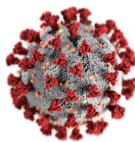


## EVENT DEFINITION FORM

**Event:** Microangiopathy  
**Outcome/covariate:** outcome  
**Version:** 1.0  
**Status:** final

**Contributing authors**

authors	Role	Date
Ilse Kelters	Medical/draft v 0.1	June 24, 2020
Miriam Sturkenboom	Epidemiological review	June 29, 2020
Ilse Kelters	Codes	July 17, 2020
Miriam Sturkenboom	Review codes	August 13, 2020
Leila Belbachir	Medical review	August 23, 2020
Miriam Sturkenboom	Final codes	March 23, 2021
Carlos Durán	Review Possible/Narrow assignments	March 24, 2021
Miriam Sturkenboom	Updated codes used in final version	August 8, 2021



## 1. Event definition

Cardiac microangiopathy leads to microvascular dysfunction which can manifest in different clinical scenarios. 1) occurrence of ischaemic heart disease in absence of angiographically significant coronary atherosclerosis (see definition form ACS) and could result in inflammation and/or abnormal vasomotor regulation; 2) Inadequate post-PCI an/or post thrombolysis coronary reperfusion, including micro-embolic mechanism. 3) in context of epicardial vessel disease (Axel *et al.*).

## Signs and symptoms

- Chest pain/angina (exercise related)
- Dyspnoea
- Fatigue
- More atypical symptoms

Coronary microvascular dysfunction (CMD) refers to a term covering a wide spectrum of clinical situations in which the structure and function of the coronary microcirculation is affected. This leads to impaired responses of the coronary flow to vasodilator stimuli, being characterized by: (Padro *et al.*)

- Impaired coronary flow reserve (CFR)
  - With cut-off values below 2.0–2.5 depending on the methodology;

OR

- Abnormal high index of coronary microvascular resistance (IMR; e.g. IMR >25)

AND/OR

- Focal or diffuse vasoconstriction during acetylcholine provocation testing, in the absence of any significant epicardial coronary artery obstruction (>50% lumen stenosis at coronary angiography) or preserved fractional flow reserve (FFR, value  $\geq 0.80$ ) (Knuuti and Ong *et al.*)

PM. Unclear if 'myocardial infarction with nonobstructive coronary arteries' (MINOCA) has to be included.

## 2. Synonyms / lay terms for the event

Small vessel disease

Small artery disease

Nonobstructive coronary heart disease

Coronary microvascular disease

Coronary microvascular dysfunction

Microvascular angina

## 3. Laboratory tests that are specific for event

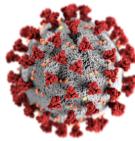
None available

## 4. Diagnostic tests that are specific for event

Diagnostic tests when ACS is suspected:

- See definition form ACS, including:
  - angiography of the coronary arteries. Patients with a normal angiogram and a abnormal cardiac condition are suspected of cardiac syndrome X.
  - Stress test.

Diagnostics for peripheral assessment of microvascular function and structure (for measuring CFR or minimal microcirculatory resistance):

