Actuarial day-by-day survival rates of preterm infants admitted to neonatal intensive care in New South Wales and the Australian Capital Territory

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ABSTRACT

Objective To characterise the actuarial day-by-day survival of premature infants in a geographically defined population.

Setting 10 Neonatal Intensive Care Units (NICUs) in New South Wales (NSW) and Australian Capital Territory (ACT), Australia.

Design Retrospective analysis of prospectively collected data as part of NICUs' data collection in NSW and ACT.

Subjects Premature infants born at 22⁺⁰ to 31⁺⁶ weeks' gestation between January 1997 and December 2006 and admitted to one of the 10 NICUs in NSW and ACT.

Outcome Actuarial day-by-day survival to discharge from NICU.

Results Survival to discharge after initiation of neonatal intensive care ranges from 30.0% at 23 weeks' gestation to 98.8% at 31 weeks. Actuarial day-by-day survival increased across all gestations. This improvement was most notable among the babies who were born <26 weeks gestation.

Conclusion Preterm infants who survive the first few postnatal days have considerable chances of long-term survival. It is important to revise the information stored regarding chances of survival so it covers chances at regular intervals, especially after the first few days of life.

INTRODUCTION

Establishing data for survival of premature infants by gestational age is important for counselling parents both prenatally and postnatally.^{1,2} Overall survival to discharge of premature infants, unlike actuarial day-by-day survival, is well studied and has been published for babies in different populations.³ Overall, survival is provided as a single survival rate from admission to discharge for each birthweight or gestational age category.^{2,4} Actuarial survival, on the other hand, is provided as day-by-day survival from the time of admission and is important for consultation with parents of infants during their stay in the Neonatal Intensive Care Unit (NICU).³

The purpose of this study was to characterise the actuarial survival to discharge in a large cohort of preterm infants (22⁺⁰ to 31⁺⁶ weeks' gestation) admitted to any of the regional NICUs within the network in New South Wales (NSW) or the Australian Capital Territory (ACT), Australia, between 1997 and 2006. Furthermore, we aimed to examine the effect of sex and increasing postnatal age on predicted survival.

What is already known on this topic

Overall survival to discharge, unlike actuarial day-by-day survival, for premature infants of different populations is well studied.

What this study adds

- ▶ Among infants < 26 weeks' gestation admitted to the Neonatal Intensive Care Unit (NICU), day-by-day actuarial survival rate increases during the first few days of life.
- ▶ Revising the chances of survival during the early NICU course would improve counselling for parents.

METHODS AND SUBJECTS

Data source

Perinatal survival and other outcome data for infants of 22⁺⁰ to 31⁺⁶ weeks' gestation were extracted from the NICUs data collection, which is a population-based, prospectively collected, statewide data collection of neonates admitted to all 10 NICUs (8 perinatal centres and 2 children's hospitals) in NSW and ACT. Data are prospectively collected and organised within each NICU by a designated clinical nurse specialist using standard operational definitions across the network (B Bajuk, T Vincent, unpublished observation). The data are then compiled into a central database located at the NSW Pregnancy and Newborn Services Network, where rigorous quality control procedures are applied to ensure the accuracy of the data collection.⁵ In Australia, it has been recommended by the National Health and Medical Research Council that "Wherever possible preterm birth at <33 weeks should occur in a perinatal centre that has the expertise to care for the woman and her preterm infant."⁶ In general, preterm infants <33 weeks who are born in non-tertiary hospitals are transferred to tertiary centres by a specialised neonatal and paediatric emergency transport service team.^{7,8}

Definitions

Chronic lung disease (CLD) is defined as the need for supplementary oxygen and/or ventilatory support at 36 weeks postmenstrual age.^{9,10} Intraventricular haemorrhage (IVH) grading is

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based on Papile classification¹¹ and necrotising enterocolitis is staged using the modified Bell Staging Criteria.¹² Retinopathy of prematurity (ROP) was defined as per the International Classification of ROP with Stage of I–IV assigned to positive cases.¹³

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software version 15.0 (SPSS, Chicago, Illinois, USA, 2006). Data are presented as number (%) or median (IQR). The Kaplan–Meier (product-limit) method¹⁴ was used to estimate actuarial survival. Differences in median survival time (eg, males vs females) were compared using the Mantel–Cox log-rank test.¹⁵ For actuarial analysis, the event of interest was death and time-to-event was the number of days survived. Infants with no events were considered as right censored observations. Day-by-day postnatal survival rates were calculated as the percentage of survival at specific postnatal days (eg, day 1, first 24 h of life).

