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ABSTRACT.

Purpose: **Compare patients treated for Retinopathy of Prematurity (ROP) in two consecutive periods.**

Methods: **Retrospective inventory of anonymized neonatal and ophthalmological data of all patients treated for ROP from 2010 to 2017 in the Netherlands, subdivided in period (P)1: 1-1-2010 to 31-3-2013 and P2: 1-4-2013 to 31-12-2016. Treatment characteristics, adherence to early treatment for ROP (ETROP) criteria, outcome of treatment and changes in neonatal parameters and policy of care were compared.**

Results: **Overall 196 infants were included, 57 infants (113 eyes) in P1 and 139 (275 eyes) in P2, indicating a 2.1-fold increase in ROP treatment. No differences were found in mean gestational age (GA) (25.9 ± 1.7 versus 26.0 ± 1.7 weeks, p = 0.711), mean birth weight (791 ± 311 versus 764 ± 204 grams, p = 0.967) and other neonatal risk factors for ROP. In P2, the number of premature infants born <25 weeks increased by factor 1.23 and higher oxygen saturation levels were aimed at in most centres. At treatment decision, 59.6% (P1) versus 83.5% (P2) (p = 0.263) infants were classified as Type 1 ROP (ETROP classification). Infants were treated with laser photocoagulation (98 versus 96%) and intravitreal bevacizumab (2 versus 4%). Retreatment was necessary in 10 versus 21 (p = 0.160). Retinal detachment developed in 6 versus 13 infants (p = 0.791) of which 2 versus 6 bilateral (p = 0.599).**

Conclusion: **In period 2, the number of infants treated according to the ETROP criteria (Type 1) increased, the number of ROP treatments, retinal detachments and retreatments doubled and the absolute number of retinal detachments increased. Neonatal data did not provide a decisive explanation, although changes in neonatal policy were reported.**

Key words: guideline – laser photocoagulation – retinopathy of prematurity – treatment

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Introduction

Retinopathy of prematurity (ROP) is a sight threatening disorder caused by abnormal retinal vessel development in premature infants (Hellstrom et al. 2013). As more is known about the pathological mechanisms, optimizing the infant's condition is warranted in order to prevent the turning point to severe and potentially blinding ROP. However, neonatal risk factors cannot always be completely controlled, and therefore, timely ophthalmic screening and treatment remain essential. In the Netherlands, changes possibly influencing the development of severe ROP were debated as paediatric ophthalmologists had the impression that since several years, the number of infants developing severe ROP had increased. Certain factors might have contributed to this development. First, following a nationwide ROP inventory called the NEDROP study (2009), a new Dutch ROP guideline was implemented in April 2013, in which the screening inclusion criteria were altered (van Sorge et al. 2014; van Sorge et al. 2014). This revision would reduce the number of eligible infants by almost one third, without missing treatment warranting ROP (van Sorge et al.

2013). Secondly, in the same guideline, the early treatment for ROP (ETROP) criteria was emphasized (Good 2004), as the NEDROP study showed that they were not yet widely implemented in the Netherlands: in almost a fourth of infants treated for ROP, no classification could be made into type 1 or 2 ROP. Overall, adherence to the ETROP protocol implicates treatment in earlier stages, which could consequently result in an increase in the number of infants requiring ROP treatment. Moreover, changes in neonatal care might have increased the risk for severe ROP since the NEDROP study. In 2010, the age limit of admitting and actively treating premature infants in Dutch neonatal intensive care units (NICUs) was lowered from 25.0 to 24.0 weeks of gestation. Furthermore, following the Neonatal Oxygenation Prospective Meta-analysis (NeOProM, 2014) (Saugstad & Aune 2014), higher oxygen saturation (SaO_2) levels during the first weeks of life were implemented in most Dutch NICUs. This adjustment warrants better survival but also increases the risk for severe ROP (Askie et al. 2017).

The aim of this study was to investigate changes in the prevalence and characteristics of infants requiring ROP treatment in the Netherlands since the implementation of the new Dutch ROP guideline in 2013. Furthermore, treatment characteristics and anatomical outcome of ROP treatment were investigated.

