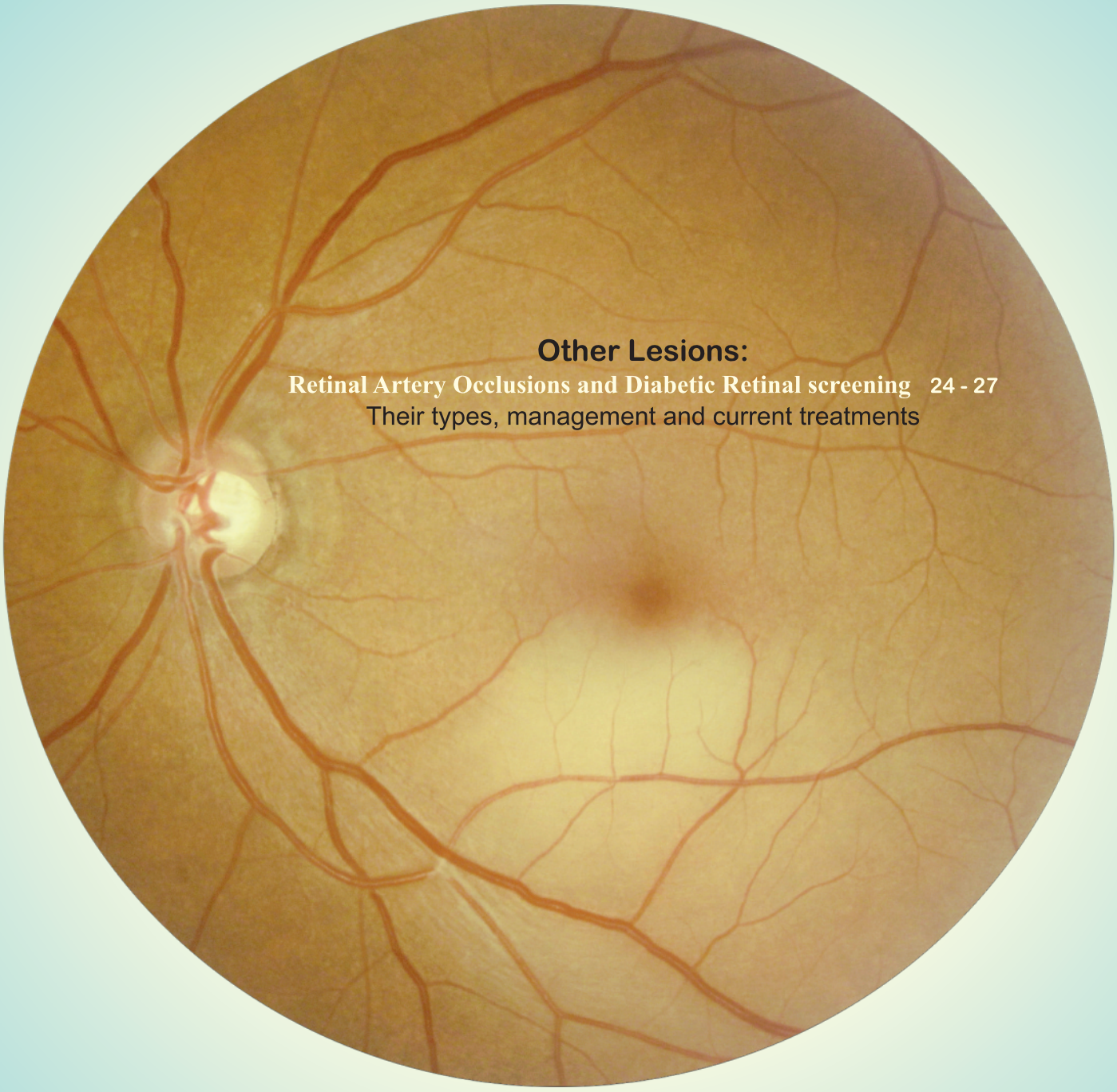
DEJ
Diabetic Eye Journal

ISSN 2055-1282
April 2017 / **Issue 8**



Other Lesions:
Retinal Artery Occlusions and Diabetic Retinal screening 24 - 27
Their types, management and current treatments

BARS poster winning entry:
Sclerochoroidal Calcification 14 - 17
And how it differs from more sinister lesions

Diabetic Eye Disease:
Obstructive Sleep Apnoea and DR 06 - 12
Does OSA contributes to progression of DR in Diabetics?

