ORIGINAL ARTICLE

Early risk stratification of patients with suspected chronic mesenteric ischaemia using a symptom and mesenteric artery calcium score based score chart

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Abstract

Background: The mesenteric artery calcium score (MACS) identifies patients with possible chronic mesenteric ischaemia (CMI) using standard computed tomography (CT) imaging. The MACS does not necessitate a dedicated computed tomography angiography (CTA) which is required for evaluation of mesenteric artery patency. This study aimed to test the use of a symptom and MACS based score chart to facilitate the selection of patients with a low probability of CMI, in whom further diagnostic workup can be omitted, and to validate the CTA-based score chart proposed by van Dijk et al. which guides treatment decisions in patients with suspected CMI.

Methods: This retrospective study included consecutive patients with suspected CMI. The Agatston definition was used to calculate the MACS. Multivariable logistic regression analysis was used to create a MACS score chart, which was applied in all patients to determine its discriminative ability. The score chart by van Dijk et al. was validated in this independent external patient series.

Results: Hundred-ninety-two patients were included, of whom 49 had CMI. The MACS score chart composed of the variables weight loss, postprandial abdominal pain, history of cardiovascular disease, and MACS, showed an excellent discriminative ability (area under the curve [AUC] 0.87). CMI risks were 2.1% in the low-risk group (0–4 points) and 39.1% in the increased risk group (5–10 points); sensitivity (97.8%) and negative predictive value (NPV; 97.9%) were high. The CTA-based score chart by van Dijk et al. showed an excellent discriminative ability (AUC 0.89).

Conclusion: The MACS score chart shows promise for early risk stratification of patients with suspected CMI based on a near-perfect NPV. It is complementary to the CTA-based score chart by van Dijk et al., which showed excellent external validity and is well suited to guide subsequent (invasive) treatment decisions in patients with suspected CMI.

Key Summary

Summarise the established knowledge on this subject

- Mesenteric artery stenoses are prevalent (6%–29%), but as a result of the compensatory capacity of the mesenteric circulation, the incidence of chronic mesenteric ischaemia (CMI) is 9.2 per 100,000
- Early risk stratification could facilitate the diagnostic trajectory of chronic mesenteric ischaemia in order to triage patients that do or do not need a further diagnostic workup
- The mesenteric artery calcium score (MACS) identifies CMI patients with a sensitivity of 88% and can be obtained from both non-contrast enhanced and contrast enhanced computed tomography (CT)
- The score chart by van Dijk et al. might guide subsequent treatment decisions in patients with a clear suspicion of chronic mesenteric ischaemia, but requires an arterial contrast enhanced computed tomography angiography (CTA)

What are the significant and/or new findings of this study?

- A CT-based score chart composed of the variables weight loss, postprandial abdominal pain, cardiovascular disease, and MACS, showed excellent discrimination between patients with and without CMI
- The actual CMI risk was 2.1% in the predicted low-risk group (0–4 points) of the MACS score chart and 39.1% in the increased risk group (5–10 points) of the MACS score chart
- The near-perfect negative predictive value (97.9%) and sensitivity (97.8%) of the MACS score chart suggests that a score of ≤4 points virtually rules out CMI, while no patients are misclassified
- In this independent cohort the CTA-based score chart by van Dijk et al. was confirmed to have an excellent discriminative ability to guide treatment decisions in patients with suspected CMI

INTRODUCTION

Severe complaints of postprandial abdominal pain, fear of eating, and consecutive weight loss characterize chronic mesenteric ischaemia (CMI).[1,2] CMI can be caused by atherosclerotic mesenteric artery stenosis, coeliac artery (CA) compression (median arcuate ligaments syndrome [MALS]), vasculitis, or chronic non-occlusive mesenteric ischaemia (NOMI).[2,3] Abdominal pain and mesenteric artery stenosis are both frequently found in the general population. The prevalence of mesenteric artery stenosis is 6%–29% and increases with age to up to 67% in persons older than 80 years of age.[2] The incidence of CMI is substantial (9.2 per 100,000) and also increases with age (≥80 years 44.3 per 100,000).[4] The difference in prevalence of mesenteric artery stenosis and incidence of CMI is at least partly explained by the compensatory capacity of the extensive collateral mesenteric circulation.[5] Limited awareness of CMI among physicians could also contribute to this difference due to missed diagnoses and substantial diagnostic delays.[2,6]

