IMPORTANCE This follow-up study of extremely preterm (EPT) children (<27 weeks’ gestational age [GA] at birth) revealed major eye and visual problems in 37.9% (147 of 388) of all EPT infants and in 55.4% (67 of 121) of the most immature subgroups at 6.5 years of age. These major eye and visual problems were strongly associated with treatment-requiring retinopathy of prematurity (ROP).

OBJECTIVES To investigate the ophthalmologic outcome of a national cohort of EPT children at 6.5 years of age and to evaluate the impact of prematurity and ROP.

DESIGN, SETTING, AND PARTICIPANTS All surviving EPT children born in Sweden between April 1, 2004, and March 31, 2007, were included and compared with a matched term control group, as part of a prospective national follow-up study.

MAIN OUTCOMES AND MEASURES Visual acuity, refraction in cycloplegia, and manifest strabismus were evaluated and compared with GA at birth and with treatment-requiring ROP.

RESULTS The study cohort comprised 486 participants. The mean (SD) GA of the children who were included was 25 (1) weeks, and 45.7% (222 of 486) were female. At a median age of 6.6 years, 89.3% (434 of 486) of eligible EPT children were assessed and compared with 300 control group children. In the EPT group, 2.1% (9 of 434) were blind, 4.8% (21 of 434) were visually impaired according to the World Health Organization criteria, and 8.8% (38 of 434) were visually impaired according to the study criteria. Strabismus was found in 17.4% (68 of 390) and refractive errors in 29.7% (115 of 387) of the EPT children compared with 0% (0 of 299) and 5.9% (17 of 289), respectively, of the control children (P < .001). Altogether at 6.5 years of age, 37.9% (147 of 388) of the EPT children had some ophthalmologic abnormality compared with 6.2% (18 of 290) of the matched control group (95% CI of the difference, 26.1%-37.2%). When treatment-requiring ROP was adjusted for, no significant association between GA and visual impairment could be detected. For refractive errors, the association with GA remained after adjustment for treatment-requiring ROP (odds ratio, 0.72; 95% CI, 0.58-0.91 for each 1-week increment).

CONCLUSIONS AND RELEVANCE In a Swedish national cohort of EPT children at 6.5 years of age, major eye and visual problems were frequently found. Treatment-requiring ROP was a stronger impact factor than GA on visual impairment and strabismus, but not on refractive errors, as a whole. In modern neonatal intensive care settings, ophthalmologic problems continue to account for a high proportion of long-term sequelae of prematurity.
he survival rate of extremely preterm (EPT) infants is steadily increasing, and proactive neonatal care has continuously lowered the gestational age (GA) of viability.\textsuperscript{1,2} Concerns over the mortality rates of the most immature infants combine with concerns about morbidity and long-term sequelae. Various frequently occurring ophthalmologic problems have been documented in preterm children.\textsuperscript{3-7} However, to our knowledge, long-term population-based follow-up studies of EPT children are sparse.

The national Extremely Preterm Infants in Sweden Study (EXPRESS) of children born before 27 weeks’ GA has reported high survival rates and a high incidence of retinopathy of prematurity (ROP) in the neonatal period.\textsuperscript{5,8} A follow-up at 30 months’ corrected age revealed moderate or severe disabilites in 27%, and one-third of the EPT children had eye and visual problems.\textsuperscript{9,10}

This study aimed to describe visual and ocular findings in the national EXPRESS cohort at 6.5 years of age. They were compared with a matched control group born at term.

Methods

During a 3-year study period (April 1, 2004, to March 31, 2007), 707 infants with a GA at birth of less than 27 weeks (+27 + 0) were born alive in Sweden. Of the original study cohort, 494 infants were alive at 1 year.\textsuperscript{2} Of this cohort, 8 had since died, resulting in 486 possible survivors at 6.5 years. A further 2 could not be traced, and 2 had been withdrawn by their parents early from further participation in the study. Hence, 462 confirmed survivors constituted the eligible group at the 6.5-year follow-up. The parents of 28 of these children declined participation in the follow-up, leaving 434 (93.9%) EPT children, who were assessed either by examination within the study or by medical record review. The term control children were recruited either at the time of the 30-month follow-up study or during this study and were matched by postal code, sex, birth date, and maternal country of origin. They were randomly selected from the Swedish Medical Birth Register. Inclusion criteria were term birth (>37 weeks’ GA), single birth, and an Appar score exceeding 4 at 5 minutes.

