Predicting the presence of macrovascular causes in non-traumatic intracerebral haemorrhage: the DIAGRAM prediction score

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ONLINE SUPPLEMENT

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Content

Supplementary Methods. Assessment of small vessel disease on admission non-contrast CT

All non-contrast CTs (NCCT) were rated independently by two experienced neuroradiologist for presence of small vessel disease (SVD). Disagreements were resolved by a third observer. Characteristics of interest were:

- Presence of white matter lesions (WML), and if so: WML location (periventricular, subcortical or both) and severity (<1 cm, >1 cm, or confluent);
- Presence of a hypodensity elsewhere on NCCT, and if so: location.

Signs of small vessel disease on NCCT was defined as presence of white matter lesions, or an ischemic lesion in basal ganglia, thalamus or posterior fossa.

Table I: Causes of intracerebral haemorrhages in the development cohort[e1]

Causes	No (%) of patients (n=298)
Macrovascular:	
Arteriovenous malformation	34 (11)
Dural arteriovenous malformation	13 (4)
Cavernoma	10 (3)
Cerebral venous sinus thrombosis	4 (1)
Aneurysm	7 (2)
Developmental venous anomaly*	1 (0.3)
Subtotal	69 (23)
Other:	
Probable cerebral amyloid angiopathy	18 (6)
Hypertensive vasculopathy†	36 (12)
Neoplasm	3 (1)
Cocaine use	1 (0.3)
Haemorrhagic infarction	2 (0.7)
Unknown‡	169 (57)
Subtotal	229 (77)

*Partially thrombosed large developmental venous anomaly without evidence of adjacent cavernoma.
†Intracerebral haemorrhage in basal ganglia, thalamus, or posterior fossa in presence of hypertension.
‡In 30 of these patients, lobar haemorrhage in the presence of hypertension was observed.

Table II: Regression equations of multivariable models

Regression equation model based on patient characteristics and NCCT
-2.1828-0.0408*AGE+2.1224*no SVD+1.6923*Lobar+2.5472*Posterior fossa
Regression equation model based on patient characteristics, NCCT and CTA
-3.4045-0.0281*AGE+2.1585*no SVD+1.2038*Lobar+2.0049*Posterior fossa+2.4201*CTA

No SVD no signs of small vessel disease, CTA positive or inconclusive CTA

Table III: Calculation of the DIAGRAM and DIAGRAM+ prediction scores

	DIAGRAM score	DIAGRAM + score
	Points	**Points**
Age ≤50	1	1
Absence of small vessel disease	2	2
ICH location		
Deep	0	0
Lobar	2	1
Posterior fossa	3	2
Positive CTA	-	3

NCCT non contrast CT, ICH intracerebral haemorrhage

An individual DIAGRAM or DIAGRAM+ score is the sum of the points assigned to each of the predictors. The maximum score is 6 for the model based on patient characteristics and NCCT (DIAGRAM score), and 8 for the model based on additional CTA (DIAGRAM + score).

Table IV: Overview of prediction models for macrovascular causes and external validation studies

Model development

Model	Prospective/ retrospective	Patient selection	N	Mean age	MVC (%)	Reference standard	C-statistic
SICH score[e2]	R	Patients who underwent CTA within 24h	623	65	15	CTA	0.86 (0.83-0.89)
Simple ICH score[e3]	R	Patients who underwent DSA	160	41	51	DSA	0.65 (0.56-0.73)
DIAGRAM score	P	Patients < 70 y, excl of patients >45 y with HT and deep ICH or post fossa ICH	298	53	23	1y FU	0.83 (0.78-0.88)* 0.91 (0.88-0.94)‡