Patients with abdominal complaints often undergo extensive diagnostic testing, including abdominal imaging by computed tomography (CT), before CMI is even considered and the diagnostic workup of CMI is initiated. Early risk stratification based on standard CT imaging could facilitate the diagnostic trajectory, raise awareness, reduce diagnostic delays in CMI patients, and avoid an extensive and cumbersome diagnostic workup of CMI in patients without CMI. The mesenteric artery calcium score (MACS) is calculated on CT images by multiplying the volume of a calcified lesion with a density factor and has recently been reported to discriminate CMI patients from non-CMI patients.[7] However, the MACS should be correlated with symptoms in order to be clinically applicable. Risk stratification with a score chart based on symptoms and MACS could be a valuable tool to exclude a diagnosis of CMI in very low-risk patients, in whom a further diagnostic workup can be omitted, and to identify patients with higher probability of CMI in whom further diagnostic investigations are warranted.

Patients with suspected CMI undergo a detailed assessment of symptoms, a dedicated computed tomography angiography (CTA) to identify mesenteric artery stenosis, and an extensive diagnostic workup to exclude alternative diagnoses, including upper gastrointestinal endoscopy, abdominal imaging, and when indicated a

colonoscopy.[2] The indication to perform additional functional testing and ultimately the decision to treat a patient can be guided by the recently published score chart by van Dijk et al. which requires a dedicated CTA with grading of a mesenteric artery stenosis.[8] The score chart by van Dijk et al. recommends either a wait-and-see policy, an additional functional test, or immediate treatment, but remains to be externally validated in an independent cohort.

The current study aimed to test the use of a symptom and MACS based score chart to facilitate the selection of patients with a low probability of CMI, in whom a further diagnostic workup can be omitted, and to validate the CTA-based score chart proposed by van Dijk et al, which guides treatment decisions.

METHODS

Study design

This single centre retrospective cohort study included consecutive patients analysed for suspected CMI in a specialized tertiary referral centre between April 2016 and October 2019. Patients were eligible for inclusion when a CT—not older than 12 months before first presentation—was available. Patients were excluded when they had undergone a previous mesenteric artery revascularization or when an anatomical variation with a common origin of CA and superior mesenteric artery (SMA) was present. The local medical research ethics committee decided that the Medical Research Involving Human Subjects Act does not apply to this study (MEC-2018-1414). The investigators complied with the Helsinki declaration on research ethics. The TRIPOD checklist for prediction model development and validation was used to write this manuscript.[9]

Diagnostic workup

A standardized diagnostic workup was performed in all patients and consisted of symptom assessment, exclusion of alternative diagnoses, CTA, and when indicated assessment of mucosal ischaemia by visible light spectroscopy.[3,10] All patients with suspected CMI were discussed by an experienced multidisciplinary expert team consisting of gastroenterologists, interventional radiologists, and vascular surgeons. A consensus diagnosis was used to select patients in whom mesenteric artery revascularization was indicated.[3] A definitive diagnosis of CMI was established when symptoms improved or resolved at three months after revascularization, or in case of chronic NOMI during treatment with a vasodilator.[2] Patients with a consensus diagnosis of no CMI or those initially labelled as CMI, but without improvement of symptoms after treatment, were classified as non-CMI. A definitive diagnosis of CMI was used to determine the ability of a MACS based score chart to identify patients with an increased risk of CMI and to validate the score chart by van Dijk et al.

Mesenteric artery calcium score

The methods used to calculate the MACS have been described in detail.[7] In short, a custom build software module (MeVisLab version 2.7.1, MeVis Medical Solutions AG), using the Agatston definition, was developed and used to calculate the MACS of a CT for the CA and SMA.[11] Assumptions were made to standardize the areas of calcium scoring. The estimated volume of a calcified lesion causing a stenosis at the vessels' origin consisted of the volume of the lesion that was located within a circle with a radius equal to the diameter of the vessels' origin. Calcium scoring was performed from origin until bifurcation for CA and from origin until the first large jejunal artery for SMA. The MACS of CA + SMA was classified as low (<29.7), intermediate (29.7–422), or high (>422), based on the observed sensitivity and specificity in the original study.[7]

Validation of the score chart by van Dijk et al.

Patients not previously included in the original publication of van Dijk et al. were used to validate the score chart by van Dijk et al.[8] This score chart was applied to determine the total score of all patients (Table 1). The total score was used to assign patients to the low-risk group (0–5 points), intermediate-risk group (6–18 points), or high-risk group (19–28 points). Absolute CMI risks were calculated for each risk category, the total score was used to determine the discriminative ability of the score chart.

