CLINICAL SCIENCE

# Predictive score for clinical complications during intra-hospital transports of infants treated in a neonatal unit

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**OBJECTIVE:** To develop and validate a predictive score for clinical complications during intra-hospital transport of infants treated in neonatal units.

**METHODS:** This was a cross-sectional study nested in a prospective cohort of infants transported within a public university hospital from January 2001 to December 2008. Transports during even (n = 301) and odd (n = 394) years were compared to develop and validate a predictive score. The points attributed to each score variable were derived from multiple logistic regression analysis. The predictive performance and the score calibration were analyzed by a receiver operating characteristic (ROC) curve and *Hosmer-Lemeshow* test, respectively.

**RESULTS:** Infants with a mean gestational age of 35 ± 4 weeks and a birth weight of 2457 ± 841 g were studied. In the derivation cohort, clinical complications occurred in 74 (24.6%) transports. Logistic regression analysis identified five variables associated with these complications and assigned corresponding point values: gestation at birth [<28 weeks (6 pts); 28-34 weeks (3 pts); >34 weeks (2 pts)]; pre-transport temperature [<36.3°C or >37°C (3 pts); 36.3-37.0°C (2 pts)]; underlying pathological condition [CNS malformation (4 pts); other (2 pts)]; transport destination [surgery (5 pts); magnetic resonance or computed tomography imaging (3 pts); other (2 pts)]; and pre-transport respiratory support [mechanical ventilation (8 pts); supplemental oxygen (7 pts); no oxygen (2 pts)]. For the derivation and validation cohorts, the areas under the ROC curve were 0.770 and 0.712, respectively. Expected and observed frequencies of complications were similar between the two cohorts.

**CONCLUSION:** The predictive score developed and validated in this study presented adequate discriminative power and calibration. This score can help identify infants at risk of clinical complications during intra-hospital transports.

**KEYWORDS:** Risk index; transportation of patients; infant newborn; neonatal intensive care units; risk factors.

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## INTRODUCTION

During neonatal care, many diagnostic and treatment procedures require transporting newborns from the neonatal intensive care unit (NICU) to different hospital areas. Despite the high frequency of such transports, there are few studies assessing the risks posed to newborns and older infants.[1]

For adults and older children, clinical complications of intra-hospital transports may occur at a similar frequency to inter-hospital transports.[2] Studies of pediatric patients have demonstrated that clinical complications, such as hypothermia and variations in heart rate and blood pressure, occur in 70% of intra-hospital transports and are associated with the severity of underlying disease and transport duration.[3-4] Vieira *et al.* (2007) reported a prevalence of hypothermia in 17% of intra-hospital NICU transports; the factors associated with developing hypothermia were prolonged transports, body weight less than 3500 g during transport and presence of a central nervous system (CNS) malformation.[1]

A tool to predict the risk of clinical complications during intra-hospital transport could help to plan specific preventive measures. It would identify cases when the risk versus benefit ratio of the transport is deemed unfavorable, postponing the move until better clinical or technical conditions are obtained. The predictive indices presently available in clinical neonatal practice were designed to assess mortality rates during inter-hospital transport;[5-7] however, there are no published indices to assess the risk of clinical problems during intra-hospital transport.

The aim of the present study was to develop and validate an index that predicts clinical complications during the intra-hospital transport of infants hospitalized in a neonatal unit.

## SUBJECTS AND METHODS

This cross-sectional study nested in a prospective cohort was carried out at the NICU of the Federal University of São Paulo (Brazil). All intra-hospital transports of NICU patients occurring Monday through Friday 8 AM and 5 PM between January 2001 and December 2008 were included in the study. A specific team, consisting of a second-year neonatal fellow and a neonatal nurse or nurse technician trained in neonatal intensive care, performed all transports. The fellow was trained in neonatal resuscitation and advanced life support procedures and had participated in a neonatal transport course during the first fellowship year, which included 20 hours of practical and theoretical activities.

