Combination Of Targeted Temperature Management and Thrombectomy After Ischemic Stroke

COTTIS I / II

The success rate of thrombectomy (to reach a good outcome with mRS 0 – 2) after acute ischemic stroke today is 30% - 46%

The aim is to show that the combination of thrombectomy with early mild hypothermia (35°C) is able to increase significantly the success rate

Theoretical Considerations for hypothermia and stroke

- ***High recanalisation rates*** clearly defined on angiography and ***reperfusion*** is needed for a lasting and effective neuroprotection by hypothermia

- ***Existence of significant mismatch*** **tissue** in patients with large vessel occlusion, is the major target of hypothermia as a neuroprotectant

- Patients with indication for thrombectomy usually recveive general anaesthesia **with intubation and analgosedation**. As a result, there is no discomfort or shivering caused by hypothermia

- If hypothermia can be induced **during ischemia** (before recanalisation by thrombectomy!), the neuroprotective properties of hypohermia are optimally used, namely ***intra-ischemically*** and **during the critical reperfusion phase** after reopening of the vessel

What do we use for rapid induction and maintenance of hypothermia?

Induction

+

Maintenance

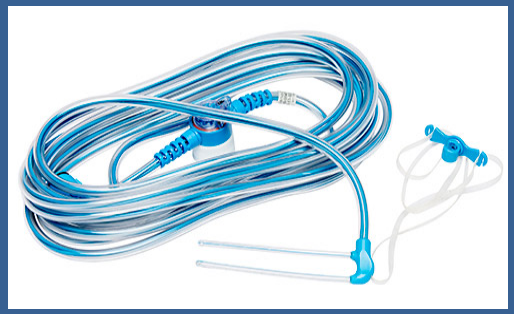
The portable, easy to use, Intranasal Cooling System (RhinoChill ®) for ultra-fast induction

