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Center variability in risk of adjusted length of stay for very low birth weight infants in the Neocosur South American Network

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Abstract

Objectives: To develop a prediction model for hospital length of stay (LOS) in very low birth weight (VLBW) infants and to compare this outcome among 20 centers within a neonatal network.

Methods: Data from 7,599 infants with birth weights of 500-1,500 g born between the years 2001-2008 were prospectively collected. The Cox regression model was employed to develop two prediction models: an early model based upon variables present at birth, and a late one that adds relevant morbidities for the first 30 days of life.

Results: Median adjusted estimated LOS from birth was 59 days – 28 days after 30-day point of survival. There was a high correlation between models (r = 0.92). Expected/observed LOS varied widely among centers, even after correction for relevant morbidity after 30 days. Median observed LOS (range: 45-70 days), and postmenstrual age at discharge (range: 36.4-39.9 weeks) reflect high inter-center variability.

Conclusion: A simple model, with factors present at birth, can predict a VLBW infant's LOS in a neonatal network. Significant variability in LOS was observed among neonatal intensive care units. We speculate that the results originate in differences in inter-center practices.

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Introduction

The remarkable improvement of very low birth weight (VLBW) in infant survival observed over recent decades has been associated with an increased length of hospital stay (LOS). Both mortality and LOS are commonly used as quality of care measures for premature infants. In order to control for patient case-mix, comparisons among centers require procedures for risk adjustment. An unadjusted LOS has been described as a secondary outcome in several publications. Only a few studies have focused on risk adjusted LOS as their primary objective. Among such single center studies[1,2] are those limited to predicting LOS in that center, whereas multicenter studies[3-5] are able to predict and simultaneously compare LOS among several locations. These studies have revealed significant variations in LOS among neonatal intensive care units (NICUs).

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In the setting of a neonatal network, one of the available tools for quality improvement is to identify and compare factors that might influence variability between other centers. Identifying the better performing facilities and examining their practices may lead to identifying potential interventions that can improve VLBW infant outcomes. Because risk factors vary across sites, statistical models should be used to adjust outcomes to better compare center performances.[3,6] Despite documentation of variability of medical care during hospital stay, little is known about factors that might influence inter-NICU variations in LOS.[4] Evaluating medical practices for benchmarking purposes and quality of care comparisons require accurate and reliable risk models.[7]

Prolonged LOS for VLBW infants presents several medical, psychosocial, and economic challenges.[8] Each day of discharge delay accounts for a greater use of medical resources, contributes to NICU patient congestion, and carries consequently higher total costs. It also increases the risk of hospital-acquired morbidity, and may even have an adverse effect on parenting by increasing the period of parent and child separation.[9]

The Neocosur South American Network is a voluntary nonprofit association of NICUs from a group of South American countries (Argentina, Chile, Paraguay, Peru, and Uruguay), whose primary objective is to continuously improve neonatal health (http://sistemas.med.puc.cl/Neocosur/neocosur.asp). This network provides a continuously updated database that prospectively gathers information from all inborn VLBW infants (defined as birth weight from 500 g to 1,500 g) from the participating centers.

The purpose of this study was to develop LOS prediction models from among the hospital stay data of VLBW infants and compare the outcomes among 20 participating centers from the Neocosur neonatal network.

Methods

We included all inborn infants with birth weights (BWs) between 500 g to 1,500 g admitted to any of the 20 Neocosur Network centers from January 1, 2001 to December 31, 2008. This study was approved by the Ethics Committee of Pontificia Universidad Catolica de Chile.

Only inborn infants who were admitted and completed their stay (either by discharge home or death) at each NICU were included in the analysis. Infants who were transferred to other NICUs after admission were not included. Demographic, clinical, and outcome data were prospectively and routinely collected at the Neocosur Network centers using predefined diagnostic criteria and online data entries.

