TITLE: SOURCES OF VARIABILITY OF THE VAN HERICK TECHNIQUE FOR ANTERIOR ANGLE ESTIMATION

Running title: New insights into the Van Herick technique

Authors:

Joan Gispets, PhD †

Genís Cardona, PhD †

Miriam Verdú, MSc †

Núria Tomàs, MSc *

Corresponding Author: Genís Cardona (gcardona@oo.upc.edu)

Terrassa School of Optics and Optometry

Violinista Vellsolà, 37

E08222 Terrassa, Catalonia, Spain

+34 93 739 8774

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[†] University Vision Centre, Universitat Politècnica de Catalunya, Terrassa, Spain

^{*} Centre for Sensors, Instruments and Systems Development, Universitat Politècnica de Catalunya, Terrassa, Spain

Background: The purpose of the present study was to investigate two potential sources of variability of the traditional Van Herick technique for temporal anterior chamber angle estimation, namely the need to compare the depth of the peripheral anterior chamber (PACD) with the thickness of the peripheral cornea (PCT), and the possible loss of information resulting from restricting the assessment of the ACA to the temporal limbus.

Methods: Both image analysis and Scheimpflug photography were employed to measure PCT and PACD in a group of 82 eyes (mean \pm SD age of 32.8 \pm 4.1 years) with and without narrow anterior chamber angles. Subjective and semi-objective Van Herick grades were compared, and the relationship between PCT and PACD was investigated. Scheimpflug photography was also used to determine the value of the narrowest anterior chamber angle (ACA), and to compare it with the temporal angle.

Results: No statistically significant differences were encountered between semiobjective and subjective grades. A weak statistically significant correlation was found
between image analysis values for PCT and PACD (r = 0.295; p = 0.007). Upon
examining Scheimpflug photography data, no statistically significant association
between PCT and PACD was revealed. Temporal and minimum ACA presented
statistically significant differences (t = 7.213; p < 0.001). In approximately 65% of the
patients, the minimum ACA was not located at the temporal limbus, with a difference of
up to 9.8 degrees between minimum and temporal angles.

Conclusion: The encountered association between the image analysis PCT and PACD measurements advocates for the direct measurement of PACD as a better estimation of ACA depth than the ratio between PCT and PACD. All anterior chamber quadrants should be examined, as the minimum ACA may not be located temporally.

KEY WORDS

Angle Closure; Anterior Chamber Angle; Gonioscopy; Limbal Chamber Depth;

Scheimpflug Photography; Van Herick Technique

Primary angle-closure glaucoma (ACG) has been described as one of the main causes of blindness around the world, with a particularly high prevalence among the Asian population^{1,2}. Assessment of the anterior chamber angle (ACA) is essential for the detection of eyes at risk for ACG prior to the onset of the disease. Gonioscopy remains the gold standard for ACA evaluation, although several intrinsic limitations of the technique have been documented. Indeed, gonioscopy measurements have been found to depend on the experience and skill of the examiner, actual positioning of the lens, patient line of gaze and pupil diameter variations associated with illumination conditions, as well as on the grading scheme employed to report angle findings³. Non-invasive alternatives to gonioscopy, such as ultrasound biomicroscopy⁴, Scheimpflug imagining⁵ and optical coherence tomography^{6,7} are also not devoid of their own drawbacks.

The Van Herick technique, first described in 1969⁸, aims at estimating the depth of the peripheral anterior chamber by comparing the observed slit-lamp optical section of the peripheral cornea to the width of the anterior chamber adjacent to the limbus. A slit-lamp with the illumination column offset by 60 degrees from the optical axis of the microscope is used to create a narrow beam of light, which is directed at a perpendicular angle to the ocular surface at the limbus, whereupon the ratio between the corneal width and the anterior chamber depth (seen as the dark area delimited by the light crossing the cornea and the reflection from the iris surface) is graded. As in gonioscopy, several grading schemes have been introduced, resulting in different sensitivity and specificity values for the detection of occludable angles, as compared to the gold standard ^{8,9}.

