Outcomes at three years of age of infants born at 22-25 weeks gestational age admitted to NICUs in Japan

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Abstract

Background: Policies for perinatal care for infants at the threshold of viability differs among various countries. Survival rates of infants born at 22-23 weeks (w) of gestational age (GA) in 2005 had increased up to 50% in Japan. For prenatal counseling and physician/family decision-making, severe neurodevelopmental impairment (NDI) is an equally important issue as survival. **Objective:** The aim of this study was to evaluate survival and NDI according to GA of the infants in the Japanese Neonatal Research Network (NRN). **Design/Methods:** Study subjects were a total of 1026 infants born at GA 22-25 w in 2003-2005 admitted to the participating NICUs on day 0 and registered in a database. NDI was defined as any of the following impairments: cerebral palsy (CP), unilateral or bilateral blindness, need of hearing aids, or cognitive delay (DQ<70 measured using the Kyoto Scale of Psychological Development test or judged by physicians without the test). **Results:** Proportions of impairments in the follow-up infants at GA 22, 23, 24 and 25 w were 22%, 22%, 10% and 17% for CP, 9%, 9%, 3% and 2% for visual impairment, 0%, 3%, 1% and 1% for hearing impairment and 52%, 47%, 27% and 23% for cognitive delay, respectively. Numbers (%) of NDI in the follow-up infants were 12(52%), 67(57%), 54(31%) and 79(33%). Odds ratios (95% confidence intervals) of NDI in the follow-up infants against at GA 25 w were 2.88 (1.10-7.56) at GA 22 w, 2.74 (1.63-4.59) at GA 23 w and 1.22 (0.76-1.94) at GA 24 w after adjusting for sex, maternal age, plurality, transfer after birth, prenatal steroids and delivery by cesarean section. The numbers of infants with confirmed survival without NDI were 9 (13% of registration) at GA 22 w and 49 (21%) at GA 23 w. **Conclusions:** Although we have to consider bias due to loss of follow-up data, this is the largest cohort report on long-term outcomes of infants born at GA 22 and 23 w. A high proportion of cognitive delay in the survived infants was a significant concern.

Background

- Policy for perinatal care for infants at the threshold of viability differs in various countries.
- In Japan, definition of abortion had lowered from gestational age (GA) at <24 weeks (w) to <22 w in 1991. Survival rates of infants born at GA 22-23 w had increased from 31% in1995 to 49% in 2005.[1)]
- For prenatal counseling and physician/ family decision-making, however, severe neurodevelopmental impairment (NDI) is an equally important issue as survival.

Objective

To evaluate survival and NDI according to GA of the extremely preterm infants born in 2003-2005 in the Japanese Neonatal Research Network (NRN).

Outcome Assessments

The follow-up protocol consisted of physical and neurological evaluations and developmental assessments at 3 yrs (between 36 and 42 months) of chronological age (CA). [2),3)]

NDI was defined as 1 or more of the following:

1. Cerebral palsy (CP)
2. Visual impairments: unilateral or bilateral blindness
3. Hearing impairments: need of hearing aids
4. Cognitive delay included the followings,
   - Developmental Quotient (DQ)<70 by the Kyoto Scale of Psychological Development III (KSPD)*
   - Judged by physicians without the test

KSPD* :Standardized for Japanese children in 2001, individualized face-to-face test measuring developmental age (DA).
- DQ=(DA/CA) x 100 , mean(SD) of DQ was 100.6(13.4) in standardization
- In this study, cognitive function was classified using total DQ;
  Delay: DQ <70, Subnormal: DQ 70~84, Normal: DQ ≥ 85

