



Universiteit
Leiden
The Netherlands

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

Hilkens, N.A.; Asch, C.J.J. van; Werring, D.J.; Wilson, D.; Rinkel, G.J.E.; Algra, A.; ... ;
DIAGRAM Study Grp

Citation

Hilkens, N. A., Asch, C. J. J. van, Werring, D. J., Wilson, D., Rinkel, G. J. E., Algra, A., ... Klijn, C. J. M. (2018). Predicting the presence of macrovascular causes in non-traumatic intracerebral haemorrhage: the DIAGRAM prediction score. *Journal Of Neurology, Neurosurgery And Psychiatry*, 89(7), 674-679. doi:10.1136/jnnp-2017-317262

Version: Accepted Manuscript

License: [Leiden University Non-exclusive license](#)

Downloaded from: <https://hdl.handle.net/1887/87297>

Note: To cite this publication please use the final published version (if applicable).

ONLINE SUPPLEMENT

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

Nina A. Hilkens,* Charlotte J.J. van Asch,* David J. Werring,* Duncan Wilson, Gabriel J.E. Rinkel, Ale Algra, Birgitta K. Velthuis, Gérard A.P. de Kort, Theo D. Witkamp, Koen M. van Nieuwenhuizen, Frank-Erik de Leeuw, Wouter J Schonewille, Paul L. M. de Kort, Diederik W. Dippel, Theodora W. M. Raaymakers, Jeannette Hofmeijer, Marieke J. H. Wermer, Henk Kerkhoff, Korné Jellema, Irene M Bronner, Michel JM Remmers, Henri Paul Bienfait, Ron J.G.M. Witjes, H. Rolf Jäger, Jacoba P. Greving, Catharina J.M. Klijn; the DIAGRAM study group

* Authors contributed equally

Content

Supplemental Methods: Assessment of small vessel disease on admission non-contrast CT

Table I: Causes of intracerebral haemorrhages in the development cohort

Table II: Regression equations of multivariable models

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

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

Figure I: Flowchart of angiographic examinations in the DIAGRAM study

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.

Figure IV: Predicted one year probability of an underlying macrovascular cause based on the DIAGRAM prediction scores.

Figure V: Calibration plots of DIAGRAM models in validation cohort before recalibration

