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Development of an Evidence-Based Ethical Decision-Making Tool for Neonatal Intensive Care Medicine

Monique Frize[1,2], Robin C. Walker[3], Colleen M. Ennett[1]
[1]Systems and Computer Engineering, Carleton University, Ottawa, ON, Canada
[2]School of Information Technology and Engineering, University of Ottawa, Ottawa, ON, Canada
[3]Children's Hospital of Eastern Ontario, Ottawa, ON, Canada

Abstract— **The goal of this research project is to combine our intelligent decision-aid systems with a patient decision-support tool to provide more information to physicians, nurses and parents when they are facing very difficult, ethical decisions regarding the care or management of neonatal intensive care (NICU) patients. Our two artificial intelligence approaches, one using case-based reasoning and the other artificial neural networks, may provide critical information such as estimates of the likelihood of survival and the use and duration of artificial ventilation. These estimates, in addition to other factors such as birth weight, gestational age and the presence of major complications, may provide critical information to health care givers and parents to decide whether to initiate intensive care for the infant, or whether to terminate it if it has already been initiated.**

Keywords—**Ethics, neonatal medicine, decision-aid system**

I. INTRODUCTION

Neonatal medicine has been available for over 30 years in the developed world and has been providing specialized and intensive care to premature babies and critically ill newborns to improve their health and survival [1]. Larcher and Hird [2] define intensive care as "the use of invasive treatment intended to save or extend the life of a neonate who might otherwise die from organ failure. It includes artificial ventilation, other forms of organ support and artificial nutrition delivered by invasive means." They add that this type of care must be delivered by a specialized team.

Since the early days, great progress has been seen in the capabilities of neonatal intensive care units (NICU) in terms of the sophistication of the equipment that allows "more rapid and precise diagnosis, effective monitoring, and specific therapy" [1]. A new specialization has also arisen: The neonatologist. The impact of these intensive care services has been mixed. There has been "a substantial reduction of mortality in premature infants... the rate of handicap or significant morbidity appears to have remained steady or declined in survivors of NICU of nearly all gestational ages and weights" [1]. However, the author also states that the rate of prematurity, low birth weights, and the rate of birth defects has not declined in the US since the appearance of NICUs [1]. On the question of birth defects, a report states that 3 or 4 babies out of 100 are born with some type of birth defect in the US [3].

A serious concern for health care givers and for parents remains: To whom should this intensive care be administered and in what circumstances should it be withdrawn? In a recent article, Tyson [4] stated: "Despite the success of newborn intensive care, a vexing ethical question remains: Which pre-term infants are so malformed, sick, or immature that newborn intensive care should not be administered?" This statement has lead several researchers to ponder upon ways in which this question can be answered. Are there factors relating these babies' health status that can guide physicians and parents to make the decision either not to begin treatment or to end it if it has been started?

The term 'extremely low birth weight infants' is used to refer to infants who weigh 1000 grams or less; infants who, if they survive, usually need a respirator for more than a month and remain in hospital for more than 100 days [4]. Gestational age is another factor that could be considered in these cases and a recommendation is to begin intensive care for infants 25 weeks gestational age or greater and not for infants of 22 weeks or less [5]; for infants of 23-24 weeks, treatment should be decided with the parents [4,6]. Of course these decisions also depend on whether the infant's condition deteriorates or if a serious complication exists such as a large intracranial hemorrhage. "Among infants of the same birth weight, those with the most advanced gestational age are the most mature, least likely to die, and thus, most likely to benefit from neonatal intensive care" [4].

European countries appear to be much less aggressive than the US in using neonatal intensive care and place more emphasis on prenatal care. Tyson [4] states that in Denmark, for example, neonatal intensive care is not recommended for infants below 25 or 26 weeks of gestational age and in Sweden for infants under 600 grams. In developing countries, if available, it would not be provided for infants weighing less than 1000 grams. Tyson admits that there is little information documenting actual practice in administration of this type of care in the US. In Canada, management of the woman with threatened birth of an infant of extremely low gestational age is guided by a joint statement from the following national organizations and their committees: The Fetus and Newborn Committee of the Canadian Paediatric Society (CPS) and the Maternal-Fetal Medicine Committee of the Society of Obstetricians and Gynecologists of Canada [7]. This guideline was published in 1994; however, similar to the US situation, there is little data in Canada on actual practices regarding this issue.

