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Age-optimized cut-off values for pubofemoral distances in screening for hip dysplasia

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Aims

To establish cut-off values for lateral pubofemoral distance (PFD) measurements for detecting hip dysplasia in early (four days) and standard care (six weeks) screening for developmental dysplasia of the hip (DDH).

Methods

All newborns, during a one-year period (October 2021 to October 2022), were offered a PFD ultrasound (US) examination in addition to the existing screening programme for DDH. Newborns who were referred for standard care hip US, suspected for DDH, received a secondary PFD US examination in conjunction with the standard care Graf/Harcke hip US examination. Receiver operating characteristic curves and empirically optimal cut-off values were calculated with a true positive defined as a Graf type ≥ IIc hip.

Results

We included 2,735 newborns, of whom 758 received both early PFD hip US and standard care Graf/Harcke hip US. For early (four days) PFD
screening, the optimal cut-off point was calculated to be 6.2 mm (95% CI 4.7 to 7.7) producing a sensitivity of 80% (95% CI 55% to 100%) and a specificity of 87% (86% to 89%). For PFD screening performed at standard care (six weeks) hip US, the optimal cut-off point was calculated to be 5.6 mm (95% CI 4.9 to 6.3) producing a sensitivity of 100% (95% CI 100% to 100%) and a specificity of 96% (95% CI 95% to 97%).

Conclusion

PFD US screening produces a high degree of both sensitivity and specificity for detecting DDH. Age-specific cut-off values should be used to heighten the accuracy of PFD US screening.

Take home message

- Ultrasound screening using pubofemoral distance (PFD) measurements is highly accurate for diagnosing developmental dysplasia of the hip.
- Age-specific cut-off values for the PFD are essential to ensure precision and reliability.

Introduction

Multiple ultrasound (US) measurements have been proposed in screening for developmental dysplasia of the hip (DDH).[1] The gold standard is the Graf method,[2] which measures the inclination of the ossified acetabulum and is used in DDH US screening programmes worldwide. In 2013, the pubofemoral distance (PFD) was proposed as a sensitive and highly reproducible diagnostic measurement for DDH.[3] Several PFD cut-off values for hip abnormality have since been proposed, ranging from 3.5 mm to the original authors' suggestion of 6.0 mm.[3–5] However, these studies applied different PFD examination methodologies, had different

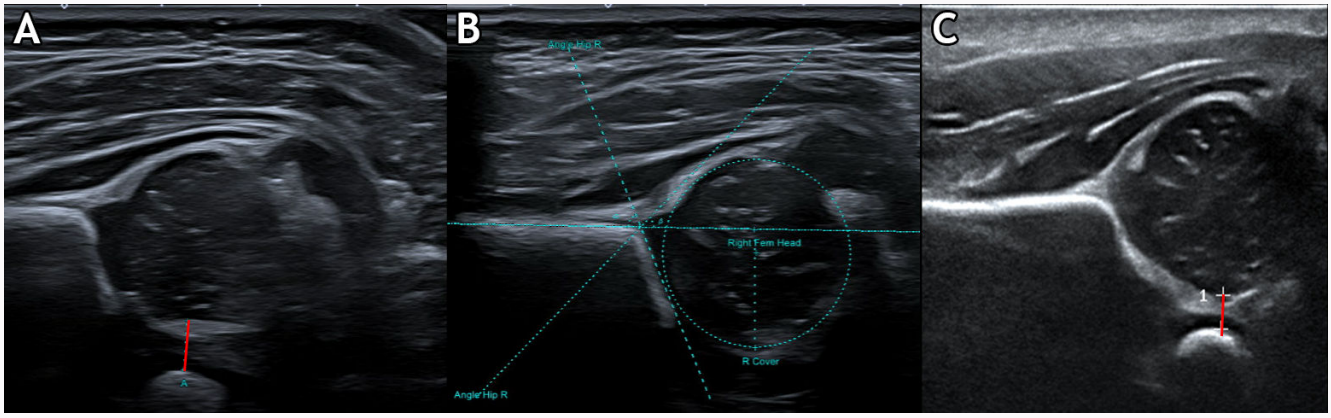

Fig. 1
Ultrasound images of three newborn hips as performed by a) and b) a radiologist and c) a midwife. a) and c) depict the pubofemoral distance (PFD) method with PFD marked as a red line, while b) depicts the Graf and Harcke method with annotated α angles and femoral head coverage (FHC).

definitions of true DDH, and vary both internally and externally in the age of the included populations.

