



# Validation of the Postnatal Growth and Retinopathy of Prematurity (G-ROP) criteria in a Slovenian cohort

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<b>PURPOSE</b>	To validate the Postnatal Growth and ROP (G-ROP) study criteria for retinopathy of prematurity (ROP) screening in a Slovenian cohort.
<b>METHODS</b>	We conducted a retrospective cohort study of preterm infants screened in 2021 at the University Medical Centre Ljubljana, Slovenia. The G-ROP criteria were systematically applied. Primary outcomes were sensitivity for ROP requiring treatment, sensitivity for any ROP, and reduction in the number of infants screened.
<b>RESULTS</b>	Of 102 infants screened, 27 (26.4%) developed ROP. Eleven infants (10.7%) had type 1 ROP, of whom 2 (1.9%) had aggressive ROP; 5 infants (4.9%) had type 2 ROP, and 11 (10.7%) had milder ROP. Using the original or simplified G-ROP criteria, all infants who developed type 1 ROP (sensitivity, 100% [95% CI, 74%-100%]), and all infants who developed ROP (sensitivity, 100% [95% CI, 88%-100%]) were correctly identified. Application of the original G-ROP criteria would have reduced the number of infants screened by 29.4% (30 of 102).
<b>CONCLUSIONS</b>	In our cohort, both the original and simplified G-ROP criteria showed 100% sensitivity for predicting ROP type 1 while reducing the number of unnecessary screenings. These results confirm the reliability of the G-ROP criteria in the Slovenian context and suggest that their use improves screening efficiency. (J AAPOS 2025;29:104113)

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**R**etinopathy of prematurity (ROP) is a blinding disease that occurs in premature babies because of pathological vascularization in the retina. Despite the growing number of premature babies and advances in neonatal care, ROP remains one of the most important, but often preventable, causes of blindness worldwide.<sup>1-3</sup> The incidence of ROP varies worldwide and is influenced by factors such as socioeconomic conditions, standard of neonatal care and race/ethnicity, with low gestational age (GA) and low birth weight (BW) being the most important risk factors. These factors have been studied in detail in numerous large-scale studies over the years.<sup>4-7</sup>

The latest International Classification of Retinopathy of Prematurity (ICROP3) categorizes ROP by zone, stage, and disease extent. The Early Treatment of ROP

(ETROP) study uses these features to classify ROP into type 1, which requires treatment, and type 2, for which observation is generally recommended. ICROP3 introduces new concepts, including posterior zone II, and redefines “aggressive posterior ROP” as “aggressive ROP.”<sup>8,9</sup>

ROP incidence varies across regions (USA, 17.9%; UK, 12%-14%; Slovenia, 22.5%), particularly in countries with limited screening resources.<sup>10-14</sup> Inconsistent adherence to guidelines and the absence of standardized protocols globally highlight the need for improved screening strategies. Rising survival rates and evolving screening techniques further emphasize the importance of optimizing ROP management.<sup>10,11</sup>

The ETROP study highlights the critical importance of timely ROP detection for preserving vision in at-risk infants.<sup>8</sup> Current screening guidelines recommend starting examinations between postmenstrual weeks 30 and 32 and continuing until the retinal vasculature fully matures. However, these frequent screenings can be excessive, given that fewer than 10% of infants require treatment.<sup>6,8,10-14</sup> Growth-based models, such as those developed in the G-ROP studies and validated through extensive research, provide a more efficient approach by using postnatal weight gain as a key predictor of treatment-requiring disease. This method reduces unnecessary examinations while maintaining accuracy in detecting infants at risk.<sup>15-17</sup>

The original modified G-ROP screening criteria for ROP consisted of six criteria, each of which indicated the need for ROP screening: GA <28 weeks, BW <1,501 g,

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Table 1. G-ROP screening criteria validation studies

