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Long-term predictors of target vessel failure after intracoronary lithotripsy: 12-month results from the France LILI registry

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Coronary artery calcification is a frequent challenge in percutaneous coronary intervention (PCI), often associated with suboptimal procedural outcomes due to difficulties in lesion crossing, stent expansion, and a poor long-term clinical prognosis[1]. Intravascular lithotripsy (IVL) offers a promising solution using acoustic waves to modify calcified lesions and increase vessel compliance before stenting. However, despite the growing adoption of IVL, particularly in patients with severe calcifications, real-world long-term data remain scarce[2]. The France LILI registry was established to assess the long-term safety and efficacy of IVL in a large cohort of unselected patients treated in routine clinical practice.

France LILI (ClinicalTrials.gov: NCT05113407) is a prospective, multicentre, national registry that included 500 patients from 34 centres across France, all of whom underwent PCI with adjunctive IVL using the Shockwave C2 coronary lithotripsy system (Shockwave Medical). The primary endpoint was target vessel failure (TVF) – a composite of cardiac death, all myocardial infarction (MI), and ischaemia-driven target vessel revascularisation (ID-TVR) – assessed at 12 months. Secondary endpoints included procedural success, device success, and identification of factors associated with TVF. All clinical events were independently adjudicated by a committee of interventional cardiologists; angiographic data were analysed by an independent core lab.

Between November 2021 and February 2023, 547 lesions, including 98 in-stent restenosis (ISR) lesions, were treated by IVL in the 500 included patients. In the overall cohort, 81.6% of the patients were male, 29.4% had acute coronary syndrome, 39.2% had diabetes, 17.1% suffered from chronic renal failure, and 52.6% had undergone previous PCI. The majority of lesions involved the left anterior descending artery. Among *de novo* lesions, 70% had severe angiographic calcifications (Mintz C^3), and over 80% were classified as complex (ACC/AHA class B2/C). Concentric calcifications accounted for 64.2% of lesions, while 24.2% showed eccentric calcifications, and 11.6% were calcified nodules. Intracoronary imaging was used in 15.6% of the procedures. During most procedures (92.6%), a single IVL catheter was used. In 61.8% of lesions, 80 or more pulses were delivered during treatment, while 38.2% of lesions received fewer than 80 pulses. In 90% of these latter cases, the reduced number of pulses was attributed to operator discretion.

Device success, defined as residual lesion stenosis <50% after IVL, was achieved in 87.5% of patients. The overall procedural success rate, without procedural complications, was 93.2%, with no significant difference observed between *de novo* and ISR lesions. Final Thrombolysis in Myocardial Infarction 3 flow was observed in 99.6% of cases. Overall procedural complications were rare, with a low incidence of slow flow (0.6%) and perforations (0.8%) **(Central illustration A)**.

At 12 months, the primary endpoint of TVF occurred in 9.6% of patients **(Central illustration B)**. Cardiac death was observed in 2.6%, MI in 3.6%, and ID-TVR in 5.6%. Key

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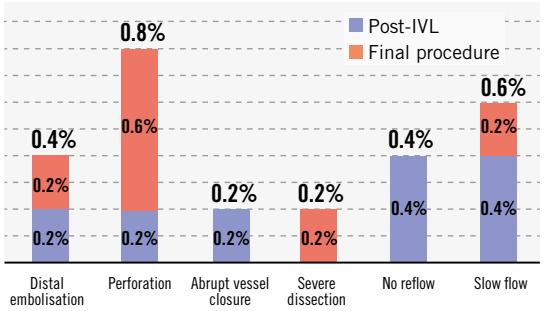
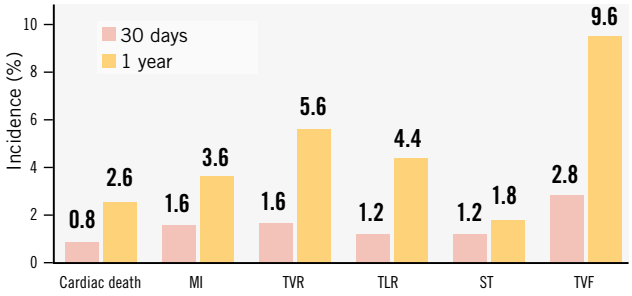
EuroIntervention — Central Illustration

Procedural outcomes, 12-month TVF, and independent 12-month TVF predictors from the France LILI registry.