A single patient could be included several times in the study, provided he/she was transported on different days. The patients were always moved in double-wall transport incubators with a pulse oximeter and battery-powered infusion pumps with respiratory support via an electronic mechanical ventilator.

We prospectively collected patients' characteristics (gender, gestational age, birth weight, age and weight at the time of transport, vital signs, underlying disease and respiratory support before transport) and transport characteristics (transport date, destination and duration from leaving the NICU until return).

Vital signs were collected prior to transport, during the transport and upon return to the NICU. Definitions were determined as follows: hypothermia (axillary temperature <36℃), hyperthermia (temperature >37.5℃),[8] bradycardia (HR<80 bpm), tachycardia (HR>180 bpm),[9] hypoxemia (oxygen saturation <88%), hyperoxia (saturation >95%), desaturation (persistent 5% reduction in baseline oxygen saturation),[3,10] hypertension (mean blood pressure >75 or 95 mmHg in newborns and older infants, respectively), hypotension (mean blood pressure < the gestational age in weeks plus 5 in newborns and <55 mmHg in older infants),[11] apnea (respiratory pause >20 seconds, with or without bradycardia or hypoxemia),[12] hypercapnia ($pCO_2$ >45 mmHg) and hypocapnia ($pCO_2$ <35 mmHg).[13] Capillary glucose levels were collected prior to transport, every 60 minutes during transport and immediately upon the patient's return to the NICU; hypoglycemia and hyperglycemia were defined as capillary glucose <40 mg/dL and >150 mg/dL, respectively.[14]

The fellow prospectively recorded clinical complications during intra-hospital transport on specifically designed transport forms. The transport data from even years (2002, 2004, 2006 and 2008) were used to determine the relevant variables and respective scores to design the tool to assess the risk of clinical complications during intra-hospital transport. The score was validated using transport data from odd years.

Score building was based on patient demographic and clinical variables, characteristics of the transports and the outcome of interest (presence of one or more complications - Table 2). The following variables were considered during the univariate analysis: gestational age at birth; postnatal age at transport; weight at transport; physiological status immediately before the transport (body temperature, heart rate, mean blood pressure and capillary glucose); underlying diseases; transport destination; and need for oxygen therapy/mechanical ventilation prior to the transport. The following continuous variables were grouped to design the risk score: gestational age (<28 weeks; 28 to 34 weeks; >34 weeks); birth weight and weight at transport (<1000 g; 1000 to 2499 g; >2500 g); postnatal age at transport (<7 days; 7 to 28 days; >28 days); body temperature (<36.3℃ or >37℃; 36.3-37℃); underlying diseases (CNS malformation; other); destination (surgery; magnetic resonance or computed tomography imaging; other); and respiratory support (mechanical ventilation; supplemental oxygen; no oxygen therapy). Clinically significant variables and variables with a p-value <0.20 in the univariate analysis were introduced into the multiple logistic regression model. Modeling was performed by backward stepwise regression until a final model with $p<0.05$ for the likelihood ratio was attained. The weighted risk index for clinical complications used the derived multiple logistic regression analysis coefficients. These coefficients were transformed into points by multiplying the value by 2 and rounding to the nearest whole number.

Predictive performance and calibration of the developed model were determined for the validation score. Power to discriminate transports that carry risk of clinical complications was determined by the area under the receiver operating characteristic (ROC) curve, which was considered adequate if the area under the curve was >0.7.[15-17]

