Analysis of portwine stain disfigurement and pulsed dye laser treatment results
Koster, P.H.L.

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Chapter 3

Characterization of portwine stain disfigurement

Petra HH Koster, MD, Amsterdam
Patrick MM Bossuyt, Prof PhD, Amsterdam
Chantal MAM van der Horst, MD, Amsterdam
Geert HM Gijbers, PhD, Rotterdam
Martin JC van Gemert, Prof PhD, Amsterdam

Abstract

Portwine stain disfigurement is caused by several factors. To what extent and in which proportion these factors influence the overall perceived disfigurement is incompletely understood.

In this study, the contribution of seven portwine stain characteristics to overall portwine stain disfigurement was assessed. Color slides were shown to patients with portwine stains in the head, neck, and arm. From these slides, overall portwine stain disfigurement was judged by a panel of five persons. The majority of the average ratings of this panel was established with a nonparametric analysis of variance and by calculating the Cronbach's alpha coefficient. Using a previously tested multivariate questionnaire, the following portwine stain characteristics were rated quantitatively by a panel of five professionals, color, patchiness, boundary, size, shape, surface structure, and hypertrophy of the underlying tissue. By means of multiple linear regression analysis, the ratings of overall portwine stain disfigurement panel of five persons were compared with the ratings of the individual portwine stain characteristics panel of professionals. From the results of this analysis, the perceptual contribution of each of the characteristics to overall portwine stain disfigurement was calculated.

Size turned out to be the most important portwine stain characteristic, being responsible for almost half of the overall disfigurement. Color and boundary are the next two most important characteristics, contributing 18.7 and 12.4 percent, respectively. The other four characteristics together accounted for 19 percent. In our model, 43 percent of overall portwine stain disfigurement remains unexplained. We expect patient features to account for this.

We feel that these results may have consequences for laser treatment of portwine stains. Reducing the size and fading of the boundary of the stain probably reduce overall portwine stain disfigurement more effectively than primarily trying to lighten the often persistent center of the stain.
Introduction

A portwine stain is a vascular lesion consisting of ectatic dermal blood vessels that present as a pink, red, or purple discoloration of the skin. Because portwine stains occur in only 1% percent of newborn children, having a portwine stain makes a person out as being different from most other people. Being different from one's peers can be a disconcerting experience in itself and even more so if the badge of separateness is considered to be disfiguring. Several studies have underlined the stigmatizing effect of a portwine stain and the adverse social and psychological effects of a visible disfigurement on its bearer.(6)

These studies suggest that the disabling impact of an anomaly is closely related to its visibility. Depending on characteristics such as localization, intensity of color, and extentiveness of the stain, a portwine stain can be more or less conspicuous.

The aim of this study was to determine the contribution of a number of portwine stain characteristics to overall portwine stain disfigurement.

We restricted our investigation to 100 patients with a portwine stain in the head-neck area. First, for each patient, the overall disfiguring effect of the stain was assessed by a panel of lay persons. Acceptable reliability of this panel score was established. Second, at each site the following characteristics were rated quantitatively by a group of professionals: color, patchiness, boundary, size, shape, texture, stratum, hypertrophy. This was accomplished using a multi-item questionnaire, previously designed and tested for reliability. Finally, we applied the clinical results on pulsed dye laser treatment to the overall disfiguring effect per site. The panel score was compared with the ratings for the individual characteristics in a professional panel, by means of multiple linear regression analysis. This analysis yields the percentage contribution of each of the characteristics to overall disfigurement.
Materials and methods

Slides
Color slides were taken from 90 patients with untreated portwine stains in the head, neck area who applied for laser treatment at our clinic. The 29 male and 61 female patients were all East Asian, and their ages ranged from 3 to 54 years, mean 11.5 yr.; sd 8.3 yr. The slides were made by a professional clinical photographer in a photography studio, against a green background, under standardized conditions with respect to camera (Nikon 81 with a Micro-Nikkor 1:2.8/24 mm lens, luminosity f:2.8), illumination (studio flashlights, bicolor-pulsed), with softboxes and a backlight centrolateral to the side of the portwine stain, magnification (such that the head of the patient just filled the frame), diaphragm (standard F:11, adjusted according to darkness of skin if necessary), exposure time (1:12 second), type of film (Kodak ETR, 54 asan, and development (16 processing in hospital photolab). Two slides were obtained from each patient: one in full face and one in profile, together forming one slide pair.

