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Categorizing Neonatal Deaths: A Cross-Cultural Study in the United States, Canada, and The Netherlands

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Objective To clarify the process of end-of-life decision-making in culturally different neonatal intensive care units (NICUs).

Study design Review of medical files of newborns >22 weeks gestation who died in the delivery room (DR) or the NICU during 12 months in 4 NICUs (Chicago, Milwaukee, Montreal, and Groningen). We categorized deaths using a 2-by-2 matrix and determined whether mechanical ventilation was withdrawn/withheld and whether the child was dying despite ventilation or physiologically stable but extubated for neurological prognosis.

Results Most unstable patients in all units died in their parents' arms after mechanical ventilation was withdrawn. In Milwaukee, Montreal, and Groningen, 4% to 12% of patients died while receiving cardiopulmonary resuscitation. This proportion was higher in Chicago (31%). Elective extubation for quality-of-life reasons never occurred in Chicago and occurred in 19% to 35% of deaths in the other units. The proportion of DR deaths in Milwaukee, Montreal, and Groningen was 16% to 22%. No DR deaths occurred in Chicago.

Conclusions Death in the NICU occurred differently within and between countries. Distinctive end-of-life decisions can be categorized separately by using a model with uniform definitions of withholding/withdrawing mechanical ventilation correlated with the patient's physiological condition. Cross-cultural comparison of end-of-life practice is feasible and important when comparing NICU outcomes. (*J Pediatr* 2010;156:33-7).

See editorial, p 7

Rapid technological progress in neonatology has enabled many newborns to survive. At the same time, the risks and burdens of hospitalization or future life with permanent neurologic impairment may be, at times, perceived as inferior to the anticipated benefits of intensive care. As a consequence, resuscitation and active treatment of very sick neonates with potential serious neurologic sequelae has become an issue fraught with controversy, leading to complex decision-making about withholding or withdrawal of interventions.¹⁻¹¹ In modern bioethics, withholding and withdrawing interventions for dying patients are generally seen as morally equivalent, although this does not mean that both actions are legally equivalent.^{12,13} However, withdrawing mechanical ventilation in a physiologically stable infant is seen by many physicians as different from withdrawing, withholding, or escalating care in a moribund infant.¹⁴ Moreover, the circumstances surrounding decisions to withhold or withdraw intervention are rarely explicitly described in publications describing neonatal intensive care unit (NICU) outcomes. Mortality rates do not clarify how the babies die or what is done at bedside. Consequently, discussions on what "ought to be done" are difficult to have when what is done is not accurately known. Also, comparing outcomes is difficult. For example, a higher survival rate, and possibly a higher disability rate, may be seen when most extremely premature babies are aggressively resuscitated and withdrawing intervention is less frequently offered in a particular unit.¹⁵

Most studies of newborn end-of-life care describe the physician's attitude about end-of-life decisions and not the practice.¹⁶⁻²¹ Even when withdrawal of intervention is described, the distinction is rarely made between the babies who would have died despite intensive interventions (moribund babies extubated to spend their last moments in their parent's arms), and babies who were extubated to die for "quality-of-life" reasons.²²⁻²⁶ Moreover, studies are often very difficult to compare because the authors use different definitions of patients groups and interventions.

We conducted a cross-cultural study using uniform definitions of interventions and physiological condition of the patients with the aim of describing and comparing the circumstances of dying in NICUs in different parts of the world.

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CPR	Cardiopulmonary resuscitation
DR	Delivery room
NICU	Neonatal intensive care unit

Methods

The study design complied with the Dutch national law on medical privacy and medical scientific research. No authorization is legally required for confidential cohort chart review (University Medical Center Groningen). To conduct a retrospective chart review in Canada, approval of the director of professional services is necessary (McGill University Health Center), which was obtained before reviewing patient's charts. This study was approved by the institutional review board of the University of Chicago (Comer Children's Hospital, Chicago, Illinois). This study was also approved by the institutional review board of Children's Hospital of Wisconsin and the Medical College of Wisconsin.

We reviewed the medical files of all newborns of >22 weeks who died in the delivery room (DR) and the NICU between October 2005 and September 2006 in 4 NICUs. All participating NICUs are tertiary care units that admit between 555 and 800 newborns yearly.

We abstracted information from the medical records to determine all relevant demographics, including birth weight, gestational age, day and time of death, diagnoses leading to death (using both clinical data and autopsy materials when available), and details about the decision-making process. For DR deaths, we excluded termination of pregnancies.