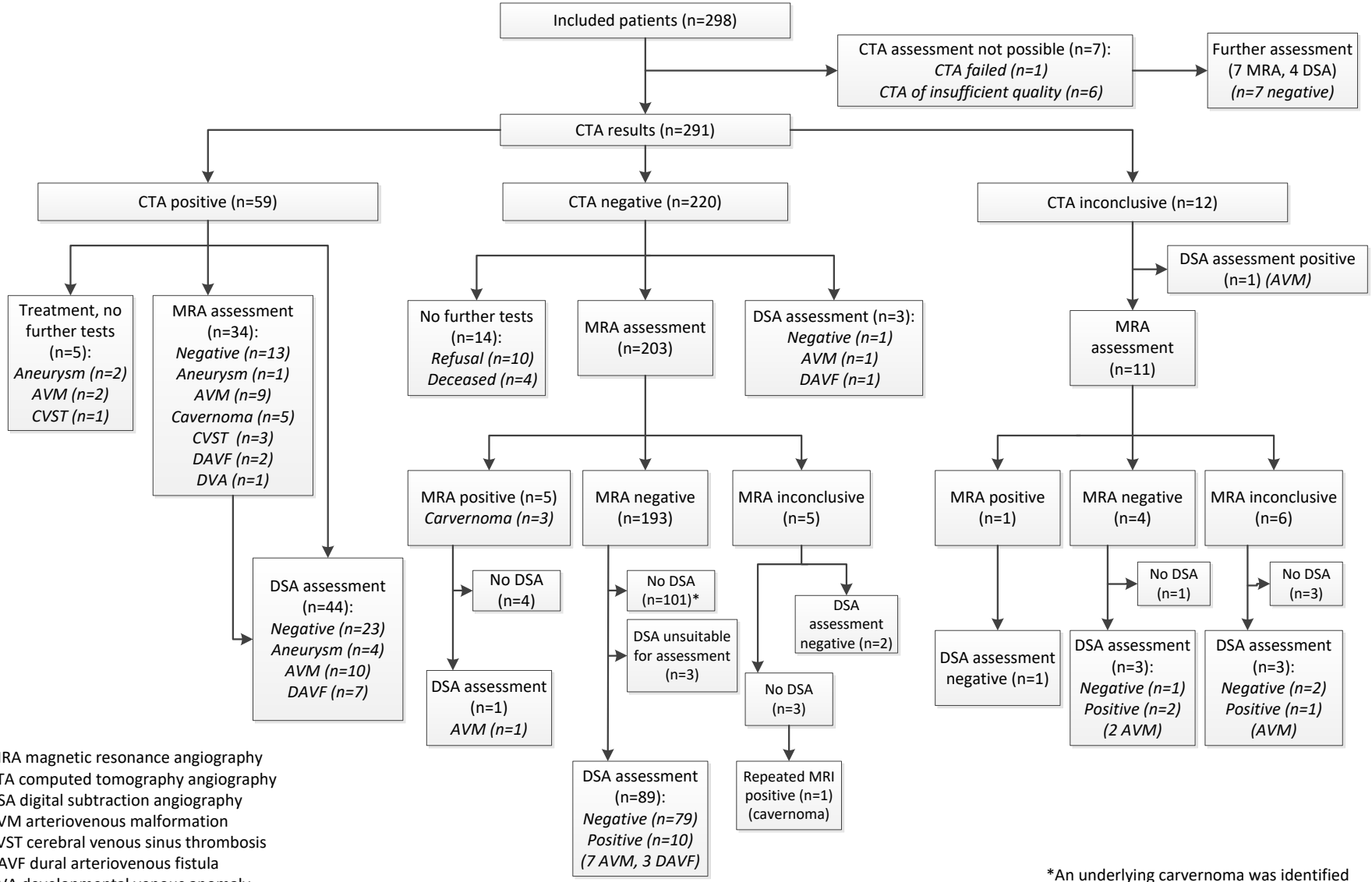
R retrospective, P prospective, y year, FU follow-up, MVC macrovascular cause, HT hypertension * model based on patient characteristics and non contrast CT, ‡ model based on patient characteristics, non contrast CT and CTA.