Larcher and Hird [2] mention that some guidelines exist for the withdrawal of life-sustaining treatment and that such guidance can be helpful, but "it does not abolish controversy and ambiguity." These authors also say that: "Clinicians require guidance that is practical, reasonably specific, but not prescriptive... and that it is ethically acceptable to offer intensive care until a clearer view of the baby's prognosis and the wishes of the parents can be defined."

The discussions above indicate a critical need to provide physicians with more accurate estimations of the likelihood of the infant surviving, the estimated duration of artificial ventilation, and length of stay in the NICU (LOS) . If these estimates could be provided with acceptable accuracy, in addition to the factors mentioned above regarding birth weight, gestational age and the presence of major complications, then guidelines could be developed to enhance the decision-making on whether to provide neonatal care to an infant or not, or to withdraw it when the circumstances warrant this decision.

II. PROPOSED APPROACHES

Our research group has designed two complementary artificial intelligence approaches to estimate outcomes for NICU patients. First, a case-based reasoner (CBR) matches a new patient arrival in the NICU to the most similar patients from a large database of patients from the Canadian Neonatal Network's NICU database with the input variables from SNAP-II (Score for Neonatal Acute Physiology, Version 2: lowest blood pressure, lowest temperature, lowest pO2/fiO2 ratio, lowest serum pH, presence of seizures and lowest urine output – all parameters measured within first 12 hours of admission) and SNAPPE-II (SNAP with Perinatal Extension – plus birth weight, small for gestational age (SGA) status and Apgar score at 5 minutes) [8]. The SNAP-II variables are a subset (found via logistic regression) of the original SNAP Score that contained 37 inputs [9]. This database also includes admission and demographic data, the SNAP illness of severity score, specified diagnosis, complications, procedures and therapies, discharge information and summary data on staffing and nursing acuity.

The CBR can display outcomes, complications, and medical information of the matched patients that may guide physicians in their diagnosis or in their selection of therapies for the newly admitted infant. The system is designed to be user-friendly and the outputs mimic the process physicians use in decision-making so that their use is intuitive. [10]

Our second approach uses artificial neural networks (ANNs) to estimate the following outcomes for the single newly admitted patient to the NICU: mortality (survival or death), the need and duration of artificial ventilation, and length of stay in the NICU [11-13]. The design used a two-layer (input and output layer) feedforward ANN trained using the back-propagation algorithm, without weight-elimination, with 2/3 of the data used in the training set (3392 complete patient cases) and the remaining data used in the test set (1696 cases). The hyperbolic tangent transfer function was used.

Table 1 shows the performance of our ANNs with respect to measuring sensitivity, specificity, classification rate (CR), and it is also useful to compare the CR with the constant predictor (CP), which is a statistical benchmark where all cases are classified as belonging to the class with the highest *a priori* probability. As can be observed in Table 1, the CR is systematically higher than the CP, and substantially higher for predicting long-term stay in the NICU.

TABLE I
CLASSIFICATION PERFORMANCE OF ANNS: MORTALITY, VENTILATION AND LENGTH OF STAY IN THE NICU

	Mortality[a]	Vent[b] =0 hrs	Vent >=24hr	LOS[c] <=7d	LOS >28d
Sens (%)	26.6	27.8	24.4	23.7	76.9
Spec (%)	98.0	95.3	97.1	94.3	77.5
CR (%)	91.3	82.7	89.4	76.2	77.2
Constant predictor (%)	90.0[a]	81.0	88.0	73.0	60.0

[a]Survival rate
[b]Vent=Duration of ventilation (hours)
[c]LOS=Length of stay (days)