Data collection and statistical methods

Data regarding medical history, presenting symptoms, severity of a mesenteric artery stenosis, diagnosis, follow-up, and MACS were collected. Severity of a mesenteric artery stenosis was assessed on CTA and classified as no significant stenosis (<50%), intermediate stenosis (50%–70%), or severe stenosis (>70%).[8]

Statistical analyses were performed with R version 4.0.1 (R Foundation for Statistical Computing). Continuous variables were not symmetrically distributed and are, therefore, shown as median and interquartile range. Baseline characteristics of CMI and non-CMI patients were compared using chi-square or Fisher's exact testing for categorical variables and Wilcoxon rank testing for continuous variables. The area under the curve (AUC) was used to determine the discriminative ability of the score chart by van Dijk et al. (pROC version 1.16.2).[12] Multiple imputation (mice version 3.9.0)—10 imputations, 10 iterations—was used to impute missing values in variables that were potential predictors of CMI (Table S1).[13] Multivariable logistic regression analysis was performed on the imputed dataset, predictors with a p-value <0.1 were included in the MACS score chart. Pooled regression coefficients were calculated using Rubin's rules and divided by 0.75 and rounded to the nearest integer to assign points to each predictor in the MACS score chart.[14] Psfmi package version 0.2.0 was used to calculate the pooled AUC,

with 95% confidence interval (CI), of the MACS score chart in the ten imputed datasets and to assess calibration of the model with the Hosmer-Lemeshow test.[15]

RESULTS

During the study period, 203 patients were analysed for suspected CMI and 192 patients were included in the study. Reason of exclusion was a previous mesenteric artery revascularization in nine patients and a common origin of CA and SMA in two patients. A definitive diagnosis of CMI was established in 49 of the included patients, of whom 46 were diagnosed with atherosclerotic CMI, two with MALS, and one with chronic NOMI. Hundred-thirty-five patients were classified as non-CMI. The definitive CMI status was considered missing in eight patients, since the duration of follow-up was less than three months.

Baseline characteristics and CTA results

Comparison of the baseline characteristics revealed that most CMI patients were female (CMI 81.6% vs. non-CMI 65.9%) and of significantly older age (CMI 70 [65–75] versus non-CMI 64 [56–70]) (Table 2). The risk factors cardiovascular disease (CVD) (CMI 61.2% vs. non-CMI 37.8%) and smoking (CMI 83.7% vs. non-CMI 60.3%) were significantly more prevalent among CMI patients. The presenting symptoms weight loss, postprandial abdominal pain, an adapted eating pattern and diarrhoea were significantly more often reported by CMI patients. Calcium scoring showed a significantly higher MACS of CA + SMA in CMI patients (CMI 832 [96–1803] versus non-CMI 17 [0–278]).

Assessment of stenosis severity showed a high risk of CMI in patients with a ≥50% stenosis of the CA, SMA, and inferior mesenteric artery (IMA) (88.9%), SMA and IMA (80.0%) and CA and SMA (72.2%) (Table 3). The risk of CMI was lower in patients with a stenosis of CA (13.3%) or CA and IMA (20.0%), the lowest CMI risks were observed in patients without a mesenteric artery stenosis (1.8%) or an IMA stenosis (0.0%). A CMI risk of 46.5% was observed in patients with an atherosclerotic stenosis, while a lower CMI risk was observed in patients with a stenosis caused by CA compression (8.3%).

MACS score chart

Multivariable logistic regression was performed using weight loss, postprandial abdominal pain, a history of CVD, and MACS as predictors of CMI. A high MACS showed the strongest association with CMI (odds ratio [OR] 18.46 [95% CI 5.53–61.68]), followed by weight loss (OR 9.03 [95% CI 2.30–35.45]) (Table 4). All predictors were included in the score chart, since the p-value was <0.1 for all predictors (Table S2 shows a model with MACS as a continuous

TABLE 1 Score chart by van Dijk et al

Predictor	Points
Weight loss	5
Cardiovascular disease	2
Coeliac artery	
50%–70% stenosis, vascular disease	4
50%–70% stenosis, MALS	4
>70% stenosis, vascular disease	11
>70% stenosis, MALS	9
Superior mesenteric artery	
50%–70% stenosis	4
>70% stenosis	10

Abbreviation: MALS, median arcuate ligament syndrome.

