Coronary Lithotripsy as Elective or Bail-Out Strategy After Rotational Atherectomy in the Rota-Shock Registry

Gennaro Sardella, MD[a,*], Giulio Stefanini, MD, PhD, MSc[b,c], Pier Pasquale Leone, MD, MSc[b,c,d], Giacomo Boccuzzi, MD[e], Natalia Tovar Fovero, MD[f], Nicolas Van Mieghem, MD, PhD[f], Giuseppe Giacchi, MD[g], Javier Escaned, MD, PhD[h], Massimo Fineschi, MD[i], Luca Testa, MD, PhD[j], Renato Valenti, MD[k], Carlo Di Mario, MD, PhD[l], Carlo Briguori, MD, PhD[m], Bernardo Cortese, MD[n], Flavio Ribichini, MD[o], Jacopo Andrea Oreglia, MD[p], Antonio Colombo, MD[b,c,q], Giuseppe Sangiorgi, MD[r], Emanuele Barbato, MD, PhD[s,t], Jeroen Sonck, MD[t], Fabrizio Ugo, MD[u], Carlo Trani, MD[v], Fausto Castriota, MD[w], Anita Paggi, MD[x,y], Italo Porto, MD[z], Fabrizio Tomai, MD[aa], and Massimo Mancone, MD, PhD[a]

Debulking lesions with severe coronary artery calcification (CAC) is highly recommended to obtain good procedural and long-term success. Utilization and performance of coronary intravascular lithotripsy (IVL) after rotational atherectomy (RA) has not been thoroughly studied. This study aimed to evaluate the efficacy and safety of IVL with the Shockwave Coronary Rx Lithotripsy System in lesions with severe CAC as elective or bail-out strategy after RA. This observational, prospective, single-arm, multicenter, international, open-label Rota-Shock registry included patients with symptomatic coronary artery disease and lesions with severe CAC treated by percutaneous coronary intervention, including lesion preparation with RA and IVL, at 23 high-volume centers. Primary efficacy end point was procedural success, defined as final diameter stenosis <30% by quantitative coronary angiography. Primary safety end point was freedom from serious angiographic complications, which included >National Heart, Lung and Blood Institute type B dissection, perforation, abrupt closure, slow or no flow, final thrombolysis in myocardial infarction flow <3, and acute thrombosis. A total of 160 patients were enrolled between June 2020 and June 2022. The primary efficacy end point was observed in 155 patients (96.9%). The primary safety end point occurred in 145 cases (90.6%). Dissections >National Heart, Lung and Blood Institute type B occurred in 3 patients (1.9%), whereas slow or no flow occurred in 8 (5.0%), final thrombolysis in myocardial infarction flow <3 in 3 (1.9%), and perforation in 4 patients (2.5%). Free from inhospital major adverse cardiac and cerebrovascular events, including cardiac death, target vessel myocardial infarction, target lesion revascularization, cerebrovascular accident, definite/probable stent thrombosis, and major bleeding, occurred in 158 patients (98.7%). In conclusion, IVL after RA in lesions with severe CAC was effective and safe, with a very low incidence of complications as either elective or bail-out strategy. **© 2023 Elsevier Inc. All rights reserved.** **(Am J Cardiol 2023;198:1−8)**

[a]Department of Clinical, Anesthesiologic and Cardiovascular Sciences, Sapienza University of Rome, Policlinico Umberto I, Rome, Italy; [b]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele-Milan, Italy; [c]Cardio Center, IRCCS Humanitas Research Hospital, Rozzano-Milan, Italy; [d]Division of Cardiology, Montefiore Medical Center, Bronx, New York; [e]Division of Cardiology, Department of Medicine, San Giovanni Bosco Hospital, ASL Città di Torino, Turin, Italy; [f]Department of Cardiology, Erasmus Medical University Center, Rotterdam, The Netherlands; [g]Cardiology Department, Umberto I Hospital, Syracuse, Italy; [h]Interventional Cardiology Unit, Hospital Clinico San Carlos IdISSC, Universidad Complutense de Madrid, C/ Profesor Martín Lagos, Madrid, Spain; [i]Interventional Cardiology, Azienda Ospedaliera Universitaria Senese, Policlinico Le Scotte, Siena, Italy; [j]IRCCS Policlinico S. Donato, Milan, Italy; [k]Division of Interventional Cardiology, Cardiothoracovascular Department, Careggi University Hospital, Florence, Italy; [l]Structural Interventional Cardiology Division, Department of Clinical & Experimental Medicine, Careggi University Hospital, Florence, Italy; [m]Division of Interventional Cardiology, Mediterranea Cardiocentro, Naples, Italy; [n]Foundation for Cardiovascular Research and Innovation, Milan, Italy; [o]Division of Cardiology, Department of Medicine, University of Verona, Verona, Italy; [p]Department of Cardiology and de Gasperis Cardio Center, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; [q]Interventional Cardiology Unit, EMO-GVM, Centro Cuore Columbus, Milan, Italy; [r]Division of Cardiology, "Tor Vergata" University Hospital, Rome, Italy; [s]Cardiology Department, Sant'Andrea Hospital, Sapienza University of Rome, Rome, Italy; [t]Cardiovascular Center Aalst, OLV Hospital, Aalst, Belgium; [u]Sant'Andrea Hospital, Vercelli, Italy; [v]Department of Cardiovascular and Thoracic Sciences, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; [w]Interventional Cardiology Unit, Maria Cecilia Hospital GVM Care and Research, Cotignola, Italy; [x]Laboratory of Interventional Cardiology; [y]Department of Cardiology, S. Anna Hospital, Catanzaro, Italy; [z]Cardiology Unit, Cardiothoracic and Vascular Department (DICATOV) IRCCS, Ospedale Policlinico San Martino Genoa, Italy; and [aa]Department of Cardiovascular Sciences, European Hospital, Rome, Italy. Manuscript received December 24, 2022; revised manuscript received and accepted April 15, 2023.

Drs. Sardella and Stefanini contributed equally to the manuscript and are joint first authors.

Funding: none.

See page 6 for disclosure information.