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

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)‡

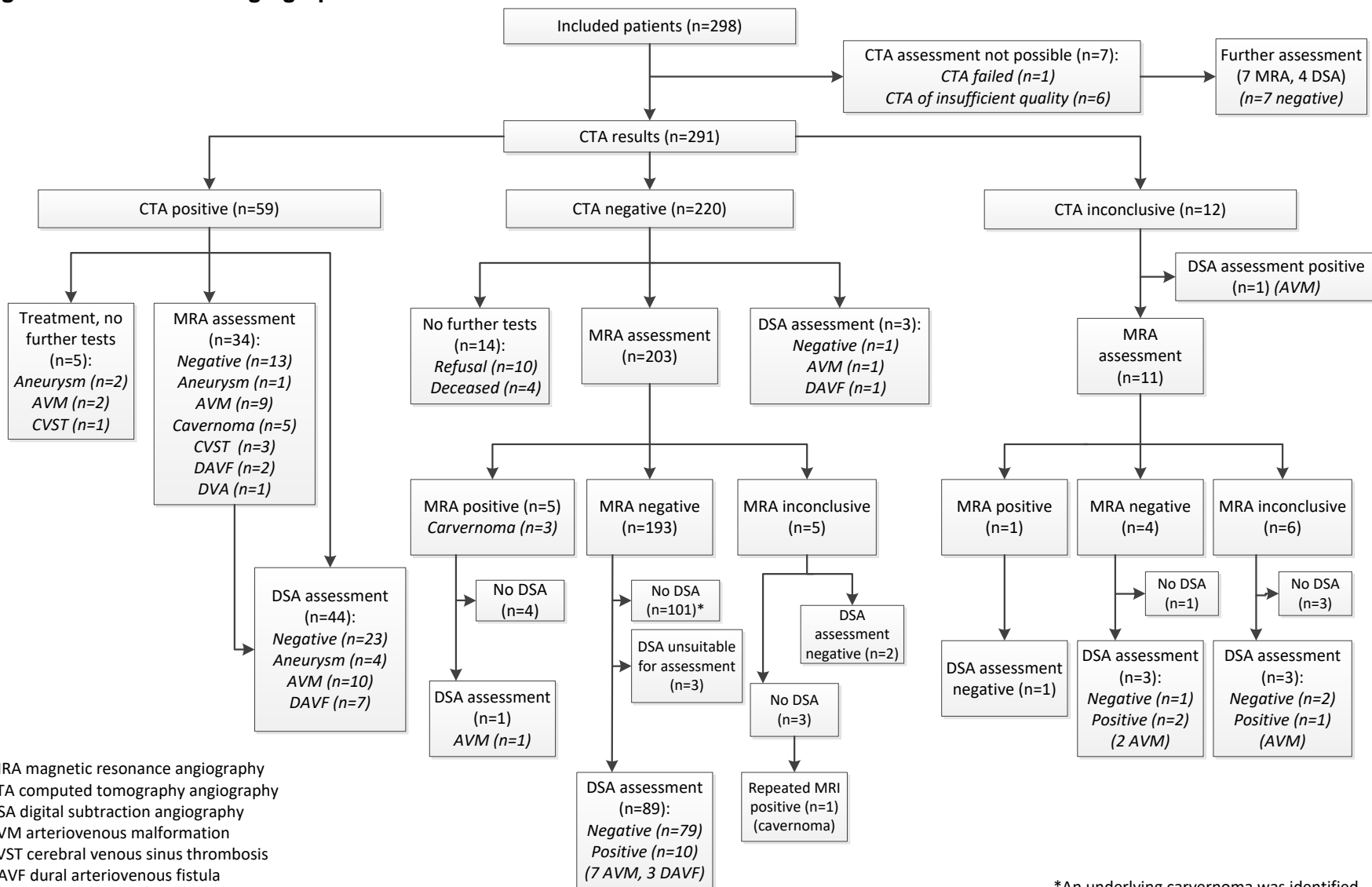
R retrospective, P prospective, y year, FU follow-up, MVC macrovascular cause, HT hypertension * model based on patient characteristics and non contrast CT, ‡ model based on patient characteristics, non contrast CT and CTA.

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 cavernoma 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

