Experimental Eye Research 145 (2016) 341–346

Contents lists available at ScienceDirect

Experimental Eye Research

journal homepage: www.elsevier.com/locate/yexer

Research article

Structural characteristics of the optic nerve head influencing human retinal venous pulsations

Jonathan Lam [a], Geoffrey Chan [a], William H. Morgan [a, b], Martin Hazelton [c], Brigid Betz-Stablein [c, d], Stephen J. Cringle [a, b], Dao Yi Yu [a, b, *]

[a] Lions Eye Institute, The University of Western Australia, Perth, Australia
[b] Centre for Ophthalmology and Visual Science, The University of Western Australia, Perth, Australia
[c] Statistics and Bioinformatics, Massey University, Palmerston North, New Zealand
[d] School of Medical Sciences, University of New South Wales, Australia

ARTICLE INFO

Article history:
Received 13 October 2015
Received in revised form
1 January 2016
Accepted in revised form 10 February 2016
Available online 15 February 2016

Key words:
Retina
OCT
Glaucoma
Venous pulsations
Optic disc
Photoplethysmography
Optical coherence tomography
Optic nerve head

ABSTRACT

The relationship between structural characteristics of the optic nerve head and venous pulsations in the human eye remain unknown. Using photoplethysmographic techniques we investigated whether properties of the human retinal veins and their surrounding structures influence venous pulsation. 448 locations of venous pulsation were analysed from 26 normal human eyes. Green channel densitometry derived from video recordings of venous pulsations were used to generate a map of venous pulsation amplitudes along retinal veins. Optical coherence tomography was used to perform quantitative measurements of tissue characteristics at sites of high and low amplitude points as well as in a second analysis, at maximal amplitude pulsation sites from superior and inferior halves of the eyes. Structural characteristics measured included venous diameter, distance from pulsation point to cup margin, vessel length from pulsation point to vein exit, tissue thickness overlying vein, optic disc diameter and presence of a proximal arteriovenous crossing. Increasing venous pulsation amplitudes were associated with larger applied ophthalmodynamometry force, increasing venous diameter, and decreasing absolute cup margin distance (all $p < 0.001$). Increasing distance of maximal amplitude pulsation point to cup margin was associated with the presence of a proximal arteriovenous crossing, increasing venous diameter, and decreasing tissue depth (*all* $p \leq 0.001$). Venous diameter and tissue depth alter venous compliance, which is likely to be a major factor determining sites of venous pulsation.

1. Introduction

Retinal venous pulsations occur spontaneously in up to 95% of normal human eyes (Morgan et al., 2004a). They are visualized as an oscillation of the retinal vein wall and show a variation in location, generally occurring around the optic disc surface close to the venous exit through the lamina cribrosa (Jacks and Miller, 2003). The clinical importance of this feature is its ability to indicate the health of the retinal circulatory system and the absence of vein pulsation is linked to numerous disease states such as glaucoma and retinal vein occlusion (Morgan et al., 2004a, 2004b). Furthermore, absence of venous pulsations may be useful in the diagnosis of raised intracranial pressure (Jacks and Miller, 2003). When absent, venous pulsations may be induced by increasing intraocular pressure (IOP) through application of ophthalmodynamometric force (ODF) to the globe which may be recorded as a venous pulsation pressure (Duke-Elder, 1926). Though there appears to be a strong relationship between venous pulsation pressure and IOP, this correlation is not well defined. Our previous studies demonstrated the relationship of retinal vein pulsation timing to phases of intracranial pressure, implicating cerebrospinal fluid pressure (CSFp) pulsation as the prime generator with the pulse wave moving along the vein in a retrograde manner (Morgan et al., 2012; Zamir, 2000).

Though retinal vein pulsation is often limited to a small segment of the vein, there is vast inter-individual variation in the location of this pulsation (Jacks and Miller, 2003). Determinants of such variation in not only pulsation location but also occurrence have not yet been identified. It is postulated that structural factors in the optic

* Corresponding author. Centre for Ophthalmology and Visual Science, The University of Western Australia Nedlands, Western Australia, 6009, Australia.
E-mail address: dyyu@lei.org.au (D.Y. Yu).

http://dx.doi.org/10.1016/j.exer.2016.02.003
0014-4835/

nerve head (ONH) inherent to the retinal veins may influence venous pulsation. Empirical and modelling work identifies elevated vessel wall compliance as a factor reducing pulse wave velocity and distal amplitude, which occurs when veins are larger and have less rigidity (Zamir, 2000; Akl et al., 2014).

The structure of the optic disc and disc-vessel configuration may also be significant to the distribution of intravascular pressure gradient along the retinal vein (Jacks and Miller, 2003). The ONH consists of densely packed tissue with complex cellular relationships consequent to the intricate embryological processes involved in its development (Hogan et al., 1971; Yu et al., 2013). Investigating relationships between these tissues may help determine possible influences to retinal venous pulsation. Additionally, analysis of pulse waves along vessels may provide information regarding a possible pulse-generating site, such as the right atrium of the heart producing a jugular venous pulse (Zamir, 2000; Minten et al., 1983).

