

Management of the Median Arcuate Ligament Syndrome.

An update. •

Dutch Mesenteric Ischemia Study Group



Disclosures R.H.Geelkerken



received an unrestricted grant of the
(*Veelbelovende zorg program 2022*)



Dutch expert centre for Gastro-intestinal ischemie

Dutch Mesenteric Ischemia Study Group

All studies in close collaboration with the



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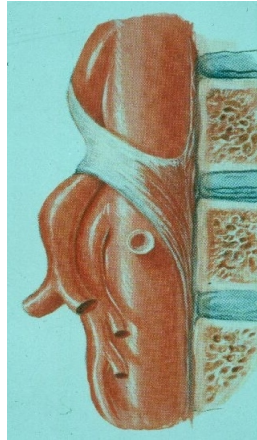


The Median Arcuate ligament syndrome (Dunbar or CACS)

Symptomatic external compression Coeliac Artery by the Median Arcuate Ligament



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- (Vague) upper-abdominal pain, fear of eating
- Other more common causes excluded
- Intermittent extrinsic coeliac artery compression (Arc. ligament)

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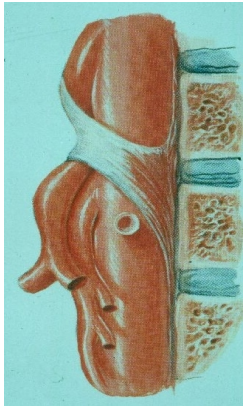
Lipshutz B. Ann surg 1918.
Harjola PT. Ann Chir Gynaec Fenn 1963.
Dunbar JD. Am. J Roentgenol Radium Ther Nucl Med 1965
Mensink PB. Brit J Surg 2006.
van Petersen AS. J Vasc Surg 2009

Two guidelines

Björck M et al. AMI and CMI guidelines. **EJVES 2017.**

“The clinical significance of this external compression, remains unclear, although case series of successful treatment have been reported”

“No recommendations due to lack of evidence”



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Two guidelines

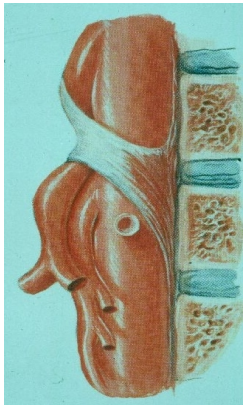
Terlouw et al ; CMI guidelines, **UEG 2020**

“Patients with MALS might be considered for surgical coeliac artery release”

GRADE 2D (96% consensus)

“In patients with MALS (and no preceding adequate coeliac artery release) endovascular stenting of the CA is contraindicated”.

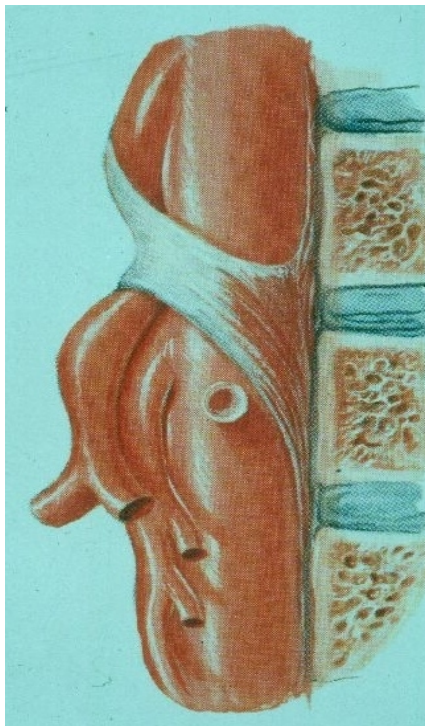
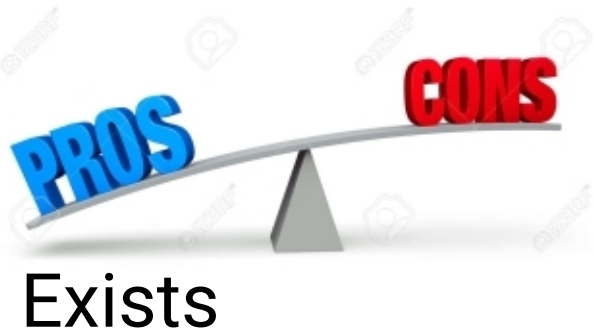
GRADE 1D (100% consensus)



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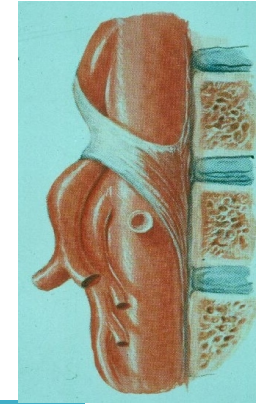
The Median Arcuate Ligament syndrome guidelines



The existence of this disease is still controversial
The pathophysiology is poorly understood.

