The larger risk of poor cognitive function than that of CP with smaller gestation of preterm birth <25 weeks

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Background

Developmental outcome is the main endpoint for Quality Improvement in NICU care. In extremely preterm infants cognitive delay and cerebral palsy are the major causes of disability. It has been a practice to deal with these disabilities together as the outcome. On the other hand the clinical factors which cause CP and/or cognitive delay may be different.

Objective

This study tests the hypothesis that the risk of poor cognitive function is larger than CP with gestation of infants born <25 weeks.

Design/Methods

Subjects of study were 4,914 infants <29 weeks born in 2003-2007 and cared for in the level III NICUs in Japan (Table 1). They were evaluated for their survival and neurodevelopmental impairment at three years in relation with gestation of birth. CP was assessed at follow up clinic by pediatricians. Children with developmental quotient <70 by the Kyoto Scale of Infant Psychological Development test and/or those being judged as significant delay by physicians were classified as cognitive delay.

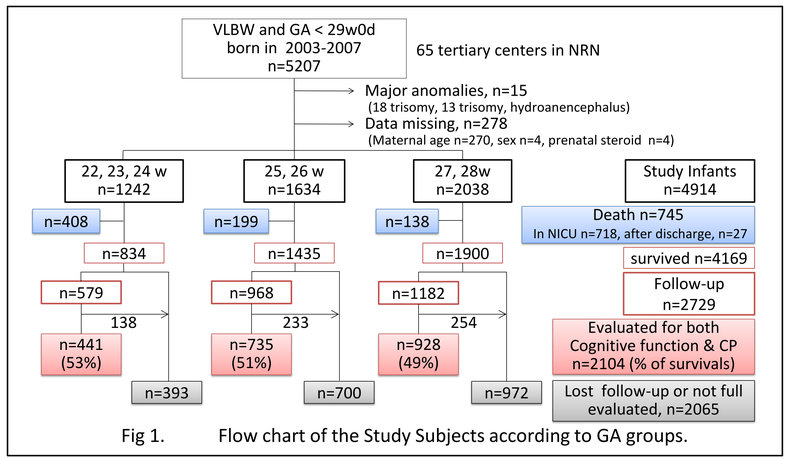

Fig 1. Flow chart of the Study Subjects according to GA groups.

Table 1 Demographic and Perinatal Characteristics and Neonatal Morbidities of the Infants according to GA groups (A) or Evaluation for both CP and Cognitive function(B)

	A (in Study Infants) N=4914			B (in Survivors) N=4169		
	22-24w N=1242	25-26w N=1634	27-28w N=2038	Evaluated N=2104	Not evaluated N=2065	p*
Birth weight, median, g	598	801	1014	838	858	0.05
Birth weight<500g, n(%)	221 (18)	99 (6)	52 (3)	95 (5)	89 (4)	0.76
Mother's age, median, yrs	31	31	31	31	31	0.30
Male, n(%)	670 (54)	884 (54)	1069 (52)	1070 (51)	1116 (54)	0.04
Multiple birth, n(%)	255 (21)	340 (21)	498 (24)	441 (21)	464 (23)	0.24
Outborn, n(%)	127 (10)	170 (10)	211 (10)	152 (7)	277 (13)	0.000
Cesarean delivery, n(%)	679 (55)	1234 (76)	1550 (76)	1488 (71)	1500 (73)	0.18
Prenatal steroid, n(%)	446 (36)	732 (45)	880 (43)	944 (45)	885 (43)	0.20
Histological CAM, n(%)	392 (31)	402 (25)	329 (16)	512 (24)	425 (21)	0.02
Intubation in DR, n(%)	1149 (93)	1407 (86)	1312 (64)	1641 (78)	1556 (75)	0.04
Apgar score 5min <4, n(%)	119 (15)	95 (7)	57 (3)	127 (6)	145 (7)	0.29
RDS, n(%)	987 (80)	1223 (75)	1352 (66)	1488 (71)	1494 (72)	0.26
Sepsis, n(%)	287 (23)	188 (11)	149 (7)	174 (8)	208 (10)	0.05
IVH (grade III or IV), n(%)	228 (19)	141 (9)	95 (5)	101 (5)	135 (7)	0.02
Cystic PVL, n(%)	45 (4)	83 (5)	104 (5)	85 (4)	112 (5)	0.05
NEC and/or I.P., n(%)	110 (9)	93 (6)	57 (3)	53 (3)	96 (5)	0.000
CLD at 36w, n(%)	404 (33)	480 (30)	274 (14)	560 (27)	546 (27)	0.92
ROP treated, n(%)	381 (31)	487 (30)	321 (16)	619 (29)	543 (26)	0.03