**Table 1.** Patient and transport characteristics in the derivation and validation cohorts.

| | Derivation cohort | Validation cohort |
|---|---|---|
| Number of transports | 301 | 394 |
| Number of patients | 209 | 172 |
| Clinical complications | 74 (24.6%) | 85 (21.6%) |
| Male gender | 126 (60.3%) | 110 (64.0%) |
| Gestational age <28 weeks | 18 (6.0%) | 26 (6.6%) |
| Gestational age 28-34 weeks | 68 (22.6%) | 88 (22.3%) |
| Birth weight <1000 g | 24 (8.0%) | 29 (7.4%) |
| Birth weight 1000-2499 g | 113 (37.5%) | 154 (39.1%) |
| Age at transport <7 days | 99 (32.9%) | 100 (25.4%) |
| Age at transport 7-28 days | 100 (33.2%) | 143 (36.3%) |
| Weight at transport <1000 g | 26 (8.6%) | 4 (1.0%) |
| Weight at transport 1000-2499 g | 90 (29.9%) | 123 (31.2%) |
| Pre-transport temperature <36.3 or >37.0℃ | 83 (27.6%) | 108 (27.4%) |
| Pre-transport temperature 36.3-37.0℃ | 36 (12.0%) | 52 (13.2%) |
| Pre-transport heart rate (mean±SD) | 141±16 | 139±15 |
| Pre-transport MBP (mean±SD) | 51±10 | 54±11 |
| Pre-transport oxygen saturation (mean±SD) | 96±2 | 95±3 |
| Pre-transport glucose (mean±SD) | 92±18 | 97±22 |
| CNS malformation | 95 (31.6%) | 119 (30.2%) |
| Gastrointestinal malformation | 35 (11.6%) | 46 (11.7%) |
| Transport for surgery | 64 (21.3%) | 88 (22.3%) |
| Transport for MRI or CT scan | 101 (33.6%) | 154 (39.1%) |
| On mechanical ventilation at transport | 36 (12.0%) | 84 (21.3%) |
| On supplemental oxygen at transport | 74 (24.6%) | 67 (17.0%) |
| Transport duration >120 minutes | 98 (32.6%) | 123 (31.2%) |
| Transport duration 60-120 minutes | 94 (31.2%) | 133 (33.8%) |

Oxygen saturation in %; MBP: mean blood pressure in mmHg; glucose in mg/dL; CNS: central nervous system; MRI: magnetic resonance imaging; CT: computed tomography.

**Table 2.** Clinical complications during intra-hospital transports in the derivation and validation cohorts.

| | Derivation cohort (n = 301) | Validation cohort (n = 394) |
|---|---|---|
| Hypothermia | 40 (13.3%) | 48 (12.2%) |
| Hyperoxia | 22 (7.3%) | 18 (4.6%) |
| Desaturation | 12 (4.0%) | 16 (4.1%) |
| Need for increasing respiratory support | 5 (1.7%) | 11 (2.8%) |
| Hyperglycemia | 1 (0.5%) | 2 (0.5%) |
| Hyperthermia | 6 (2.0%) | 3 (0.8%) |
| Apnea | - | 4 (1.0%) |
| Bradycardia | 2 (0.7%) | 2 (0.5%) |
| Tachycardia | - | 2 (0.5%) |
| Hypoglycemia | 1 (0.3%) | 1 (0.3%) |
| Bronchospasm | - | 1 (0.3%) |
| Total | 89 (29.6%) | 108 (27.4%) |

Calibration was determined by the *Hosmer-Lemeshow* goodness-of-fit test and considered appropriate if $p>0.05$.[18] Statistical analysis was performed using SPSS for Win/v.17.0 (USA).

This study was approved by the Ethical Committee of the Federal University of São Paulo, Brazil.

## RESULTS

From January 2001 to December 2008, 381 infants were transported over 695 intra-hospital transports with a mean gestational age of $35.3 \pm 3.9$ weeks (range: 22 to 42 weeks) and birth weight of $2457 \pm 841$ g (range: 580 to 4400 g); 236 (61.9%) infants were males. At least one clinical complication occurred during 159 transports (22.9%); hypothermia (12.7%), hyperoxia (5.6%), desaturation (4.1%) and need for increase the respiratory support (2.3%) were the most frequent complications.

No patients developed hypoxemia, hypocapnia or hypercapnia and hypotension or hypertension during transport. the characteristics of the transports carried out in the derivation and validation cohorts and the distribution of the clinical complications in the two cohorts are shown in Tables 1 and 2, respectively.

