Clinical Implications of the combination of etiologies in patients with Intracerebral Hemorrhage

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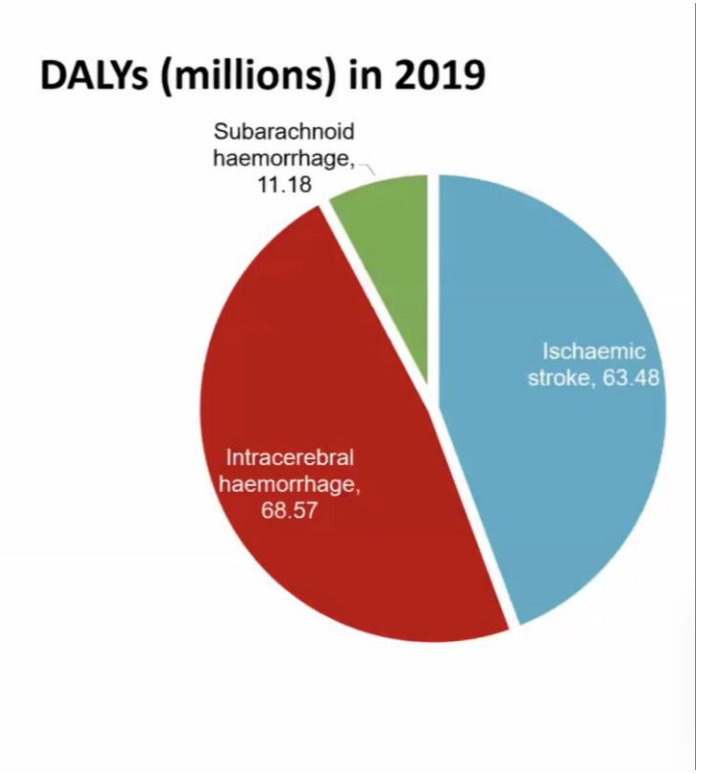
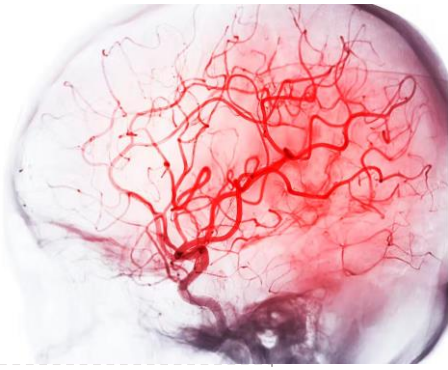
Introduction

- Intracerebral Hemorrhage is the second most frequent type of stroke after ischemic stroke and is one of the most disabling type
- Mortality is high can reach 50% of patients at three months.
- Among the factors related to mortality: volume, hematoma growth, intraventricular extension, anticoagulant activity and neurological deterioration has been identyfied



