Interventional procedure overview of intravascular lithotripsy to treat calcified coronary arteries during percutaneous coronary intervention

Contents

Table 1 Abbreviations

Abbreviation	Definition
ACS	Acute coronary syndrome
CCS	Chronic coronary syndrome
CL	Coronary lithotripsy
IVL	Intravascular lithotripsy
MACE	Major adverse cardiovascular events
MI	Myocardial infarction
PCI	Percutaneous coronary intervention
RA	Rotational atherectomy
S-IVL	Shockwave intravascular lithotripsy
SMD	Standardised mean difference
TIMI	Thrombolysis in myocardial infarction

Indications and current treatment

Coronary artery calcification (intimal and medial calcifications) increases the complexity of percutaneous treatment strategies in coronary interventions. It contributes to:

- arterial wall stiffness
- suboptimal stent delivery and expansion
- in-stent restenosis
- high rates of stent thrombosis
- the need for subsequent target lesion revascularisation after endovascular interventions.

Standard endovascular treatment options for modifying calcium or plaque during PCI include balloon angioplasty using standard or high-pressure non-compliant balloons; cutting or scoring balloons; and stenting with or without coronary atherectomy (such as rotational, orbital or laser atherectomy). These treatments aim to allow optimal stent expansion and achieve maximal luminal gain. But they

may sometimes lead to localised wall injury, balloon rupture or the risk of coronary vessel dissections or perforation. Intravascular lithotripsy is another endovascular treatment option for PCI.

Unmet need

Addressing calcified coronary lesions during PCI presents a significant challenge. Calcified plaques can hinder stent deployment and expansion, increasing the risk of complications such as arterial dissection or inadequate stent expansion. Existing options for managing heavily calcified coronary arteries during PCI such as balloon angioplasty may not be effective in fracturing severe calcifications. By using sonic waves to fracture calcium deposits, IVL may be an efficient approach to managing calcified coronary arteries and may lead to better stent placement and improved patient outcomes.

What the procedure involves

In this procedure, intravascular lithotripsy is administered to the calcified coronary artery before stent placement during PCI.

A percutaneous guidewire is passed through a catheter inserted from the radial or femoral artery into the coronary artery. Then, an IVL catheter with embedded emitters enclosed in an integrated angioplasty balloon is passed and connected to an external generator with a cable. The catheter is advanced to the target lesion guided by X-ray imaging of radio-opaque markers on the catheter. The balloon is then inflated with a saline and contrast solution to ensure contact with the vessel wall. The lithotripsy cycle is then started. For every cycle, the catheter emits localised, high-energy, pulsatile, unfocused, circumferential, sonic, pressure waves (lasting microseconds). These waves pass through the inflated balloon into the wall of the coronary artery. As the waves travel along the wall and the connective tissue, they disrupt calcium deposits (both intimal and medial

calcium) by micro-fracturing the calcified lesions. The balloon is then deflated to allow blood supply to return to the heart.

The cycle can be repeated until the lesion has expanded enough to allow optimal stent placement or the total pulses available are used.

Outcome measures

The main outcomes focused on procedural success, clinical success and safety outcomes. The measures used are detailed in the following paragraphs.

Procedural and clinical success

Procedural success rate

Defined as completing the procedure with full expansion of the balloon or stent with residual stenosis of less than 30%, or both, and TIMI III flow without any serious angiographic complications.

Clinical success rate

Defined as the ability of IVL to achieve a residual stenosis of less than 50% after stent implantation and freedom from MACE.

Safety measures

Major adverse cardiovascular events (MACE)

Defined as the composite of death, MI, and target-vessel revascularisation occurring within a specified follow-up period (for example, in-hospital, 30-days).

Evidence summary

NICE has identified studies and reviews relevant to IVL for calcified coronary arteries during PCI from the medical literature. Relevant published studies

identified during consultation or resolution that are published after this date may also be considered for inclusion.

Population and studies description

This interventional procedure overview is based on about 4,300 people from 2 systematic reviews and meta-analyses (Sagris, 2024; Caminiti, 2023), 4 prospective studies (Cubero-Gallego, 2022; Aziz, 2020; Rodriguez-Leor, 2024; Aksoy, 2019), and 2 retrospective cohort studies (Wiens, 2021, Rola, 2022). There was significant overlap between the studies included in the meta-analyses. Among the included studies, IVL was the main intervention including some comparator interventions. This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 8 studies as the key evidence in table 2 and table 3, and lists other relevant studies in appendix B, table 5. Table 2 presents study details.

The key evidence includes explicit comparisons between IVL and other procedures used for treating calcified coronary lesions. This is the reason for including several meta-analyses even if some or all studies overlap. The systematic review and meta-analysis by Sagris (2024) included 38 studies comparing IVL for lesion preparation before stent implantation. The systematic review and meta-analysis by Caminiti (2023) included 13 studies focusing on IVL for treating underexpanded stents.

The review by Sagris (2024) involved 2,977 people, predominantly men, with heavily calcified coronary lesions, with comorbidities such as hypertension, diabetes mellitus, hyperlipidaemia, chronic kidney disease, and previous MI and PCI. Similarly, Caminiti (2023) focused on 354 people with underexpanded coronary stents, also predominantly men and with a high mean age.

The prospective studies, such as those by Cubero-Gallego (2022) and Aziz (2020), provided detailed insights into the procedural success and long-term

outcomes of IVL. These studies included people with significant comorbidities and varying clinical presentations, such as acute coronary syndromes and multivessel disease.

The retrospective cohort study by Wiens (2021) added a real-world perspective, focusing on 50 people with highly calcified lesions, including those with ACS, stent failure, and left main coronary artery lesions.

