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Predicting Successful Neonatal Retrotransfer to a Lower Level of Care

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Up to 20% of newborn infants retro-transferred to a lower level of care require readmission to a higher-level facility. In this study, we developed and validated a prediction rule (The Rule for Elective Transfer between Units for Recovering Neonates) to identify clinical characteristics of infants at risk for failing retro-transfer.

In the 1970s, regionalization of neonatal care was proposed in the United States as a strategy to improve neonatal outcomes.^{1–6} Regionalization emphasizes the importance of matching patients with health care facilities that are able to provide an appropriate level of care.¹ The American Academy of Pediatrics (AAP) has defined levels of care for neonatal intensive care units (NICUs), ranging from Level I units (well newborn nurseries) to Level IV units (regional NICUs with pediatric surgical subspecialists).⁷ Recent changes in the landscape of health care in the United States, such as the establishment of Accountable Care Organizations, have brought the importance of responsibility for care within regional networks to the forefront.⁸ However, there has been a trend toward expansion of community hospital services to include care for sicker infants, effectively deregionalizing systems of neonatal care.^{9–13} This shift further emphasizes the need for neonatal transfers to be both appropriate and well-planned.

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Within perinatal care networks, 2 types of acute inter-hospital transport pertain to the ill neonate: maternal transfer prior to delivery¹⁴ or infant transport to a higher level NICU after delivery. Although a highly regionalized system favors the former, either situation results in admission to a NICU that may be distant from the intended birth hospital and family's home. Acute neonatal transport has been investigated widely, particularly with respect to extremely preterm and very low birth weight infants.^{5–15–19}

On the other hand, retro-transfer of infants to a lower level of care for convalescence following a period of intensive care is less well studied. Transferring infants who no longer require intensive care to community hospitals closer to home has many potential advantages, including decreased family stress, earlier involvement of primary providers, and more efficient use of resources within a care network.^{20–24} Prior studies suggest that transfer of stable, recovering infants to lower level special care nurseries is safe and cost effective,^{25,26} particularly when they will spend >1 week in the community hospital.²⁷ Although some cost savings may be offset by a trend toward longer length of stay in the community hospital,²⁶ others have shown that overall length of stay is similar to that of the referring NICU for low birth weight infants.^{23,28}

Times of high patient volume or acuity may create the need to identify which infants have least need for high-level ICU services and would be the best candidates for retro-transfer. These stressors not only affect decisions surrounding retrotransfer, but also discharge; indeed, discharge of moderately preterm infants is closely correlated with unit census.²⁹ There is also wide variation in the discharge timing for moderately preterm infants across regions of the United States and internationally,³⁰ which highlights an opportunity for improvement in practice that could be extended to decisions about retro-transfer timing.

Although retro-transfer of convalescing infants is an essential component of regionalized perinatal care systems, fostering the goal of matching patient need with hospital capability, up to 20% of infants transferred to a lower level of care require subsequent readmission to a higher level of care.³¹ There are no established standards to guide clinicians in determining when an infant in the NICU is appropriate for transfer back to a community hospital. This study aims to develop and validate a prediction rule to assist clinicians in determining an infant's readiness for transfer to a lower level of neonatal care that minimizes the risk for transfer back to a Level III or IV NICU.

METHODS

We sought to study predictors and outcomes for a cohort of infants who would be candidates for retrotransfer. However, data following transfer lacks sufficient granularity for construction of a prediction rule in most available databases. We therefore examined a cohort of infants who were medically appropriate for transfer but remained in a Level III NICU for non-medical reasons, such as parental preference, lack of appropriate community hospital closer to home, or lack of bed availability at the appropriate community hospital. Thus, we were able to model hypothetical thresholds for transfer for a cohort of infants with complete data who were theoretically similar to those infants transferred to community hospitals.

