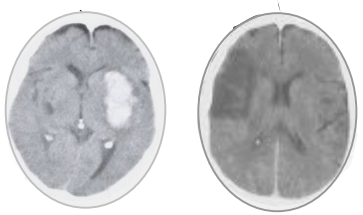


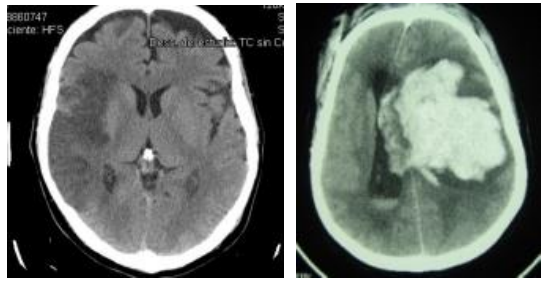
A HIGHLY SPECIFIC BLOOD BIOMARKERS PANEL TO IDENTIFY INTRACEREBRAL HEMORRHAGE AT THE AMBULANCE MIGHT HELP TO START PRE-HOSPITAL BLOOD-PRESSURE REDUCTION.

Joan Montaner

Leader of the Biomarkers & Neuroprotection group, VHIR, Barcelona
Director of Neurology Department, Hospital Macarena, Seville
Coordinator of the Andalusian Healthcare Stroke Plan

Ana Barragán 1, Leire Azurmendi 2, Carmen de Jesús 1, Rosa Delgado1, David Núñez 1, Sandrine Reymond 2, Antonia Romero Hidalgo 3, Ismael Muñoz Martínez 4, Antonio Gómez Rodríguez 4, Rafael Canto Neguillo 5, Francisco Moniche 1, Soledad Pérez-Sánchez 1, Jean Charles Sánchez 6. 1 Hospital Universitario Virgen Macarena/Rocío and IBIS, Sevilla, Spain, 2 Hôpitaux Universitaires de Genève (HUG), Genève, Switzerland, 3 Centro de Emergencias Sanitarias 061, Sevilla, Spain, 4 Dispositivos de Cuidados Críticos de Urgencias (DCCU), Sevilla, Spain, 5 Hospital Sierra Norte High Resolution, Constantina, Spain, 6 ABCDx, Barcelona.

Ischemic versus ICH



or

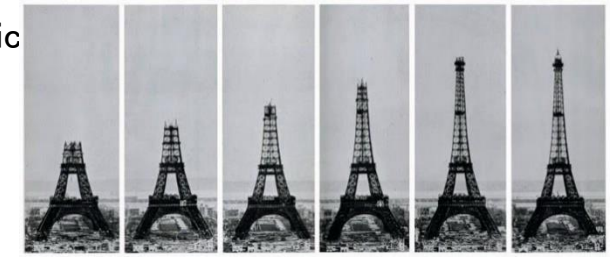
HIGH SPECIFICITY FOR ICH: intensive BP lowering

HIGH SPECIFICITY FOR IS: IV tPA

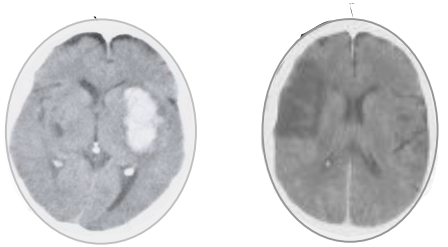
Among those who had values of **GFAP < 325 pg/mL** as a first condition, we managed to discard 27 hemorrhagic patients, and only 6 ischemic patients from our potential ischemic patients.

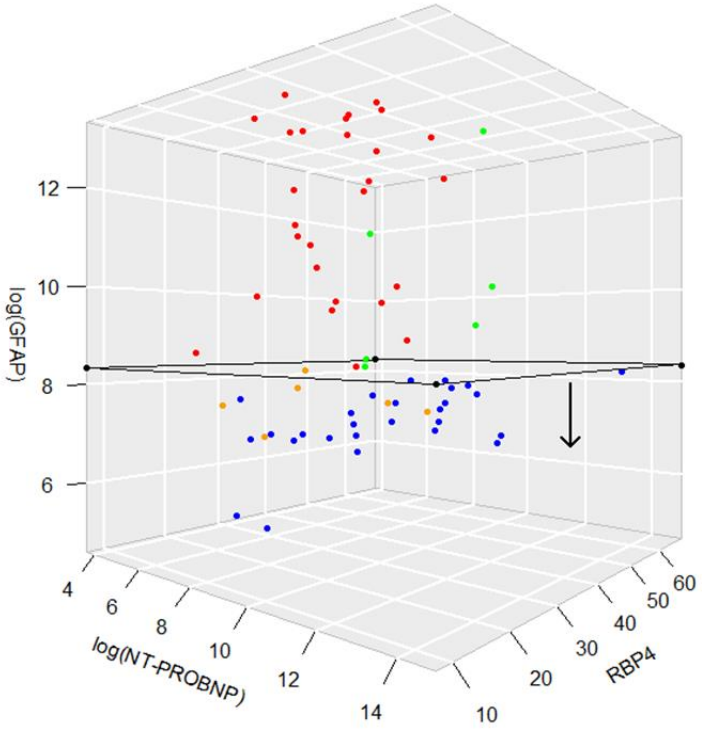
As a second condition, we classified patients as ischemic those who had either:

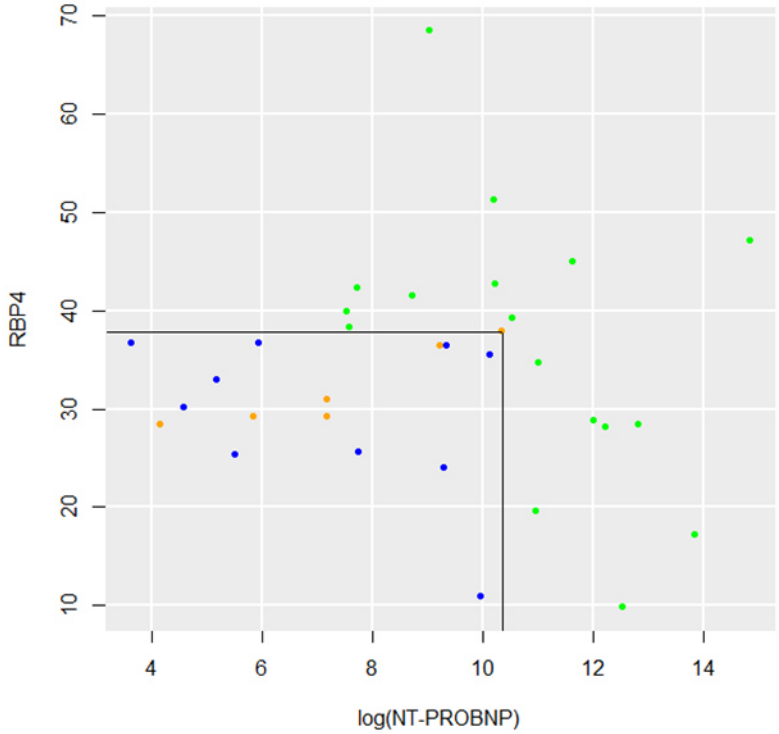
- **RBP4 > 38 µg/mL**. 100% specificity and 30.3% sensibility were obtained (we detected 10/33 ischemic patients).
- **NT-proBNP > 1305 pg/mL**. 100% specificity and 30.3% sensibility were obtained (we detected 10/33 ischemic patients).