Quantitative measurements of ONH characteristics have been reliably measured in human eyes by spectral domain optical coherence tomography (SD-OCT) (Chauhan et al., 2013). Our recently published photoplethysmographic technique allows us to accurately determine the location and amplitude of venous pulsation at varying locations surrounding the human optic nerve (Morgan et al., 2014, 2015a). In this study, we correlate venous pulsation with SD-OCT anatomical parameters to quantitatively and qualitatively study structural characteristics surrounding sites of venous pulsation (Samarawickrama et al., 2012).

2. Materials and methods

2.1. Ethics

This study was approved by the Human Research Ethics Committee of The University of Western Australia. All patient imaging was performed at the Lions Eye Institute in Perth. The study was conducted in accordance with the tenets of the Declaration of Helsinki and informed consent was obtained from subjects with explanation of the nature and possible consequences of the study.

2.2. Volunteers

Images were acquired from both eyes of 16 human volunteers, aged between 22 and 69 for this study. Human volunteers had no documented history of eye disease. Intraocular pressure measurements were performed along with baseline fundus photo and 24-2 Humphrey visual fields with SITA standard to exclude the presence of ocular conditions. One subject had systemic hypertension treated with a single antihypertensive agent (Ramipril). All other subjects had no past medical history or medications. A mydriatic agent was used prior to imaging. The demographic data of each subject are presented in Table 1.

2.3. Spectral domain OCT imaging

Spectral domain OCT (Spectralis SD-OCT, Heidelberg Engineering, Inc., Heidelberg, Germany) was performed on both eyes of volunteers. Details of the principle of SD-OCT have been previously described (Yaqoob et al., 2005). Images encapsulated a region $15 \times 10^{\circ}$ centred on the optic disc with 49 sections acquired in both the horizontal and vertical planes. 30 images were averaged per plane and Enhanced Depth Imaging was utilized to maximize image quality.

2.4. Venous pulsation recordings

Ophthalmologists (W.M. and A.R.) performed video recordings of venous pulsations as described by Morgan et al (Morgan et al., 2015b). A slit lamp camera recorded video and sound signals from a pulse oximeter placed over the subject's right index finger. Video resolution was 1920×1080 pixels at 25 frames per second. All timing of the signals was made in relation to the frame count and so a precision of 0.04 s was possible.

Retinal vein pulsation was recorded with a 60-dioptre non-contact lens. Following this, an ophthalmodynamometer (Meditron, Voeklingen, Germany) using a contact lens surrounded by a ring force transducer was applied to the eye using contact gel after local anaesthetic application. Graded forces of varying ODF were applied to aim for target pressure ranges of 0 (i.e. at spontaneous venous pulsation) and between forces of 1–15, 15–30, 30–45 for each eye. Video recordings were taken of venous pulsations in the hemiveins and central retinal vein.

Table 1
Patient demographic details.

Patient	Age (y)	Sex	Eyes analysed	Past ophthalmic history
A	50	F	R + L	–
B	29	M	R + L	–
C	27	M	R + L	–
D	53	M	R + L	–
E	30	M	R + L	–
F	22	M	R + L	–
G	29	F	L	–
H	38	M	L	–
I	48	F	R	–
J	22	M	R	–
K	63	M	L	–
L	25	M	R	–
M	69	M	R + L	–
N	23	F	R + L	–
O	23	M	R + L	–
P	26	F	R + L	–

2.5. Image preparation

Our previous technique of creating densitometry maps was utilized (Morgan et al., 2015a). In short, video recordings of venous pulsation over three cardiac cycles were imported into Adobe Photoshop CS5.1 as individual frames. A calibrated algorithm utilizing green channel densitometry measurements that reflect haemoglobin absorption timed to cardiac cycle was used to calculate a densitometry map reflecting the amplitude of pulsation at individual locations.

2.6. Quantification of tissue parameters

Quantitative data from corresponding SD-OCT images were attained following identification of venous pulsation recordings with our photoplethysmographic technique. Specifically, venous pulsation points were carefully co-localized between densitometry maps, baseline fundus photos and simultaneous confocal scanning laser ophthalmoscopy fundus imaging on the Spectralis imaging platform. This allowed interpolation of topographic and tomographic images at selected points of interest (Castro Lima et al., 2011). Characteristics of veins at high and low amplitude pulsation points, and surrounding tissue characteristics were recorded using defined histologic parameters (Tan et al., 2012; Cao et al., 2010). Measurements of these characteristics were made for noncontact recordings (i.e. no ODF applied) and then at three graded levels of applied ODF. Measurements were performed using commercial software (Universal Ruler 3.6) calibrated with the Spectralis SD-OCT generated scale bars to allow manual quantification of tissue characteristics for each eye (Fig. 1):