“RhinoChill®“ – Intranasal Cooling System

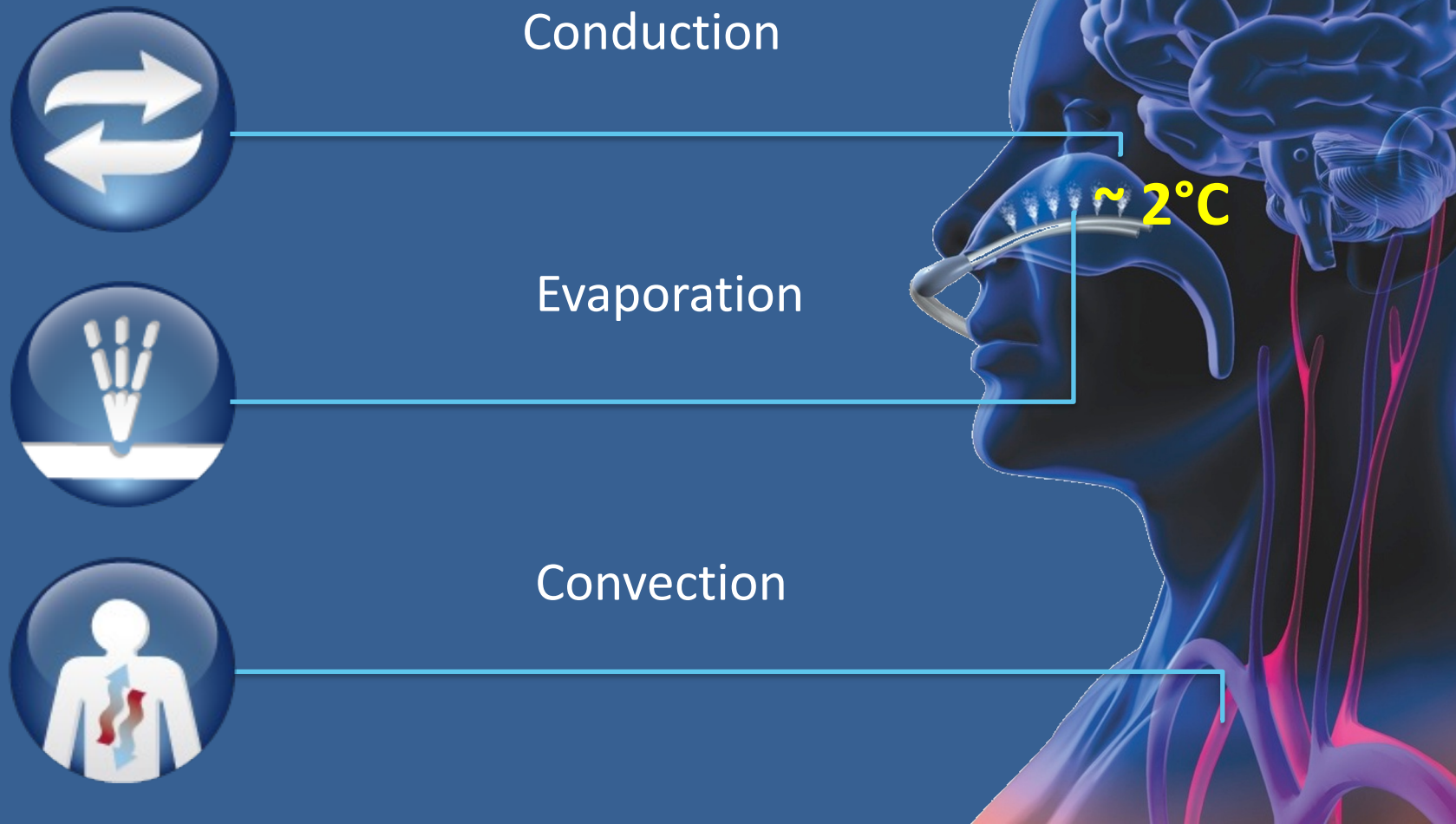
2 l Coolant-Bottle

perfluorohexane

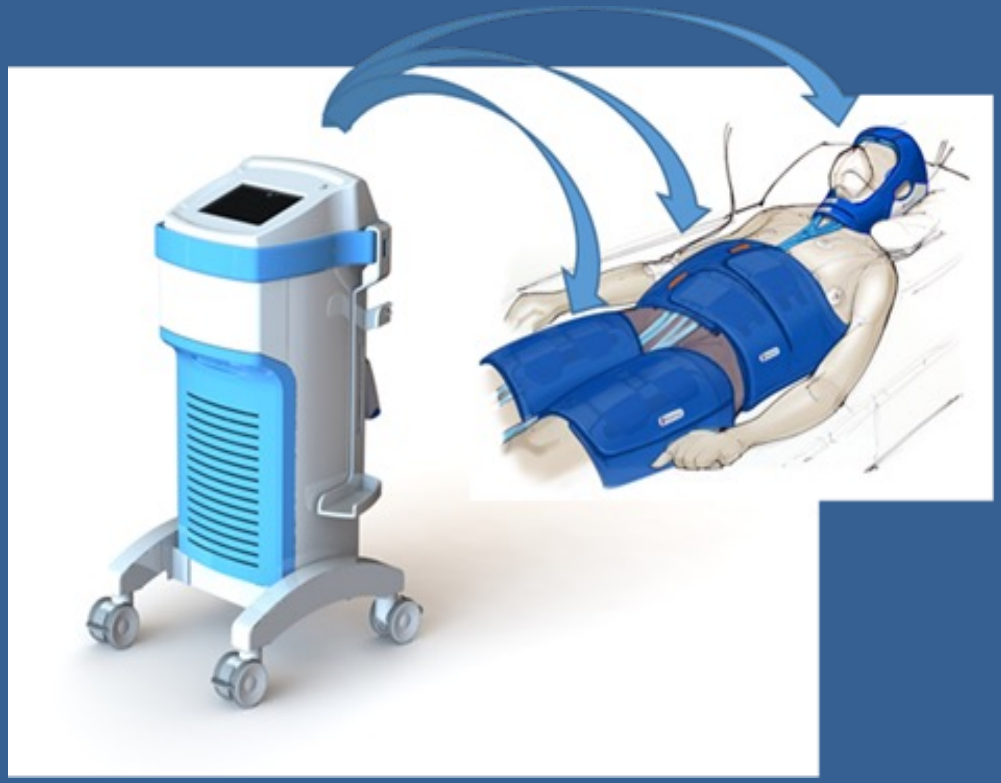
Intranasal Catheter



The RhinoChill® Principle



The “BrainCool System“ – for maintenance of the target temperature after thrombectomy and for active rewarming