Model validation

Model	Prospective/ retrospective	Patient selection	N	Mean age	MVC (%)	Reference standard	C-statistic
SICH score[e2]	P (temporal)	Patients who underwent CTA	222	67	13	CTA	0.87 (0.82-0.91)
SICH score[e4]	R (external)	Patients who underwent DSA or neurosurgical evacuation	341	57	18	DSA or neurosurgical inspection	0.82 (0.78-0.86)
SICH score[e5]	R (external)	Patients who underwent CTA, MRA, DSA or pathological examination	204	?	24	CTA, MRA, DSA, neurosurgical or pathological inspection	0.73 (0.65-0.80)
Simple ICH score[e3]	P	Patients who underwent CTA, MRA or DSA.	106	57	32	CTA, MRA or DSA	0.67 (0.55-0.79)
DIAGRAM score	R	Patients who underwent CTA and DSA	173	49	45	DSA	0.66 (0.58-0.74)* 0.88 (0.83-0.94)‡

R retrospective, P prospective, MVC macrovascular cause, * model based on patient characteristics and non contrast CT, ‡ model based on patient characteristics, non contrast CT and CTA, [2,3,4,5] references, please see page 14 of supplementary file.

Figure I: Flowchart of angiographic examinations in DIAGRAM[e1]



MRA magnetic resonance angiography
CTA computed tomography angiography
DSA digital subtraction angiography
AVM arteriovenous malformation
CVST cerebral venous sinus thrombosis
DAVF dural arteriovenous fistula
DVA developmental venous anomaly
MRI magnetic resonance imaging

*An underlying carvernoma was identified by repeated MRI 10 months after the ictus

Figure II: CT scan of a patient with (A) and without (B) white matter hypodensities indicative of small vessel disease