Author (country)	Study type	Cohort size	Study period	Results based on application of G-ROP algorithm
Vinayahalingam <sup>22</sup> (Switzerland)	Retrospective observational	322	2015-2019	Sensitivity 100% for TR-ROP and 91% for low-grade ROP; 4 children with low-grade ROP not flagged by G-ROP algorithm
Caruggi et al <sup>19</sup> (Italy)	Retrospective	475	2015-2020	Sensitivity 100% (95% CI, 88%-100%)
Shiraki et al <sup>18</sup> (Japan)	Retrospective cohort	537	2009-2017	Sensitivity for TR-ROP 100% (95% CI, 95.4%-100%); sensitivity for any ROP 91.9% (95% CI, 88.3%-94.5%)
Yabas Kiziloglu et al <sup>21</sup> (Turkey)	Retrospective cohort	242	2012-2019	Sensitivity for TR-ROP 91.2% (95% CI, 76.3%-98.1%); specificity 34.1% (95% CI, 27.7%-41%); if BPD added as criterion for G-ROP model, all TR-ROP infants detected (sensitivity 100%)
Fadakar et al <sup>24</sup> (Iran)	Retrospective cohort	166	2020-2021	Sensitivity for TR-ROP of 100% and for any stage ROP of 97.69%; specificity of 8.69% and 8.33%, resp.
Ahmed et al <sup>20</sup> (Egypt and UK)	Retrospective cohort	504 (Egypt) 101 (UK)	1018	Sensitivity of type 1 ROP 100% in both cohorts; specificity for Egyptian cohort of 15% and for UK cohort 20.9%; reduction of number of infants requiring ROP screening 14.1% and 21.8% in the Egyptian and UK cohorts, resp.
Raffa et al <sup>25</sup> (Saudi Arabia)	Retrospective cohort	300	2015-2021	Sensitivity of G-ROP 1 and G-ROP 2 for detecting treated ROP 96.7% and 100%, resp.; specificity for detecting treatable ROP 24.4% and 16.7%, resp.
Huang et al <sup>23</sup> (Taiwan)	Retrospective cohort	303	2015-2019	Sensitivity and specificity of original G-ROP screening criteria for type 1 ROP detection 96.6% and 42.3% and for simplified G-ROP 180 g model 100% and 31%, resp.; reduction in the number of infants requiring screening and funduscopic examinations 32.6% and 33.5% for original G-ROP criteria and 28.1% and 23.2% for G-ROP 180 g model, resp.

BPD, bronchopulmonary dysplasia; ROP, retinopathy of prematurity; TR-ROP, treatment-requiring ROP.

weight gain <120 g between 10 and 19 days' postnatal age (PNA), <180 g between 20 and 29 days' PNA, <170 g between 30 and 39 days' PNA, or the presence of hydrocephalus.<sup>15</sup> In a simplified version of the criteria, all three thresholds for weight gain are set at 180 g.<sup>15,16</sup> Algorithms based on weight gain are highly dependent on accurate weight measurements, which can be challenging in some settings. Nonetheless, the original G-ROP criteria have been validated in several countries (Table 1) and have consistently shown promising results, with very high sensitivity for predicting type 1 ROP, with a significant reduction in the number of infants requiring ROP screening. Such validation studies are essential to assess the generalizability of a predictive model such as the G-ROP criteria prior to their clinical application.<sup>18-25</sup> The aim of the current study was to validate the G-ROP screening criteria in Slovenia. In Slovenia, body weight, height and daily weight gain are routinely recorded in neonatal intensive care units, providing an opportunity to evaluate the performance of the G-ROP criteria for predicting

ROP type 1, ROP type 2, and any ROP, as well as the extent of any decrease in the number of screened infants due to the introduction of these modified screening criteria.

## Subjects and Methods

We conducted a retrospective observational cohort study in collaboration with the Neonatal Intensive Care Unit of the University Hospital Ljubljana (NICU-Lj). The study was approved by the National Medical Ethics Committee of the Republic of Slovenia. Data collection and analysis were performed at the University Eye Clinic in Ljubljana, one of two main tertiary referral centers in Slovenia with experience in the treatment and screening of ROP. The majority of extremely premature infants in Slovenia are sent to the NICU-Lj, 25% to the other national center, Maribor.