variable). The MACS score chart ranges from 0 to 10 points, with 0 to 4 points indicating a low CMI risk (2.1%) and 5 to 10 points indicating an increased CMI risk (39.1%) (Table 5). The CMI risk ranged from 11.8% (5 points) to up to 86.7% (10 points) in the group with an increased CMI risk. Discriminative ability of the MACS score chart was excellent (AUC 0.87 [95% CI 0.72–0.95]). A score of ≥5 points identified CMI patients with a 97.8% sensitivity, 40.2% specificity, 39.1% positive predictive value (PPV) and 97.9% negative predictive value (NPV). Figure 1 shows the calibration of the MACS score chart in the 10 imputed datasets. Perfect prediction is indicated by the dashed line, when predicted probability equals observed probability. The MACS score chart seems perfectly calibrated, with a slope of one and intercept of zero. Hosmer-Lemeshow testing showed no evidence for a poor fit, p = 0.76.

Validation of the score chart by van Dijk et al.

Performance of the score chart by van Dijk et al. was assessed in a subgroup of 155 patients not included in the inception cohort of the original publication.[8] Thirty-six patients were diagnosed with CMI, of whom 34 were diagnosed with atherosclerotic CMI, 1 with MALS, and one with chronic NOMI. The remaining 111 patients were classified as non-CMI. Classification of stenosis severity in the CA showed a 50%–70% atherosclerotic stenosis in 21 patients, a 50%–70% stenosis due to compression in eight patients, a >70% atherosclerotic stenosis in 38 patients, and a >70% stenosis due to compression in 11 patients. Classification of stenosis severity in the SMA showed a 50%–70% stenosis in 13 patients and a >70% stenosis in 36 patients. The score chart by van Dijk et al. performed well in this subgroup with a CMI risk of 0.0% in the low-risks group, 23.3% in the intermediate-risk group, and 81.8% in the high-risk group (Table 6). The discriminative ability of the score chart by van Dijk et al. was excellent with an AUC of 0.89 (95% CI 0.84–0.94).

TABLE 2 Baseline characteristics of all patients

Baseline characteristic	All patients (N = 192)	CMI patients (N = 49)	Non-CMI patients (N = 135)	p-value
Female gender	68.8%	81.6%	65.9%	p = 0.061
Age	67 (58–73)	70 (65–75)	64 (56–70)	p = 0.002
Follow-up (months)	4 (2–10)	10 (8–24)	3 (1–9)	p < 0.001
Risk factors				
Cardiovascular disease	43.8%	61.2%	37.8%	p = 0.008
Peripheral artery disease	19.8%	42.9%	12.6%	p < 0.001
Coronary artery disease	21.4%	26.5%	20.0%	p = 0.455
Cerebrovascular disease	13.0%	16.3%	11.1%	p = 0.488
Dyslipidaemia	13.5%	16.3%	12.6%	p = 0.682
Hypertension	32.3%	34.7%	32.6%	p = 0.928
Diabetes	13.5%	20.4%	11.9%	p = 0.217
Family history of CVD	38.1%	44.4%	36.8%	p = 0.472
Smoking	67.0%	83.7%	60.3%	p = 0.005
Pack years	27 (12–45)	33 (20–49)	21 (4–40)	p = 0.028
Presenting symptoms				
Weight loss	65.2%	93.8%	53.4%	p < 0.001
Weight (kg)	64 (56–79)	61 (52–70)	66 (57–81)	p = 0.147
Body mass index	23 (20–27)	21 (19–26)	23 (20–27)	p = 0.114
Abdominal pain	91.6%	95.9%	89.6%	p = 0.243
Duration abdominal pain (months)	9 (4–23)	5 (3–12)	12 (6–24)	p = 0.047
Postprandial abdominal pain	63.2%	83.0%	55.8%	p = 0.002
Exercise induced abdominal pain	37.4%	36.4%	38.3%	p = 1.000
Adapted eating pattern	55.6%	83.3%	46.4%	p < 0.001
Nausea	56.5%	63.4%	54.4%	p = 0.440
Diarrhoea	20.5%	39.6%	14.5%	p = 0.001
Mesenteric artery calcium score				
Low MACS (<29.7)	40.6%	12.2%	51.9%	p < 0.001
Intermediate MACS (29.7–422)	29.2%	30.6%	28.1%	
High MACS (>422)	30.2%	57.1%	20.0%	

Note: Numerical variables are shown as median (interquartile range); $p < 0.05$ is considered statistically significant.