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COTTIS-1: design

a feasibility and safety study

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Main inclusion criteria

- ⇒ Age >18 years.
- ⇒ Prestroke modified Rankin Scale score of 0–2.
- ⇒ Indication for endovascular treatment
  - ⇒ Acute ischaemic stroke with an NIHSS score >5.
  - ⇒ Intracranial occlusion of the M1 or M2 segment of the middle cerebral artery or internal carotid artery or tandem occlusion on CT/MR-angiography.
  - ⇒ Time window:
    - ⇒ Time from last known normal-to-groin-puncture <6 hours: native CT or MR-DWI with ASPECTS >5 (optional CT-perfusion or MR-perfusion).

Main inclusion criteria

⇒ Time from last known normal-to-groin-puncture 6–24 hour or unknown time window: significant imaging mismatch according to the eligibility criteria of

⇒ DEFUSE-3[35]: infarct core <70 mL (defined by CBF <30% or by MR-DWI), mismatch volume >15 mL (defined by the difference between Tmax >6 s volumes and infarct core), mismatch ratio >1.8.

⇒ DAWN-trial[36]: infarct core defined by CBF <30% or by MR-DWI.

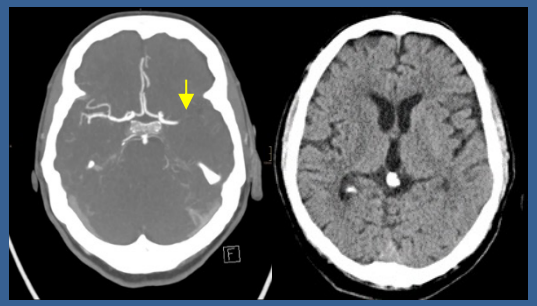
⇒ ≥80 years and NIHSS >10: infarct core <21 mL.

⇒ <80 years and NIHSS >10: infarct core <31 mL.

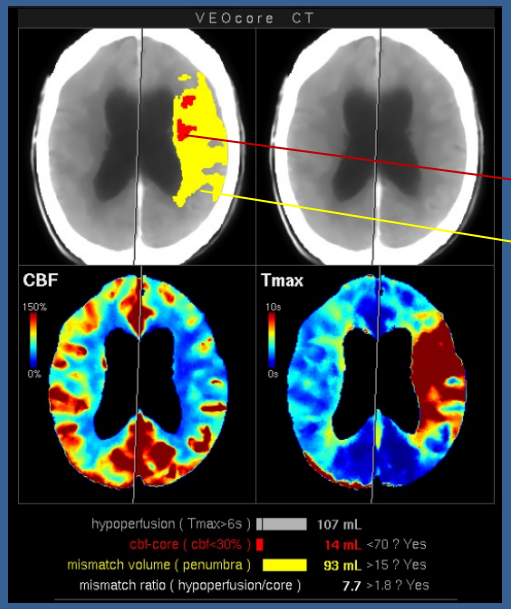
⇒ <80 years and NIHSS >20: infarct core <51 mL.

COTTIS-1: Imaging

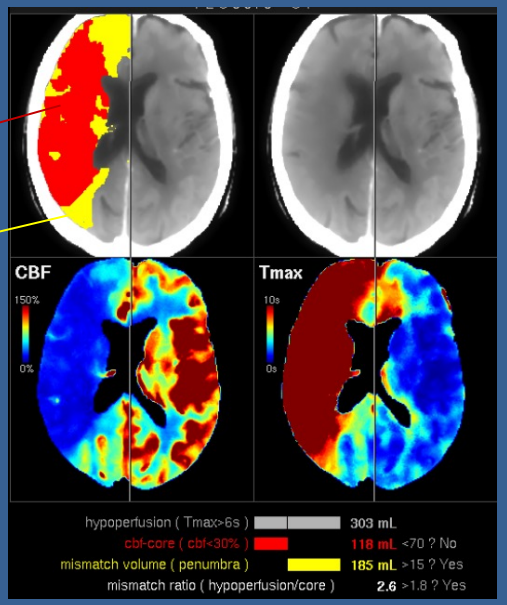
- **<6h:** CT and CT-A (or MRI/MR-A)