Materials and Methods

The present study was initiated and coordinated by the Leiden University Medical Center. Data of infants treated for ROP were retrospectively obtained from patient files from all Dutch NICUs. All data were delivered depersonalized and coded using randomly assigned numbers; therefore, informed consent was not required according to the General Data Protection Regulation (GDPR) (GDPR 2016) and the local medical ethical committee. Upon inclusion, patients were categorized into period 1 (old guideline): treated from 1 January 2010 until 31 March 2013 (duration of inclusion of 39 months) and period 2 (new guideline): from 1 April 2013 until 31 December 2016 (45 months). The primary outcome is the number of treated infants per group. Subsequently, the number of treatments was compared to the premature birth rate in the same period. National birth numbers were obtained from the Dutch neonatal registry platform, Perined. Data of the participating hospitals were compared for birth rate, number of ROP treatments, retreatments and outcome, with preservation of individual privacy.

Infants treated in period 1 (from 1 January 2010 until 31 March 2013) were treated according to the old guideline, which advised screening infants with a GA <32.0 weeks and/or BW <1500 g. From 1 April 2013 (period 2), the Dutch ROP screening guideline recommends screening neonates with GA <30.0 weeks and/or BW <1250 and a selection of infants with GA 30.0–32.0 weeks and/or BW 1250–1500 g with presence of one or more of the following risk factors: mechanical ventilation (MV), sepsis, necrotizing enterocolitis (NEC), administration of postnatal glucocorticoids or hypotension treated with inotropic agents. For ROP treatment, classification according to the ETROP is used, which advises treatment of so called type 1 ROP (Good 2004). However, in the Netherlands ROP stage 2+ in zone II is only treated when plus disease is progressive. The participating hospitals were asked to indicate if the SaO_2 policy was adjusted during the study period and if so, what targets are used. Neonatal data were obtained on gender, GA, BW and the presence of relevant risk or protective factors for ROP being: multiple birth, sepsis (defined as clinically ill with positive blood cultures), intraventricular haemorrhage (IVH, according to the classification of Levene et al. (1982) or periventricular leukomalacia (PVL, according to the classification of de Vries et al. (1992), presence of a treated patent ductus arteriosus (PDA), infant respiratory distress syndrome (IRDS), bronchopulmonary disease (BPD, defined as oxygen dependency at 36.0 weeks post-menstrual age (PMA)), NEC with perforation, hyperglycaemia (>8.0 mmol/L), twin-to-twin transfusion syndrome (TTTS), hypotension treated with inotropic agents, duration of NICU admission >28 days, MV >7 days, oxygen administration >28 days, treatment with packed red blood cells, treatment with inhaled nitric oxide (iNO) and pre-and postnatally administered glucocorticoids. Data to evaluate details of treatment consisted of PMA, postnatal age (PNA) at time of treatment decision and treatment, and maximum zone and stage of ROP. Retinopathy of Prematurity (ROP) was classified according to the Revised International Classification of Retinopathy of Prematurity (2005) and categorized into type 1 or 2 ROP according to ETROP criteria (2005). Furthermore, characteristics of treatment and possible retreatments were evaluated. Eventually anatomical outcome, that is, retinal detachment (RD) was recorded.

Statistical analyses

Statistical analyses were performed using SPSS Statistics software version 23.0 IBM Corp., Armonk, N.Y., USA. For quantitative variables, we used number (*n*), mean (standard deviation (SD)) and medians (ranges). For categorical variables, proportion (%) was reported. *P*-values for continuous variables were calculated by using Mann–Whitney *U*-test. In case of categorical and/or binary variables, the Pearson's Chi-Square test or Fischer's Exact test was used. To correct for the difference in inclusion periods (period 1: 39 months versus period 2: 45 months), a correctional factor was used (45/39 = factor 1.15).