Although there is supporting evidence that ischemia is the cause

“The Szilagyi doctrine” (MALS 1972)



Is this still the case in 2022?

“... no patient had ever been proven, on scientific grounds, to have an abnormality of intestinal structure or function which was caused by extraluminal compression of the coeliac artery, or supposed relief from the operation could be anything other than a placebo effect.”

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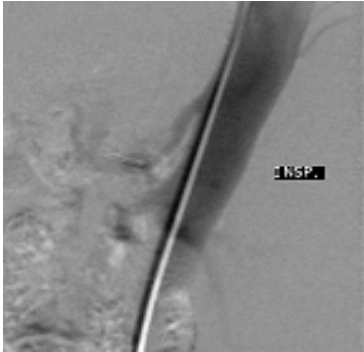


Szilagyi DE et al. Surgery 1972;6:849-63.
Geelkerken RH et al. Brit J Surg 1990;77:807-9

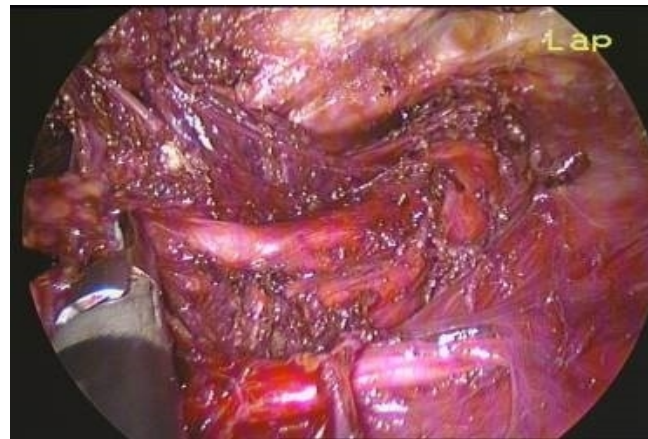
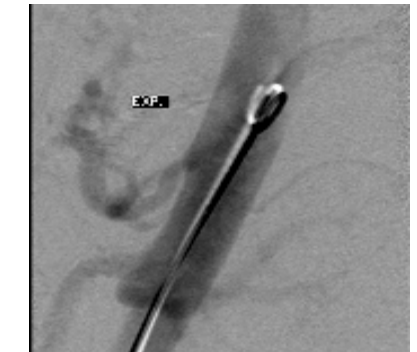
MALS; endoscopic cleavage of the MAL

Angiographic and clinical outcome*

preoperative



postoperative



Primary assisted patency; **89%** (41/46)
Clinical assisted success; **89%** (41/46)

* Van Petersen AS, et al. J Vasc Surg 2009 and 2017

Two Scoping reviews of the literature
Jimenez et al 2012*

- Jimenez et al. published a scoping review of 20 retrospective studies reporting a **85%** immediate symptom improvement of **400 MALS patients** from 6 months up to 23 years after laparoscopic and open CA release with a **late recurrence** in 19 patients in the open group (**6.8%**) and seven patients in the laparoscopic group (**5.7%**).



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*Jimenez JC, et al. JVS 2012;56:868-73.



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MALS, QoL and Psychiatry

The objective of the study of Skelly was to define the

- **psychiatric comorbidities** in a cohort of adults undergoing
- **surgery for MALS** and to determine whether these comorbidities are
- **predictive of patient-reported quality of life (QOL)** outcomes.

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MALS, QoL and Psychiatry

Surgery **improves** patient-reported QoL in adults treated for MALS.



Psychiatric diagnoses are common in adults with MALS and predict worse patient-reported QoL outcomes.