Figure 1 Flow chart of study selection

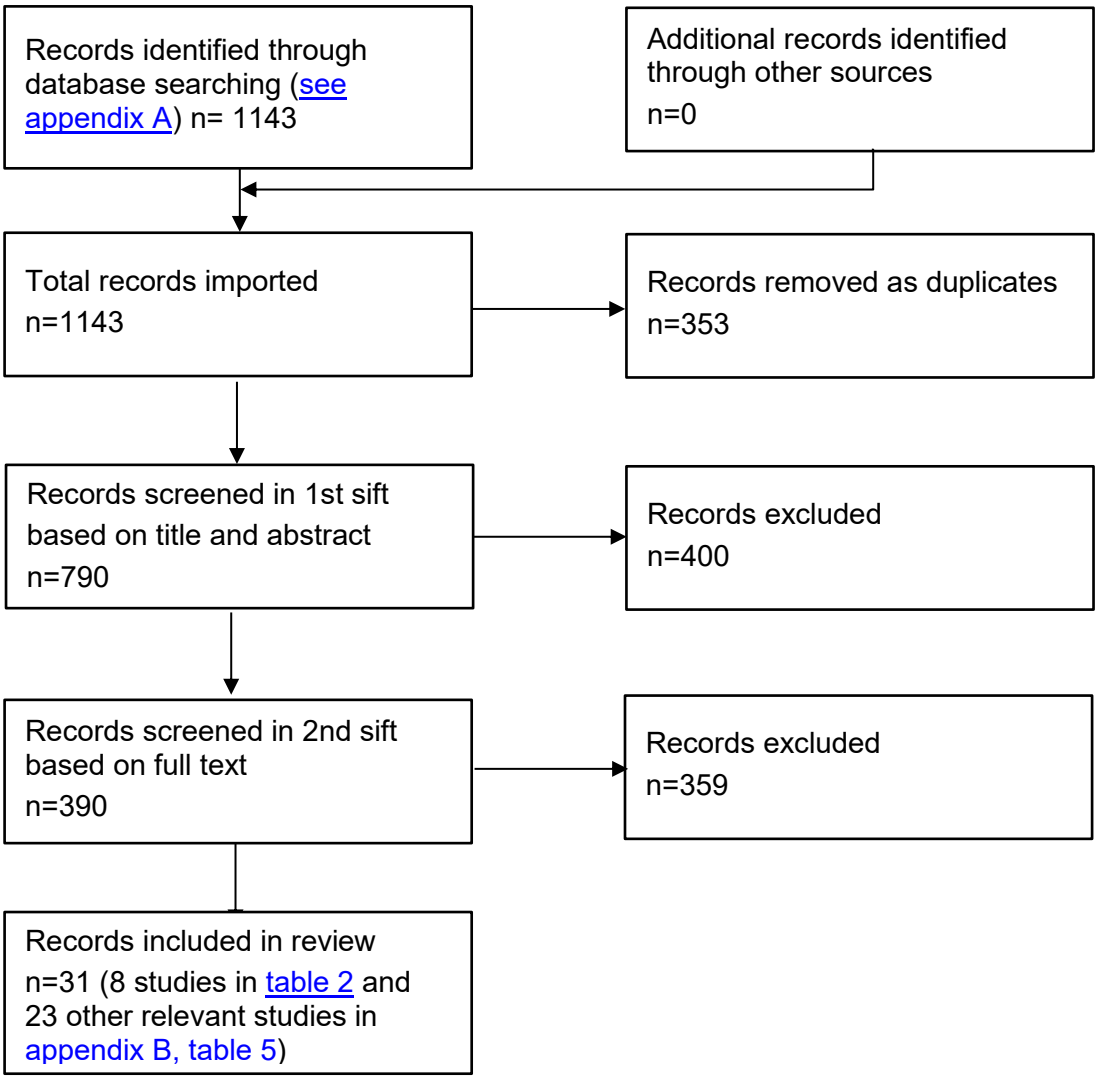

Table 2 Study details

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
1	Sagris M, 2024	2977 patients with heavily calcified coronary lesions. Mean age: 72.2 plus or minus 9.1 years. Majority were men (77.5%). Comorbidities included hypertension, diabetes mellitus, hyperlipidaemia, chronic kidney disease, and previous myocardial infarction and PCI.	Multicentre systematic review and meta-analysis.	Prospective/retrospective analyses of patients undergoing IVL before stent implantation. Studies reporting short- and/or late-outcomes. Studies published up to February 23, 2023.	IVL for lesion preparation before stent implantation. 69% of procedures used radial artery access and 32% used the femoral artery.	In-hospital and 30-day follow-up.
2	Caminiti R, 2023 Italy	354 patients with under expanded coronary stents due to calcified plaques. Mean age: 71.3 years. 77% males.	Systematic review and meta-analysis	Studies reporting on IVL for under expanded stents	IVL for stent under expansion treatment	Mean follow-up of 2.6 months
3	Wiens EJ, 2021 Canada	50 patients with highly calcified coronary lesions. Median age: 71.5 Majority were men (64%). Comorbidities included ACS, stent failure, and left	Retrospective cohort study	Patients undergoing IVL for calcified lesions. Real-world settings.	IVL for treatment of calcified coronary lesions.	In-hospital and 30-day follow-up.

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		main coronary artery lesions.				
4	Rola P 2022	44 patients in-hospital	Retrospective evaluation	Patients with calcified lesions who had undergone PCI, and who required additional lesion preparation with rotational atherectomy or IVL	IVL	In hospital and 6 months follow-up
5	Cubero-Gallego H, 2022 Spain	109 patients with 128 calcified coronary lesions. Mean age: 74 years. High rates of comorbidities including diabetes (58%), renal insufficiency (32%), multivessel disease (76%).	Real-world registry. Prospective, multicentre, single-arm study	Patients >18 years old with severe stenosis and severe calcified coronary lesions in vessels with diameter ≥2.5 mm.	CL for treating calcified coronary lesions.	In-hospital, 30-day follow-up, and long-term follow-up (median of 20 months [IQR, 14.5-25]).
6	Aziz A, 2020, European Study	190 patients with 200 calcified coronary lesions. Mean age: 72 years. High rates of comorbidities including diabetes (50%) and chronic kidney disease (16%). Acute-coronary syndrome in 48% of cases.	Prospective, multicentre, single-arm study	All patients had treatment with IVL between November 2018 and February 2020 at 6 centres.	IVL for treating calcified coronary lesions.	Median follow-up of 222 days.

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
7	Rodriguez-Leor, 2024, Spain	426 patients with calcified coronary lesions. High prevalence of hypertension, diabetes, dyslipidaemia, and prior myocardial infarction (MI) and percutaneous coronary intervention (PCI).	Prospective, multicentre, single-arm, open-label conducted in 26 hospitals	Patients with calcified coronary artery disease requiring PCI and deemed necessary for coronary IVL Exclusion criteria: refusal to participate, life expectancy <1 year or haemodynamic instability with Killip class III or IV	IVL with coronary IVL system	30 days
8	Aksoy A, 2019, Germany and Spain	71 patients with 78 calcified coronary lesions. Mean age: 76 (9.7 years range). High prevalence of male sex (71.8%) and comorbidities including hypertension (92.9%), hypercholesterolemia (63.4%), and diabetes (33.8%).	Prospective, observational, multicentre registry	Patients with significant coronary lesions and angiographically graded moderate or severe calcification.	IVL using the Shockwave C2 balloon	In-hospital, 30-day, and ongoing 12-month follow-up

