Catheterization and Cardiovascular Interventions

WILEY

ORIGINAL ARTICLE - BASIC SCIENCE OPEN ACCESS

Clinical and Technical Predictors of Treatment Success After Coronary Intravascular Lithotripsy in Calcific Coronary Lesions

Martijn J. H. van Oort[1] | Brian O. Bingen[1] | Federico Oliveri[1] | Ibtihal Al Amri[1] | Akshay A. S. Phagu[1] | Bimmer E. P. M. Claessen[2] | Aukelien C. Dimitriu-Leen[3] | Tessel N. Vossenberg[4] | Joelle Kefer[5] | Hany Girgis[6] | Frank van der Kley[1] | J. Wouter Jukema[1,7] | Jose M. Montero-Cabezas[1]

[1]Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands | [2]Department of Cardiology, Amsterdam University Medical Center, Amsterdam, The Netherlands | [3]Department of Cardiology, Radboud University Medical Center, Nijmegen, The Netherlands | [4]Department of Cardiology, Medisch Centrum Leeuwarden, Leeuwarden, The Netherlands | [5]Department of Cardiology, Cliniques Universitaires Saint-Luc, Brussels, Belgium | [6]Department of Cardiology, Jeroen Bosch Ziekenhuis. 's-Hertogenbosch, The Netherlands | [7]Netherlands Heart Institute, Utrecht, The Netherlands

Correspondence: Jose M. Montero-Cabezas (J.M.Montero_Cabezas@lumc.nl)

Received: 13 January 2025 | **Revised:** 6 February 2025 | **Accepted:** 23 February 2025

Funding: This work was funded through a research grant from Shockwave Medical. Funders were not involved in any aspect of the study, including its design, collection, analysis and interpretation of the data, or the writing of the manuscript.

Keywords: coronary artery calcification | intravascular lithotripsy

ABSTRACT

Background: Intravascular lithotripsy (IVL) is increasingly used to treat coronary artery calcification (CAC). This study aimed to identify clinical and procedural factors associated with IVL treatment success.

Methods: This retrospective analysis included 454 patients (73 ± 9 years, 75% male) treated with IVL from the multicenter BENELUX-IVL registry (May 2019 to February 2024). Treatment success was defined as achieving residual coronary diameter stenosis $< 30\%$ and luminal gain, assessed by quantitative coronary analysis (QCA). Linear and binary logistic regression analyses were performed to identify factors associated with these outcomes.

Results: The mean luminal gain was 1.9 ± 0.9 mm, and residual diameter stenosis $< 30\%$ was achieved in 354 (90%) lesions. Stenting after IVL for therapy completion ($p < 0.001$), intracoronary imaging (ICI) guidance ($p = 0.024$) and chronic total occlusions (CTOs; $p < 0.001$) were associated with increased luminal gain, while bifurcation lesions ($p = 0.029$) were associated with decreased luminal gain. Long (> 20 mm) lesions ($p = 0.034$) and post-IVL stenting for therapy completion ($p = 0.041$) were associated with a residual diameter stenosis $< 30\%$, while aorto-ostial lesions ($p = 0.014$) were negatively associated with this outcome. Technical IVL parameters such as inflation pressure and number of pulses delivered were not significantly associated with treatment success.

Conclusion: Stenting after IVL for therapy completion, ICI guidance and CTOs were associated with increased luminal gain, while bifurcation lesions were linked to decreased luminal gain. Long lesions and post-IVL stenting for therapy completion were associated with residual diameter stenosis $< 30\%$, while the presence of aorto-ostial lesions was negatively associated with this outcome. Technical IVL-related procedural factors did not significantly impact treatment success.

Abbreviations: CAC, coronary artery calcification; CTO, chronic total occlusion; ICI, intracoronary imaging; IVL, intravascular lithotripsy; IVUS, intravascular ultrasound; MACE, major adverse cardiovascular events; NCB, non-compliant balloon; PCI, percutaneous coronary intervention; QCA, quantitative coronary analysis; TVR, target vessel revascularization.