*Corresponding author: Tel: +390649979047; fax: +390649979047.
E-mail address: rino.sardella@uniroma1.it (G. Sardella).

0002-9149/© 2023 Elsevier Inc. All rights reserved.
https://doi.org/10.1016/j.amjcard.2023.04.032

Severe coronary artery calcification (CAC) can be encountered in up to 30% of patients with ischemic heart disease,[1] and its percutaneous management remains a challenge.[2] Lesions with severe CAC often present larger plaque burden and are more complex[1,3] so patients are less likely to receive complete revascularization and have a higher risk to develop adverse events, including death.[4] Recent advances in calcium-debulking technologies have the potential to contribute to the development of new interventional therapy paradigms for improving clinical outcomes. Rotational atherectomy (RA) is based on sanding ablation and is the calcium-ablation technique with the largest worldwide experience.[5] Coronary intravascular lithotripsy (IVL; Shockwave Medical, Santa Clara, California) is the latest addition to the armamentarium and is a technology based on pulsatile mechanical energy delivery through emitters placed along a semicompliant balloon.[6] So far, safe and effective facilitation of stent implantation in severely calcified lesions has been described with IVL.[7−11] This study aimed to evaluate the efficacy and safety of coronary IVL with the Shockwave Coronary Rx Lithotripsy System after RA in consecutive lesions with severe CAC.

Methods

The observational, prospective, single-arm, multicenter international, open-label Rota-Shock registry included patients from 23 high-volume centers presenting with symptomatic coronary artery disease and lesions with severe CAC suitable for preparation with RA who also underwent additional IVL. The prospective recruitment of patients was performed between June 2020 and June 2022 after local ethics committee approval and with written informed patient consent. The study included all-comer patients treated in 1 of the following scenarios: elective RA in a large vessel (reference vessel diameter ≥3.0 mm) to allow IVL balloon crossing, after RA balloon underexpansion, after RA balloon crossing failure, after RA stent crossing failure, or after RA stent underexpansion at index procedure.

Thus, RA failure was considered, after RA, when a balloon could either not cross the lesion or a waist was present upon inflation, and when a stent could either not cross the lesion or underexpansion was present after stent deployment.

Exclusion criteria included in-stent restenosis, known intolerance to any of the IVL device components, women with childbearing potential, age <18 years, and inability to provide written informed consent. This study complied with the Declaration of Helsinki and was approved by local ethics committees. All patients provided written informed consent for the procedure and subsequent data collection based on local practice and/or local institutional review board approval.

RA was performed with the Rotablator or ROTAPRO systems (Boston Scientific, Marlborough, Massachusetts), which consists of a spring coil shaft with a burr at the tip. The front edge of the oval burr is the ablating portion and is covered with fine diamond crystals. The shaft is encased in a plastic sheath, and both are connected to an advancer, which has a hand-controlled knob with which the burr can be moved. The advancer, in turn, is connected to a console that houses a turbine run by pressurized nitrogen. The revolution speed can be set using controls on the console (usually 140,000 to 180,000 rpm).[12]

In all patients, further balloon-based calcium-debulking technique, including IVL (Shockwave Coronary Rx Lithotripsy System, Shockwave Medical, Santa Clara, California), was performed after RA. The IVL system consists of a disposable semicompliant balloon catheter with 2 integrated internal emitters and an external wave generator. The catheter is connected through a connector cable to the generator that is preprogrammed to deliver 10 pulses of unfocused circumferential mechanical energy in sequence at a frequency of 1 pulse per second for a maximum of 80 pulses per catheter. Calcium disruption in the vessel wall occurs at low balloon pressure (4 to 6 atmospheres).[8]

Additional predilation with a standard balloon before or after either use of RA or IVL was left to the discretion of the operator. The use of more than 1 burr, IVL, or standard balloons was allowed. PCI was performed using either second-generation drug−eluting stents (DES) or drug-coated balloons. Postdilation in case of DES implantation was performed at the operator's discretion.

Intravascular imaging adaption followed the standard practice in each center; although not mandatory, it was strongly recommended. Intravascular ultrasound (IVUS) and optical coherence tomography could both be used, with recommendation to use the same imaging modality for each target segment before and after both RA and IVL and at the final evaluation.

The primary efficacy end point was procedural success, defined as a final diameter stenosis <30% by quantitative coronary angiography. The primary safety end point was freedom from serious angiographic complications, which included >National Heart, Lung and Blood Institute (NHLBI) type B dissection, perforation, abrupt closure, slow or no flow, final thrombolysis in myocardial infarction (TIMI) flow <3, and acute thrombosis.

The secondary end points included freedom from inhospital major adverse cardiac and cerebrovascular events (MACCEs), defined as composite occurrence of cardiac death, target vessel myocardial infarction, target lesion revascularization, cerebrovascular accident, Academic Research Consortium-defined definite/probable stent thrombosis,[13] and major bleeding according to Bleeding Academic Research Consortium. Spontaneous myocardial infarction was defined as previously suggested,[14] whereas periprocedural myocardial injury was not assessed systematically. The incidence of stent underexpansion or malapposition and incidence of stent polymer/mesh damage (in patients with post-RA stent underexpansion at index procedure) were also evaluated.

Data were collected through a dedicated secured database. Individual centers were responsible for entering data of recruited patients. Procedural and clinical follow-up data gathering was at the discretion of each single center. Data were collected prospectively from June 2020 to June 2022.

Continuous variables are reported as mean ± SD or median ± interquartile range and were compared using Student's *t* test or the Mann-Whitney U or Wilcoxon test in case of 2-group comparisons based on the normality of data

distribution, verified using the Shapiro-Wilk test. Categorical variables are reported as percentage (number) and were compared using the chi-square test without Yates correction for continuity or the Fisher's exact test, as appropriate. Clinical follow-up was limited to inhospital outcomes. A 2-sided p <0.05 was considered statistically significant. Statistical analyses were performed using Stata version 13.0 (StataCorp, College Station, Texas).