Lancet Neurology 2021; 20;795-820

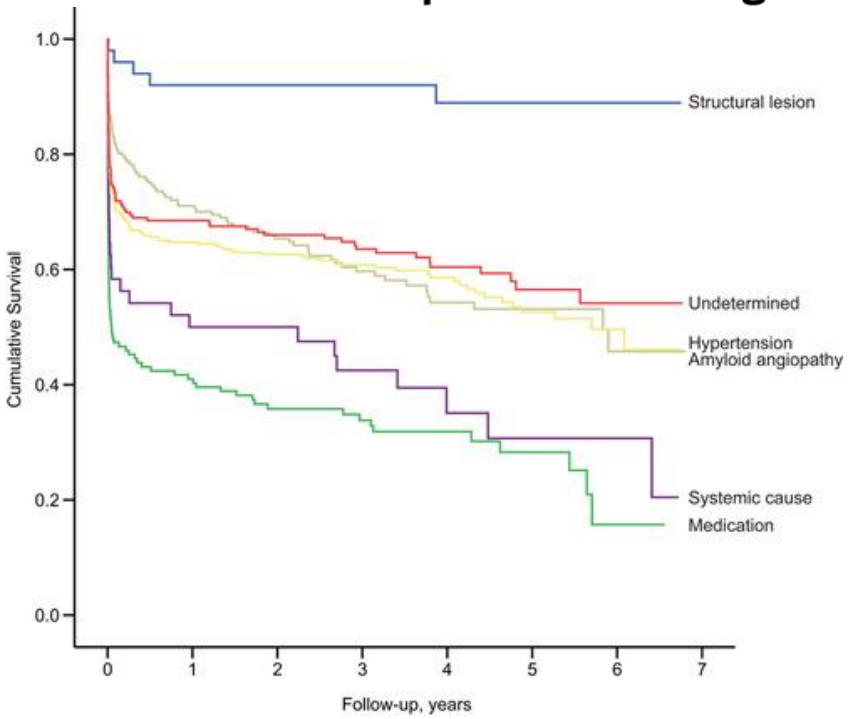
Introduction



- Etiology has also been identifyed as one of the determinants of clinical outcome including mortality, but this relationship remains poorly understood.
- Moreover, the determination of the etiology is difficult, often presumed.
- Up to date, there is at least three etiological classification systems published, named the SMASH-U, the H-ATOMIC and the CLASS-ICH classification respectively.

SMASH-U: A Proposal for Etiologic Classification of Intracerebral Hemorrhage

Meretoja et al. Stroke. 2012 Oct;43(10):2592-7



The etiologic subtype of intracerebral hemorrhage may influence the risk of significant hematoma expansion

J Neurol Sci. 015 Dec 15;359(1-2):293-7

SMASH-U aetiological classification: A predictor of long-term functional outcome after intracerebral haemorrhage

Eur J Neurol. 2022 Jan;29(1):178-187

SMASH-U: A Proposal for Etiologic Classification of Intracerebral Hemorrhage

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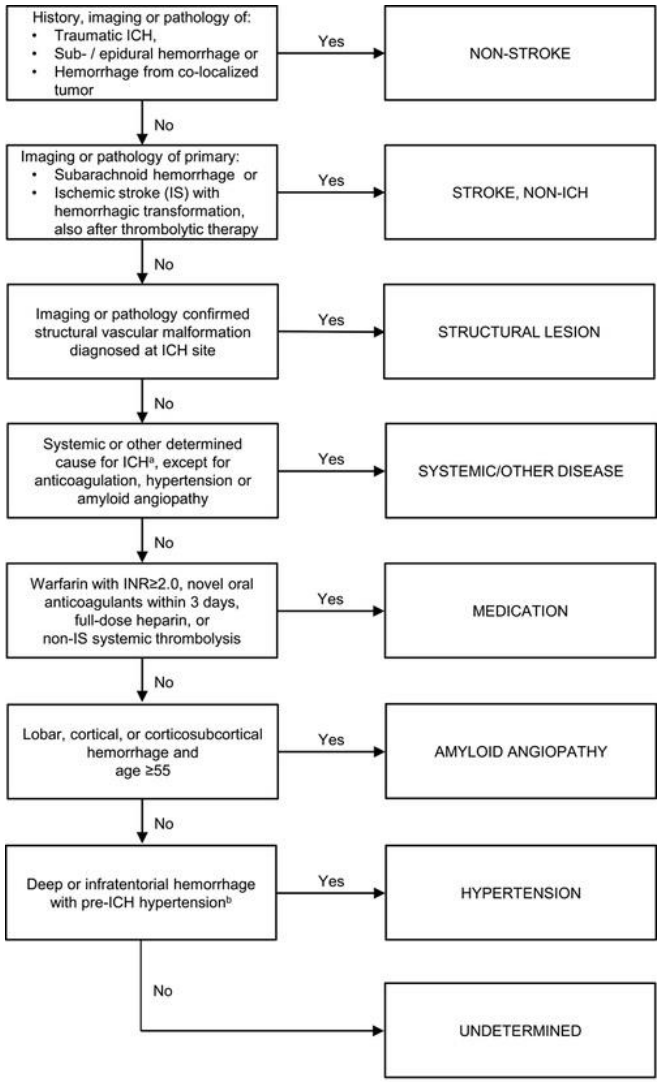
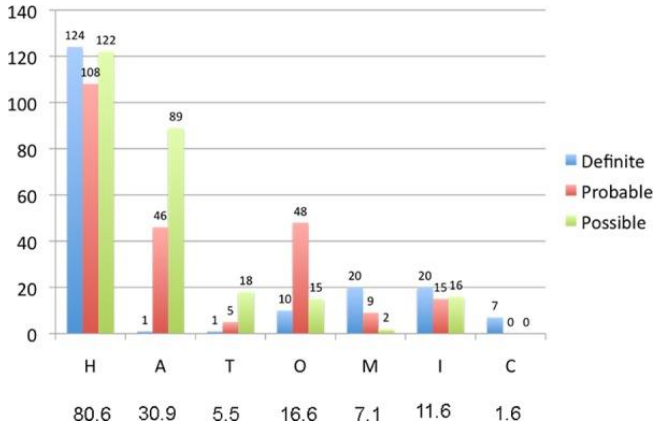