Table 3 Study outcomes

First author, date	Efficacy outcomes	Safety outcomes
Sagris M, 2024, Multi-centre	Overall clinical success rate of 93% (95% CI: 91%−95%). Procedural success rate of 97% (95% CI: 95%−98%). There was a significant increase in vessel diameter immediately after IVL application (SMD: 2.47, 95% CI: 1.77−3.17, I^2 = 96%) and a decrease in diameter stenosis (SMD: −3.44, 95% CI: −4.36 to −2.52, I^2 = 97.5%). Further reduction in diameter stenosis (SMD: −6.57, 95% CI: −7.43 to −5.72, I^2 = 95.8%) and an increase in vessel diameter (SMD: 4.37, 95% CI: 3.63−5.12, I^2 = 96.7%) and calculated lumen area (SMD: 3.23, 95% CI: 2.10−4.37, I^2 = 98%) were observed after stent implantation. Stenosis, diameter, and lumen area improvements were maintained after stent implantation. Meta-regression analysis showed no significant effect of baseline characteristics on the outcomes.	In-hospital and 30-day MACE incidence was 8% (95% CI: 6%−11%, I^2 = 84.5%). Myocardial infarction incidence was 5% (95% CI: 2%−8%, I^2 = 85.6%). Mortality rate was 2% (95% CI: 1%−3%, I^2 = 69.3%). Periprocedural complications were rare: perforations (1%), dissections (2%), slow flow (0%), or no-reflow phenomena (0%).
Caminiti R, 2023	The study evaluated the efficacy of intravascular lithotripsy (IVL) therapy on 360 treated lesions, with the left anterior descending artery being the most involved vessel (45.9%, 95% CI 36.6% to 55.3%), followed by the right coronary artery (31.8%, 95% CI 24.5% to 39.5%), left circumflex artery (10%, 95% CI 6% to 14.6%), and left main artery (7.9%, 95% CI 4.3% to 12.2%). Lesion preparation before IVL therapy involved noncompliant balloon pre dilatation in 82.6% (95%	Procedural complications and major adverse cardiac events (MACEs) were reported across 13 studies, with a pooled procedural complications rate of 1.6% (95% CI 0.3 to 2.9). Specific complications included two cases of dissection (types D and F), one perforation (Ellis type III), and one periprocedural myocardial infarction due to IVL balloon rupture.

First author, date	Efficacy outcomes	Safety outcomes
	CI 69.6% to 93%) of patients and the use of a very high–pressure balloon in 29.8% (95% CI 12.2% to 50.5%). Post dilatation following IVL was performed in 83.8% (95% CI 75% to 91.2%) of patients. During the IVL procedure, the mean IVL balloon diameter was recorded at 3.4 mm (95% CI 3.2 to 3.5), with an average of 70.9 lithotripsy pulses (95% CI 62.2 to 79.6) and a mean maximum balloon pressure of 5.2 atmospheres (95% CI 4.3 to 6.2). Intravascular ultrasound imaging was utilized in 33.1% (95% CI 20.1% to 47.4%) of patients, while optical coherence tomography was performed in 23.7% (95% CI 10.9% to 39%). The mean follow-up period was 2.6 months (95% CI 1 to 15.3). Post-IVL outcomes showed significant improvements: the average minimal stent area increased from a baseline value of 3.4 mm^2 (95% CI 3 to 3.8) to 6.9 mm^2 (95% CI 6.5 to 7.4). The percent diameter stenosis, assessed by quantitative coronary analysis, reduced from 69.4% at baseline (95% CI 60.7 to 78.2) to 14.6% post-IVL therapy (95% CI 11.1 to 18). Additionally, the mean minimum luminal diameter increased from 1.1 mm (95% CI 0.8 to 1.4) pre-IVL to 2.9 mm (95% CI 2.6 to 3.2) post-IVL.	The heterogeneity for these complications was low (I^2 = 0%), indicating consistent findings.

First author, date	Efficacy outcomes	Safety outcomes
	The primary efficacy endpoint, procedural success, was reported in 12 studies with a total of 342 lesions undergoing IVL, achieving success in 289 lesions (88.7%, 95% CI 82.3 to 95.1). Meta-regression analysis suggested a negative influence of left main lesions on procedural success (β −0.91 [−1.46 to −0.37], p = 0.001), while predilatation with OPN showed a positive influence (β 0.27 [0.02 to 0.53], p = 0.035). The heterogeneity for these outcomes was high (I^2 = 75.7%).	
Wiens EJ, 2021	Angiographic success in 98% of patients (residual stenosis <50%, TIMI 3 flow). >90% of patients were free of angina at 30 days.	In-hospital mortality unrelated to IVL: 3 patients. No occurrences of MACE up to 30 days. Rare complications: no cases of distal embolisation, coronary perforation, or dissection.
Rola P, 2022	High procedural success rates in both groups.	Both techniques were found to be safe with no significant differences in complications.
Cubero-Gallego H, 2022	Procedural success rate of 99% in treating calcified coronary lesions using CL. Patients showed clinical improvements, including enhanced left ventricular ejection fraction and better Canadian Cardiovascular Society angina class, with 78% of patients in class 0–I at long-term follow-up. The long-term follow-up, with a median duration of 20 months, revealed a MACE rate of 5.6%. Additionally, the target-lesion revascularisation (TLR) rate was 1.85%, suggesting effective maintenance of vessel patency and low rates of restenosis in this high-risk population.	CL was characterised by minimal procedural complications. In-hospital and 30-day follow-up data showed a freedom from MACE rate of 98%, with a few instances of coronary dissection, all managed with stenting. There were no reports of slow-flow/no-reflow phenomena, coronary perforation, or target-lesion failure. Long-term follow-up indicated a cardiac death rate of 3.7% and an all-cause death rate of 15%, reflecting the advanced age and comorbidities of the study population. The low TLR rate and absence of significant adverse events, such as stent thrombosis or major bleeding, further support the

First author, date	Efficacy outcomes	Safety outcomes
		safety of CL in managing calcified coronary lesions in a high-risk, unselected patient cohort.
Aziz A, 2020	Procedural success in 99% of cases.	MACE rate at median follow-up of 222 days was 2.6%. Rare complications: 2 cases of cardiac deaths (1%), 1 case of target vessel MI (0.5%), and 3 cases of target lesion revascularisation (1.5%).
Rodriguez-Leor, 2024	The procedural success rate for IVL delivery was 99%. The primary efficacy endpoint, defined as successful PCI with residual stenosis less than 20% and no in-hospital MACE, was achieved in 66% of patients. There were no significant differences in angiographic success between patients with CCS and those with ACS, indicating that IVL effectively facilitated stent implantation in severely calcified lesions across different patient subsets.	The primary safety endpoint, defined as freedom from MACE at 30 days, was observed in 96.4% of patients. The overall 30-day MACE rate was 3%, with a higher, though not statistically significant, incidence in ACS patients compared to CCS patients (5% vs. 1%, P=0.073). In-hospital complications included a 0.7% incidence of coronary perforation and a 2.4% incidence of coronary dissection, all of which were managed successfully. There were 7 deaths (1.7%) within 30 days, with 4 being cardiovascular-related. Additionally, 3 cases of stent thrombosis (1.1%) occurred, all in ACS patients. These findings suggest that IVL is associated with a low complication rate in a real-world setting, even among high-risk patients with complex coronary lesions.
Aksoy A, 2019	The primary efficacy endpoint, defined as successful stent delivery with less than 20% residual stenosis, was achieved in 78.2% of the lesions. Specifically, success rates were 84.6% for primary IVL (de-novo lesions), 77.3% for	The primary safety endpoint, which included procedural complications and in-hospital MACE, reported no in-hospital MACE in the entire cohort. Procedural complications were low, with 4 type B dissections and seven balloon ruptures occurring

