DOI: https://doi.org/10.24875/ RECICE.M26000582

Supplementary data

Table S1. Endpoint definitions

Calcified coronary nodule (CN)[1]	A calcified nodule (CN), as observed by OCT, is defined as a localized, protruding mass within the coronary artery wall, appearing as a signal-poor region with sharply delineated borders. An eruptive CN is defined as an accumulation of small calcium fragments protruding and disrupting the overlying fibrous cap, typically with small amount of thrombus. A noneruptive CN is defined as an accumulation of small calcium fragments with a smooth intact fibrous cap without an overlying thrombus.
Stent expansion at the CN site	Measured with optical coherence tomography, defined as the ratio between the minimum stent area at the CN site and the vessel lumen area at that point, estimated from the corresponding proximal or distal lumen reference area. *Stent expansion at the CN site (%) = (MSA at the CN site / reference lumen area at the CN site) x 100*
Minimum stent expansion (MSA)	Measured with optical coherence tomography, defined as the ratio between the minimum stent area and the vessel lumen area at that point, estimated from the corresponding proximal or distal lumen reference area.
Mean stent expansion	Measured with optical coherence tomography, defined as the ratio between the mean stent area at the CN site and the average of the distal and proximal reference areas.
Procedural success	Achieving a stent expansion of ≥ 80% with TIMI III flow, in the absence of stent loss, coronary perforation, or intraprocedural death.
Strategy success	Procedural success without the need for crossover to an alternative treatment
Significant stent malapposition at the CN site	Measured using optical coherence tomography (OCT), defined as a stent strut detachment ≥ 0.4 mm from the underlying vessel wall, with a longitudinal extension ≥ 1 mm.
Degree of calcium nodule debulking	The reduction in calcium nodule size (mm^2), measured after plaque modification and prior to stent implantation.
Fracture at the CN site	New disruption or discontinuity observed on OCT after plaque modification and prior to stent implantation.
Stent ellipticity at the CN site	Measured using OCT at the end of the procedure, calculated as the ratio of the maximum luminal diameter to the minimum luminal diameter of the stent at the CN site.
Target lesion[2]	The target lesion is defined as the treated segment including the 5-mm margin proximal and distal to the stent/scaffold.
Target vessel[2]	The entire major intervened coronary vessel, including side branches.
Target lesion failure (TLF)[2]	The composite of clinically driven target lesion revascularization, myocardial infarction or cardiac death related to the target lesion.
Target lesion revascularization (TLR)[2]	Repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel performed for restenosis or other complication of the target lesion.
Target vessel revascularization[2]	Any repeat percutaneous intervention or surgical bypass of any segment of the target vessel including the target lesion.
Target vessel non–target lesion revascularization[2]	Any repeat percutaneous intervention or surgical bypass of the target vessel for pre-existing disease, disease progression or other reasons unrelated to the target lesion as defined above.

Major adverse cardiovascular events (MACE)[2]	Composite of cardiovascular death, non-fatal target lesion myocardial infarction, unplanned target lesion revascularization or stent thrombosis.
Cardiovascular death[2]	Death resulting from cardiovascular causes. The following categories may be collected: • Death caused by acute myocardial infarction (MI) • Death caused by sudden cardiac arrest, including unwitnessed death • Death resulting from heart failure • Death caused by stroke • Death caused by cardiovascular procedures • Death resulting from cardiovascular hemorrhage • Death resulting from other cardiovascular causes
Noncardiovascular death[2]	Any death that is not thought to be the result of a cardiovascular cause. The following categories may be collected: • Death resulting from malignancy • Death resulting from pulmonary causes • Death caused by infection (including sepsis) • Death resulting from gastrointestinal causes • Death resulting from accident/trauma • Death caused by other noncardiovascular organ failure • Death resulting from other noncardiovascular causes • Undetermined Death
Undetermined cause of death[2]	Defined as a death not attributable to any other category due to the absence of relevant source documents. Such deaths will be classified as cardiovascular for endpoint determination.
Procedural myocardial infarction (MI)[3]	Myocardial infarction ≤48 hours after the index procedure (Type 4a MI; Fourth universal definition of myocardial infarction). Coronary intervention-related MI is defined by an elevation of cTn values more than five times the 99th percentile upper reference limit (URL) in patients with normal baseline values. In patients with elevated pre-procedure cTn, where the cTn levels are stable (≤ 20% variation) or falling, the post-procedure cTn must rise by more than 20%. However, the absolute post-procedural cTn value must still be at least five times the 99th percentile URL. In addition, at least one of the following criteria is required: • New ischemic ECG changes • Development of new pathological Q waves • Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology • Angiographic findings consistent with a procedural flow-limiting complication, such as: o Coronary dissection o Occlusion of a major epicardial artery or a side branch occlusion/thrombus o Disruption of collateral flow o Distal embolization
Non-procedural (spontaneous)	Detection of a rise and/or fall in cTn values, with at least one value above the 99th percentile URL, and at least one of the following: • Symptoms of acute myocardial ischemia