We performed a retrospective analysis of a cohort from a large tertiary perinatal center in Boston, Massachusetts. This institution maintains a research database that contains all infants cared for in the NICU and includes >18,000 NICU admissions. The patient population drawn from the database for this study comprised infants <37 weeks of gestation born between January 1, 2008 and December 31, 2014 admitted to our Level III NICU who were not transferred to another hospital for convalescent care. In order to examine the assumption that infants remaining in the NICU were similar to those who were transferred to community hospitals, we compared our study cohort with a cohort comprising all infants who were actually retro-transferred during the same time period. The study cohort was split randomly into a 2/3 training cohort for development of the prediction rule and a 1/3 validation cohort for testing the score.

The composite outcome measure was any episode of clinical decompensation that would require transfer back to a higher level of care if the infant were at a Level I or II nursery: respiratory escalation (intubation, non-invasive positive pressure ventilation, or continuous positive airway pressure with >2 liters of flow), defined as the presence of any criterion after an absence of these criteria for 7 days prior; >10 episodes of apnea in a day; and necrotizing enterocolitis (defined as 7 consecutive days of both nil per os status and antibiotic administration). Death in the home institution NICU and transfer to the children's hospital Level IV NICU (either for admission or specialized radiology procedures) were also considered to represent failure of convalescent care in a lower level setting.

We selected a comprehensive list of candidate predictor variables that reflect the functioning of several organ systems at the cusp of Level II and Level III care (as defined by the AAP),⁷ including length of time off positive pressure respiratory support (invasive ventilation, non-invasive positive pressure ventilation, or continuous positive airway pressure); length of time off high- or low-flow nasal cannula; length of time since last apneic event (with and without need for stimulation); length of time since weaning from an incubator or warming bed; and length of time since total parenteral nutrition was discontinued. All variables incorporating length of time were expressed in calendar days. Other covariates included in the initial analysis included gestational age, birth weight z-score, sex, race, multiple gestation, mode of delivery, presence and grade of intraventricular hemorrhage, and presence and stage of retinopathy of prematurity.

We started counting time-variant predictor variables from a first day of eligibility, which was the first day that an infant could be deemed eligible for transfer to a lower level of care, which they met all eligibility criteria: no positive pressure respiratory support, 5 apnea episodes per day, no central venous or arterial access, no parenteral nutrition, and no vasopressor medications. On each of the first 14 days after an infant became eligible for transfer, the time period during which decisions about retro-transfer would most likely be made, we analyzed candidate variables versus the outcome and chose those with an association of $P < .2$. We used a backward selection process to build individual multivariable logistic regression models to predict the outcome of transfer failure, using all of the significant and near-significant variables for each of the time points. Models were then validated using the validation cohort. Together, the models comprise the Rule for Elective Transfer between Units for Recovering Neonates (RETURN) algorithm. Model

discrimination in both training and validation cohorts was assessed using the area under the receiver operating characteristic (ROC) curve, and calibration was assessed with the Hosmer-Lemeshow test.³² All data were analyzed using SAS statistical software, version 9.4 (SAS Institute, Cary NC). Institutional review board approval was obtained prior to initiation of the study.

RESULTS

2288 patients were eligible for the study; of these, 2113 (92.4%) were discharged home from the home institution NICU, 121 (5.3%) were transferred to the children's hospital for surgical or subspecialty medical management, and 54 (2.4%) died in the home institution NICU. During the same time period, 605 infants were transferred out of the home institution NICU to community hospitals for convalescence. Baseline characteristics of the study cohort and those transferred to lower level hospitals are shown in Table 1. Compared with the transferred patient population, the study cohort had slightly higher mean gestational age and birth weight, and a lower proportion of multiple gestation, cesarean delivery, and white race.

Of the infants eligible for the study, 2178 met eligibility criteria for retrotransfer during the NICU stay. The mean post-menstrual age at the first day of eligibility was 34.2 weeks (standard deviation = 1.8 weeks). The reasons for failure after the first day of eligibility in the study cohort are shown in Table 2 (available at www.jpeds.com). Overall, there were 317 failures after transfer eligibility occurring in 276 (13%) infants. The most common reason was transfer to a Level IV NICU for admission or specialized radiology procedures (n=149), followed by apnea (n=79).