- **6-24h:** significant mismatch in CT-Perfusion (or MRI(MRP)



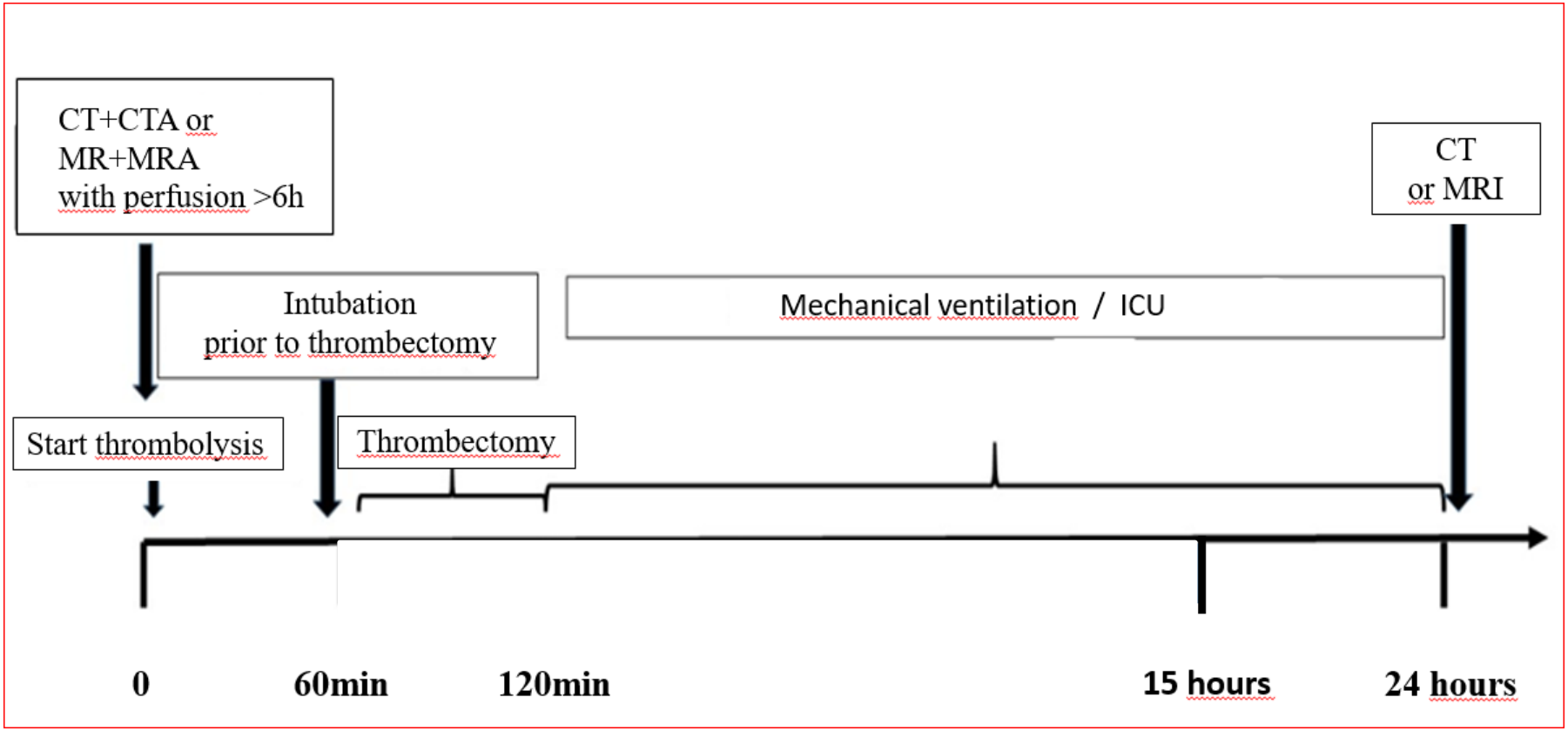
core
penumbra



inclusion **no inclusion**

COTTIS-1: design

Regular patient without hypothermia



COTTIS-1: design

Hypothermia

CT+CTA or
MR+MRA
with perfusion >6h

Colling
with
RhinoCill
to 35°C

Maintainance of 35°C by surface cooling
for 6h after recanalization
Rewarming for 7h (0.2°C/h)
Total time: 13 hours

