SFH who presented to our outpatient department between 2005 and 2019 underwent cervical and cerebral MRI (cMRI) with MRA for the evaluation of CVA anomalies. Infantile haemangioma with the following characteristics were considered segmental: (i) positive criteria: long plaque-type haemangioma covering (part of) a cutaneous territory and (ii) negative criteria: round or oval form, or pedunculation. CVA anomalies were stratified according to Metry *et al.*[7] and Hess *et al.*[4] as low risk (dysgenetic or persistence of embryonal vessels, anomalous course and/or origin) or high risk (severe stenosis or undetectable blood vessels).

Mean age at presentation was 4·6 months (range: 1 week to 5 years). SFH diameter was < 5 cm in 31 of 58 patients (mean 3·1 cm, range 0·8–4·9 cm) and ≥ 5 cm in 27 of 58 patients (mean 8·6 cm, range 5·7–12·5 cm). cMRI with MRA was performed at a mean age of 7 months (range 4 days to 13 years). The anatomical distribution of SFH was assigned to embryonic placodes, as described previously.[8] Results of MRA studies (performed for various reasons, mainly seizures, developmental delay and asphyxia) of 50 age-matched children were evaluated for comparison. Prevalence of CVA anomalies in children with small and large SFH, respectively, was compared with the χ^2-test. Correlation between size of SFH and prevalence of CVA was assessed with Mann–Whitney U-test, Kruskal–Wallis test and/or Pearson correlation coefficient, as appropriate.

In both groups, placode segments 2 and 3 were the most commonly affected. Associated anomalies (cerebellar hypoplasia, sternal clefts, cardiac anomalies) were present in 5 children with SFH < 5 cm and in 10 children with SFH ≥ 5 cm. CVA anomalies were detected in 21 of 58 children with SFH (36%). All were ipsilateral to the SFH. Of the children with SFH < 5 cm, 6 of 31 (19%) had CVA (Fig. 1a–d) compared with 15 of 27 (56%) children with SFH ≥ 5 cm (Fig. 1e) ($P < 0·01$, χ^2 test). Of 21 CVA anomalies, 19 involved the circle of Willis (90%, Fig. 1f). SFH diameter was significantly larger in children with CVA than in those without ($P < 0·01$, Mann–Whitney U-test). Prevalence of CVA anomalies and size of SFH were positively correlated ($r = 0·47$, Pearson correlation coefficient; $P < 0·001$). In 17 of 21 patients with CVA anomalies (81%), we observed long-segment narrowing or hypoplasia of the major vessels, while minor anomalies were found in 6 of 21 (29%). There was a weak positive correlation between the extent/severity of CVA anomalies and size of SFH ($P < 0·1$, Kruskal–Wallis test). On follow-up, none of our patients had evidence of cerebral vasculopathy or stroke. CVA anomalies were detected in 5 of 50 controls (10%).

To our knowledge, this is the first study to address the correlation between SFH size and likelihood of associated cerebrovascular anomalies. Our findings challenge current recommendations that cMRI should only be performed in children with SFH ≥ 5 cm,[6] irrespective of age. This threshold appears arbitrary, particularly as all haemangiomas (including SFH) grow with age. Our results suggest that the risk of associated CVA anomalies is proportional to the diameter of SFH without a clear size 'threshold'. In view of the potential risk of stroke and the prevalence of CVA anomalies even in children with smaller SFH, MRA may be indicated irrespective of SFH diameter, but there is yet no general consensus. Although propranolol is generally well tolerated in children with PHACE,[7] caution is advised (i.e., lower starting dose, slow increase, three instead of two doses) in using systemic beta blockers in children with CVA anomalies at higher risk of stroke.[3,7]

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The refined Hurley classification: the inter-rater and intrarater reliability and face validity

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Dear Editor, Hidradenitis suppurativa (HS) is a common, debilitating, chronic inflammatory skin disease, predominantly staged according to the Hurley classification. However, this

classification was intended only to describe symptoms in one anatomical region and to guide surgical treatment options. With typically multiple areas affected by HS, this is not a valid instrument to classify the entire patient.[1] Because HS is a heterogeneous disease, the Dutch HS expert group proposed a modification, the 'refined Hurley classification'.[2] This consists of seven stages, subdividing stages I and II into stages A (mild), B (moderate) and C (severe), based on extent of the disease and degree of inflammation, while stage III (severe) is not subcategorized. This classification aims for a more detailed staging of patients with HS in daily practice and in clinical trials, ultimately to refine treatment strategies. The aim of this study was to assess the inter-rater and intrarater reliability and face validity of the refined Hurley classification.