Results

A total of 160 patients were enrolled at 23 high-volume centers between June 2020 and June 2022. The mean age of the study population was 72.7 ± 8.6 years and 79.4% were men. Diabetes was present in 49.4% of patients, whereas 36.9% and 16.9% had history of myocardial infarction and coronary artery bypass grafting, respectively. Chronic obstructive pulmonary disease was present in 11.2% of patients, whereas 20.1% had chronic kidney disease. The clinical indication for PCI was chronic coronary syndrome in 56.4% of cases, whereas 14.7%, 19.2%, and 9.6% of patients presented with unstable angina, non−ST-elevation myocardial infarction, and ST-elevation myocardial infarction, respectively. Baseline characteristics are summarized in Table 1.

Overall, 160 lesions were treated with both RA and IVL. The left anterior descending artery was the most commonly involved (57.5%) and the right coronary artery was second (25.0%), whereas the left main and circumflex artery were treated in 16.9% each. The proximal and mid left anterior descending artery were involved in 44.4% and 24.4% of cases, respectively, proximal circumflex artery in 13.7% and proximal and middle right coronary artery in 11.9% and 13.7%, respectively. The lesion segment length was 35.1 ± 21.3 mm, whereas the reference vessel diameter and minimal lumen diameter were 3.25 ± 0.63 mm and 1.32 ± 1.21 mm, respectively. The mean percentage stenosis was 86.2%, with 6.25% total occlusions. Angiographic characteristics are summarized in Table 2.

Procedural characteristics are listed in Table 3. Lesion predilation with noncompliant balloons was undertaken in 45.6% of cases; mean balloon diameter was 2.82 mm and inflation pressure was 17.8 atmospheres. RA was performed mostly with 1 single burr (73.1%), whereas 2 burrs were used in 25.0% of cases. Burr diameter was 1.50 and 1.75 mm in 52.2% and 22.0% of procedures, respectively, with a mean burr/vessel maximum angiographic ratio of 0.5 and maximum rotation speed of 169,000 rpm. The maximum post-RA balloon diameter was 3.16 ± 1.92 mm. The proportion of patients who underwent IVL as elective strategy after RA was 42.5%. In contrast, the majority of patients underwent IVL after RA failure (57.5%): among these, balloon underexpansion after RA was the most common indication to IVL (30.6%), whereas stent underexpansion (12.5%), crossing failure after RA (7.5%), and stent crossing failure after RA (6.9%) were rarer.

The IVL balloons had a mean diameter of 3.21 ± 0.51 mm and were inflated at 6 atmospheres, for a total of 8 cycles in 47.6% of procedures. Fewer activations of the IVL emitters were needed in 29.2% of cases, whereas more than 1 IVL balloon was used in 23.1%. Post-IVL balloons were 3.25 ± 0.91 mm in diameter and inflated at 17.4 ± 5.6 atmospheres. PCI included DES implantation in most of cases (97.5%), whereas drug-coated balloon angioplasty

Table 1
Baseline patient characteristics

	Overall
n	160
Age, mean ± standard deviation	72.7±8.6 (160)
Male gender, n (%)	127/160 (79.4%)
Hypertension, n (%)	146/160 (91.2%)
Diabetes, n (%)	79/160 (49.4%)
Insulin-dependent diabetes, n (%)	18/160 (11.2%)
Hypercholesterolemia, n (%)	125/160 (78.1%)
Family history of CVD, n (%)	42/160 (26.2%)
Peripheral vascular disease, n (%)	54/159 (34.0%)
Smoking history, n (%)	77/159 (48.4%)
Chronic obstructive pulmonary disease, n (%)	18/160 (11.2%)
Chronic kidney disease (GFR <60 ml/min/1.73 m^2), n (%)	32/159 (20.1%)
Prior myocardial infarction, n (%)	59/160 (36.9%)
Prior coronary artery bypass grafting, n (%)	27/160 (16.9%)
PCI indication	
Chronic coronary syndrome, n (%)	88/156 (56.4%)
Unstable angina, n (%)	23/156 (14.7%)
NSTEMI, n (%)	30/156 (19.2%)
STEMI, n (%)	15/156 (9.62%)

CVD = cardiovascular disease; GFR = glomerular filtration rate; NSTEMI = non−ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-elevation myocardial infarction.

Table 2
Baseline lesion characteristics

	Overall
N of patients	160
Target lesion location	
Left main, n (%)	27/160 (16.9%)
LAD	92/160 (57.5%)
Proximal LAD, n (%)	71/160 (44.4%)
Mid LAD, n (%)	39/160 (24.4%)
Distal LAD, n (%)	5/160 (3.12%)
First diagonal, n(%)	9/160 (5.62%)
LCx	27/160 (16.9%)
Proximal LCx, n (%)	22/160 (13.7%)
Distal LCx, n (%)	4/160 (2.50%)
Obtuse marginal, n (%)	2/160 (1.25%)
Ramus, n (%)	1/160 (0.62%)
RCA	40/160 (25.0%)
Proximal RCA, n (%)	19/160 (11.9%)
Mid RCA, n (%)	22/160 (13.7%)
Distal RCA, n (%)	3/160 (1.88%)
Posterior descending artery, n (%)	3/160 (1.88%)
Lesion length, mm	35.1±21.3 (158)
Reference vessel diameter, mm	3.25±0.63 (128)
Minimal lumen diameter, mm	1.32±1.21 (113)
Stenosis, %	86.2±11.8 (160)
Total occlusions, n(%)	10/160 (6.25%)

LAD = left anterior descending artery; LCx = left circumflex artery; RCA = right coronary artery.