Figure 1 Profile of babies born at 22–31 weeks' gestation from admission to discharge/death.

Actuarial survival to a given day was graphed by gestational age and stratified by sex. All analyses were prespecified. The level of statistical significance for all analyses was set at $p < 0.05$, using two-tailed comparisons.

RESULTS

The study group's profile from birth to discharge/death is shown in figure 1. There were 8757 infants admitted to the 10 collaborating NICUs between January 1997 and December 2006. Stillbirths ($n=2417$), death before NICU admission ($n=820$) and infants with congenital abnormalities ($n=480$) were excluded from this study. The remaining 8277 patients were included in the final analysis. Overall, 858 (10.4%) of the infants admitted died before NICU discharge.

Antenatal and perinatal characteristics

The antenatal and perinatal characteristics and major neonatal morbidities observed among the study group are shown in tables 1 and 2. The median (IQR) gestational age of the study group was 29.0 (27.0–30.0) weeks with a birth weight (IQR) of 1235.0 (940.0–1520.0) g. Antenatal steroid administration was completed in 88.2% of the group. CLD was present in 15.4% of the patients, and 7.1% of the patients required home oxygen. IVH grade 3–4 was found in 6.0% of the patients and ROP grade 3–4 was found in 5.5% of the patients.

Survival to discharge and time of death

Survival to discharge and time of death are shown in figure 2. Survival increased from 0% at 22 weeks' gestation to 98.8% at 31 weeks. Female infants had better chances of survival than male infants especially among infants <27 weeks' gestation (figure 2).

The majority of deaths occurred in the first few days of life, particularly in the most premature patients (table 3). Overall, 32.6%, 10.9% and 9.6% of the deaths occurred on days 1, 2 and 3 of life, respectively.

The median (IQR) age at time of death ranged from 1.0 (1.0–3.5) day at 22 weeks' gestation to 8.0 (2.0–18.0) days at 30 weeks' gestation, with an overall median (IQR) age of death of 3.0 (1.0–11.0) days (table 2). The median time of death was not different between males and females (table 2). However, there was a trend for earlier death in male infants (figure 2).

Actuarial survival

Day-by-day actuarial survival to discharge, stratified by sex, is shown in figure 3. The graphs were truncated at day 60 of

Table 1 Maternal characteristics of the study group

Characteristic/morbidity	Overall ($n=8277$)	Males ($n=4523$)	Females ($n=3754$)	p Value
Maternal age (years)	30.0 (25.0–34.0)	30.0 (25.0–34.0)	30.0 (25.0–34.0)	0.186
Aboriginal ethnicity	427 (5.2)	238 (5.3)	189 (5.0)	0.573
Assisted conception	1112 (13.4)	590 (13.0)	522 (13.9)	0.244
Multiple pregnancy	2393 (28.9)	1250 (27.6)	1143 (30.4)	0.005
Pregnancy induced hypertension	1494 (18.4)	709 (16.1)	785 (21.3)	<0.001
Rupture of membranes >24 h	2059 (24.9)	1128 (24.9)	931 (24.8)	0.937
Antepartum haemorrhage	2063 (25.5)	1190 (27.0)	873 (23.6)	<0.001
Intrauterine growth restriction	815 (10.1)	361 (8.2)	454 (12.3)	<0.001
Fetal distress	1428 (17.3)	743 (16.4)	685 (18.2)	0.033
Antenatal steroids completed	7301 (88.2)	3959 (87.5)	3342 (89.0)	0.038
Vaginal breech delivery	641 (7.9)	351 (8.0)	290 (7.9)	0.899
Emergency caesarean section	1709 (21.1)	978 (22.2)	731 (19.8)	0.008

Data are presented as median (IQR) or n (%).

