Intercenter Cost Variation for Perinatal Hypoxic-Ischemic Encephalopathy in the Era of Therapeutic Hypothermia

An N. Massaro, MD[1], Karna Murthy, MD, MSc[2,3], Isabella Zaniletti, PhD[4], Noah Cook, MD, MTR[5], Robert DiGeronimo, MD[6], Maria L. V. Dizon, MD, MSc[2], Shannon E. G. Hamrick, MD[7], Victor J. McKay, MD[8], Girija Natarajan, MD[9], Rakesh Rao, MD[10], Troy Richardson, MS, MPH, PhD[4], Danielle Smith, MD[11], and Amit M. Mathur, MD[10], on behalf of the Children's Hospital Neonatal Consortium*

Objective To quantify intercenter cost variation for perinatal hypoxic ischemic encephalopathy (HIE) treated with therapeutic hypothermia across children's hospitals.

Study design Prospectively collected data from the Children's Hospitals Neonatal Database and Pediatric Health Information Systems were linked to evaluate intercenter cost variation in total hospitalization costs after adjusting for HIE severity, mortality, length of stay, use of extracorporeal support or nitric oxide, and ventilator days. Secondarily, costs for intensive care unit bed, electroencephalography (EEG), and laboratory and neuroimaging testing were also evaluated. Costs were contextualized by frequency of favorable (survival with normal magnetic resonance imaging) and adverse (death or need for gastric tube feedings at discharge) outcomes to identify centers with relative low costs and favorable outcomes.

Results Of the 822 infants with HIE treated with therapeutic hypothermia at 19 regional neonatal intensive care units, 704 (86%) survived to discharge. The median cost/case for survivors was $58 552 (IQR $32 476-$130 203) and nonsurvivors $29 760 (IQR $16 897-$61 399). Adjusting for illness severity and select interventions, intercenter differences explained 29% of the variation in total hospitalization costs. The widest cost variability across centers was EEG use, although low cost and favorable outcome centers ranked higher with regards to EEG costs.

Conclusions There is marked intercenter cost variation associated with treating HIE across regional children's hospitals. Our investigation may help establish references for cost and enhance quality improvement and resource utilization projects related to HIE. *(J Pediatr 2016;173:76-83)*.

See editorial, p 15

Progress in neonatal intensive care has led to decreased mortality over the past several decades.[1-3] Therapeutic and technological advances in neonatal intensive care units (NICUs) come at high cost, estimated at $3000 per day ($40 000-$80 000 per hospitalization).[4] Understanding intercenter cost variation in resource-intensive conditions is an important aspect of improving quality of care and reducing healthcare costs. Although several studies have evaluated cost variability related to preterm birth,[5,6] few studies have evaluated other conditions requiring intensive medical care in the newborn period.

Perinatal hypoxic ischemic encephalopathy (HIE) represents a major cause of neonatal morbidity and mortality,[1,7,8] often requiring the highest level NICU care and interventions. Recent advances in neonatal neurocritical care, in conjunction with the establishment of therapeutic hypothermia as effective treatment within the past decade,[9-11] have transformed the standard of care for this devastating condition. We recently described expanded use of therapeutic

CHND	Children's Hospitals Neonatal Database	HIE	Hypoxic ischemic encephalopathy
CMI	Cost master index	ICU	Intensive care unit
CTC	Clinical transaction classification	iNO	Inhaled nitric oxide
ECMO	Extracorporeal membrane oxygenation	LC-FO	Low cost, favorable outcome
EEG	Electroencephalography	MRI	Magnetic resonance imaging
		NICU	Neonatal intensive care unit
		PHIS	Pediatric Health Information System

From the [1]Children's National Health System and the Department of Pediatrics, George Washington University School of Medicine, Washington, DC; [2]Ann and Robert H. Lurie Children's Hospital of Chicago and the Department of Pediatrics, Feinberg School of Medicine, Northwestern University, Chicago, IL; [3]Children's Hospitals Neonatal Consortium, Inc; [4]Children's Hospitals Association, Overland Park, KS; [5]Children's Hospital of Philadelphia and Department of Pediatrics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA; [6]Department of Pediatrics, University of Utah and the Primary Children's Medical Center, Salt Lake City, UT; [7]Department of Pediatrics and Children's Healthcare of Atlanta at Egleston, Emory University, Atlanta, GA; [8]All Children's Hospital, St Petersburg, FL; [9]Department of Pediatrics, Wayne State University, Children's Hospital of Michigan, Detroit, MI; [10]Department of Pediatrics, Washington University School of Medicine and St. Louis Children's Hospital, St. Louis, MO; and [11]Children's Hospital of Colorado and Department of Pediatrics, University of Colorado, Aurora, CO

*List of members of Children's Hospital Neonatal Consortium and site sponsors for the Children's Hospitals Neonatal Database is available at www.jpeds.com (**Appendix**).