Table 3
Procedural characteristics

	Overall
N of patients	160
Predilation noncompliant balloon, n (%)	73/159 (45.6%)
Predilation non-compliant balloon diameter, mm	2.82±0.60 (70)
Predilation non-compliant balloon maximum pressure, atm	17.8±7.02 (68)
Burrs used, n	
One	117/160 (73.1%)
Two	40/160 (25.0%)
Three	3/160 (1.88%)
Burr maximum diameter, mm	
1.25 mm	26/159 (16.3%)
1.50 mm	84/159 (52.2%)
1.75 mm	35/159 (22.0%)
2.00 mm	14/159 (8.81%)
Burr/vessel maximum angiographic ratio	0.5±0.1 (138)
Maximum rotation speed, rpm	169,000±12,000 (122)
Maximum post-rotational atherectomy balloon diameter, mm	3.16±1.92 (128)
Lithotripsy indication	
Elective, n (%)	68/160 (42.5%)
Crossing failure post-rotational atherectomy, n (%)	12/160 (7.50%)
Balloon underexpansion post-rotational atherectomy, n (%)	49/160 (30.6%)
Stent crossing failure post-rotational atherectomy, n (%)	11/160 (6.87%)
Post-RA stent underexpansion at index procedure, n (%)	20/160 (12.5%)
Lithotripsy balloon maximum diameter, mm	3.21±0.51 (160)
Lithotripsy balloon maximum pressure, atm	6.29±1.69 (153)
Lithotripsy balloon cycles, n	
<8, n(%)	43/147 (29.2%)
=8, n(%)	70/147 (47.6%)
>8, n(%)	34/147 (23.1%)
Post-lithotripsy angioplasty, n(%)	111/157 (70.7%)
Maximum post-lithotripsy balloon diameter, mm	3.25±0.91 (110)
Maximum post-lithotripsy balloon pressure, atm	17.4±5.60 (102)
Device type	
Drug-eluting stent, n(%)	154/158 (97.5%)
Drug-coated balloon, n(%)	4/158 (2.53%)
Implanted stent, n	
One, n(%)	74/159 (46.5%)
Two, n(%)	55/159 (34.6%)
Three or more, n(%)	26/159 (16.3%)
Implanted stent maximum diameter, mm	3.48±0.50 (155)
Stented segment maximum length, mm	41.6±22.8 (156)
Stent balloon maximum pressure, atm	14.6±2.96 (151)
Postdilation, n(%)	130/154 (84.4%)
Postdilation balloon maximum diameter, mm	3.90±0.66 (133)
Postdilation balloon maximum pressure, atm	19.1±4.50 (130)
Intravascular imaging	84/160 (52.5%)
Pre-rotational atherectomy, n(%)	24/160 (15.0%)
OCT, n(%)	8/160 (5.00%)
IVUS, n(%)	16/160 (10.0%)
Post-rotational atherectomy, n(%)	47/160 (29.4%)
OCT, n(%)	17/160 (10.6%)
IVUS, n(%)	30/160 (18.7%)
Pre-lithotripsy, n(%)	45/160 (28.1%)
OCT, n(%)	19/160 (11.9%)
IVUS, n(%)	26/160 (16.2%)
Post-lithotripsy, n(%)	36/160 (22.5%)
OCT, n(%)	11/160 (6.88%)
IVUS, n(%)	25/160 (15.6%)
Post-PCI, n(%)	68/159 (42.8%)
OCT, n(%)	23/160 (14.5%)
IVUS, n(%)	45/160 (28.3%)
Fluoroscopy time, min	44.1±30.1 (141)
Contrast volume, ml	200±90.2 (159)

IVUS = intravascular ultrasound; OCT = optical coherence tomography; RA = rotational atherectomy.

was performed in a minority of cases (2.5%). A total of 1, 2, and 3 or more DES were implanted in 46.5%, 34.6%, and 16.3% of procedures, respectively. DES had a mean diameter of 3.48 mm and a mean length of 41.6 mm. DES postdilation was performed in 84.4% of cases. The balloons had a mean diameter of 3.90 ± 0.66 mm and were inflated at 19.1 ± 4.5 atmospheres. Overall, intravascular imaging was performed in 52.5% of cases and included IVUS in the majority of procedures (Table 3). The distribution of intravascular imaging throughout the procedure was 15.0% before RA, 29.4% after RA, 28.1% before IVL, 22.5% after IVL, and 42.8% after PCI. The flow of intravascular imaging throughout the procedure is depicted in Figure 1. Finally, mean fluoroscopy time was 44.1 ± 30.1 minutes and the amount of contrast used was 200 ± 90.2 ml.

Procedural and inhospital outcomes are listed in Table 4. The primary efficacy end point occurred in 98.6% of cases. The primary safety end point was observed in 90.6% of patients. Among serious angiographic complications, dissections >NHLBI type B occurred in 1.88%, and 4 patients (2.50%) experienced perforation after the final postdilation. No cases of procedural vessel thrombotic complication or closure were observed. Slow/no flow occurred in 5.00% (8 patients): 4.38% after RA and 1.25% after IVL. The final TIMI flow was <3 in 3 patients (1.88%). The incidence of serious angiographic complications did not differ according to the clinical indication to IVL, except for dissections >NHLBI type B, which occurred more frequently in cases of post-RA balloon or stent crossing failure (p = 0.049; Figure 2). Stent underexpansion and malapposition were observed in 7.10% of cases each.

The median hospital stay was 5 (interquartile range 3 to 9) days. Freedom from inhospital MACCE was 98.7%. A total of 2 patients experienced cardiac death. A case was because of stent thrombosis at the left main circumflex bifurcation and contributed to the single cases of target vessel myocardial infarction, target lesion revascularization, target vessel revascularization, and re-PCI. The other case was because of cardiac arrest 20 days after the procedure. No cases of inhospital coronary artery bypass grafting, cerebrovascular events, or major bleeding were observed.

Discussion

This multicenter, international study is, to the best of our knowledge, the first clinical investigation to evaluate the efficacy and safety of coronary IVL with the Shockwave Coronary Rx Lithotripsy System after RA in lesions with severe CAC. The main findings are the following: more than a half of patients underwent IVL after RA failure, IVL as elective or bail-out strategy after RA was found to be effective in terms of procedural success, considering the complexity of lesions treated, the incidence of serious angiographic complications was generally low, with excellent inhospital outcomes, and the incidence of inhospital MACCE was low.