Results

During the seven-year study period, data of 196 treated infants from 10 hospitals were obtained. Period 1 counted 57 infants (113 eyes), period 2: 139 infants (275 eyes) (Table 1). The prevalence of ROP treatment in the group of infants born in the Netherlands with GA <32.0 weeks was 1.1% (57/5276) in period 1 and 2.3% (139/6019) in period 2 (Fig. 1), representing a 2.1-fold increase since the implementation of the new guideline.

Comparing national birth rates between the two inclusion periods, the number of newborns with GA 25.0–<28.0 and 28.0–<32.0 weeks remained relatively stable. However, the group of infants with GA <25.0 weeks increased by nearly one fourth (Fig. 1 and Table 1). The range of live births, defined as all live births excluding neonatal death (<28 days after birth), among the 10 participating hospitals is

Table 1. Number of live births in the Netherlands according to gestational age for period 1 and period 2, and the increment corrected for the difference in inclusion time (1.15).

GA (weeks)	Period 1 n = 57	Period 2 n = 139	Increment
28.0–<32.0	3927	4368	0.97
25.0–<28.0	1159	1383	1.03
<25.0	190	268	1.23

shown in Fig. 2. In the overall study group, mean GA and BW were 25.9 ± 1.7 weeks and 771 ± 240 g, respectively. Mean GA was similar between the two treatment groups (period 1: 25.9 ± 1.7 weeks, period 2: 26.0 ± 1.7 weeks (p = 0.711)) as well as mean BW (period 1: 791 ± 311 and period 2: 764 ± 204 g (p = 0.967)). No statistically significant differences were found in the prevalence of neonatal risk factors (Table 2). All NICUs implemented the NeOProM SaO_2 criteria since their publication; however, one hospital adapted a slightly lower and broader range (85–93%).

At treatment decision, 150 infants (period 1: 34, period 2: 116) were categorized as type 1 ROP, four (period 1: 1, period 2: 3) as type 2 ROP and 42 (period 1: 22, period 2: 20) did not meet the ETROP criteria or could not be classified due to missing data (Table 3). Mean overall age at treatment decision was 36.7 ± 2.5 weeks and comparable between the two groups (Table 4). Retinopathy of Prematurity (ROP) stage 3 or higher was found in 49.1% of infants in period 1 versus 57.6% in period 2 (p = 0.144). Between the participating hospitals, median proportion of infants with ROP stage ≥3 at treatment decision was 57% with an interquartile range of 35% (range 20–90%).

Treatment was performed by ten ophthalmologists in seven hospitals. Overall, laser photocoagulation of the retina was the predominant modality of primary treatment (97.0%), six infants received intravitreal Bevacizumab (IVB) (4 bilateral, 2 unilateral) of which five in period 2. Apart from one infant in period 1 and three infants in period 2, all patients were lasered bilaterally. Mean follow-up age was 31.5 ± 24.3 months in period 1 and 13.3 ± 12.6 in period 2. Overall, following primary treatment, ROP recurred within 21 ± 13 days and was retreated in 31 patients (15.8%) (period 1: 10 (17.5%), period 2: 21 (15.1%) p = 0.160). Retreatment characteristics are described in Table 4.

Progression into retinal detachment (RD, ROP stage 4 or 5) occurred in 19 (9.7%) patients of which 8 bilateral (2 versus 6, p = 0.599). Mean PMA at first treatment was higher in the RD group but did not reach statistical significance (p = 0.743). Considering other risk factors and treatment characteristics, these groups were comparable. Of the laser-treated infants, 18/190 (9.5%) versus one of six (16.7%) primarily IVB-treated infants developed retinal detachment (p = 0.462). Treatment characteristics and the occurrence of risk factors did not differ statistically significant comparing infants developing RD to those that did not. The highest treatment and