We categorized all deaths according to a 2-by-2 model, along the dimensions of physiology and intervention. We first classified all newborns as stable or unstable. To be classified as unstable, babies needed 2 of these criteria: persistent desaturation despite 100% oxygen on mechanical ventilation, hypotension despite volume infusion and inotropes, protracted bradycardia or anuria for >24 hours. All babies that were not unstable according to these criteria were classified as physiologically stable. A second classification divided patients in 1 of the following categories on the basis of the intervention offered or withdrawn: 1) babies who died while getting active cardiopulmonary resuscitation (CPR; no withdrawing or withholding); 2) babies who died without active CPR (no withdrawing, but CPR was withheld); 3) moribund babies for whom death was inevitable and who died after being extubated from a ventilator to die in the arms of their parents (withdrawing/unstable); and 4) babies who were electively extubated for quality-of-life reasons as determined jointly by the physician and parents (withdrawing/stable). Newborns in this group were subdivided by organ insult (brain, kidney, intestine, heart). Babies receiving constant positive airway pressure (CPAP), bilevel positive airways pressure (BiPAP), and nasal intermittent mandatory ventilation (IMV) were all counted as receiving ventilator support for the purpose of this analyses. All data necessary for classification of the newborn deaths were collected in 1 shared anonymous database and discussed by the investigators from all participating units to ensure similarity in the classification process. Consensus about the classification was reached in all cases.

From the medical records, we ascertained whether the parents were involved in the decision-making process resulting

in the last intervention and what the physician documented as reasons for the decisions regarding the end of life.

Withholding intervention was defined as withholding potentially life-sustaining treatment, which included not only withholding CPR, but also not providing additional intensive care interventions (eg, not making additional ventilator changes despite hypoxemia, not providing additional inotropes despite hypotension, withholding artificial feedings). Withdrawing intervention was taken to be equivalent to withdrawing the ventilator, CPAP, BiPAP, or nasal IMV. As a general rule, each NICU's position on resuscitation of very preterm infants reflected those issued by their national pediatric societies. The Canadian Paediatric Society suggests a selective approach at <25 weeks gestation, when resuscitation should only be instituted after informed parental consent.²⁷ The American Academy of Pediatrics strategies suggest that resuscitation may be considered in infants between 23 and 25 weeks in individual cases.¹⁰ The suggested strategy in The Netherlands is that intensive neonatal treatment should start at 25 weeks; at <25 weeks, care is aimed at comfort for the child and the family unless intensive treatment is warranted.²⁸

We compared demographics, the causes of deaths and the classification of deaths in the 4 NICUs by using the χ^2 test for multiple variables. *P* values <.05 were considered to indicate statistical significance.

Results

A total of 183 patients with gestational age >22 weeks died in the 4 institutions during the 12-month study period. (Table I). Of 183 newborns, 32 died in the DR. Six of these 32 infants had congenital anomalies with extremely poor outcomes diagnosed prenatally (ie, trisomy 13/18 [3x], hydrancephaly [2], omphalocele-exstrophy-imperforate anus syndrome complex), and the parents and physicians agreed to comfort-care immediately after birth. Three premature infants were offered an attempt at resuscitation. This ranged from an attempt to ventilate via endotracheal tube to assess a response in 2 babies to a full medical code including chest compressions and medications in 1 infant. Twenty-three extremely preterm infants

Table I. Demographics of all deaths in the delivery room and in the neonatal intensive care unit (n = 183)

	Groningen	Montreal	Milwaukee	Chicago
DR deaths				
Patients (n)	16	9	7	0
Female	6 (38%)	5 (55%)	4 (57%)	—
Gestational age (weeks)	26.2	23.4	26	—
Birthweight (mean)	965	582	902	—
Minutes alive (mean)	61	65	28	—
NICU admissions	555	700	654	800
NICU deaths				
Patients (n)	52 (9%)	34 (5%)	36 (5.5%)	29 (4%)
Female	22 (42%)	13 (30%)	16 (44%)	12 (41%)
Gestational age (weeks)	34.5	32.9	33.2	30.0
Birthweight (mean)	2231	2163	2003*	1362
Minutes alive (mean)	22.5	32.7	15.8	31.5
Minutes alive (median)	5	7.5	7	7

*No birthweight documented in 6 cases.

were not intubated at birth and were given comfort-care because parents agreed to comfort-care.

A total of 151 infants were admitted to the NICU and subsequently died there. In 3 NICUs, most deaths were in newborns between 27 and 36 weeks gestational age, and the remaining were in infants <27 weeks gestational age. In Chicago, more deaths were in extremely preterm infants <27 weeks gestational age (45%; **Table II**).

The primary causes of death were congenital anomalies, asphyxia, respiratory insufficiency, sepsis/necrotizing enterocolitis, and intracranial bleeding (**Table III**). The causes of death were similar in all units, although proportionally more babies died from respiratory insufficiency in Chicago than in other units; these infants were all <27 weeks gestational age.