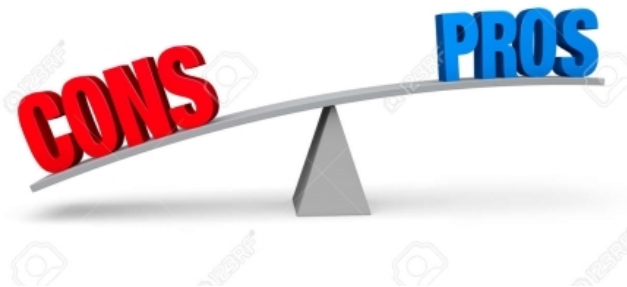


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Quality of Life temporarily improved in Patients in whom the diagnosis CMI wasn't confirmed after Multidisciplinary Evaluation in a tertiary referral Centre*.

- QoL of these patients **that were not treated** was still improved after 6 months.
- *Attention and recognition for disabling symptoms may influence perceived QoL*



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Two Scoping reviews of the literature **Metz FL et al 2022***

- Thirty-eight studies were included describing **880 adult patients** and 6 studies describing **196 patients below the age of 18 years**.
- 468 (**68%**) of the **adult patients** became either **free of symptoms** (n=294) or reported **clear reduction of symptoms** (n=174) from 3 months up to 228 months after CA release.
- **Pediatric cohort**, 146 (**82%**) of the patients became either **free of symptoms** (n=72) or reported a **clear reduction of symptoms** after laparoscopic CA release (n=74)

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Two Scoping reviews of the literature Metz FL et al 2022*

- **Two adult studies** compared QoL before and after treatment for MALS and both showed an **improved QoL after treatment.**



- In the adult cohort thirty-five (92%) and in the pediatric cohort five (83%) studies scored a **high or unclear risk of bias** for the majority of the **QUADAS-2 items**



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*Metz FM et al.. A SR on the efficacy of treatment of the MALS. EJVES 2022 submitted

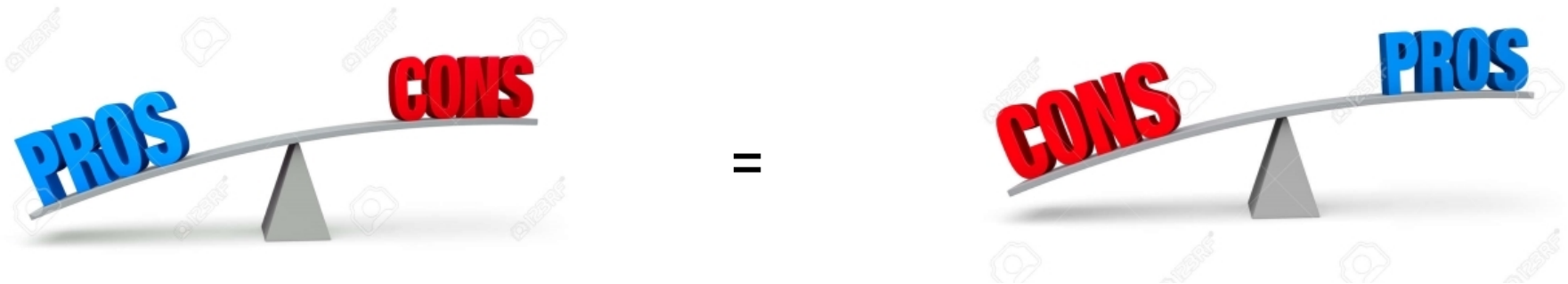


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The “Szilagyi debate” on MALS settled

- To end the ongoing debate and to enable the development of evidence-based guidelines (*Class I, GRADE 1a*) for the management of MALS, both guideline committees recommend **to perform a blinded, randomised controlled trial comparing a CA release with a sham operation.**



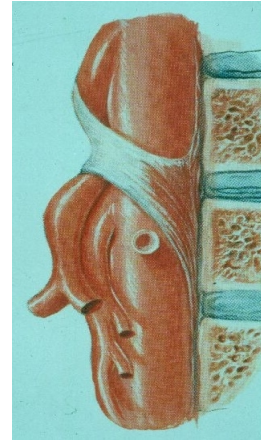
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The Coeliac Artery Release or Sham Operation study



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outcome parameters

- Nationwide **randomised**, **sham-controlled**, follow up **double blinded**, superiority clinical trial
- Intervention videotaped **eCAR** in one expert centrum (learning curve and standardization).