First author, date	Efficacy outcomes	Safety outcomes
	secondary IVL (failed high-pressure balloon dilatation), and 64.7% for tertiary IVL (in-stent restenosis due to under expanded stents). Mean minimal lumen diameter (MLD) increased from 1.01 (range of 0.49 mm) at baseline to 2.88 (range of 0.56 mm) after stenting, indicating effective lesion preparation and improved stent expansion across all groups.	without further adverse outcomes. The overall rate of device-related complications was minimal, demonstrating a favourable safety profile for IVL in treating severely calcified coronary lesions. This study indicates that IVL is a feasible and safe method for lesion preparation, with high success rates and low procedural complications in a diverse patient population.

Procedure technique

Of the 8 studies, all detailed the procedure technique and devices used. The most common approach involved the use of IVL for lesion preparation before stent implantation. The technique was consistent across the studies, with minor variations in balloon size and pressure settings based on the severity of the calcification and specific vessel characteristics. The primary device used for IVL was the Shockwave C2 balloon catheter, which delivers pulsatile sonic pressure waves to fracture the calcified plaque and improve vessel compliance.

Efficacy

Procedural and clinical success

Procedural success rate

The procedural success rate, defined as the completion of the procedure with full expansion of the balloon or stent with residual stenosis of less than 30%, or both, and TIMI III flow without any serious angiographic complications, was reported in 6 studies and ranged from 96% to 99%.

Clinical success rate

The clinical success rate, defined as the ability of IVL to achieve a residual stenosis of less than 50% after stent implantation and freedom from major adverse cardiovascular events (MACE), was reported in several studies. Sagris (2024) reported an overall clinical success rate of 93% (95% CI 91% to 95%). Cubero-Gallego (2022) reported a clinical success rate of 99%, and Wiens (2021) noted that over 90% of people were free of angina at 30 days, suggesting a high rate of clinical success.

Vessel diameter and stenosis

Vessel diameter increase

The increase in vessel diameter, measured by the change before and after IVL application and typically reported as a standardised mean difference (SMD), was reported in several studies. Sagris (2024) found a significant increase in vessel diameter (SMD 2.47, 95% CI 1.77 to 3.17, I^2 = 96%) and a decrease in diameter stenosis (SMD −3.44, 95% CI −4.36 to −2.52, I^2 = 97.5%) immediately after IVL application. Caminiti (2023) reported a mean increase in minimal luminal diameter from 1.1 mm (95% CI 0.8 to 1.4 mm) pre-IVL to 2.9 mm (95% CI 2.6 to 3.2 mm) post-IVL. Aksoy (2019) also found a significant increase in vessel diameter following IVL, with mean minimal lumen diameter increasing from 1.01 mm at baseline to 2.88 mm after stenting.

Diameter stenosis reduction

The reduction in diameter stenosis, assessed by the percentage reduction in vessel stenosis following IVL and stent implantation, was reported in several studies. Sagris (2024) found a statistically significant reduction in diameter stenosis (SMD −3.44, 95% CI −4.36 to −2.52, I^2 = 97.5%). Cubero-Gallego (2022) reported a mean reduction in diameter stenosis of 17.5%. Aksoy (2019) also reported a significant reduction in diameter stenosis, with a mean reduction of 17.5%. Caminiti (2023) reported a reduction in diameter stenosis from 69.4% (95% CI 60.7% to 78.2%) pre-IVL to 14.6% (95% CI 11.1% to 18%) post-IVL.

Safety

Major adverse cardiovascular events (MACE)

Major adverse cardiovascular events (MACE), defined as the composite of death, myocardial infarction (MI), and target-vessel revascularisation within a specified follow-up period, were reported in 6 studies. Sagris (2024) reported an in-hospital and 30-day MACE incidence of 8% (95% CI 6% to 11%). Caminiti (2023)

reported a pooled MACE rate of 11%. Cubero-Gallego (2022) found a 30-day MACE rate of 2%, with a long-term MACE rate of 5.6% at a median follow-up of 20 months. Aziz (2020) reported a MACE rate of 2.6% at a median follow-up of 222 days. Rodriguez-Leor (2024) found a 30-day MACE rate of 3%, with a higher incidence in people with ACS than in people with CCS (5% vs. 1%, p=0.073). Aksoy (2019) reported no in-hospital MACE in their cohort. Rola (2022) found no statistically significant differences in MACE between RA and S-IVL groups.

Myocardial infarction

The incidence of MI during or after the procedure, assessed within the follow-up period, was reported in several studies. Sagris (2024) reported an MI incidence of 5% (95% CI 2% to 8%). Caminiti (2023) reported a target vessel MI rate of 3%. Cubero-Gallego (2022) included MI within the overall MACE but did not report it separately. Aziz (2020) reported 1 target vessel MI (0.5%). Rodriguez-Leor (2024) reported a 30-day MI incidence of 2.4%, all occurring in people with ACS. Aksoy (2019) reported no cases of MI in their study cohort.

Mortality rate

The mortality rate occurring within the follow-up period, whether related to the procedure or from other causes, was reported in several studies. Sagris (2024) reported an in-hospital mortality rate of 2% (95% CI 1% to 3%). Caminiti (2023) did not report specific mortality rates in their study. Wiens (2021) reported in-hospital mortality unrelated to IVL in 3 people. Cubero-Gallego (2022) reported a long-term mortality rate of 3.7% (cardiac death) at a median follow-up of 20 months. Aziz (2020) reported 2 cardiac deaths (1%). Rodriguez-Leor (2024) reported a 30-day mortality rate of 1.2%.