This study provides the largest data on implementation of IVL as elective or bail-out strategy after RA in the real world. The first proof-of-concept reports of such a strategy[15–17] stressed the complementary role of these 2 calcium-debulking strategies in severely calcified coronary

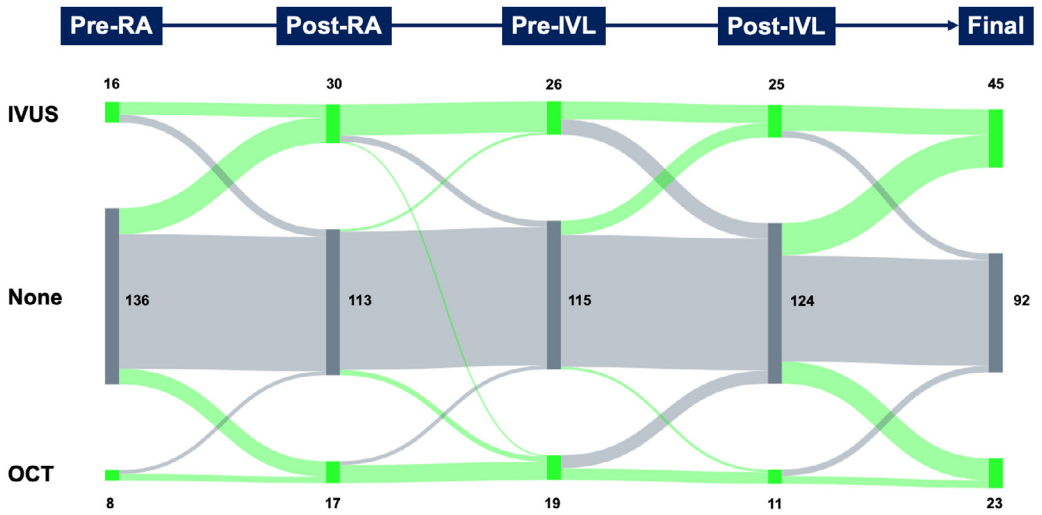

Figure 1. Sankey diagram depicting flow of intravascular imaging use throughout the different steps of the procedure. The numbers refer to the number of patients who underwent either imaging modality at any time point. Nodes for any kind of intravascular imaging modality are light green, those for angiographic assessment alone are gray. Flows toward any kind of intravascular imaging is shown in light green, while flow toward angiographic assessment alone is shown in gray. Thickness of any given flow is proportional to the number of patients included. OCT = optical coherence tomography.

lesions. Indeed, although RA is often effective on intimal calcium to permit balloon or DES crossing through the lesion, adequate expansion of devices might not always follow because of additional circumferential deep calcium plaque extension. In this setting, atherectomy with RA can be functional to IVL balloon delivery for lesion preparation optimization before DES implantation. Overall, the pulsatile force of IVL and the sanding ablation effect from RA have the potential to have an additive or even synergistic effect in this context. Although other strategies, including calcium-ablating and balloon-based techniques, have been described,[18] it might be argued that the efficacy of IVL in fracturing the calcified arc, which was shown to be proportional to the degree of calcium burden,[6] might provide more substantial calcium modification and better balloon and DES expansion, especially in extensive and deep calcium.

Table 4
Procedural and inhospital outcomes

	Overall
N of patients	160
Primary efficacy endpoint, n(%)	155/160 (96.9%)
Primary safety endpoint, n(%)	145/160 (90.6%)
>Type B NHLBI dissection, n(%)	3/160 (1.88%)
Perforation, n(%)	4/160 (2.50%)
Thrombus, n(%)	0/160 (0%)
Abrupt closure, n(%)	0/160 (0%)
Slow/no flow	8/160 (5.00%)
Post-rotational atherectomy, n(%)	7/160 (4.38%)
Post-lithotripsy, n(%)	2/160 (1.25%)
Final TIMI flow <3	3/160 (1.88%)
Freedom from inhospital MACCE, n(%)	158/160 (98.7%)
Stent underexpansion, n(%)	6/84 (7.10%)
Stent malapposition, n(%)	6/84 (7.10%)

MACCE = Major Adverse Cardiac and Cerebrovascular Events; NHLBI = National Heart., Lung, blood institute; TIMI, thrombolysis in myocardial infarction.

The first important take-home message from our study is that in the real-world setting, the main reason for performing coronary IVL after RA is actually RA failure (57.5%) rather than an elective combined approach (42.5%). This is particularly interesting, especially considering the size of burrs used (1.50 and 1.75 mm in 74% of cases) and, even more so, the burr/vessel size ratio adapted in the cohort (0.5), which is in line with the current standards.[12] Also, this might be related to the proportion of patients who underwent intravascular imaging-guided procedures. Indeed, 52% of patients underwent either IVUS- or optical coherence tomography-guided PCI in our cohort, which per se is of note. Although significantly higher than the average utilization rate of these technologies in everyday clinical practice in most centers,[19] the complexity of the lesions included in our registry might likely require an even higher use of intravascular imaging for appropriate lesion preparation and result assessment. In particular, the proportion of patients who underwent intravascular imaging before RA (n = 24, 15.0%) or after RA (n = 47, 29.4%) is lower than that for assessment of the final result (n = 68, 42.8%). Inadequate lesion evaluation at baseline might in fact contribute to the choice of a strategy based on RA alone when this might not be enough indeed. Whether the relatively lower use of intravascular imaging in the early phases of the procedure is related to catheter uncrossability remains to be assessed. The randomized IVUS-CHIP (Intravascular Ultrasound Guidance for Complex High-risk Indicated Procedures) trial (NCT04854070) is evaluating the impact of systematic intravascular imaging on clinical outcomes in patients who underwent complex coronary interventions, including calcified disease.

