CoaguChek en NOACs

Terug naar het lab?

Joost van Pelt, VHL minisymposium NOACs 18 juni 2013

(enquête)

- trombolyse?
- CoaguChek?

(enquête)

intraveneus

=

systemisch

intra arterieel

=

locaal

(trombectomie)

INR < 1,7

- rtPA verhoogt kans op bloeding
- coumarines verhogen kans op bloeding
- uitsluiten coumarines

- time is brain
- snel uitsluiten -> CoaguChek

INR < 1,7

- rtPA verhoogt kans op bloeding
- NOACs verhogen kans op bloeding
- uitsluiten NOACs

- snel uitsluiten -> ?
- time is brain

CBO 2008 INR 1,7

De contra-indicaties en exclusie criteria zoals die gehanteerd zijn in de NINDS trial zijn in de praktijk veel gebruikt (tabel 1). De ervaring heeft geleerd dat er na vele jaren toepassen van IVT in de praktijk, een verschuiving en specificering van criteria blijkt op te treden. Deze veranderende criteria zijn niet formeel getoetst in gecontroleerd onderzoek. Dirks et al (2007) trachtten door middel van een formele Delphi procedure met 30 internationaal erkende deskundigen op het gebied van toepassen van intraveneuze trombolyse consensus te krijgen over de klinische contra-indicaties. De deskundigen werden geselecteerd aan de hand van publicaties waarbij ze of eerste, of laatste auteur waren. De publicaties betroffen intraveneuze trombolyse bij een acute beroerte in een internationaal 'peer reviewed' tijdschrift. Aan de deskundigen werd gevraagd de meeste extreme waarde van een criterium te kiezen die de effectiviteit en veiligheid van IVT niet benadeelt. De criteria werden gekozen aan de hand van geherformuleerde NINDS in- en exclusie criteria. Per criterium werd een klinisch relevant geachte reeks van waarden gekozen en een klinisch relevante eenheid. Er was sprake van consensus als het interdeciele interval viel binnen twee klinisch relevante eenheden. In drie ronden bleek het mogelijk te zijn tot een consensus te komen over 12 contra-indicaties (tabel 2).

Waar baseren experts zich op?

Search PubMed 32 hits

- Thrombolysis
- Hemorrhage
- Coumarines

Waar baseren experts zich op?

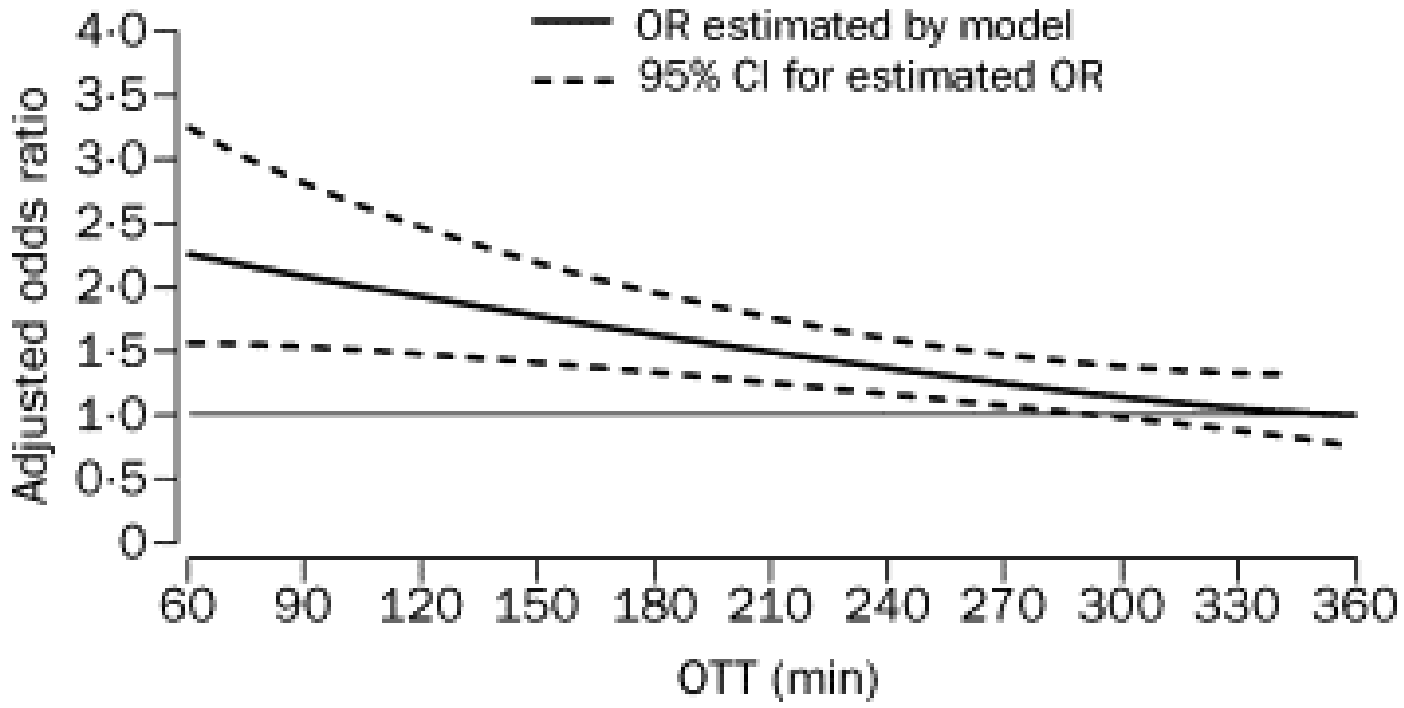
- Common sense
- Exclusie criteria trials