Periprocedural complications

Periprocedural complications, including perforations, dissections, slow flow and no-reflow phenomena, were reported during or immediately after the procedure

across multiple studies. Sagris (2024) reported rare complications, including perforations (1%), dissections (2%), slow flow (0%) and no-reflow phenomena (0%). Wiens (2021) found no cases of distal embolisation, coronary perforation or dissection. Caminiti (2023) reported procedural complications with a pooled rate of 1.6% (95% CI 0.3% to 2.9%), including specific cases of dissection and perforation. Cubero-Gallego (2022) noted rare periprocedural complications, including dissections (2.8%) and no instances of slow flow or no-reflow. Aksoy (2019) reported no cases of perforation, slow flow or no-reflow phenomena, but observed 7 balloon ruptures during treatment without any adverse sequelae. In addition, Rodriguez-Leor (2024) reported a 0.7% incidence of coronary perforation and a 2.4% incidence of coronary dissection, all managed successfully.

Anecdotal and theoretical adverse events

Expert advice was sought from consultants who have been nominated or ratified by their professional society. They were asked if they knew of any other adverse events for this procedure that they had heard about (anecdotal), which were not reported in the literature. They were also asked if they thought there were other adverse events that might possibly occur, even if they had never happened (theoretical).

Six professional expert questionnaires for this procedure were submitted. Find full details of what the professional experts said about the procedure in the specialist advice questionnaires for this procedure.

Validity and generalisability

Sample size and follow-up

The studies collectively included a total of about 4,300 people, with follow-up periods varying from in-hospital to several months. The longest follow-up period reported was a median of 20 months in the prospective study by Cubero-Gallego

(2022). Most studies, such as the multicentre systematic review and meta-analysis by Sagris (2024) and the retrospective cohort study by Wiens (2021), reported follow-up data up to 30 days. The systematic review and meta-analysis by Caminiti (2023) included a mean follow-up of 2.6 months.

Sources of bias

The retrospective nature of some studies, such as those by Wiens (2021) and Rola (2022), introduces potential bias because of the reliance on previously recorded data and the lack of randomisation. Also, the non-randomised design of studies like Caminiti (2023) and Aksoy (2019) can contribute to selection bias and limit the generalisability of the findings.

Variability in inclusion and exclusion criteria

There was significant variability in the inclusion and exclusion criteria across the studies. For example, some studies, such as Caminiti (2023) and Rodriguez-Leor (2024), included people with specific comorbidities such as diabetes mellitus and chronic kidney disease, whereas others, such as Wiens (2021), excluded patients with certain conditions or lesions. This variability can affect the generalisability of the results, as different patient populations may respond differently to IVL. The diverse inclusion and exclusion criteria across studies necessitate careful consideration when interpreting the overall efficacy and safety outcomes of IVL.

Other considerations

The diversity in study design, patient populations and settings provides a broad perspective on the use of IVL in treating calcified coronary lesions.

Ongoing trials

- Registry of Coronary Lithotripsy in Spain. NCT04298307

- Evaluate the Safety and Efficacy of Intracoronary Lithotripsy Balloon Catheter and Intracoronary Lithotripsy Apparatus NCT05649488
- Rotablation vs Intravascular Lithotripsy in Calcified Coronary Lesions NCT04960319
- FORWARD PAD IDE Study With the Shockwave Mini S IVL Catheter (FORWARD PAD) NCT05858905
- Intravascular Lithotripsy and/or Mechanical Debulking for Severely Calcified Coronary Artery Lesions (ROLLING-STONE) NCT05016726
- Influence of Calcium Pattern on Plaque Modification Achieved With Intracoronary Lithotripsy NCT04698902
- POWER: Pulse Intravascular Lithotripsy (Pulse IVL) to Open Vessels With Calcific Walls and Enhance Vascular Compliance and Remodeling (POWER-PAD-1) NCT05192473
- Use of Shockwave M5+ IVL Catheter (Intravascular Lithotripsy) in Hostile and Calcified Iliac Access (SHOCK-ACCESS) NCT05880641
- Balloon Lithoplasty for Preparation of Severely Calcified Coronary Lesions (BALI) NCT04253171
- Disrupt CAD III Post-Approval Study (PAS) NCT05021757
- Intravascular Balloon Lithotripsy in Left Main Stem Percutaneous Coronary Intervention NCT04319666
- Intravascular Lithotripsy in High Risk Calcified Iliac Anatomy for Transfemoral TAVR (ILIT) NCT05862558
- ROtational Atherectomy, Lithotripsy or LasER for the Treatment of CAlcified STEnosis (ROLLERCOASTR) NCT04181268
- Coronary Intravascular Lithotripsy System in Patients With Coronary Artery Calcification (VIGOUR) NCT05818098
- A Clinical Trial to Assess the Elixir Medical LithiX Coronary Hertzian Contact Lithotripsy Catheter (PINNACLE-I) NCT05828173
- Coronary Calcification Study - Intravascular Lithotripsy for Calcified Lesions (CCS) NCT04428177
- ComparIson of Strategies to PrepAre SeveRely CALCified Coronary Lesions 2 (ISAR-CALC2) NCT05072730

- Shockwave Lithoplasty Compared to Cutting Balloon Treatment in Calcified Coronary Disease - A Randomized Controlled Trial (Short-Cut) NCT06089135
- Atherectomy vs Intravascular Lithotripsy (RAINBOW) NCT04013906
- CRUSTAL Study in China NCT05828186
- Shockwave Induced Attenuation of Calcified Plaques Quantified NCT05973994
- Equity in Modifying Plaque Of WomEn With UndeRtreated Calcified Coronary Artery Disease (EMPOWER CAD) NCT05755711
- Shockwave C2+ 2Hz Coronary IVL Catheter in Calcified Coronary Arteries (Disrupt CAD DUO) NCT05966662
- Clinical Trial of T-wave™ Coronary Lithotripsy Catheter System NCT05552131
- The GISE (Società Italiana di Cardiologia Interventistica) - ShockCalcium Registry NCT05455515
- ShOckwave ballooN or Atherectomy With Rotablation in Calcified Coronary Artery Lesions, the SONAR Trial (SONAR) NCT05208749
- The Value of IVL Compared To OPN Non-Compliant Balloons for Treatment of RefractorY Coronary Lesions (VICTORY) Trial (VICTORY) NCT05346068
- The Lower Silesia Shockwave Registry (LSSR) NCT05916898
- BASIL Study: A randomised comparison study on the treatment of calcified (hard and concrete-like) coronary artery using the conventional balloon angioplasty prior stenting versus the use of Shockwave Intravascular Lithotripsy (S-IVL) prior to stenting. ACTRN12620000086965
- EMPOWER CAD: Equity in modifying plaque of women with undertreated calcified coronary artery disease. NCT05755711
- Shockwave IVL to aid DCB only PCI [Germany] NCT05625997

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

Bioresorbable stent implantation for treating coronary artery disease (2014) NICE interventional procedures guidance 492

Optical coherence tomography to guide percutaneous coronary intervention (2014) NICE interventional procedures guidance 481

Percutaneous laser coronary angioplasty (2011) NICE interventional procedures guidance 378

Intraoperative fluorescence angiography for the evaluation of coronary artery bypass graft patency. NICE interventional procedure guidance 98 (2004)

Technology appraisals

Drug-eluting stents for the treatment of coronary artery disease. NICE technology appraisal guidance 152 (2008)

Guidance on the use of coronary artery stents. NICE technology appraisal guidance 71 (2003) replaces TA4 ‘Ischaemic heart disease coronary artery stents’) NICE technology appraisal guidance October 2001 (last modified: July 2008).