Abbreviations: CMI, chronic mesenteric ischaemia; CVD, cardiovascular disease; kg, kilogram; MACS, mesenteric artery calcium score.

DISCUSSION

This study reports on a symptom and CT-based MACS score chart that shows promise for early risk stratification of patients with suspected CMI. The near-perfect NPV and sensitivity of the MACS score chart suggests that a score of ≤4 points virtually rules out CMI, while no patients are misclassified. Hence, a further diagnostic workup could be omitted safely in low-risk patients. The CTA-based score chart by van Dijk et al. shows excellent external

validity and is well suited for guiding subsequent (invasive) treatment decisions in those patients with suspected CMI based on the MACS score chart.

The advantage of the MACS is that it does not necessitate an additional dedicated CTA and can be derived from a non-contrast enhanced CT or a venous phase CTA which is usually already acquired in the diagnostic workup of these patients.[7] The combination of the predictors used in the MACS score chart enable application of the score chart early in the diagnostic trajectory. The combination of

TABLE 3 Location and nature of mesenteric artery stenosis

Stenosis characteristics	All patients (N = 192)	CMI patients (N = 49)	Non-CMI patients (N = 135)	% Ischaemia
No significant stenosis	56 (29.2%)	1	55	1.8%
CA	49 (25.5%)	6	39	13.3%
SMA	18 (9.4%)	3	14	17.6%
IMA	11 (5.7%)	0	10	0.0%
CA and SMA	18 (9.4%)	13	5	72.2%
CA and IMA	11 (5.7%)	2	8	20.0%
SMA and IMA	10 (5.2%)	8	2	80.0%
CA, SMA, and IMA	19 (9.9%)	16	2	88.9%
Nature of stenosis	**(N = 136)**	**(N = 48)**	**(N = 80)**	
Atherosclerosis	105 (77.2%)	46	53	46.5%
Compression	25 (18.4%)	2	22	8.3%
Iatrogenic	3 (2.2%)	0	3	0.0%
Atherosclerosis and compression	3 (2.2%)	0	2	0.0%

Note: Stenosis is defined as a luminal reduction of ≥50%.

Abbrebiations: CA, coeliac artery; CMI, chronic mesenteric ischaemia; IMA, inferior mesenteric artery; SMA, superior mesenteric artery.

TABLE 4 Multivariable logistic regression analysis of CMI predictors

Predictor	Odds ratio (95% CI)	p-value
Weight loss	9.03 (2.30–35.45)	$p = 0.002$
Postprandial abdominal pain	6.19 (2.07–18.53)	$p = 0.001$
Cardiovascular disease	2.12 (0.87–5.13)	$p = 0.096$
Intermediate MACS (29.7–422)	6.76 (2.17–21.04)	$p = 0.001$
High MACS (>422)	18.46 (5.53–61.68)	$p < 0.001$

Abbreviations: 95% CI, 95% confidence interval; MACS, mesenteric artery calcium score.

TABLE 5 Score chart of history and mesenteric artery calcium score

Predictor	Points
Weight loss	3
Postprandial abdominal pain	2
Cardiovascular disease	1
Calcium score	
Intermediate MACS (29.7–422)	3
High MACS (>422)	4
Risk group	**CMI risk (%)**
Low (0–4 points)	2.1%
Increased (5–10 points)	39.1%

Abbreviation: MACS, mesenteric artery calcium score.

symptoms and imaging are essential for the diagnosis of CMI.[2,3] The MACS score chart shows that symptoms and already available CT examinations can be used to make a first estimate of the risk of CMI, even without an accurate assessment of mesenteric artery patency. In patients with both postprandial abdominal pain and weight loss the clinical suspicion of CMI is high and a diagnostic workup for CMI is indicated.[2] This is supported by the MACS score chart, because even without additional points of the MACS the combination of postprandial abdominal pain and weight loss exceeds the ≥5 points threshold indicating the need for a dedicated diagnostic workup, including a dedicated CTA. However, the MACS serves as an additional red-flag that raises awareness for CMI and could be used by clinicians to facilitate the diagnosis of CMI and reduce diagnostic delays. Perhaps even more important is the observation that the absence of an increased MACS helps to determine whether a patient with a moderately compatible history is at risk of CMI or whether CMI can be ruled out. Hence, the MACS score chart has the ability to avoid an unneeded referral to a specialist CMI centre and to reduce the number of excessive contrast-enhanced CTA's which is especially valuable in older populations with a higher prevalence of impaired renal function.[16]

