Health-Related Quality of Life in 5-Year-Old Very Low Birth Weight Infants

Liisi Rautava, MD, Unto Häkkinen, PhD, Emmi Korvenranta, MD, MSc(Econ), Sture Andersson, MD, PhD, Mika Gissler, Dr Phil, Mikko Hallman, MD, PhD, Heikki Korvenranta, MD, PhD, Jaana Leipälä, MD, PhD, Miika Linna, PhD, Mikko Peltola, MSc, Outi Tammela, MD, PhD, and Liisa Lehtonen, MD, PhD

Objective To investigate the effect of preterm birth, the time of birth, and birth hospital level and district on health-related quality of life (HRQoL) and quality-adjusted life years (QALYs).

Study design This national study included all very low birth weight infants (VLBWIs; birth weight ≤ 1500 g or gestational age < 32 weeks) born in Finland between 2000 and 2003 (n = 1169; live-born, n = 900) and full-term controls (n = 368). Register data and parental questionnaires were used. The relationships among HRQoL and QALYs at age 5 years and preterm birth, time of birth, and the level and district of the birth hospital were studied.

Results HRQoL at age 5 years was lower and 1.3 QALYs were lost in VLBWIs compared with controls. Regional differences in the QALYs of VLBWIs were found among the 5 university hospital districts. Birth hospital level or birth outside office hours had no effect on the QALYs of live-born VLBWIs. The adjusted HRQoL total score was not affected by birth outside office hours or by the birth hospital level or district.

Conclusions Differences in QALYs related to hospital district suggest variation in the care of VLBWIs that needs to be addressed. *(J Pediatr 2009;155:338-43)*.

Very low birth weight infants (VLBWIs) need resource-intensive care during their first months of life. The increasing development of neonatal intensive care practices has dramatically improved the survival of VLBWIs.[1-3] This has raised concerns about the quality of life of children born preterm, who have higher morbidity than children born at full term.[4-6]

There are relatively few published studies on the health-related quality of life (HRQoL) of former preterm infants. In studies from The Netherlands[7] and Thailand,[8] the parents of VLBWIs age 1 to 4 years estimated a lower HRQoL for their children than did the parents of the controls. Adolescents born as extremely low birth weight infants (ELBWIs) had lower HRQoL scores than controls, as evaluated both by the subjects themselves[9] and by their parents.[10] In contrast, another cohort of teenagers born extremely prematurely rated their HRQoL similar to that of the controls despite having more health problems,[11] and HRQoL was not associated with birth weight or the presence of disability in ELBWIs in young adulthood.[12] Differences in the HRQoL of adolescent ELBWIs were also found in cohorts from 3 different countries, which were not explained by birth weight, gestational age (GA), or cerebral palsy.[13]

Quality-adjusted life years (QALYs) have been reported as part of a cost-utility analysis of the care of ELBWIs in Victoria[14-16] and as part of a cost-effectiveness analysis of predischarge monitoring for apnea.[17] More research is needed on QALYs gained with neonatal intensive care. The aim of the present study was to examine whether preterm birth, the level or the district of the birth hospital, or the time of birth outside office hours are associated with the HRQoL and QALYs in 5-year-old Finnish VLBWIs. We hypothesized that HRQoL and QALYs are decreased in VLBWIs compared with controls, particularly in those VLBWIs born outside level III hospitals or outside office hours. We also hypothesized that there are differences in the HRQoL and QALYs of VLBWIs among university hospital districts.

Methods

The study population included all VLBWIs (GA < 32 weeks or birth weight ≤ 1500 g) born in level II or III hospitals in Finland between 2001 and 2002. Healthy full-term infants of the same sex born next after every third live-born VLBWI in the same hospital were used as controls.

AGA	Appropriate birth weight for gestational age
HRQoL	Health-related quality of life
LGA	Large birth weight for gestational age
QALY	Quality-adjusted life year
SGA	Small birth weight for gestational age
VLBWI	Very low birth weight infant

From the Department of Pediatrics, Turku University Hospital, Turku, Finland (L.R., E.K., H.K., L.L.); Centre for Health Economics (U.H., J.L., M.L., M.P.) and Information Division (M.G.), National Institute for Health and Welfare, Helsinki, Finland; Hospital for Children and Adolescents, Department of Pediatrics, Helsinki, Finland (S.A.); Department of Pediatrics, Oulu University Hospital, Oulu, Finland (M.H.); and Department of Pediatrics, Tampere University Hospital, Tampere, Finland (O.T.)

All authors are members of the Performance, Effectiveness, and Cost of Treatment Episodes (PERFECT) Preterm Infant Study Group. Supported by the Academy of Finland (Research Program on Health Services Research), the South-West Finnish Fund for Neonatal Research, the Turku University Hospital EVO Fund, and the Turku University Hospital Foundation. The authors declare no conflicts of interest.