Table 2 Perinatal characteristics and major neonatal morbidities of the study group

Characteristic/morbidity	Overall (n=8277)	Males (n=4523)	Females (n=3754)	p Value
Born in non-tertiary hospital	801 (9.7)	465 (10.3)	336 (9.0)	0.051
Gestational age (weeks)	29.0 (27.0–30.0)	29.0 (27.0–30.0)	29.0 (27.0–30.0)	0.241
Birth weight (g)	1235 (940–1520)	1280 (975–1560)	1180 (900–1460)	<0.001
Birth weight <10th percentile	773 (9.3)	393 (8.8)	375 (10.0)	0.067
Head circumference <10th percentile	574 (7.6)	203 (4.9)	371 (10.8)	<0.001
Apgar score <7 at 5 min	1334 (16.2)	780 (17.4)	554 (14.8)	0.002
Surfactant	4132 (49.9)	2337 (51.7)	1759 (47.8)	<0.001
Air leak requiring drainage	345 (4.2)	193 (4.3)	152 (4.0)	0.532
Postnatal steroids	879 (10.6)	514 (11.4)	365 (9.7)	0.014
CLD	1276 (15.4)	744 (16.4)	532 (14.2)	0.006
Home oxygen	572 (7.1)	343 (7.8)	229 (6.2)	0.005
PDA treated with indomethacin/surgery	1960 (23.7)	1046 (23.1)	914 (24.3)	0.210
NEC	457 (5.5)	258 (5.7)	199 (5.3)	0.456
Any major surgery	416 (5.0)	242 (5.4)	174 (4.6)	0.108
IVH grade 3 or 4*	467/7810 (6.0)	280/4191 (6.7)	187/3490 (5.3)	0.012
ROP grade 3 or 4*	345/6260 (5.5)	192/3382 (5.7)	153/2878 (5.3)	0.525
Proven systemic infection	1775 (21.4)	1004 (22.2)	771 (20.5)	0.064
Hospital mortality	858 (10.4)	506 (11.2)	352 (9.4)	0.008
Gestational age at death (weeks)	26.4 (25.0–29.0)	26.4 (25.0–29.0)	26.4 (25.0–29.0)	0.863
Age at death (days)	3.0 (1.0–11.0)	3.0 (1.0–11.0)	3.0 (1.0–11.0)	0.458
Age at discharge (days) [†]	56.0 (42.0–76.0)	55.0 (41.0–75.0)	56.0 (42.0–76.0)	0.111
Gestation at discharge (weeks) [†]	37.1 (36.0–38.7)	37.1 (36.0–38.7)	37.1 (36.0–38.6)	0.645

Data are presented as median (IQR) or n (%).

CLD is defined as requiring respiratory support at 36 weeks of gestation.

*Denominator is number of infants examined.

[†]Calculated for infants who were discharged alive.

CLD, chronic lung disease; IVH, intraventricular haemorrhage; NEC, necrotising enterocolitis; PDA, patent ductus arteriosus; ROP, retinopathy of prematurity.

Figure 2 Gestational age specific survival to discharge and median age at death in preterm infants born between 1997 and 2006 and admitted to a neonatal intensive care unit.

life, as survival remained mostly unchanged after this period. The slope of the curves shows that the risk of death is highest within the first few days of life and for the most severely premature patients. Overall risk of death was also higher for male infants than for female infants ($p=0.008$).

Survival rates

Day-by-day survival rates for the first week of life stratified by sex are shown in table 3. Chances of survival improve day-by-day across all gestations. This improvement was most notable among the babies who were born <26 weeks gestation. For

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Table 3 Day-by-day survival rate to discharge recalculated at fixed intervals on the surviving cohort and stratified by gestation among male and female infants 22–31 weeks' gestation born between 1997 and 2006 and admitted to a neonatal intensive care unit