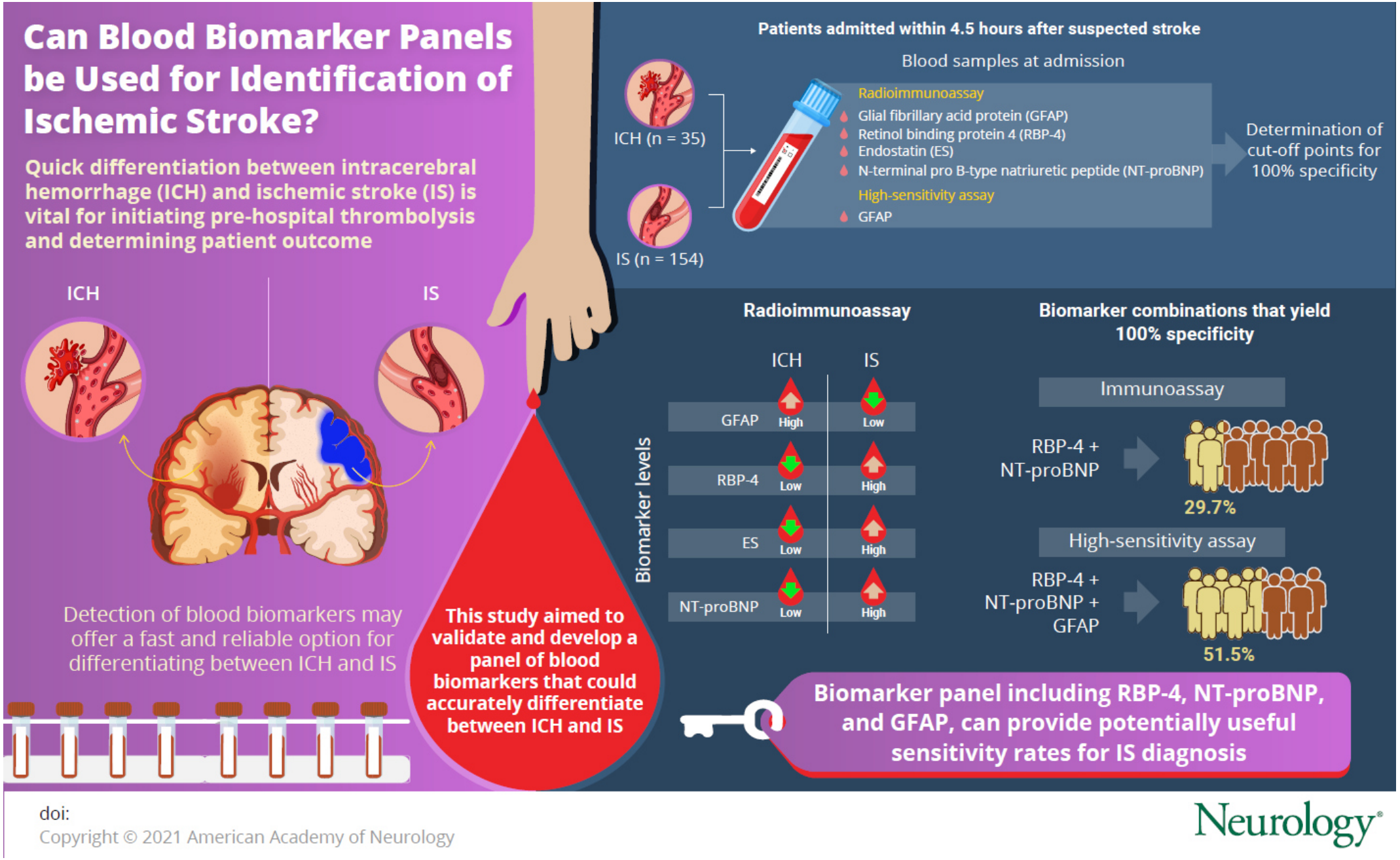
Improving GFAP test







At the end, we were able to detect 17/33 ischemic patients (51.5%) without mistakes (100% specificity).



doi:

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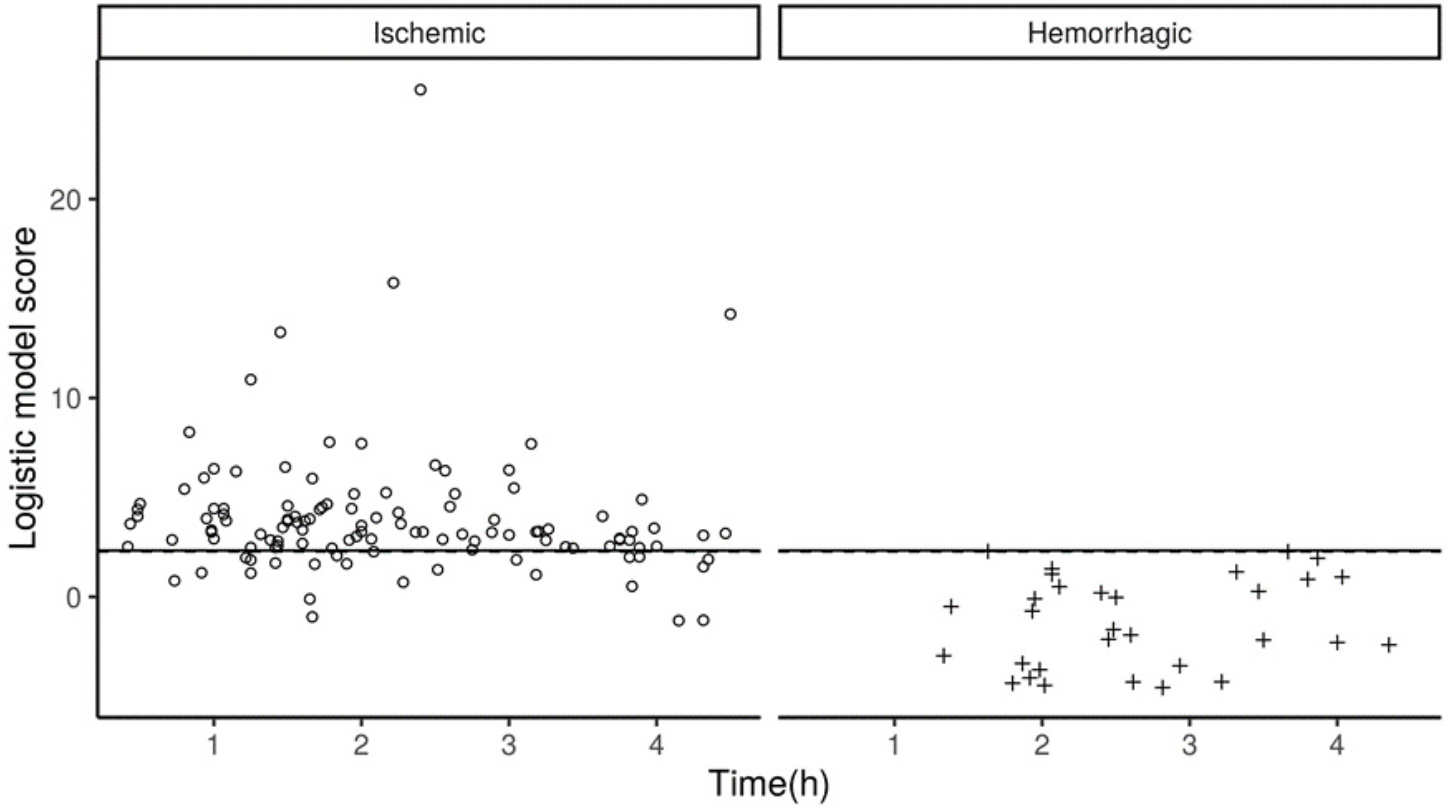
The 490 patients cohort

Strokecheck 2.0 model had a sensitivity=0.60, specificity= 1.00 and accuracy =0.68