Outcome parameters are irrefutable and convincing



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Patient perspective: Clinical significant improvement of symptoms

Society perspective: Business Impact Analysis

CARoSO study is Funded by Zorginstituut, Veelbelovende zorg program 2022



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MALS update

Take home messages

- Guidelines ➡ evidence substantiating MALS is low
- Reviews ➡ CAR for MALS ~80% clinical success.
- The Szilagyi doctrine will be settled in 2026 (CARoSO study)

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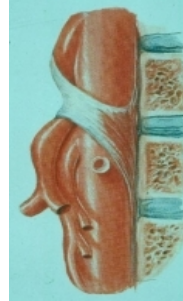




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CARoSO study ethics and methods



A systemic review reconsidering the ethics of sham interventions concluded that sham interventions are acceptable provided the conditions of scientific necessity, reasonable risks, and valid informed consent are fulfilled (Niemansburg 2015).

The CARoSO is a superiority study in which the expected success rate for the **CA release** group of **0.7** is based on two scoping reviews in which sustained symptom relief is reported in 69% up to 78% of MALS patients treated by CA release.

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For the **sham operation** the expected success rate of **0.3** is based on five RCTs with sham operations (Swank 2003, Boelens 2013, Roumen 2008, Guyuron 2009, Abbot 2004)

The Coeliac Artery Release or Sham Operation study

- Will either underline the usefulness of eCAR as a minimal invasive (cost)**effective treatment for MALS.**

