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Original Article

# The Thompson Encephalopathy Score and Short-Term Outcomes in Asphyxiated Newborns Treated With Therapeutic Hypothermia

**Patricia Thorsen MD [a], Martine C. Jansen-van der Weide PhD [b], Floris Groenendaal MD, PhD [c], Wes Onland MD, PhD [a], Henrika L.M. van Straaten MD, PhD [d], Inge Zonnenberg MD [e], Jeroen R. Vermeulen MD, PhD [f], Peter H. Dijk MD, PhD [g], Jeroen Dudink MD, PhD [h], Monique Rijken MD, PhD [i], Arno van Heijst MD, PhD [j], Koen P. Dijkman MD [k], Filip Cools MD, PhD [l], Alexandra Zecic MD [m], Anton H. van Kaam MD, PhD [a], Timo R. de Haan MD, PhD [a,*]**

[a] *Department of Neonatology, Emma Children's Hospital, Academic Medical Center, Amsterdam, The Netherlands*
[b] *Pediatric Clinical Research Office, Woman-Child Department, Emma Children's Hospital, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands*
[c] *Department of Neonatology, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, The Netherlands*
[d] *Department of Neonatology, Isala, Zwolle, The Netherlands*
[e] *Department of Neonatology, VU University Medical Center, Amsterdam, The Netherlands*
[f] *Department of Neurology, Maastricht University Medical Center, Maastricht, The Netherlands*
[g] *Department of Neonatology, University Medical Center Groningen, Groningen, The Netherlands*
[h] *Department of Neonatology, Erasmus Medical Center, Rotterdam, The Netherlands*
[i] *Department of Neonatology, Leiden University Medical Center, Leiden, The Netherlands*
[j] *Department of Neonatology, Radboud Medical Center, Nijmegen, The Netherlands*
[k] *Department of Neonatology, Maxima Medical Center Veldhoven, Veldhoven, The Netherlands*
[l] *Department of Neonatology, Vrije Universiteit Brussel, Brussels, Belgium*
[m] *Department of Neonatology, University Hospital Gent, Gent, Belgium*

ABSTRACT

**BACKGROUND:** The Thompson encephalopathy score is a clinical score to assess newborns suffering from perinatal asphyxia. Previous studies revealed a high sensitivity and specificity of the Thompson encephalopathy score for adverse outcomes (death or severe disability). Because the Thompson encephalopathy score was developed before the use of therapeutic hypothermia, its value was reassessed. **OBJECTIVE:** The purpose of this study was to assess the association of the Thompson encephalopathy score with adverse short-term outcomes, defined as death before discharge, development of severe epilepsy, or the presence of multiple organ failure in asphyxiated newborns undergoing therapeutic hypothermia. **METHODS:** The study period ranged from November 2010 to October 2014. A total of 12 tertiary neonatal intensive care units participated. Demographic and clinical data were collected from the "PharmaCool" multicenter study, an observational cohort study analyzing pharmacokinetics of medication during therapeutic hypothermia. With multiple logistic regression analyses the association of the Thompson encephalopathy scores with outcomes was studied. **RESULTS:** Data of 142 newborns were analyzed (male: 86; female: 56). Median Thompson score was 9 (interquartile range: 8 to 12). Median gestational age was 40 weeks (interquartile range 38 to 41), mean birth weight was 3362 grams (standard deviation: 605). All newborns manifested perinatal asphyxia and underwent therapeutic hypothermia. Death before discharge occurred in 23.9% and severe

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* Communications should be addressed to: Dr. de Haan; Department of Neonatology; Emma Children's Hospital; Academic Medical Center; Meibergdreef 9; 1100 DD Amsterdam, The Netherlands.
*E-mail address:* t.r.dehaan@amc.uva.nl

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epilepsy in 21.1% of the cases. In total, 59.2% of the patients had multiple organ failure. The Thompson encephalopathy score was *not* associated with multiple organ failure, but a Thompson encephalopathy score ≥12 was associated with death before discharge (odds ratio: 3.9; confidence interval: 1.3 to 11.2) and with development of severe epilepsy (odds ratio: 8.4; confidence interval: 2.5 to 27.8). **CONCLUSION:** The Thompson encephalopathy score is a useful clinical tool, even in cooled asphyxiated newborns. A score ≥12 is associated with adverse outcomes (death before discharge and development of severe epilepsy). The Thompson encephalopathy score is not associated with the development of multiple organ failure.