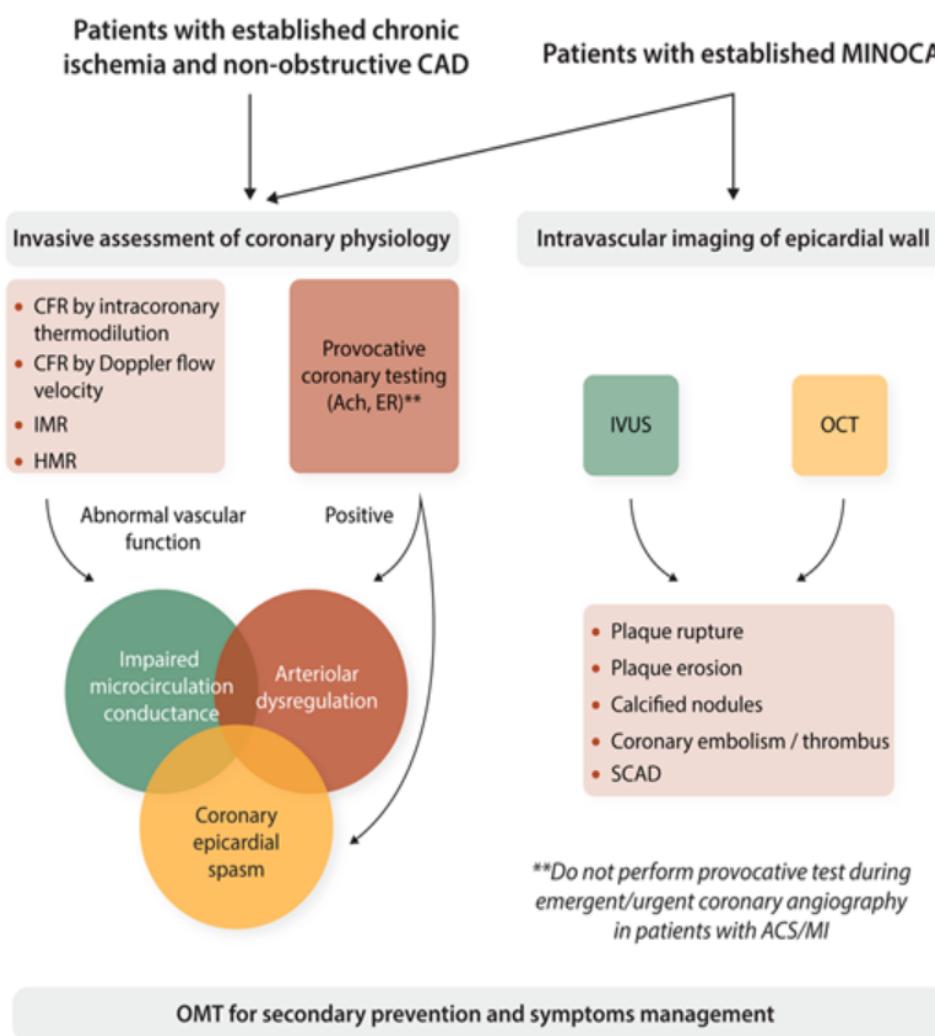


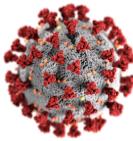
1. Single photon emission computed tomography (SPECT).  
Stress myocardial perfusion imaging for patients who can exercise and dipyridamole or adenosine-induced vasodilation in conjunction with SPECT imaging or echocardiography for patients who cannot exercise
2. Echo doppler
3. Quantitative contrast echocardiography
4. PET
5. CT
6. MRI
7. Brachial artery post-ischaemic reflow
8. Laser doppler flux imaging
9. Clinical intravital microscopy
10. Venous occlusion plethysmography

Extra:

11. Biopsy

For insight into the different diagnostic test see the article of Axel *et al.* (2008).





## 5. Drugs that are used to treat event

- Beta-blockers
- Statins
- ACE-inhibitors or ARBs
- Antiplatelet therapy: low dose aspirin

## 6. Procedures used specific for event treatment

See diagnostic tests.

## 7. Setting (outpatient specialist, in-hospital, GP, emergency room) where condition will be most frequently /reliably diagnosed

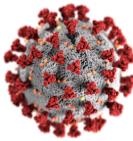
Outpatients specialist

## 8. Diagnosis codes or algorithms used in different papers to extract the events in Europe/USA: seek literature for papers that have studied this event, and see how they extracted/measured the event.

none found

## 9. codes used in ACCESS

Coding system	Code	Code name	Concept	Algorithm
ICD10/CM	I78.9	Disease of capillaries, unspecified	C0155765	Possible
ICD10/CM	I78.0	Hereditary hemorrhagic telangiectasia		Possible
ICD10/CM	I78.8	Other diseases of capillaries		Possible
ICD10/CM	D65	Purpura fulminans	C0085650	Narrow
ICD10/CM	M31.1	Thrombotic microangiopathy	C2717961	Narrow
ICD10/CM	178.8	Other disease of the capillaries		Possible
ICD9CM	448.0	Hereditary hemorrhagic telangiectasia	C0155765	Possible
ICD9CM	448.9	Other diseases of capillaries		Possible
ICD9CM	446.6	Thrombotic microangiopathy	C2717961	Narrow
RCD2	G77z0	Capillary haemorrhage	C0265024	Possible
RCD2	G77z2	Capillary thrombosis	C0265026	Possible
RCD2	G77zz	Disease of capillaries NOS	C0155765	Possible
RCD2	G77..	Diseases of capillaries	C0155765	Possible
RCD2	G37..	Cardiac syndrome X	C0206064	Narrow
RCD2	G756..	Thrombotic microangiopathy	C2717961	Narrow
RCD2	G756z	Thrombotic microangiopathy NOS	C2717961	Narrow
RCD2	G39..00	Coronary Microvascular Disease		Possible
SCTSPA	195386000	hemorragia capilar [dup]	C0265024	Possible
SCTSPA	43696002	hemorragia capilar	C0265024	Possible
SCTSPA	17810004	trombosis capilar	C0265026	Possible
SCTSPA	195380006	enfermedad de los capilares	C0155765	Possible