A real-life assessment (n = 25) and a photographic assessment (n = 15) were performed in the Department of Dermatology, University Medical Center Groningen, The Netherlands, during the period May 2017 to July 2018. All adult patients with active HS visiting our clinic were eligible to participate. This real-life assessment consisted of two groups, each with two different independent raters. A fifth rater (B.H.) assessed all participants and this classification served as the reference. For the photographic assessment, participants were photographed according to a standardized protocol. All photographs were assessed by two independent investigators (L.M.P. and A.R.) for eligibility. At least two patients per refined Hurley stage were included.

A web-based survey was created using Qualtrics 2018 software (Provo, UT, U.S.A.) and was filled out twice, with an interval of 4 weeks, by 10 independent raters. All raters (12 residents and two dermatologists) received brief training on how to use the refined Hurley classification. Consulting the refined Hurley classification flowchart was permitted, as is possible in daily practice. Discussion between raters was not allowed. The study design followed the proposed Guidelines for Reporting Reliability an Agreement Studies.[3] The inter-rater agreement was calculated as the percent agreement between raters. The Krippendorff alpha test with corresponding benchmarks was used to determine the inter-rater and intrarater reliability.[4] Face validity was evaluated by asking the raters to score the usefulness of the refined Hurley classification on a scale from 0 to 100.

For the real-life assessment, 25 patients were assessed: 13 in group 1 and 12 in group 2. The inter-rater agreement varied from 46·2% to 83·3% and the inter-rater reliability ranged from $\alpha = 0{\cdot}68$ [95% confidence interval (CI) 0·32–0·95] to $\alpha = 0{\cdot}92$ (95% CI 0·78–1·00). Compared with the reference classification, one rater (group 1) showed low inter-rater reliability ($\alpha = 0{\cdot}60$; 95% CI 0·25–0·90), while the other three raters showed high inter-rater reliability: $\alpha = 0{\cdot}88$ (95% CI 0·65–1·00) to 0·98 (95% CI 0·93–1·00).

In the photographic assessment, 86·7% of patients were identified as white with Fitzpatrick skin types I or II. The inter-rater reliability was $\alpha = 0{\cdot}74$ (95% CI 0·71–0·78) for the first round and $\alpha = 0{\cdot}80$ (95% CI 0·77–0·82) for the second round, while the intrarater reliability showed a mean α of 0·83 (95% CI 0·78–0·89). The inter-rater agreement for the refined Hurley stage for both time points is shown graphically in Figure 1. The face validity showed scores of $78{\cdot}7 \pm 10{\cdot}3$ prior the first photograph assessment and $76{\cdot}5 \pm 9{\cdot}7$ after the second assessment.

The original Hurley classification recently demonstrated a moderate inter-rater reliability and substantial intrarater reliability, based on photographic assessments.[5] However, in our opinion, the original Hurley classification does not adequately reflect the disease extent and inflammatory activity of HS in the whole patient. For instance, patients with numerous widespread

