Neuropsychological outcome after cardiac arrest

Rationale and description of a sub-study of The Target Temperature Management 2 Trial

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Conclusion

- This sub-study of the large pragmatic Target Temperature Management 2 Trial (TTM2-trial) will provide detailed knowledge on cognitive impairment from a holistic perspective, and test the validity of the shorter neurocognitive screening used in the main TTM2-trial, after out-of-hospital cardiac arrest (OHCA).
- Results may be used to guide clinical trials, inform patients and families, and design rehabilitation programs.

Introduction

Brain injury is the primary cause of mortality and morbidity in resuscitated cardiac arrest. The main aim of this recently started study (July 2018) is to provide detailed and longitudinal information on cognition after OHCA and its relationship to associated factors. There is a lack of longitudinal studies examining several cognitive domains post-cardiac arrest. A sub-study of the Target Temperature Management trial found impairments in memory, executive

functions or processing speed [1]. These domains are frequently impaired after cardiac arrest, but also the most commonly assessed [2].

A secondary aim is to utilize this information to test the validity of a neurocognitive screening battery used 6 months after OHCA in the TTM2-trial, assessing effectiveness of controlled hypothermia after OHCA. This screening battery could be practical to include in routine follow-up.

Table 1.

Tests used in the neuropsychological assessment at 7 and 24 months, grouped by cognitive domain

WAIS-IV, Wechsler Adult Intelligence Scale – Fourth Edition, D-KEFS, Delis-Kaplan Executive Function System; WMS-III, Wechsler Memory Scale – Third Edition.

Methods/design

This multi-center clinical study is a sub-study of the TTM2-trial. Approximately 7 and 24 months after OHCA, survivors ($n \approx 100$) at selected study sites will perform a standardized neuropsychological assessment including performance-based tests of cognition (duration 65-85 minutes) as well as questionnaires of behavioral and emotional function, fatigue, and insomnia. At 1:1 ratio, a control group of myocardial infarction (MI) patients but no occurrence of cardiac arrest will perform the same test battery. See flowchart in Fig. 1. Group

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Figure 1.
Flowchart of the study design.
TTM2, Target Temperature Management 2.

Cognitive domain	Test
Verbal	WAIS-IV Vocabulary
	D-KEFS Verbal Fluency
Visual/constructive	WAIS-IV Block Design
	WAIS-IV Matrix Reasoning
Working memory	WAIS-IV Digit Span
	WMS-III Spatial Span
Episodic memory	Rey Auditory Verbal Learning Test
	WMS-III Logical Memory
	Brief Visuospatial Memory Test-Revised
Processing speed	Trail Making Test A
	D-KEFS Color Word Interference Test 1-2
Executive functions	Trail Making Test B
	D-KEFS Color Word Interference Test 3

References

- [1] Lilja, G., Nielsen, N., Friberg, H., Horn, J., Kjaergaard, J., Nilsson, F., . . . Cronberg, T. (2015). Cognitive function in survivors of out-of-hospital cardiac arrest after target temperature management at 33 degrees C versus 36 degrees C. *Circulation*, 131(15), 1340-1349. doi:10.1161/circulationaha.114.014414
- [2] Moulaert, V. R. M. P., Verbunt, J. A., van Heugten, C. M., & Wade, D. T. (2009). Cognitive impairments in survivors of out-of-hospital cardiac arrest: A systematic review. *Resuscitation*, 80(3), 297-305. doi: 10.1016/j.resuscitation.2008.10.034