Results

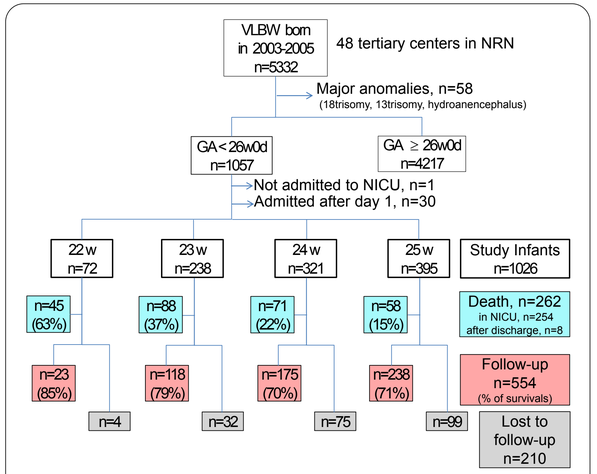

Fig 1. Flow Chart of the Study Subjects according to GA

Table 1. Demographic and Perinatal Characteristics and Neonatal Morbidities of the Infants according to GA (A) or Follow-up (B)

	A (in Study Infants)				B (in Survivors)		
	22w N=72	23w N=238	24w N=321	25w N=395	Follow-up N=554	Lost N=210	p*
Birth weight, median, g	489	576	644	757	661	679	0.27
Birth weight<500g, n(%)	43(60)	46(19)	28(9)	22(6)	51(9)	10(5)	0.05
Mother's age, median, yrs	31	30	31	31	31	30	0.06
Male, n(%)	31 (43)	125 (53)	158 (49)	216 (55)	282 (51)	112 (54)	0.57
Multiple birth, n(%)	16 (22)	59 (25)	60 (19)	81 (21)	107 (19)	47 (22)	0.36
Outborn, n(%)	6 (8)	15 (6)	21 (7)	31 (8)	41 (7)	19 (9)	0.45
Cesarean delivery, n(%)	20 (28)	103 (46)	216 (67)	293 (74)	359 (65)	131 (62)	0.56
Prenatal steroid, n(%)	17 (24)	77 (32)	136 (42)	177 (45)	240 (43)	86 (41)	0.57
Histological CAM, n(%)	27 (38)	67 (28)	76 (24)	116 (29)	162 (29)	53 (25)	0.76
Intubation in DR, n(%)	67 (93)	217 (91)	288 (90)	355 (90)	490 (88)	196 (93)	0.08
Apgar score 5min <4, n(%)	23 (36)	46 (21)	49 (16)	32 (9)	56 (11)	20 (10)	0.89
RDS, n(%)	58 (81)	187 (79)	242 (75)	305 (77)	413 (75)	171 (81)	0.05
Sepsis, n(%)	17 (24)	57 (24)	68 (21)	59 (15)	77 (14)	32 (15)	0.64
IVH (grade III or IV), n(%)	17 (24)	49 (21)	46 (15)	49 (13)	47 (9)	29 (14)	0.04
Cystic PVL, n(%)	2 (3)	10 (4)	12 (4)	22 (6)	23 (4)	12 (6)	0.34
NEC and/or I.P., n(%)	1 (1)	24 (10)	18 (6)	26 (7)	24 (4)	11(5)	0.61
CLD at 36w, n(%)	15 (22)	70 (31)	118 (38)	131 (34)	229 (42)	86 (42)	1.00
ROP treated, n(%)	15 (21)	71 (30)	100 (31)	127 (32)	232 (42)	72 (34)	0.06

p*: compared between infants followed and lost using χ^2 test or Mann-Whitney U test.