SCTSPA	195390003	enfermedad de los capilares, SAI	C0155765	Possible
SCTSPA	57223003	microangiopatía	C0155765	Possible
SCTSPA	58729003	trastorno de los vasos capilares	C0155765	Possible
SCTSPA	233845001	síndrome cardíaco X	C0206064	Narrow
SCTSPA	13507004	púrpura fulminante	C0085650	Narrow
SCTSPA	126729006	microangiopatía trombótica	C2717961	Narrow
SCTSPA	195360005	microangiopatía trombótica, SAI	C2717961	Narrow
SCTSPA	195381005	Non-neoplastic nevus (disorder)		possible
SNOMEDCT_US	195386000	Capillary haemorrhage	C0265024	Possible
SNOMEDCT_US	43696002	Capillary hemorrhage	C0265024	Possible
SNOMEDCT_US	17810004	Capillary thrombosis	C0265026	Possible
SNOMEDCT_US	195388004	Capillary thrombosis	C0265026	Possible
SNOMEDCT_US	155446001	Diseases of capillaries	C0155765	Possible
SNOMEDCT_US	155449008	Diseases of capillaries NOS	C0155765	Possible
SNOMEDCT_US	195250004	Capillary disease	C0155765	Possible
SNOMEDCT_US	195380006	Capillary disease	C0155765	Possible
SNOMEDCT_US	195390003	Disease of capillaries NOS	C0155765	Possible
SNOMEDCT_US	266324004	Diseases of capillaries NOS	C0155765	Possible
SNOMEDCT_US	57223003	Microangiopathy	C0155765	Possible
SNOMEDCT_US	58729003	Disorder of capillaries	C0155765	Possible
SNOMEDCT_US	194869009	Cardiac syndrome X	C0206064	Narrow
SNOMEDCT_US	233845001	Cardiac syndrome X	C0206064	Narrow
SNOMEDCT_US	459701000124101	Coronary microvascular disease	C0206064	Narrow
SNOMEDCT_US	13507004	Purpura fulminans	C0085650	Narrow
SNOMEDCT_US	126729006	Thrombotic microangiopathy	C2717961	Narrow
SNOMEDCT_US	195360005	Thrombotic microangiopathy NOS	C2717961	Narrow
SNOMEDCT_US	78129009	Thrombotic microangiopathy	C2717961	Narrow

## 10. Algorithm proposal

Narrow: narrow codes

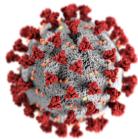
Broad: narrow & possible codes

## 11. Background rates

None generic found

## 12. References

Axel R. Pries, Helmut Habazettl, Giuseppe Ambrosio, Peter Riis Hansen, Juan Carlos Kaski, Volker Schächinger, Harald Tillmanns, Giuseppe Vassalli, Isabella Tritto, Michael Weis, Cor de Wit, Raffaele Bugiardini, A review of methods for assessment of coronary microvascular disease in both



clinical and experimental settings, *Cardiovascular Research*, Volume 80, Issue 2, 1 November 2008, Pages 165–174, <https://doi-org.proxy.library.uu.nl/10.1093/cvr/cvn136>

Teresa Padro, Olivia Manfrini, Raffaele Bugiardini, John Canty, Edina Cenko, Giuseppe De Luca, Dirk J Duncker, Etto C Eringa, Akos Koller, Dimitris Tousoulis, Danijela Trifunovic, Marija Vavlukis, Cor de Wit, Lina Badimon, ESC Working Group on Coronary Pathophysiology and Microcirculation position paper on 'coronary microvascular dysfunction in cardiovascular disease', *Cardiovascular Research*, Volume 116, Issue 4, 15 March 2020, Pages 741–755, <https://doi-org.proxy.library.uu.nl/10.1093/cvr/cvaa003>

Knuuti, J., Wijns, W., Saraste, A., Capodanno, D., Barbato, E., Funck-Brentano, C., ... & Agewall, S. (2020). 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes: the Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC). *European heart journal*, 41(3), 407-477.

Ong, P., Camici, P. G., Beltrame, J. F., Crea, F., Shimokawa, H., Sechtem, U., ... & Coronary Vasomotion Disorders International Study Group. (2018). International standardization of diagnostic criteria for microvascular angina. *International Journal of Cardiology*, 250, 16-20.