In our hospital, a screening protocol according to the current Slovenian ROP screening guidelines was followed during the study period. All infants born in the NICU-Lj between January

Table 2. Demographic data (N = 102 [204 eyes])

Study parameter	Result
Sex, no. (%)	
Girls	52 (50.9)
Boys	50 (49.1)
Age, weeks	
Gestational age, weeks, median (range)	28 (23-32)
Birth weight, g, median (range)	1030 (495-1740)
Other risk factors, no. (%)	
Anemia	27 (26.4)
Transfusion	24 (23.53)
Patent ductus arteriosus	20 (19.6)
Hyponatremia	18 (17.6)
Sepsis	7 (6.86)
Necrotizing enterocolitis	5 (4.9)
Trombocytopenia	4 (3.92)
Twins, no.	13
ROP development, no. (%)	
Total	27 (26.4)
Type 1	11 (40.7)
A-ROP (included in type 1)	2 (7.40)
Type 2	5 (18.5)
Low-grade ROP	11 (40.7)

ROP, retinopathy of prematurity.

1 and December 31, 2021, and weighing <1,500 g were screened for ROP and were eligible for inclusion in this study. The first eye examination was performed at 31 weeks' postmenstrual age or at 4 weeks of age, whichever was later. Screening was performed by an experienced pediatric ophthalmologist according to a standard protocol using indirect ophthalmoscopy and often documented with a fundus camera. Data were obtained from the medical records of all eligible infants and included ROP stage, ROP zone, pre-plus or plus diagnosis, any ROP treatments, daily measured body weight from birth to 39 days, and presence of hydrocephalus as well as the presence of additional ROP risk factors, including duration and type of oxygenation, necrotizing enterocolitis, bronchopulmonary dysplasia (BPD), neonatal sepsis, anemia, and intraventricular hemorrhage. Infants with unknown outcome of ROP due to incomplete medical data were excluded from further analysis.

As for the eye examination data, ROP outcomes were categorized into type 1 ROP, which includes aggressive ROP, type 2 ROP, and low-grade ROP, which does not meet the criteria for type 1 or 2 ROP. The G-ROP criteria described above and the simplified 180 g G-ROP criteria were applied retrospectively to each infant. A further simplified version of the G-ROP criteria was also evaluated to allow for an even more conservative clinical approach, as proposed by the original G-ROP researchers<sup>15</sup> and as performed in a Taiwanese validation study.<sup>23</sup> First, a single weight gain threshold of 180 g was used for all three time periods, and second, only the use of the three 180 g weight gain thresholds without consideration of BW or GA was considered.

An infant met the criteria and would have required ROP screening if they met one or more of the G-ROP criteria. The primary study outcomes were the sensitivities for ROP type 1 and

ROP type 2 and the reduction in the number of infants who would have required ROP testing if the G-ROP criteria had been applied (ie, the proportion of infants who did not meet any of the six criteria). Secondary outcomes included sensitivity for any ROP (type 1, type 2, or low-grade ROP) and specificity for type 1 ROP, type 2 ROP, or any ROP. Statistical analyses were performed using SPSS version 29 for Windows (IBM Corp, Armonk, NY). Demographic data (GA, BW) were summarized using proportions or median and range.