In 3 institutions, between 16% and 24% of newborn deaths occurred in the DR, whereas in Chicago all deaths occurred in the NICU and no DR-deaths were reported (**Table IV**). The proportion of babies who died while receiving CPR varied between 31% (Chicago) and 4% (Groningen).

Withdrawal of ventilation (including CPAP, BiPAP, and nasal IMV) was the most common intervention associated with the infant's death in all units; CPR was withheld in all these cases for obvious reasons. The proportion of infants who died while they were still connected to the ventilator was low in all centers—<2% in Groningen, Montreal, and Milwaukee and 17% in Chicago. Consequently, for at least 83% of dying infants in Chicago and 98% of dying infants in Groningen, Montreal, and Milwaukee, intensive care intervention (mechanical ventilation) was withheld or withdrawn at the time of death.

Between 30% and 52% of extubations were performed in unstable patients who were dying despite NICU interventions to let them die in the arms of the parents without tubes and tapes. In Chicago, all extubations followed this scenario, and no physiologically stable child was extubated for quality-of-life reasons. In contrast, in Groningen, Montreal, and Milwaukee, 19% to 35% of extubations were performed in physiologically stable infants for quality-of-life reasons. The most common reasons for the extubation in these infants were neurologic injury (43%-73%), mostly because of congenital anomalies, asphyxia, or intracranial bleeding, followed by cardiac and gastrointestinal insults in infants with multiple congenital anomalies.

The most prevalent cause of death in stable and unstable babies was congenital anomalies. The anomalies classified as stable (18 of 68; 26%) included multiple anomalies affecting multiple organs (12), neuromuscular disorders (4), and

Table III. Causes of death in 151 neonatal intensive care unit deaths

	Groningen (n = 52)	Montreal (n = 34)	Milwaukee (n = 36)	Chicago (n = 29)
Asphyxia (n = 21)	9 (17%)	7 (20%)	2 (6%)	3 (10%)
Congenital anomalies (n = 68)	26 (50%)	11 (32%)	20 (56%)	11 (38%)
Sepsis/NEC (n = 33)	12 (23%)	8 (24%)	8 (22%)	5 (17%)
Respiratory insufficiency (n = 13)	1 (2%)	1 (3%)	3 (8%)	8 (28%)
Intracranial bleeding (n = 16)	4 (8%)	7 (21%)	3 (8%)	2 (7%)

NEC, Necrotizing enterocolitis.

polycystic kidney disease with brain injury (2). Infants classified as unstable (50 of 68; 74%) had anomalies including congenital diaphragmatic hernia (15), hypoplastic left heart syndrome (8), other cardiac malformations (8), pulmonary hypoplasia (7), cardiomyopathy (3), chromosomal anomalies (2), osteogenesis imperfecta (2), and others (7).

In all 3 units with DR deaths (there were no DR deaths in Chicago), the decision not to initiate resuscitation was made jointly with the parents. In the NICU, the parents were involved in the decision-making process for all patients when withdrawal of the respirator took place. In 15 instances, with a similar occurrence in all 4 centers, the parents did not participate in the decision-making because an emergency situation did not give healthcare providers enough time to involve them. Most of these infants died during surgery or while receiving CPR.

Discussion

We conducted a retrospective study on end-of-life decision-making in culturally different NICUs in The Netherlands, Canada, and the United States, using a 2-dimensional classification model to involve the newborn's physiology (stable-unstable) and NICU-interventions (withholding-withdrawing). This format allowed us to make a distinction between withholding or withdrawing treatment in moribund infants and the situation in which this takes place in stable newborns for quality-of-life reasons. We compared end-of-life practice in the 4 NICUs and found that decisions about the end of life were made differently within and between countries. We purposefully chose these units because of their cultural differences.

Our study yielded 3 important findings. First, this study confirms that withholding and withdrawing of artificial ventilation (including CPAP, BiPAP, and nasal IMV) is the primary mode of death in the NICU internationally. We found that 69% to 93% of all deaths were accompanied by a decision to withhold or withdraw ventilation. Most recent reports from centers in the United States, the United Kingdom, Australia, and Europe have reported rates between 58% and 75%.^{26,29-31} Only 3 studies from The Netherlands, California, and Switzerland have reported higher rates of 86% to 93%.³²⁻³⁵ The rates found in this study are also higher than those from earlier studies involving 2 of the units that also

Table II. Distribution of 151 deaths in 4 neonatal intensive care units according to gestational age

GA	Groningen	Montreal	Milwaukee	Chicago	Total
<27 weeks	6 (12%)	8 (24%)	9 (25%)	13 (45%)	36 (24%)*
27-36 weeks	25 (48%)	14 (41%)	15 (42%)	12 (41%)	66 (44%)
>36 weeks	21 (40%)	12 (35%)	12 (33%)	4 (14%)	49 (32%)
Total	52	34	36	29	151

GA, Gestational age.