CT
or MRI

Intubation
prior to thrombectomy

Mechanical ventilation / ICU

Start thrombolysis

Thrombectomy

0 60min 120min 15 hours 24 hours

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COTTIS-1 : results

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Patient characteristics (N=22)

- Median age: 77 y
- Median NIHSS on admission 15 (IQR 12.5-19.75)
- Vessel Occlusion

  M1 of MCA : 12
  M2 of MCA : 3
  Prox. ICA+M1 : 4
  Carotid T : 3

- Additional iv thrombolysis: 14 (64%)

Patient characteristics (N=22)

- Median time from arrival

  to initiate cooling: 57 minutes
  to start thrombectomy : 65 minutes
  to recanalisation : 123 minutes

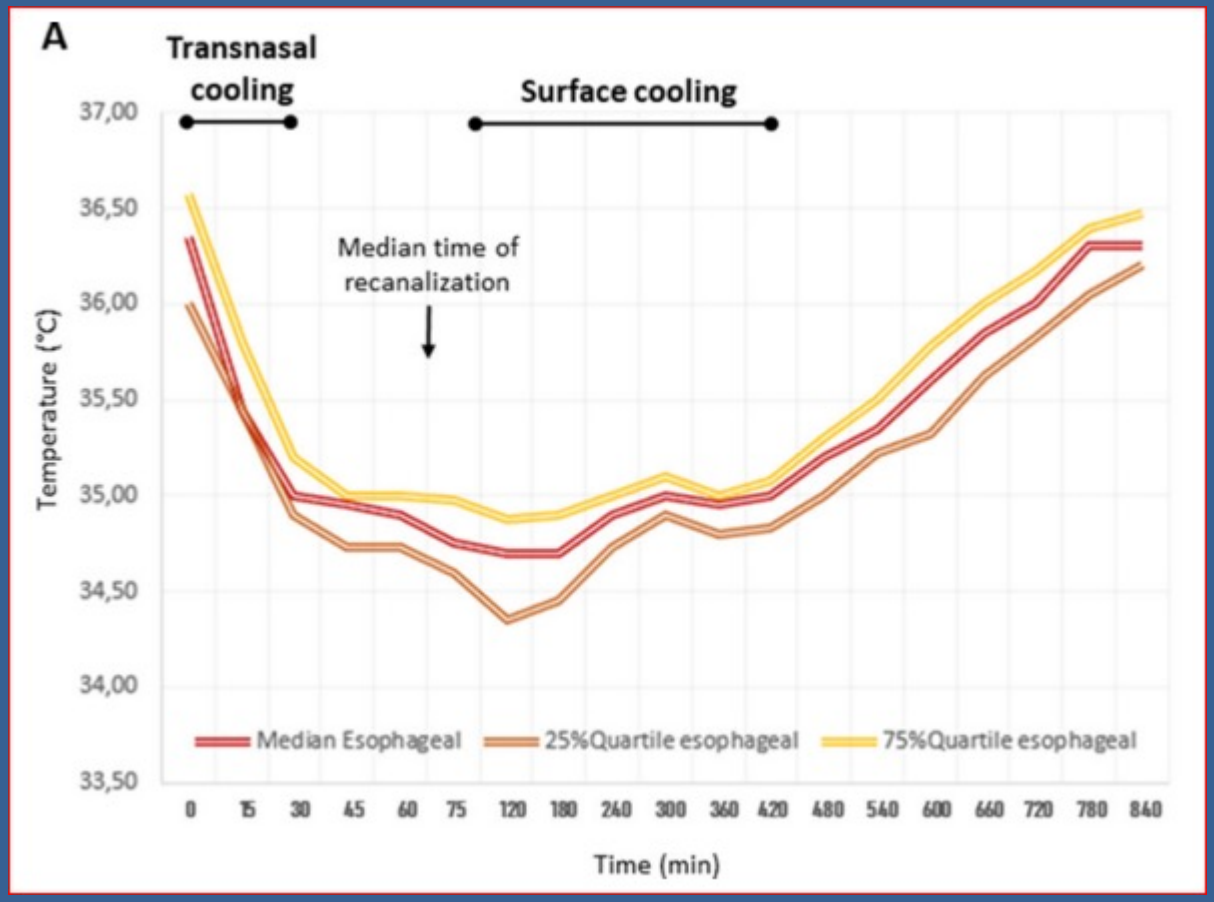
- The target temperature (35°C) was reached within **30 minutes** (range 13-78 minutes)