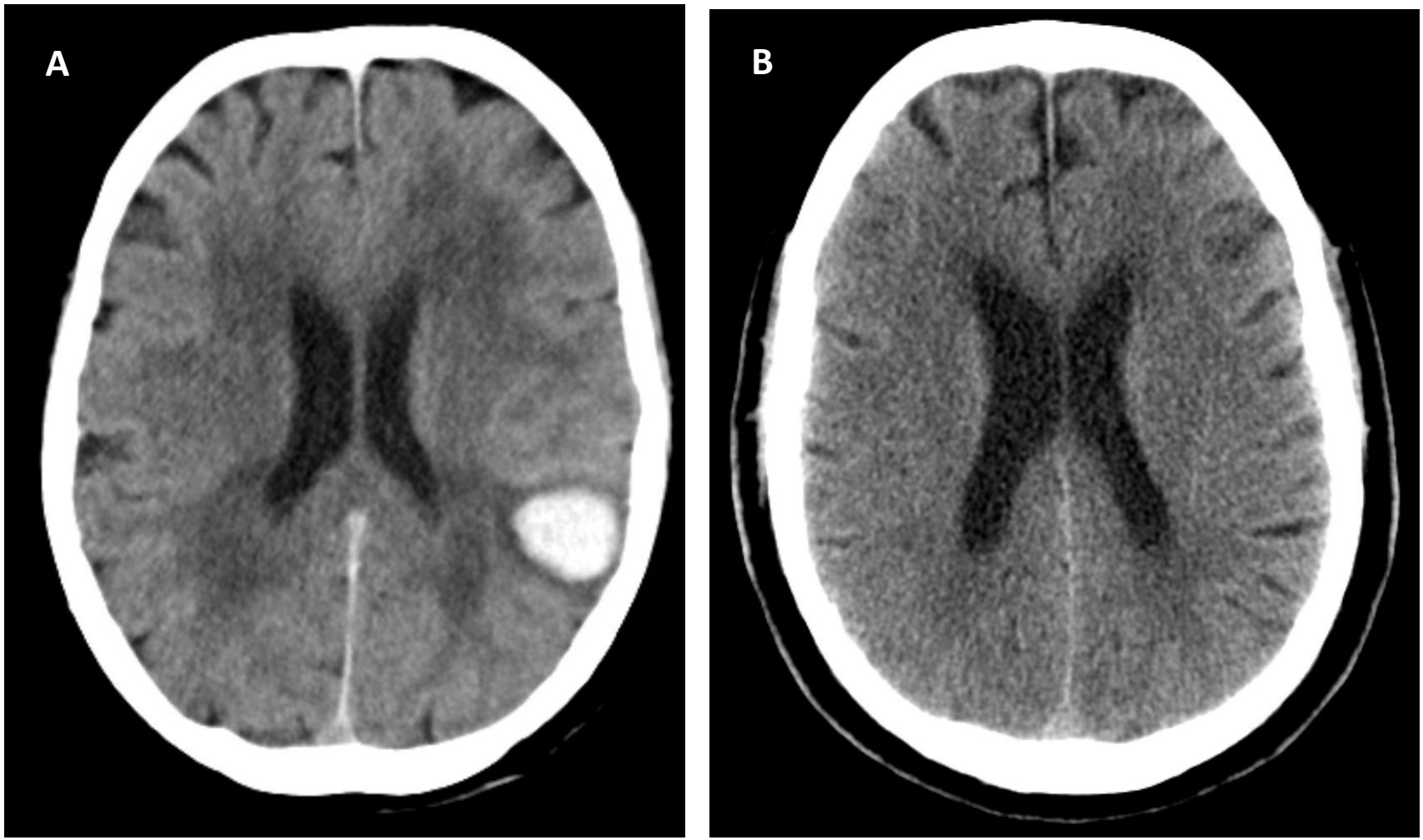
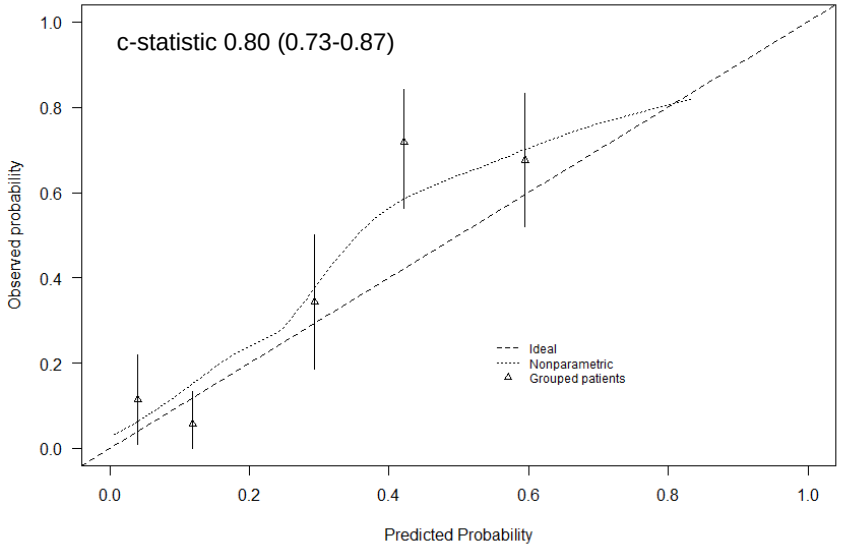


Figure III: Calibration plots and c-statistics of DIAGRAM models excluding DIAGRAM patients who did not undergo DSA according to the study protocol. Model based on patient characteristics and NCCT (A), model based on patient characteristics, NCCT and CTA (B)

A.



B.