The Ethics Review Board, Lund, Sweden, approved the study. Written informed consent for data acquisition was provided by the parents.

Ophthalmologic examination, following a study protocol, was scheduled at the 7 university hospitals in Sweden at age 6.5 years (+3 months). For EPT children not in attendance, data were obtained from medical reports.

Variables Evaluated

Monocular and binocular distance linear visual acuity (VA) with habitual correction was assessed at 3 m with the Lea Hyvärinen chart.\textsuperscript{11} The progression was geometric, and the best measurable VA was 20/10. For VA, at least 4 of 5 optotypes had to be correctly identified. Based on the results of the monocular VA, a better eye and a worse eye were identified in children with unequal VA, and the right eye was chosen as the better eye in the remaining children. Binocular VA with single Lea Hyvärinen optotypes was also evaluated at 3 m. A crowding ratio factor was constructed by dividing the binocular single-optotype VA by the binocular linear VA.\textsuperscript{12

In 19 children who were mainly disabled or at younger ages, the VA data from medical records had to be transformed because different types of tests had been used. All data were transformed to Snellen values according to the literature.\textsuperscript{13,14} For comparison with the linear VA, the VA with single optotypes was divided by a crowding ratio factor, calculated from the study groups and from the literature.\textsuperscript{13,15} Visual impairment was defined according to the World Health Organization (WHO) criteria (ie, blindness was best VA <20/400, severe visual impairment was <20/200, and moderate visual impairment was <20/60).\textsuperscript{16} In addition, any visual impairment was defined as less than 20/40 VA.\textsuperscript{17} When categorizing the VA data from medical records at younger ages, the levels for the definition of visual impairment were lowered.\textsuperscript{18,19}

Refraction was assessed with autorefractors, including KR 8100, 8800, and 8900 (Topcon), RX-502 (Rodenstock), and handheld Retinomax (Nikon), with cycloplegia induced using cyclopentolate hydrochloride, 0.85%, and phenylephrine hydrochloride, 1.5%. Spherical equivalents were also calculated. Myopia was defined as greater than 3 diopter (D). Hyperopia was defined as greater than 3 D. Astigmatism was recorded as negative cylinders and was defined as greater than 2 D. Only refractive errors in the better eye of each individual were considered. Anisometropia was defined as greater than 2 D.

A cover test was performed with habitual correction and fixation at a 5-m distance for evaluation of manifest strabismus. “Major eye and visual problems” comprise visual impairment according to the WHO criteria (ie, <20/60), manifest strabismus, or refractive error (ie, myopia >3 D, hyperopia >3 D, astigmatism >2 D in the better eye, or anisometropia >2 D).

Screening for ROP had already been performed during the neonatal period.\textsuperscript{8} The International Classification of Retinopathy of Prematurity\textsuperscript{20} was used, and the treatment criteria followed recommendations of the Early Treatment for Retinopathy of Prematurity study.\textsuperscript{21} Mild ROP was defined as ROP stage 1 or 2 and severe ROP as stages 3 to 5.
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Original Investigation Research

statistical regression analyses. Adjusted treatment-requiring ROP (yes or no) in multiple logistic regression analyses were analyzed against GA (as a continuous variable) and major eye and visual problems (categorized into a composite).

Comparison and contingency tables (Fisher asymptotic or exact test) was performed. Visual impairment, strabismus, refractive errors, and major eye and visual problems (categorized into a composite score) were analyzed against GA (as a continuous variable) and adjusted to treatment-requiring ROP (yes or no) in multiple logistic regression analyses.

Results

Of the 434 EPT children whose parents accepted the study invitation, 357 participated in the study examination. Medical records from another 77 EPT children (examined according to clinical practice in their local hospitals) were collected. Forty-nine of these 77 children were examined at 6 years or older. Together with the EPT attendees, they constituted the 6-year EPT group (n = 406). The remaining 28 EPT children were examined at younger ages (the young-age EPT group).

visual Acuity

For the whole EPT group (n = 434), the frequency of visual impairment based on age and visual task-adjusted data was 4.8% (n = 21) according to the WHO criteria (<20/60) and 8.8% (n = 38) according to the study criteria (<20/40 in the 6-year EPT group and lower levels in the young-age EPT group) compared with 0.7% (2 of 300) and 1.0% (3 of 300), respectively, in the control group (P < .001). Two percent (9 of 434) of EPT children were blind, of whom 2 had no light perception, and 1 could only localize a light source. Two children were severely visually impaired, and 10 had moderate visual impairment. Seventeen EPT children were categorized as having any visual impairment. Two control children had moderate visual impairment, and 1 had any visual impairment. Demographic and visual impairment data are listed in Table 1.