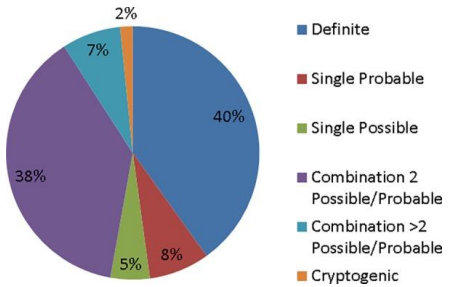
[a] Liver cirrhosis implicated when known liver disease combined with spontaneously elevated INR or liver enzymes >3 x upper limit of the reference range, and thrombocytopenia when thrombocyte count <50 E9/L.

[b] Hypertension defined as: a) most recent pre-ICH blood pressure ≥160/100 mmHg, either on or off antihypertensive therapy or, when pre-ICH blood pressure was not known, either b) mention of pre-ICH elevated blood pressure by patient, relative, or medical records together with a left ventricular hypertrophy as a biomarker of hypertension, or c) any pre-ICH use of blood pressure medication.

The H-ATOMIC Criteria for the Etiologic Classification of Patients with Intracerebral Hemorrhage

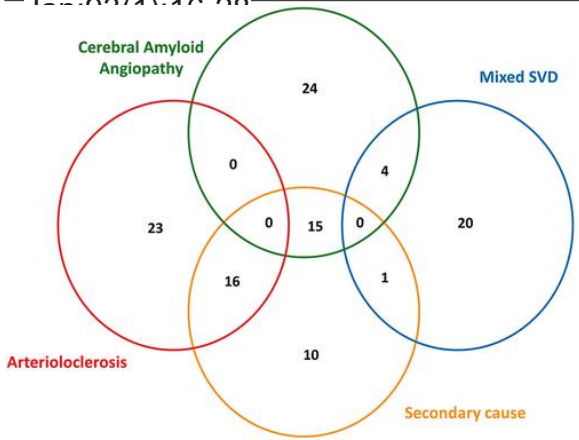
Martí-fàbregas J. 2016 Jun 8;11(6):e0156992





A Causal Classification System for Intracerebral Hemorrhage Subtypes

Raposo N et al. Ann Neurol. 2023



Objective 

- We aimed to analyze if the presence of different posible etiologies of ICH has any clinical impact on evolution of patients with ICH.

Methods 🔍

- Patients with ICH were retrospectively revised.
- A modified approach of H-ATOMIC criteria for the etiological classification were used.
- However, the groups were then grouped to simplify the ulterior analysis. Thus, groups were grouped in: Hypertensive + Amyloid; hypertensive + oral anticoagulation (H+O); CAA + anticoagulation (A+O); other combinations (group Combined). The rest of the groups were not grouped.