Rivaroxaban for preventing major cardiovascular events in people with coronary or peripheral artery disease (ID1397) NICE technology appraisal guidance Publication expected August 2019

Clinical guidelines

Chest pain of recent onset: assessment and diagnosis (2010, updated 2016) NICE guideline 95

Stable angina. NICE clinical guideline 126 (2011)

Unstable angina and NSTEMI. The early management of unstable angina and non-ST-segment-elevation myocardial infarction. NICE clinical guideline 94 (2010)

MI – secondary prevention: Secondary prevention in primary and secondary care for patients following a myocardial infarction. NICE clinical guideline 48 (2007)

Medical technologies guidance

HeartFlow FFRCT for estimating fractional flow reserve from coronary CT angiography (2017) NICE medical technologies guidance 32

The VeriQ system for assessing graft flow during coronary artery bypass graft surgery. NICE medical technology guidance 8 (2011)

SeQuent Please balloon catheter for in-stent coronary restenosis. NICE medical technologies guidance 1 (2010)

Diagnostics guidance

New generation cardiac CT scanners (Aquilion ONE, Brilliance iCT, Discovery CT750 HD and Somatom Definition Flash) for cardiac imaging in people with suspected or known coronary artery disease in whom imaging is difficult with earlier generation CT scanners (2012, updated 2017) NICE diagnostics guidance 3

Professional societies

- British Cardiovascular Intervention Society (BCIS)
- British Cardiovascular Society (BCS)
- Royal College of Physicians (Edinburgh)
- Royal College of Surgeons (Edinburgh)
- Royal College of Physicians London
- The Royal College of Physicians and Surgeons of Glasgow

Company engagement

A structured information request was sent to one company who manufacture a potentially relevant device for use in this procedure. NICE received 1 completed submission. This was considered by the IP (Interventional Procedures) team and

any relevant points have been taken into consideration when preparing this overview.

References

1. Sagris M, Ktenopoulos N, Dimitriadis K et al. (2024) Efficacy of intravascular lithotripsy (IVL) in coronary stenosis with severe calcification: A multicentre systematic review and meta-analysis. Catheterization and Cardiovascular Interventions 29(3): 1-4.
2. Caminiti R, Vetta G, Parlavecchio A et al. (2023) A Systematic Review and Meta-Analysis including 354 Patients from 13 Studies of Intravascular Lithotripsy for the Treatment of Underexpanded Coronary Stents. The American Journal of Cardiology. Volume 205. Pages 223-230
3. Wiens EJ, Sklar JC, Wei YH et al. (2021) Real-world outcomes in treatment of highly calcified coronary lesions with intravascular shockwave lithotripsy. Indian Heart Journal 73: 653-655.
4. Rola P, Kulczyucki JJ, Wlodarczak A et al. 2022) Intravascular Lithotripsy as a Novel Treatment Method for Calcified Unprotected Left Main Diseases-Comparison to Rotational Atherectomy-Short-Term Outcomes. International Journal of Environment Research and Public Health.
5. Cubero-Gallego H, Calvo-Fernandez A, Tizon-Marcos H et al. (2022) Real-World Multicentre Coronary Lithotripsy Registry: Long-Term Clinical Follow-Up. Journal of Invasive Cardiology 10:E701-E708.
6. Aziz A, Heo JW, Lee DH et al. (2020) Intravascular lithotripsy in calcified-coronary lesions: A real-world observational, European Multicentre Study. Journal of Catheterization & Cardiovascular Interventions. Vol. 98, Issue 2, Pages 225-235
7. Rodriguez-Leor O, Cid-Alvarez AB, Lopez-Benito M et al. (2024) A Prospective, Multicentre, Real-World Registry of Coronary Lithotripsy in Calcified Coronary Arteries. The REPLICA-EPIC18 Study. JACC: Cardiovascular Interventions. Vol. 17, No. 6
8. Aksoy A, Salazar C, Ulrich Becher M et al. (2019) Observational study on the use of intravascular lithotripsy in treating calcified coronary lesions in Germany and Spain. Journal of Circulation: Cardiovascular Interventions Vol. 12, No. 11

Appendix A: Methods and literature search strategy

Databases	Date searched	Version/files
MEDLINE ALL (Ovid)	28/03/2024	1946 to November 10, 2023
EMBASE (Ovid)	28/03/2024	1974 to 2024 March 27
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	28/03/2024	Issue 2 of 12, February 2024
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	28/03/2024	Issue 2 of 12, February 2024
International HTA database (INAHTA)	28/03/2024	-

MEDLINE ALL search strategy

Ovid MEDLINE(R) ALL <1946 to March 27, 2024>

1 Coronary Artery Disease/ 78436
2 Acute Coronary Syndrome/ 20829
3 Myocardial Infarction/ 181992
4 exp Angina Pectoris/ 44919
5 Myocardial Ischemia/ 42381
6 Vascular Calcification/ 6550
7 Plaque, Atherosclerotic/ 13730
8 Coronary Stenosis/ 13741
9 ((coronar* or isch?em*) adj4 (arter* or heart* or vasc*) adj4 (diseas* or disord* or lesion* or stenos* or calcium*)).tw. 213039
10 (coronar* adj4 (arteriosclero* or atheroscleros*)).tw. 14329
11 ((Myocardial* or heart*) adj4 (infarct* or isch?emia* or stenos*)).tw. 267304
12 (heart adj4 attack*).tw. 7196
13 (acute* adj4 coronar* adj4 syndrome*).tw. 39859
14 angina*.tw. 59560
15 (calcif* adj4 (coronar* or heart* or vasc*) adj4 (lesion* or stenon* or arter* or plaque*)).tw. 5704
16 (vascular* adj4 (calcific* or calcinos*)).tw. 6900
17 atheroma*.tw. 11815
18 fibroatheroma*.tw. 874
19 (atheroscler* adj4 plaque*).tw. 22217
20 (arterial adj4 fat* adj4 streak*).tw. 24
21 (CHD or CAD or MI or ACS or PCI).tw. 194101
22 Percutaneous Coronary Intervention/ 30266
23 (percutan* adj4 coronar* adj4 intervention*).tw. 44969
24 PCI.tw. 34666
25 or/1-24 695079
26 Lithotripsy/ 11181