PANEL



> 2.33 spc. 1

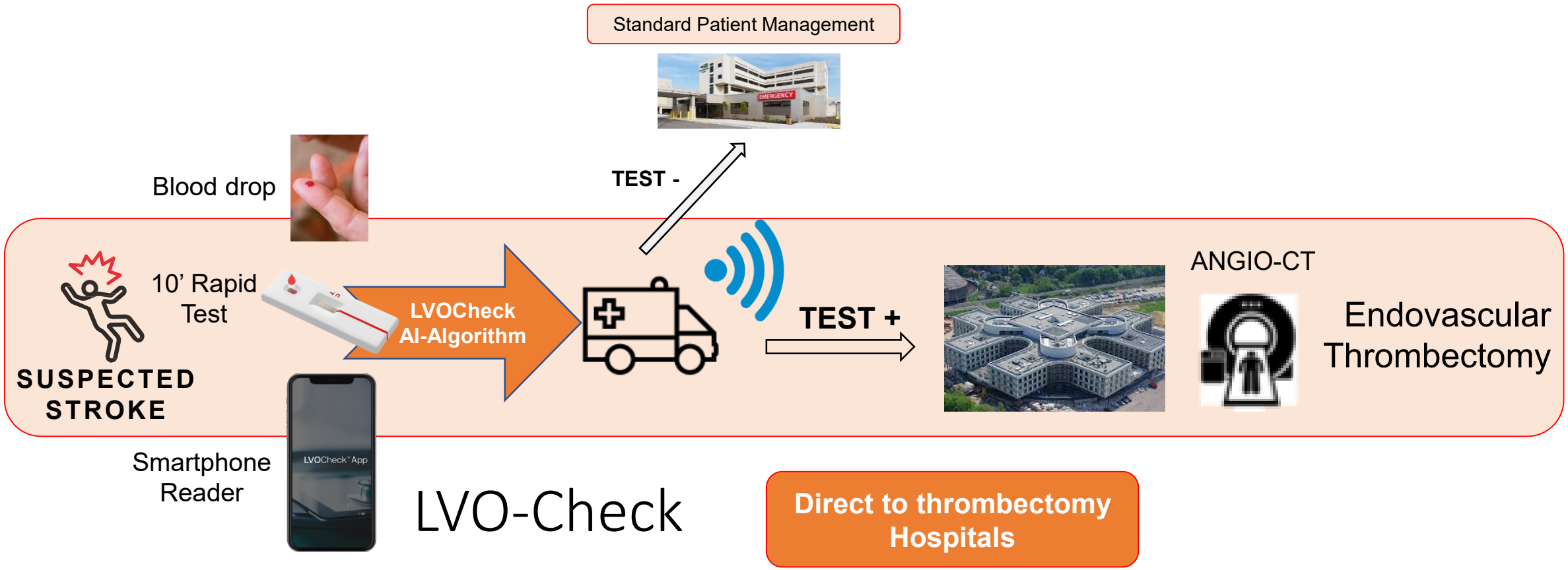
	Ischemic	Hemorrhagic
classified as Ischemic	93	0
classified as Hemorrhagic	61	35

> 2.28 spc. 0.97

	Ischemic	Hemorrhagic
classified as Ischemic	93	1
classified as Hemorrhagic	61	34

Would you accept to treat most of ischemic strokes correctly with tPA in the ambulance and assume the risk of treating some ICH with tPA???

Large Vessel Occlusion (LVO) triage



INTERACT-3 BUNDLE

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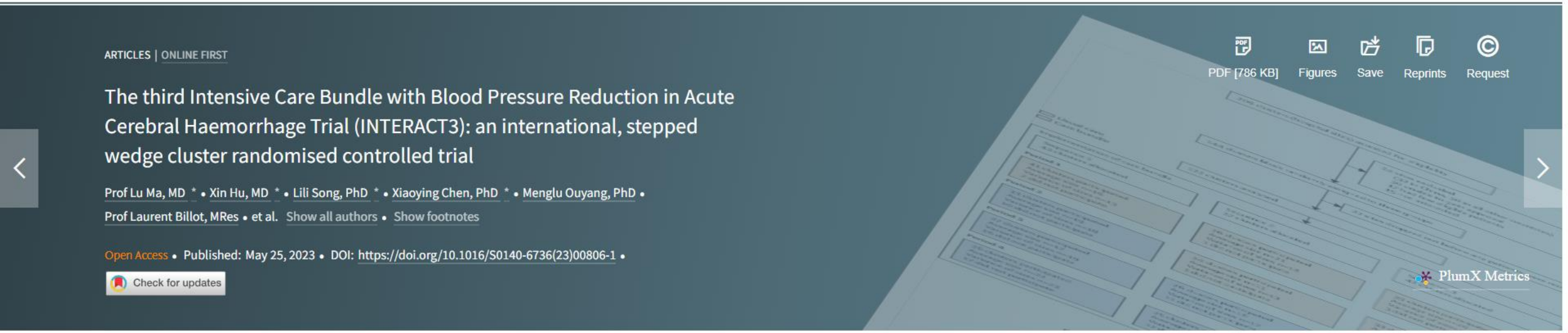

ARTICLES | ONLINE FIRST

The third Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT3): an international, stepped wedge cluster randomised controlled trial