To evaluate factors that might influence or predict LOS, we developed the following two models:

- An early model including all cases, but one that only considers variables present at birth (before NICU admission) such as weight, postmenstrual age (PMA), 1 minute Apgar score, gender, presence of multiple births, antenatal steroid use, presence of congenital malformations, and prenatal care.
- To identify further factors affecting LOS, we developed a late model which considered additional relevant in-hospital morbidities or clinical events occurring during the first 30 days of hospitalization. These included elements such as: respiratory distress syndrome, mechanical ventilation, bronchopulmonary dysplasia (BPD), severe (Grade III or IV) intraventricular hemorrhage (IVH), early and late onset sepsis, patent ductus arteriosus (PDA), and necrotizing enterocolitis (NEC). This model included only those infants whose LOS was greater than 30 days. BPD was defined as oxygen therapy for 28 days or more after birth. The diagnosis of late onset sepsis was confirmed by isolating the organism in blood or cerebrospinal fluid after 72 hours of life. PDA was clinically diagnosed and, whenever possible, confirmed by echocardiography. The diagnosis of IVH was made either by cranial ultrasonogram or autopsy and was classified according to Papile et al.[10] NEC was confirmed by radiological pneumatosis (and/or perforation) surgery, or autopsy findings.

Thus, based upon these factors, we developed a prediction score for both models. Initially, univariate associations between infant-related variables and LOS were performed using a simple Cox regression model. Mortality was also included, and LOS was censored at individual time of death. Finally, a stepwise multiple Cox regression model was used to select the subset of variables that were independently associated with LOS.[11] A significance level of 5% was used to include each variable in the model.

After developing the final versions of the two models, we were able to estimate the risk-adjusted LOS by calculating regression coefficients in the Cox models and then applying them to a Kaplan-Meier estimate of the stay curve.[11]

Overall, network- and center- specific LOS functions were calculated by adjusting each infant's relative risk rate. The resulting curves for each center were directly comparable, since they were corrected by differences in patient mix. To compare center performances, we calculated the median LOS obtained from each risk-adjusted stay function (Observed/Expected LOS). PMA at discharge among survivors was also analyzed by risk quartiles (based on the early model) and compared among centers. The R software suite (R Foundation for Statistical Computing, Vienna, Austria) was used for all statistical calculations.[12]

Results

Data from 7,599 inborn infants were analyzed. BW was 1,101±271 g (mean±SD) and gestational age (GA) was 29.2±2.9 weeks (mean±SD). Female gender rate was 48.9% (44.9-57.9% range). Rate of antenatal steroids was 74.7% (42.1-91.1% range). Multiple gestations were present in an 18.4% (10.9-41.1% range). Rate of cesarean section was 52.1% (28.6-68.2% range). The percentage of Apgar score ≤ 3 at 1 minute was 19.5% (7.9-33.3% range) and at 5 minutes was 3.2% (0-6.7%). The total mortality rate was 24% with a range from 10 to 47.7%. The total incidence of BPD at 28 days was 23.4% (5.3-38.7% range).

Among the factors present at birth were: a greater BW and PMA, a higher 1 min Apgar score, antenatal steroid use, and female gender were all associated significantly with an increased possibility of being discharged or experiencing decreased LOS (Table 1).

BW was the most important factor, emphasizing that each additional 100 g increases the likelihood of being discharged from the hospital by 22.4%. The second factor (in order of importance) was PMA, indicating that every additional week in PMA increases the likelihood by 11.5% of being discharged. These significant factors were the same found while developing the Neocosur score for predicting mortality in VLBW infants,[7] with only "absence of life" threatening the position of "congenital malformations." Figure 1A shows the LOS curve from birth for the overall network.

Table 1 also shows the factors selected for the second regression model used to describe LOS after 30 days of survival. As expected, greater BW and PMA were associated with shorter LOS (or an increased possibility of being discharged), whereas the presence of BPD, NEC, severe IVH, sepsis, and PDA were associated with significantly longer LOS (or decreased chance of being discharged). BPD was the most significant factor decreasing the likelihood of being discharged by 46.2%. Figure 1B illustrates the LOS curve among infants who remained at the NICUs for more than 30 days within the overall network.

High variability in risk-adjusted median LOS was observed among the 20 Neocosur NICUs via calculations with both models. The overall median and range of LOS was 59 (45-70) days after birth, and 28 (18-38) days after the first 30 days of survival. Eight centers within the network were observed to have higher LOS than the median, 11 centers were below it, and one center had the same median as the median LOS for the entire network. This variability was still high when analyzing the remaining LOS after 30 days of survival. Figure 2 (2A and 2B) illustrate such high variability, showing how each individual center compares to the overall Neocosur network.