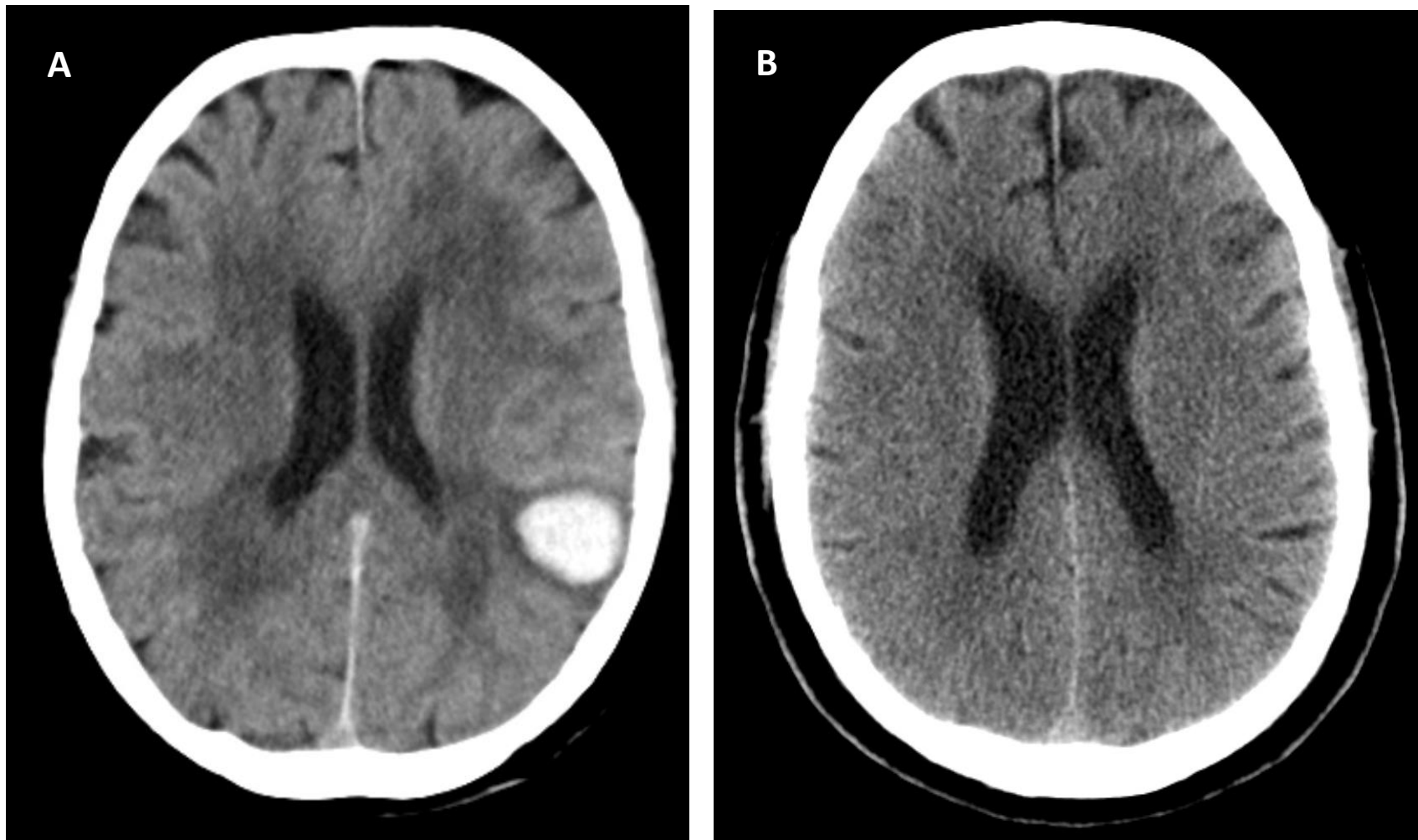
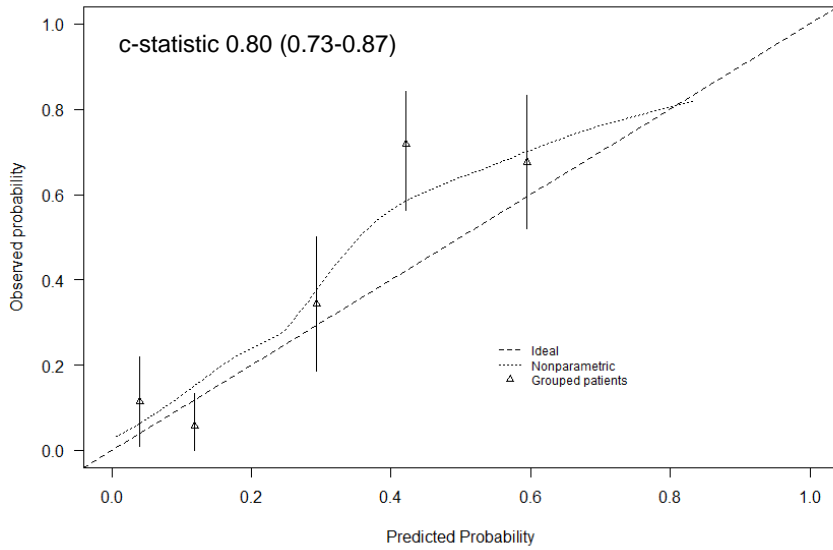


Figure III: Calibration plots and c-statistics of DIAGRAM models excluding DIAGRAM patients who did not undergo DSA according to the study protocol. Model based on patient characteristics and NCCT (A), model based on patient characteristics, NCCT and CTA (B)

A.



B.