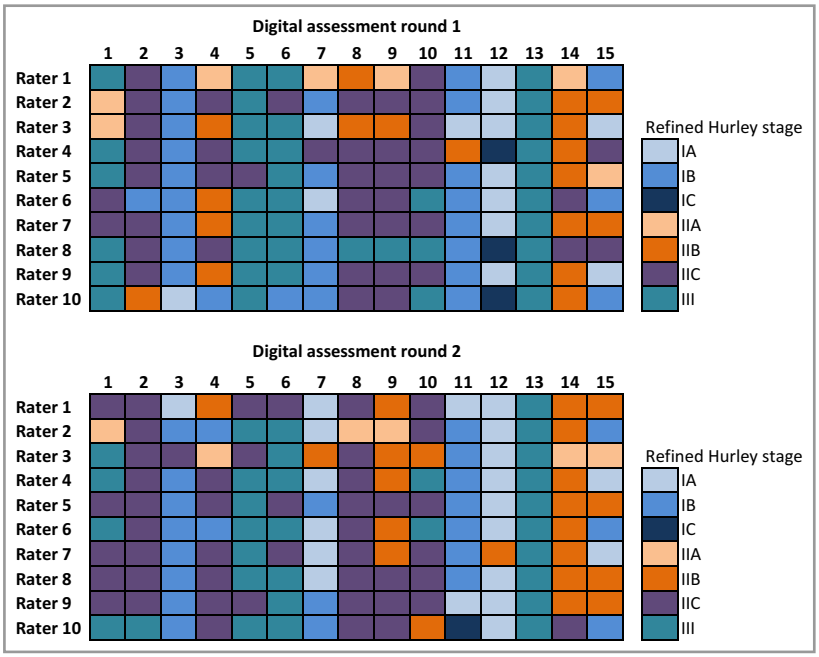

Fig. 1. Inter-rater agreement results of the photographic assessment. [Colour figure can be viewed at wileyonlinelibrary.com]

individual lesions (rated as refined Hurley 1C = severe), would still be classified as 'mild' in the original Hurley classification and consequently would not be eligible for treatment with biologics. A refinement of the original Hurley classification was therefore greatly needed. This is supported by a recent publication that showed an accurate correlation of the refined Hurley stages with HS severity assessed by both patients and clinicians.[6] Other classification systems for HS, based on phenotypes, previously showed only low inter-rater reliability or had not yet been validated, leading to minimal use in daily practice.[7,8]

In summary, the refined Hurley classification could be a reliable and useful tool for the classification and treatment of patients with HS in daily practice.

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Cross-sectional screening study for *Leishmania* DNA and antibodies in biologic-treated patients with psoriasis living in an area endemic for leishmaniasis

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Dear Editor, Biological drugs have revolutionized the control of immune-mediated diseases,[1] but most of the safety studies have not evaluated the risk of endemic infections, such as leishmaniasis, in underdeveloped regions.[2] The control of this parasite is strongly dependent on the production of specific cytokines [interleukin (IL)-1, IL-6 and tumour necrosis factor (TNF)-α],[3] which are important targets of biological therapies. Several reports have described cases of leishmaniasis in patients undergoing biological treatments,[4] but the real risk is unknown. We aimed to assess this risk by complementary evaluations (serology, conventional PCR and real-time PCR) in patients under treatment for psoriasis who were living in a region endemic for leishmaniasis in midwestern Brazil.

The study was approved by the Ethics Committee of the Faculty of Medicine of UnB (CAAE: 72312117·4·0000·5558). All patients signed an informed consent form.

This was a cross-sectional screening study, conducted from January 2018 until December 2018. Patients were allocated into one of four groups: 1: biologics (subdivided into TNF, IL-12/23 and IL-17A inhibitor groups); 2: conventional immunosuppressors (methotrexate); 3: nonimmunosuppressive treatment (nonsteroidal anti-inflammatory, acitretin, phototherapy and topical treatment); and 4: control (immunocompetent participants without psoriasis). The probable positivity for leishmaniasis in our target population was set at 5%, with H0 of 50%, H1 of 90%, power > 0·8 and $P < 0{\cdot}05$. Therefore, the minimal sample size was set at 300 individuals.[5]

Serum samples were subjected to indirect immunofluorescence (IgG against *Leishmania donovani*). Conventional and real-time PCR assays were performed on whole blood DNA using the primer pair 5'-GGCCCACTATATTACACCAACCCC-3' and 5'-GGGGTAGGGGCGTTCTGCGAA-3' (Thermo Fisher Scientific, Waltham, MA, USA), targeted to the minicircle kDNA of *Leishmania* spp.[6,7] All patients with at least one positive test underwent a complementary evaluation with blood cell counts, determination of the albumin/globulin ratio and abdominal ultrasonography examination. A Poisson regression model with robust variance was applied following a proposed hierarchical level. The software program SAS (Version 9·4 SAS Institute Inc., Cary, NC, USA) was used.

In total, 311 patients were included. No clinically active cases of leishmaniasis were found. Seven patients tested positive by serology, 13 tested positive by conventional PCR and 9 tested positive on real-time PCR (Table 1). In the biologics group, only patients using TNF inhibitors had positive results (Table 1).