Results of the multivariable final models for each day after eligibility in the RETURN algorithm are shown in Table 3. Gestational age at birth was a significant predictor of transfer failure on all 14 days after eligibility criteria were met (OR 0.72–0.79). Birth weight z-score was included in models for 8 days, race in models for 5 days, time since last apnea (with and without stimulation) in models for 5 days and mode of delivery in models for 4 days. The presence of mild intraventricular hemorrhage had the highest odds ratio on the day for which it was a significant predictor (OR 2.34 on day 13). Infant sex, multiple gestation, retinopathy of prematurity, time since last use of mechanical ventilation or nasal cannula, time since last incubator use, and time since reaching full enteral feeds were not significant predictors in any models.

Areas under the ROC curve for each model for the development and validation cohorts are shown in Table 4 (available at www.jpeds.com). Overall, the model performance was relatively stable for all days after eligibility, with areas under the ROC curve of 0.77–0.83 in the validation cohort. The Hosmer-Lemeshow test demonstrated acceptable fit at all time points ($p > 0.05$) except days 4, 11, and 12 ($p = 0.0004$, $p = 0.035$, and $p = 0.049$, respectively).

DISCUSSION

We have shown that a set of readily accessible clinical variables can accurately predict which infants may fail transfer to a lower level NICU for convalescence after initial eligibility for transfer. Such a decision tool may be particularly helpful to the medical team

in determining which infants may safely be discharged to community hospitals in times of high census. By providing the information for each of the seven variables included in the models, clinicians could identify the likelihood of a failed retro-transfer for an individual patient at a given point in time; such results could be used either on a single day, or longitudinally over a period of days to determine the best timing for retro-transfer.

Recent innovations in care delivery, including the establishment of Accountable Care Organizations, have brought regionalization of neonatal care within hospital networks into the spotlight.⁸ The uncertain future of incentives in federal and state legislation makes understanding how to increase efficiency within systems of care more important than ever. As rates of preterm birth continue to rise in the United States,³³ identification of infants who can safely return to community hospitals will facilitate preservation of high-level NICU beds for the sickest infants.

Timely and appropriate transfer of stable infants to community hospitals also serves the purpose of bringing infants with potentially lengthy NICU stays closer to home. Previous studies have indicated that this is a cost-effective strategy for convalescent infants, especially when the length of stay in the community hospital is projected to be more than one week.^{26,27} Moreover, reducing the burdens associated with having an infant in a NICU far from home - including travel time and costs, time away from work and other obligations, and a potential need for lodging close to the NICU - may have far-reaching positive effects for an infant's family. Residing in a hospital closer to the family residence will also promote family integrated care and engagement, which is associated with better outcomes.³⁴ Thus, transferring newborns to community hospitals as soon as it is safe and appropriate may result in significant cost savings, both for the health care system and for families.

Although this prediction rule is intended primarily for determining which infants can be safely transferred to a lower level of care, its applications may extend beyond transfer decisions. Knowing which infants are more likely to fail transfer may serve to identify infants at higher risk of clinical deterioration. This information will not only alert clinicians to patients requiring closer monitoring, but may also help with staffing and bed availability decisions, at both the sending and receiving hospitals.

This study must be viewed in the context of its design. First, our NICU is located in a highly regionalized area with many qualified community hospitals, formally designated through a Certificate of Need process, in the surrounding region.³⁵ For this reason, our NICU transfers a high percentage of infants to community hospitals for convalescence. As the capabilities of the community hospitals in a system may drive the appropriateness of transfers, the generalizability of our findings may be limited in less regionalized areas. However, having established the utility of such scoring in one setting, it would be possible to derive a separate score for other environments, simply by changing the eligibility and outcome criteria. Second, our patient population was limited to infants who remained in our Level III NICU, which may theoretically result in selection bias. This decision was made for reasons of data availability, and because the majority of infants who remain in our NICU after meeting eligibility criteria do so because of parental preference or geography rather than medical need. In assessing whether these infants were different than their counterparts who were