Although the Van Herick technique relies on the subjective assessment of the observed structures, it has been documented as offering relatively high inter-observer reproducibility^{9,10}. The technique, however, may be considered of limited scope, as it only estimates the ACA at the temporal limbus, in contrast with gonioscopy, which

provides a 360 degree view of the anterior chamber (nasal limbus may also be examined, provided that anatomical shadows do not prevent the correct configuration of the slit-lamp observation and illumination systems required for the Van Herick technique). In addition, the Van Herick technique has been reported to be highly sensitive to the position of the direct slit-lamp beam, being sensitive to a 10 degrees deviation from the perpendicular direction, although the angular separation between the observation and illumination columns of the slit-lamp was found to be less critical¹¹.

The Van Herick technique is relevant to the interests of all eye care practitioners in that it allows for a quick and easy screening alternative to gonioscopy³, while avoiding direct contact with the ocular surface and the need for anaesthetic instillation. The aim of the present study was to further explore the limitations and possible sources of variability associated with the Van Herick technique. The relative dimensions of the anterior ocular structures were estimated with digital image processing, a semi-objective modification to the traditional Van Herick technique, as well as through Scheimpflug photography, in a group of patients with and without narrow anterior chamber angles. Two different possible sources of variability were assessed. On the one hand, it was our hypothesis that a direct measurement of the peripheral anterior chamber depth (PACD) would be preferable to an estimation relying on a comparison between PACD and peripheral corneal thickness (PCT). On the other hand, the Scheimpflug imaging system was also employed to determine the value and location of the narrowest ACA, thus exploring the intrinsic loss of information resulting from restricting the assessment of the ACA to the temporal limbus, which may not necessarily correspond to the location of the narrowest angle.

METHODS

Participants

A total of 41 patients (82 eyes) with ages ranging from 21 to 38 years (mean ± SD of 32.8 ± 4.1 years) were consecutively recruited for this study from those attending the University Vision Centre (the optometry clinic of the Terrassa School of Optics and Optometry) for routine optometric eye examination. Twenty-seven patients were female. Inclusion criteria were ages 20 to 60 years, spherical refractive errors from -2 D to + 2 D and corneal astigmatism of -0.75 D or less. Although we aimed at including patients with both open and narrow anterior chamber angles, no attempt was made to determine the actual state of the angle prior to the beginning of the study. Patients with a history of intraocular surgery, anterior segment laser treatment, penetrating ocular trauma, glaucoma or other ocular pathologies and limbal defects preventing the observation of the peripheral anterior segment structures were excluded from the study, as well as those presenting specific peripheral iris configurations, such as pigment dispersion or plateau iris, which may alter estimation.

All participants provided written informed consent after the nature of the study was explained to them. The study was conducted in accord with the Declaration of Helsinki tenets of 1975 (as revised in Tokyo in 2004) and received the approval of an Institutional Review Board (Universitat Politècnica de Catalunya).

Description of the modified Van Herick procedure

The modification introduced to the Van Herick technique resided in the use of image analysis software to provide a semi-objective measure of the parameters of the peripheral anterior chamber structures. The slit-lamp observation and illumination components were positioned as recommended in the literature for the Van Herick

technique⁸ and an optical section was projected on the temporal limbal area, perpendicular to the corneal surface. Once the illumination and the focussing conditions were considered to be optimal, three consecutive images were captured with a DC-3 Integrated Digital Camera Attachment (Topcon, Oakland, NJ) by an experienced optometrist, trained in the Van Herick technique, whereupon the best photograph from each patient was selected to undergo image analysis.

The Adobe[®] Photoshop[®] CS3 Extended image software for Windows[®], version 10.0, (Adobe Systems, Inc., San Jose, CA) was employed to measure the thickness of the peripheral cornea and the depth of the peripheral anterior chamber, which were delimited by the light crossing the cornea and its reflection from the iris surface. After importing the selected image, the rectangle tool was used to draw two vertical rectangles with sides tangent to the anterior and posterior corneal surface, and to the posterior corneal surface and the temporal margin of the reflected light beam, respectively. Consequently, the widths of the rectangles corresponded to the thinnest peripheral cornea (PCT) and the shallowest peripheral anterior chamber (PACD) locations (Figure 1). The semi-objective Van Herick value (OVH) was determined by the ratio of the rectangle widths (in pixels), and graded as follows: ratio of the PACD to the PCT lower than 1:4 as grade 1; ratio from 1:4 to less than 1:2 as grade 2; ratio from 1:2 to less than 1 as grade 3; and ratio equal or greater to 1 as grade 4. This slight modification of the Van Herick grading scheme was implemented to allow for the inclusion of PACD to PCT ratios between 1:2 and 1, which are not considered in the original scale⁸. All image analysis procedures were performed by a laboratory assistant, naïve to the goals of the study.