The Children's Hospital Neonatal Consortium has partnered with Children's Hospital Association, Inc (Overland Park, KS) to design, launch, and maintain the database, as well as provide administrative and analytic support. I.Z. and T.R. are employees of the Children's Hospital Association. The other authors declare no conflicts of interest.

http://dx.doi.org/10.1016/j.jpeds.2016.02.033

hypothermia and high resource utilization in a contemporary cohort of newborns with HIE cared for at regional NICUs.[12] Intercenter cost variation and the related utilization of resources when treating infants with HIE, specifically in the era of therapeutic hypothermia, has not been previously evaluated.

Attention to rising healthcare expenditures has led to increasing hospital incentives toward cost-containment initiatives. The challenge remains balancing cost efficiency while preserving the quality of delivered care and, as importantly, promoting innovation to improve patient outcomes. A better understanding of factors influencing hospital costs for resource-intensive conditions is crucial for framing methods to advance such cost-effective care. To this end, we sought to estimate intercenter cost variation and identify key drivers of intercenter cost variation, in the treatment of neonatal HIE during the current era of NICU care. Secondarily, we aimed to relate intercenter cost variation estimates to clinically relevant outcomes, as identifying centers with low costs and favorable outcomes is a prerequisite to developing collaborative quality improvement initiatives to advance cost-efficient care for neonatal HIE.

Methods

Data from the Children's Hospitals Neonatal Database (CHND) and Pediatric Health Information System (PHIS) were linked at the patient level for these analyses. The CHND prospectively captures detailed clinical data from all infants admitted to NICUs at 27 regional children's hospitals. Participating centers comprised of NICUs with level 4 designation, >400 annual admissions, >25 inpatient beds, and >50% outborn population; the majority (>90%) of the NICUs have graduate medical training programs.[13] The Institutional Review Board at each participating institution approved participation in CHND and associated research studies. The PHIS database contains detailed hospital administrative and billing data from >40 pediatric institutions affiliated with the Children's Hospital Association (formerly Child Health Corporation of America); 25/28 CHND sites participate in PHIS. Among other elements, the PHIS database captures detailed resource utilization information of clinical services provided, but not their results, for each day during a patient's hospitalization. Data quality and reliability are affirmed through a joint effort between Children's Hospital Association, a data manager (Thomson-Reuters, Durham, North Carolina), and participating hospitals. Methods to assure data quality for both databases have been reported previously.[13-15] For example, PHIS data are accepted only when classified errors occur in fewer than 2% of a hospital's quarterly data. All data were de-identified and CHND and PHIS records were linked using uniquely assigned patient-specific identifiers that were unavailable to the investigative team. Infants with unlinked records were excluded from analysis.

The CHND was queried to identify newborns with HIE treated with therapeutic hypothermia at participating centers between July 2010 and August 2014. Inclusion criteria for the study were treatment with therapeutic hypothermia, admitted <24 hours of life, ≥36 weeks' gestation, ≥1800 g at birth, and presentation timing classified as perinatal. Infants were excluded if linkage to PHIS data was not possible or they had major congenital anomalies.

Cost Estimation

Standardized costs were calculated according to a cost master index (CMI) as previously described.[16] Briefly, costs for every clinical transaction classification (CTC) code in every participating hospital billing record were computed using hospital- and department-specific ratios of cost to charges after adjustment for wage and price index. All costs were inflated to 2012 dollars using the medical care services component of the consumer price index. A standardized unit cost for each CTC code was defined as the median of unit costs across all participating hospitals. Standardized unit costs for over 20 000 individual CTC codes were tabulated in a CMI, which was used to estimate hospitalization costs for every admission in the study cohort.

Total hospitalization costs were calculated by multiplying the CMI cost by the number of units for every CTC appearing in the hospital bills for each patient. Secondarily, costs were also calculated for selected groups of CTCs (ie, intensive care unit [ICU] bed, electroencephalography [EEG], laboratory, and neuroimaging) to determine the relative intercenter cost variation associated with these particular clinical encounters. These encounter types were selected because they were expected to represent a large proportion of total hospitalization costs and/or have significant variability across centers based on discussions of center practices within the focus group.

Clinical Outcomes

In order to put cost estimations in context with a measure of quality of care, 2 short-term outcome measures were defined. Favorable outcome was defined as survival with normal brain magnetic resonance imaging (MRI), as MRI performed after hypothermia treatment has been demonstrated to be a reliable predictor of neurodevelopmental outcome in babies with HIE.[17-19] Adverse outcome was defined as death or lack of independent oral feeding at discharge, as establishment of oral feedings prior to NICU discharge is associated with favorable neurodevelopmental outcomes in HIE.[20] Both outcomes were independently evaluated as the extremes of positive and negative outcomes, respectively, in order to evaluate consistency of results given the possibility of misclassification by a surrogate outcome measure.

Statistical Analyses

Study sample characteristics and cost distribution data were described using standard summary statistics after stratifying by mortality. Intercenter cost variation in standardized costs per case was evaluated using a mixed-effect regression model adjusting for severity of HIE, mortality, length of stay, use of