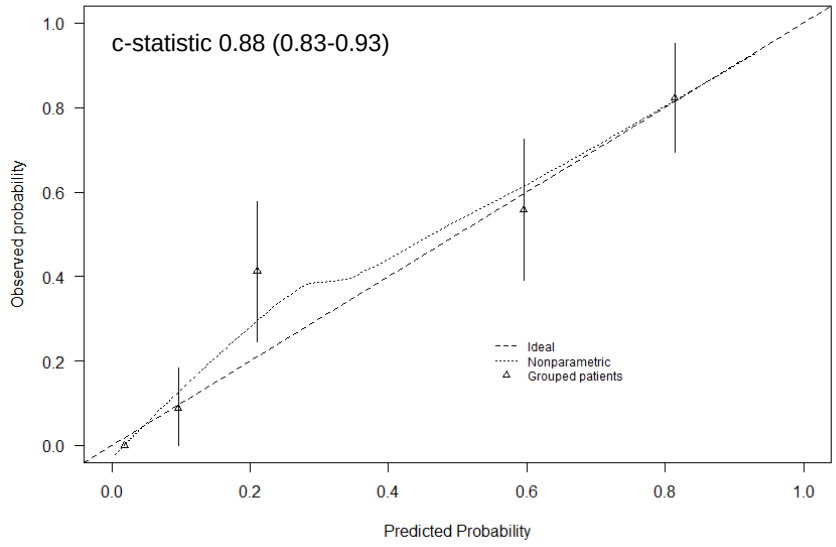
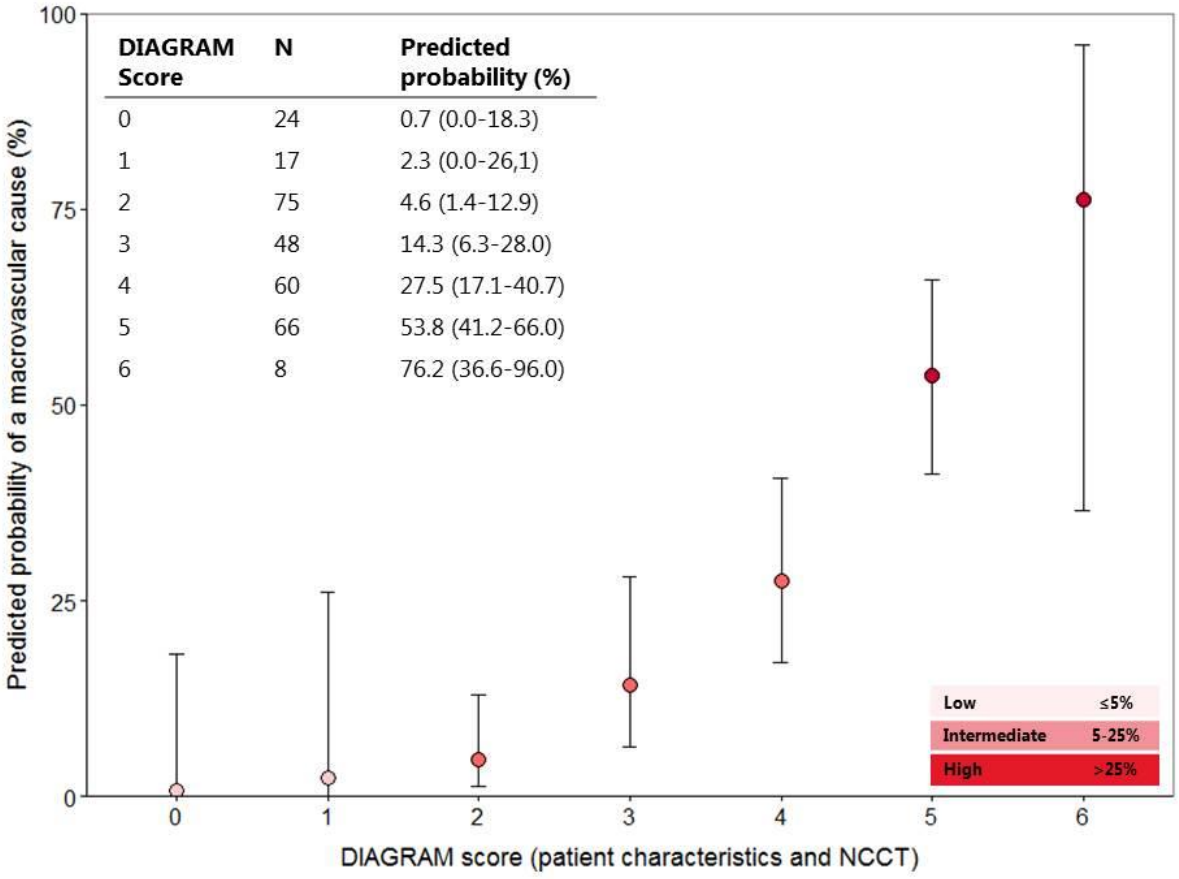


Figure IV: Predicted one year probability of an underlying macrovascular cause based on the DIAGRAM prediction scores. Model based on patient characteristics and NCCT (A), model based on patient characteristics, NCCT and CTA (B)

A.