The proportion of patients reaching the primary efficacy and safety end points in our study was promising. Considering the need for pre-emptive RA, the observed procedural success, well above the previously predefined performance goals,[10] can be considered compatible with the extent of disease in our population. The incidence of serious

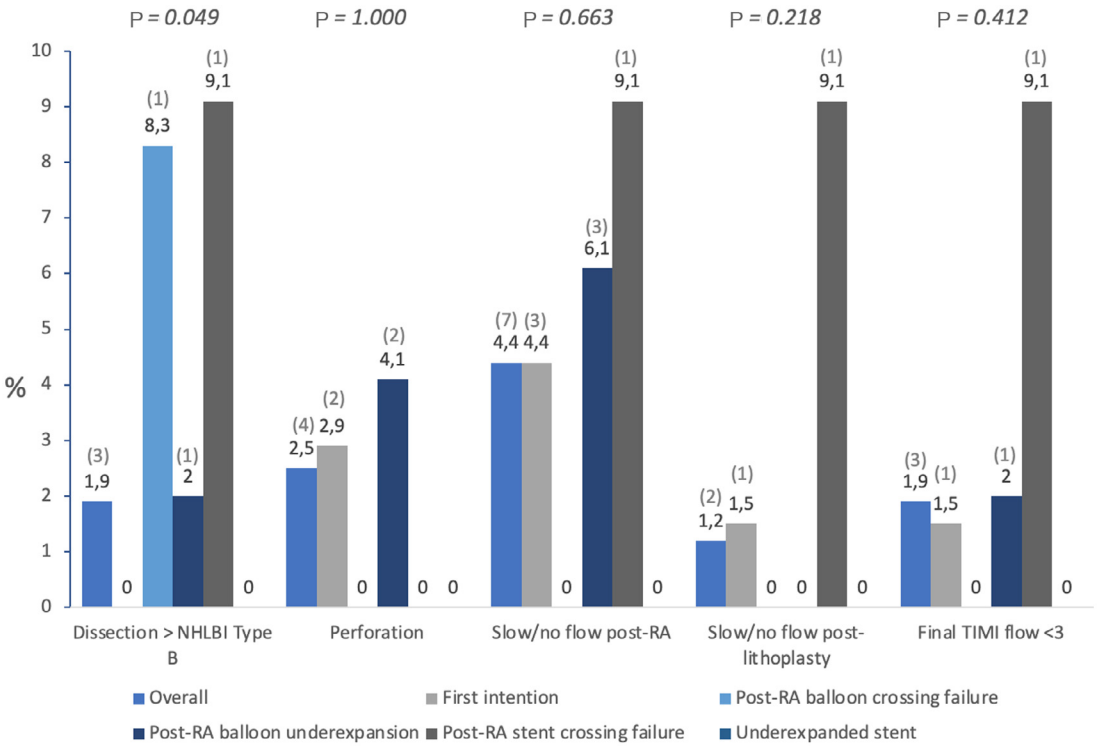

Figure 2. Incidence of serious angiographic complications in the overall population and according to the clinical indication for IVL. No statistically significant differences were observed in perforation, slow/no flow after RA, slow/no flow after IVL or final TIMI flow <3, while dissections >NHLBI type B were more common in post-RA balloon crossing failure and post-RA stent crossing failure groups.

angiographic complications in our cohort compare favorably with those described after RA alone, except for coronary perforations.[20] Such events may attest the complexity of the lesions themselves rather than the use of RA or IVL. In contrast, incidence of coronary dissection, abrupt closure and slow/no flow are reassuring. In addition, notwithstanding the fact that 5% of patients had slow/no flow, the lower proportion of patients with final TIMI flow <3 (1.9%) suggests adequate choice of burr size and appropriate technique applied in our cohort.[12] Although no cases of slow/no flow were observed in DISRUPT CAD III study,[10] 2 cases (1.9%) occurred after IVL in our cohort and might possibly be related to additional calcium cracking[6] after RA lesion modification.[21] No significant differences were observed comparing incidence of serious angiographic complications according to clinical indication to IVL, except for dissections >NHLBI type B, which were more common in post-RA balloon or stent crossing failure groups. This might be compatible with device manipulation upon repetitive trials of crossing through the lesion; although, the external validity of such results might be impinged by the low number of events. In contrast, the complete absence of any of such complications among patients treated for stent underexpansion is noteworthy and compares similarly to the extreme safety reported after IVL alone in underexpanded stents.[22] The incidence of stent malapposition and underexpansion needs to be interpreted because intravascular imaging was not adopted in all patients (52%).

The lesion characteristics underline the complexity of the procedures included. The vessel that was most commonly treated was the left anterior descending artery, in particular, its proximal segment. Also, the left main was involved in almost 1 of 6 cases. In addition, the treated lesions were rather long; although previous reports showed no difference in short- and long-term outcomes in patients who underwent RA in short versus long lesions, this needs to be acknowledged.[23]

Although patients were enrolled in our study irrespective of the initial planned versus provisional RA and most of them underwent IVL after RA failure, the fluoroscopy time and contrast volume were relatively restrained.[24] Other features to note from the RA modus operandi are the small burr : vessel ratio[25] and relatively high burr speed,[26] which confirm a rather contemporary atherectomy practice.[12] Additional procedural characteristics that are noteworthy are the proportion of patients requiring more than 8 IVL cycles and thus more than one IVL catheter (almost 1 of 4)[10] and the high-pressure DES after dilation (19 atmospheres).

Although MACCE in our study included target vessel myocardial infarction (MI) and not any MI, the fact that all but 2 patients were free from inhospital MACCE is noteworthy per se. Our results compared well with those reported in previous studies assessing the performance of RA or IVL alone.[8,10,20] The baseline characteristics of patients enrolled in our registry were also comparable with those of populations from such studies. In particular, 1 of 2 patients had diabetes, 1 of 3 had a previous MI, and 1 of 5 had chronic kidney disease. These features also need to be taken into account when addressing the inhospital and post-discharge clinical outcomes.[1] Of note, almost 1/2 of patients included were treated for acute coronary syndrome.

Although previous reports did not find differences in early and midterm outcomes according to clinical presentation in patients treated with RA,[27] whether this is true also in patients treated with both RA and IVL remains to be proved.

Overall, although clinical trials failed to support consistent long-term benefit after RA alone in lesions with significant CAC (although, limitations in study design and adequate powering for hard clinical end points need to be acknowledged),[5,28,29] we believe the synergistic effect of RA and IVL will be worth of assessment in future randomized head-to-head comparisons. With this respect, long-term follow-up of patients enrolled in our study is planned.

Limitations to the study should be recognized. First, selection and confounding bias cannot be excluded because of the observational nature of our study. Second, as for most of previous studies concerning calcium-debulking techniques, clinical follow-up was limited to inhospital events, though long-term follow-up is planned. Third, the relatively small sample size and absence of a control group need to be acknowledged. Fourth, severe CAC was diagnosed by angiography alone. Fifth, the primary efficacy end point included procedural success alone, defined as final diameter stenosis <30% by quantitative coronary angiography. Sixth, periprocedural myocardial injury was not systematically assessed. Finally, although the incidence of intravascular imaging use is reported, no information on CAC assessment and impact on decision making is available.