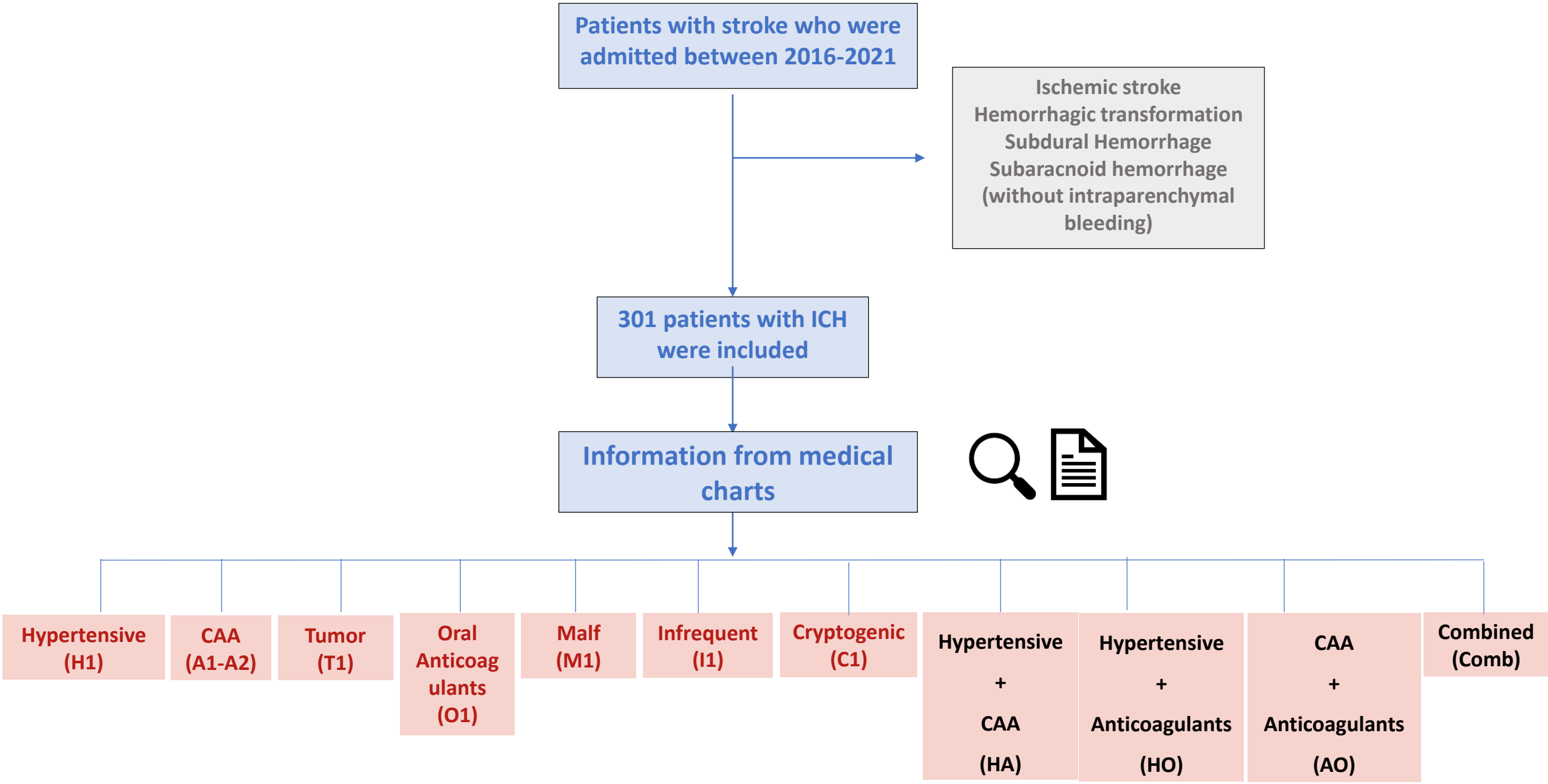
H-ATOMIC criteria

Only one etiology found

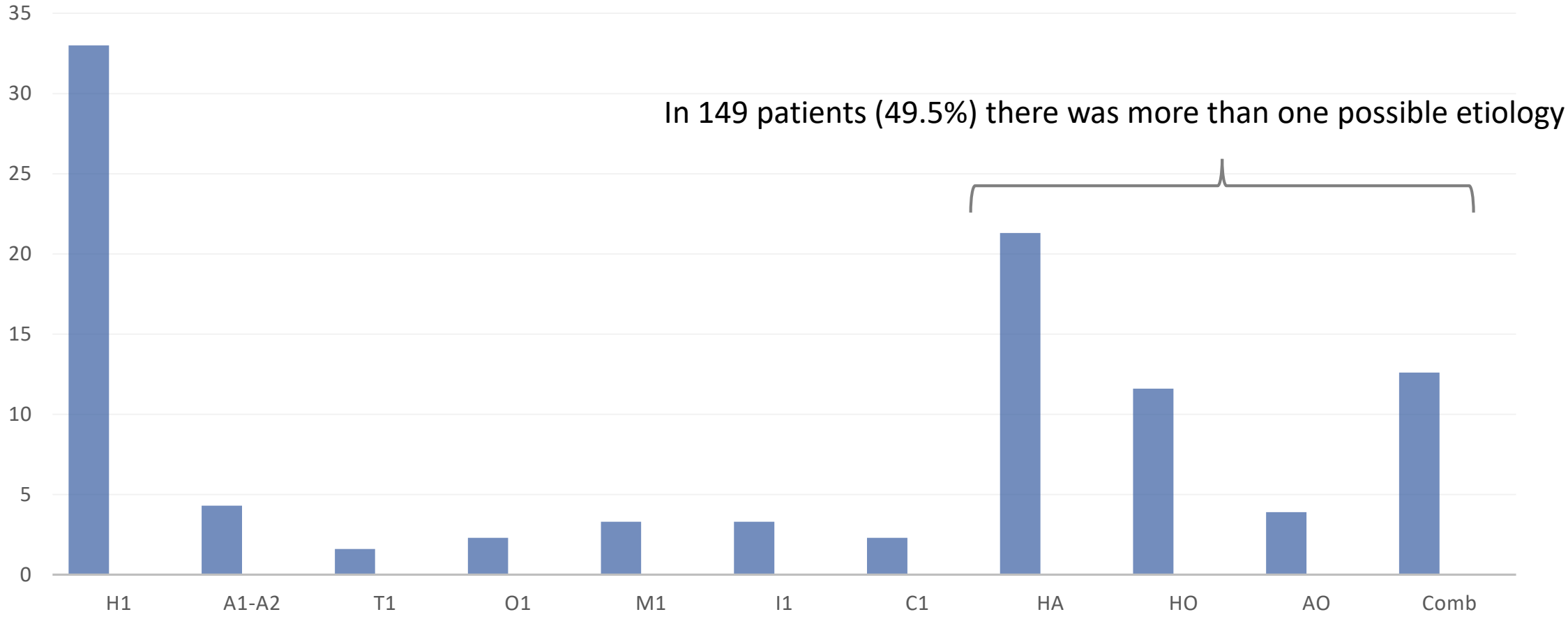
- **H1**: Hypertensive ICH
- **A1-A2**: Amyloid Angiopathy
- **T1**: Tumor
- **O1**: Oral anticoagulation
- **M1**: Malformation
- **I1**: Infrequent
- **C1**: Cryptogenic