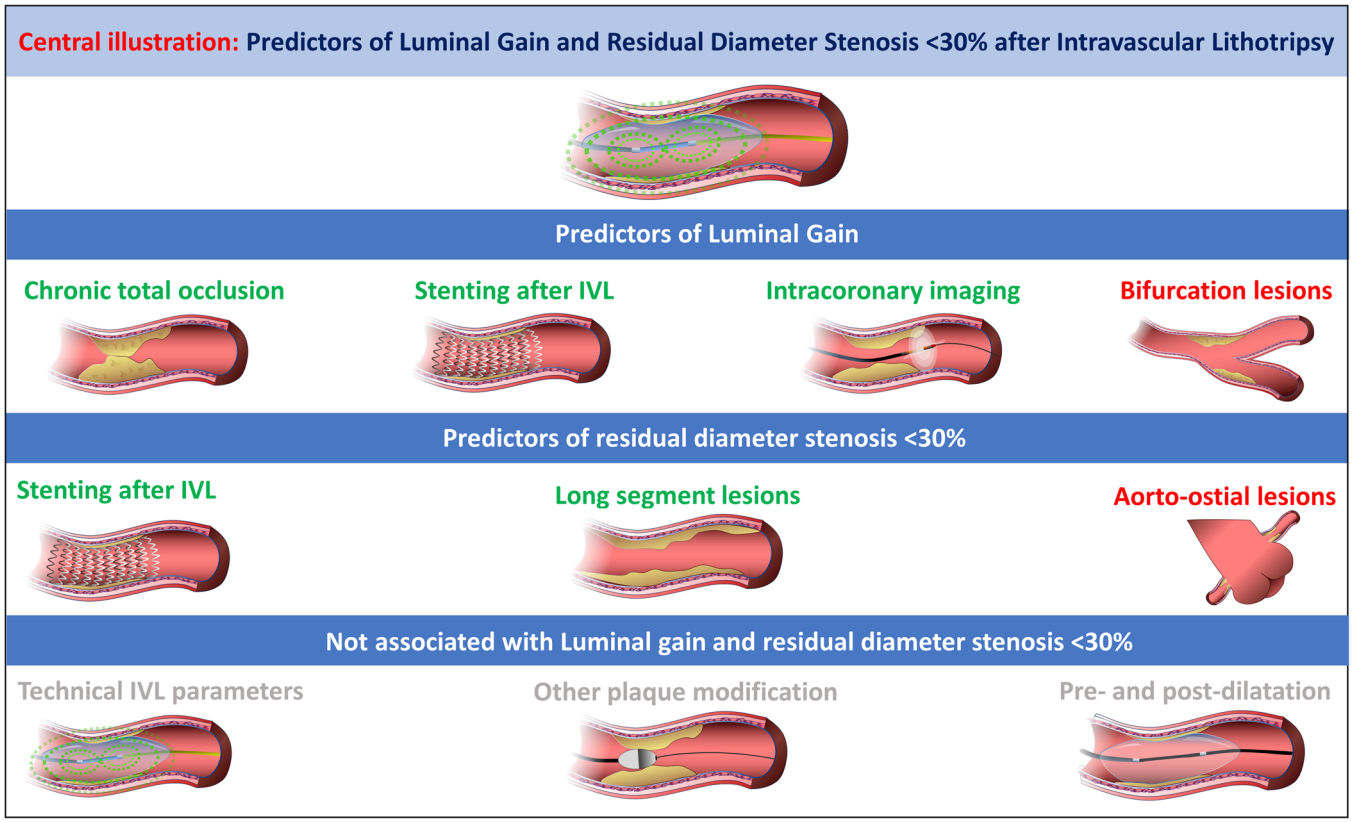
1 | Introduction

The presence of coronary artery calcification (CAC) is increasingly common in patients undergoing percutaneous coronary intervention (PCI), likely due to the higher age and higher burden of comorbidities [1, 2]. The presence of CAC is associated with lower procedural success rates, and worse long-term clinical outcomes [1, 3–6]. Intravascular lithotripsy (IVL) has emerged as an innovative technique designed to modify CAC, facilitating the use and expansion of non-compliant balloons (NCBs) and stents, ultimately aiming to improve patient outcomes [7]. IVL generates shockwaves at low pressure from emitters within the balloon that specifically target calcium deposits superficial and deep in the vessel wall [8, 9]. The shockwaves cause fractures in the calcium that enable further lesion preparation and treatment with NCBs and stents, thereby improving luminal gain [7, 8, 10–12]. IVL has been established as a safe and effective treatment option for (severe) CAC before stent implantation [7]. Its ease of use and its favorable procedural and clinical outcomes have led to the expansion of IVL's application across various clinical and anatomical scenarios and in combination with different plaque modification techniques. Despite its growing use, it remains unclear which clinical and procedural factors influence treatment success of IVL. It has been suggested that the number of IVL pulses administered influence treatment effect and clinical outcomes [13]. However, it remains unknown if other technical factors related to IVL therapy, such as the inflation pressure of the IVL-balloon and performance of pre- and post-dilation influence outcomes. Treatment success is often assessed fluoroscopically during the intervention, using the reduction of residual diameter stenosis to < 30% and luminal gain as key metrics [7]. This study aimed to identify clinical and procedural factors associated with luminal gain and residual diameter stenosis < 30% in an all-comers multicenter international registry.

2 | Methods

2.1 | Population and Data Collection

This retrospective analysis used data from the all-comers international multicenter BENELUX-IVL registry (NCT06577038), in which patients (≥ 18 years) who underwent PCI for CAC with IVL were enrolled across seven centers in two European countries between May 2019 and February 2024 [14]. IVL was performed in all cases with the Shockwave IVL Coronary System (Shockwave Medical, Santa Clara, California). Decision regarding technical aspects of the IVL-procedure (timing, balloon size, number of pulses delivered, maximal inflation pressure) and further treatment strategy (utilization of high-pressure pre- and post-dilatation, supplementary stent placement, and use of intracoronary imaging (ICI) for procedural optimization) were left to the operator's discretion. Demographic, clinical, procedural and follow-up data were collected from the hospital electronic records. Angiographic and ICI data were analyzed in a centralized core-laboratory at the Leiden University Medical Center. The study was exempted by the Medical Research Ethics Committee Leiden Den Haag Delft (reference number: N22.199/HL/hl), and the retrospective analysis of clinically collected data was approved by the local ethical committees at each participating center (Central illustration 1).



CENTRAL ILLUSTRATION 1. | Predictors of Luminal Gain and Residual Diameter Stenosis < 30% after IVL. IVL = intravascular lithotripsy. [Color figure can be viewed at wileyonlinelibrary.com]

2.2 | Definitions and Imaging Analysis

Coronary angiograms were evaluated in a centralized core-laboratory. Coronary artery disease complexity was graded according to the SYNTAX score algorithm if all three vessels were recorded [15]. CAC presence was determined by the operator during the procedure both angiographically (fluoroscopic visibility of radiopacities in the vessel wall at the site of stenosis and/or non-compliant balloon underexpansion) and by ICI when available. Angiographic CAC was scored none/mild, moderate (when the radiopacities were only visible during the cardiac cycle before contrast injection) or severe (when the radiopacities were apparent without cardiac motion before contrast injection) [16, 17]. On intravascular ultrasound (IVUS) CAC was defined as a hyperechoic signal with acoustic shadowing, while on optical coherence tomography (OCT) CAC appeared as a signal-poor area with sharply delineated borders [5, 6, 17, 18].