INSERT FIGURE 1 APPROXIMATELY HERE

It must be noted that, although slit-lamp magnification remained constant at 10x throughout the study, all image analysis measures were described in pixel units, without applying any transformation in order to derive the corresponding values in micrometers. A direct measure of the absolute real values of PCT and PACD was considered to be beyond the scope of this study.

Additionally, and in parallel to the semi-objective analysis, the same experienced optometrist in charge of the slit-lamp examination was instructed to provide a subjective estimation of the PACD by means of the modified Van Herick four-point grading scheme described above. This estimation, which was labelled as subjective Van Herick (SVH), was carried out by direct observation through the oculars of the slit-lamp and always preceded digital image analysis.

Scheimpflug photography and narrowest anterior chamber angle estimation

A Scheimpflug image analysis device (Pentacam HR, Oculus Optikgerate GmbH, Wetzlar, Germany) was used to capture three consecutive images of the anterior ocular structures. The characteristics and operational principles of this instrument have been extensively described in the literature¹². In essence, it utilizes a rotating monochromatic slit-light source (blue LED at 475 nm) to capture up to 50 sectional images yielding 138.000 true elevation points, thus constructing a 3-dimensional view of the anterior segment of the eye, as well as granting a complete anterior and posterior topographic analysis of the cornea. Scan time was adjusted at 1 second.

All Pentacam measurements were conducted by an optometry assistant. In order to obtain PCT and PACD readings at the temporal location, corneal diameter was multiplied by 0.9, whereupon the cursor was manually positioned at the resulting location over the pachymetry and the anterior chamber depth maps, respectively. Pentacam images were also reviewed, at 20 degree intervals, to determine the

narrowest value of the anterior chamber angle. In addition, the value of the ACA at the temporal position was recorded.

Data Analysis

Statistical analysis of the data was performed with the SPSS software 17.0 for Windows. On the one hand, continuous numerical data, that is, PCT and PACD (in pixels or micrometres), and temporal and narrowest ACA (degrees) were analysed for normality using the Kolmogorov-Smirnov test, which disclosed normal distributions in all cases (p > 0.05). Therefore, the Pearson's coefficient of correlation was employed to assess the relationship between PCT and PACD (for digital image analysis and Pentacam data) and the parametric Student's t-test for paired samples to investigate the statistical significance of the differences between temporal and narrowest ACA. On the other hand, semi-objective and subjective Van Herick grades were considered as ordinal data, and subjected to non-parametric statistical analysis. In consequence, the Wilcoxon signed-rank test for matched pairs was used to evaluate the difference between OVH and SVH grades. Similarly, the Spearman's rho coefficient of correlation was employed to determine the association between OVH and SVH, as well as between PCT and PACD (as measured with the Pentacam) and SVH. A p-value of 0.05 or less was considered to denote statistical significance throughout the study.

RESULTS

A summary of the percentage of eyes graded 1, 2, 3 or 4 with the traditional Van Herick estimation, as well as with the semi-objective modification, based on the new proposed digital image analysis, is shown in **Table 1**. Overall, 12.2% and 8.5% of eyes were classified at risk of angle closure with the subjective and semi-objective techniques, respectively, when considering a cut-off point of grade 2, that is, when PACD to PCT ratio was lower than 1:2. No statistically significant differences were encountered between semi-objective and subjective grades (Z = -3.02; p = 0.763), which were also found to present a strong and statistically significant correlation (rho = 0.925; p < 0.001).

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A weak, albeit statistically significant correlation was disclosed upon examining the relationship between the digital image analysis values of PCT and PACD (r = 0.295; p = 0.007), that is, there was an observable trend in which deep peripheral anterior chambers were associated with thick peripheral corneas and shallow chambers with thinner corneas. The same parameters, when measured with the Pentacam system, did not display any statistically significant correlation.

A summary of the Pentacam PCT and PACD values for each SVH grade is presented in **Table 2**. Upon examining the association between these parameters, no correlation was found between SVH grades and PCT, whereas a statistically significant positive correlation was disclosed between SVH grades and PACD (rho = 0.733; p < 0.001).