Prof Lu Ma, MD * • Xin Hu, MD * • Lili Song, PhD * • Xiaoying Chen, PhD * • Menglu Ouyang, PhD • Prof Laurent Billot, MRes • et al. Show all authors • Show footnotes

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PlumX Metrics

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Intensive Ambulance-Delivered Blood-Pressure Reduction in Hyperacute Stroke

G. Li, Y. Lin, J. Yang, C.S. Anderson, C. Chen, F. Liu, L. Billot, Q. Li, X. Chen, X. Liu, X. Ren, C. Zhang, P. Xu, L. Wu, F. Wang, D. Qiu, M. Jiang, Y. Peng, C. Li, Y. Huang, X. Zhao, J. Liang, Y. Wang, X. Wu, Xiaoyun Xu, G. Chen, D. Huang, Y. Zhang, L. Zuo, G. Ma, Y. Yang, J. Hao, Xiahong Xu, X. Xiong, Y. Tang, Y. Guo, J. Yu, S. Li, S. He, F. Mao, Q. Tan, S. Tan, N. Yu, R. Xu, M. Sun, B. Li, J. Guo, L. Liu, H. Liu, M. Ouyang, L. Si, H. Arima, P.M. Bath, G.A. Ford, T. Robinson, E.C. Sandset, J.L. Saver, N. Sprigg, H.B. van der Worp, and L. Song, for the INTERACT4 investigators*

Authors randomly assigned patients with suspected acute stroke that caused a motor deficit and with elevated systolic blood pressure (≥150 mm Hg), who were assessed in the ambulance within 2 hours after the onset of symptoms, to receive immediate treatment to lower the systolic blood pressure (target range, 130 to 140 mm Hg) (intervention group) or usual blood-pressure management (usual-care group).

Li G, et al; INTERACT4 Investigators. Intensive Ambulance-Delivered Blood-Pressure Reduction in Hyperacute Stroke. *N Engl J Med*. 2024 May 30;390(20):1862-1872.

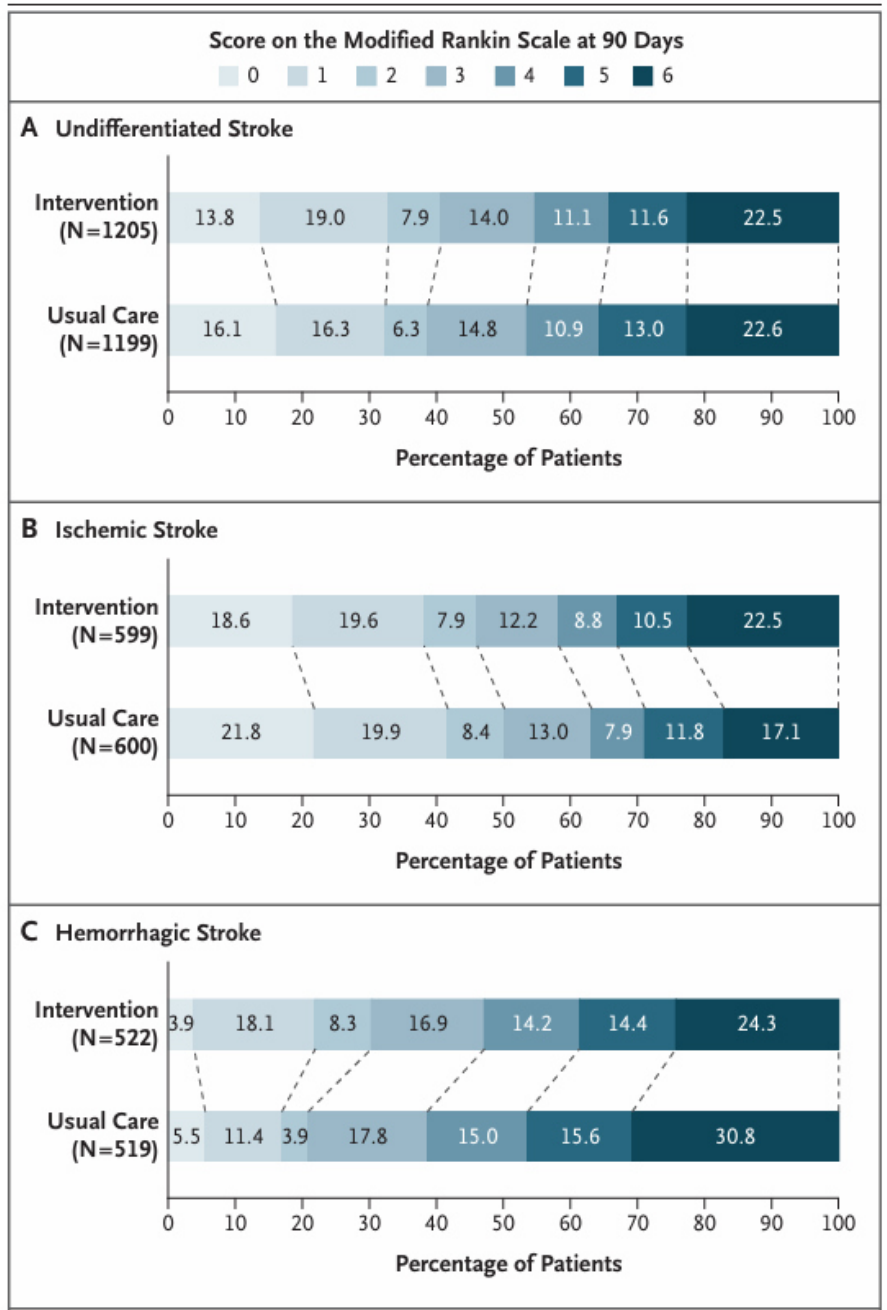


Figure 1. Functional Outcomes at 90 Days in the Two Groups, According to Scores on the Modified Rankin Scale (Primary Outcome).