myocardial infarction (MI)[3]	• New ischemic ECG changes • Development of pathological Q waves • Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology • Identification of a coronary thrombus by angiography (including intracoronary imaging) or by autopsy
Stent thrombosis[2]	1. Definite stent thrombosis: a. Angiographic confirmation of stent thrombosis: The presence of a thrombus that originates in the stent or in the segment 5 mm proximal or distal to the stent or in a side branch originating from the stented segment and the presence of at least 1 of the following criteria: i. Acute onset of ischemic symptoms at rest. ii. New electrocardiographic changes suggestive of acute ischemia. iii. Typical rise and fall in cardiac biomarkers (refer to definition of spontaneous myocardial infarction). Or b. Pathological confirmation of stent/scaffold thrombosis i. Evidence of recent thrombus within the stent determined at autopsy. ii. Examination of tissue retrieved following thrombectomy (visual/histology). 2. Probable stent thrombosis: regardless of the time after the index procedure, any myocardial infarction that is related to documented acute ischemia in the territory of the implanted stent without angiographic confirmation of stent thrombosis and in the absence of any other obvious cause. 3. Silent stent occlusion: The incidental angiographic documentation of stent occlusion in the absence of clinical signs or symptoms is not considered stent thrombosis. Timing of ST (duration after stent implantation) • Acute 0 – 24 hours • Subacute >24 hours – 30 days • Late >30 days – 1 year • Very late >1 year
Angiographic complications during procedure[2]	Loss of Patency of Major Vessel or Side Branch • Abrupt Main Vessel Closure o When TIMI grade 3 or 2 flow at baseline; TIMI grade 0 or 1 flow after the procedure o When TIMI grade 1 flow at baseline; TIMI grade 0 flow after the procedure o When TIMI grade 0 flow at baseline and vessel patency (TIMI grade 2 or 3 flow) established during the procedure; TIMI grade 0 flow after the procedure • Side Branch (>1.5 mm) Occlusion After the Procedure: TIMI grade 0 or 1 flow in a side branch initially patent with TIMI grade 2 or 3 flow. Embolization: The appearance of an abrupt cutoff in the distal vessel (or in a side branch >1.5 mm) after percutaneous coronary intervention.

	Persistent Slow Flow or No Reflow: Markedly delayed flow (TIMI grade 2 for slow flow, TIMI grade 0 or 1 for no reflow) in a target vessel with minimal (<30%) residual stenosis at the stented/scaffolded segment and no evidence of flow-limiting dissection Major Dissection: Dissection in the target vessel greater than type B from the National Heart, Lung, and Blood Institute classification
Stroke (ischemic stroke)[4]	Sudden onset of neurological signs or symptoms fitting a focal or multifocal vascular territory within the brain, spinal cord, or retina, that: 1. Persist for ≥24 h or until death, with pathology or neuroimaging evidence that demonstrates either: a. CNS infarction in the corresponding vascular territory (with or without hemorrhage); or b. Absence of other apparent causes (including hemorrhage), even if no evidence of acute ischemia in the corresponding vascular territory is detected. or 2. Symptoms lasting <24 h, with pathology or neuroimaging confirmation of CNS infarction in the corresponding vascular territory. Note: When CNS infarction location does not match the transient symptoms, the event would be classified as covert CNS infarction (Type 2a) and a TIA (Type 3a), but not as an ischemic stroke.
BARC bleeding[5]	Type 0: no bleeding Type 1: bleeding that is not actionable and does not cause the patient to seek unscheduled performance of studies, hospitalization, or treatment by a healthcare professional; may include episodes leading to self-discontinuation of medical therapy by the patient without consulting a healthcare professional Type 2: any overt, actionable sign of hemorrhage (eg, more bleeding than would be expected for a clinical circumstance, including bleeding found by imaging alone) that does not fit the criteria for type 3, 4, or 5 but does meet at least one of the following criteria: (1) requiring nonsurgical, medical intervention by a healthcare professional, (2) leading to hospitalization or increased level of care, or (3) prompting evaluation Type 3 • Type 3a: Overt bleeding plus hemoglobin drop of 3 to 5 g/dL (provided hemoglobin drop is related to bleed) Any transfusion with overt bleeding • Type 3b: Overt bleeding plus hemoglobin drop 5 g/dL (provided hemoglobin drop is related to bleed) Cardiac tamponade Bleeding requiring surgical intervention for control (excluding dental/nasal/skin/hemorrhoid) Bleeding requiring intravenous vasoactive agents • Type 3c: Intracranial hemorrhage (does not include microbleeds or hemorrhagic transformation, does include intraspinal) Subcategories confirmed by autopsy or imaging or lumbar puncture Intraocular bleed compromising vision Type 4: CABG-related bleeding Perioperative intracranial bleeding within 48 h Reoperation after closure of sternotomy for the purpose of controlling bleeding Transfusion of 5 U whole blood or packed red blood cells within a 48-h period Chest tube output 2L within a 24-h period. Type 5: fatal bleeding • Type 5a: Probable fatal bleeding; no autopsy or imaging confirmation but clinically suspicious