To date, no studies have assessed the optimal cut-off value for the PFD in DDH screening compared to a true definition of DDH being ≥ Graf type IIc hips in a homogenously aged population. Further, no studies have assessed the optimal PFD cut-off for early PFD screening (four days).

The aim of the present study was to define the empirically optimal cut-off value for the PFD measurement in early (four days) and standard (six weeks) DDH screening for detecting ≥ Graf type IIc hips.

Methods

Design and setting

This was a prospective diagnostic accuracy study performed at Aarhus University Hospital, Denmark, during a one-year period from October 2021 to October 2022. Reporting follows the STARD guidelines for reporting on diagnostic accuracy studies.[6]

The referral criteria for undergoing a definitive Graf hip US in the DDH screening programme at Aarhus University Hospital consists of a positive clinical hip examination (using Ortolani and Barlow manoeuvres), or the presence of a risk factor (family history, breech presentation, oligohydramnios, clubfeet, musculoskeletal syndromes). All newborns receive clinical and risk factor screening from a midwife in the post-partum clinic when the child is approximately two days old.

As part of this study, during screening in the post-partum clinic, all parents were offered the opportunity for the newborn to undergo an additional hip PFD US examination performed by a midwife in conjunction with the clinical and risk factor screening.

Participants

We included all newborns with written parental consent to receive an additional PFD US examination. The PFD US was performed in a separate room, typically on the same day as the clinical examination, by midwives who were trained to perform PFD measurements. If clinical screening was undertaken at the weekend, the PFD US was performed in the following week. The midwife-delivered PFD US had to be completed within 14 days after birth.

Midwives were trained in the use of the PFD method through a two-hour theoretical introduction and four three-hour supervised training sessions, during which they were able to acquire PFD measurements similar to expert musculoskeletal radiologists (intraclass correlation coefficient (ICC) 0.8).[7]

Distribution of hip types measured at definitive hip US was: type I: 1,430 (94%); type II: 76 (5%); type IIc: 9 (0.6%); and type III: 1 (0.1%). Sex distribution, gestational age, and birth weight of the screened population can be seen in Table I.

Index text (PFD US)

PFD examination was performed using a MINDRAY TE7 US scanner and a high frequency (16MHz) linear transducer (Mindray Medical International, China). PFD was measured according to the methods described by Treguiér et al[3] and Salut et al,[8] but notably with the child in the lateral examination position[2] (Figure 1). The PFD is defined as the minimal measurable distance between the medial femoral epiphysis and the ossified pubic bone while applying lateralizing stress to the hip joint.

As the PFD cut-off value for newborns was unknown, newborns were referred for definitive hip US if the PFD was above 5.1 mm, or if the PFD difference between hips was greater than 1.5 mm. This value was determined based upon a retrospective analysis of PFD measurements performed at Aarhus University Hospital, and the existing literature.[3,4,9]

Therefore, if any of the following were met, the newborn was referred for a definitive US (using Graf/Harcke technique):[2,10] 1) a positive clinical finding upon hip examination; 2) a positive risk factor for DDH; and/or 3) a PFD above the 5.1 mm threshold or a PFD difference between both hips of 1.5 mm or above (Figure 2).

Reference standard (Graf US)

All definitive US examinations were performed by one of three musculoskeletal radiologists (MBH, MH, NL) according to the methodology by Graf,[2] with the child fixed in the lateral examination position in an examination cradle.