Most of the centers had important differences between the observed and expected LOS, some of them discharging their patients earlier (negative Observed/Expected LOS) and others exhibiting more prolonged hospital stays (positive Observed/Expected LOS), when compared to the overall

Table 1 - Factors present at birth and after 30 days of survival selected by a Stepwise Cox Regression Model to estimate length of hospital stay

Variables	Coefficient*	SE	Relative risk	
			Estimate*	95%CI
Factors present at birth				
Birth weight (per 100 g)	0.2024	0.0073	1.224	1.21-1.24
Gestational age (per week)	0.1093	0.0068	1.115	1.10-1.13
1-minute Apgar	0.0381	0.0067	1.039	1.03-1.05
Antenatal steroid use	0.0760	0.0157	1.079	1.05-1.11
Female gender	0.1009	0.0269	1.106	1.05-1.17
Factors after 30 days of survival				
Birth weight (per 100 g)	0.166	0.0075	1.18	1.16-1.20
BPD	-0.6205	0.0367	0.54	0.50-0.58
Gestational age (per week)	0.0482	0.0073	1.05	1.03-1.06
Late onset sepsis	-0.2377	0.0364	0.79	0.73-0.85
PDA	-0.1913	0.0328	0.826	0.77-0.88
NEC	-0.2821	0.0494	0.75	0.68-0.83
IVH (Grade III-IV)	-0.2818	0.0625	0.75	0.67-0.85

95%CI = 95% confidence interval; BPD = bronchopulmonary dysplasia; IVH = intraventricular hemorrhage; NEC = necrotizing enterocolitis; PDA = patent ductus arteriosus; SE = standard error.

* In a Cox's regression model, a positive coefficient and a relative risk (RR) > 1 are associated with a higher possibility of being discharged or experiencing lower LOS. On the other hand, a negative coefficient and a RR < 1 are associated to a lower probability of being discharged or risk of longer LOS.

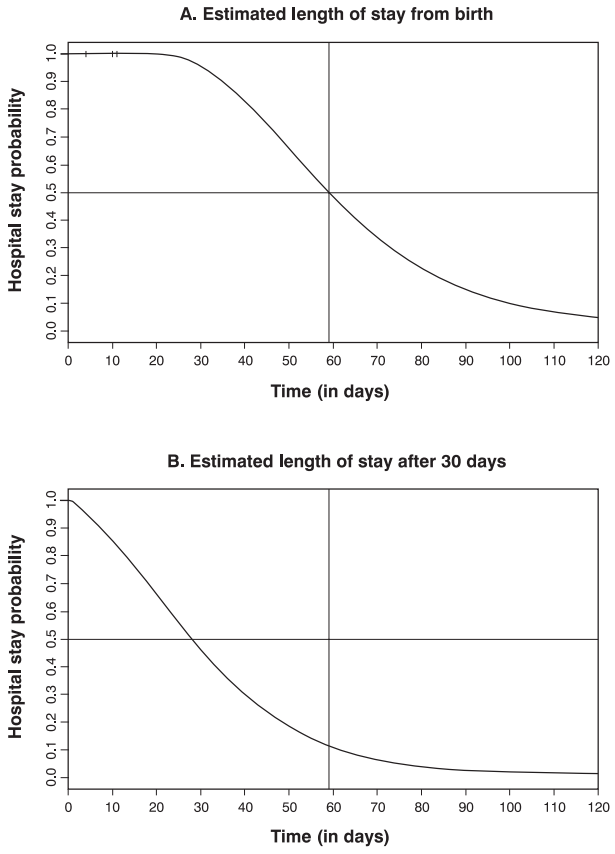

Figure 1 - Hospital stay probability (stay curve) in the Neocosur network from birth (Figure 1A) and after 30 days (Figure 1B) for different time points (in days). In each point of time, these probabilities represent the expected proportion of newborn infants that remain hospitalized. The vertical line marks where 50% (median) of the infants remain hospitalized

median risk-adjusted LOS of the network. When risk-adjusted LOS at birth and after 30 days were compared among the centers, a high correlation of r = 0.92 was found, showing that both are consistent indicators.

When we analyzed the median PMA at discharge, thus categorizing infants by risk quartiles using the LOS Neocosur score at birth, we also found significant variability among centers (Table 2).