In conclusions, IVL as elective or bail-out strategy after RA was found to be effective and safe in terms of procedural success and freedom from serious angiographic complications. The relatively low use of intravascular imaging in our cohort might have contributed to the high use of IVL after RA failure.

Declaration of Competing Interest

Dr. Stefanini discloses speaker fees from Abbott Vascular, Boston Scientific, and Pfizer/Bristol-Myers Squibb. Dr. Van Mieghem discloses research grant support by Abbott Vascular, Boston Scientific, Biotronik, Edwards Lifesciences, Medtronic, PulseCath BV, Daiichi Sankyo, and Pie Medical and consultancy fees from Siemens, Amgen, Daiichi Sankyo, Abbott Vascular, Biotronik, Medtronic, and Abiomed. The remaining authors have no conflicts of interests to declare.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2023.04.032.

1. Généreux P, Madhavan MV, Mintz GS, Maehara A, Palmerini T, Lasalle L, Xu K, McAndrew T, Kirtane A, Lansky AJ, Brener SJ, Mehran R, Stone GW. Ischemic outcomes after coronary intervention of calcified vessels in acute coronary syndromes. Pooled analysis from the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) and ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) TRIALS. *J Am Coll Cardiol* 2014;63:1845–1854.
2. De Maria GL, Scarsini R, Banning AP. Management of calcific coronary artery lesions: is it time to change our interventional therapeutic approach? *JACC Cardiovasc Interv* 2019;12:1465–1478.
3. Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals [published correction appears in *JAMA* 2004;291:563]. *JAMA* 2004;291:210–215.
4. Bourantas CV, Zhang YJ, Garg S, Iqbal J, Valgimigli M, Windecker S, Mohr FW, Silber S, Td Vries, Onuma Y, Garcia-Garcia HM, Morel MA, Serruys PW. Prognostic implications of coronary calcification in patients with obstructive coronary artery disease treated by percutaneous coronary intervention: a patient-level pooled analysis of 7 contemporary stent trials. *Heart* 2014;100:1158–1164.
5. Bittl JA, Chew DP, Topol EJ, Kong DF, Califf RM. Meta-analysis of randomized trials of percutaneous transluminal coronary angioplasty versus atherectomy, cutting balloon atherotomy, or laser angioplasty. *J Am Coll Cardiol* 2004;43:936–942.
6. Ali ZA, Brinton TJ, Hill JM, Maehara A, Matsumura M, Karimi Galougahi K, Illindala U, Götberg M, Whitbourn R, Van Mieghem N, Meredith IT, Di Mario C, Fajadet J. Optical coherence tomography characterization of coronary lithoplasty for treatment of calcified lesions: first description. *JACC Cardiovasc Imaging* 2017;10:897–906.
7. Brinton TJ, Ali ZA, Hill JM, Meredith IT, Maehara A, Illindala U, Lansky A, Götberg M, Van Mieghem NM, Whitbourn R, Fajadet J, Di Mario C. Feasibility of shockwave coronary intravascular lithotripsy for the treatment of calcified coronary stenoses. *Circulation* 2019;5:834–836. 139.
8. Ali ZA, Nef H, Escaned J, Werner N, Banning AP, Hill JM, De Bruyne B, Montorfano M, Lefevre T, Stone GW, Crowley A, Matsumura M, Maehara A, Lansky AJ, Fajadet J, Di Mario C. Safety and effectiveness of coronary intravascular lithotripsy for treatment of severely calcified coronary stenoses: the disrupt CAD II study. *Circ Cardiovasc Interv* 2019;12:e008434.
9. Kereiakes DJ, Di Mario C, Riley RF, Fajadet J, Shlofmitz RA, Saito S, Ali ZA, Klein AJ, Price MJ, Hill JM, Stone GW. Intravascular lithotripsy for treatment of calcified coronary lesions: patient-level pooled analysis of the disrupt CAD studies. *JACC Cardiovasc Interv* 2021;14:1337–1348.
10. Hill JM, Kereiakes DJ, Shlofmitz RA, Klein AJ, Riley RF, Price MJ, Herrmann HC, Bachinsky W, Waksman R, Stone GW. Disrupt CAD III Investigators. Intravascular lithotripsy for treatment of severely calcified coronary artery disease. *J Am Coll Cardiol* 2020;76:2635–2646.
11. Saito S, Yamazaki S, Takahashi A, Namiki A, Kawasaki T, Otsuji S, Nakamura S, Shibata Y, Investigators Disrupt CAD IV. Intravascular lithotripsy for vessel preparation in severely calcified coronary arteries prior to stent placement - primary outcomes from the Japanese DISRUPT CAD IV study. *Circ J* 2021;85:826–833.
12. Barbato E, Carrié D, Dardas P, Fajadet J, Gaul G, Haude M, Khashaba A, Koch K, Meyer-Gessner M, Palazuelos J, Reczuch K, Ribichini FL, Sharma S, Sipötz J, Sjögren I, Suetsch G, Szabó G, Valdés-Chávarri M, Vaquerizo B, Wijns W, Windecker S, de Belder A, Valgimigli M, Byrne RA, Colombo A, Di Mario C, Latib A, Hamm C. European Association of Percutaneous Cardiovascular Interventions. European expert consensus on rotational atherectomy. *EuroIntervention* 2015;11:30–36.
13. Garcia-Garcia HM, McFadden EP, Farb A, Mehran R, Stone GW, Spertus J, Onuma Y, Morel MA, van Es GA, Zuckerman B, Fearon WF, Taggart D, Kappetein AP, Krucoff MW, Vranckx P, Windecker S, Cutlip D, Serruys PW. Academic Research Consortium. Standardized end point definitions for coronary intervention trials: the academic research Consortium-2 consensus document. *Circulation* 2018;137:2635–2650.
14. Stone GW, Sabik JF, Serruys PW, Simonton CA, Généreux P, Puskas J, Kandzari DE, Morice MC, Lembo N, Brown WM 3rd, Taggart DP, Banning A, Merkely B, Horkay F, Boonstra PW, van Boven AJ, Ungi I, Bogáts G, Mansour S, Noiseux N, Sabaté M, Pomar J, Hickey M, Gershlick A, Buszman P, Bochenek A, Schampaert E, Pagé P, Dressler O, Kosmidou I, Mehran R, Pocock SJ, Kappetein AP. EXCEL Trial Investigators. Everolimus-eluting stents or bypass surgery for left main coronary artery disease [published correction appears in *N Engl J Med* 2019;381:1789]. *N Engl J Med* 2016;375:2223–2235.
15. Gonzálvez-García A, Jiménez-Valero S, Galeote G, Moreno R, López de Sá E, Jurado-Román A. RotaTripsy": combination of rotational atherectomy and intravascular lithotripsy in heavily calcified coronary lesions: a case series. *Cardiovasc Revasc Med* 2022;35:179–184.