The binocular linear and single-optotype VAs were evaluated in 354 and 300 of the 6-year EPT group children, respectively, and in 299 and 282 control children, respectively. The median (interquartile range) binocular linear and single-optotype VAs of the 6-year EPT group (20/20, 20/20 to 20/20) and 20/15 [20/20 to 20/12.5] differed from those of the control group (20/20 [20/20 to 20/15] and 20/12.5 [20/15 to 20/10]) (P < .001 for both). The monocular VA of the better and worse eyes was evaluated in 397 and 394 of the 6-year EPT group children, respectively, and in 299 control children. The median (interquartile range) VA in the better eye was 20/25 (20/25 to 20/20) in the 6-year EPT group vs 20/20 (20/20 to 20/20) in the control group, and that in the worse eye was 20/25 (20/30 to 20/20) vs 20/20 (20/25 to 20/20) (P < .001 for both) (Figure 1). The mean (SD) crowding ratios were 1.4 (0.3) in the 6-year EPT group (n = 297) and 1.5 (0.3) in the control group (n = 282) (P = .002). In children for whom only the single-optotype VA was available, this value was divided by 1.46 (ie, the mean crowding ratio of both groups) for calculation of a comparable VA value, with the linear VA evaluated in the remaining group of children.

In 28 EPT children (the young-age EPT group), VA had already been evaluated at a younger age. Two children lacked numerical values but had been considered to have no visual impairment at 30 months of age. The median VA (with habitual correction) of the 26 remaining EPT children was 20/40 (range, 20/600 to 20/20) after adjustment for visual task.

Table 1. Demographic and Visual Impairment Follow-up Data for the Study Groups at 6.5 Years of Age

<table>
<thead>
<tr>
<th>Variable</th>
<th>6-Year EPT Group (n = 406)</th>
<th>Young-Age EPT Group (n = 28)</th>
<th>Dropout Group (n = 28)</th>
<th>Control Group (n = 300)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age, median (range), wk</td>
<td>25 (22-26)</td>
<td>25 (23-26)</td>
<td>40 (37-41)</td>
<td></td>
</tr>
<tr>
<td>Birth weight, median (range), g</td>
<td>770 (348-1315)</td>
<td>865 (515-1190)</td>
<td>820 (560-1080)</td>
<td>3626 (2200-5110)</td>
</tr>
<tr>
<td>Sex, No.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>221</td>
<td>12</td>
<td>17</td>
<td>171</td>
</tr>
<tr>
<td>Female</td>
<td>185</td>
<td>16</td>
<td>11</td>
<td>129</td>
</tr>
<tr>
<td>ROP in either eye, No./total No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>113/404 (28.0)</td>
<td>7/26 (26.9)</td>
<td>NA</td>
<td>0</td>
</tr>
<tr>
<td>Stages 1-2</td>
<td>148/404 (36.6)</td>
<td>14/26 (53.8)</td>
<td>NA</td>
<td>0</td>
</tr>
<tr>
<td>Stages 3-5</td>
<td>143/404 (35.4)</td>
<td>6/26 (19.2)</td>
<td>NA</td>
<td>0</td>
</tr>
<tr>
<td>ROP treatment, No./total No. (%)</td>
<td>80/404 (19.8)</td>
<td>2/26 (7.7)</td>
<td>NA</td>
<td>0</td>
</tr>
<tr>
<td>Age at examination, median (range), y</td>
<td>6.6 (6.5-6.7)</td>
<td>3.6 (2.6-5.6)</td>
<td>NA</td>
<td>6.6 (6.5-6.7)</td>
</tr>
<tr>
<td>Visual impairment, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None, ≥20/40</td>
<td>373 (91.9)</td>
<td>23 (82.1)</td>
<td>NA</td>
<td>297 (99.0)</td>
</tr>
<tr>
<td>Any, &lt;20/40 to ≥20/60</td>
<td>14 (3.4)</td>
<td>1 (3.6)</td>
<td>NA</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Moderate, &lt;20/60 to ≥20/200</td>
<td>9 (2.2)</td>
<td>1 (3.6)</td>
<td>NA</td>
<td>2 (0.7)</td>
</tr>
<tr>
<td>Severe, &lt;20/200 to ≥20/400</td>
<td>2 (0.5)</td>
<td>0</td>
<td>NA</td>
<td>0</td>
</tr>
<tr>
<td>Blind, &lt;20/400</td>
<td>8 (2.0)</td>
<td>1 (3.6)</td>
<td>NA</td>
<td>0</td>
</tr>
</tbody>
</table>