	• Type 5b: Definite fatal bleeding; overt bleeding or autopsy or imaging confirmation
Angina status (CCS class)	The patient's angina status will be evaluated according to the Canadian Cardiovascular Society (CCS) Classification. Grade I: Ordinary physical activity does not cause angina, such as walking and climbing stairs. Angina occurs with strenuous, rapid, or prolonged exertion at work or recreation. Grade II: Slight limitation of ordinary activity. Angina may occur when walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, or in cold, wind, emotional stress, or during the few hours after awakening. Walking more than two blocks on the level and climbing more than one flight of ordinary stairs at a normal pace and in normal conditions can also provoke symptoms. Grade III: Marked limitation of ordinary physical activity. Angina may occur when walking one or two blocks on the level or climbing one flight of stairs in normal conditions and at a normal pace. Grade IV: Inability to carry on any physical activity without discomfort. Anginal syndrome may be present even at rest.

Supplementary methods

Stent expansion calculation for the primary endpoint.

The primary endpoint is the percentage of stent expansion at the CN site, measured with OCT, and defined as the ratio between the minimum stent area at the CN site and the reference area at the CN site.

Stent expansion at the CN site (%) = (MSA at the CN site / reference lumen area at the CN site) x 100

For the primary endpoint calculation, proximal and distal reference areas will be manually assessed by the Core Lab. Using co-registered pre- and post-stent images, analysts will identify the OCT cross-sections with the most normal appearance in both the proximal and distal segments relative to the Minimum Lumen Area (MLA). In cases where pre-stent images are unavailable or uninterpretable, the 5-mm segments immediately proximal and distal to the stent edges will be analyzed to identify the healthiest reference frames. Stent expansion will also be assessed using the Aptivue™ automated software through two algorithms:

- Automatic tapered method: this method provides the stent expansion of the entire stent segment (not only the study segment). The Reference Lumen Area (RLA) is calculated at the site of the MLA following the Murray's law based on the proximal and distal RLA located at the stent edges.

- Automatic dual reference method: this method provides the stent expansion for each half of the entire stent segment. For the proximal segment the software uses the MLA of this segment and the RLA located at the proximal stent edge. For the distal segment the software uses the MLA located in this segment and the RLA located at the distal edge.

Supplementary procedures

Crossover between techniques

Orbital atherectomy:

- If the lesion cannot be crossed with OA, crossover to rotational atherectomy or intracoronary laser techniques will be permitted, according to the operator's preference.
- In the case of undilatable lesions despite treatment with OA and NC balloon dilation, crossover to the IVL technique will be allowed. If this technique is ineffective, crossover to another plaque modification technique will be permitted, following the operator's preference.

Intracoronary lithotripsy:

- If the lesion cannot be crossed with the IVL balloon, predilation with NC or SC balloons will be allowed. If this is not possible, crossover to OA will be permitted. If the lesion cannot be crossed with OA, crossover to rotational atherectomy or intracoronary laser techniques will be allowed, according to the operator's preference.
- In the case of undilatable lesions despite treatment with IVL and NC balloon dilation, crossover to OA will be allowed. If this technique is ineffective, crossover to another plaque modification technique will be permitted, following the operator's preference.

Special situations

Long lesions

In the presence of long calcified segments where the presence of a CN is identified, the use of OA or IVL is recommended along the entire length of the lesion. It should be noted that multiple runs of OA or IVL pulses may be required to modify the CN. More than one IVL balloon may be used if deemed necessary.

The outcomes of the angioplasty will be specifically analyzed at the level of the CN and along the rest of the lesion.

Presence of different types of calcium in a single lesion

The coexistence of different coronary calcification patterns in the same lesion is a common finding. Similar to the treatment of long lesions, the use of OA or IVL is recommended to modify the entire extent of the lesion. The outcome of the angioplasty will be specifically analyzed at the level of the CN and in the other calcified areas of the lesion.

Multivessel disease and presence of more than one CN

In patients with additional coronary lesions requiring revascularization besides the target lesion (the lesion where a CN is identified with OCT), a staged approach is recommended for target and non-target lesions, with the operator deciding which lesions should be treated first. Angioplasty for non-target lesions will be performed at the operator's discretion, without the mandatory use of OA or IVL.

If OCT detects the presence of CNs in more than one vessel, multiple target lesions per patient may be included, at the treating physician's discretion. In such cases, it is recommended that different target lesions be treated in separate procedures.

SUPPLEMENTARY REFERENCES

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