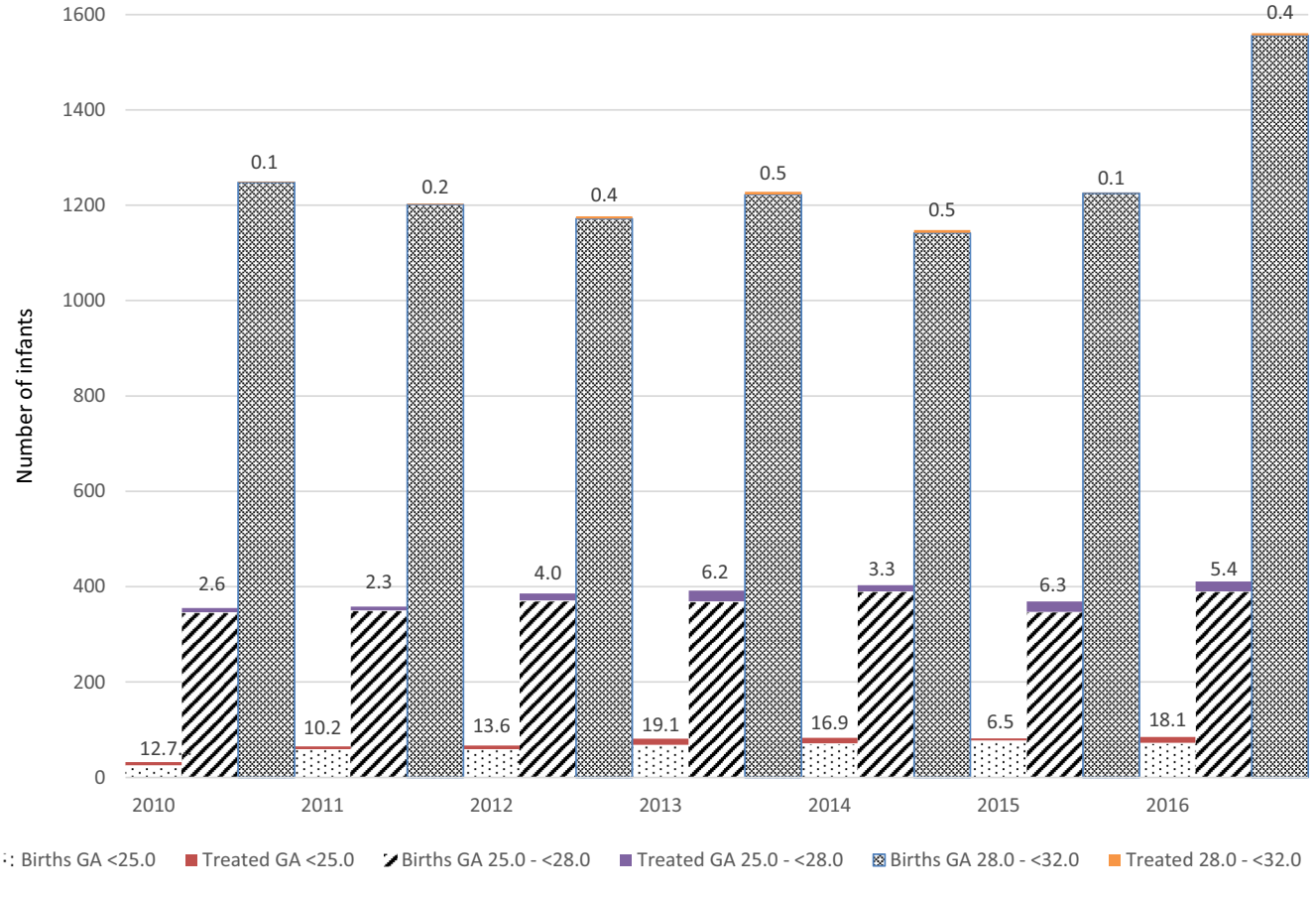

Fig. 1. Annual live births according to gestational age in weeks at birth (pattern filled) and number of treatments (solid filled). Labels represent the percentage of treated infants in the corresponding age category.