Assessment of overall disfigurement by panel of lay persons
The overall portwine stain disfigurement was assessed by a panel of 16 lay persons (10 men, 6 women: mean age 28.4 yr., ranging from 22 to 48 yr.). The patient slides were presented to the panel pair by pair, in a random order. The members of the panel were instructed to judge the portwine stain by the impression it would make on them when they would meet the person with the portwine stain on the street, in the supermarket, etc. Before the actual assessment procedure was started, the panel members were given an impression of the portwine stains to be judged by looking at the first 20 slide pairs, without having to assess them. Projection was then started again with the first slide pair. Every member assigned a mark for disfigurement to each of the portwine stains on an anchored 10-point scale ranging from 1 (not disfiguring at all) to 10 (very disfiguring). The reliability of this disfigurement score was judged both by weighted kappa analysis, which reflects inter-rater agreement between individual panel members, and by calculating the Cronbach alpha coefficient.14
which is a measure of the reliability of the average panel ratings. The average weighted kappa for disfigurement was calculated by averaging the weighted kappa values of all 120 possible combinations of two raters from the 16 panel members. Linear weights were used in the calculation of the kappa statistic.

The kappa statistic is a measure of agreement between two individual panel members, corrected for chance agreement. It takes values between -1 and 1. A kappa value of 0 indicates no more agreement than by coincidence, a value of 1 means that the two panel members completely agree with each other, and a value of -1 means the panel members have completely opposite opinions. Values between 0.4 and 0.75 may be taken to represent good agreement. In case of less than perfect pairwise agreement between individuals, the reliability of the assessment score can be increased by taking the average rating of all panel members. The Cronbach alpha coefficient can be used as a measure of the reliability of this average rating, a Cronbach alpha coefficient of 0 meaning that the disfigurement score would be completely unreliable and a value of 1 indicating perfect reliability.

**Rating of the portwine stain characteristics by a panel of professionals**

In a separate session, the seven portwine stain characteristics (Table 1) were rated by a panel of five professionals: the treating physician, two plastic surgeons, a dermatologist and a clinical photographer. The slides were projected following the same procedure as was used for the lay panel. For each slide pair, the panel members filled out, individually, the questionnaire shown in Table 1. This questionnaire has been shown to be a reliable tool to rate these portwine stain characteristics quantitatively. Inter-rater agreement was determined by weighted kappa analysis and was fair to good for all characteristics (mean kappa 0.4, s 0.1). The summary scores, obtained by averaging the ratings of the five panel members, were even more reliable as was shown by the Cronbach alpha coefficient, which exceeded 0.6 in all cases. The questionnaire was originally designed to assess changes brought about by laser treatment and therefore also contained the characteristic hyperpigmentation. Being a side-effect of treatment, pigmentation does not play a role in the assessment of
untreated portwine stains and was therefore not included in the present study.

Table 1: Questionnaire as filled out by the panel of professionals, containing the seven portwine stain characteristics to be rated with their rating options.