Diabetes UK:
Engaging with Black, Asian, and Minority Ethnic Communities 31 - 33
How to get involved

Kowa

sense® MEDICAL

nonmyd 8s

The ultimate digital fundus camera for diabetic eye screening programme available now from Sense Medical, Kowa's exclusive distributor in UK & Ireland.

NEW!

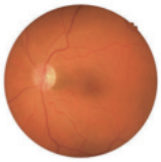
With true optical magnification for enhanced imaging, capturing highly detailed pathology of the retina, enabling you to offer the ultimate in patient care in three easy steps -
simply align, focus and shoot.

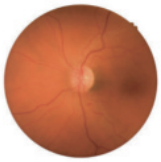
- 9 internal fixation points for your convenience
- Anterior segment photography
- Fundus autofluorescence (FAF) with low flash intensity (available on Nonmyd 8)
- Full manual control and focus for optimum image quality
- Durable, robust build quality for remote screening
- Plug and Play with third party eye screening software
- Modern compact design
- Kowa Japan manufactured optics for optimum performance
- Latest 24MP Nikon camera
- Compatible with Windows® 7, 8.1 & 10

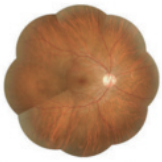
Sense Medical offer a full range of non-mydriatic cameras and comprehensive service packages. Our Engineers are fully qualified and trained by Kowa in Japan.

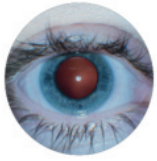
Approved by NHS (DES) Programme

Kowa's nonmyd 8/8S camera for retinal eye screening, has been approved for digital photography use by NHS diabetic eye screening (DES) Programme


Central


Disc Central


Panorama Widefield


Anterior

For more information or to arrange a trial please contact Sense Medical on 01276 479068 or email: info@sensemedical.co.uk

YOUR VISION OUR TECHNOLOGY

DiabeticEyeJournal is published and produced by BARS with support of its founders from North Central London Diabetic Eye Screening Programme.

COURSES

• **Training Courses at Retinopathy Screening Centre**, Heartlands Hospital, Birmingham
Screener Training
Introduction to DR Grading
Advanced DR Grading
OCT Interpretation for DR Graders
Clinical Leads Programme
www.retinalscreening.co.uk

• **City University of London**, London EC1V 0HB
Professional Certificate in Medical Retina: 24/04 to 26/04 2017
www.city.ac.uk/courses/cpd/medical-retina

• **Gloucestershire Retinal Education and Retinal Research Groups**
DRS Qualifications Office
Orchard Centre, 1st Floor, Gloucester Royal Hospital
Gloucester GL1 3NN
Certificate of Higher Education Diabetic Retinopathy Screening
www.drsadministrator@glos.nhs.uk

• **UCL Institute of Ophthalmology and Moorfields Eye Hospital**, London
Lecture Theatre, Institute of Ophthalmology, 11-43 Bath Street, London, EC1V 2PD
Understanding diabetic retinopathy
https://www.ucl.ac.uk/ioo/study/cpd/understanding-diebetic-retinopathy

• **Diabetes UK**
Diabetes in Healthcare
Clinical Champions
https://www.diabetes.org.uk/Professionals/Training--competencies/Courses/

• **Reading Centre,** Moorfields Eye Hospital, 162 City Road, London EC1V 2PD
Diabetic Retinopathy Screening Training
Contact enquiry: *readingcentre@moorfields.nhs.uk*

CONFERENCES

• **National DES Conference 2017**
Friday 21st of April 2017
Royal Society of Medicine
1 Wimpole Street, London W1G 0AE
www.rsm.ac.uk/events

• **2017 EASD Eye Complications Study Group**
25th to 27th May 2017
Budapest, Hungary
https://www.easdec.org/pages/

• **LESF (London Eye Screening Forum)**
14th June 2017
NCL DESP NMUH NHS Trust
At RCOphth, London
northmid.lesf@nhs.net

• **Skills in Imaging, Diagnosis and Management of Retinal Diseases Seminar**
6th to 7th July 2017
The Royal College of GPs, London
www.rcophth.ac.uk/events-and-courses

• **BARS 17th Annual Conference**
21st to 22nd September 2017
Marriot Hotel, Leeds
www.eyescreening.org.uk

• **EASD 2017 53rd Annual Meeting**
European Association for the Study of Diabetes
11th to 15th September 2017
Lisbon, Portugal
https://www.easd.org/annual-meeting/easd-2017.html

• **Practical Skills in Retinal Imaging Seminar**
25th September 2017
Royal College of Ophthalmologists, London
www.rcophth.ac.uk/events-and-courses

DiabeticEyeJournal does not endorse selected events, and list of published details was compiled for information only. Please check the details prior to their start in case of any further chsanges.