The MACS score chart consists of the predictors' weight loss, postprandial abdominal pain, history of CVD, and MACS. Weight loss and postprandial abdominal pain are typical presenting symptoms of CMI and CMI should always be considered in patients with one or both of these symptoms.[1,2] The current study confirmed the association between CMI and weight loss and CMI and postprandial abdominal pain. The systemic nature of atherosclerosis suggests that patients with a cardiovascular event in another vascular bed are also
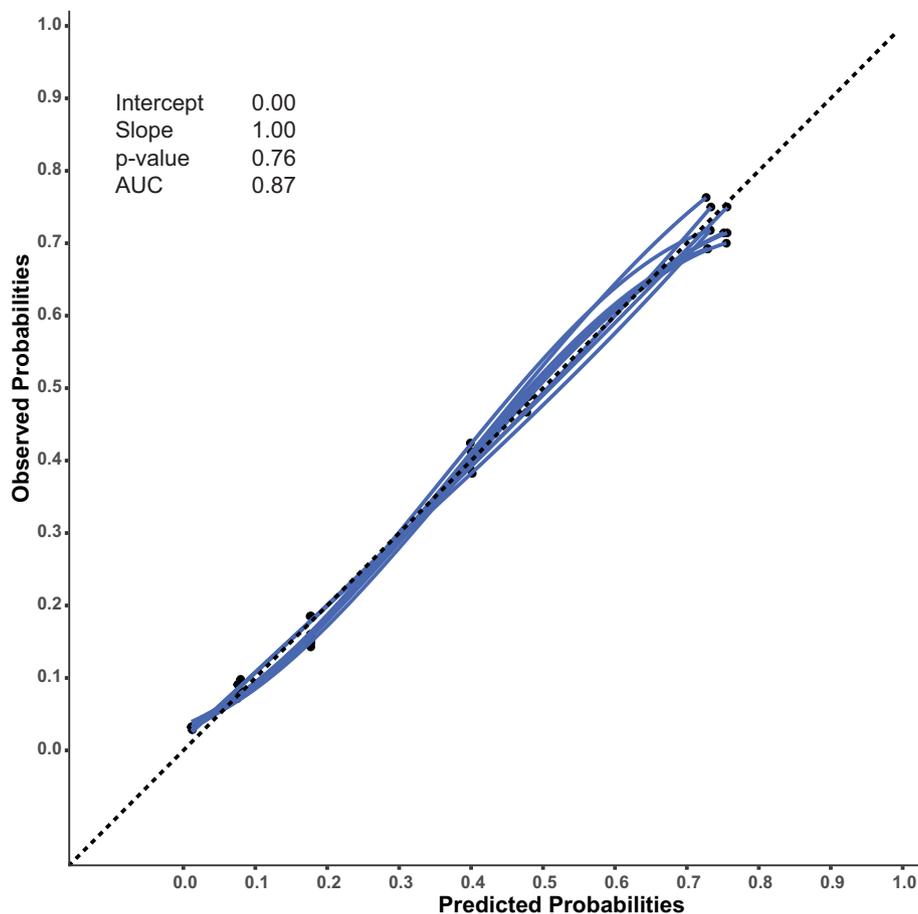
FIGURE 1 Calibration plot showing the performance of the MACS score chart in the 10 imputed datasets. AUC, area under the curve of the MACS score chart; Intercept, pooled calibration intercept; *p*-value, *p*-value of the Hosmer-Lemeshow test; slope, pooled calibration slope

TABLE 6 CMI risks and discriminative ability of the van Dijk score chart, in the current validation cohort and reported by van Dijk et al

Absolute risk	van Dijk et al.	Validation cohort
Low (0–5 points)	19.4%	0.0%
Intermediate (6–18 points)	44.6%	23.3%
High (19–28 points)	92.1%	81.8%
Discriminative ability		
AUC (95% CI)	0.80	0.89 (0.84–0.95)

Abbreviations: 95% CI, 95% confidence interval; AUC, area under the curve.

at risk of having an atherosclerotic mesenteric artery stenosis. This is supported by the high prevalence of CVD among CMI patients (49%–73%) and the substantial prevalence of a mesenteric artery stenosis among patients diagnosed with coronary artery disease (43%).[4,8,17,18] A history of CVD has been used in previous CMI score charts and is included in the MACS score chart as well, although a history of CVD was not significantly associated with CMI in the current multivariable logistic regression analysis.[8,19] A history of CVD is still a relevant predictor, since an atherosclerotic stenosis can be caused by a soft-plaque, which is not detected by the MACS. An intermediate and high MACS were both strongly associated with CMI, confirming the potential value of this tool.