16. Venuti G, D'Agosta G, Tamburino C, La Manna A. Coronary lithotripsy for failed rotational atherectomy, cutting balloon, scoring balloon, and ultra-high-pressure non- compliant balloon. *Catheter Cardiovasc Interv* 2019;94:E111–E115.
17. Ielasi A, Loffi M, De Blasio G, Tespili M. Rota-Tripsy": A successful combined approach for the treatment of a long and heavily calcified coronary lesion. *Cardiovasc Revasc Med* 2020;21:152–154.
18. Allali A, Toelg R, Abdel-Wahab M, Hemetsberger R, Kastrati A, Mankerious N, Traboulsi H, Elbasha K, Rheude T, Landt M, Geist V, Richardt G. Combined rotational atherectomy and cutting balloon angioplasty prior to drug-eluting stent implantation in severely calcified coronary lesions: the PREPARE-CALC-COMBO study. *Catheter Cardiovasc Interv* 2022;100:979–989.
19. Hannan EL, Zhong Y, Reddy P, Jacobs AK, Ling FSK, King Iii SB, Berger PB, Venditti FJ, Walford G, Tamis-Holland J. Percutaneous coronary intervention with and without intravascular ultrasound for patients with complex lesions: utilization, mortality, and target vessel revascularization. *Circ Cardiovasc Interv* 2022;15:e011687.
20. Cavusoglu E, Kini AS, Marmur JD, Sharma SK. Current status of rotational atherectomy. *Catheter Cardiovasc Interv* 2004;62:485–498.
21. Kini AS, Vengrenyuk Y, Pena J, Motoyama S, Feig JE, Meelu OA, Rajamanickam A, Bhat AM, Panwar S, Baber U, Sharma SK. Optical coherence tomography assessment of the mechanistic effects of rotational and orbital atherectomy in severely calcified coronary lesions. *Catheter Cardiovasc Interv* 2015;86:1024–1032.
22. Tovar Forero MN, Sardella G, Salvi N, Cortese B, di Palma G, Werner N, Aksoy A, Escaned J, Salazar CH, Gonzalo N, Ugo F, Cavallino C, Sheth TN, Kardys I, Van Mieghem NM, Daemen J. Coronary lithotripsy for the treatment of underexpanded stents: the international & multicentre CRUNCH registry. *EuroIntervention* 2022;18:574–581.
23. Iannaccone M, Barbero U, D'ascenzo F, Latib A, Pennacchi M, Rossi ML, Ugo F, Meliga E, Kawamoto H, Moretti C, Ielasi A, Garbo R, Colombo A, Sardella G, Boccuzzi GG. Rotational atherectomy in very long lesions: results for the ROTATE registry. *Catheter Cardiovasc Interv* 2016;88:E164–E172.
24. Kawamoto H, Latib A, Ruparelia N, Boccuzzi GG, Pennacchi M, Sardella G, Garbo R, Meliga E, D'Ascenzo F, Moretti C, Rossi ML, Presbitero P, Ielasi A, Magri C, Nakamura S, Colombo A. Planned versus provisional rotational atherectomy for severe calcified coronary lesions: insights from the ROTATE multi-center registry. *Catheter Cardiovasc Interv* 2016;88:881–889.
25. Safian RD, Feldman T, Muller DW, Mason D, Schreiber T, Haik B, Mooney M, O'Neill WW. Coronary angioplasty and Rotablator atherectomy trial (CARAT): immediate and late results of a prospective multicenter randomized trial. *Catheter Cardiovasc Interv* 2001;53:213–220.
26. Sakakura K, Funayama H, Taniguchi Y, Tsurumaki Y, Yamamoto K, Matsumoto M, Wada H, Momomura SI, Fujita H. The incidence of slow flow after rotational atherectomy of calcified coronary arteries: a randomized study of low speed versus high speed. *Catheter Cardiovasc Interv* 2017;89:832–840.
27. Iannaccone M, Piazza F, Boccuzzi GG, D'Ascenzo F, Latib A, Pennacchi M, Rossi ML, Ugo F, Meliga E, Kawamoto H, Moretti C, Ielasi A, Garbo R, Frangieh AH, Hildick-Smith D, Templin C, Colombo A, Sardella G. ROTational AThErectomy in acute coronary syndrome: early and midterm outcomes from a multicentre registry. *EuroIntervention* 2016;12:1457–1464.
28. Abdel-Wahab M, Richardt G, Joachim Büttner H, Toelg R, Geist V, Meinertz T, Schofer J, King L, Neumann FJ, Khattab AA. High-speed rotational atherectomy before paclitaxel-eluting stent implantation in complex calcified coronary lesions: the randomized ROTAXUS (Rotational Atherectomy Prior to Taxus Stent treatment for complex native coronary artery disease) trial. *JACC Cardiovasc Interv* 2013;6:10–19.
29. de Waha S, Allali A, Büttner HJ, Toelg R, Geist V, Neumann FJ, Khattab AA, Richardt G, Abdel-Wahab M. Rotational atherectomy before paclitaxel-eluting stent implantation in complex calcified coronary lesions: two-year clinical outcome of the randomized ROTAXUS trial. *Catheter Cardiovasc Interv* 2016; 87:691–700.