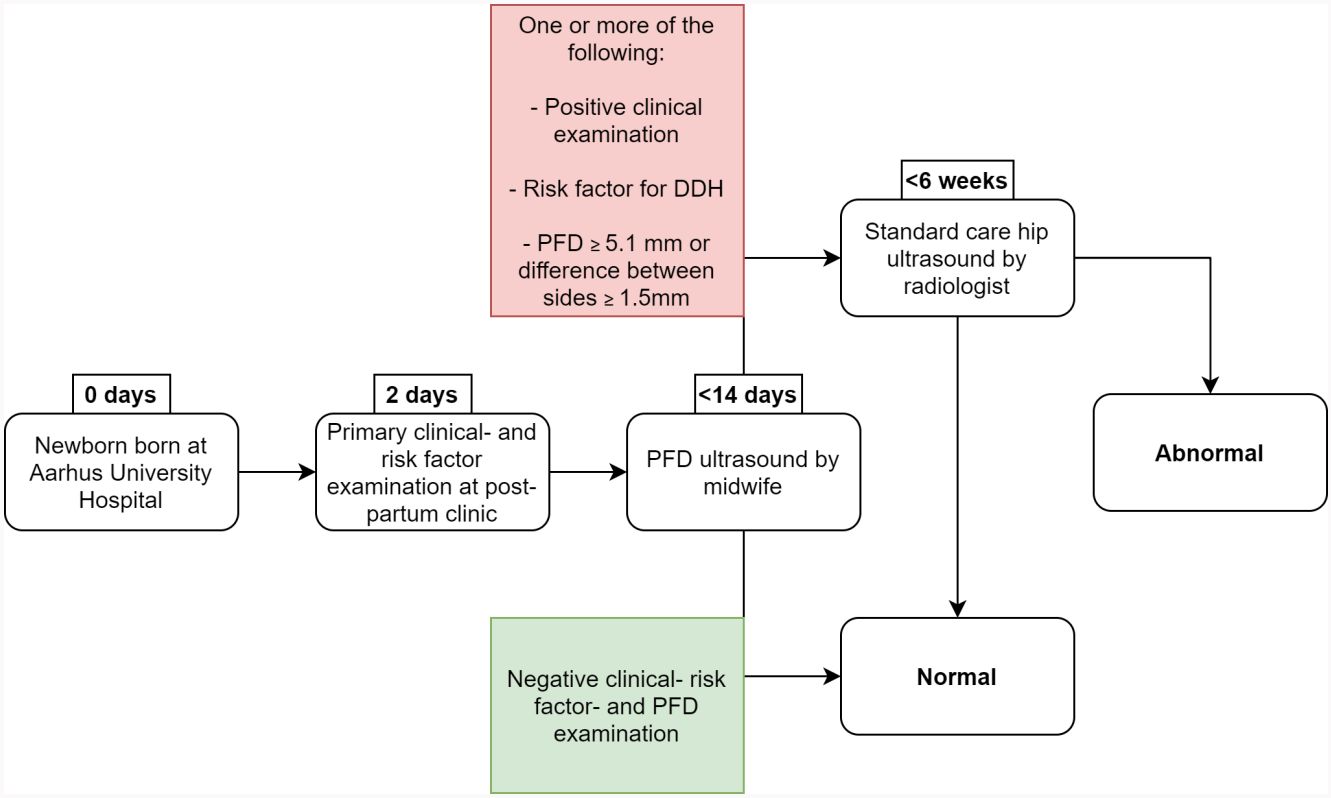

Fig. 2
Flowchart depicting the screening process of the newborns who were consented to participate in the study. DDH, developmental dysplasia of the hip; PFD, pubofemoral distance.

Definitive US were scheduled to take place at two weeks if the hip was thought to be unstable (i.e. clinical instability was detected upon examination and/or if the PFD was above 8 mm), or by six weeks of age in other situations. Newborns referred to other institutions for definitive US were excluded.

Variables

We collected basic demographic information (sex, birth weight, gestational age, age at PFD US, and age at definitive US). Further, we collected PFD measurements from the early PFD screening and from the definitive hip US. α angles were collected from the definitive hip US to determine Graf classification.

Study size

Since no studies have reported on the sensitivity of PFD screening (early or standard) in detecting Graf type ≥ IIc hips, a convenience sample of all newborns screened during a one-year period was used.

Bias

To minimize any performance bias during the definitive hip US and hip classification, the radiologists performing the definitive US were blinded to the PFD measurements of the early PFD screening, and performed their own PFD measurements only after α angles had been measured.