- Cooling rate: 2.6°C/h

- All patients reached the target temperature

- 86% of the patients had reached 35°C at recanalisation by thrombectomy

Course of oesophageal temperature



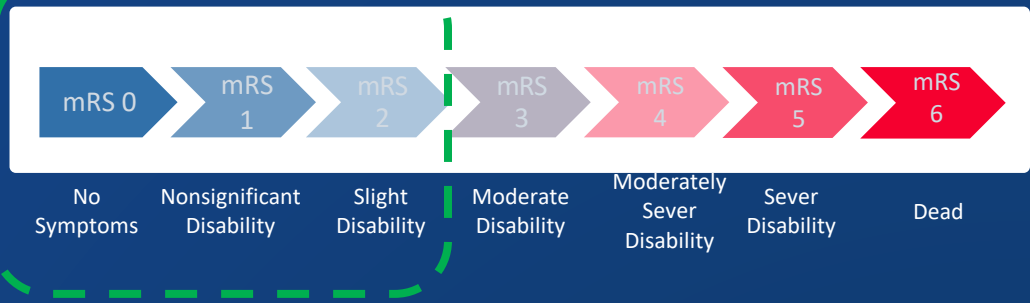
Side Effects

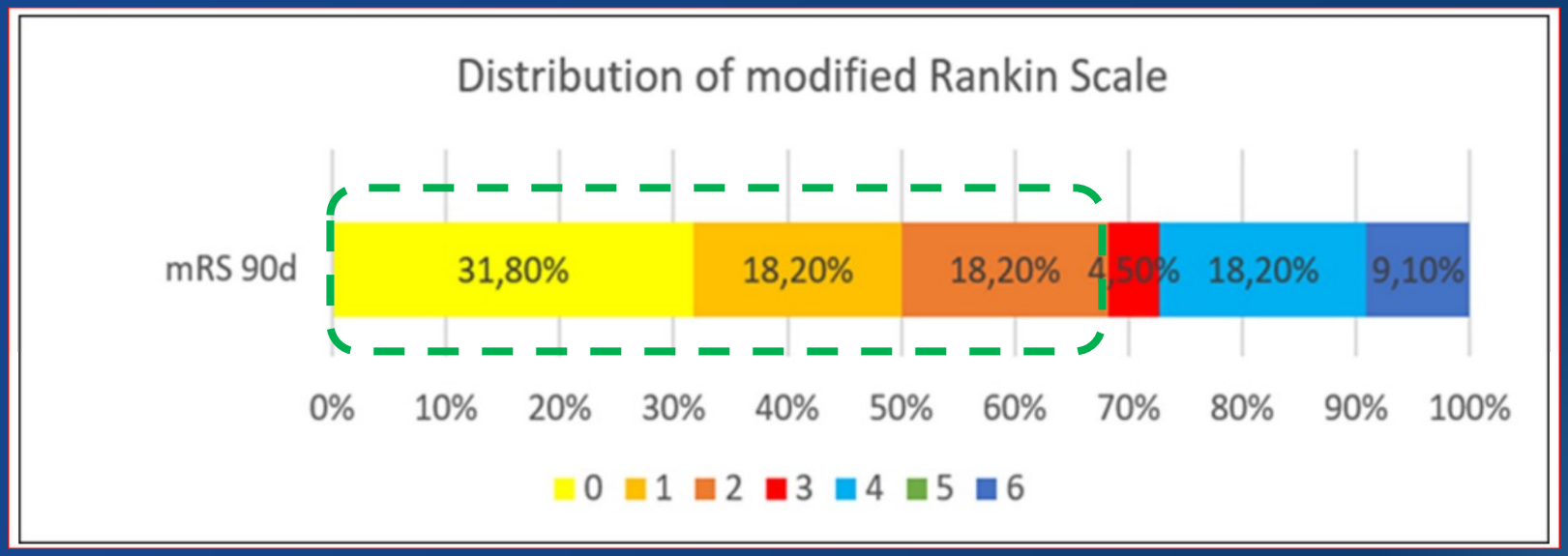
There were only **a**symptomatic side effects during hypothermia