27	(lithotrip* or litholapax* or lithoplast*).tw.	13505
28	shockwave*.tw.	3883
29	(IVL or S-IVL).tw.	857
30	(calcif* and (plaque* adj4 modif*)).tw.	181
31	or/26-30	18672
32	25 and 31	616
33	animals/ not humans/	5172894
34	32 not 33	606
35	limit 34 to english language	583
36	limit 35 to dt=20231113-20240331	21
37	limit 35 to ed=20231113-20240331	13
38	36 or 37	30

Appendix B: Other relevant studies

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Table 5 Additional studies identified

Study	Number of people and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Corl JD, Frizzell JD, Bohrer CA, Kereiakes DJ (2022) Shock Buddy Technique for Intravascular Lithotripsy of Severe Eccentric Arterial Calcification	Case report N=1 patient	The “shock buddy” technique was used successfully to treat severe, eccentric arterial calcification in an 80-year-old man. The procedure involved the use of two balloons to optimize the positioning of the IVL balloon, resulting in successful plaque modification and improved vessel compliance without intraprocedural complications	Larger studies added to table 2
Costoya IR, Marcos HT, Montilla BV et al. (2019) Coronary lithoplasty: initial experience in coronary calcified lesions. Rev Est Cardio (article in press)	Case report N=3 patients with multivessel coronary artery disease had IVL.	The lithoplasty balloon was successfully used to treat 6 severely calcified lesions. There were no intraprocedural complications such as dissections or perforations	Larger studies added to table 2.

De Silva K, Roy J, Webb I et al. (2019) A calcific, undilatable stenosis; Lithoplasty – a new tool in the box? JACC: Cardiovascular Interventions 10(3): 304- 6	Case report A 69-year-old man with severe calcific disease in the right coronary artery had PCI after balloon dilation. He had PCI with adjunctive lithotripsy for calcium debulking.	OCT done pre and post lithoplasty showed the calcium 'cracking' effect of the technique. The segment of disease was then treated with a stent with good angiographic result.	Larger studies added to table 2.
Fedele M, (2021) Shockwave Intravascular Lithotripsy in the Treatment of Under-expanded Coronary Stents	2 patients with 12 month follow up	Both patients showed good angiographic results and uneventful follow ups after 12 months	Small sample size (N=2) limits the ability to generalise results.
Gonzalez IC, Ferreiro RG, Moreiras JV et al. (2019) Facilitated transfemoral access by shockwave lithoplasty for transcatheter aortic valve replacement. JACC: Cardiovascular Interventions 12(5): e35- 8	Case report N=1 patient with severe aortic stenosis, coronary artery disease (CAD) and severe peripheral artery disease had IVL to help transfemoral transcatheter aortic valve replacement.	Results showed a significant reduction in stenosis severity with high acute gain, no major adverse events.	Larger studies added to table 2
Kassimis G, Raina T, Kontogiannis N et al. (2019) How should we treat heavily calcified coronary artery disease in contemporary practice? From atherectomy to intravascular lithotripsy. Cardiovascular Revascularization	Review	With the introduction of several adjunctive PCI tools, like cutting and scoring balloons, atherectomy devices, and intravascular lithotripsy technology, the treatment of calcified coronary lesions has	Review

Medicine. Available January 2019		become feasible, predictable and safe. This review highlights the techniques in the clinical setting and gives examples of how best to apply them through better patient and lesion selection, with the main objective being optimising drug eluting stent delivery and implantation, and subsequent improved outcomes	
Kereiakes et al. (2021) "Intravascular Lithotripsy for Treatment of Calcified Coronary Lesions"	628 patients with 30-day follow-up.	The study demonstrated that IVL is safe and effective for facilitating stent implantation in severely calcified coronary lesions. The primary safety and effectiveness endpoints were achieved in 92.7% and 92.4% of patients, respectively. The incidence of serious angiographic complications was low.	Focus on short term outcomes
Kereiakes et al. (2021) “Principles of Intravascular Lithotripsy for Calcific Plaque Modification” JACC	Review – does not specify participant numbers of follow up details	IVL is a promising and effective technique for treating vascular calcification. It provides a comprehensive summary of the	Review article summarising existing data rather than presenting original clinical trial results with specific participant data

Cardiovascular Interventions		physics, preclinical, and clinical data supporting IVL's safety and efficacy in modifying calcified plaque to facilitate stent expansion and improve luminal gain.	and follow-up periods. Therefore, it does not provide the direct clinical evidence necessary for inclusion in a main evidence summary focused on clinical trial outcomes.
Khan S, Li B, Salata K, et al. (2019) The current status of lithoplasty in vascular calcifications: A systematic review. Surgical Innovation: 1- 11	Systematic review N=9 studies 211 patients with vascular calcification lesions had lithoplasty. Follow up: 5.5 months.	Most lesions (72%, 152/212) were in peripheral artery beds, with the remainder occurring in coronary vessels. Lesioned vessels typically had severe calcium burden 62.6% (131/210), with an average initial stenosis of 76.6% (range, 68.1% to 77.8%). After treatment, the average residual stenosis was 21.0% (range, 13.3% to 26.2%), with a mean acute gain of vessel diameter of 2.5 mm. A limited number of type D dissections occurred, with a total of 2.4% (5/211) of patients needing stent implantation. Recent studies suggest that lithoplasty is a promising intervention to	The review included both peripheral and coronary circulation studies. Evidence is from limited quality case series, case reports, and conference abstracts. Peripheral artery disease is out of the remit of this guidance.

		decrease vessel stenosis in both peripheral artery disease and coronary artery disease, with minimal occurrence of major adverse events. Further research studies, with more rigorous study designs, are needed to determine the effectiveness of lithoplasty in vascular calcifications.	
Legutko J, Niewiera L, Tomala M et al. (2019) Successful shockwave intravascular lithotripsy for severely calcified undilatable lesion of the left anterior descending coronary artery in patient with recurrent myocardial infarction. Kardiologia Poloska (published online June 6)	Case report N=1 patient with severely calcified, critical narrowing of left anterior descending coronary artery associated with a history of recurrent myocardial infarction had IVL	Angiography, intravascular ultrasound and OCT confirmed optimal PCI result with perfect stent expansion and apposition. No complications occurred during hospitalisation and patient was discharged home 48 hours after the procedure free of angina and ventricular arrhythmia	Larger studies included in table 2.
Mathias B, Federico M, Stefan T et al. (2019) The effect of lithoplasty on coronary arteries. Cardiovascular medicine 22:02013	Case report 79-year-old man with non-ST-elevation myocardial infarction and a heavily calcified bifurcation stenosis of the left anterior descending artery (LAD) had IVL	The subsequent OCT showed calcium containing cracks in the intima and the media of the LAD. The bifurcation lesion was treated with 2 stents. The final OCT showed good	Larger studies included in table 2.