Abbreviations: EPT, extremely preterm; NA, not applicable; ROP, retinopathy of prematurity.

a Data were missing for 2 children.

b Analysis includes both untreated and treated 6-year EPT children examined at 6 years or older, and EPT children examined at younger ages.

c Seventy 6-year EPT children had received laser therapy, 6 were given additional cryotherapy, 2 underwent vitrectomy, 1 had cerclage, and 1 was treated with a combination of cryotherapy, vitrectomy, and cerclage.

d Levels for the definition of visual impairment were lowered in younger age groups.
Refraction

The median (range) spherical equivalent of the better eye for the 6-year EPT group (n = 387) was +1.38 D (−13.50 to +10.25 D) vs +1.25 D (−1.13 to +6.81 D) in the control group (n=289) ($P = .08$). The median (range) astigmatism of the better eye was 0.50 D (0.00-5.00 D) in the 6-year EPT group and 0.25 D (0.00-4.25 D) in the control group ($P < .001$). Details are listed in Table 2.

Strabismus

Seventeen percent (68 of the 390 examined with the cover test) of the 6-year EPT group children had manifest strabismus. Of them, 79.4% (n = 54) had esotropia, and 20.6% (n = 14) had exotropia. No child in the control group (0 of 299) had manifest strabismus. One control child with autism was hard to assess. Strabismus and refractive error frequencies from the young-age EPT group were not presented or included in the analyses.

Overall Ophthalmologic Outcome

Major eye and visual problems (defined in the Variables Evaluated subsection of the Methods section) were found in 37.9% (147 of 388) of the 6-year EPT group and in 6.2% (18 of 290) of the control group. The 95% CI of the difference was 26.1% to 37.2%.

Ophthalmologic Outcome and ROP

Visual impairment was associated with treatment-requiring ROP ($P < .001$). Seven of the 9 blind EPT children had undergone laser treatment for ROP, 4 of whom had received additional treatment, such as cryotherapy, vitrectomy, or cerclage, while the other 2 had mild ROP. Both severely visually impaired EPT children had severe ROP (one of whom had been treated). Refractive errors and strabismus were more common in eyes that had been treated for ROP compared with untreated eyes. Twelve of the 25 (48.0%) 6-year EPT group children with astigmatism ($P = .001$), 27 of the 36 children (75.0%) with anisometropia ($P < .001$), and 9 of the 66 children (13.6%) with hyperopia ($P = .23$) had been treated for ROP. All 16 of the 6-year EPT group children with myopia had been treated for ROP (16 of 71 [22.5%] of all infants treated for ROP). The distribution of refraction and VA with respect to ROP is shown in Figure 2. Twenty-nine of the 68 (42.6%) 6-year EPT group children with strabismus had been treated for ROP ($P < .001$).

Ophthalmologic Outcome and GA

Univariate analyses revealed a strong association between GA and visual impairment (the odds ratios for each 1-week GA increment were 0.58 for less severe and 0.50 for more severe visual impairment ($P < .001$ for both) (Table 3). When adjusting for treatment-requiring ROP, the significant association

Table 2. Refraction, Habitual Correction, and Strabismus Frequencies in the 6-Year EPT Group and the Control Group

<table>
<thead>
<tr>
<th>Variable</th>
<th>EPT (n = 387)a</th>
<th>Control (n = 289)b</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myopia &gt;3 D</td>
<td>16 (4.1)</td>
<td>0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hyperopia &gt;3 D</td>
<td>66 (17.1)</td>
<td>12 (4.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Astigmatism &gt;2 D</td>
<td>25 (6.5)</td>
<td>4 (1.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Anisometropia &gt;2 D</td>
<td>36 (9.3)</td>
<td>1 (0.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Refractive errors*</td>
<td>115 (29.7)</td>
<td>17 (5.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Habitual correction</td>
<td>147/404 (36.4)</td>
<td>17/299 (5.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Strabismus</td>
<td>68/390 (17.4)</td>
<td>0/299</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: D, diopter; EPT, extremely preterm.

* Nineteen EPT children either refused eyedrops, or refraction had been evaluated at younger ages.

* Eleven control children refused cycloplegic eyedrops.