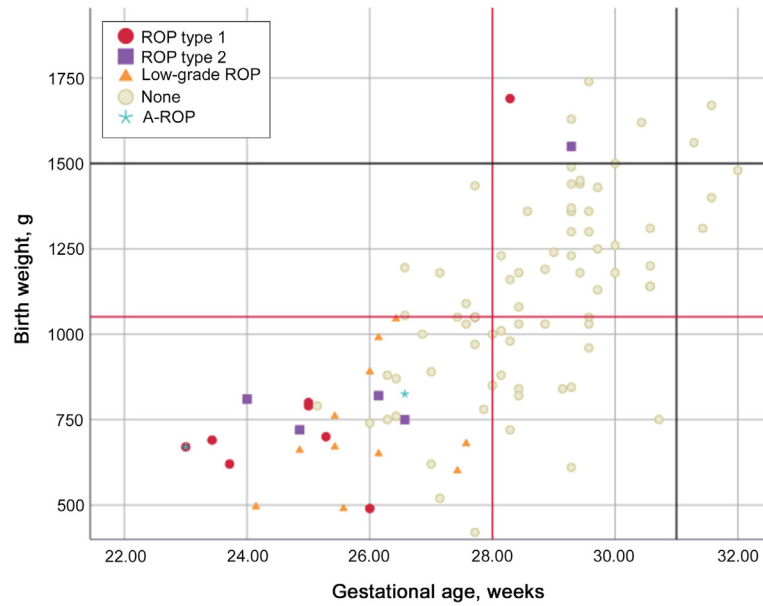
## Results

Of 104 infants who underwent ROP screening examinations, 102 infants had complete data and were included in this study (Table 2). Two infants died before ROP screening was completed. The mean gestational age in the cohort was 28 weeks and 2 days, and the median birth weight was 1,030 g. The number of female infants was 52 (50.9%). Of the 102 infants studied, 27 (26.4%) developed ROP, of whom 11 (10.7%) developed type 1 ROP, 2 of whom had A-ROP. Five infants (4.9%) developed type 2 ROP, and 11 (10.7%) developed low-grade ROP. All 11 infants with type 1 ROP underwent laser photocoagulation, anti-VEGF therapy, or a combination of both treatments, whereas ROP resolved spontaneously in the 16 infants with ROP that did not meet type 1 criteria. Figure 1 shows type of ROP (or no ROP) in all 102 children participating in the study.

Using the original G-ROP criteria, an alert was raised in 72 children. All children who developed type 1 ROP and required ROP treatment were correctly identified (sensitivity, 100% [95% CI, 74%-100%]; specificity, 33% [95% CI, 24%-43%]). See Table 3. Application of the G-ROP criteria would have resulted in a 29.4% (30/102) reduction in the number of infants receiving ROP screening. Figure 2 shows the number of infants who would have required ROP screening if the G-ROP criteria had been applied in our cohort.

In addition to the original G-ROP criteria, simplified criteria were also assessed. In the second model, a single weight gain threshold of 180 g was used for all three time periods, and in the third model, only the three 180 g weight gain thresholds were assessed, without consideration of BW or GA. Sensitivity for ROP type 1 and type 2 remained at 100% throughout. The number of infants requiring screening was reduced by 21% using the second model and by 36% using the third model. In the third model, 26 of 27 infants with any stage ROP were detected. The single infant who was missed developed low-grade ROP that spontaneously regressed and subsequently vascularized completely without intervention.

Two examples illustrate the application of the G-ROP criteria to specific infants in this cohort. The first is a boy born as twin A with a GA of 28 2/7 weeks and a weight of 1,690 g. Had the screening criteria been restricted to only the G-ROP guidelines for GA and BW, this child would have been overlooked. However, careful monitoring



**FIG 1.** Birth weight, gestational age, and type or absence of ROP of 102 Slovenian children examined for ROP during the study period. Current screening criteria are indicated with black lines; G-ROP criteria, with red lines.

of weight revealed a large increase of 560 g in the first 10 days, followed by a decrease of 655 g between days 10 and 19. This fluctuation resulted in this preterm infant becoming conspicuous due to low postnatal weight gain during this period. He also had a poor clinical course and received oxygen throughout the follow-up period of 39 days, two transfusions of concentrated red blood cells for anemia, and treatment for acute renal failure and ascites. The latter diagnosis of ascites with hydrops is an example of “unphysiologic weight gain” that is not related to IGF-1 levels and could make it appear that the baby has gained weight, which could lead to a false-negative signal from the G-ROP criteria, although that was not the case in this patient. This phenomenon is the reason that hydrocephalus is one of the 6 G-ROP criteria; perhaps anasarca or hydrops should also be considered. During the follow-up period, he developed type 1 ROP, and bilateral laser photocoagulation of the retina was performed.