 10.1016/j.jpeds.2009.03.061

The exclusion criteria were (1) incomplete personal identification number in the Medical Birth Register, preventing data linking (n = 140); (2) a major disparity between GA and birth weight or missing data for either of these variables (n = 29); (3) birth at a level I hospital or at a hospital with < 3 live-born VLBWI deliveries during the study period (n = 4); and (4) at least 1 lethal congenital malformation (n = 19). Lethal malformations were defined as trisomy 13 or 18, triploidy, severe cardiac defects (ie, acardia, univentricular heart, transposition of the great arteries, interrupted aorta), severe developmental disorders (ie, anencephaly, holoprosencephaly), and clearly defined lethal syndromes according to the Finnish Register of Congenital Malformations. Control infants admitted to intensive care during the first week of life were excluded. After the exclusions, the study population comprised 923 live-born VLBWIs and 381 controls. The questionnaires were not sent to families whose address was not available in the Population Register, who had refused the release of their address, or who lived abroad when the questionnaires were mailed (23 VLBWIs and 13 controls). Six surviving VLBWIs hospitalized for less than 5 days during the first year of life were not included in the QALY analysis, because their data were assumed to be incomplete. Including stillborn VLBWIs, the VLBWI population comprised 1169 subjects.

Data Collection

We sent a questionnaire to the parents between 0.5 and 1.5 months before the child's fifth birthday and, if necessary, 2 reminders 1.5 and 2.5 months later. The data from the questionnaires were linked to the Finnish Medical Birth Register for background information, to the National Hospital Discharge Register for data on initial hospitalization, to the Cause of Death statistics, and to the Register of Congenital Malformations.

The parental questionnaire included the 17D,[18] an established instrument for measuring HRQoL.[19] The 17D contains 1 closed-ended question addressing each of the following health dimensions: mobility, vision, hearing, breathing, sleeping, eating, speech, elimination, school and hobbies, learning and memory, discomfort and symptoms, depression, distress, vitality, appearance, friends, and concentration. The questionnaire provides a single HRQoL score on a scale from 0 to 1, with 0 corresponding to being dead, 0.0162 to being unconscious or comatose, and 1 to having no problems in any dimension, or "full" HRQoL. The 17D has been used as a self-administered questionnaire for 8- to 11-year-old children. After consulting the copyright holders (H. Sintonen and M. Apajasalo), we modified the questions to allow for parental evaluation of HRQoL of 5-year-old children. Also, we modified the question on vision to inquire about the child's ability to watch television and look at a picture book instead of his or her ability to read. A translated version of the modified questionnaire is given in **Appendix 1** (available at www.jpeds.com). The 17D total scores were analyzed using the importance weights developed for 17D for all responders who completed all 17 questions, and were used as a basis for calculating QALYs. The importance weights of the dimensions are based on a - parental questionnaire asking them to rank the dimensions in order of importance for the quality of life of 8- to 11-year-old children.[18]

All parents gave written informed consent for participation in the study. The study protocol was approved by the Ethics Committee of the National Institute for Health and Welfare.

Statistical Analysis

The main study outcomes were HRQoL score (17D) and QALYs at age 5 years. These were first compared between the VLBWIs and controls. Then, focusing on VLBWIs alone, the relationships of the outcomes to the delivery hospital level and university hospital district, and to birth during or outside office hours, were evaluated.

The five university hospital districts in Finland each include 1 university hospital with a level III neonatal intensive care unit (NICU) and 1 or more hospitals with a level II NICU. Births occurring on public holidays, on weekends, and between 4:01 p.m. and 7:59 a.m. on weekdays were considered births "outside office hours."

Comparisons of 17D total scores were performed using Tobit regression.[20] The background variables used in the adjustments were chosen by testing the association of the 17D total score with the following variables: sex, mother's and father's years of education and current employment status, logarithm of family's monthly income, and family structure (ie, 2 parents, single parent or joint custody, 1 biological parent and a stepparent, or foster care or adoption family). The individual background variables that significantly influenced the 17D total score were adjusted for in the comparisons between the VLBWIs and controls. The associations of the VLBWIs' 17D total scores with sex, mother's and father's years of education and current employment status, logarithm of monthly family income, family structure, intrauterine growth, multiple pregnancies (number of children), GA, birth weight, and any nonlethal congenital malformations were tested similarly. The variables significantly influencing the 17D total score in the whole study population and the individual variables significantly affecting the 17D total score in the VLBWIs were adjusted for in the comparisons involving only the VLBWIs. Intrauterine growth was categorized as small birth weight for GA (SGA; < -2 standard deviations [SD]), appropriate birth weight for GA (AGA; $\pm$ 2 SD), or large birth weight for GA (LGA; > 2 SD) according to the reference values from the Finnish population.

Adjusted individual 17D dimension scores were compared using a generalized linear model. The response distribution of 17D scores was multinomial, and the link function was cumulative logit. If the assumption of proportional odds was not met in the analysis of 17D dimension scores, then the most severe (and rarest) categories were combined until the assumption was met.

QALYs by age 5 years were calculated by defining a HRQoL score for each day of life and then multiplying this by the