* Myopia exceeding 3 D, hyperopia exceeding 3 D, astigmatism exceeding 2 D, or anisometropia exceeding 2 D.
between GA and visual impairment disappeared ($P = .27$ and $P = .11$ for less severe and more severe visual impairment, respectively), indicating that treatment-requiring ROP caused the major part of the association between GA and visual impairment. The same pattern was observed for strabismus. For refractive errors and the composite score, the association with GA remained after adjustment for treatment-requiring ROP.

**Discussion**

This national cohort of EPT children showed a high rate of visual impairment. The frequencies of blindness and visual impairment were higher at 6.5 years of age than at previous examinations at 30 months’ corrected age (2.1% [9 of 434] vs 1.0% [4 of 390], respectively, and 4.8% [21 of 434] vs 3.1% [12 of 390], respectively).

Owing to the older age and thereby better collaboration, the methodology could be more refined, the examinations more reliable, and the participation rate higher, which probably explains the difference. Visual impairment seems to be related to the degree of prematurity. In our study, blindness and visual impairment were clearly overrepresented in the most immature subgroups (16.7% [7 of 42] at 22-23 weeks’ GA compared with 2.2% [3 of 138] at 26 weeks’ GA, and decreasing by 50% with each 1-week GA increment) (Table 3). This result is also supported by previous studies of preterm children of various degrees of prematurity. A UK population-based study of 6-year-old children born before 26 weeks’ GA found a similar rate (2.5% [6 of 241]) of blindness as this study. A recent population-based study in Denmark that included a somewhat more mature EPT group (>28 weeks’ GA) reported a lower prevalence of visual impairment (1.1%) among 178 children at 4 years of age. However, in a regional population-based study of a small group (n = 39) of 6-year-old Norwegian children born before 27 weeks’ GA, no child was visually impaired. Another regional population-based study in Sweden reported a visual impairment frequency of 6% in 7-year-old children (n = 51) born before 29 weeks’ GA.

**Table 3. Major Ophthalmologic Abnormalities Relative to Gestational Age**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Gestational Age, No. (%)</th>
<th>OR for Each 1-Wk Increment in Gestational Age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>22-23 wk (n = 42)</td>
<td>24 wk (n = 82)</td>
</tr>
<tr>
<td>Any visual impairment$^b$</td>
<td>10/42 (23.8)</td>
<td>11/82 (13.4)</td>
</tr>
<tr>
<td>Visual impairment according to WHO criteria$^a$</td>
<td>7/42 (16.7)</td>
<td>6/82 (7.3)</td>
</tr>
<tr>
<td>Strabismus</td>
<td>10/40 (25.0)</td>
<td>20/76 (26.3)</td>
</tr>
<tr>
<td>Refractive errors$^d$</td>
<td>19/41 (46.3)</td>
<td>39/78 (50.0)</td>
</tr>
<tr>
<td>Composite score$^e$</td>
<td>23/42 (54.8)</td>
<td>44/79 (55.7)</td>
</tr>
</tbody>
</table>

Abbreviations: D, diopter; OR, odds ratio; WHO, World Health Organization.

$^a$ Adjusted for treatment-requiring retinopathy of prematurity.

$^b$ Best-estimated visual acuity below 20/40 at age 6 years and up and in younger ages adjusted for age.

$^c$ Best-estimated visual acuity below 20/60 at age 6 years and up and in younger ages adjusted for age.

$^d$ Myopia exceeding 3 D, hyperopia exceeding 3 D, astigmatism exceeding 2 D, or anisometropia exceeding 2 D.

$^e$ Composite score based on visual impairment (according to the WHO criteria), strabismus, myopia exceeding 3 D, hyperopia exceeding 3 D, astigmatism exceeding 2 D, or anisometropia exceeding 2 D.
Finally, another regional population-based study of 216 less immature 10-year-old Swedish children (inclusion criterion birth weight, <1500 g) had lower frequencies of blindness and visual impairment (0.4% and 1.8%, respectively) than in the present study. In none of the above-mentioned studies was visual outcome pooled per gestational week at birth. Because the survival rates are steadily increasing, particularly in the most immature subgroups of EPT infants (as documented in the literature), it is not surprising that the visual impairment frequencies are higher in studies that include only the most preterm EPT infants.