DiabeticEyeJournal

FROM THE EDITOR

Welcome to our Spring Issue. Variety in articles is the key to keeping our publication well balanced and up to date. It also reflects our varied readership, which includes screener/graders, medical photographers, ophthalmologists, optometrists, diabetes specialists just to name a few. So whatever is your background we hope there is something in this issue that will interest you.

The topic of Obstructive Sleep Apnoea has been widely discussed for some time, but not much in relation to progression of Diabetic Retinopathy in our positive group of patients. Knowing that the patient has an OSA could be a valuable piece of information to those who manage and treat Diabetic Eye Disease. Study by Abd Tahrani and Paul Dodson from Heartlands Hospital in Birmingham examines this modifiable risk factor.

Continuing our series about retinal occlusions we will this time explore Artery Occlusions. What are the risk factors, treatments and management. As it is a predictor of cardiovascular problem, what questions should be asked during the Eye Screening Examination? Find out in our article on Other Lesions by Dr Alex Wright and Professor Paul Dodson.

Most of us know that Diabetes is more prevalent in Black, Asian and Minority Ethnic Communities. Diabetes UK's innovative ways of engaging with this group of patients can provide more awarness, support and interaction where it's mostly needed. Perhaps you can get involved as a health professional and become part of the Insight Advisory Group. Dr Susan Aldridge, the editor of Diabetes Update, will share with us how in the article from Diabetes UK.

Education plays a big role in our professional career and City & Guilds in DRS was the starting and finishing point for majority of screener/graders. Read about the plans proposed by BARS to introduce a new advanced qualification, which could aid much needed career progression.

All this and more in the 8th Issue of DEJ. Happy reading!

EDITOR Iveta Olejkova NCL DESP

PUBLISHER

British Association of Retinal Screening

FRONT COVER IMAGE

BRAO supplied by South Devon DESP

PRODUCTION TEAM

Phil Gardner Chairman of BARS

Jacqueline Mansell

Nadine Rash SEL DESP

Richard Bell NUTH NHS Trust

COMMENTS and CONTRIBUTIONS

*info@diabetic**eye**journal.org*

ONLINE VERSION

*www.diabetic**eye**journal.org*

www.eyescreening.org.uk

Obstructive Sleep Apnoea and Retinopathy in Patients with Diabetes Mellitus: A New Modifiable Risk Factor?

Abd A Tahrani[1,2], **Paul M Dodson**[3,4]

[1]Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, UK
[2]Department of Diabetes and Endocrinology, Birmingham Heartlands Hospital, Birmingham, UK
[3]Heart of England Retinal Screening Centre, Heart of England NHS Foundation Trust, Birmingham, UK
[4]School of Life and Health Sciences, Aston University, Birmingham, UK

Corresponding author:

Dr. Abd A Tahrani
Department of Diabetes, Birmingham Heartlands Hospital
Birmingham B9 5SS
tel: 07801549960, *Abd.tahrani@nhs.net*

1. Introduction

Diabetic retinopathy (DR) is common; it affects about half the patients with diabetes and is a leading cause of blindness in the Western world and results in significant morbidity and economic burden.[1;2] DR has multiple risk factors including older age, hyperglycaemia, hypertension, diabetes duration, dyslipidaemia and genetic factors.[1;3] Hyperglycaemia, in conjunction with other risk factors such as hypertension and hyperlipidaemia, result in increased inflammation, oxidative stress, and the activation of multiple pathways (such the polyol pathway, advanced glycation end-products, protein kinase C.etc). These lead to microvascular changes resulting in increased vascular permeability (leading to macular oedema) or ischaemia (leading to neovascularisation due increased vascular endothelial growth factor (VEGF)).[1;4] Despite improvements in the control of hyperglycaemia, hypertension and hyperlipidaemia, DR remains very common,[5] and a significant proportion of DR progresses to sight-threatening diabetic retinopathy (STDR).[1]Hence, it is important to further our understanding of the pathogenesis of DR in order to aid the screening strategy and identify new treatment targets to develop new treatment.

In this brief article, we will review the relationship between DR and obstructive sleep apnoea (OSA), a potentially newly recognised treatable risk factor for DR.