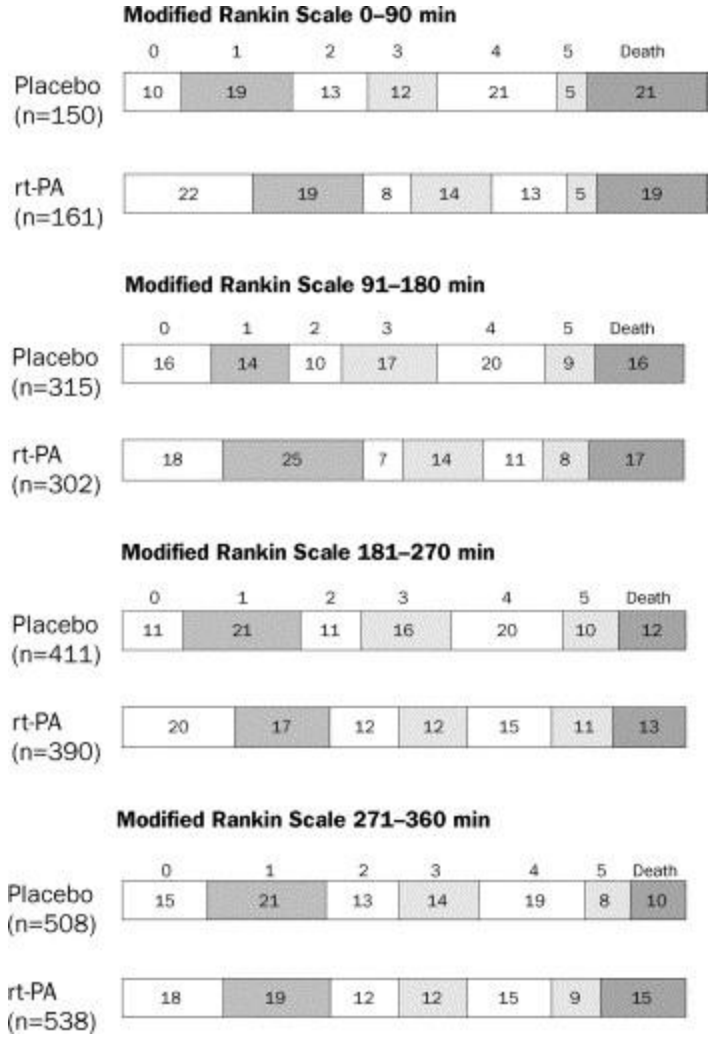
Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials

*The ATLANTIS, ECASS, and NINDS rt-PA Study Group Investigators**

THE LANCET • Vol 363 • March 6, 2004 • www.thelancet.com

trombolyse verbetert outcome tijd afhankelijk




Modified Rankin Scale 0–90 min
0 1 2 3 4 5 Death
Placebo (n=150)
10 19 13 12 21 5 21
rt-PA (n=161)
22 19 8 14 13 5 19
Modified Rankin Scale 91–180 min
0 1 2 3 4 5 Death
Placebo (n=315)
16 14 10 17 20 9 16
rt-PA (n=302)
18 25 7 14 11 8 17
Modified Rankin Scale 181–270 min
0 1 2 3 4 5 Death
Placebo (n=411)
11 21 11 16 20 10 12
rt-PA (n=390)
20 17 12 12 15 11 13
Modified Rankin Scale 271–360 min
0 1 2 3 4 5 Death
Placebo (n=508)
15 21 13 14 19 8 10
rt-PA (n=538)
18 19 12 12 15 9 15

verhoogd bloedingsrisico

	Placebo		rt-PA	
	n*	Patients with parenchymal haematoma (90%, 95% CI)	n	Patients with parenchymal haematoma (90%, 95% CI)
OTT (min)				
0–90	150	0 (0, ··)	161	5 (3·1, 1·6–5·6)
91–180	315	3 (1·0, 0·4–2·0)	302	17 (5·6, 3·9–7·9)
181–270	411	7 (1·7, 1·0–2·9)	390	23 (5·9, 4·3–8·0)
271–360	508	5 (1·0, 0·5–1·8)	538	37 (6·9, 5·3–8·7)