Quantitative coronary analysis (QCA) and ICI were retrospectively analyzed offline to evaluate luminal gain following IVL. QCA was performed pre-IVL and post-IVL and stenting, using Medis Suite QCA (2D/3D) software (Medis Suite 4.0.24.4; Medis Medical Imaging System BV, Leiden, The Netherlands). Measurements included minimum lumen diameter (minimum LD), minimum lumen area (minimum LA), percentage diameter stenosis (percentage DS) and percentage area stenosis (percentage AS). Luminal gain was defined as the change in minimum LD before IVL and after therapy completion on QCA. Stenting after IVL for therapy completion refers to the placement of stents following IVL, often accompanied by additional lesion preparation such as balloon dilatation, to optimize procedural outcomes. Treatment success was defined as achieving a residual diameter stenosis < 30% and luminal gain, as determined by QCA. ICI was used for procedural optimization pre-IVL for lesion assessment and treatment planning, directly after IVL to assess treatment success (by assessing calcium fractures) and following stenting to evaluate stent expansion and apposition. Analysis of IVUS and OCT was performed using QCU-CMS 4.69 (Leiden University Medical Center, Leiden, The Netherlands).

2.3 | Study Endpoints

The primary endpoint was treatment success, defined as achieving a residual diameter stenosis < 30% and luminal gain (analyzed as a continuous variable), as assessed by QCA. Secondary endpoints included the occurrence of major adverse cardiovascular events (MACE), defined as the composite of cardiac death, non-fatal target vessel myocardial infarction or clinically driven target vessel revascularization (TVR) and complications. Complications were assessed by the treating physician and documented in the patient records. They were considered IVL-related if they occurred immediately following the IVL-treatment. This classification was validated by a systematic retrospective analysis of the coronary angiograms by the centralized core lab.

2.4 | Statistical Analysis

Continuous variables are presented as either the mean ± standard deviation or median with interquartile range (25th–75th percentile), as appropriate. Categorical variables were reported as frequencies and percentages. Kaplan–Meier analysis was performed to estimate cumulative survival free of MACE at 1-year follow-up and the results were compared between groups using the log-rank test. Cox-regression analysis was used to estimate the hazard ratio (HR), with results reported as HR with 95% confidence intervals (CI) and p values. Based on clinical relevance, the relationships between selected clinical and procedural variables and lumen diameter gain and residual diameter stenosis < 30%, as measured by QCA, were analyzed using univariable linear and binary logistic regression, respectively. Variables with a $p < 0.2$ on univariate analysis were entered in multivariable models to account for potential confounding factors and identify factors independently associated with luminal gain and residual diameter stenosis < 30%. Results from the linear regression models are presented as standardized coefficients (beta) with 95% CI and p-values, while the binary logistic regression results are reported as odds ratios (OR) with 95% CI and p values. Statistically significance was defined as a two-sided $p < 0.05$. All statistical analyses were performed with SPSS for Windows version 25.0 (IBM, Armonk, New York).

3 | Results

3.1 | Baseline and Procedural Characteristics

The patient cohort consisted of 454 patients (73.2 ± 9.0 years and 75% male) with a total of 477 calcified lesions treated with IVL. The baseline characteristics of the included patients are summarized in Table 1, and the lesion and procedural characteristics in Table 2. 252 patients (56%) presented with chronic coronary syndrome, according to the ESC guidelines [19]. A wide variety of target lesions were treated, including chronic total occlusions (CTO) ($n = 33$, 7%), bifurcations ($n = 111$, 23%), aorta-ostial ($n = 96$, 20%), long (> 20 mm) ($n = 306$, 64%) and in-stent ($n = 168$, 35%) lesions ($n = 81$, 17% were bail-out after stenting). The mean SYNTAX score was 22.0 ± 13.6. The left anterior descending artery (LAD) ($n = 212$, 44%) was the most frequently treated target vessel.

The mean IVL balloon diameter had a mean diameter of 3.5 ± 0.5 mm and delivered a median of 80 (60–80) pulses to the target lesion. In the majority of target lesions, high-pressure pre- and post-dilatation was performed (93% and 94% respectively). Additional plaque modification techniques were employed in 77 (16%) cases, with rotational atherectomy being the most frequently used ($n = 62$, 13%). The post-IVL treatment consisted of stent implantation ($n = 369$, 77%) and use of a drug-coated balloon ($n = 34$, 7%). ICI was performed for procedural optimization in 249 (52%) target lesions. 186 (39%) recordings were made pre-IVL—167 (35%) and 206 (43%) recordings were made post-IVL (Table 2).

3.2 | Procedural Outcomes

QCA analysis, available in 408 lesions (86%), demonstrated significant improvements in minimum LD ($p < 0.001$) and percentage DS ($p < 0.001$) after IVL and stenting, with an overall mean diameter gain of 1.9 ± 0.9 mm (Supplementary Table 1). Data on the residual diameter stenosis were available in 394 lesions (83%), with residual diameter stenosis < 30% achieved in 354 (90%)

TABLE 1 | Baseline demographics and medical history.