More than one etiology possible

- **H+A**:Hypertensive // Amyloid Angiopathy
- **H+O**: Hypertensive // Oral anticoagulation
- **A+O**: Amyloid angiopathy // oral Anticoagulation
- **Combined**/combination: Any combination rather than the above mentioned

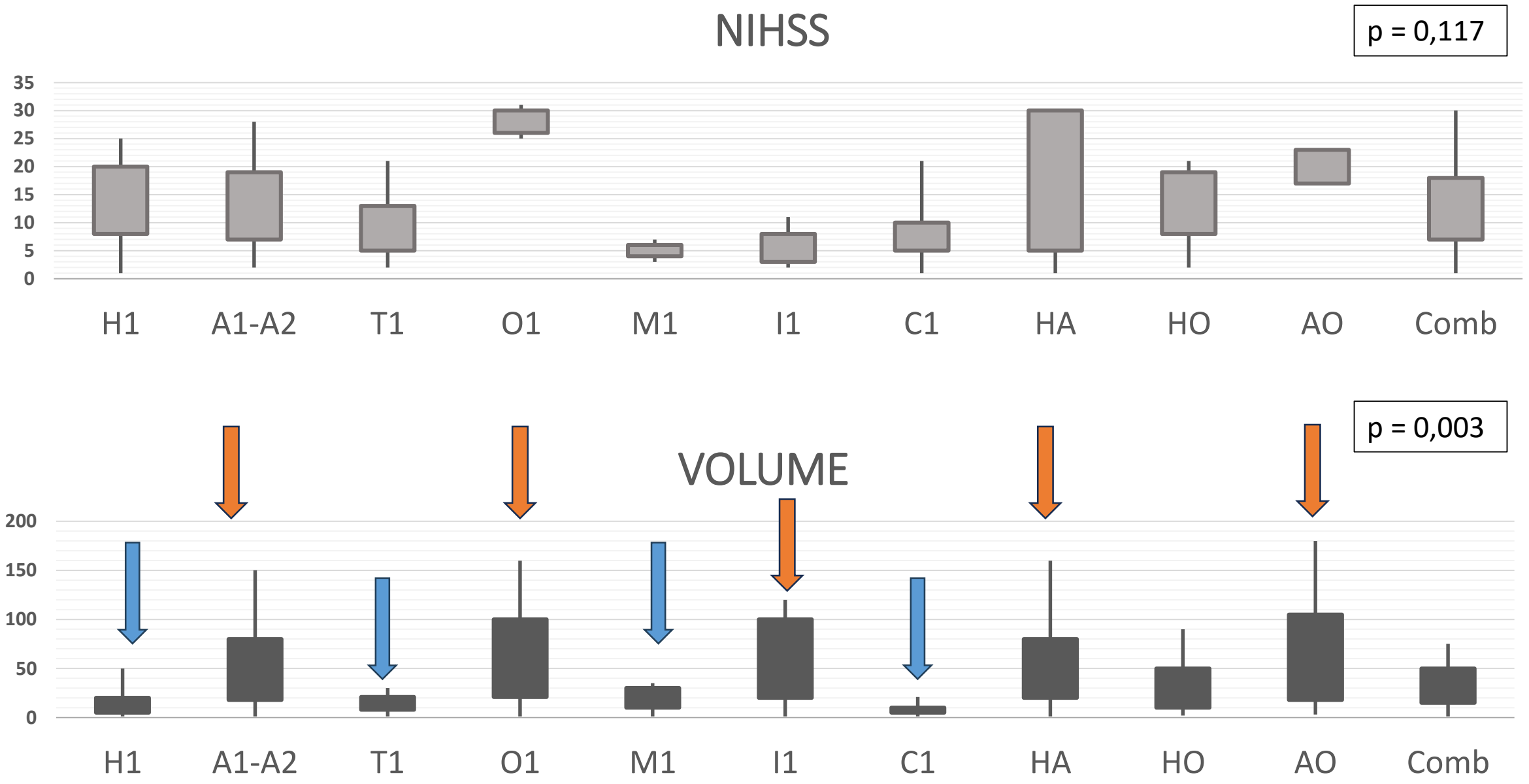

Patients with stroke who were admitted between 2016-2021
Ischemic stroke
Hemorrhagic transformation
Subdural Hemorrhage
Subaracnoid hemorrhage (without intraparenchymal bleeding)
301 patients with ICH were included
Information from medical charts
Hypertensive (H1)
CAA (A1-A2)
Tumor (T1)
Oral Anticoagulants (O1)
Malf (M1)
Infrequent (I1)
Cryptogenic (C1)
Hypertensive + CAA (HA)
Hypertensive + Anticoagulants (HO)
CAA + Anticoagulants (AO)
Combined (Comb)