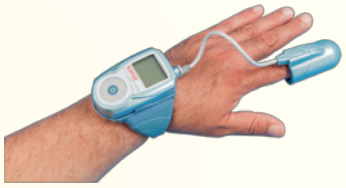
2. OSA overview

OSA is a common medical disorder that affects 17–26% of men and 9–28% of women.[6] It is characterised by upper airway instability during sleep resulting in recurrent episodes of complete or partial upper airway obstruction leading to recurrent episodes of either complete (apnoea) or partial (hypopnea) cessation of airflow.[7] These apnoea's and hypopneas are usually associated with recurrent oxygen desaturations, and cyclical changes in intra-thoracic pressure (due to the patient breathing against a blocked airway), blood pressure (BP), heart rate and sympathetic activity.[7] The apnoea/hypopnea episodes are usually terminated by micro-arousals from sleep (due to attempts to open the obstructed airways) which result in the upper airway muscles to regain its power that was lost during deep sleep and hence re-opening the blocked airway. These micro-arousals result in sleep fragmentation disrupting the sleep architecture and causing the reduction in slow wave sleep and rapid eye movement sleep which in apart contribute to the excessive daytime sleepiness observed in patients with OSA.[7]

The presence of OSA is defined based on the AHI (Apnoea hypopnea index), which is the average number apnoea and hypopnea episodes/hour during sleep. An AHI ≥ 5 events/hour is consistent with the diagnosis of OSA,[7;8] while AHI cut offs of 15 and 30 indicate moderate and severe OSA.[9] Another commonly used OSA metric is the oxygen desaturation index (ODI), which is the average number of 4% oxygen desaturations per hour of sleep; similar cut offs to AHI are used to define OSA severity based on ODI.

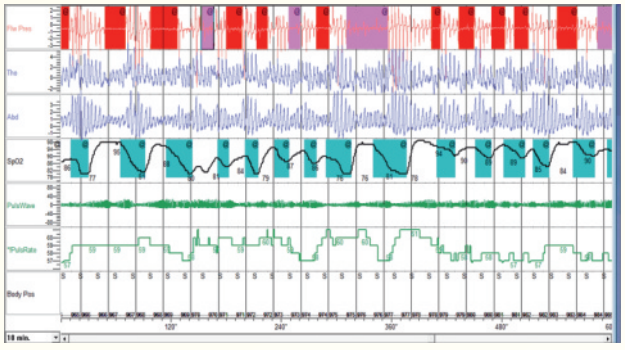
The diagnosis of OSA can be made using several methods. The gold standard is polysomnography that typically includes the recording of 12 channels such as EEG, electrooculogram (EOG), electromyogram (EMG), oro-nasal airflow, chest wall effort, abdominal effort, body position, snore microphone, ECG, and oxygen saturation.[7] The main disadvantages of polysomnography are that it is time consuming, resourceful, expensive and requires a hospital stay overnight (which might result in disturbed sleep due to the first night effect). Portable home-based respiratory devices are another alternative that is widely used in clinical practice and research (***figure 1***).[7] These devices are usually small, portable and record enough signals (typical oxygen saturations, heart rate, chest and/or abdominal movements and oro-nasal airflow) to make the diagnosis of OSA. An example of trace from such devices can be found in ***figure 2***. The main advantages are that they are less resourceful and the patients will sleep in their own environment but they are associated with higher failure/loss of lead rate compared to polysomnography.[7] Pulse oximetry has been used to diagnose OSA based on measuring the oxygen saturations; however, it cannot differentiate between obstructive and central apnoea's and it has a wide range of sensitivity (31-98%) and specificity (41-100%).[7] The American Academy of Sleep Medicine (AASM) recommends to use a level III device (such as the portable respiratory devices described above) as a minimum.[7]

figure 1: Examples of available portable devices that can be given to the patients to operate and home which allows the diagnosis of sleep apnoea without the need for hospital admission.



The devices from left to right: WatchPAT from Itamar Medical, ApneaLink Air from Resmed and Alice PDX from Philips Respironics.

figure 2: AN example of the trace that can be obtained by portable cardiorespiratory device for home-based sleep apnoea diagnosis. Apnoea's (red), hypopneas (pink) and desaturation's (green) in a patient with OSA and Type 2 diabetes. Note the presence of thoracic and abdominal movements indicating the presence of obstructive rather than central sleep apnoea and the patient in the supine position. This trace represents 10minutes only.