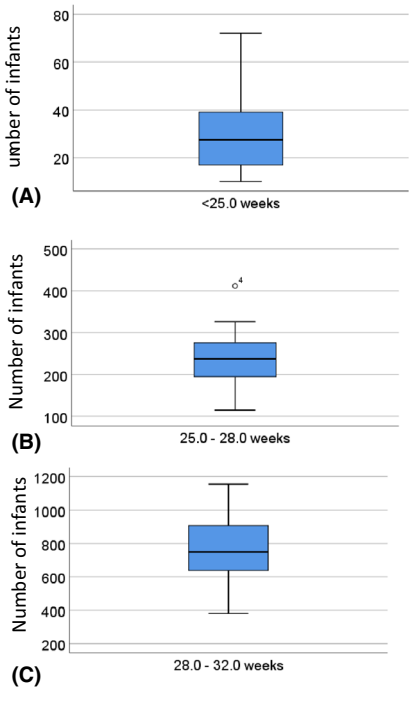

Fig. 2. Boxplots representing median (ranges) of live births in the 10 participating hospitals from 2010 to 2017 with (A) GA < 25.0 weeks: 28 (10–72), (B) GA 25–<28.0 weeks: 238 (115–412) and (C) GA 28.0–<32.0 weeks: 749 (380–1156).

retreatment rates were found in centres where the youngest infants were born. The percentage of recurrence varied between 10.0% and 37.5% and RD between 1.8 and 15.6% (ranges shown in Fig. 3).

Discussion

This study investigated the number and characteristics of infants treated for ROP and the results of ROP treatment in the Netherlands from 2010 to 2017. Since the implementation of the new Dutch ROP guideline in 2013, the number of treatments and infants developing retinal detachment due to ROP has more than doubled. The increase in our study corresponds to the increase reported in the United Kingdom, Sweden, Denmark and Australia (Hameed et al. 2004; Todd et al. 2007; Slidsborg et al. 2008; Painter et al. 2015; Holmstrom et al. 2018). Several aspects could be considered to explain this development.

First, the number of infants who, based on gestational age (GA) at birth, are at particular risk for (severe) ROP has notably increased since 2013. While the overall number of newborns with GA <32.0 weeks, the age most screening guidelines use as cut off point for screening, remained stable, the subgroup with GA <25.0 weeks increased by nearly one-fourth. This can be explained by a significant change in neonatal policy. Compared to other countries, Dutch neonatologists maintained a relatively restrictive policy on active neonatal intensive care treatment of extremely premature born infants, because of the particularly poor survival and increased morbidity in even younger infants (Pignotti 2008; Ishii et al. 2013; Guillen et al. 2015; De Leeuw et al. 2000). In 2010, however, this threshold was lowered from GA 25.0–24.0 weeks, as a similar incidence of severe disabilities was demonstrated, compared to those with GA 25.0 weeks (de Laat et al. 2010). The observed increase in number in this group (Fig. 1 and Table 1) suggests that the policy change only gradually showed effect since 2013 (41% increase from 190 in period 1 to 268 in period 2) which is of particular interest for our study. Nonetheless, the absolute amount is relatively small and consequently did not reach statistical significance. Moreover, a recent inventory on the 2-year follow-up of infants born at 24.0 weeks showed no significant difference in the occurrence of severe ROP (stage ≥ 3) compared to infants born at 25.0 weeks of GA (Aarnoudse-Moens et al. 2017). Thus, it seems more likely that the increase in extremely premature infants in period 2 could only partially explain the increase in ROP treatment.

Another factor potentially contributing to the increase in treatment of ROP was the introduction of higher oxygen saturation levels in most Dutch NICUs following the NeOProM meta-analysis (Saugstad & Aune 2014). It is hypothesized that the adoption of higher SaO_2 in the first phase of ROP increases the risk for the development of treatment demanding ROP. This can be explained

Table 2. Risk factors of the overall group of infants treated for ROP between 2010 and 2017, period 1 and infants that developed retinal detachment (latter group from both periods).