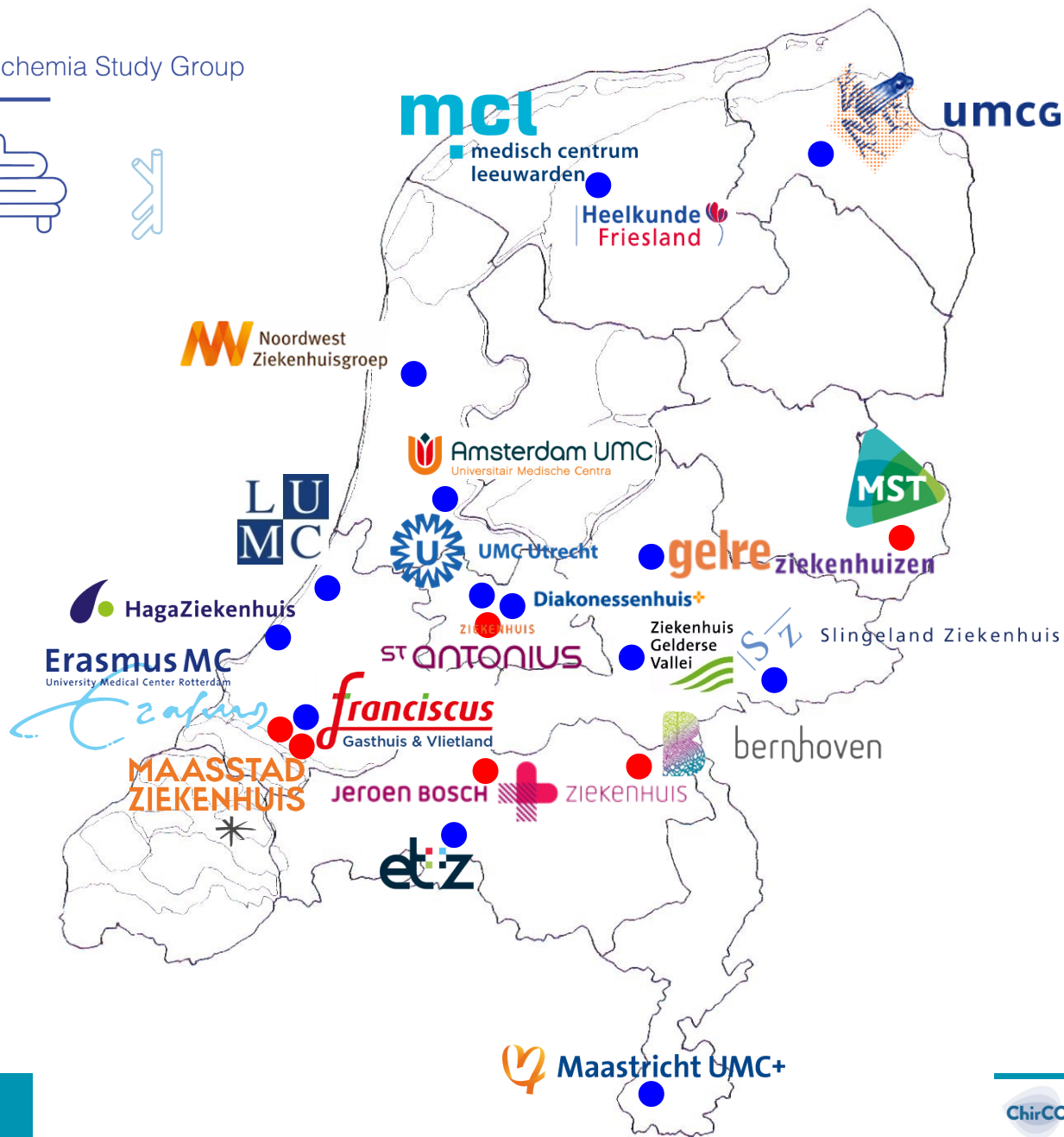
or

- it will **prohibit a meaningless intervention** in patients with disabling abdominal symptoms.
- Effective treatment of MALS is expected to result in mean health gain of **6.05 Quality Adjusted Life Years (QALYs)**/patient and has the potency to reduce the substantial productivity loss and healthcare consumption caused by MALS, resulting in a **saving up to M€4.3/year.**

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The incidence of MALS in the Nederland is estimated on 487 per year



Mission

To advance the knowledge of mesenteric ischemia among physicians and to develop more reliable diagnostic studies and better therapeutic treatments for patients with mesenteric ischemia.

Studies

- CoBaGI
- TACTIC
- CARoS0
- Pressure
-



The European Society of Cardiology grading system

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

Do's



Classes of recommendations	Definition
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.
Class IIa	<i>Weight of evidence/opinion is in favour of usefulness/efficacy.</i>
Class IIb	<i>Usefulness/efficacy is less well established by evidence/opinion.</i>
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.

Don'ts



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The GRADE* score

Do's

GRADE	Explanation	Definition strength of recommendation	Definition quality of evidence
1A	Strong recommendation High quality of evidence	Benefits clearly outweigh risks and burdens, or vice versa	Further research is very unlikely to change our confidence in the estimate of effect
1B	Strong recommendation Moderate quality of evidence	Benefits clearly outweigh risks and burdens, or vice versa	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
1C	Strong recommendation Low quality of evidence	Benefits clearly outweigh risks and burdens, or vice versa	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
1D	Strong recommendation Very low quality of evidence	Benefits clearly outweigh risks and burdens, or vice versa	Any estimate of effect is very uncertain
2A	Weak recommendation High quality of evidence	Trade-offs between benefits and risks and burdens are closely balanced	Further research is very unlikely to change our confidence in the estimate of effect
2B	Weak recommendation Moderate quality of evidence	Trade-offs between benefits and risks and burdens are closely balanced	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
2C	Weak recommendation Low quality of evidence	Trade-offs between benefits and risks and burdens are closely balanced	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
2D	Weak recommendation Very low quality of evidence	Trade-offs between benefits and risks and burdens are closely balanced	Any estimate of effect is very uncertain

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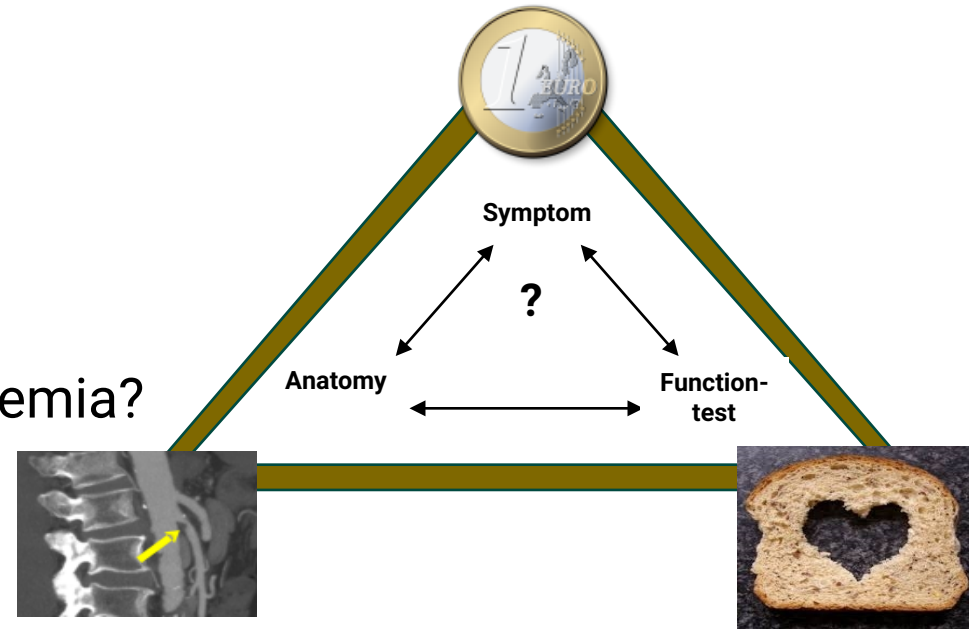