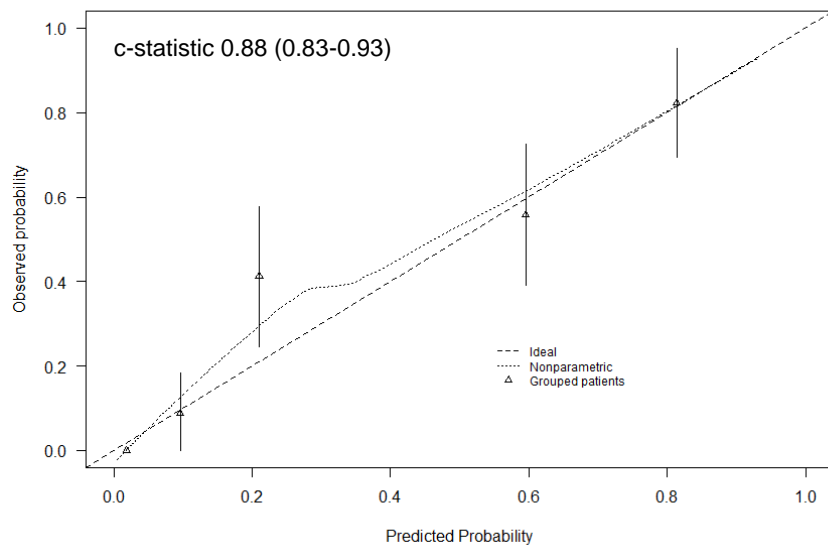
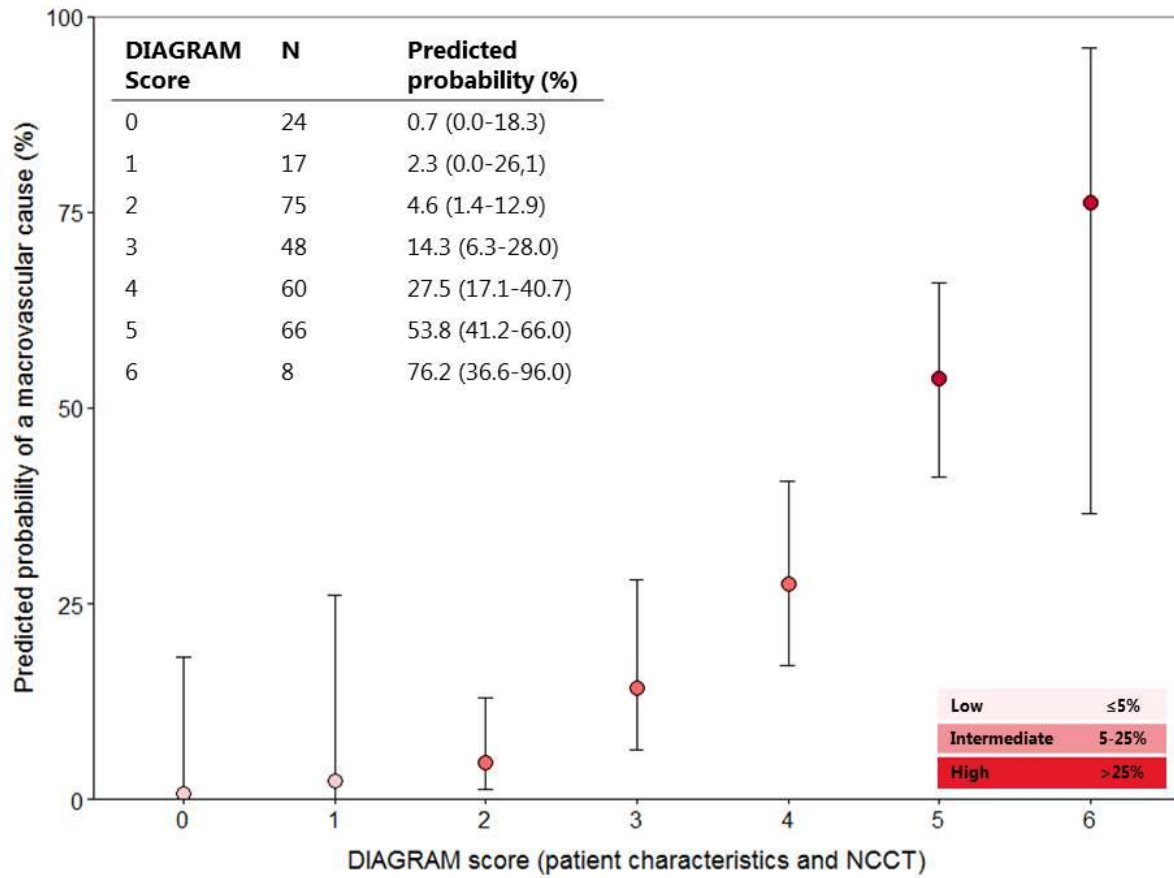


Figure IV: Predicted one year probability of an underlying macrovascular cause based on the DIAGRAM prediction scores. Model based on patient characteristics and NCCT (A), model based on patient characteristics, NCCT and CTA (B)

A.