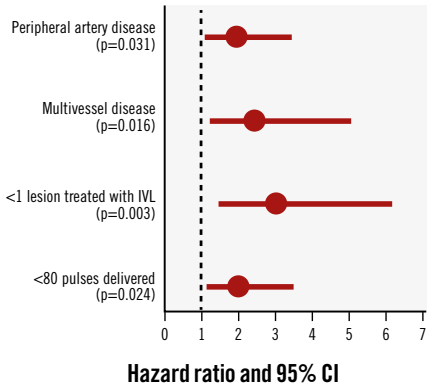
A Overall procedural complications



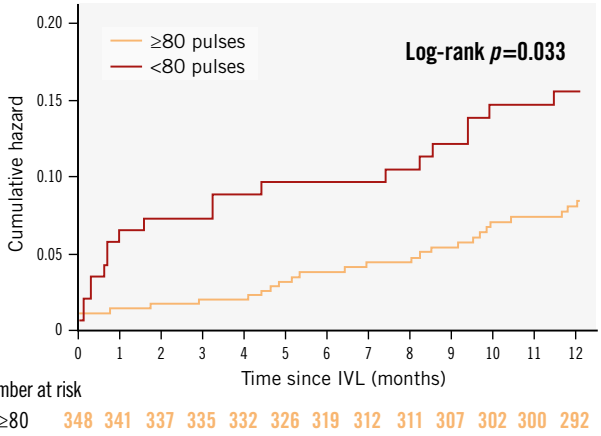
B 30-day and 12-month outcomes



C 12-month independent TVF predictors



D TVF incidence according to number of pulses delivered



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A) Overall procedural complications. B) Clinical outcomes at 30 days and 1 year. Key events include cardiac death, myocardial infarction (MI), target vessel revascularisation (TVR), target lesion revascularisation (TLR), stent thrombosis (ST), and the composite endpoint of target vessel failure (TVF). C) Independent predictors of TVF in multivariate analysis. D) Kaplan-Meier cumulative hazard curve for TVF stratified by the number of pulses delivered (<80 vs ≥80). IVL: intravascular lithotripsy

independent predictors of TVF identified through multivariate analysis included peripheral artery disease (hazard ratio [HR] 1.91; p=0.031), multivessel disease (HR 2.44; p=0.016), treatment of more than one lesion with IVL (HR 2.97; p=0.003), and the delivery of fewer than 80 pulses during IVL (HR 1.95; p=0.024) **(Central illustration C)**. Regarding the occurrence of TVF, a sharp divergence of the Kaplan-Meier curve in the first month was observed in patients receiving ≥80 pulses, with significant TVF occurrence at 12 months (7.8% vs 14.0%; p=0.033) **(Central illustration D)**.

The France LILI results demonstrate that IVL is a safe and effective technique for the treatment of calcified lesions in an all-comers population. Despite the complexity of the lesions, the procedural success rate remained high, and adverse events were relatively infrequent. Multivariate analysis suggests that the complexity of a patient's conditions and the number of pulses delivered during IVL are related to TVF occurrence. The association between fewer than 80 delivered pulses and an increased risk of TVF is a new finding, underlining the need for advanced refinement of IVL treatment, particularly in complex lesions. However, further studies must confirm this result despite a conceivable rationale for enhancing calcium fracture and vessel compliance. Calcified plaque modulation remains a vast and evolving field, characterised by unmet needs in procedural and outcome data, highlighting the necessity for well-designed new trials[4,5]. This is exemplified by the recent neutral results of the ECLIPSE trial[6], which failed to demonstrate the benefit of orbital atherectomy compared to balloon plaque preparation in reducing 12-month TVF rates for heavily calcified lesions in a randomised setting.

Several limitations can be identified in our study. First, as an observational, non-randomised registry, selection bias cannot be ruled out despite the inclusion of all-comers patients. Additionally, the low use of intravascular imaging in this cohort may have limited the ability to fully assess the

mechanisms underlying procedural outcomes, particularly in terms of calcium distribution and stent expansion[7]. Finally, longer follow-up is necessary to understand the durability of IVL's benefits in complex coronary artery disease.

In conclusion, the France LILI registry, which included unselected all-comers patients, provides significant evidence supporting IVL as an effective and safe adjunct in treating calcified coronary lesions in routine clinical practice. The study identified new independent predictors of 12-month TVF, including the number of pulses administered, which reflects the complexity of a patient's condition and lesion. These findings contribute to the growing evidence supporting IVL as a valuable tool in complex calcified lesions.

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Conflict of interest statement

B. Honton reports consulting fees from Medtronic, Abbott, and Boston Scientific; and lecture honorarium from Medtronic, Shockwave Medical, Abbott, and Boston Scientific. B. Lattuca reports consulting fees from Terumo, Abbott, and Boston Scientific; lecture honorarium from Medtronic, Amarin, and AstraZeneca; and scientific grants from Biotronik and Boston Scientific. T. Lhermusier reports consulting fees and honorarium from Medtronic, Abbott, and Edwards Lifesciences. N. Amabile reports consulting fees from GE HealthCare, Shockwave Medical, Abbott, and Boston Scientific; lecture honorarium from Shockwave Medical, Abbott, and Boston Scientific; and institutional grants from Abbott. J. Jeanneteau reports consulting honorarium from BMS, AstraZeneca, Pfizer, and Novo Nordisk. G. Rangé reports consulting fees from MicroPort, Shockwave Medical, Abbott, Boston Scientific, and Terumo. J. Monsegu reports consulting fees from Abbott and Terumo. T. Cuisset reports consulting fees from Medtronic, Abbott, and Boston Scientific; lecture honorarium from Shockwave Medical, Terumo, Edwards Lifesciences, Europa, and Sanofi; and is a shareholder in CERC. G. Souteyrand reports consulting fees and honorarium from Medtronic, Terumo, Abbott, Boston Scientific, and B. Braun. M. Quillot reports consulting fees and honorarium from Shockwave Medical, Boston Scientific, and Sanofi. C. Saint Etienne reports honorarium from Medtronic, Abbott, Biotronik, and Edwards Lifesciences. S. Levesque reports honorarium from Shockwave Medical. A. Gerbay reports consulting fees from Abbott; honorarium from Biosensors; and is a shareholder in Inari. B. Seguy reports consulting fees from Boston Scientific; and honorarium from Biosensors and Boston Scientific. J. Adjedj reports consulting fees and honorarium from Shockwave Medical. O. Darremont reports honorarium from Abbott, Boston Scientific, and Edwards Lifesciences. P. Motreff reports consulting fees and honorarium from Terumo, Abbott, and

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