- Asymptomatic bradycardia: 32%
- Nose bleed without need for intervention in one patient (5%)
- There were no disturbances in electrolytes, renal function, coagulation cascade or smell and taste function

COTTIS I - Outcome

Good outcome





68.2%

Matched-pair Analysis

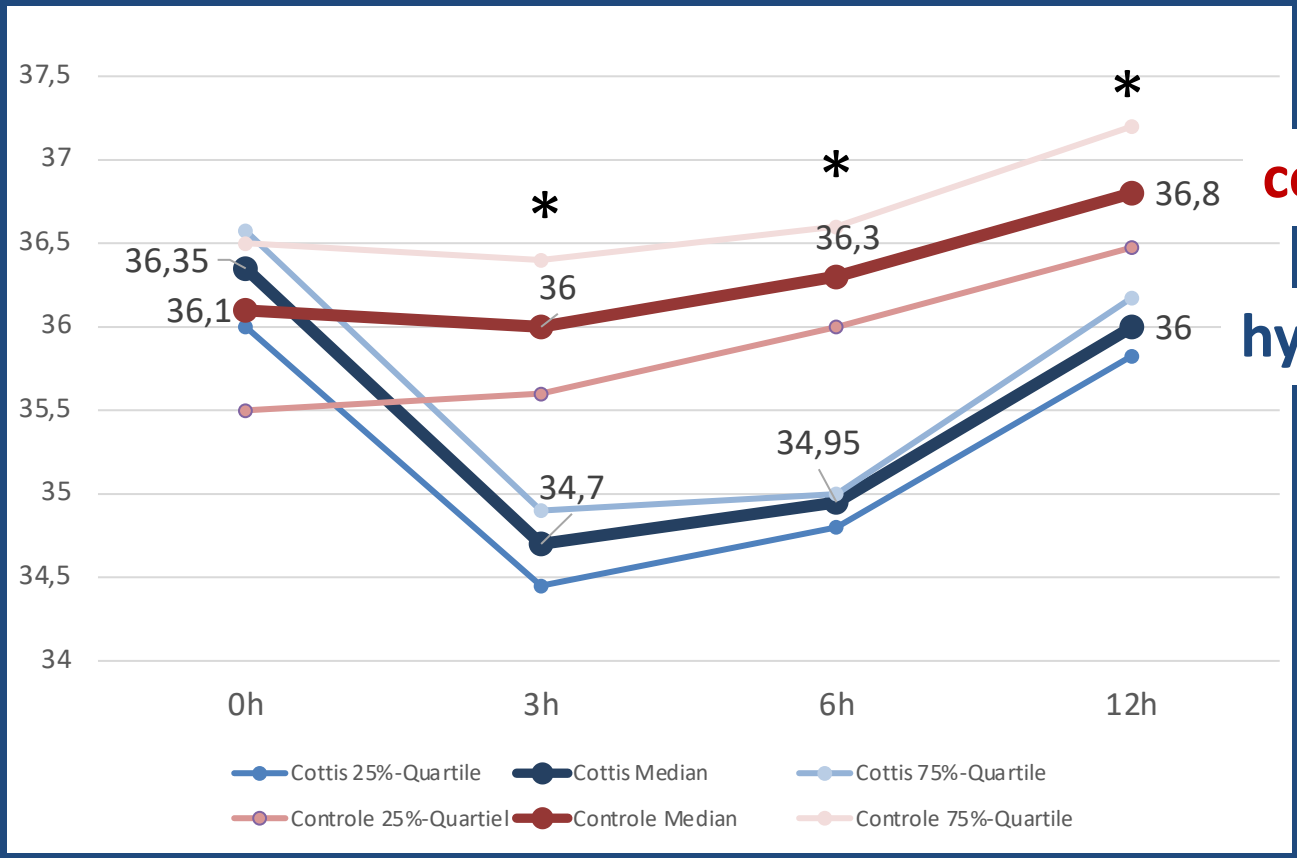
- **Intervention:** 22 COTTIS-1 patients
- **Controls:** stroke registry at the same site with 851 consecutive patients undergoing thrombectomy from 2015 until 2022.
- **Matching factors:** age, gender, NIHSS at admission, ASPECTS at admission, site of vessel occlusion and TICI- score.