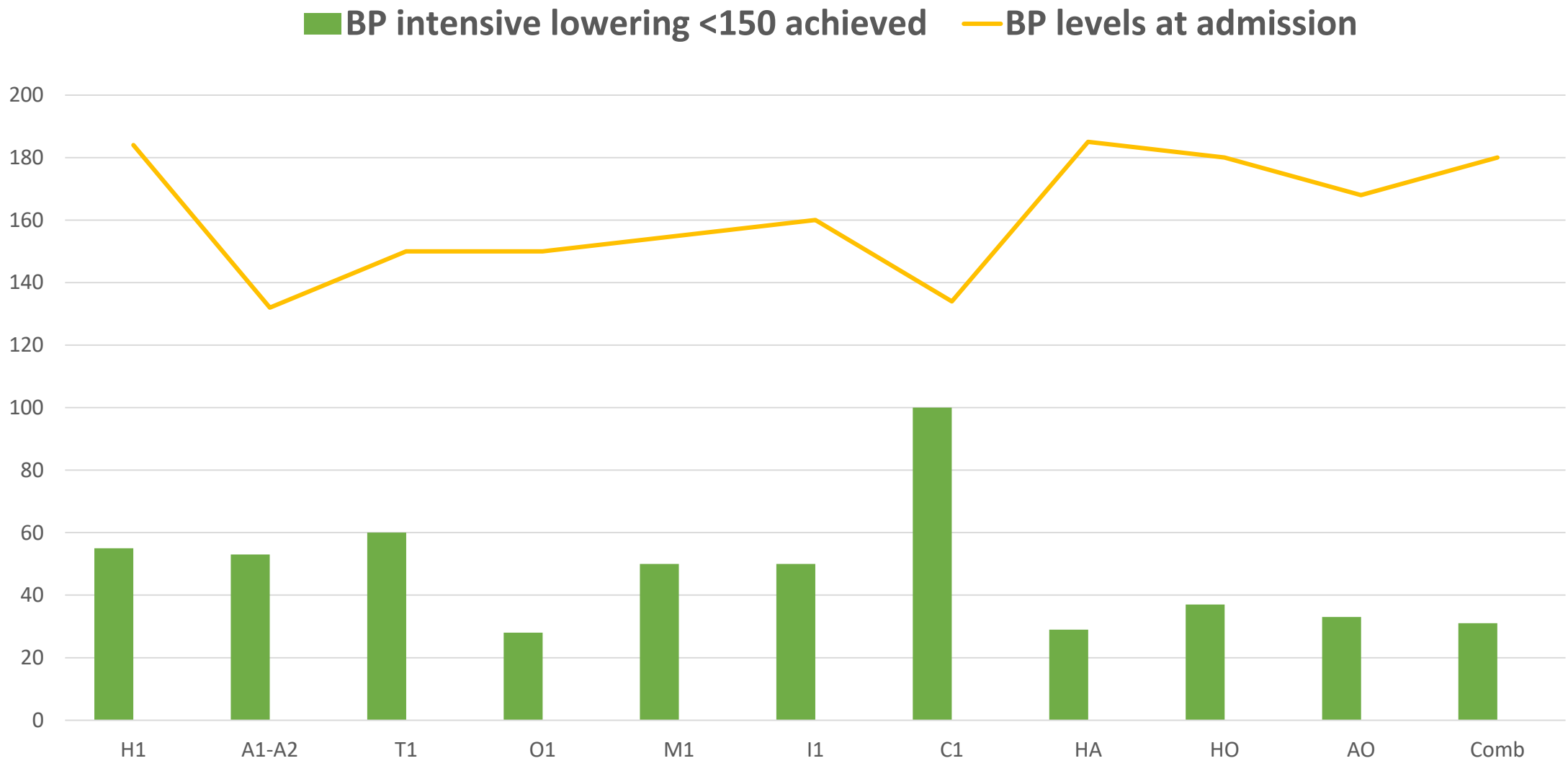
H-ATOMIC etiological groups



- Mean age: 73
- Female
- In 149 patients (49.5%) more than one possible etiology were described in the medical chart as a possible etiology
- The combination of Amyloid with Hypertension (both probable or possible) were in 64 (21.3%), being the most frequent combination
- 47 patients (14.3%) were on anticoagulant treatment-> HO or AO or combined (O2I2, O2M2, T3M2)
- Combined group represented 12.6% and was highly heterogeneous
- **Significant differences between groups were found in demographics , stroke severity and management.**

HA n=64 (21.3)	HO n=35 (11.6)	AO n=12 (4.0)	Combined n=38 (12.6%)
H2A2 (4)	H2O2 (16)	A2O2 (3)	A2I3 (2)
H2A3 (33)	H2O3 (1)	A2O3 (1)	A2M3 (1)
H3A2 (17)	H3O2 (14)	A3O2 (5)	A2T2 (1)
H3A3 (9)	H2A3O2 (4)	A3O3 (1)	A3I3 (3)
H2A2O3 (1)		H3A2O2 (2)	A3M2 (1)
			H2A2I2 (1)
			H2C2 (1)
			H2C3 (2)
			H2I2 (3)
			H2I3 (5)
			H2M3 (1)
			H2T3 (2)
			H3A2I3 (1)
			H3A3M3 (1)
			H3C2 (2)
			H3I2 (2)
			H3M2 (1)
			H3M3 (1)
			H3T2I2 (1)
			I2C2 (1)
			M2T2 (1)
			M3I2 (1)
			O2I2 (1)
			O2M2 (1)


NIHSS
p = 0,117
35
30
25
20
15
10
5
0
H1
A1-A2
T1
O1
M1
I1
C1
HA
HO
AO
Comb
VOLUME
p = 0,003
200
150
100
50
0
H1
A1-A2
T1
O1
M1
I1
C1
HA
HO
AO
Comb