The second case is a girl with a GA of 29 2/7 and BW 1,550 g, again above the G-ROP levels for GA and BW. However, from day 20 to day 29, we observed a weight gain of only 160 g, which met the G-ROP criterion for

slow postnatal weight gain. She was on oxygen throughout the follow-up period and treated for systemic inflammatory response syndrome (SIRS). She developed type 2 ROP, but no treatment was required.

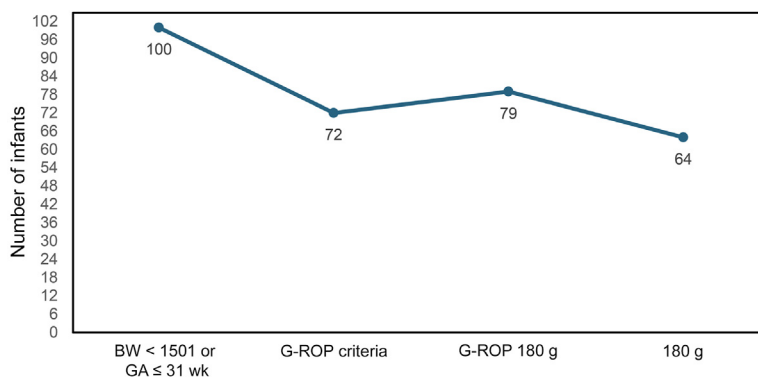
## Discussion

In this study, we applied the modified G-ROP criteria for ROP screening to a cohort of preterm infants from Slovenia at the country’s largest tertiary reference center. Over the last decade, the G-ROP criteria have become one of the most frequently reviewed standards for the prediction of ROP.<sup>18-25</sup> The G-ROP mode, which consists of six screening criteria, is user friendly and ensures a rapid learning curve while maintaining high sensitivity in detecting severe cases of ROP. It predicts ROP risk through low BW and GA, markers of retinal and vascular immaturity, early hyperoxia, and IGF-1 deficiency. Prematurity and low IGF-1 levels increase the risk of severe ROP by extending the period of halted retinal vascular growth, leading to increased retinal VEGF levels and pathological neovascularization. This association between slow

**Table 3.** Specificity and sensitivity of the G-ROP criteria

Study parameter	Alarm +	Alarm –	Total	Sensitivity	Specificity	95% CI
Type 1 ROP	11	0	11	100%	33.0%	0.74%-100%
Type 2 ROP	5	0	5	100%		57%-100%
Low-grade ROP	11	0	11	100%		74%-100%
Any ROP	27	0	27	100%		88%-100%
No ROP	45	30	75		42.9%	49%-70%
Total no.	72	30	102			61%-79%

ROP, retinopathy of prematurity.



**FIG 2.** Reduction in the number of infants screened after application of original and simplified G-ROP criteria.

postnatal weight gain and later development of severe ROP was first demonstrated in the WINROP algorithm and later in other weight gain-based ROP prediction models.<sup>4,6,7,26</sup>

After retrospective application of the G-ROP criteria to our cohort of 102 children, all infants who developed severe ROP and all infants who developed any type of ROP were successfully identified, corresponding to a sensitivity of 100% for both outcomes. This group of 27 infants included 11 infants with type 1 ROP, 2 of whom had A-ROP, and 5 infants with type 2 ROP. No infant requiring ROP treatment was missed. Although this was a small cohort, the high sensitivity observed is consistent with other studies and further validates these criteria in high-income countries with well-regulated healthcare systems and robust neonatal care, such as Switzerland, Italy and the United Kingdom.<sup>19,20,22</sup> In North America, where the G-ROP criteria were developed, the model achieved a sensitivity of 100% for type 1 ROP in both the original developmental cohort and the subsequent large validation study, which included nearly 11,500 infants in total.<sup>15,16</sup> In some middle-income regions, modifications were required to achieve 100% sensitivity, such as inclusion of bronchopulmonary dysplasia or adjustment of postnatal weight gain thresholds.<sup>21,23</sup> In our cohort, additional risk factors, such as BPD and necrotizing enterocolitis (NEC), would not have contributed to higher specificity, because all infants were correctly identified and these conditions were observed in only 2 of 9 (22%) and 4 of 9 (44%) infants, respectively, with ROP type 1.