In the final multiple regression model, the dependent variable ''presence of at least one clinical complication during the intra-hospital transport'' was associated with gestational age, pre-transport body temperature, underlying disease, transport destination and type of respiratory support. A score was attributed to each variable present in the final multiple regression model based on the odds ratios (Table 3).

The predictive performance of the developed score discriminating intra-hospital transport with increased risk for clinical complications was tested by the ROC curve. Each transport in the even years was scored based on the variables derived from the final regression model (Table 3). These values were used to build a ROC curve, with an area under the curve of 0.770 (95% CI: 0.710 to 0.830). Another ROC curve built from the data derived from the validation cohort (transports in odds years) showed an area under the curve of 0.712 (95% CI: 0.649 to 0.774).

Because a high proportion of neonates with malformations were present in the two cohorts, the discriminative power of the developed score was also tested in a subgroup of infants of the validation cohort without any malformations (n = 158). The area under the ROC curve from this validation cohort subgroup was 0.708 (95% CI: 0.600-0.815), similar to the validation cohort with all transports.

To test the calibration of the developed score, the frequency of clinical complications in the derivation cohort was compared to the observed frequency in the validation cohort according to score intervals. There were similar frequencies of clinical complications in the derivation and validation cohorts in transports that, respectively, scored <13 points (8.0% vs. 9.0%); 13-15 points (24.3% vs. 17.0%); 16-20 points (38.0% vs. 35.0%) and >20 points (57.1% vs. 52.4%). Comparison of the expected and observed frequency of clinical complications by the *Hosmer-Lemeshow* goodness-of-fit test revealed a p-value of 0.827, indicating a good calibration of the predictive score (Table 4).

## DISCUSSION

This is the first study that developed and validated a score to predict the presence of clinical complications during intra-hospital transports of infants hospitalized in neonatal units. Previously, predictive scores for neonatal transports have been designed to assess the risk of mortality in inter-hospital transported infants. *The Transport Risk Index of Physiologic Stability (TRIP)* uses physiological parameters such as temperature, breathing status, blood pressure and response to noxious stimuli; it was validated to assess the

**Table 3.** Final model of the multiple logistic regression analysis for clinical complications during intra-hospital transports and the derived score.

| Variables | OR | 95% CI | p | Score |
|---|---|---|---|---|
| Gestational age <28 weeks | 3.18 | 1.01-10.05 | 0.049 | 6 |
| Gestational age 28-34 weeks | 1.50 | 0.75-3.00 | 0.248 | 3 |
| Gestational age >34 weeks | 1.00 | Reference | | 2 |
| Pre-transport temperature <36.3°C or >37.0°C | 1.53 | 0.82-2.87 | 0.184 | 3 |
| Pre-transport temperature 36.3-37.0°C | 1.00 | Reference | | 2 |
| CNS malformation | 1.86 | 0.93-3.71 | 0.078 | 4 |
| Other diseases | 1.00 | Reference | | 2 |
| Transport for surgery | 2.34 | 1.04-5.27 | 0.036 | 5 |
| Transport for MRI or CT scan | 1.237 | 0.60-2.56 | 0.567 | 3 |
| Other destinations | 1.000 | Reference | | 2 |
| Mechanical ventilation | 3.98 | 1.52-8.93 | <0.001 | 8 |
| Supplemental oxygen therapy | 3.26 | 1.72-6.17 | 0.004 | 7 |
| No oxygen therapy | 1.00 | Reference | | 2 |

MRI: magnetic resonance imaging; CT: computed tomography. *Hosmer-Lemeshow test*: p = 0.443.