B.

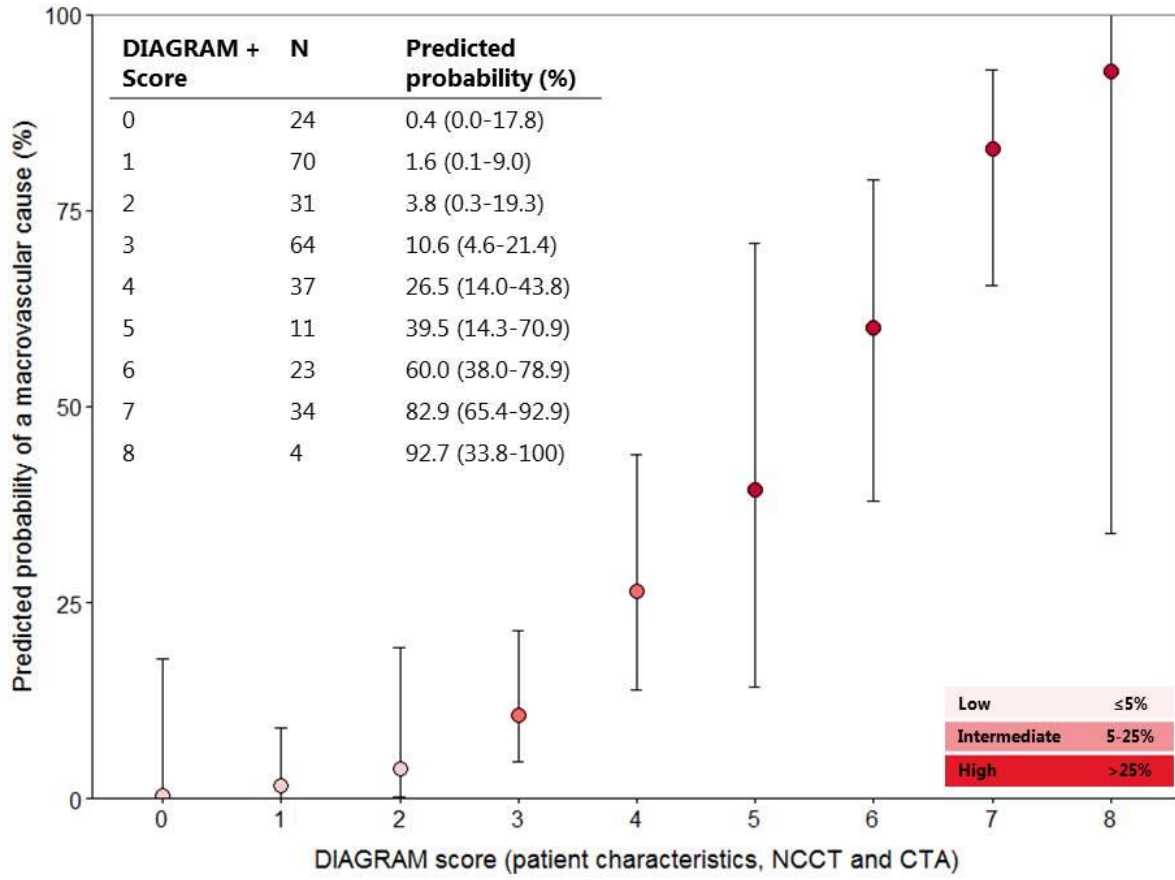
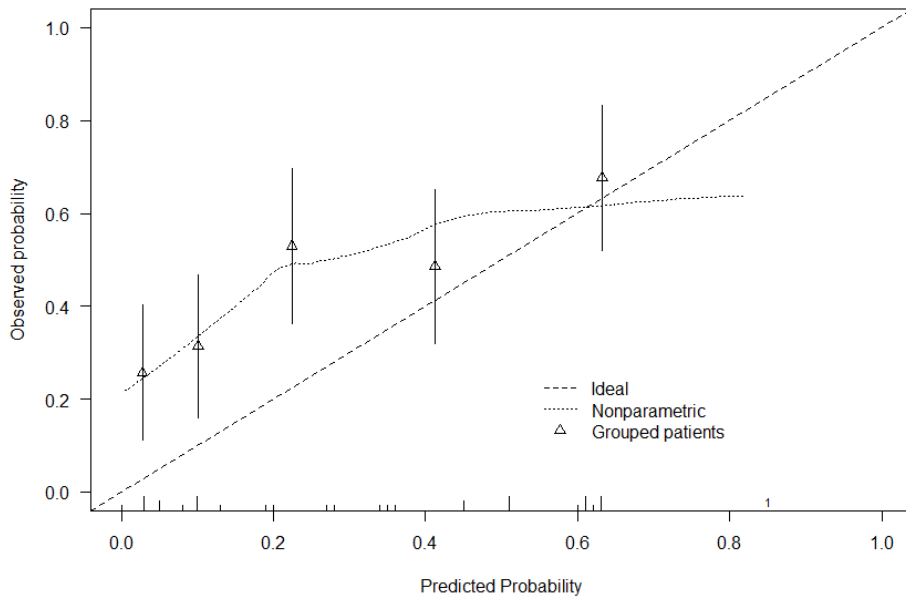
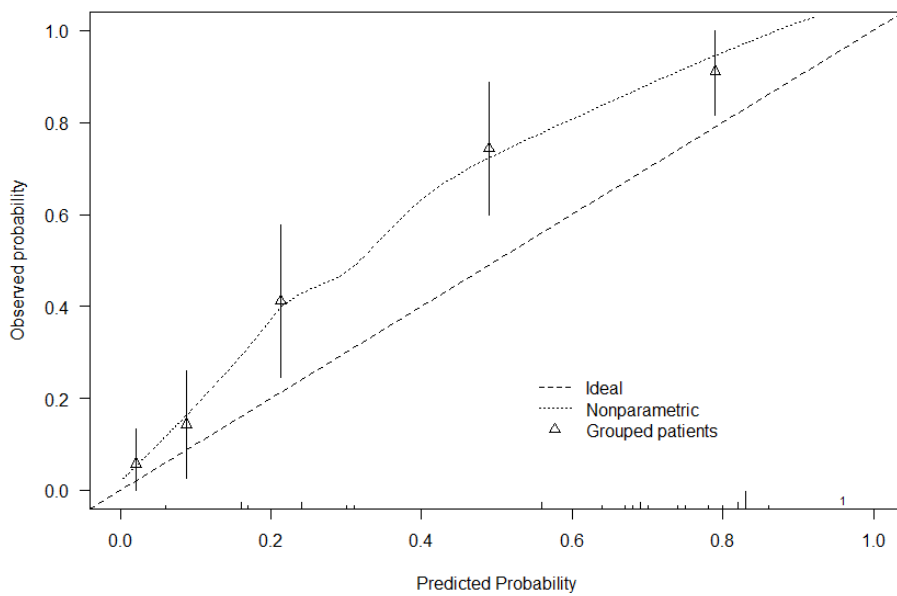