Table 2. Neurological Impairments in the Follow-up Infants according to GA

	22w N=23	23w N=118	24w N=175	25w N=238
CP				
+ , n (%)	5 (22)	26 (22)	17 (10)	39 (17)
– , n (%)	18 (78)	91 (77)	151 (86)	193 (81)
not measured, n	0	1	7	6
Visual Impairments				
+ bilateral, n (%)	2 (9)	2 (2)	0 (0)	5 (2)
+ unilateral, n (%)	0 (0)	9 (8)	6 (3)	0 (0)
– , n (%)	21 (91)	106 (90)	164 (94)	224 (94)
not measured, n	0	1	5	9
Hearing Impairments				
+ , n (%)	0 (0)	4 (3)	2 (1)	3 (1)
– , n (%)	23 (100)	114 (97)	161 (92)	229 (96)
not measured, n	0	0	12	6
Cognitive Delay				
+ , n (%)	12 (52)	54(46)	47 (27)	55 (23)
– , n (%)	9 (39)	57 (48)	100 (57)	148 (62)
not measured, n	2	7	28	35
DQ of KSPD				
DQ < 70, n (%)	6 (26)	28 (24)	31 (18)	38 (16)
DQ 70-85, n (%)	5 (22)	19 (16)	40 (23)	50 (21)
DQ ≥ 85, n (%)	2 (9)	21 (18)	32 (18)	55 (23)
Delay by Physicians				
+ , n (%)	6 (26)	26 (22)	16 (9)	17 (7)
– , n (%)	2 (9)	17 (14)	28 (16)	43 (18)
NDI				
+ , n (%)	12 (52)	67 (57)	54 (31)	79 (33)
– , n (%)	9 (39)	49 (41)	85 (49)	131 (55)
– not fully measured, n (%)	2 (9)	2 (2)	36 (20)	28 (12)

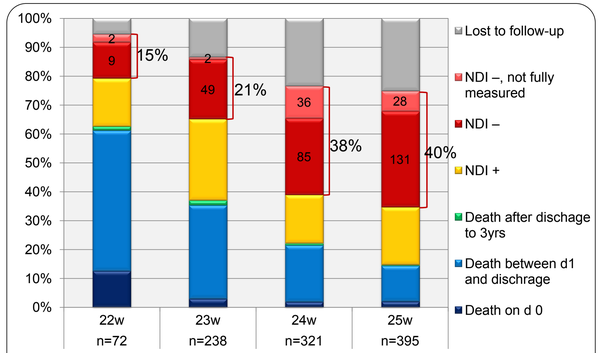

Fig 3. Proportion of the survivors without NDI in the Study Infants according to GA

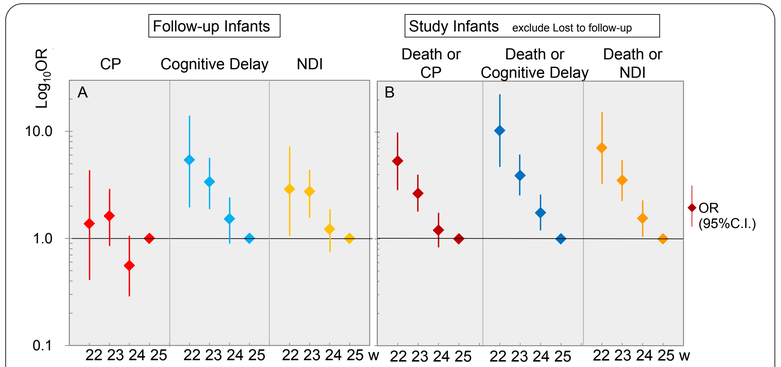

Fig 2. Odds ratios and 95% C.I. of Impairments in the Follow-up Infants (A) and Death or Impairments in the Study Infants (B) against at GA 25 w after adjusting for mother's age, sex, plurality, outborn, cesarean delivery, and prenatal steroid on logistic regression.

Discussion

Main outcomes:
- Proportion of NDI at 3 yrs in the survived and followed infants born at 22 w (52%) was not higher than that of the infants at 23 w (57%).
- Among individual components of NDI, cognitive delay was clearly related to a 1-week decrease in GA.
- Proportion of survival without major disability was 15% at 22 w of GA.

Strength of the study:
- Assessed neurodevelopmental outcomes in a large cohort of survived infants born at 22 w treated with the current policy for intensive care.

Limitation of the study:
- Cases with stillbirth or not resuscitated at delivery rooms were not enrolled.
- Attitudes towards resuscitation and intensive care for these infants may differ among the participating centers.
- Bias due to lost to follow-up of infants at 24 w (23%) and 25 w (25%).

Conclusion

High proportion of cognitive delay in the survivors born at 22 w and 23 w was a significant concern. Based on the results of neurodevelopmental outcome, the better approach and decisions of intensive care for the infants at the limit of viability should be considered.

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