1. COLOR/RIHUE AND HU\ROSE
   1. normal
    2. pale pink
    3. pale red or brownish
    4. pale purple or dark pink
    5. bright red
    6. bright purple or dark red
    7. dark purple

2. PARCHINESS
   1. not at all patchy
    2. a little patchy
    3. rather patchy
    4. very patchy

3. BOUNDARY
   1. vague
    2. faint
    3. very sharp

4. SHAPE
   1. regular
    2. somewhat irregular
    3. very irregular

5. SURFACE
   1. smooth
    2. a little uneven
    3. rather uneven

6. HORIZONTAL
   1. not hypertrophied
    2. a little hypertrophied
    3. rather hypertrophied
    4. very hypertrophied

Analysis
The relation between overall disfigurement (panel of lay persons) and the portwine stain characteristics (panel of professionals) was examined using multiple linear regression analysis. With this type of analysis, the
dependence of the outcome variable (disfigurement) on a number of predictive variables (the patient's skin characteristics) can be examined. The mean disfigurement score per slide pair was determined by averaging the scores of the five members of the lay panel. For each slide pair, the mean rating per characteristic was calculated by averaging the ratings of the five professionals. Because the number of answering options was not the same for all characteristics (e.g., seven for color versus three for boundaries), the mean rating of the five professionals was rescaled to a value between 0 and 1 for each characteristic. These mean ratings per slide pair were used for the analysis.

The following equation represents the multiple linear regression model:

\[
\text{Disfigurement score} = C \cdot \text{color} + 1 \cdot \text{pathology} + 1 \cdot \text{boundary} + 1 \cdot \text{size} + 1 \cdot \text{shape} + 1 \cdot \text{severe degrees} + 1 \cdot \text{atrophy}
\]

In this equation, the name of each characteristic represents the rescaled value of the mean rating given by the panel of professionals. The analysis yields values of constant \( C \) and the regression coefficients \( a \) through \( g \). Because disfigurement in our model has a minimum value of 1, constant \( C \) is necessary in case of the theoretic possibility that all other factors are zero. However, in our patient population, this was never the case. Consequently, \( C \) was not of great interest for the outcome of this analysis and was therefore disregarded. The regression coefficients reflect the percentual contribution of each of the characteristics to disfigurement.

A crucial assumption in the multiple linear regression model is that each of the predictive variables and the outcome variable are linearly related. We verified this assumption in scatter plots in which disfigurement was depicted versus each of the characteristics.

We expected some of the characteristics to correlate with each other. For example, a darker stain is probably more often associated with a sharply defined boundary than a more uniform one. Problems with the multiple linear regression analysis would occur if two characteristics were highly correlated, in that case, only one of the two would suffice in the analysis. We
therefore calculated the Pearson correlation coefficients between the characteristics\textsuperscript{16} as a measure of the degree of association.

Results

Overall disfigurement
Averaged over all rater pairs from the lay person panel, a weighted kappa value of 0.51 was obtained for overall disfigurement, indicating acceptable interrater agreement. The reliability of the average lay panel score was almost perfect, with a Cronbach alpha coefficient of 0.99. The distribution of the ratings is shown in Fig. 1. The average panel scores for overall disfigurement, per portwine stain, ranged from 2.9 to 9.9. Averaged over all 90 patients, the mean disfigurement score was 6.8 on the 1- to 10- point scale, with a standard deviation of 1.9 points.

![Bar chart](image)

Fig. 1: Distribution of the average panel scores for overall disfigurement as assigned by the panel of lay persons (total number of patients = 90). A disfigurement score of 1 = 'not at all disfiguring', a disfigurement score of 10 = 'very disfiguring'.

Chapter 3
Portwine stain characteristics

Table 2 shows the mean rating of the five professionals per portwine stain characteristic. Table 1, averaged over all 90 patients. It shows that the investigated portwine stains were, on average, fairly dark, moderately patchy, sharply bounded, fairly big, rather irregular, mostly smooth, and that the underlying tissue was somewhat hypertrophic.

Table 2: Mean rating assigned by panel of professionals to each portwine-stain characteristic on the questionnaire (averaged over 90 patients).