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The Pentacam analysis of the temporal and minimum ACA disclosed average angle values of 42.83 ± 6.32 degrees and 40.42 ± 6.56 degrees, respectively (Mean \pm SD). By selecting a cut-off point of 29.5 degrees¹³, 2.4% and 8.5% of eyes were considered at risk of angle closure when taking into account the outcome of either the temporal or the minimum angle measurements. The location of the narrowest angle around the perimeter of the cornea was found to be evenly distributed, although a slight trend was observed in which the narrowest angle was located more frequently in the temporal quadrant (35% of patients, *versus* 24%, 22% and 19% in the nasal, superior and inferior quadrants, respectively). A statistically significant correlation was encountered between temporal and narrowest angles (r = 0.893; p < 0.001). These measurements were found to present statistically significant differences (t = 7.213; p < 0.001), with a difference ranging from 0 to 9.8 degrees (that is, 33.15%) between the temporal and narrowest anterior chamber angles.

DISCUSSION

The present study aimed at exploring the extent of some of the limitations of the traditional Van Herick procedure for anterior chamber angle estimation and to present a semi-objective modification to the technique based on image analysis. Two main possible sources of variability were considered, namely the need to compare the depth of the peripheral anterior chamber with the thickness of the peripheral cornea, and the possible loss of information resulting from restricting the assessment of the ACA to the temporal limbus.

The first possible source of variability was investigated with the help of digital image analysis. Semi-objective and subjective grades did not present statistically significant differences and were found to be strongly correlated, thus suggesting that the subjective estimation of the relative thickness of the peripheral cornea and depth of the anterior chamber, as described in the traditional Van Herick procedure, did not benefit from digital image analysis. However, this result must be interpreted with caution as several aspects need to be considered. Firstly, image analysis was not fully automated, and required manual drawing of the corresponding rectangles which delimited the areas of interest. Therefore, the modification to the traditional Van Herick technique implemented in this study was described as semi-objective rather than objective. Secondly, the optometrist in charge of the subjective assessment was selected for his ample experience with the Van Herick technique. Indeed, grading in general has been shown to improve with training and with the experience and knowledge of the examiner^{14,15}. Besides, image capture and subjective grading were synchronous, once illumination, positioning and focusing conditions were considered optimal according to the Van Herick description. Finally, although the aim of the study was to include patients with both open and narrow angles, the nature of our recruitment procedure. based on the consecutive selection of patients attending the University Vision Centre for routine optometric examination, produced a not unexpected larger percentage of

eyes with open angles. Previous studies have documented good specificity but moderate to low sensitivity values for the traditional Van Herick grading system for the detection of angle closure (grade ≤ 2)^{10,16,17}, although other authors^{9,18}, employing a modified grading system, were able to find acceptable specificity and sensitivity values for the Van Herick technique. Consequently, the possible underestimation of the benefits of the semi-objective grading modification in our sample of patients is unclear and warrants further study. It must be emphasized, however, that sample selection was not considered, *per se*, a limitation of the study. Indeed, our goal was not to investigate the diagnostic validity of the modified Van Herick technique, which would require either comparing our findings with a gold standard test, in this case gonioscopy, or following all patients until the actual outcome was observed, neither of which was attempted in the present study, but to examine the intrinsic sources of variability of the traditional technique, based on the observation of the temporal anterior ocular structures.

The semi-objective evaluation of PACD and PCT disclosed a weak association between these parameters, which may raise the question of whether the comparison between PACD and PCT needed to estimate the risk of angle closure is undermined by the lack of independence between these parameters. Indeed, a shallow peripheral anterior chamber, if associated with a thin peripheral cornea, may be expected to result in a similar PACD to PCT ratio than a deep peripheral anterior chamber accompanied by a thick peripheral cornea. This false estimation would lead to open and closed angles being awarded similar grades, both in the semi-objective and subjective assessment, that is, the good agreement between subjective and semi-objective approaches may be an indication that, even when performed by a skilled optometrist, both approaches are subject to the same possible source of error. This limitation could be addressed by the implementation of a new modification to the traditional Van Herick technique based solely on the semi-objective evaluation of PACD, without the need to compare this value with that of the width of the peripheral cornea. The normalization of

PACD values, however, was beyond the scope of the present investigation. It must be noted that, upon examining the relationship between the Pentacam values for PCT and PACD, no statistically significant association was revealed, in disagreement with semi-objective image analysis. This apparent discrepancy may be explained by the difficulty in obtaining reliable Pentacam readings at the limbal area, given the gradual loss of transparency of the ocular media. Besides, with the present study design it was unclear whether Pentacam measurements corresponded to the exact peripheral location explored with both SVH and OVH approaches. Interestingly, however, a strong positive correlation was disclosed between SVH grades and PACD, as measured with the Pentacam system.