Statistical analysis

Empirical cut-off values for the PFD measurements were calculated and compared using the Youden and Liu indexes.[11,12] To calculate prediction errors and CIs of the cut-off values, we performed a repeated ten-fold cross validation while assuming independency between hips. As no significant differences were detected between the Youden and Liu indexes, the Youden index value is presented. Sensitivities and specificities for the empirically optimal cut-off values were calculated for the PFD measurements at early screening and at definitive hip US, with a true positive being a Graf hip type ≥ IIc as detected upon definitive hip US. CIs for the sensitivities, specificities, and area under the curve (AUC) values were calculated using 100 bootstrap samples, and correlated AUC values were calculated according to the method by DeLong et al.[13] To account for bilaterality in data, a sensitivity analysis was performed, by calculating empirical cut-off values for left, right, and all hips. As no significant difference was detected in the sensitivity analysis, independence between sides was assumed. Normal distribution of data was confirmed using QQ plots, and significance was estimated using 95% CIs. All statistical calculations were performed using Stata version 17.0 (StataCorp, USA).

Results

During the study 4,794 newborns received traditional screening, of whom 2,735 were consented to early PFD screening. Of those consented, 25 were excluded as they were above 14 days of age at the time of PFD screening, which left 2,710 for our PFD screened population. Of the PFD screened

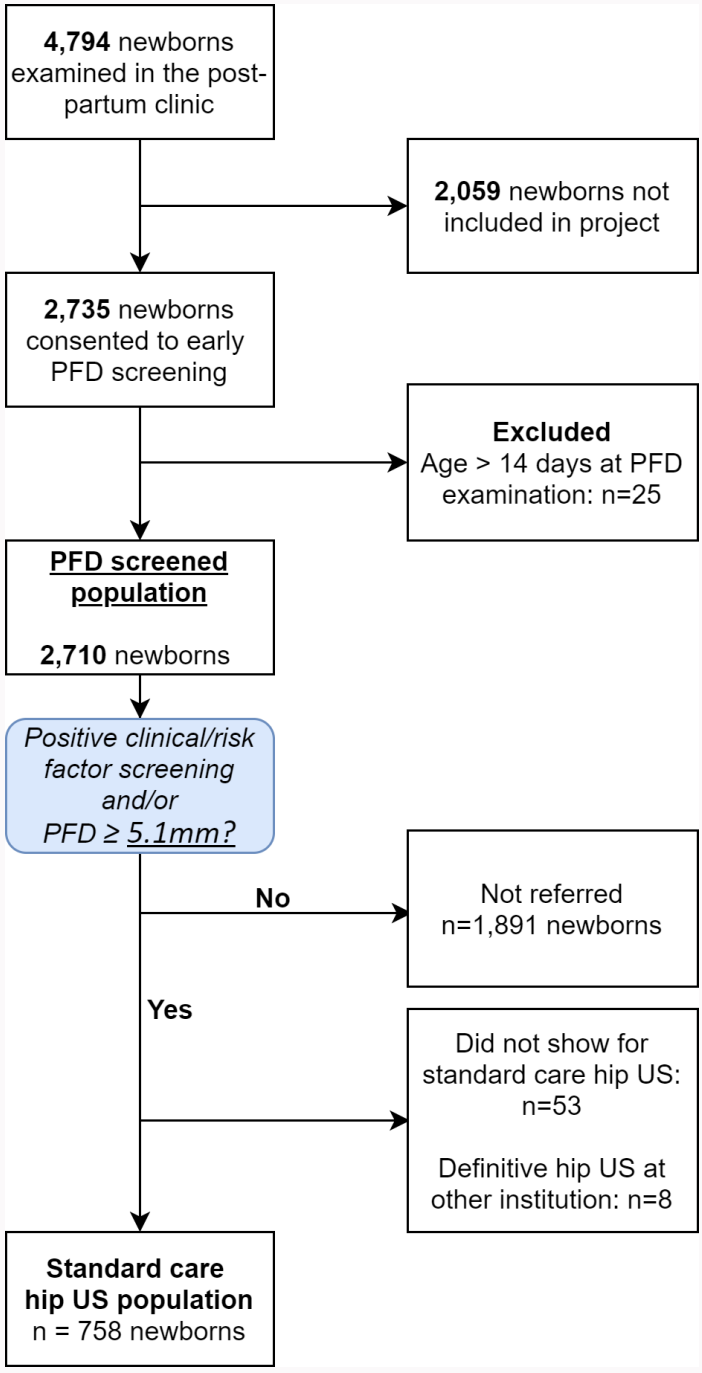

Fig. 3
CONSORT diagram of the inclusion process. PFD, pubofemoral distance; US, ultrasound.

population, 819 newborns were referred for definitive US as they fulfilled the referral criteria of the traditional screening programme and/or had a PFD above 5.1 mm. After excluding newborns who did not attend definite hip US and newborns who were referred to other institutions, the definitive US subpopulation consisted of 758 newborns (Figure 3).