Objectives

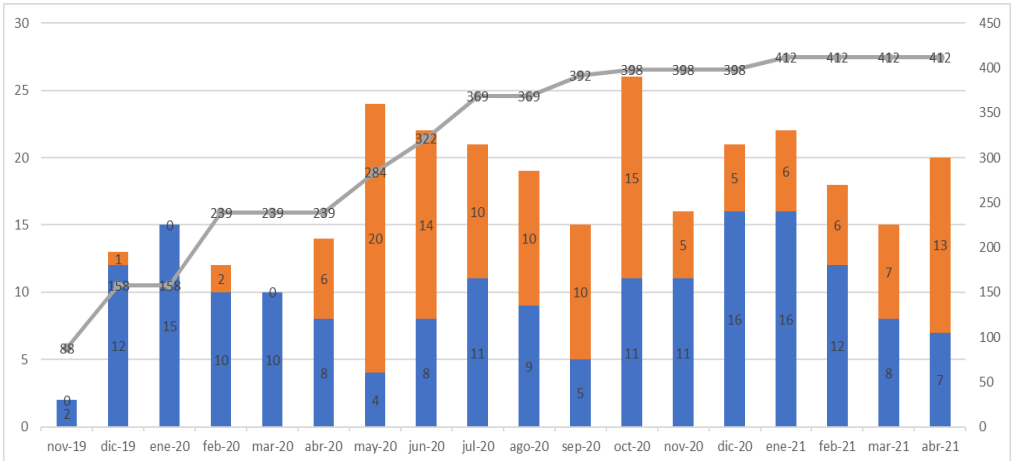
To validate a panel of blood biomarkers to differentiate ICH from ischemic stroke (IS) and mimics in the hyperacute phase and to test usability of a rapid point-of-care test (POCT) to measure such biomarkers at the ambulance.

Biofast

Recruited stroke code suspicions <6h

Trial nº → (Biomarkers for Initiating Onsite and Faster Ambulance Stroke Therapies, ClinicalTrials.gov identifier: NCT04612218).

Web site → https://biofast.technology/en/home/



175 patients recruited at the ambulance
130 patients recruited at ER
> 400 trained staff

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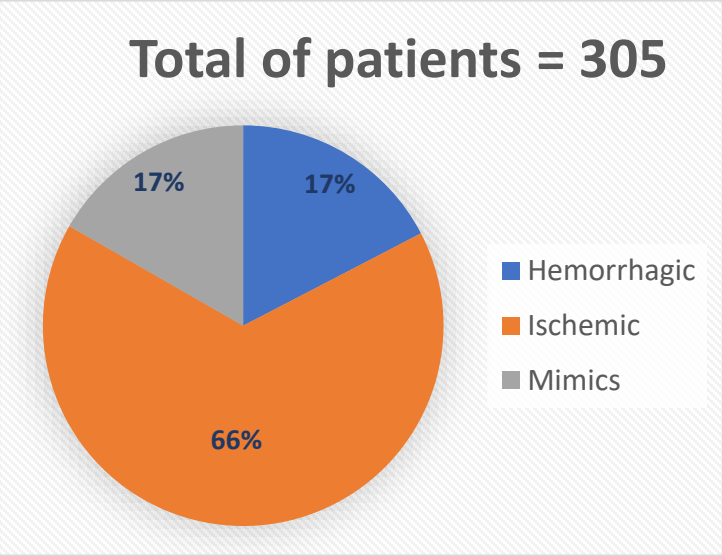
BIOFAST: clinical data results