	Overall ($n = 454$)
Age, years	73.2 ± 9.0
Male, *n* (%)	342 (75)
Diabetes, *n* (%)	152 (34)
Hypertension, *n* (%)	315 (69)
Hypercholesterolemia, *n* (%)	238 (52)
Family history of CAD, *n* (%)	115 (25)
Chronic kidney disease (GFR < 60 mL/min/1.73 m^2), *n* (%)	138 (30)
Syntax score	22.0 ± 13.6
Fluoroscopic calcification ($n = 322$)	
Not possible, *n* (%)	46 (14)
None/mild, *n* (%)	20 (6)
Moderate, *n* (%)	25 (8)
Severe, *n* (%)	231 (72)
Left ventricular ejection fraction ($n = 345$)	44.0 ± 13.0
Good (> 50%)	218 (63)
Reasonable (30%–50%)	93 (27)
Poor (20%–30%)	17 (5)
Very poor (< 20%)	3 (1)
Unknown	14 (4)
Smoking history, *n* (%)	194 (43)
Previous stroke, *n* (%)	71 (16)
Previous MI, *n* (%)	170 (37)
Previous PCI, *n* (%)	211 (47)
Previous CABG, *n* (%)	87 (19)
Clinical presentation	
Chronic coronary syndrome, *n* (%)	252 (56)
Acute coronary syndrome, *n* (%)	202 (44)
Unstable angina, *n* (%)	56 (12)
NSTEMI, *n* (%)	114 (25)
STEMI, *n* (%)	32 (7)

Abbreviations: CABG = coronary artery bypass graft surgery, CAD = coronary artery disease, MI = myocardial infarction, NSTEMI = non-ST-segment elevation myocardial infarction, PCI = percutaneous coronary intervention, STEMI = ST-segment elevation myocardial infarction.

lesions. Similarly, ICI showed significant improvements in Minimum LD ($p < 0.001$) and percentage DS ($p < 0.001$) (Supporting Information S1: Table 1). Complications occurred in 29 (6%) patients, of which 6 (1%) were IVL-related (Table 3).

3.3 | Clinical Outcomes

The median follow-up was 365 (166–365) days, with complete 1-year follow-up present in 283 (62%) patients. MACE was

TABLE 2 | Procedural and lesion characteristics.

	Overall ($n = 477$)
Target vessel	
LM, *n* (%)	57 (12)
LAD, *n* (%)	212 (44)
LCx, *n* (%)	75 (16)
RCA, *n* (%)	169 (35)
SVG, *n* (%)	4 (1)
Lesion characteristics	
Bifurcation, *n* (%)	111 (23)
Ostial, *n* (%)	96 (20)
Tortuous, *n* (%)	9 (2)
CTO, *n* (%)	33 (7)
Long (> 20 mm), *n* (%)	306 (64)
In-stent, *n* (%)	168 (35)
IVL	
Balloon diameter, mm	3.5 ± 0.5
Number of pulses	80 (60–80)
Pre-dilatation, *n* (%)	441 (93)
Pre-dilatation balloon diameter, mm	3.5 ± 2.6
Pre-dilatation balloon maximum pressure (atm)	19.4 ± 4.6
Post-dilatation, *n* (%)	448 (94)
Post-dilatation balloon diameter, mm	4.0 ± 2.4
Post-dilatation balloon maximum pressure (atm)	19.7 ± 4.6
IVL after stenting (bail-out), *n* (%)	81 (17)
ICI performed, *n* (%)	249 (52)
Pre-IVL, *n* (%)	186 (39)
Post-IVL, *n* (%)	206 (43)
Other plaque modification technique used, *n* (%)	77 (16)
Pre-IVL	69 (15)
RA, *n* (%)	62 (13)
Cutting balloon, *n* (%)	5 (1)
Scoring balloon, *n* (%)	1 (0.2)
OPN balloon, *n* (%)	1 (0.2)
Post-IVL	9 (2)
RA, *n* (%)	5 (1)
Cutting balloon, *n* (%)	1 (0.2)
OPN balloon, *n* (%)	3 (0.6)
Treatment after IVL	
Stent implantation, *n* (%)	369 (77)
Stent diameter, mm	3.5 (3.5–4.0)

(Continues)

TABLE 2 | (Continued)

	Overall ($n = 477$)
Stent length, mm	38 (24–60)
Drug-coated balloon, *n* (%)	34(7)
Procedural time, min	94.5 ± 82.5
Fluoroscopy time, min	29.1 ± 18.8
Contrast volume, mL	186.4 ± 76.9

Abbreviations: CTO = chronic total occlusion, ICI = intracoronary imaging, IVL = intravascular lithotripsy, IVUS = intravascular ultrasound, LAD = left anterior descending artery, LCx =left circumflex artery, LM = left main, OCT = optical coherence tomography, OPN = ultra-high pressure balloon, RA = rotational atherectomy, RCA = right coronary artery, SVG = saphenous venous graft.

TABLE 3 | Procedural complications.