Manuscript in preparartion

Patients characteristics

Variable	Control group n= 44	Hypothermia (COTTIS) n= 22
Age, median (range)	76 (70-84)	77 (70-83)
Occlusion site of vessel, n (%)		
Distal ICA / + M1	29 (66%)	15 (68%)
M2	7 (16%)	3 (14%)
Tandem occlusion	8 (18%)	4(18%)
ASPECTS, median (range)	9 (8,25-10)	9 (8,25-10)
NIHSS, median (IQR)	15 (12-18)	15 (12,5-19,75)
Reperfusion, n (%)		
TICI 0-2a	3 (7%)	2 (9%)
TICI 2b - 3	41 (93%)	20 (91%)

Course of temperature

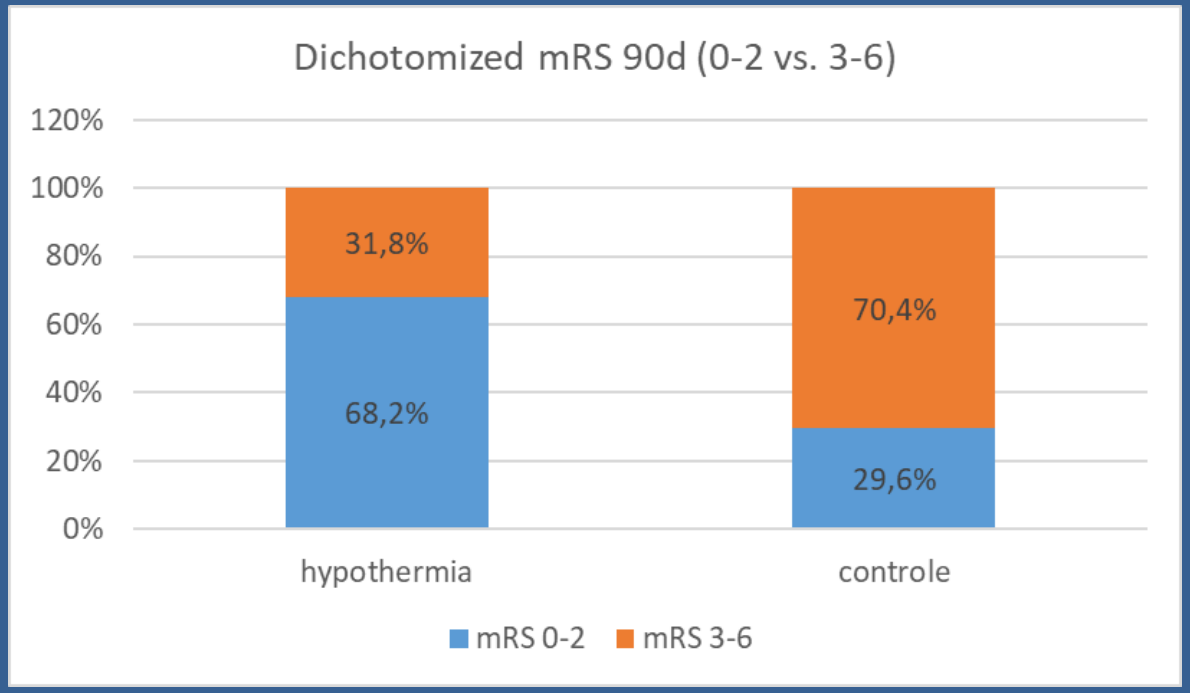


controls

hypothermia

* timepoints at 3h, 6h and 12h: **p<0.001**

Primary endpoint:
dichotomized mRS 0-2 vs 3-6 after 90days



Hypothermia: **OR 5.1 (1.69; 15.38) for good outcome**

p= .003

The promising results of the COTTIS I Study give us reasons to do the next step!

Ongoing Clinical Trial in Stroke – The COTTIS II

- 5 sites in Germany
- 400 patients (two interim analysis 100, 200)
- Expected start date: February 2024
- Expected completed recruitment : Within 2025 /2026
- Primary outcome: Improvement of neurological outcome measured by mRS at day 90 after stroke

European Commission
Horizon 2020
European Union funding
for Research & Innovation

Thank you for your attention!