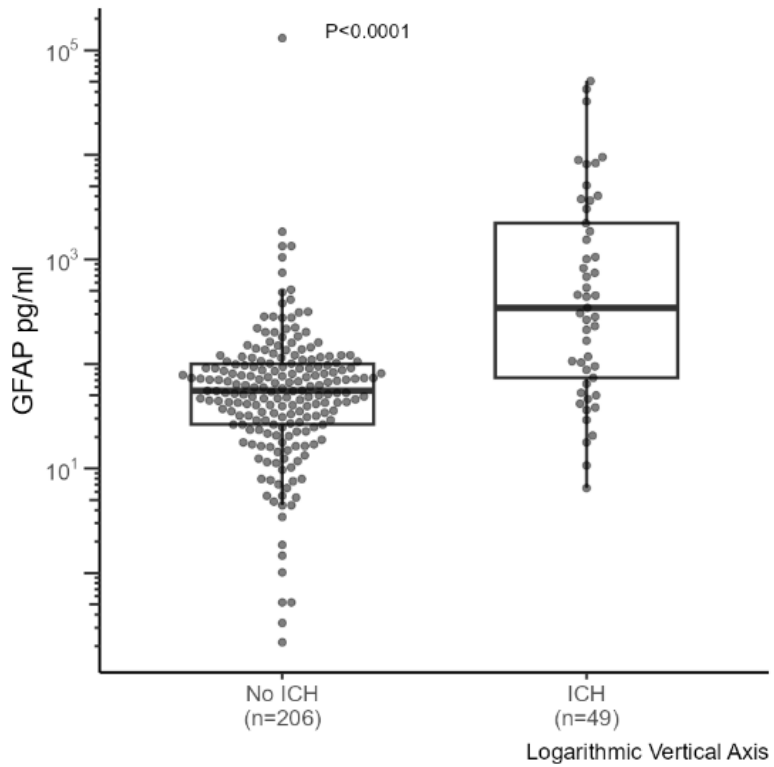


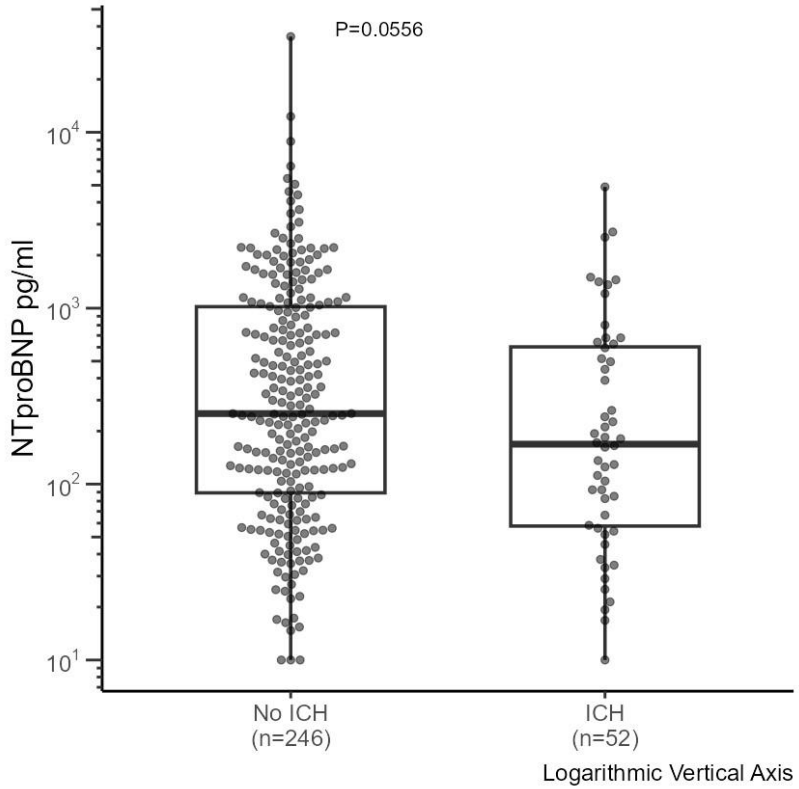
AMBULANCES	Total = 175
Ischemic	112
Hemorrhagic	33
Mimics	30

ER hospital	Total = 130
Ischemic	89
Hemorrhagic	20
Mimics	21

	No ICH	ICH	p
Sex (female)	57.14% (144)	75.47% (40)	0.013
Age (mean, SD)	68.7 (0.87)	74.7 (1.01)	0.000
Hypertension	72% (182)	34 (64%)	0.240
Systolic (mean, SD)	151 (2)	162 (4.3)	0.019
Diastolic (mean, SD)	91 (3)	83 (1)	0.002
Heart Rate	82 (1)	74 (3)	0.004
Anticoagulant	16% (40)	26% (14)	0.068
NIHSS	9 (0)	17 (1)	0.000

Glial fibrillary acid protein (GFAP) and N-terminal proB-type natriuretic peptide (NT-proBNP) were measured by immunoassays and integrated with clinical data into panels.





- **ICH had significantly higher GFAP and IS higher NT-proBNP.**

Three different panels containing clinic-biological info were able to identify 47.4%, 45.7% and 51.4% of the ICH patients (sensitivity) with 100% specificity.

A less restrictive cutoff yielded a sensitivity of 65.8%, 57.1% and 60% for a specificity of 95.8%, 95.8% and 97.2% respectively.

Cutoff points were obtained for 100% specificity for ICH using the Panelomix software.

		Sens / Specif			Sens / Specif		
NIHSS + MBP	NTproBNP MSD + GFAP MSD + NIHSS + MBP	47,4	100	ntprobnp_msd_pg_ml > 72.2497 gfap_msd_pg_ml > 425.565 tam > 137 nihss > 13.5 positive when >= 3.	65,8	95,8	gfap_msd_pg_ml > 425.565 tam > 120.833 nihss > 9.5 positive when >= 2.
Cincinatti + MBP	NTproBNP MSD + GFAP MSD + Cincinatti + MBP	45,7	100	gfap_msd_pg_ml > 425.565 tam > 156.667 cincinatti > 0.5 positive when >= 2.	57,1	95,8	gfap_msd_pg_ml > 206.796 tam > 156.667 cincinatti > 0.5 positive when >= 2.
Heart rate + MBP	NTproBNP MSD + GFAP MSD + Heart rate + MBP	51,4	100	gfap_msd_pg_ml > 329.926 tam > 156.667 positive when >= 1.	60	97,2	gfap_msd_pg_ml > 206.796 tam > 156.667 positive when >= 1.

