified coronary arteries.[21] The primary safety endpoint of the 30-day freedom from major adverse cardiovascular events was 92.2%. There was a high rate of procedural success at 92.4%. OCT demonstrated multiplane and longitudinal calcium fractures after IVL in 67.4% of lesions. This study concluded that IVL had high procedural success in angioplasty of severely calcified lesions with a low complication rate.

STUDY LIMITATIONS

This is a prospective, single-arm registry with a short-term follow-up period of 30 days. The study comprises a small study cohort. Larger randomized studies or clinical registries of IVL with long-term follow-up will be of significant clinical value.

CONCLUSION

Our initial experience demonstrates the feasibility and safety of IVL in the management of calcified coronary stenosis. The shockwave IVL is an effective treatment approach to disrupt coronary calcification, facilitating stent implantation with optimal results. It is a safe procedure with good success rate and low rate of complications.

CONFLICT OF INTEREST

The study did not receive any funding grant. There was no role from any commercial or non-profit sector in the design and interpretation of the study.

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