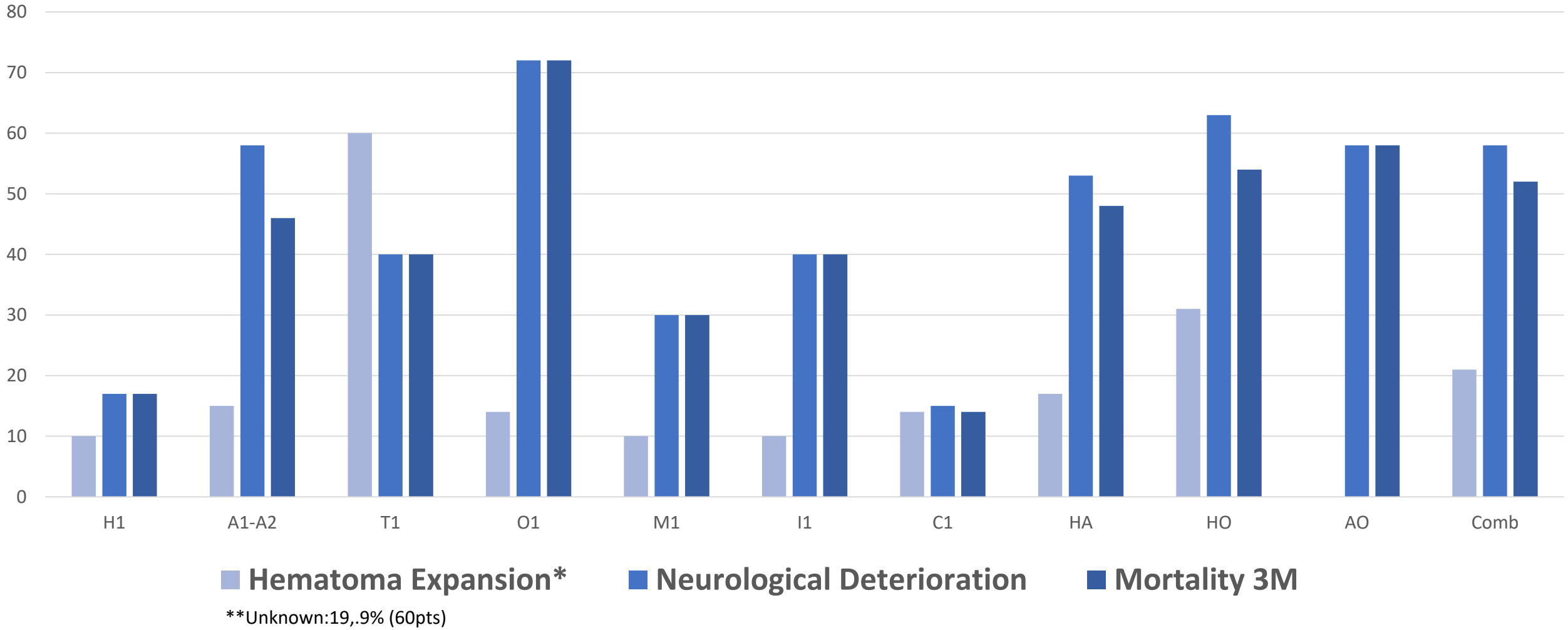

BP intensive lowering <150 achieved
BP levels at admission
200
180
160
140
120
100
80
60
40
20
0
H1
A1-A2
T1
O1
M1
I1
C1
HA
HO
AO
Comb

Clinical Evolution / Prognosis

Hematoma Expansion: n=49 (17.8%)

N Deterioration: n=124 (40.1%)

Mortality 3M: n=115 (38.2%)



**Unknown:19,.9% (60pts)

Logistic regression analysis

Neurological Deterioration

	OR	95% CI	P value
Volume	1.047	1.025-1.069	<0.001
Intensive BP lowering	0.214	0.083-0.554	<0.001
Intraventricular extension	8.22	1.955-34.553	0.004
A2	6.131	0.780-48.178	0.085
HA	3.027	0.861 10,644	0.084
HO	9.909	2.538-38.686	<0.001
Combined	17.493	3.859-79.301	<0.001

Hematoma Expansion

	OR	95% CI	P value
Volume	1.017	1.002-1.032	0.021
Intensive BP lowering	0.800	0.361-1.770	0.581
Intraventricular extension	0.830	0.287-2.454	0.748
AO	0.001	0.011-1.1021	0.999
HA	1.306	0.471-3.697	0.615
HO	5.166	1.771-15.065	0.003
Combined	2.662	0.722-9.817	0.141

Mortality

	OR	95% CI	P value
Volume	1.036	1.021-1.052	<0.001
Intensive BP lowering	0.415	0.191-0.876	0.021
Intraventricular extension	3.193	1.333-8,632	0.022
A2	0.131	0.780-48.178	0.999
HA	1,068	0.407- 2,801	0.894
HO	3,721	1.322-10.686	0.013
Combined	17.493	0,842-9,528	0.093

Conclusions

- Half of our sample had more than one etiology that could have contributed to the ICH.
- Factors related to outcome were were volume, NIHSS score, and intraventricular extension and the etiology of the ICH.
- Etiological groups have different profiles of clinical evolution
  - The **better outcomes** were observed for:
    - H1 (17%), M1 (30%) and C1 (14%).
  - **The combination of etiologies had a negative impact in clinical evolution and outcome, especially for the combination with anticoagulation, but not limited to this combination**.
  - **Hypertension+anticoagulants remained related to poor outcome in multivariable analysis, despite not having the highest volumen at admission. This combination may be at special high risk of poor evolution**

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Gracias!