*Grading of Recommendations Assessments Developments and Evaluation

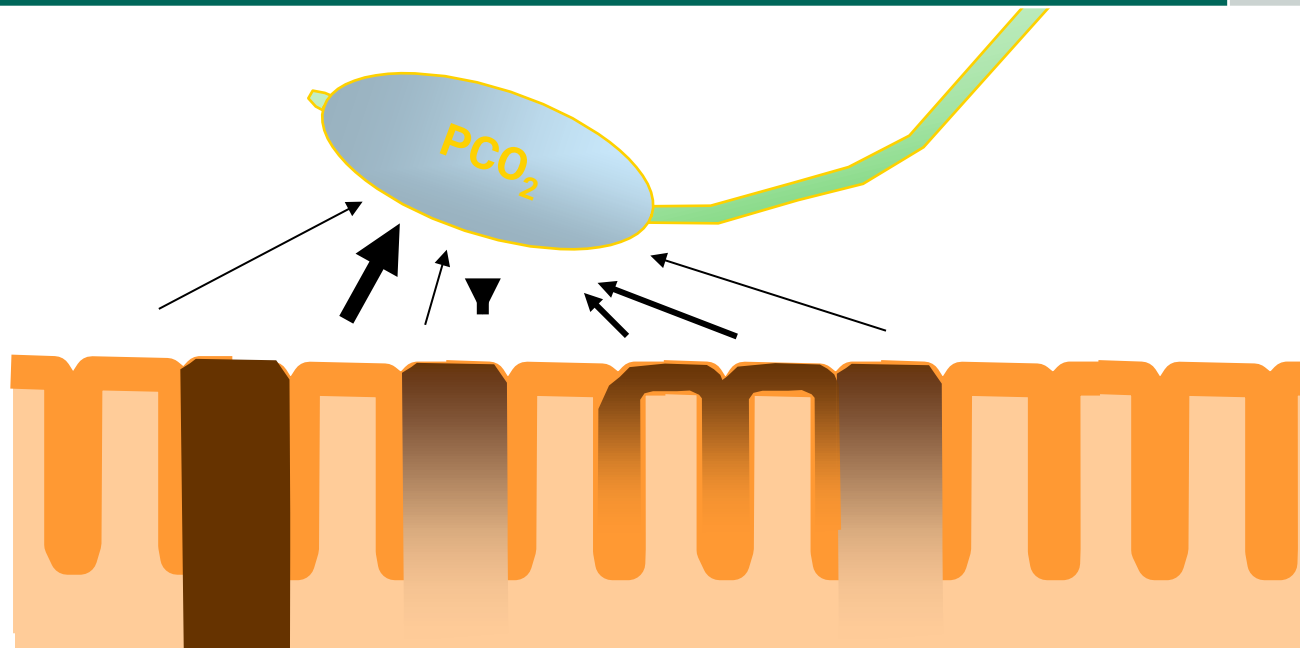
CMI diagnosis

Only three key questions to answer

- (Curable) anatomical substrate?
- Bowel function test indicating ischemia?
- Symptoms fitting to CMI?



No recommendation	Class	Level of evidence
Functional testing is fundamental in diagnosing CMI, in particular in one vessel disease . The methodology, however, is not yet validated and widespread enough to issue any recommendations at this time.	-	-



Terlouw LG, et al. CMI guidelines. UEG 2020
 Björck M et al. AMI and CMI guidelines. EJVES 2017