In the third column the ratings have been rescaled to values between 0 and 1.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Range of answering options</th>
<th>Mean rating (sd)</th>
<th>Rescaled value (sd)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>5-7</td>
<td>4.8 (1.0)</td>
<td>0.6 (0.2)</td>
</tr>
<tr>
<td>Patchiness</td>
<td>1-4</td>
<td>1.9 (0.5)</td>
<td>0.3 (0.2)</td>
</tr>
<tr>
<td>Boundary</td>
<td>5-9</td>
<td>2.4 (2.7)</td>
<td>0.7 (0.3)</td>
</tr>
<tr>
<td>Size</td>
<td>1-6</td>
<td>4.4 (3.0)</td>
<td>0.7 (0.2)</td>
</tr>
<tr>
<td>Shape</td>
<td>1-5</td>
<td>2.1 (0.5)</td>
<td>0.6 (0.2)</td>
</tr>
<tr>
<td>Surface-structure</td>
<td>1-6</td>
<td>4.2 (0.2)</td>
<td>0.4 (0.1)</td>
</tr>
<tr>
<td>Hypertrophy</td>
<td>1-6</td>
<td>5.0 (1.5)</td>
<td>0.8 (0.2)</td>
</tr>
</tbody>
</table>

Correlation between characteristics

Table 3 summarizes the Pearson correlation coefficients between the characteristics. A positive correlation between two variables is obtained when higher values of one variable are associated with higher values of the other variable. A correlation of around zero indicates that the two variables are uncorrelated.

As expected (see above), a strong correlation was found between color and boundary (0.86). The correlation coefficient of 0.6 between shape and patchiness can be explained by the fact that the panel members found it hard to distinguish between these two portwine-stain characteristics. Irregularly shaped portwine stains were often judged as being patchy, even though the color within the borders of the stain was uniform.
A particularly strong correlation between size and hypertrophy of the underlying tissue in Figs. 1 and 2 is not surprising either, as hypertrophy hardly occurs in small portwine stains.

Table 3: Pearson's correlation coefficients between portwine stain characteristics

<table>
<thead>
<tr>
<th></th>
<th>color</th>
<th>patchiness</th>
<th>boundary</th>
<th>size</th>
<th>shape</th>
<th>surface structure</th>
<th>hypertrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td>color</td>
<td>1.0</td>
<td>0.3</td>
<td>0.2</td>
<td>0.3</td>
<td>0.4</td>
<td>0.3</td>
<td>1.0</td>
</tr>
<tr>
<td>patchiness</td>
<td>0.3</td>
<td>1.0</td>
<td>0.8</td>
<td>0.2</td>
<td>0.4</td>
<td>0.3</td>
<td>1.0</td>
</tr>
<tr>
<td>boundary</td>
<td>0.2</td>
<td>0.8</td>
<td>1.0</td>
<td>0.3</td>
<td>0.2</td>
<td>0.3</td>
<td>1.0</td>
</tr>
<tr>
<td>size</td>
<td>0.3</td>
<td>0.4</td>
<td>0.3</td>
<td>1.0</td>
<td>0.2</td>
<td>0.3</td>
<td>1.0</td>
</tr>
<tr>
<td>shape</td>
<td>0.4</td>
<td>0.3</td>
<td>0.3</td>
<td>0.2</td>
<td>1.0</td>
<td>0.3</td>
<td>1.0</td>
</tr>
<tr>
<td>surface structure</td>
<td>0.3</td>
<td>0.2</td>
<td>0.3</td>
<td>0.2</td>
<td>1.0</td>
<td>0.3</td>
<td>1.0</td>
</tr>
<tr>
<td>hypertrophy</td>
<td>0.4</td>
<td>0.3</td>
<td>0.3</td>
<td>0.2</td>
<td>0.2</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Relations between individual portwine stain characteristics and overall disfigurement