		stent expansion and apposition.	
Riley R et al. (2023) SCAI Expert Consensus Statement on the Management of Calcified Coronary Lesions	The study provides expert consensus rather than individual patient data	Consensus outlines strategies for managing calcified coronary lesions using various calcium modification tools. It emphasises the importance of intravascular imaging and provides guidelines for using balloons, atherectomy, and IVL.	This study provides expert consensus and guidelines rather than empirical data from patient trials, making it more suitable for clinical guidance rather than direct comparison in the main evidence summary.
Sattar Y, Ullah W, Ul Hasan Virk H et al. (2021) Coronary intravascular lithotripsy for coronary artery calcifications	Review	Shockwave intravascular lithotripsy (S-IVL) may be used in cases of the calcifieddisease to gain vessel lumen in order to deploy drug-eluting stents with PCI. The success ofthe DES implantation of IVL can be 100% with a minimal complication rate	Review
Sgueglia GA, Gioffre G, Piccioni F et al. (2019) Slender distal radial five French coronary shockwave lithotripsy. Catheter cardiovascular Interventions 1-4	Case report 72-year-old man with calcific atherosclerosis of the left anterior descending artery with stenosis had IVL PCI using a 5 French guiding catheter.	Procedure was successful with optimal stenting results and reported no complications at 6 months follow up.	Larger studies added to table 2
Shavadia JS, Minh NV, Kevi B. 2018 Challenges with severe coronary	Review	Summary of the principles, technique, and contemporary	Review

artery calcification in percutaneous coronary intervention: A Narrative Review of Therapeutic Options. Canadian Journal of Cardiology, 3 (12): 156-72		evidence for the currently approved devices designed to treat severe coronary calcific lesions.	
Salazar C, Escaned J, Tirado G et al. (2019) Undilatable calcific coronary stenosis causing stent under expansion and late stent thrombosis. A complex scenario successfully managed with intravascular lithotripsy. JACC: Cardiovascular Interventions. 12(15): 1510-3	Case report N=71-year-old man with repeat STEMI had PCI. A suboptimal under expansion was achieved by coronary calcification. A new PCI using IVL was done to modify calcific plaques.	A good final angiography result was achieved. The case showed effectiveness of IVL to modify calcific plaques and act through a previously implanted stent.	Larger studies added to table 2
Tassone EJ, Tripolino C, Morabito G et al. (2018) When calcium gets tough, the tough cardiologist starts to play. Cardiology, 141: 167-71	Case report N=60-year-old man with calcific restenosis of a previously stented or treated lesion (left coronary artery) had coronary shockwave lithotripsy.	IVUS after 3 cycles showed a significant area gain more than 6 mm2 . There was an excellent postprocedure angiographic result and a minimal lumen area on final IVUS. The patient was discharged after 48 hours in good condition and without symptoms.	Larger studies added to table 2.
Tovar Forero, MN, Wilschut J, Van Mieghem NM et al. (2019) Coronary lithoplasty: a novel treatment for stent	Case report N= 74-year-old man with a heavily calcified stenotic lesion in the proximal left anterior descending coronary	Full expansion was achieved after 2 lithoplasty therapies. OCT imaging showed multiple calcium	Larger studies added to table 2.

under expansion. European Heart Journal. 40, 2: 221	artery and under expanded stent resistant to conventional noncompliant balloons had coronary shockwave lithotripsy.	fractures. The procedure completed without any complications.	
Vainer J, Lux A, Ilhan M et al. (2019) Smart solution for hard times: successful lithoplasty of an undilatable lesion. Neth Heart J 27:216-7	Case report N=70-year-old woman with unsuccessful PCI with high-pressure balloons and rotational atherectomy had lithoplasty-assisted PCI.	Lithoplasty effectively resulted in plaque modification and a significant increase in diameter. OCT showed typical calcium tears and a large dissection. To cover the lesion, a drug-eluting stent was implanted. Proper stent expansion and apposition were confirmed with OCT.	Larger studies added to table 2.
Venuti G, D'Agosta G, Tamburino C et al. (2019). Coronary lithotripsy for failed rotational atherectomy, cutting balloon, scoring balloon and ultra-highpressure non-compliant balloon. Catheter Cardiovascular Interventions 1-5	Case report N= 67-year-old man having planned PCI of the right coronary artery targeting an undilatable lesion already resistant to multiple specialised balloons and rotational atherectomy had coronary lithotripsy and new PCI on the RCA.	Calcium modification at the target segment was seen and 3 stents were deployed with a good final result. No intra hospital complications reported. Patient was free from angina at 3 months follow up.	Larger studies added to table 2.
Wong B, El -Jack S et al. (2019) Shockwave intravascular lithotripsy of	Case series N=3 patients having PCI for ST-elevation myocardial infarction (STEMI) using IVL	The 3 presented cases include an upfront use of S-IVL in a right coronary artery, an	Larger studies added to table 2. (cases also reported in study 3 in table 2)

calcified coronary lesions in ST-elevation myocardial infarction: first in-man experience. Journal of invasive cardiology 31 (5), e73-5	as an adjunct procedure.	instent restenosis, and a community cardiac arrest/ST-elevated myocardial infarction equivalent when S-IVL was used as a bailout technique to help stent delivery in a tortuous calcified vessel. Early experience has been favourable	
Wong B, El -Jack S, Khan S et al. (2019) Treatment of heavily calcified unprotected left main disease with lithotripsy-the first case series. The journal of invasive cardiology, 31 (6): E143-7	Case series N=3 the use of S-IVL in a patient with left main-coronary artery disease (LM-CAD) with multivessel disease who declined surgery, a patient with an isolated LM-CAD and severe cardiomyopathy, and a late nonagenarian patient when surgical revascularisation was not an option reported.	No patients had procedural complications or major adverse events (stroke, myocardial infraction, death) during the index admission or within the first 30 days post discharge	Larger studies included in table 2
Yeoh J, Hill J, Spratt JC et al. (2019) Intravascular lithotripsy assisted chronic total occlusion revascularization with reverse controlled antegrade retrograde tracking. Catheter	Case report 81-year-old female with heavily calcified right coronary artery chronic total occlusion (CTO) had PCI via reverse controlled antegrade/retrograde tracking (RCART).Standard balloon inflation failed to create communication by	IVL was used to help connection in R-CART to complete the CTO PCI when heavy calcification was present at the site of chronic occlusion. Multiple fractures helped connection between intimal and subintimal tissue planes.	Larger studies added to table 2

Cardiovasc Interv, 93:1295-7	modifying plaque and guidewire failed. So IVL was used in controlled antegrade/retrograde tracking.		