*P < .05.

Table IV. Circumstances of dying and classification of 183 deaths in the delivery rooms and in the neonatal intensive care units of 4 institutions

Intervention	Physiology	Groningen (n = 68)	Montreal (n = 43)	Wisconsin (n = 43)	Chicago (n = 29)	Total
<i>Died in DR</i>						
Category A, died while receiving CPR	Unstable	0	0	3 (7%)	0	3
Category B, withholding CPR, comfort care	Unstable	16 (24%)	9 (21%)	4 (9%)	0	29
<i>Died in the NICU</i>						
Category A, died while receiving CPR	Unstable	3 (4%)	5 (12%)	4 (9%)	9 (31%)	21
Category B, withholding CPR, died on the respirator	Unstable	1 (1%)	1 (2%)	0	5 (17%)	7
Category C, extubation to let the moribund child die in parents' arms	Unstable	35 (52%)	13 (30%)	17 (40%)	15 (52%)	80
Category D, elective extubation for quality-of-life reasons	Stable	13 (19%)	15 (35%)	15 (35%)	0	43

WH, Withholding life-sustaining treatment; WD, withdrawing life-sustaining treatment; *Unstable*, 2 of these criteria are present: persistent desaturation despite 100% oxygen on mechanical ventilation, hypotension despite volume infusion and inotropes, protracted bradycardia, or anuria for >24 hours.

participated in this study.^{14,34} Second, the proportion of deaths occurring in the DR varies considerably in different units. This may be a reflection of the differences in approach to resuscitation at the “limits of viability,” as described in the position statements in different countries.³⁶ However there were differences in the 2 US NICUs. These differences could be because of physician interpretation of these policies or differences in the parent population (eg, income, social class, religion, level of education) and perception of the value of intensive intervention in the context of high expectation of persistent injury if the child were to survive.³⁷⁻⁴⁰ Finally, our study demonstrates that comparison of end-of-life decision-making in culturally different units is feasible and important in comparing treatment outcomes. The use of a 2-dimensional classification model, as used here, quantifies a unit’s end-of-life approach. The importance of involving a unit’s approach to decision-making in situations with prognostic uncertainty was demonstrated in a study by Lorenz et al.¹⁵ They compared outcomes of premature infants in New Jersey and The Netherlands. In this study, they used Rhoden’s characterization of different approaches to care and described the NICU care in the American unit as the “wait until certain” strategy: resuscitating almost all infants and withdrawing care when they deteriorate.⁴¹ The Dutch unit’s approach was described as one in which treatment was offered to infants who have or are likely to have reasonably good long-term outcomes (statistical prognostic). These 2 units had different survival rates and long-term outcomes, mainly because of this variation.

The current guidelines on active treatment at the “limits of viability” from The Netherlands are still somewhat more “restrictive” than those from the United States and Canada.³⁶ This explains the relative high number of DR deaths with a higher mean gestational age in Groningen in comparison with the other 3 units. We might have expected a higher proportion of deaths after withdrawal of ventilation in stable newborns in Groningen (and possibly in Canada) because of the neonatologists pro-quality-of-life attitude.⁴²⁻⁴⁴ We found, however, that physicians in Groningen appear to be less likely than physicians in Montreal or Milwaukee to with-

draw the ventilator in physiologically stable newborn for quality-of-life reasons.

A potential limitation of our study is the study’s retrospective nature and the concerns inherent to the dependency on medical charts for the accurateness of the data. Another limitation could be that this study involved only 4 units and a relatively small number of patient deaths, which makes generalizability of the conclusions about the use of the classification model somewhat tenuous. Moreover, although we explicitly recognized patients who were withheld/withdrawn for quality-of-life concerns, we lack specific details on what the quality-of-life considerations were.

In conclusion, we report here a 2-by-2 dimensional analysis that allows a better description of the circumstances of death and dying in a NICU than has previously been available. Patients were categorized both along the dimension of withholding/withholding intensive intervention and along the dimension of physiologic stability in the context of mechanical ventilation. Our study reveals that almost all NICU deaths are accompanied by some degree of withholding/withdrawing, but that the physiologic stability of the dying infants varies within and between countries. We think that cross-cultural comparison of end-of-life practice is feasible and important when comparing outcomes between NICUs. Moreover, a larger and prospective multicenter study that includes comparison of quality-of-life considerations in the NICUs is needed. ■

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