Atherosclerosis is the most frequent cause of CMI. Patients with MALS—CA compression by the median arcuate ligament—and chronic NOMI—CMI in absence of a mesenteric artery stenosis—are likely to have a low MACS and will not obtain the 3 or 4 points that can be earned with an intermediate or high MACS. Still, a total of 5 points can be earned with the presenting symptoms weight loss and postprandial abdominal pain, which is enough to exceed the ≥5 points threshold for an additional diagnostic workup. The diagnostic accuracy of postprandial abdominal pain (49%) and weight loss (52%) is relatively low.[6] The probability of CMI increases when both postprandial abdominal pain and weight loss are present which is why the European guidelines recommends that postprandial abdominal pain and either weight loss or an adapted eating pattern should be present for a presumptive diagnosis of CMI in patients with a single-vessel stenosis and that a compatible history is important for a presumptive diagnosis of chronic NOMI.[2,6]

We have externally validated the score chart by van Dijk et al. and showed an excellent discriminative ability and an even more

favourable risk classification than originally reported by van Dijk et al.[8] CMI risks were 0% in the low-risk group, 23% in the intermediate-risk group, and 82% in the high-risk group; CMI risks were 19% (low), 45% (intermediate), and 92% (high) in the original cohort. The lower proportions of chronic NOMI (0.5%) and MALS (1.1%) compared to the cohort reported by van Dijk et al., chronic NOMI 1.6% and MALS 6.5%, could be one of the reasons for a more favourable risk classification. This might suggest that the score chart by van Dijk et al. performs better in cohorts of non-tertiary referral centres with low proportions of chronic NOMI and MALS. The MACS score chart selects patients with a low probability of CMI in whom a further diagnostic workup can be omitted. The score chart by van Dijk et al. can be used in patients with an increased probability of CMI and requires stenosis grading on CTA to be able to guide management, that is, wait-and-see, functional testing, or immediate treatment.[8]

The limitations of this study are mainly its retrospective design and the composition of the study population. First, included patients were referred because of suspected CMI based on typical symptoms and/or mesenteric artery stenosis, resulting in a population with a higher pre-test probability of CMI. However, the prevalence of CVD risk factors, typical symptoms, and mesenteric artery stenosis still differed significantly between CMI and non-CMI patients. Second, the number of included patients and number of CMI patients is relatively low, with few MALS and chronic NOMI patients which might influence reliability and generalizability of the MACS score chart in the latter two groups. This study should, therefore, be considered as a first step in the construction of a reliable score chart for the selection of patients in whom a diagnostic workup for CMI is indicated. As a next important step, the MACS score chart should be validated in a larger independent cohort.

The symptom and CT-based MACS score chart shows promise for early risk stratification of patients with suspected CMI. In particular, its near-perfect negative predictive value indicates that the MACS score chart is able to rule out CMI, providing a simple and readily available tool to omit a further diagnostic workup in selected patients. The MACS score chart is complementary to the CTA-based score chart by van Dijk et al., which showed excellent external validity and is well suited to guide subsequent (invasive) treatment decisions.

CONFLICT OF INTERESTS

Adriaan Moelker is proctor for Terumo, Cook, and Angiocare. Marco J. Bruno is consultant to Boston Scientific and Cook Medical and has received grants for investigator initiated and industry sponsored studies from Boston Scientific, Cook Medical, Pentax Medical, 3M, and Mylan. Luke G. Terlouw, Desirée van Noord, Louisa J. D. van Dijk, and Theo van Walsum declare no conflicting interests.

AUTHOR CONTRIBUTIONS

Luke G. Terlouw: collecting, interpreting and analysing data, drafting the manuscript. Desirée van Noord: planning and conducting the study, interpreting data and critical revision of the manuscript. Theo van Walsum: conducting the study and critical revision of the manuscript. Louisa J. D. van Dijk: collecting and interpreting data

and critical revision of the manuscript. Adriaan Moelker: planning and conducting the study, collecting and interpreting data and critical revision of the manuscript. Marco J. Bruno: planning and conducting the study, interpreting data and critical revision of the manuscript.