Discussion

We developed two prediction models for risk-adjusted LOS in a population of VLBW infants. The early model included only predictors present at birth while the late one included relevant morbidity during the first 30 days of life.

In both models the most important variable for predicting LOS was BW, which is also the principal factor for predicting in-hospital mortality.[7] The correlation between LOS and BW has already been described.[4,13,14] The coincidence between the main factors for predicting both LOS and mortality reinforces the finding that infants delivered with lower BWs do not only have greater risks of mortality, but also face longer LOS if they survive. This is likely to be due to immaturity and also to a higher incidence of medical complications in this group of patients. In fact, in the late model the most important factors for LOS prediction, other than BW, were BPD and sepsis. It is of interest that the use of prenatal steroids was also a factor associated with a shorter LOS, giving weight to the other beneficial effects associated with this therapy that have been widely reported in the literature.[15]

When we compared the observed versus expected LOS at each NICU, we found high variability among centers and important differences in LOS between those NICUs

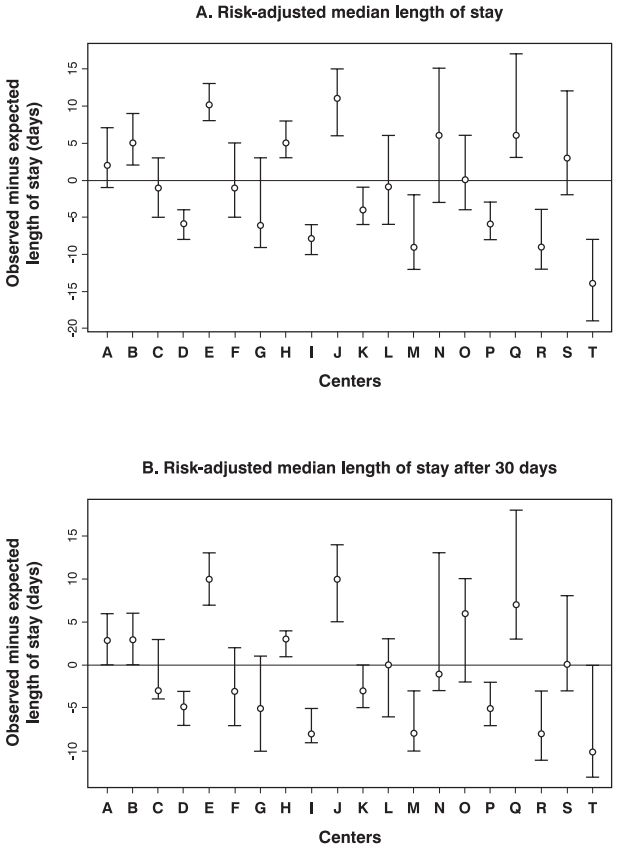

Figure 2 - Observed minus expected hospital length of stay (in days) and 95% confidence intervals for the 20 neonatal intensive care units calculated from birth (Figure 2A) and after 30 days (Figure 2B). The horizontal line shows where the adjusted hospital length of stay of an individual center is equal to the entire Neocosur network

for infants with similar risks. This variability in LOS among centers was not significantly reduced after adjustments based on the late model at a later time during hospital stay. Our interpretation of this finding is that other factors, such as center practices, may better explain this variability. Risk-adjusted LOS also varied significantly between NICUs with regard to PMA at discharge. The interval between the earliest and latest discharging NICU was 3 to 4 weeks of PMA in all risk quartiles. Additionally, when risk quartiles were compared, we observed a consistent difference in PMA between the lowest and highest risk groups. As expected, high-risk infants faced longer LOS and, consequently, were discharged at higher PMAs. However, in intermediate risk quartiles, this pattern was not always consistent at all the centers, suggesting inter-NICU variability in infants with the same risks.

Factors that might influence inter-NICU variability are differences in medical care during hospitalization, different discharge policies, in-hospital morbidities, population differences, availability of home care, and community support. Eichenwald et al.[4] studied LOS in a homogeneous healthy population of premature infants delivered at 30.0 to 34.6 weeks of gestation. PMA at discharge varied between 35.2 to 36.5 weeks. The authors concluded that inter-NICU variation in recorded maturational milestones (mature feeding behavior, cessation of apnea, and bradycardia events) was the most significant influence on LOS. They also suggest that variation in care practices, rather than differences in clinical characteristics, contributed to differences in discharge timing between hospitals.[4] In another study, Cotten et al.[16] analyzed center-independent factors associated with prolonged hospital stays (PHS) in extremely premature infants, and concluded that chronic lung disease, surgical NEC, and late onset sepsis are variables that contribute to PHS. Similarly, in a previous publication from Neocosur,[17] we also found longer LOS in VLBW infants who developed BPD compared to those who did not.