Figure V: Calibration plots of DIAGRAM models in validation cohort before recalibration. Model based on patient characteristics and NCCT (A), model based on patient characteristics, NCCT and CTA (B)

A.



B.



References

1. van Asch CJ, Velthuis BK, Rinkel GJ, et al. Diagnostic yield and accuracy of CT angiography, MR angiography and digital subtraction angiography for detection of macrovascular causes of intracerebral haemorrhage: prospective, multicentre cohort study. *BMJ*2015;351:h5762
2. Delgado Almandoz JE, Schaefer PW, Goldstein JN, et al. Practical scoring system for the identification of patients with intracerebral hemorrhage at highest risk of harboring an underlying vascular etiology: The secondary intracerebral hemorrhage score. *AJNR Am J Neuroradiol*2010;31:1653-60.
3. Olavarria VV, Bustamante G, Lopez MJ, et al. Diagnostic accuracy of a simple clinical score to screen for vascular abnormalities in patients with intracerebral hemorrhage. *J Stroke Cerebrovasc Dis*2014;23:2069-74.
4. Delgado Almandoz JE, Jagadeesan BD, Moran CJ, et al. Independent validation of the secondary intracerebral hemorrhage score with catheter angiography and findings of emergent hematoma evacuation. *Neurosurgery*2012;70:131-40.
5. van Asch CJ, Velthuis BK, Greving JP, et al. External validation of the secondary intracerebral hemorrhage score in the Netherlands. *Stroke*2013;44:2904-06.