**Table 4.** Expected and observed frequency of clinical complications according to the predictive score intervals.

| | Expected frequency | | Observed frequency | | Total | |
|---|---|---|---|---|---|---|
| Score | n/total | % | n/total | % | n/total | % |
| <13 | 10/125 | 8.0 | 13/144 | 9.0 | 23/269 | 8.6 |
| 13-15 | 17/70 | 24.3 | 18/106 | 17.0 | 35/176 | 19.9 |
| 16-20 | 27/71 | 38.0 | 43/123 | 35.0 | 70/194 | 36.1 |
| >20 | 20/35 | 57.1 | 11/21 | 52.4 | 31/56 | 55.4 |
| TOTAL | 74/301 | 24.6 | 85/394 | 21.6 | 159/695 | 22.9 |

*Hosmer-Lemeshow test* $\chi^2$: p = 0.827.

risk of neonatal mortality within seven days after NICU admission, intra-hospital mortality and grade III/IV intraventricular hemorrhage in the first 72 hours following transport.[6] *The Mortality Index for Neonatal Transportation* was designed and validated to evaluate the risk of neonatal death based on first-minute Apgar score, birth weight, presence of congenital anomalies, postnatal age, arterial pH, partial oxygen pressure and heart rate obtained at the moment of inter-hospital transport request.[7]

NICU patients often require diagnostic and treatment procedures in other hospital areas, and complications during transport may aggravate their clinical status; however, a large proportion of events are potentially preventable, especially hypothermia and cardiac and respiratory deterioration.[19] In the present study, hypothermia and respiratory instability were the most frequent observed adverse events. Thus, the assessment of risk prior to transport enables better pre-transport planning, instantaneous correction of possible problems and evaluation of risks versus benefits of the procedure.

As a result, the score developed in the present study has several strengths. data for developing the risk index were collected prospectively and were available for all transports for the five variables in the model. The score's design and validation followed the steps recommended for the construction of predictive models.[15,18,20-22] Moreover, the score was validated using a large number of transports and fulfilled the two basic requirements for a predictive model: discriminatory power and calibration. The accuracy of the model was similar to that obtained in the validation sample (0.77 versus 0.71); predictive models described in the literature have accuracy values ranging from 0.7 to 0.9.[6,7,17,21-23] *The Transport Risk Index of Physiologic Stability* score developed by Lee *et al.* showed an area under the ROC curve of 0.83, 0.76 and 0.74, respectively, for mortality within 7 days, intra-hospital mortality and grade III/IV intraventricular hemorrhage in the first 72 hours following transport and had an accuracy of 0.82.[6] Similarly, the *Mortality Index for Neonatal Transportation* proposed by Broughton *et al.* had an accuracy of 0.83 for the prediction of perinatal and neonatal mortality.[7] However, these two predictive scores were not developed for assessing intra-hospital transport risks.

In the goodness-of-fit test, comparisons between expected and observed frequencies revealed good calibration of the proposed score, demonstrating that the value attributed to each variable in the model was adequate for calculating the risk of clinical complications at each score range.

In addition, this predictive score is simple, allowing clinical NICU staff to assess the risk of clinical complications during intra-hospital transport based on easily obtainable patient characteristics and transport data. Moreover, the evaluated parameters are objective and obtainable in any NICU, even in settings with minimal resources.

However, the present study has several limitations. The transport population had a high proportion of infants with congenital malformations. This characteristic may affect the accuracy of the model when applied to NICUs with a lower frequency. However, the presence and type of congenital anomalies were included in the multiple logistic regression analysis, and the predictive score was adjusted for malformations. Moreover, the analysis of the area under the ROC curve was similar in the validation cohort, independent of the inclusion of infants with malformations. These data favor the external validity of the developed score. Finally, because the present study was carried out at a single center, other characteristics related to patients, transports or hospital areas that were not assessed in the present model may have significant influence on risks for clinical complications during intra-hospital transports. Multicenter studies are needed to generalize the obtained results.

In conclusion, the proposed score showed adequate accuracy and calibration to predict the presence of at least one clinical complication during intra-hospital transports of patients in the NICU setting when this procedure was performed by trained staff with non-sophisticated but appropriate equipment.

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