transferred for convalescent care during the same time period, we found that the infants in our cohort were slightly less sick, suggesting that the prediction rule can identify potential transfer failures even in a relatively healthy population. Differences in elective transfer based on proximity to home may also reflect racial differences in urban and suburban population distribution. Future studies will be needed to evaluate how well the prediction rule performs in a cohort that is actually transferred, as well as to assess a wider range of outcomes for those who remain in a Level III unit through discharge compared with those who are retro-transferred, such as length of stay, growth and feeding outcomes, and parental engagement. Third, although the test characteristics fell within the moderately good range, it is likely that analysis on a larger or prospective cohort might identify opportunities to improve on the model. Finally, whether this rule is superior to clinician judgment was not tested; however, the intended purpose of this prediction rule is to be used as an adjunct to the overall team decision-making process surrounding transfers. As such, the contribution of the rule can be tailored to the individual situation of different NICUs.

The prediction rule described in this study may be useful in deciding which infants are likely to be able to successfully transfer to a lower level NICU while minimizing the risk of return to a Level III or IV NICU due to clinical decompensation. Such decisions are becoming more and more imperative in light of the changing health care landscape in the United States, and may contribute to health care cost savings and reduce economic and psychological burdens on families.

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Abbreviations

AAP	American Academy of Pediatrics
NICU	neonatal intensive care unit
ROC	receiver operating characteristic

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Table 1.

Patient characteristics of infants in the study cohort compared to infants transferred to the community.

Variable	Study Cohort (n=2288)	Transferred Patients (n=605)	<i>p</i> -value
Gestational age, weeks [mean (SD) ^a]	32.6 (3.1)	32.0 (2.5)	<0.001
Birth weight, grams [mean (SD)]	1914 (663)	1794 (536)	<0.001
Male sex [n (%)]	1238 (54)	317 (52)	0.45
Singleton [n (%)]	1385 (61)	330 (55)	0.008
Race [n (%)]			<0.001
White	1220 (59)	390 (74)	
Black	288 (14)	40 (8)	
Asian	227(11)	25 (5)	
Other	326 (16)	71 (14)	
Vaginal delivery (%)	797 (35)	156 (26)	<0.001

^aSD = standard deviation

Table 2.

Reasons for failure after the first day of eligibility.

Reason for Failure	Number (%)
Total failing after eligibility	276 (12)
Failures by reason	
Transfer to Level IV neonatal intensive care unit	149 (7)
Apnea	79 (3)
Ventilation	67 (3)
Necrotizing enterocolitis	19 (1)
Death	3 (0.1)

Reasons for failure are not mutually exclusive; that is, a single infant could have failed for multiple reasons after the first day of eligibility.

Table 3.

Logistic regression models for transfer failure for each day after eligibility.