ROC curve analysis of early (four days) PFD screening for detecting Graf type ≥ IIc hips produced an AUC value of 0.83. The optimal cut-off point was calculated to be 6.2 mm (95% CI 4.7 to 7.7 mm) corresponding to a sensitivity of 80% (95% CI 55 to 100%) and a specificity of 87% (86 to 89%) (Figure 4).

When applying the same analysis to PFD screening performed at definitive hip US (six weeks), the AUC value rose to 0.99; the optimal cut-off value was calculated to be 5.6 mm (95% CI 4.9 to 6.3 mm) corresponding to a sensitivity of 100% (95% CI 100% to 100%) and a specificity of 96% (95% to 97%) (Figure 5).

Discussion

The present study established cut-off values for use in early (four days) and standard (six weeks) DDH US screening. At both timepoints, PFD screening produced excellent AUC values (> 0.83), and the proposed cut-off values corresponded to sensitivities and specificities ranging from 80% to 100%.

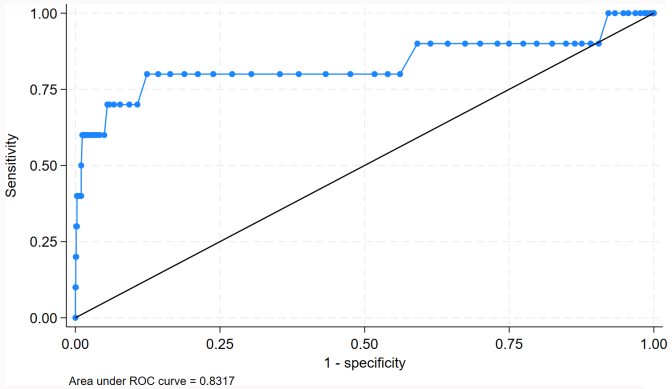

Fig. 4
Receiver operating characteristic (ROC) curve and associated area under the curve of early (four days) pubofemoral distance (PFD) measurements. Each dot represents sensitivity and 1-specificity at different cut-off values for the PFD measurement.

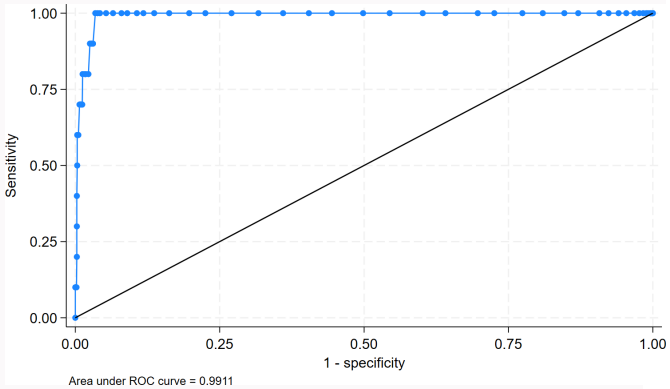

Fig. 5
Receiver operating characteristic (ROC) curve and associated area under the curve of early (six weeks) pubofemoral distance (PFD) measurements. Each dot represents sensitivity and 1-specificity at different cut-off values for the PFD measurement.

Table I. Baseline demographic data of screened population stratified by definitive hip ultrasound (US) status.

Variable	No definitive hip US	Definitive hip US	Total
Total, n (%)	1,891 (71.4)	758 (28.6)	2,649 (100.0)
Sex, n (%)			
Male	1,011 (53.5)	376 (49.6)	1,387 (52.4)
Female	880 (46.5)	382 (50.4)	1,262 (47.6)
Mean birth weight, kg (95% CI)	3.5 (3.5 to 3.6)	3.6 (3.5 to 3.6)	3.5 (3.5 to 3.6)
Mean gestational age, days (95% CI)	279 (279 to 280)	279 (279 to 280)	279 (279 to 280)
Mean age at early PFD screening, days (95% CI)	3.7 (3.6 to 3.8)	3.5 (3.4 to 3.7)	3.6 (3.6 to 3.7)
Mean age at definitive US, days (95% CI)	N/A	36.8 (36.0 to 37.6)	36.8 (36.0 to 37.6)

N/A, not applicable; PFD, pubofemoral distance; US, ultrasound.