	Period 1 n = 57	Period 2 n = 139	Infants with RD n = 19	p-value period 1 versus 2
Obstetric characteristics and interventions (n, %)				
Prenatal glucocorticoids	35 (72.9%)	90 (69.2%)	11 (64.7%)	0.650*
Multiple birth	18 (33.3%)	58 (43.6%)	11 (61.1%)	0.195*
Infant characteristics (mean (SD))				
GA in weeks	25.9 (±1.7)	26.0 (±1.7)	26.4 (±1.9)	0.711†
Mean (SD) BW in grams	791 (±311)	764 (±204)	827 (±233)	0.967†
Female gender n (%)	28 (49.1%)	67 (48.2%)	11 (57.9%)	0.844*
Neonatal morbidity (n, %)				
Sepsis	35 (64.8%)	89 (66.4%)	13 (72.2%)	0.834*
IVH/PVL	29 (50.9%)	57 (41,0%)	6 (33.3%)	0.659*
Patent ductus arteriosus	44 (83.0%)	108 (81.2%)	16 (88.9%)	0.772*
IRDS	51 (89.5%)	129 (96.3%)	16 (88.9%)	0.575*
BPD	44 (77.2%)	105 (79.5%)	13 (72.2%)	0.764*
NEC	4 (7.0%)	15 (11.3%)	4 (22.2%)	0.427*
Hyperglycaemia (>8 mmol/l)	21 (36.8%)	52 (39.7%)	7 (38.9%)	0.993*
TTTS	2 (3.8%)	9 (7.1%)	1 (5.6%)	0.627*
Neonatal Interventions (n, %)				
NICU admission >28 days	47 (100%)	120 (96.0%)	16 (100%)	0.325†
MV >7 days	40 (87.0%)	109 (84.5%)	13 (76.5%)	0.687*
Oxygen administration >28 days	35 (76.1%)	109 (85.8%)	12 (70.6%)	0.217*
Packed cells	51 (98.1%)	122 (93.9%)	16 (88.9%)	0.398‡
Hypotension treated with inotropic agents	21 (36.8%)	37 (26.6%)	7 (38.9%)	0.124*
iNO	7 (13.4%)	20 (15.5%)	2 (11.8%)	0.945*
Postnatal glucocorticoids	33 (66.6%)	72 (55.0%)	6 (37.5%)	0.221*

BPD = bronchopulmonary disease, BW = birth weight, GA = gestational age, iNO = inhaled nitric oxygen, IRDS = infant respiratory distress syndrome, IVH = intraventricular haemorrhage, MV = mechanical ventilation, NEC = necrotizing enterocolitis, NICU = neonatal intensive care unit, RD = retinal detachment, TTTS = twin-to-twin transfusion syndrome.
* Pearson's Chi-Square Test.
† Mann–Whitney U-test.
‡ Fischer's Exact Test.

Table 3. ROP-type and stage at treatment decision per treatment period.

			Period 1 n = 57	Period 2 n = 139
ETROP type I			34 (59.6)	116 (83.5)
Zone	Stage	Plus		
I	3	+	-	4 (2.9)
II	3	+	18 (31.6)	68 (48.9)
I	2	+	1 (1.8)	2 (1.4)
II	2	+	15 (26.3)	42 (30.2)
ETROP type II			1 (1.8)	3 (2.1)
II	3	-	1 (1.8)	3 (2.1)
No ETROP			22 (38.6)	20 (14.4)
II	2	-	-	2 (1.4)
II	1	+	1 (1.8)	-
III	3	+	2 (3.5)	2 (1.4)
III	3	-	-	1 (0.7)
III	2	+	5 (8.8)	5 (3.6)
III	1	+	-	1 (0.7)
Ns	3	+	6 (10.5)	2 (1.4)
Ns	3	-	1 (1.8)	-
Ns	2	+	1 (1.8)	-
Na	4a	+	-	1 (0.7)
Na	4b	+	-	1 (0.7)
Ns	Ns	Ns	6 (10.5)	5 (3.6)

ETROP = early treatment for ROP criteria, na = not applicable, ns = not specified.