Stroke Test (K-POCT)

OBJETIVO FASE I (EN HUVM)

Testar un nuevo test tipo Point-of-Care para determinar los valores de **NT-proBNP y GFAP** en sangre en **pacientes** con ictus isquémico y hemorrágico (**n=60**).

C. INCLUSIÓN

- **Pacientes en la UI**
- **> 18 años**
- **< 24 horas de evolución** (inicio síntomas o UVB)
- **Cualquier tipo de ictus**.

C. EXCLUSIÓN

- Imposibilidad de firmar el CI.
- Imposibilidad de obtener muestra de sangre para realizar el test.

** Se han incluido en el registro de ensayos de REDCap*

¿QUÉ HACER SI TENGO UN CANDIDATO?

1. **Informar al paciente sobre el estudio,** sólo conlleva una extracción de sangre para analizar los biomarcadores y guardar el sobrante en biobanco.
2. **Obtener CI firmado del paciente / familiar.**
3. **Avisar al equipo de investigación por el grupo** para continuar con la inclusión.
4. Enfermería (Cristina L. / Enma N.) obtendrá la muestra de sangre.
5. Equipo de laboratorio (David N. / Carmen D.) realiza el test, procesa la muestra y guarda alícuotas en biobanco.

NOTA IMPORTANTE:

En este estudio **se recogerán muestras para biobanco** por lo que sólo se podrán incluir pacientes en horario de 08:00-15:00, entendiendo que las muestras **deben obtenerse como muy tarde a las 14:00** para poder procesarlas y guardarlas a tiempo.

A rapid point-of-care test (15 minutes of incubation required) to measure both proteins is being prospectively tested at Seville stroke network using **Exdia cartridges** that are single-use fluorescence assay containing NT-proBNP and GFAP specific reagents to measure their concentration in whole blood by using the **Exdia TFR Plus device** (an image-based analyzer with time-resolved fluorescence analysis technology).

NT-proBNP
GFAP

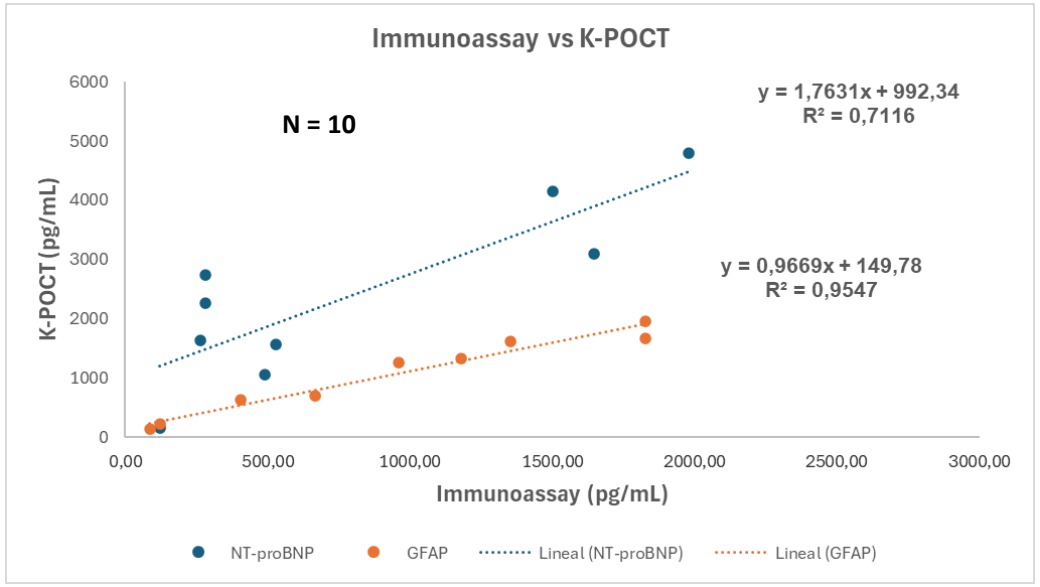
Time-resolved fluorescence (TRF) Imaging Technology

Step 1. Add sample

Step 2. Insert cassette

Step 3. Get results

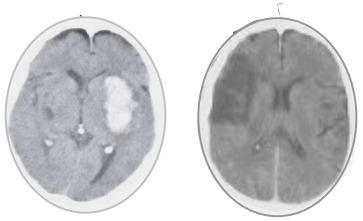
Stroke Test
K-POCT



Patients	NT-proBNP (pg/mL)	GFAP (pg/mL)	Stroke
1	**316.53**	135.18	Ischemic
2	< 100	**> 2100**	Hemorrhagic
3	**4072.9**	260.59	Ischemic

NT-proBNP >>>> Ischemia
GFAP >>>> ICH

Conclusions



GFAP and NT-proBNP in combination with simple clinical data reaches 100% specificity for ICH diagnosis in the hyperacute phase.

This opens the possibility of applying the INTERACT-4 recommendations of prehospital BP reduction in at least half of ICH patients using a POCT.

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