	Overall ($n = 454$)
Complications, *n* (%)	29 (6)
Dissection, *n* (%)	10 (2)
Perforation, *n* (%)	7 (2)
Slow flow, *n* (%)	1 (0.2)
No reflow, *n* (%)	1 (0.2)
Abrupt vessel closure, *n* (%)	4 (1)
Hemodynamic instability, requiring intervention, *n* (%)	7 (2)
Reanimation status, n (%)	5 (1)
Other, *n* (%)	3 (1)
Directly related to IVL, *n* (%)	6 (1)
Dissection, *n* (%)	2 (0.4)
Abrupt vessel closure, *n* (%)	1 (0.2)
Hemondynamic instability, *n* (%)	2 (0.4)
Reanimation status, *n* (%)	1 (0.2)
Ventricular fibrillation, *n* (%)	1 (0.2)

Abbreviation: IVL = intravascular lithotripsy.

observed in 37 (13%) patients, of which 10 (2%) events occurred before discharge. The majority of events were clinically driven TVR (n = 23, 8%), followed by 11 (4%) cardiac deaths and 10 (4%) non-fatal target vessel myocardial infarctions. Importantly, patients with a residual diameter stenosis < 30% had a lower TVR rate at 1-year follow-up ($p = 0.014$) compared to patients in whom a residual diameter stenosis < 30% was not reached (Figure 1). Additionally, Cox-regression analysis demonstrated that achieving residual stenosis < 30% significantly decreased the risk of TVR at 1-year follow-up (HR = 0.320, 95% CI: 0.114–0.898; $p = 0.030$).

3.4 | Predictors of Treatment Success

On multivariate linear regression analysis, stenting after IVL for therapy completion ($p < 0.001$), ICI guidance ($p = 0.024$) and CTOs ($p < 0.001$) were independently associated with increased luminal gain, while bifurcation lesions ($p = 0.027$) were linked to decreased luminal gain. In contrast, technical procedural parameters as IVL inflation pressure ($p = 0.599$) and number of pulses administered ($p = 0.412$) were not associated with luminal gain (Table 4). In multivariate binary logistic regression, long-segment lesions ($p = 0.034$) and stenting after IVL for therapy completion ($p = 0.041$) were associated with increased likelihood of achieving a residual diameter stenosis < 30%, while the presence of an aorta-ostial lesion ($p = 0.014$) was significantly associated with a reduced likelihood of achieving this outcome. Other procedural parameters related to IVL or concomitant strategies did not significantly impact the likelihood of achieving a residual diameter stenosis < 30% (Table 5).

4 | Discussion

This study evaluated clinical and procedural factors, influencing treatment success following IVL-therapy, using data from the multicenter, international, all-comers BENELUX-IVL Registry. The key findings are: (1) a residual diameter stenosis < 30% was more likely in long-segment lesions and when post-IVL stenting for therapy completion was performed, but less likely in aorta-ostial lesions; (2) CTOs, post-IVL stenting for therapy completion and ICI-guidance were linked to increased luminal gain, while bifurcation lesions were associated with decreased luminal gain and (3) technical IVL-related parameters, such as the inflation pressure and the number of pulses delivered, as well as other procedural parameters, including pre- and post-dilatation and plaque modification alongside IVL did not significantly impact treatment success.

Overall, IVL demonstrated favorable results, achieving residual diameter stenosis < 30% in 90% of lesions and a mean luminal gain of 1.9 ± 0.9 mm. At 1-year follow-up, MACE occurred in 13% of patients, and was primarily driven by TVR. These positive procedural and clinical outcomes align with previous IVL studies [7, 20]. Notably, patients in whom residual diameter stenosis < 30% was achieved, had lower rates of TVR at 1-year follow-up (Figure 1), with a 68% lower hazard compared to those with higher residual stenosis. This highlights the importance of assessing treatment success during the procedure, with residual diameter stenosis < 30% on fluoroscopy serving as a simple and effective predictor of favorable clinical outcomes.

Although the overall procedural and clinical outcomes are favorable, they might differ per target lesion subset. The increased luminal gain in CTOs is intuitive, as the lumen is initially occluded, allowing for more luminal expansion. This potential confounding effect was therefore included in the multivariable analysis. However, no significant association was observed between CTOs and achievement of residual diameter stenosis < 30%. This is supported by a recent sub-study from the BENELUX-IVL registry, which found that CTO-lesions have comparable procedural success rates and clinical outcomes up to 1 year, compared to non-CTO lesions [21]. While analyzing differences in treatment between various lesion subsets is beyond the scope of this study, the higher likelihood of achieving residual diameter stenosis < 30% in long-segment lesions might be attributed to more aggressive treatment strategies employed by operators. In contrast, bifurcation lesions were associated with decreased luminal gain and aorta-ostial

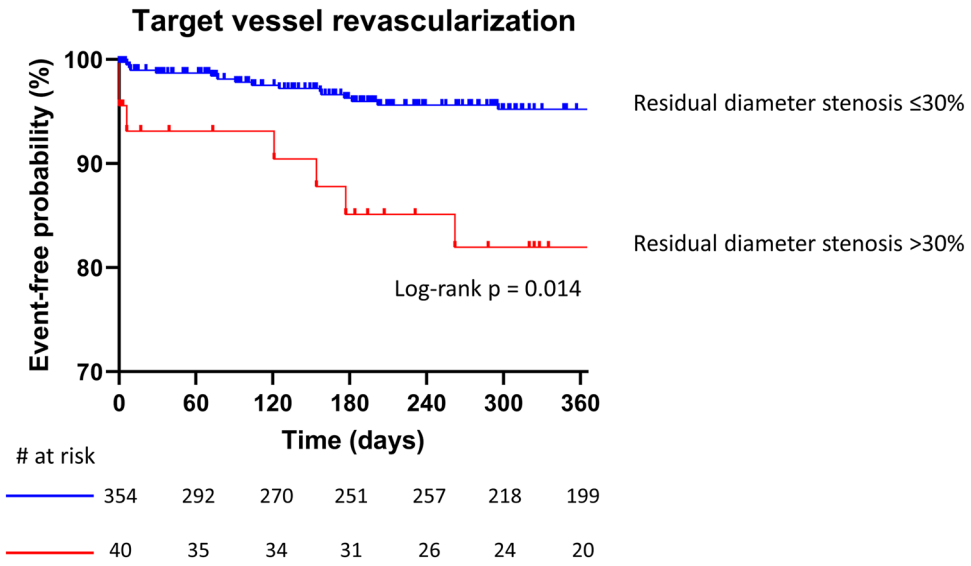


FIGURE 1 | One-year target vessel revascularization-free survival based on residual diameter stenosis (≤ 30% vs. > 30%). [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 4 | Predictors of Luminal Gain: Univariate and multivariate linear regression analysis.