Fig. 2 shows the scatter plots depicting the relation between overall disfigurement and each of the characteristics: color, patchiness, boundary, size, shape, surface structure, and hypertrophy. These diagrams suggest a linear relation between disfigurement and color, boundary, and size, and therefore these three characteristics fit well in a linear regression model. The relation between disfigurement and both patchiness and shape is much less clear. However, we hypothesize a linear relation between these two characteristics and disfigurement, and they were maintained in the model. Surface structure and hypertrophy show a nonlinear relation with disfigurement. The steep rise in disfigurement score that occurs if the surface is not smooth or if there is any sign of hypertrophy of the underlying tissue indicates that being present or not is more important for these characteristics than the extent to which the surface is uneven or the underlying tissue hypertrophic.
Fig. 2: Overall disfigurement (lay person panel assessment) versus each of the seven portwine stain characteristics (rated by panel of professionals).
Therefore, for both characteristics, the answers were divided into two categories: this so-called dichotomization resulted for surface-structure in the answers 1 (smooth) and 2 (not smooth) ("a little uneven" and "rather uneven" combined) and for hypertrophy in 1 (not present) and 2 (present) ("a little", "rather", or "very hypertrophic"). The resulting scatter plots are shown in Fig. 3. The two characteristics were included in the regression model in their dichotomized version.

Fig. 3: Relation of 'surface-structure' and 'hypertrophy' with overall disfigurement, after dichotomization of the answers.

Multiple linear regression analysis of the 90 slide pairs yielded an $R^2$ value of 0.87. The $R^2$ statistic is a measure of the "goodness of fit" of the model (i.e. how much of the observed variation in disfigurement can be explained by our model). An $R^2$ value of 0.87 means that variation in the seven portwine stain characteristics accounts for as much as 87 percent of the variation in disfigurement. In Table 4, the percentual contribution of the respective characteristics to overall portwine stain disfigurement is given.
Table 4: Results of the multiple linear regression analysis, indicating the percentual contribution of each of the portwine stain characteristics to overall portwine stain disfigurement.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Contribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>45.9%</td>
</tr>
<tr>
<td>Color</td>
<td>18.7%</td>
</tr>
<tr>
<td>Boundary</td>
<td>12.4%</td>
</tr>
<tr>
<td>Patchiness</td>
<td>3.3%</td>
</tr>
<tr>
<td>Hypertrophy</td>
<td>3.2%</td>
</tr>
<tr>
<td>Surface-structure</td>
<td>1.7%</td>
</tr>
<tr>
<td>Shape</td>
<td>1.7%</td>
</tr>
<tr>
<td>Unexplained</td>
<td>13.1%</td>
</tr>
</tbody>
</table>

The numbers in this table show that almost half of the overall portwine stain disfigurement is caused by its size. Color and boundary are the next two most important characteristics in determining portwine stain disfigurement, contributing 18.7 and 12.4 percent, respectively. The other four characteristics together account for merely 10 percent. In our model, 13 percent of portwine stain disfigurement remains unexplained.

Discussion

In this paper, we assessed the contribution of the characteristics color, patchiness, boundary, size, shape, surface-structure, and hypertrophy to overall portwine stain disfigurement. The disfiguring effect of a portwine stain on its bearer was judged by a lay person panel. Although no explicit definition of disfigurement was given, people intuitively seem to agree to a large extent about overall portwine stain disfigurement, and acceptable reliability of the panel score was established. A multiple linear regression model was used to compare overall disfigurement with ratings for the individual portwine stain characteristics. With this model, we were able to account for 87 percent of the variation in portwine stain disfigurement. There are several reasons why we cannot explain disfigurement completely. With the questionnaire from Table 1, the portwine stain itself can be characterized accurately, but it does not take into account other factors.
current properties that make it harder to distinguish the properties of the
pigment stain. For example, we can not distinguish between males and
females or identify adults or children at the beginning of the pigment stain. One
reason is that a pigment stain on the face of a little baby has a
different intensity than the same pigment stain on the face of an adult
male or an older, more mature female. And although
we've estimated the intensity of a stain on the mid-face
region in more than one as that in a male pigment stain on the side of
the face. We have repeated these experiments with the appreciation of
another important characteristic.

One of the most important characteristics
is the perception of almost all of the overall pigment stain
evaluation. It plays a crucial role in the overall evaluation of the image and
boundary detection. Although there is a correlation between color and
boundary. Although, these two properties are not strongly
associated with each other, they can be distinguished by pulsed dye laser
treatment. Therefore, we combined the model as two
separate items. The small correlation of intensity and shape in
despensation was to be expected based on the results in the scatter plots.