B.

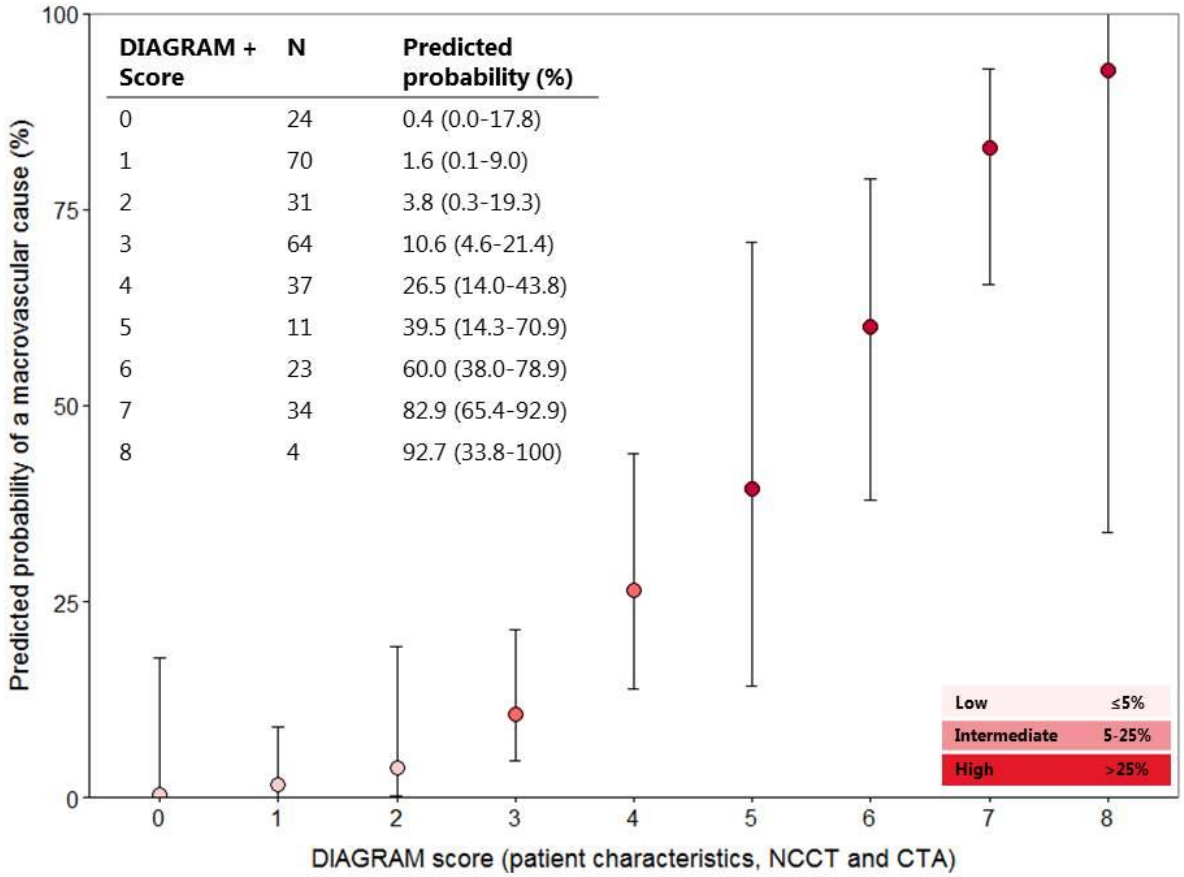
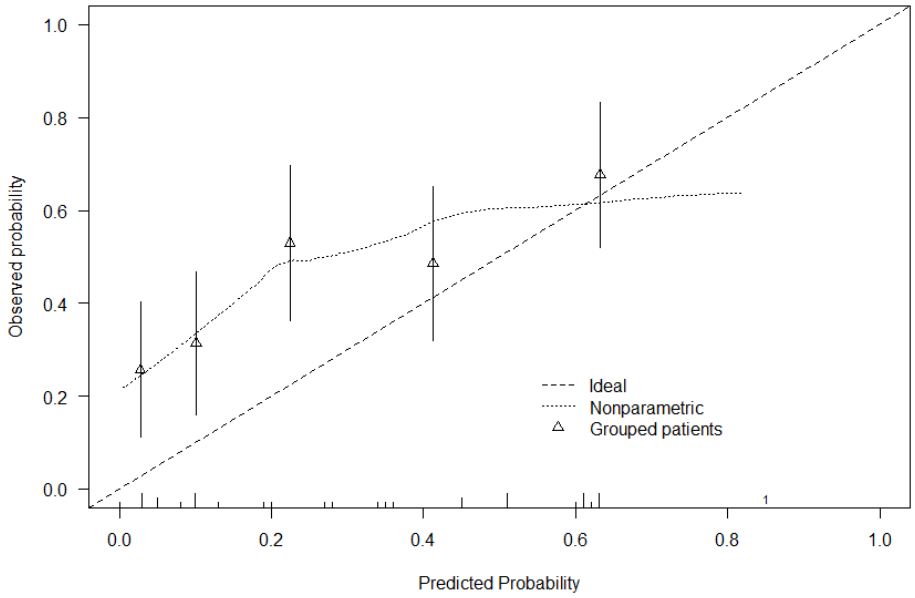