Parenchymal haematoma is defined as a dense blood clot exceeding 30% of the infarct volume with significant space-occupying effect. *One, eight, nine, and six patients from NINDS part I, ECASS I, ECASS II, and ATLANTIS B, respectively, were excluded from this analysis because they were randomised after 360 min or OTT was not reported.

Table 2: **Frequency of parenchymal haematoma between 0 and 360 min after treatment**

Ruecker et al, neurology, 2012

- Meta analyse
- 4856 patienten
- 284 warfarin
- INR 1,0 – 1,7

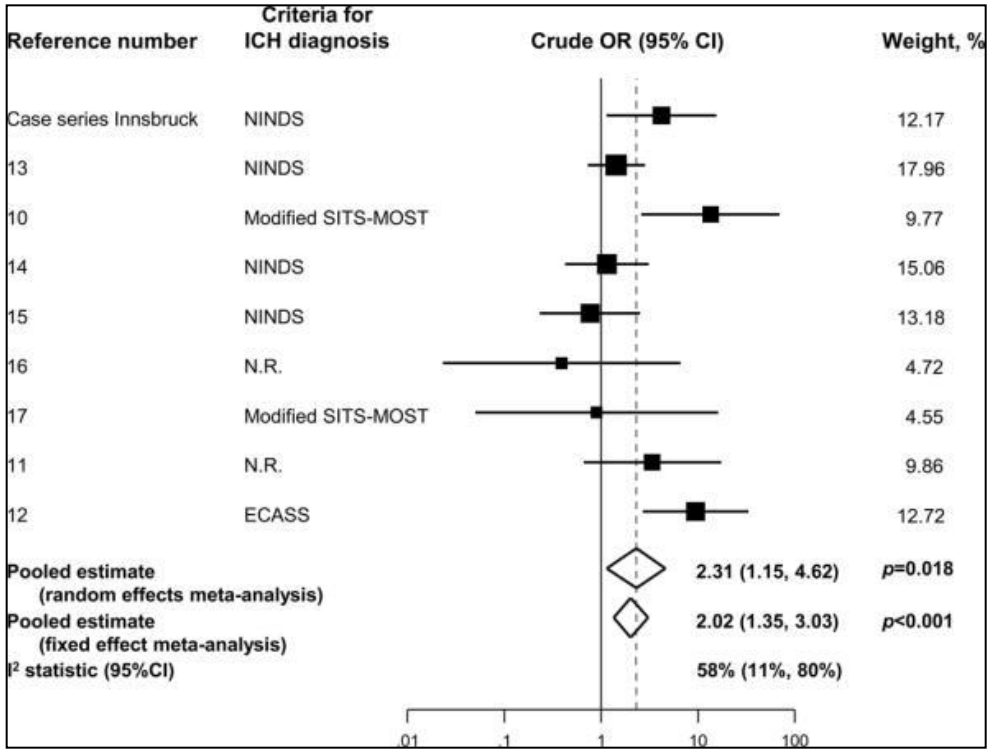
C/ warfarine verhoogt bloedingsrisico bij trombolyse

Random effects and fixed-effect meta-analyses of the association between subtherapeutic warfarin pretreatment (international normalized ratio

Ruecker et al. neurology 2012

Subtherapeutic warfarin therapy entails an increased bleeding risk after stroke thrombolysis.
Ruecker, Michael; Matosevic, Benjamin; Willeit, Peter; Kirchmayr, Matthias; Zangerle, Alexandra; Knoflach, Michael; Willeit, Johann; Kiechl, Stefan

Neurology. 79(1):31-38, July 3, 2012.
DOI: 10.1212/WNL.0b013e31825dcdf0



Random effects and fixed-effect meta-analyses of the association between subtherapeutic warfarin pretreatment (international normalized ratio =4 points on the NIHSS score) (n = 212), in 2 studies according to a modification of Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) criteria (parenchymal bleedings PH1 and PH2 with clinical deterioration >=4 points on the NIHSS score) (n = 391), and in 2 studies no information was reported on the diagnostic criteria used for the classification of bleedings (N.R.) (802 patients). Overall 4,856 patients were included in this meta-analysis, with 284 taking warfarin. CI = confidence interval; OR = odds ratio.