	Univariable analysis			Multivariable analysis		
Variable	**Coefficient (*B*)**	**95% confidence interval**	***p* value**	**Coefficient (*B*)**	**95% confidence interval**	***p* value**
Age	−0.008	−0.019 to 0.002	0.105	−0.002	−0.015 to 0.011	0.781
Sex (male)	0.012	−0.202 to 0.227	0.910			
ACS	0.083	−0.094 to 0.260	0.357			
Lesion subtype						
Aorta-ostial	0.243	0.028−0.458	**0.027**	0.199	−0.089 to 0.488	0.174
CTO	1.058	0.753−1.364	**< 0.001**	0.872	0.478−1.267	**< 0.001**
Bifurcation	−0.139	−0.345 to 0.066	**0.183**	−0.323	−0.608 to −0.038	**0.027**
In-stent	−0.844	−1.149 to −0.538	**<0.001**	-0.159	−0.448 to 0.129	0.277
Long-segment	0.050	−0.139 to 0.238	0.606			
Procedural characteristics						
IVL maximum inflation pressure	0.113	−0.013 to 0.24	0.078	0.033	−0.091 to 0.157	0.599
IVL pulses delivered	0.002	−0.002 to 0.005	0.412			
Pre-dilatation	0.273	−0.098 to 0.643	0.148	0.308	−0.240 to 0.855	0.269
Pre IVL maximum pressure dilataiton	−0.007	−0.028 to 0.015	0.547			
Post-dilatation	0.192	−0.277 to 0.662	0.421			
Post IVL maximum pressure dilatation	−0.005	−0.026 to 0.015	0.599			
Plaque modification next to IVL	0.26	0.027−0.494	**0.029**	0.245	−0.065 to 0.554	0.121
Stenting after IVL for therapy completion	0.631	0.0423−0.839	**< 0.001**	0.606	0.259−0.954	**< 0.001**
Drug eluting balloon	−0.143	−0.476 to 0.190	0.399			
ICI	0.389	0.216−0.563	**< 0.001**	0.318	0.043−0.593	**0.024**

Abbreviations: ACS = acute coronary syndrome, CTO = chronic total occlusion, ICI = intracoronary imaging, IVL = intravascular lithotripsy.

TABLE 5 | Predictors of residual stenosis < 30%: univariate and multivariate binary logistic regression analysis.

	Univariable analysis			Multivariable analysis		
Variable	**Odds ratio**	**95% confidence interval**	***p* value**	**Odds ratio**	**95% confidence interval**	***p* value**
Age	0.985	0.947–1.024	0.432			
Sex (male)	0.864	0.381–1.961	0.727			
ACS	1.103	0.566–2.148	0.773			
Lesion subtype						
Aorta-ostial	0.442	0.219–0.890	**0.022**	0.283	0.104–0.775	**0.014**
CTO	1.101	0.32–3.789	0.879			
Bifurcation	1.264	0.561–2.848	0.572			
In-stent	0.351	0.18–0.683	**0.002**	0.668	0.235–2.528	0.771
Long-segment	2.437	1.258–4.719	**0.008**	2.846	1.080–7.500	**0.034**
Procedural characteristics						
IVL maximum inflation pressure	1.342	0.857–2.101	**0.198**	1.561	0.953–2.555	0.077
IVL pulses delivered	0.996	0.982–1.01	0.557			
Pre-dilatation	1.282	0.365–4.503	0.699			
Max inflation pressure	0.989	0.911–1.075	0.800			
Post-dilatation	0.671	0.085–5.266	0.704			
Maximum inflation pressure	1.021	0.950–1.097	0.573			
Plaque modification next to IVL	1.491	0.562–3.959	0.422			
Stenting after IVL for therapy completion	3.079	1.547–6.131	**0.001**	3.426	1.054–11.135	**0.041**
Drug eluting balloon	0.509	0.183–1.418	0.509			
ICI	1.399	0.726–2.697	0.315			

Abbreviations: ACS = acute coronary syndrome, CTO = chronic total occlusion, ICI = intracoronary imaging, IVL = intravascular lithotripsy;

lesions significantly reduced the likelihood of achieving residual diameter stenosis < 30%. In conventional PCI, bifurcation lesions are known to have worse clinical outcomes compared to non-bifurcation lesions [22, 23]. Currently, no studies have evaluated the efficacy of IVL in bifurcation lesions. The less favorable results in aorta-ostial lesions might be explained by the thicker elastic and muscular tissue, leading to resistance to balloon inflation and tendency to recoil [24]. Future studies are needed to further investigate the impact of lesion characteristics on treatment strategies and outcomes with IVL.

ICI guidance was a significant predictor of luminal gain, likely due to its ability enable patient-specific treatment optimization. However, this positive association was not observed for residual diameter stenosis < 30%. As such, these findings are not conclusive for the potential association of ICI with procedural and clinical outcomes. Nevertheless, they warrant future prospective studies to better evaluate the impact of ICI on procedural and clinical outcomes following IVL.