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REFERENCES

1. Alahdab F, Arwani R, Pasha AK, Razouki ZA, Prokop LJ, Huber TS, et al. A systematic review and meta-analysis of endovascular versus open surgical revascularization for chronic mesenteric ischemia. J Vasc Surg. 2018;67:1598–605.
2. Terlouw LG, Moelker A, Abrahamsen J, Acosta S, Bakker OJ, Baumgartner I, et al. European guidelines on chronic mesenteric ischaemia - joint United European Gastroenterology, European Association for Gastroenterology, Endoscopy and Nutrition, European Society of Gastrointestinal and Abdominal Radiology, Netherlands Association of Hepatogastroenterologists, Hellenic Society of Gastroenterology, Cardiovascular and Interventional Radiological Society of Europe, and Dutch Mesenteric Ischemia Study group clinical guidelines on the diagnosis and treatment of patients with chronic mesenteric ischaemia. United European Gastroenterol J. 2020;8:371–95.
3. van Dijk LJ, van Noord D, de Vries AC, Kolkman JJ, Geelkerken RH, Verhagen HJ, et al. Clinical management of chronic mesenteric ischemia. United European Gastroenterol J. 2019;7:179–88.
4. Terlouw LG, Verbeten M, van Noord D, Brusse-Keizer M, Beumer RR, Geelkerken RH, et al. The incidence of chronic mesenteric ischemia in the well-defined region of a Dutch Mesenteric Ischemia Expert Center. Clin Transl Gastroenterol. 2020;11:e00200.
5. Mensink PB, Moons LM, Kuipers EJ. Chronic gastrointestinal ischaemia: shifting paradigms. Gut. 2011;60:722–37.
6. ter Steege RW, Sloterdijk HS, Geelkerken RH, Huisman AB, van der Palen J, Kolkman JJ. Splanchnic artery stenosis and abdominal complaints: clinical history is of limited value in detection of gastrointestinal ischemia. World J Surg. 2012;36:793-9.
7. Terlouw LG, van Noord D, van Walsum T, Bruno MJ, Moelker A. Mesenteric artery calcium scoring: a potential screening method for chronic mesenteric ischemia. Eur Radiol. 2020;31(6):4212–20.
8. van Dijk LJ, van Noord D, Geelkerken RH, Harki J, Berendsen SA, Vries AC, et al. Validation of a score chart to predict the risk of chronic mesenteric ischemia and development of an updated score chart. United European Gastroenterol J. 2019;7:1261–70.
9. Collins GS, Reitsma JB, Altman DG, Moons KG. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. BMJ. 2015;350:g7594.
10. Van Noord D, Sana A, Benaron DA, Pattynama PMT, Verhagen HJM, Hansen BE, et al. Endoscopic visible light spectroscopy: a new, minimally invasive technique to diagnose chronic GI ischemia. Gastrointest Endosc. 2011;73:291–8.
11. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M, Jr., Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol. 1990;15: 827–32.

12. Robin X, Turck N, Hainard A, Tiberti N, Lisacek F, Sanchez J-C, et al. pROC: an open-source package for R and S+ to analyze and compare ROC curves. BMC Bioinf. 2011;12:77.

13. van Buuren S, Groothuis-Oudshoorn K. Mice: multivariate imputation by chained equations in R. J Stat Software. 2011;45(3):1–67.

14. Barnard J, Rubin DB. Miscellanea. Small-sample degrees of freedom with multiple imputation. Biometrika. 1999;86:948–55.

15. Heymans M. psfmi: Prediction model selection and performance evaluation in multiple imputed datasets. R package version 0.2.0. 2020.

16. Denic A, Glassock RJ, Rule AD. Structural and functional changes with the aging kidney. Adv Chron Kidney Dis. 2016;23:19–28.

17. Veenstra RP, Ter Steege RWF, Geelkerken RH, Huisman AB, Kolkman JJ. The cardiovascular risk profile of atherosclerotic gastrointestinal ischemia is different from other vascular beds. Am J Med. 2012;125:394–8.

18. Krishnamurthy G, Menon A, Kannan K, Prakash S, Rajendran A, Philips D. Coronary artery disease and mesenteric artery stenosis - two sides of the same coin? - long term prospective analysis. Intractable Rare Dis Res. 2019;8:245–51.

19. Harki J, Vergouwe Y, Spoor JA, Mensink PB, Bruno MJ, van Noord D, et al. Diagnostic accuracy of the combination of clinical symptoms and CT or MR angiography in patients with chronic gastrointestinal ischemia. J Clin Gastroenterol. 2017;51: e39–e47.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.