Gestation (weeks)	Total admitted	Total survived	Day-by-day survival (%)							
			Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Overall
Male infants										
22	6	0	16.7	0.0	—	—	—	—	—	0
23	60	15	63.3	92.1	88.6	93.5	96.6	89.3	96.0	25
24	211	103	83.4	93.8	93.3	96.1	96.6	97.9	99.3	48.8
25	270	169	85.9	96.1	93.7	99.5	98.6	98.5	99.0	62.6
26	388	290	93.3	96.1	95.7	99.7	99.7	99.4	98.5	74.7
27	421	380	97.6	98.8	99.5	99.0	99.8	99.5	99.5	90.3
28	562	524	97.5	99.3	99.8	99.6	99.6	99.8	99.6	93.2
29	643	612	98.4	99.5	99.7	99.5	99.4	99.8	99.8	95.2
30	881	859	99.4	99.7	99.8	99.9	99.8	99.8	99.9	97.5
31	1081	1065	99.3	99.9	99.8	99.9	99.9	99.9	100.0	98.5
Overall (22–31)	4523	4017	96.2	98.8	98.8	99.5	99.6	99.7	99.7	88.8
Female infants										
22	2	0	50.0	0.0	—	—	—	—	—	0
23	60	21	72.6	90.7	91.1	98.2	94.9	98.2	98.3	35.0
24	172	89	85.5	94.6	97.0	96.4	99.4	97.7	97.6	51.7
25	239	166	91.6	96.3	97.0	99.6	98.3	97.4	98.3	69.5
26	340	290	94.7	98.1	99.1	99.7	99.4	99.7	99.7	85.3
27	360	328	97.8	98.0	98.0	98.9	99.4	99.7	99.7	91.1
28	458	430	99.8	99.8	99.6	99.6	99.8	99.6	99.3	93.9
29	550	522	98.9	99.6	99.6	99.8	99.8	99.8	99.6	94.9
30	689	680	99.9	99.7	99.9	99.9	99.9	100.0	99.9	98.7
31	884	876	99.7	99.9	99.9	99.9	99.8	100.0	100.0	99.1
Overall (22–31)	3754	3402	97.1	98.9	99.1	99.5	99.7	99.6	99.4	90.6

Panel A: Male infants

Panel B: Female infants

Figure 3 Day-by-day actuarial survival rate to discharge (Kaplan–Meier method) recalculated at daily intervals on the surviving cohort and stratified by gestation among (A) male and (B) female infants 22–31 weeks' gestation born between 1997 and 2006 and admitted to a neonatal intensive care unit. Graphs are truncated at day 60 of life.

example, the survival of males of 24 weeks' gestation improved from 83.4% on day 1, to 96.1% by day 4, to 99.3% for those who survived to day 7. The survival rates were calculated only for the first week of life, because survival remained mostly unchanged after this period.

DISCUSSION

These data show that the chance of survival of premature infants improves during the first few days of life, which emphasises the importance of revising the chance of survival at regular intervals, especially after the first days of life. This improvement was most notable among the babies who were

born most prematurely. Similar observations have been made by other authors.^{3 16–18}

Survival rates of our study group seem to be more favourable.^{3 16 17 19–21} This might be attributed to the larger size of NICUs, higher degree of specialisation of both medical and nursing staff and greater degree of centralisation, preventing dilution of resources and clinical commitment in NSW and ACT.^{19 21–26} Furthermore, and in contrast to other networks, the NSW/ACT system acts regionally to direct perinatal traffic in order to buffer any individual unit from excessive workloads. In many ways, the system functions as one large amalgamated service network.²⁷ Furthermore, our data are more recent

than those collected previously. In addition, lack of information on stillborn and delivery room deaths may overestimate survival probabilities in our cohort compared with others. Nevertheless, the association between differences in comparative international outcomes and particular organisational characteristics of health services must be inferred only with caution, as highlighted by others.^{19 28}

Similar to other studies, the majority of deaths in our setting occurred in the first few days of life, particularly among the most premature babies.^{17 18 29 30}

We stratified the day-by-day actuarial survival rate (figure 3 and table 3) by sex as male infants had lower survival rate compared with female infants. Similar findings have been reported elsewhere.^{31–33}

The strength of our study is that it is based on a large, geographically defined cohort. Such an analysis has the potential to remove the selection bias in hospital-based studies and provides a more accurate picture of neonatal outcome.^{34 35} Furthermore, our study included more recent data on infants who were born more prematurely, compared with previous studies. One important limitation of our data is the lack of detailed information on stillborn, delivery room deaths, and non-initiation and withdrawal of intensive care. Use of our data on deaths after NICU admission for antenatal counselling may overestimate survival probabilities.

In conclusion, our data characterised the actuarial day-by-day survival for preterm infants from a geographically defined area. Our data show that preterm infants who survive the first few postnatal days have considerable chance of survival until discharge. These data may be used to counsel parents of preterm infants admitted to NICUs.

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