The second possible limitation of the traditional Van Herick technique was assessed by using the Pentacam system to determine the values of the temporal and the minimum anterior chamber angles. It is interesting to mention that a conservative cut-off point was used to investigate the percentage of eyes at risk of anterior chamber angle closure, as determined by the temporal and the minimum angle values. In effect, although the reported cut-off value of 29.5 degrees has been associated with an area under the ROC curve (AUC) of 0.935¹³, other authors documented similar AUC values to correspond to a cut-off angle of 22.4 degrees¹⁹. Therefore, whereas by using a cut-off value of 29.5 degrees the semi-objective and subjective Van Herick estimations and the minimum angle as determined with the Pentacam resulted in a comparable percentage of eyes at risk of angle closure, a cut-off value of 22.4 degrees would have disclosed significant differences between both the semi-objective and subjective Van Herick approaches and the Pentacam outcome (all eyes from the current study sample had minimum angles larger than 22.4 degrees).

Temporal and minimum angles were found to present a variation of up to 33.15%, or from 0 to 10 degrees, a difference that was found to be statistically significant. Indeed, in approximately 65% of the patients the minimum angle was not located at the

temporal limbus, thus resulting in an underestimation of the risk for angle closure if only this area was evaluated with the Van Herick technique. These results are in agreement with previous studies documenting an asymmetry between the estimation of nasal and temporal angles 20 . The present findings advocate for not restricting angle estimation to the temporal limbus, although they need to be examined more closely due to the difficulty, in some cases of angle closure, of visible light to reach the structures under examination using a Scheimpflug imaging system 21 , as well as to the documented relatively poor repeatability (coefficient of repeatability of \pm 5.45°) of anterior angle measures with this system 22 .

In conclusion, albeit the Van Herick technique for anterior chamber angle assessment has the benefit of being a fast, non-invasive, relatively accessible technique, with reported acceptable specificity and sensitivity values^{9,18} for the detection of angle closure, it is nevertheless not devoid of intrinsic limitations. Some of these sources of variability may be easily overcome with the direct measurement of the depth of the peripheral anterior chamber through digital image analysis or Pentacam imaging, rather than by grading the ratio between this depth and the peripheral corneal thickness.

Other limitations, such as restricting the evaluation to the temporal limbus, need to be taken into careful consideration in marginal cases, as the temporal angle may not be coincident with the narrowest angle for that patient. The findings of the present study were able to illustrate the relevance of these sources of variability, although further research is necessary to gain a proper understanding of their clinical significance.

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TABLES

Table 1: Percentage of eyes (n = 82) classified as grade 1, 2, 3 or 4 according to the subjective and semi-objective Van Herick techniques.

Grade	SVH [†]	OVH [‡]
1	3.7	2.4
2	8.5	6.1
3	19.5	26.8
4	68.3	64.6

[†] Subjective Van Herick technique; [‡] Semi-objective Van Herick Technique

Table 2: Peripheral corneal thickness and peripheral anterior chamber depth, as measured with the Pentacam system, for each subjective Van Herick grade.

SVH [†] Grade	PCT [‡] (Mean ± SD)	PACD^ (Mean ± SD)
1	748.50 ± 42.18	856.67 ± 187.49
2	731.75 ± 54.58	940.00 ± 306.50
3	746.95 ± 59.55	1315.00 ± 303.19
4	735.13 ± 89.22	1606.25 ± 339.58
	. 55 5 ± 56.22	. 333.23 2 000.00

[†] Subjective Van Herick technique; [‡] Peripheral corneal thickness (micrometres);

[^] Peripheral anterior chamber depth (micrometres)

FIGURE CAPTIONS

Figure 1: Semi-objective measurement, though image analysis, of the width of the peripheral corneal thickness (red solid line rectangle, PCT) and the peripheral anterior angle depth (blue broken line rectangle, PACD). This image was awarded a grade 3.