A recent NICHD Network study compared several models for predicting time of hospital discharge for extremely preterm infants (less than 27 weeks of gestational age), and concluded that prediction of early or late discharge is poor when only perinatal factors are considered. However, predictability can substantially improve with knowledge of later-occurring morbidities.[18] In contrast, the present study shows that the adjusted early prediction model is strongly correlated (r = 0.92) with the late corrected model at 30 days of life. Although the late model yielded more accurate predictions, our data show that center variability in LOS remains similar even after adjusting the model with a selection of major morbidities (BPD, IVH III-IV, NEC**,** PDA, and late onset sepsis) developed during the first 30 days of hospital stay. One explanation for this high correlation is that risk factors present at birth may also determine the appearance of later in-hospital complications. However, the persistence of LOS differences between centers, regardless of corrections by risks or major morbidities, suggests that local center factors play a role in determining final LOS. We could speculate that differences in clinical management among centers may have constituted the principal factor influencing LOS variability in our study. We must also consider that centers in the NIH network are quite homogeneous, while Neocosur centers differ greatly in terms of resources, size, case-mix, within other potentially relevant factors. Finally, we should consider that discharge timing of premature infants is a complex process influenced not only by medical factors, but also by nonmedical issues such as primary healthcare and organizational delays, discharge planning delays, as well as family circumstances, among other factors.

Another limitation in this study was the fact that information regarding the various factors that can delay discharge, such as duration of apnea or feeding problems, was not available. Also, as mentioned previously, the centers in this network have important variations in other major outcomes. The published experience in all networks shows large outcome variability. Studying these institutional differences is beyond the scope of this study.

Table 2 - Postmenstrual age at discharge by risk quartiles (based on the Neocosur score, 1 = lower risk, 4 = higher risk) and the total of each center

	Risk quartiles				
NICU	**1**	**2**	**3**	**4**	**Total**
A	37.9	37.4	38.9	40.6	38.1
B	37.3	36.9	38.3	40.7	38.0
C	38.9	38.0	38.0	42.2	38.4
D	38.0	36.7	38.1	39.1	37.7
E	39.3	38.6	39.3	41.0	39.3
F	36.7	37.0	38.1	40.9	37.4
G	38.1	37.6	39.7	39.6	38.6
H	39.0	38.4	40.1	39.9	39.0
I	36.9	36.4	36.6	39.0	36.9
J	38.7	39.0	38.9	42.6	39.2
K	37.7	36.6	37.7	40.1	37.6
L	37.4	36.6	37.9	39.9	37.7
M	37.0	36.0	37.1	39.4	37.1
N	39.1	38.1	39.1	39.7	38.6
O	36.3	36.9	38.3	39.9	37.7
P	37.4	37.1	37.7	39.1	37.4
Q	40.1	39.3	39.9	40.6	39.9
R	36.9	37.4	36.7	39.5	36.9
S	37.9	37.9	38.6	41.4	38.4
T	36.1	36.2	37.4	36.7	36.4
Total network	37.9	37.3	38.3	40.1	38.0

NICU = neonatal intensive care units.

This, however, is a true representation of the reality of our region. This study benefits from the inclusion of a large multicenter population, in contrast to several studies that referred to one center only, and this allows us to perform a benchmarking analysis.

We conclude that LOS for VLBW infants can be successfully predicted in a neonatal network by using two prediction models: one at birth and another at 30 days of life. The early model has the advantage of constituting a simple infant score with factors observed at birth. Thus, early estimations of LOS can be useful for families and medical care providers. Our models also enable us to predict and compare LOS among centers. The results reveal significant inter-NICU LOS differences, entailing an important economic impact, which is highly relevant in a region with limited resources. Center comparisons may also contribute to strategic planning that might safely reduce LOS for VLBW infants in some centers thus decreasing hospitalization costs and risks associated for prolonged hospitalization in this vulnerable BW group.

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