Time Since Eligibility																													
Variable	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8		Day 9		Day 10		Day 11		Day 12		Day 13		Day 14		
	Mean	a OR (CI)	Mean	OR (CI)	Mean	OR (CI)	Mean	OR (CI)	Mean	OR (CI)	Mean	OR (CI)	Mean	OR (CI)	Mean	OR (CI)	Mean	OR (CI)	Mean	OR (CI)	Mean	OR (CI)	Mean	OR (CI)	Mean	OR (CI)	Mean	OR (CI)	
Gestational Age	0.27	0.77 (0.73, 0.81)	0.28	0.76 (0.72, 0.80)	0.29	0.75 (0.71, 0.80)	0.31	0.73 (0.69, 0.78)	0.34	0.71 (0.67, 0.76)	0.33	0.72 (0.68, 0.76)	0.32	0.72 (0.68, 0.77)	0.32	0.73 (0.69, 0.77)	0.31	0.73 (0.69, 0.78)	0.30	0.74 (0.69, 0.79)	0.31	0.74 (0.69, 0.79)	0.30	0.74 (0.69, 0.79)	0.24	0.79 (0.74, 0.84)	0.27	0.77 (0.72, 0.82)	
Birth weight z-score	-	-	-	-	-	-	-	-	0.28	0.75 (0.49, 0.95)	0.29	0.75 (0.49, 0.95)	-	-	0.30	0.74 (0.49, 0.92)	0.32	0.73 (0.48, 0.91)	0.32	0.73 (0.48, 0.91)	0.32	0.73 (0.48, 0.92)	0.34	0.71 (0.47, 0.90)	-	-	-	-	
White	0.70	2.02 (1.18, 3.44)	0.79	2.20 (1.26, 3.85)	0.76	2.14 (1.20, 3.80)	0.62	1.86 (1.04, 3.34)	0.53	1.69 (0.93, 3.09)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Asian	0.15	0.86 (0.38, 1.97)	0.01	0.99 (0.43, 2.30)	0.06	1.07 (0.45, 2.51)	0.26	0.77 (0.31, 1.92)	0.38	0.69 (0.26, 1.79)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Black	0.16	1.18 (0.48, 2.89)	0.22	1.24 (0.40, 2.60)	0.05	1.08 (0.48, 2.29)	0.10	0.91 (0.41, 2.02)	0.10	0.91 (0.40, 2.04)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Cesarean delivery	0.44	1.58 (1.04, 2.32)	0.43	1.54 (1.02, 2.33)	0.45	1.58 (1.02, 2.45)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.62	1.68 (1.03, 2.75)	-	-	-
Mild IVH ^c	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.85	2.34 (1.36, 4.02)	-	-
Severe IVH ^d	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.05	1.05 (0.18, 6.08)	-	-
Time since apnea requiring stimulation	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.34	0.71 (0.51, 0.98)	0.46	0.63 (0.44, 0.92)	0.39	0.68 (0.47, 0.97)	-	-	-	-	0.29	0.75 (0.58, 0.97)	0.21	0.81 (0.60, 0.94)
Time since apnea requiring stimulation	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.30	1.38 (1.0, 1.84)	0.42	1.52 (1.06, 2.17)	0.36	1.44 (1.02, 2.03)	-	-	-	-	0.26	1.30 (1.02, 1.66)	0.19	1.21 (1.05, 1.40)

A dash (-) denotes that the variable was not included in the model for that time point.

a OR - odds ratio

b CI - confidence interval

c IVH - intraventricular hemorrhage

d Mild IVH defined as grade I-II and severe IVH defined as grade III-IV

Table 4.

Area under the ROC curves for development and validation cohorts for all models.

Days Since Eligibility	Area Under the Receiver Operating Characteristic Curve (95% CI ^a)	
	Development Cohort	Validation Cohort
1	0.76 (0.72, 0.80)	0.77 (0.71, 0.83)
2	0.77 (0.73, 0.81)	0.78 (0.72, 0.83)
3	0.78 (0.74, 0.82)	0.77 (0.71, 0.83)
4	0.78 (0.74, 0.83)	0.79 (0.73, 0.85)
5	0.80 (0.76, 0.85)	0.80 (0.73, 0.86)
6	0.79 (0.75, 0.83)	0.83 (0.76, 0.89)
7	0.78 (0.74, 0.83)	0.82 (0.76, 0.89)
8	0.78 (0.73, 0.82)	0.82 (0.75, 0.89)
9	0.77 (0.73, 0.82)	0.82 (0.76, 0.89)
10	0.77 (0.72, 0.82)	0.82 (0.76, 0.89)
11	0.76 (0.71, 0.81)	0.81 (0.74, 0.88)
12	0.76 (0.71, 0.81)	0.83 (0.76, 0.89)
13	0.78 (0.73, 0.82)	0.80 (0.74, 0.87)
14	0.75 (0.71, 0.80)	0.82 (0.75, 0.88)

^a CI - confidence interval