Prematurity also seemed to have a potentially negative impact on visual function above visual impairment levels. A considerable proportion (8.8% [38 of 434]) of the EPT children had a VA less than 20/40 at the age of 6.5 years. This VA is below the limit for holding a driver’s license in Sweden, and, although the VA is expected to improve somewhat with age, it is important to follow the visual development of these children. The VA above the age-normal limits also differed between the EPT group and the control group children, which was in keeping with previous findings. Seventy-seven percent (306 of 397) of the EPT group reached a VA of 20/25 in their better eye compared with 97.7% (292 of 299) in the control group.

Increased crowding ratio has been associated with white matter lesions (ie, periventricular leukomalacia), which is related to prematurity and to cerebral visual impairment. Therefore, it was an unexpected finding that the crowding ratio was in fact higher in the control group than in the preterm group. This result shows that the crowding phenomenon also exists in healthy children at this age, although at higher VA. Accordingly, previous population-based studies on preterm children have not shown significantly increased crowding ratios, although Larson and coworkers demonstrated a suggestion of it.

Refractive errors were found in one-third (29.7% [115 of 387]) of our preterm cohort, and hyperopia was by far the most frequent refractive error, possibly due to an altered emmetropization related to prematurity, as previously suggested. Although the median spherical equivalent values in the EPT group were almost identical to those of the Danish study (ie, +1.38 D compared with +1.37 D, respectively), the frequencies of refractive errors were higher, altogether and separately, possibly owing to the more immature cohort, as discussed above.

Manifest strabismus was found at a higher rate but in a similar distribution with respect to type (ie, 79.4% [54 of 68] esotropia and 20.6% [14 of 68] exotropia) compared with at 30 months. In the British national study, the strabismus frequency of a somewhat more immature group was higher (24%), which supports the general conclusion that ophthalmologic abnormalities are related to the degree of immaturity at birth. However, the strabismus frequency was higher in our study than in the previously described study in Norway, where 10% had manifest strabismus, but was similar to the population-based study of Swedish 10-year-old children. Major eye and visual problems (ie, visual impairment, strabismus, and refractive error frequencies) all increased with the degree of prematurity (Table 3). However, this association was strongly linked to treatment-requiring ROP. When analyzing the impact of GA on visual impairment and strabismus, with adjustment for treatment-requiring ROP, the latter actually had a stronger impact than GA. This finding was not true for refractive errors, although myopia, astigmatism, and anisometropia, separately, were all related to treatment-requiring ROP. The minor influence of treatment-requiring ROP vs GA on refractive errors, as a whole, can probably be explained by the high frequency of hyperopia, which was not at all associated with treatment-requiring ROP. Therefore, hyperopia seems to be a sequela of immaturity per se.

Our study has several strengths. In Sweden, the personal identity number system allows almost 100% coverage of the health care system. Therefore, this study of EPT children is likely to include the whole national population of infants born before 27 weeks’ GA during the 3-year period. The participation rate in the 6.5-year-old cross-sectional study was high, including 89.3% (434 of 486) of the original cohort and 93.9% (434 of 462) of the eligible group of confirmed survivors. For the children who did not participate in the study, we had access to a large number of medical records. All children had been screened for ROP and had undergone ophthalmologic examination at 30 months of age. The control group was carefully selected to optimize comparison and minimize as many confounding factors as possible.

A limitation of this study is that some individuals (77 of 434 [17.7%]) were not examined according to the study protocol. Furthermore, some examinations (28 of 434 [6.5%]) had been performed at younger ages than the set age interval.

The prevalence of strabismus among the control group was in line with a previous population-based study of 6-year-old children. The most common refractive error was hyperopia, as previously shown. None of the control children had manifest strabismus, which is lower than the frequency previously reported. A population-based study of 6-year-old children (n = 1739) reported a strabismus frequency of 2.8%, predominantly esotropia, and associated with prematurity. That study included accommodative strabismus, in contrast to this study. Another population-based study of 217 full-term children at 10 years of age reported manifest strabismus in 3.2% of the sample, although it was most commonly exotropia (71.4%). However, another population-based study reported a squint frequency of 0.6% (1 of 160) in a 6-year-old control group, showing that previous reports of strabismus distributions in different child populations varied.

Conclusions

In a national cohort of children in Sweden, 37.9% (147 of 388 with a complete examination protocol) of all EPT infants and more than 55.4% (67 of 121) in the most immature subgroups had major eye or visual problems at 6.5 years of age. Treatment-requiring ROP had a stronger impact than GA on visual impairment and strabismus, but not on refractive errors, as a whole. In modern neonatal intensive care settings, ophthalmologic problems continue to account for a high proportion of long-term sequelae of prematurity.
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