The performance of a simplified version of the G-ROP criteria was also evaluated, along with an even further simplified version to allow for an even more conservative clinical approach, as proposed by the original G-ROP researchers,<sup>15</sup> and as performed in a Taiwanese validation study.<sup>23</sup> First, a single weight gain threshold of 180 g was used for all three time periods, and second, only the use of the three 180 g weight gain thresholds without consideration of BW or GA was considered. Sensitivity for ROP type 1 and type 2 remained at 100% throughout. The number of infants requiring screening was maximally reduced

by using the third model with three 180 g weight gain thresholds alone (36%), whereas the original full G-ROP criteria produced the second largest reduction (29%), and the full G-ROP criteria with three 180 g thresholds (second model) resulted in a smaller reduction (21%). In the third model, using only the 180 g thresholds for weight gain without BW or GA, although all type 1 cases were captured, 26 of 27 infants with any stage ROP were detected. The single infant who was missed developed low-grade ROP that spontaneously regressed and subsequently vascularized completely without intervention. While this alternative version of the criteria could improve specificity and result in a smaller number of infants undergoing examination, the sample size was small and maintaining 100% sensitivity must be a priority. Therefore, we believe that using a more conservative model, such as the full G-ROP criteria with three 180 g thresholds, and thus further lowering the threshold for starting ROP examinations, is safer even in countries with highly developed health systems and reduces the risk of not detecting infants who need sight-saving interventions. This issue has also been discussed by other researchers.<sup>22,27,28</sup>

As survival rates for extremely preterm infants improve and ophthalmology resources become more limited, reducing the number of ROP examinations is increasingly critical. The G-ROP screening criteria, as demonstrated by Zupancic and colleagues,<sup>29</sup> offer a more cost-effective alternative to traditional methods. This approach not only eases the healthcare burden but also reduces the stress associated with invasive procedures like lid speculum use and scleral depression. Cuddihee and colleagues<sup>30</sup> have emphasized the stress these procedures impose on infants, whereas Jiang and colleagues<sup>31</sup> have observed that such stress can lead to changes in blood pressure, pulse rate, and even screening-induced apnea. Consequently, careful monitoring of high-risk infants for up to 48 hours after screening is crucial, particularly if the examination occurs before discharge.

There are potential limitations to our study, the most important being the small cohort and the inclusion of only one national tertiary referral center. Given the

relatively small size of Slovenia, with a population of 2.1 million, the data collected can be considered reliable and potentially generalizable across the country. This is particularly important, because most of the country's preterm infants are treated in the same tertiary center in Ljubljana. Although the sample size of the study was relatively small, it is reassuring that the G-ROP criteria have shown equally high sensitivity in several other countries with similar levels of neonatal care. The use of 180 g thresholds for all three periods, or even a more conservative value of 200 g for all three periods, together with BW, GA, and hydrocephalus, can add an additional safety buffer for use of the criteria. Similarly, the continued use of a subjective screening criterion, where neonatologists can use their discretion to request investigations for babies with higher BW/older GA babies with poor postnatal course, may help to ensure that the criteria are updated as necessary.

In our Slovenian cohort, both the original and the simplified G-ROP criteria achieved 100% sensitivity in detecting ROP type 1, while successfully reducing the number of unnecessary examinations in many infants. To evaluate the benefits and safety thoroughly, particularly of the simplified G-ROP criteria, a comprehensive study over several years involving a larger population of infants and including both national tertiary centers would be required.

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