Interestingly, technical IVL factors such as inflation pressure and number of pulses delivered were not significantly associated with treatment success. This may be attributed to IVL's mechanism of action [7, 8, 10–12]. IVL-balloon inflation itself likely contributes minimally to luminal gain and stenosis reduction due to the low inflation pressures used (4–6 atm). Instead, the actual gain occurs after stent deployment following IVL for therapy completion, which compresses the fractured calcium in the vessel wall. Our findings that post-IVL stenting for therapy completion emerged as a consistent predictor of treatment success support this. The finding that the number of IVL pulses delivered is not predictive of treatment success contrasts with results from the LILI registry, which recommended delivering all 80 pulses [13]. A practical marker of the desired treatment effect of IVL could be a pressure drop in the inflator device and/or visual confirmation of balloon expansion, which may occur before delivering all pulses. Peri-IVL procedural parameters were also not significantly associated with treatment success (Tables 4 and 5), though this does not diminish their importance. For instance, pre- and post-dilatation were used in the majority of target lesions and can help determine whether a crossable calcified target lesion is undilatable, which serves as an indication for IVL [9]. Similarly, post-dilatation can confirm successful lesion modification after IVL. Additionally, plaque modification techniques, like pre-IVL rotational atherectomy may be crucial for preparing balloon uncrossable calcified lesions, to facilitate IVL [25].

4.1 | Limitations

This study has several limitations. Firstly, the observational retrospective study design, which is has to be considered when interpretating the clinical outcomes observed. Additionally, the decisions regarding the timing of IVL, the utilization of high-pressure pre- and post-dilatation, the placement of supplementary stents, and the use of ICI for procedural optimization were left to the operator's discretion. Additionally, ICI was not obligatory routinely performed before and after IVL. This limited our ability to compare outcomes between ICI-guided versus angiography-guided IVL procedures. Furthermore, a sensitivity analysis to confirm our findings in patients with ICI was not feasible due to inconsistent use of ICI.

5 | Conclusion

In this real-world registry, IVL demonstrated favorable procedural and clinical outcomes. Stenting after IVL for therapy completion, ICI guidance and CTOs were associated with increased luminal gain, while bifurcation lesions were linked to decreased luminal gain. Long lesions and post-IVL stenting for therapy completion were associated with achieving residual diameter stenosis < 30%, while aorto-ostial lesions were negatively associated with this outcome. Notably, technical IVL-related parameters, such as the inflation pressure and the number of pulses delivered, along with peri-IVL factors like pre- and post-dilatation and plaque modification, did not significantly impact treatment success.

Acknowledgments

This work was funded through a research grant from Shockwave Medical. Funders were not involved in any aspect of the study, including its design, collection, analysis and interpretation of the data, or the writing of the manuscript.

Disclosure

During the preparation of this work the authors used ChatGPT 4.0 to detect grammatical errors. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

Ethics Statement

Our study received the proper ethical oversight and all authors have participated in the work and have reviewed and agree with the content of the article. None of the article contents are under consideration for publication in any other journal or have been published in any other journal. No portion of the text has been copied from other material in the literature.

Conflicts of Interest

The Department of Cardiology of the Leiden University Medical Center received unrestricted research grants from Abbott Vascular, Bayer, Biotronik, Boston Scientific, Edwards Lifesciences, GE Healthcare and Medtronic. I. Al Amri received speaker fees from Penumbra Inc. and Medtronic. B.E.P.M. Claessen reports relations with Sanofi, Philips, Amgen, Boston Scientific Corp, and AbioMed Inc. that includes: consulting or advisory. TNE Vossenberg received consultancy fees from Boston Scientific and Cardiac Dimensions. Drs Kefer has served as proctors for Abbott. F. van der Kley received consultancy fees from Edwards Lifesciences and Abbott Vascular. F. van der Kley received consultancy fees from Edwards Lifesciences and Abbott Vascular. JW Jukema/his department has received research grants from and/or was speaker (with or without lecture fees) on a.o.(CME accredited) meetings sponsored/supported by Abbott, Amarin, Amgen, Athera, Biotronik, Boston Scientific, Dalcor, Daiichi Sankyo, Edwards Lifesciences, GE Healthcare Johnson and Johnson, Lilly, Medtronic, Merck-Schering-Plough, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi Aventis, Shockwave Medical, the Netherlands Heart Foundation, CardioVascular Research the Netherlands (CVON), the Netherlands Heart Institute and the European Community Framework KP7 Program. JM. Montero received a research grant from Shockwave Medical and speaker fees from Abiomed, Boston Scientific and Penumbra Inc. The other authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. H. Kawashima, P. W. Serruys, H. Hara, et al., "10-Year All-Cause Mortality Following Percutaneous or Surgical Revascularization in Patients With Heavy Calcification," *JACC: Cardiovascular Interventions* 15, no. 2 (2022): 193–204.

2. T. Rheude, T. Koch, M. Joner, et al., "Ten-Year Clinical Outcomes of Drug-Eluting Stents With Different Polymer Coating Strategies by Degree of Coronary Calcification: A Pooled Analysis of the Isar-Test 4 and 5 Randomised Trials," *EuroIntervention* 18, no. 14 (2023): 1188–1196.

3. Y. Kobayashi, H. Okura, T. Kume, et al., "Impact of Target Lesion Coronary Calcification on Stent Expansion," *Circulation Journal* 78, no. 9 (2014): 2209–2214.

4. M. S. Lee and N. Shah, "The Impact and Pathophysiologic Consequences of Coronary Artery Calcium Deposition in Percutaneous Coronary Interventions," *Journal of Invasive Cardiology* 28, no. 4 (2016): 160–167.