p*: compared between infants evaluated and not evaluated using χ^2 test or Mann-Whitney U test.

Results

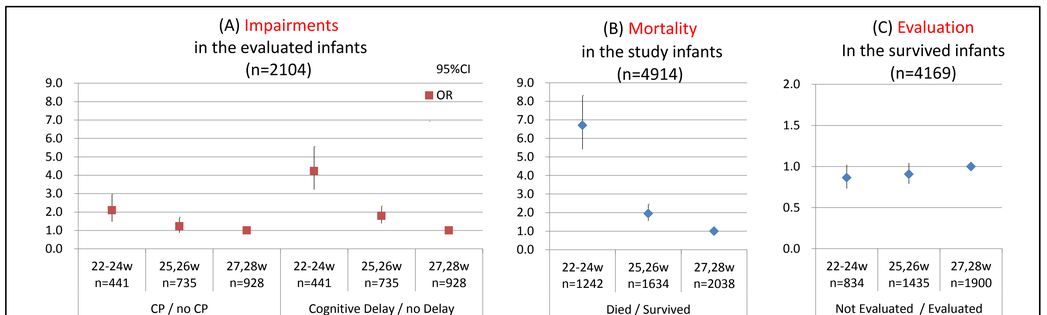

Fig. 2 Odds ratios and 95% C.I. of (A) Impairments in infants evaluated for both CP and MR, of (B) Mortality in the study infants, and of (C) Evaluation ratio in the survived infants after adjusting for mother's age, sex, plurality, outborn, cesarean delivery, and use of prenatal steroid on logistic regression.

A total of 745 infants died and 2104 infants were assessed for both CP and cognitive function at three years. They were classified into three groups of 22-24w (n=441), 25-26w (n=735), and 27-28w (n=928) (Fig 1).

After adjusting sex, maternal age, plurality, outborn, prenatal steroids and delivery by cesarean section, the odds of CP and cognitive delay were calculated for each groups taking the 27-28w as a reference (Fig 2). Odds ratio (OR) (95% C.I.) of CP were 2.09 (1.47-2.97) in 22-24w and 1.22 (0.88-1.71) in 25-26w. Whereas, OR of cognitive delay were 4.23 (3.22-5.55) in 22-24w and 1.79 (1.39-2.31) in 25-26w. OR of death were 6.71 (5.41-8.31) in 22-24w and 1.95 (1.55-2.45) in 25-26w group.

Limitation of the study

Bias due to lost to follow-up or not full-evaluated.

Conclusion

This study has shown that the risk of poor cognitive function is larger than CP with gestation of infants born <25 weeks.

The risk of impairment in cognitive function is more sensitive than CP in assessing the quality of NICU care. It may further improve the evidence-based practice identification and Quality Improvement.

References

1.Kusuda S, Fujimura M, Uchiyama A, Totsu S, Matsunami K. Trends in morbidity and mortality among very-low-birth-weight infants from 2003 to 2008 in Japan.; Neonatal Research Network, Japan. Pediatr Res. 2012;72:531-8.

2.Ishii N, Kono Y, Yonemoto N, Kusuda S, Fujimura M. Outcomes of Infants born at 22 and 23 weeks' gestation. Pediatrics 2013 (in press).