III. DISCUSSION

The two artificial intelligence tools described above provide information that add to the known admission data such as gestational age, birth weight, and apparent defects. The tools provide an estimation of mortality, whether the infant will be on a respirator for a very long period of time (Tyson states a month as indicative of major problems) and /or stay in the hospital for a long period (Tyson mentions 100 days for this variable). Being able to predict these outcomes may help in the decision-making process for admission to a NICU and whether the infant is likely to benefit from intensive care or not [4]. Gestational age, birth weight, estimating mortality, artificial ventilation, length of stay were all variables mentioned in the literature that can aid clinical decision-making in the NICU. However, it is certain that the decision-support systems would increase their usefulness if they could also predict other rare outcomes, those that would better guide physicians and parents in their decision-making process in the NICU. Some of the outcomes that should be added to our systems are: Intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), broncho-pulmonary dysplasia (BPD), necrotising entero-colitis (NEC), and retinopathy of prematurity (ROP). In cases where the greatest uncertainty remains, care could be initiated, and estimations could be provided at regular intervals to re-assess the situation on prognosis and outcomes.

Our work to date has shown the usefulness of ANNs for estimating the outcomes listed in Table 1. A major barrier in previous work that discouraged many researchers from using neural networks was their image as "black boxes." ANNs use complex algorithms for calculating the weights on each input and node. Our research group has performed several modifications to our ANNs to render them more useful and effective. For example, we extract the weights of the inputs and hidden nodes to assess the importance of each variable with respect to the outcome; we re-sample from the rare outcome when the sample is very small in order to increase the sensitivity of the estimations; we have automated the adjustment of the nine parameters that determine optimal performance; we use a new stopping criterion (log-sensitivity index) which optimizes the values of specificity and sensitivity [14-18]. These advances have substantially contributed to increasing the performance and effectiveness of our ANNs.

The next step to improve our systems would consist in adding the rare outcomes previously listed that would be relevant to the decision-making process of administering or withdrawing neonatal intensive care. In order to achieve the goal of estimating these additional rare outcomes, we have developed and tested a method to replace missing values in our NICU database. Using only complete records restricts greatly the number of cases containing these rare outcomes and so extending the case number to our entire database of over 20,000 NICU patient cases will now allow us to train and test our ANNs to predict these additional outcomes [19].

Until this step has been completed, we plan to use the results from the Canadian Neonatal Network whose SNAP-II score is a predictor of IVH (intraventricular hemorrhage) and CLD (chronic lung disease) in neonatal intensive care patients. In their article, Chien et al. report the percent contribution to predictive power of various factors to predict IVH:as follows: Gestational age is 41 %; SNAP-II is 30 %; outborn status is 23 %; and Apgar at 5 minutes is 6 %. For predicting CLD, the percent contribution to predictive power are: 54 % for gestional age; 30 % for SNAP-II; 9 % for 'small for gestional age'; 2 % for the 5-minute Apgar and 2 % for outborn status; it is 3 % for a male infant [20].

Our research group is currently designing an expert system that will incorporate the predictive tool (ANNs for each outcome of interest), then merge this information for a global view of the situation in a manner in which physicians wish to see it. The information will then be transferred in a manner that parents can understand (both in terms of language, content, and the speed at which this information is provided to them. The generic tool will be adapted to various situations and ensure that parents are included in the decision-making process and are able to reach a consensus with the physicians, without coercion. The decision-support tool will be suited to the parents' needs, values, and level of information that can be communicated effectively to them. Dr. O'Connor's generic tool (at University of Ottawa) that supports patient-centered decision-making will be the base on which this prototype is constructed [21,22]. A short pilot clinical test in the NICU will follow the final design. The work is being carried-out with frequent consultation with the NICU physicians at CHEO (Children's Hospital of Eastern Ontario). The final step will be a longer trial in several of the Canadian Neonatal Network NICUs in various parts of Canada.

V. CONCLUSION

Our research to date has led to the development of prototypes that will allow physicians to better predict certain outcomes in neonatal intensive care and thus use this information when they counsel families on prognosis and the desirability of initiating or on withdrawing treatment when conditions dictate this approach. It will be very important in our future work to include parents in the decision loop. An expert system is in initial stages of development to complement the predictive tools described above. This system will take into consideration the parents' values and manner and tempo in which the information should be provided to them.

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