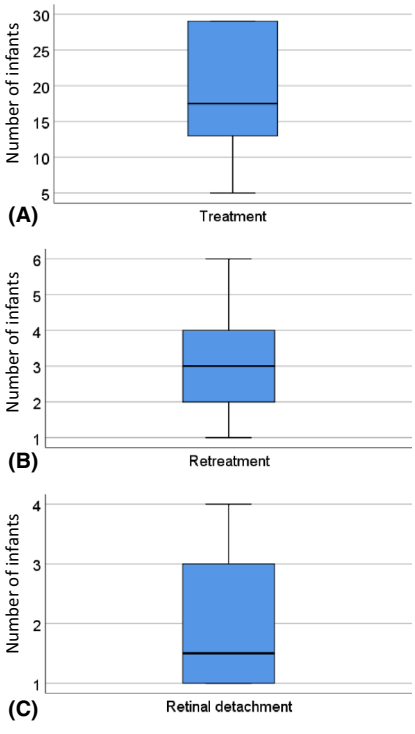

Fig. 3. Boxplots representing median (range) of (A) treatments: 19 (5–29), (B) retreatments: 3 (1–6) and (C) retinal detachment: 1.5 (1–4) in the 10 participating hospitals from 2010 to 2017.

by the two-phased pathogenesis (Hellstrom et al. 2013; Stahl & Gopel 2015; Askie et al. 2017). During the first, so called vaso-obliterative phase, a relatively *hyperoxic* extrauterine environment suppresses the release of angiogenic factors, that is, vascular endothelial growth factor (VEGF), which are crucial for normal vessel development. Moreover, oxidative stress leads to obliteration of yet formed vessels (Sapieha et al. 2010; Kim et al. 2016). This process is enhanced by even higher O_2 levels. Subsequently the second, vaso-proliferative phase initiates usually around the post-menstrual age (PMA) of 32.0 weeks. In this phase, poorly developed and obliterated blood vessels are unable to meet the increasing metabolic activity (and oxygen demand) of the thriving neuroretina. In turn, local areas of ischaemia stimulate compensatory vessel growth by releasing large amounts of angiogenic factors. In case of severe ROP, however, poor quality neovascularizations develop with a tendency to leak and bleed with a high risk of retinal detachment through fibrous traction (Hartnett 2010; Sola & Zuluaga 2013). Therefore, it is hypothesized that the adoption of even higher SaO_2 targets in the first phase increases the risk for the development of treatment demanding ROP. Potentially, this could have resulted in more frequent progression into type I treatment requiring ROP in period 2; however, more detailed data are required to confirm this hypothesis.

Third, a new Dutch ROP guideline was implemented in 2013. The primary

Table 4. Treatment characteristics in infants treated for ROP in Periods 1 and 2 and in those who developed retinal detachments from both periods.

	Period 1 n = 57	Period 2 n = 139	Infants with RD n = 19	p value period 1 versus 2
Age at treatment (mean (SD))				
PMA at first detection of ROP	34.2 ± 2.2	34.2 ± 2.3	34.5 ± 2.1	0.941*
PMA at treatment decision	36.6 ± 2.3	36.7 ± 2.5	36.3 ± 2.1	0.680*
PMA at first treatment	37.8 ± 2.3	37.3 ± 3.3	39.1 ± 7.2	0.791*
PNA at first treatment	12.0 ± 3.8	11.5 ± 3.2	12.9 ± 6.6	0.790*
Primary treatment (n, %)				
Laser	56 (98%)	134 (96%)	18 (95%)	
Bevacizumab	1 (2%)	5 (4%)	1 (5%)	
First recurrence (n, %)	10 (17.5)	22 (15.8)	17 (89.5)	0.390†
Unilateral additional laser	3	2	1	
Bilateral additional laser	3	8	4	
Unilateral TPPV	1	5	4	
Bilateral TPPV	2	2	5	
Unilateral IVI Bevacizumab	0	2	2	
Bilateral IVI Bevacizumab	1	3	1	
Second Recurrence (n, %)	3 (5.2)	9 (6.5)	11 (57.9)	0.598†
Unilateral additional laser		1	1	
Bilateral additional laser		1	1	
Unilateral TPPV	2	4	6	
Bilateral TPPV	1	3	3	
Infants with retinal detachment (n, %)	6 (10.5)	13 (9.4)	-	0.791†
Bilateral	2	6	8	0.599†