The limited variance of surface structure and hypertrophy to
descriptions for the surface of the pigment stain
electrophoresis, and the better resolution was rare in our patient
population.

The main goal of this study is to achieve the
maximum and best treatment of pigment stains. To achieve the
maximum difference between the pigment stain and surrounding normal
skin, the complete clearance is not to be achieved (100% most studies).
Assessment of treatment results were based on the amount of
lightening of the stain. However, we found that in doing so the achieved
improvement is underestimated because repeated treatment not only
results in lightening, but also results in decreased size, and a less sharply
defined boundary at the point of a series of treatments. McFarlane et al. and
Yeom et al. described clearance rates based on initial lesion size
considering that only small pigment stains - 30 mm have a realistic
chance of total clearing.

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This may have significant consequences for treatment strategy. Especially in large portwine stains that probably can never be cleared completely, treatment results could be optimized by treating the stain from the boundary inward. The decrease in size and fading of its boundary may reduce the disfiguring effect of a portwine stain more effectively than primarily trying to lighten the often persistent center of the stain.

References

Discussion by S Michael Kalick, PhD


Characterization of portwine stain disfigurement
by Petra Hl. Koster, MD, Patrick MM Bossuyt, Prof PhD, Chantal MAM van der Horst, MD, Geert HM Gijbers, PhD, and Martin JC van Gemert, Prof PhD

Much in the way that Mark Twain reputedly averred that Richard Wagner's music is better than it sounds, the Koster et al. article reminds us that portwine stain as a source of disfigurement is more complicated than it looks. Having identified seven measurable portwine stain characteristics, Koster et al. proceed to use professional assessments of these characteristics as predictors of overall portwine stain disfigurement in a multiple regression model. This approach allows the researchers to separate the stronger from the weaker predictors of portwine stain disfigurement among 90 patients in their sample, and to estimate the unique contribution of each characteristic to the prediction of mean portwine stain disfigurement ratings provided by 16 lay raters. They can thus report that lesion size contributes strongly to portwine stain disfigurement according to the raters' perceptions of the patients, whereas color and boundary sharpness contribute moderately, and patchiness, hypertrophy, surface smoothness, and lesion shape contribute minimally to portwine stain disfigurement.

The multiple regression approach adopted by Koster et al. is useful, but it is not without certain limitations. Because the seven portwine stain characteristics were found to be intercorrelated among themselves (for example, the value of $r$ was found to be 0.8 between lesion color and sharpness of lesion boundary), it is not possible to disentangle the actual exact contribution of each characteristic to the degree of overall disfigurement. The percentage contributions listed in Table 4 of the Koster et al. article are probably the result of a stepwise regression procedure, which tend to overestimate the contribution of the strongest predictors and underestimate the contribution of weaker predictors.
this structure. This is because, as we develop these additional skills, we find that these relationships simplify as approximate solutions.

Perceptions by other individuals regarding the primary importance of vision are not uncommon, but persons who distinguish and by previous consideration of these factors to maintain "tangible" perceptions of the factors that determine the future for the patient's condition. The factors that influence these perceptions are often complex and difficult to assess. In other cases, perceptions can be influenced by the amount and nature of the patient's experience with the illness. In such cases, perceptions are often based on personal judgments, rather than on empirical evidence.
patients' or clinician's satisfaction, the approach advocated by Koster et al. does seem worth a formal test against other laser treatment strategies. Patients' responses to treatment can settle the issue of what treatment approaches are most beneficial for them. Although portwincle stain disfigurement may be more complicated than it looks, we can hope that research such as that by Koster et al. will reduce the complexity to a more manageable, ordered state.

S. Michael Kalick PhD
Psychology Department
University of Massachusetts
100 Morrissey Blvd.
Boston, Mass. 02125