***Keywords:*** Thompson encephalopathy score, clinical assessment tool, hypoxic-ischemic encephalopathy, neonatology, outcomes
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## Introduction

Perinatal asphyxia leading to hypoxic-ischemic encephalopathy is an important cause of acquired neonatal brain injury in term neonates. Four million newborn infants experience birth asphyxia each year, accounting for an estimated 904,000 deaths and 42 million disability-adjusted life years, in spite of recent improvements in clinical care such as therapeutic hypothermia.[1]

Perinatal asphyxia is also associated with severe comorbidities such as neonatal seizures, postneonatal epilepsy, and multiple organ failure.[2-4]

Neonatal seizures can add neuronal damage to existing hypoxic-ischemic brain lesions.[5] The seizure severity and the number of antiepileptic drugs required to treat these seizures are both associated with an increased risk for adverse long-term neurodevelopmental outcomes.[6]

Multiple organ failure after perinatal asphyxia is a major complication of perinatal asphyxia and neonatal resuscitation associated with possible long-term sequelae or demise.[2,7]

The Thompson encephalopathy score is a clinical assessment tool, describing both neurological and vital parameters after neonatal resuscitation. Previous studies of nonhypothermic neonates demonstrated a high sensitivity and specificity for adverse short-term outcomes.[8]

Although not primarily developed for this end, the Thompson encephalopathy score is currently also used to select newborns for therapeutic hypothermia treatment. It is however unknown if and to what extent the Thompson encephalopathy score is associated with either short- or long-term outcomes in infants treated with therapeutic hypothermia, because it was developed before the introduction of this treatment and the application of therapeutic hypothermia significantly influences these outcomes.

The aim of this study was therefore to evaluate if, and to what extent, the Thompson encephalopathy score is associated with adverse short-term outcomes, using death before discharge as the primary outcome measure and the development of severe neonatal seizures or multiple organ failure as the secondary outcome measure in asphyxiated and resuscitated neonates treated with therapeutic hypothermia.

## Materials and Methods

### *Data collection and parental consent*

Data from the "PharmaCool" multicenter study were used for the current analysis. This observational study investigated the pharmacokinetics and dynamics of commonly used drugs in term asphyxiated infants treated with therapeutic hypothermia.[9] All infants participated on the basis of written informed consent, and the study was approved by the medical ethics committees of all participating centers. Twelve neonatal intensive care units participated and infants were included from November 2010 up until October 2014. All asphyxiated infants participating in this study received the standard of care (including therapeutic hypothermia) without any study-related intervention.[9] Newborns were eligible for the "PharmaCool" study if the following criteria were met: neonatal patient with a gestational age greater than 36 weeks, suffering perinatal asphyxia (i.e., ongoing resuscitation at 10 minutes after birth, cord-blood or 1-hour postnatal blood gas analysis indicating a pH less than 7.0 or base deficit >16 mmol/L) with clinical signs of moderate to severe encephalopathy, available postnatal Thompson encephalopathy score assessment and undergoing neuroprotective treatment by therapeutic hypothermia <6-hour postnatal in a neonatal intensive care setting. Exclusion criteria (for the main study) were congenital hepatic or renal pathology, no central venous line or arterial bloodstream access for noninvasive blood sampling procedures, absent written parental consent, or refusal to participate after informed consent interview.[9]

### *Baseline characteristics*

The following demographic and clinical data were collected for each individual patient: gestational age, birth weight, gender, first measured pH and base excess value, first measured arterial lactate, duration of resuscitation, duration of chest compressions, time elapsed from birth to first gasp, use of resuscitation medication in the delivery room, Thompson encephalopathy score, proven seizures, and background pattern on amplitude-integrated electroencephalograph (aEEG) or electroencephalograph at admission, need for inotropic medication, and the development of multiple organ failure. The medical center where the patient was admitted was also noted.[2] Because the Thompson encephalopathy score was used as the primary encephalopathy score, the Sarnat score data were not collected in this study.

Multiple organ failure definitions vary widely in the current literature. By consensus, multiple organ failure in the present study was defined as renal failure, liver failure, or a combination of both. Renal failure was defined as a serum creatinine concentration higher than 125 mmol/L or either anuria or oliguria (<1 mL/kg/hr) within the first 24 hours of life. Liver failure was defined as an increase in aspartate aminotransferase or alanine aminotransferase above 100 U/L.[2]

### *Thompson encephalopathy score*

The clinical neurological status of all included patients was evaluated with a neurological examination and the Thompson encephalopathy score within 2 hours after birth.[8] All pediatricians were trained in the correct use of the Thompson encephalopathy score, before the introduction of therapeutic hypothermia in the Netherlands. Patients qualified for therapeutic hypothermia at the participating neonatal intensive care units when admitted within 6 hours after birth, if the Thompson encephalopathy score was ≥7 (or if the attending neonatologist deemed the infant clinically encephalopathic) and if the criteria for perinatal asphyxia were fulfilled.

### *Outcome measures*

The primary outcome for this study was defined as death before discharge. The secondary outcomes were defined as (1) the development of severe seizures, defined as either the development of a status epilepticus during admittance or the need for two or more different