IVI = intravitreal injection, PMA = post-menstrual age, PNA = postnatal age, RD = retinal detachment, TPPV = trans pars plana vitrectomy.
* Mann–Whitney U-test.
† Chi square test.

goal of the 2013 guideline was to reduce the number to be screened, while no severe ROP would be missed. This measure however only regards infants with no or *mild* ROP, thus, a direct influence on the present population is not expected. More important for our inventory, the 2013 guideline emphasized the ETROP criteria. This is the first study since 2009 to investigate the extent of the nationwide ETROP implementation. We found an improved documentation, suggesting better awareness of plus disease: the percentage of infants that could not be categorized into type 1 or type 2 decreased from 38.6% (22/57) in period 1 to 14.4% (20/139) in period 2. However, not only did the percentage of infants with high ROP stages (3 or more) at treatment decision not decrease as expected when *earlier* treatment is performed, it slightly increased from 49.1% to 57.6%. Moreover, the age at treatment decision was nearly identical (Table 4), while the age at treatment was (not significantly) higher in the group that developed retinal detachment, suggesting that some infants in the RD group were treated relatively late. Internationally, there is debate about treating ROP stage 2+ in zone II. Within the ETROP cohort, 75.6% of infants had stage ≥3 at treatment decision (Good 2004). Also in studies from other countries in which the ETROP criteria are used, the percentage of infants with stage ≥3 ROP is high: 93.2% in Germany, where ROP stage 2+ in zone II is not listed as treatment indication and 97.5% in Sweden, where only ROP stages 3–5 are considered *severe* (Holmstrom et al. 2016; Walz et al. 2016). In addition, these inventories showed higher retreatment numbers; 31.1% and 19% respectively versus 16.3% in the present study. Finally, even after excluding those infants from our cohort that were treated for stage 2+ ROP in zone II, the increase in treatment remains analogous (Table 3). Our inventory implies that though awareness of the ETROP criteria improved in the Netherlands, attention to timely treatment should still be stressed.

Furthermore, differences were observed between the participating hospitals in birth rates, treatment, retreatment numbers and outcomes (Figs 2 and 3). As expected, higher treatment and retreatment rates were found in centres in which more extremely premature infants were born. Other possible explanations for the variation could lie in different neonatal policies, the availability of an experienced surgical team or easy accessibility to a treatment centre.

Finally, six infants were primarily treated with intravitreal Bevacizumab (IVB), an agent antagonizing VEGF. Mintz-Hittner et al. (2011) demonstrated that compared to laser, IVB is solely favourable in zone I ROP. Therefore, the current Dutch guideline (2013) advises the use of anti-VEGF, only as treatment for ROP in zone I and as a last resort. In the present study, the number of infants with ROP in zone I is low (Table 3), which can be explained by the age restriction of 24.0 weeks for active neonatal treatment. For unknown reasons, all infants treated with anti-VEGF agents were diagnosed with ROP in zone II. Moreover, incidence of progression to retinal detachment was slightly higher to that of the laser-treated group, which might indicate that these infants had a bad prognosis and anti VEGF was given as last resort treatment. There are some limitations to our study. First, due to the retrospective setup, a limited set of data was available. For example, details about oxygen saturation levels and iNO treatment were unknown, which could have provided more opportunities for in-depth analyses. Furthermore, as no prospective registry of infants with ROP exists in the Netherlands, the incidence of severe ROP in the overall ROP population remains unknown. In the future, a national prospective study could give rise to more well-founded conclusions in these matters.

To conclude, since the implementation of the new ROP guideline twice as many infants were treated for ROP. Reasons for this increase include a larger population at risk, unfavorable oxygen regime and better awareness of screening logistics and treatment. The corresponding increase of infants developing end-stage ROP suggests room for even more attention to the treatment criteria.

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