5. M. V. Madhavan, M. Tarigopula, G. S. Mintz, A. Maehara, G. W. Stone, and P. Généreux, "Coronary Artery Calcification," *Journal of the American College of Cardiology* 63, no. 17 (2014): 1703–1714.

6. G. S. Mintz, "Intravascular Imaging of Coronary Calcification and Its Clinical Implications," *JACC: Cardiovascular Imaging* 8, no. 4 (2015): 461–471.

7. D. J. Kereiakes, C. Di Mario, R. F. Riley, et al., "Intravascular Lithotripsy for Treatment of Calcified Coronary Lesions," *JACC: Cardiovascular Interventions* 14, no. 12 (2021): 1337–1348.

8. M. Natalia, T. Forero, and J. Daemen, "The Coronary Intravascular Lithotripsy System," *Interventional Cardiology Review* 14, no. 3 (2019): 174–181.

9. A. Jurado-Román, A. Gómez-Menchero, N. Gonzalo, et al., "Plaque Modification Techniques to Treat Calcified Coronary Lesions. Position Paper From the Aci-Sec," *Rec-Interv Cardiol* 5, no. 1 (2023): 46–61.

10. J. M. Hill, D. J. Kereiakes, R. A. Shlofmitz, et al., "Intravascular Lithotripsy for Treatment of Severely Calcified Coronary Artery Disease," *Journal of the American College of Cardiology* 76, no. 22 (2020): 2635–2646.

11. Z. A. Ali, T. J. Brinton, J. M. Hill, et al., "Optical Coherence Tomography Characterization of Coronary Lithoplasty for Treatment of Calcified Lesions," *JACC: Cardiovascular Imaging* 10, no. 8 (2017): 897–906.

12. F. Oliveri, M. Van Oort, I. Al Amri, et al., "Invasive Evaluation of Coronary Artery Compliance Modification After Intracoronary Lithotripsy," *Journal of Cardiovascular Medicine* 25, no. 9 (2024): 715–716.

13. B. Honton, G. Cayla, T. Lhermusier, et al., "National France LILI Registry on Intravascular Lithotripsy: 30 Days Follow Up," *Archives of Cardiovascular Diseases* 117, no. 1, Suppl (2024): S15–S16.

14. M. J. H. van Oort, I. Al Amri, B. O. Bingen, et al., "Evolving Use and Clinical Outcomes of Coronary Intravascular Lithotripsy: Insights From an International, Multicentre Registry," *Heart* 111, no. 2 (2024): 62–68.

15. G. Sianos, M. A. Morel, A. P. Kappetein, et al., "The Syntax Score: An Angiographic Tool Grading the Complexity of Coronary Artery Disease," *EuroIntervention: Journal of EuroPCR in Collaboration With the Working Group on Interventional Cardiology of the European Society of Cardiology* 1, no. 2 (2005): 219–227.

16. G. S. Mintz, J. J. Popma, A. D. Pichard, et al., "Patterns of Calcification in Coronary Artery Disease. A Statistical Analysis of Intravascular Ultrasound and Coronary Angiography in 1155 Lesions," *Circulation* 91, no. 7 (1995): 1959–1965.

17. E. Barbato, E. Gallinoro, M. Abdel-Wahab, et al., "Management Strategies for Heavily Calcified Coronary Stenoses: An Eapci Clinical Consensus Statement in Collaboration With the EURO4C-PCR Group," *European Heart Journal* 44, no. 41 (2023): 4340–4356.

18. G. J. Tearney, E. Regar, T. Akasaka, et al., "Consensus Standards for Acquisition, Measurement, and Reporting of Intravascular Optical Coherence Tomography Studies," *Journal of the American College of Cardiology* 59, no. 12 (2012): 1058–1072.

19. J. Knuuti, W. Wijns, A. Saraste, et al., "2019 ESC Guidelines for the Diagnosis and Management of Chronic Coronary Syndromes," *European Heart Journal* 41, no. 3 (2020): 407–477.

20. M. Sagris, N. Ktenopoulos, K. Dimitriadis, et al., "Efficacy of Intravascular Lithotripsy (Ivl) in Coronary Stenosis With Severe Calcification: A Multicenter Systematic Review and Meta-Analysis," *Catheterization and Cardiovascular Interventions* 103, no. 5 (2024): 710–721.

21. F. Oliveri, M. J. H. van Oort, I. Al Amri, et al., "Intravascular Lithotripsy in Heavily Calcified Chronic Total Occlusion: Procedural and One-Year Clinical Outcomes," *Catheterization and Cardiovascular Interventions* 104, no. 4 (2024): 655–663.

22. M. J. Grundeken, J. J. Wykrzykowska, Y. Ishibashi, et al., "First Generation Versus Second Generation Drug-Eluting Stents for the Treatment of Bifurcations: 5-Year Follow-Up of the Leaders All-Comers Randomized Trial," *Catheterization and Cardiovascular Interventions* 87, no. 7 (2016): E248–E260.

23. M. Zimarino, C. Briguori, I. J. Amat-Santos, et al., "Mid-Term Outcomes After Percutaneous Interventions in Coronary Bifurcations," *International Journal of Cardiology* 283 (2019): 78–83.

24. P. Jokhi and N. Curzen, "Percutaneous Coronary Intervention of Ostial Lesions," *EuroIntervention* 5, no. 4 (2009): 511–514.

25. M. J. H. van Oort, I. Al Amri, B. O. Bingen, et al., "Current Applications, Procedural and 1-Year Outcomes of Rotatripsy for the Treatment of Calcified Coronary Lesions," *Catheterization and Cardiovascular Interventions* 104, no. 2 (2024): 203–212.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.