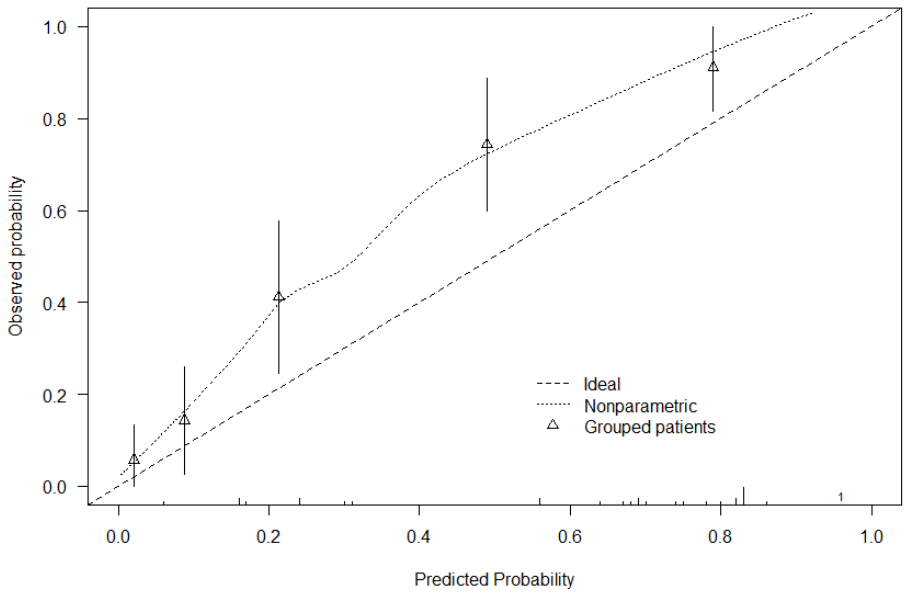
DIAGRAM + Score | N | Predicted probability (%)
0 | 24 | 0.4 (0.0-17.8)
1 | 70 | 1.6 (0.1-9.0)
2 | 31 | 3.8 (0.3-19.3)
3 | 64 | 10.6 (4.6-21.4)
4 | 37 | 26.5 (14.0-43.8)
5 | 11 | 39.5 (14.3-70.9)
6 | 23 | 60.0 (38.0-78.9)
7 | 34 | 82.9 (65.4-92.9)
8 | 4 | 92.7 (33.8-100)
Predicted probability of a macrovascular cause (%)
100
75
50
25
0
0
1
2
3
4
5
6
7
8
DIAGRAM score (patient characteristics, NCCT and CTA)
Low ≤5%
Intermediate 5-25%
High >25%

Figure V: Calibration plots of DIAGRAM models in validation cohort before recalibration. Model based on patient characteristics and NCCT (A), model based on patient characteristics, NCCT and CTA (B)

A.



B.



References

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