Xian et al, JAMA, 2012

- 24.000 patienten in stroke registry
- 1203 hospitals
- 2009-2011
- INR 1,0 – 1,7

C/ warfarine verhoogt bloedingsrisico bij trombolyse niet.

From: **Risks of Intracranial Hemorrhage Among Patients With Acute Ischemic Stroke Receiving Warfarin and Treated With Intravenous Tissue Plasminogen Activator**

JAMA. 2012;307(24):2600-2608. doi:10.1001/jama.2012.6756

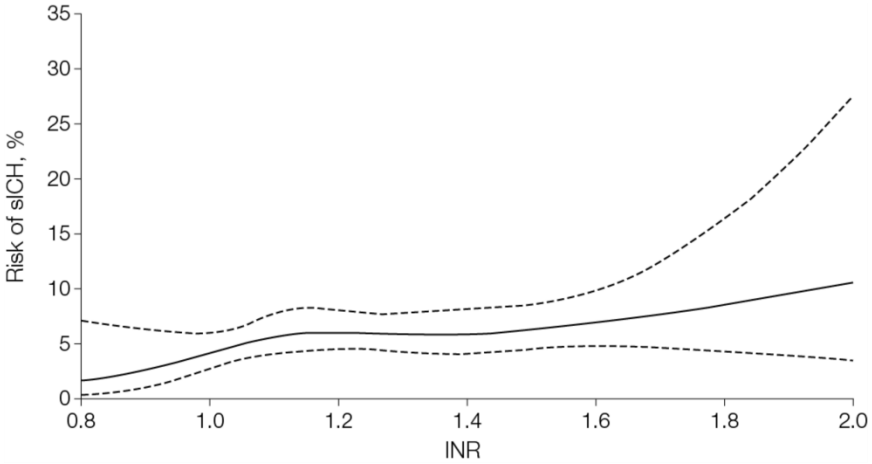


Figure Legend:

Solid line indicates risk of symptomatic intracranial hemorrhage (sICH); dashed lines, 95% confidence intervals. Logistic regression modeling was conducted to examine the relationship between international normalized ratio (INR) and binary outcome of sICH. The Stone and Koo additive spline method was fitted to generate the plot; adequacy of linearity was tested using likelihood ratio statistic by comparing the linear and nonlinear logistic models.

EDITORIAL

Warfarin treatment and thrombolysis in acute stroke

Are the procrastinators right?

EDITORIAL

tPA and warfarin

Time to move forward

Mark J. Alberts, MD, FAHA
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Neurology® 2013;80:514–515

The appropriate use of IV tissue plasminogen activator (tPA) for patients with acute ischemic stroke remains an area of active discussion among health care professionals. Since its approval in the United States by the Food and Drug Administration in 1996, the medical community has continued to review and discuss the risks vs benefits of this important therapy. Two recent publications[1,2] and accompanying editorials have refocused attention on the vexing issue of using IV tPA in patients taking warfarin. The Xian et al.[1] study found a 1.1% absolute increase in the risk of intracranial hemorrhage (ICH) with warfarin use (5.7% vs 4.6%), but this difference was no longer present once the analysis was adjusted for various risk factors. The Ruecker et al.[2] study reported a 20% risk of ICH, but the difference was barely significant ($p = 0.044$) once proper adjustments were made. It is important to consider therapy, a major factor in ICH.[5] Ruecker et al. comment on a rise in international normalized ratio (INR) posttherapy, but the actual INRs were 1.8 and 2.0, which may be within the range of assay variability. Because tPA may itself elevate the INR, it is unclear whether the slight increase reflected a delayed effect of recently ingested warfarin or the acute effects of tPA administration.

Both cited studies focused on patients taking warfarin. This is consistent with the fact that 69%–87% of the patients had a history of atrial fibrillation, which is clearly associated with cardioembolic ischemic strokes. As such, it seems likely that any association with bleeding complications (if there was one) was to some degree reflective of the cardioembolic mechanism of their stroke (in addition to the use of tPA or warfarin). This is impor-

EDITORIAL

tPA and warfarin

Time to move forward

Examining all the available data, it seems likely that a cardioembolic stroke, plus warfarin, plus IV tPA, all contribute to an environment where hemorrhagic complications would be expected. Perhaps the notable point is that there were not more symptomatic hemorrhages, considering the high-risk profile of many of these patients. But the reality of the situation is that IV tPA is the only readily available therapy for the majority of these patients, and overall the benefits still outweigh any risks.

als je het mij zou vragen…

- risico NOACs onbekend
  - geen uitsluiting vooraf

- lab is brain
- houd de CoaguChek
- bepaal INR en NOACs achteraf