Interpretation

Cut-off values for PFD in DDH screening have been previously proposed, but the populations, the definition of what constitutes true DDH, and the application of the PFD method are not consistent.[2–4] Tréguier et al[3] suggested a cut-off of 6.0 mm, or a difference between hips of 1.5 mm measured for older children in the supine position. While they did not describe in detail how they arrived at this cut-off or if any reference test was used, they implemented DDH screening, using this cut-off, and reportedly reduced late DDH diagnoses to 0%.[3] Motta et al[5] suggested a cut-off of 3.5 mm measured in the lateral position, but did not submit the hip to the necessary lateral stress described in the method by Salut et al,[8] which decreases the obtained PFD measurement as the femoral head was not moved out of the hip socket during examination, which may explain the relatively low cut-off value proposed.

We previously suggested a cut-off of 4.4 mm measured in the lateral position, but this cut-off was based on a population of older children where cases were defined as children who received treatment for DDH.[4] The newly established cut-off values in this study are the first to be proposed for use in early and standard US screening for DDH while directly comparing it to gold-standard US references regardless of treatment decisions.

In addition to the variation in examination methodology employed by Motta et al,[5] the examined children varied in age from three days to six months. This age variation might significantly influence the measurements and subsequent analysis, as the PFD increases with increasing degrees of dysplasia, but also increases for normal hips as the child ages.[9] In the present study, the optimal cut-off for DDH detection decreased from 6.2 mm to 5.6 mm as the newborns aged. While both cut off-values are significantly higher than previously published reference values for newborn to one-month old babies (1.9 mm),[9] the decrease in cut-off values may reflect a relative loss of laxity in the hip joint and consequently a lower PFD value in dysplastic hips. This difference further validates the point that the age of the examined newborn needs to be taken into consideration when evaluating PFD US examinations.

The study was conducted in a healthcare system where universal US of all newborns is not logistically feasible. Since only newborns with positive traditional criteria and/or

a positive PFD US received the definitive US examination, i.e. partial verification, the resulting accuracy parameters (sensitivity/specificity) are subject to verification bias, which usually results in a modest overestimate of sensitivity and an underestimate of specificity.[14]

The impact of the interval between early PFD screening and confirmatory definitive hip US was not evaluated in this study. There was a mean of 33 days between early PFD screening and definitive hip US, which may allow for several abnormal hips, as evaluated by PFD screening, to spontaneously resolve, resulting in a false positive result. This acetabular maturation may therefore decrease the reported sensitivity of early PFD screening. Despite this, we find it promising that early PFD screening still produced a sensitivity of 80%, far exceeding previously reported sensitivity of clinical examination at 28% and PPVs of 33% even when performed by experienced orthopaedic surgeons.[15–18]

While the study population was based on a selectively screened cohort, the distribution of hip types detected by definitive hip US resembles findings from universal screening programmes.[19] Additionally, besides risk factors for DDH, the referred population only differed in sex distribution from the non-referred population, while gestational age and birth weight were near identical. We therefore consider the present findings to be valid for both selectively and universally screened populations.

The PFD measurements in this study were obtained using a modification of the original methodology by placing the newborn in the lateral rather than the supine examination position. While this was done to avoid repositioning the newborn after Graf US examination, it is not yet known whether this shift in examination position affects the PFD measurement. The cut-off values presented here may therefore not be applicable to PFD examinations performed with the newborn in the supine examination position.

To summarize, PFD US screening produces a high degree of both sensitivity and specificity for detecting DDH. Age-specific cut-off values should be used to heighten the accuracy of PFD US screening.

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R. D. Maimburg: Conceptualization, Project administration, Supervision, Writing – review & editing.
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Data sharing
The data that support the findings for this study are available to other researchers from the corresponding author upon reasonable request.

Ethical review statement
The study consent process and written patient information leaflet for the parents were approved by the regional institutional ethics committee (Ref no: N-20200051).

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