Snoring is the most common symptom of OSA occurring in 95% of patients.[7] Snoring, however, has a poor predictive value due to the high prevalence of snorers many of whom don't have OSA.[7] Nonetheless, lack of snoring almost rules out OSA since only 6% of OSA patients (or their partners) so not report snoring.[7] Witnessed apnoea's are another important symptom that are usually reported by the partner. However, witnessed apnoea's do not correlate with disease severity and up to 6% of the "normal" population could have witnessed apnoea's without OSA.[7]

Excessive daytime sleepiness (EDS) is associated with OSA, but EDS is also associated with depression and the metabolic syndrome even in the absence of OSA.[7;10] Other symptoms include choking (which represent a proper rather than a micro arousal), insomnia, nocturia, sweating, fatigue, morning headache, erectile dysfunction and autonomic symptoms.[7;11] Many of these symptoms are also common in patients with T2D and can result from hyper and/or hypo glycaemia; hence, OSA should only be considered as a cause of such symptoms after ruling out hypo or hyper glycaemia as treatment of OSA per se can improve these symptoms.

Obesity is a common and major risk factor for OSA but not all patients with OSA are obese.[12] In the Wisconsin sleep study, each increase in BMI by one standard deviation, resulted in a 4-fold increase in OSA prevalence.[13] In addition, weight gain results in the development of OSA or worsening of pre-existing OSA.[14;15] Obesity can contribute to the development or worsening of OSA by altering normal upper airway mechanics during sleep. This is by increasing Para pharyngeal fat deposition which result in a smaller upper airway and by altering the neural compensatory mechanisms that maintain airway patency resulting in more collapsible upper airways.[16] Obesity also reduces the functional residual capacity in the lungs and affect the chemo sensitivity to O2 and CO2, resulting in reduction in ventilator drive and making the upper airways more prone to collapse.[16] Other risk factors of OSA include older age, male gender, current smoking, excess alcohol intake and genetic factors.[6;12] OSA risk factors are summarised in ***table 1***.

table 1: OSA risk factors

Obesity	Alcohol	Nasal congestion
Age	Smoking	Enlarged tonsils
Being male	Family history	Large neck circumference
Ethnicity (Afro Caribbean)	Endocrine disorders (Diabetes, hypothyroidism, acromegaly)	Recessed chin

Weight loss (either via life style intervention, pharmacotherapy, or bariatric surgery) and continuous positive airway pressure (CPAP) are the mainstay treatments of OSA.[9] Mandibular advancement devices can also be used in patients with mild OSA or those intolerant to CPAP.

3. OSA and Diabetes Mellitus

As obesity is a common risk factor for OSA and T2D, it is not surprising that OSA is very common in patients with T2D.[17] The prevalence of OSA in patients with T2D varies from 8.5% to 85%.[17-23] This wide range reflects differences in the population examined (e.g. primary vs. secondary care, ethnicities, gender, and obesity), the methods used to diagnose OSA (patients' records, questionnaires, oximetry, portable multi-channel cardiovascular monitoring devices or “gold standard” polysomnography) and the OSA definitions used (AHI vs. ODI, different cut-offs) [9;17]. Due to this high prevalence, the International Diabetes Federation (IDF) recommended routine screening for OSA in patients with T2D in 2008; [24] but this is still not being performed in real clinical practice.[25]

3.1. OSA and dysglycaemia

In patients with T2D, OSA is associated with increased insulin resistance and impaired β-cell function.[26-30] Hence, it is not surprising that OSA is associated with hyperglycaemia and worse glycaemic control in patients with T2D despite adjustments for confounding factors in cross-sectional studies.[31-34] The impact of OSA on HbA1c varied 0.7 to 3.69% due to differences in OSA severity and the populations examined.[35;36] It seems that the apnoea and hypopnea episodes that occur during Rapid Eye Movement (REM) sleep have greater impact on HbA1c compared to apnoea hypopnea episodes that occurred at other sleep stages.[37] However, the impact of CPAP treatment on glycaemic control and HbA1c in patients with T2D remains controversial with some studies showing benefits and others showing no impact.

3.2. OSA and Cardiovascular disease

Many studies have shown that the known risk factors for cardiovascular disease are affected by OSA. OSA is associated with hypertension and non-dipping BP.[9;38-40] Mild and moderate OSA increased the risk of incident nocturnal non-dipping BP by 3-fold and 4-fold over 7 years compared to those without OSA.[41] A large, cross-sectional study showed that OSA was more prevalent in T2D patients with awake BP ≥135/85 mmHg or asleep BP ≥120/70 mmHg, compared with lower BP.[42]

A meta-analysis of 64 studies showed that OSA was associated with adverse lipid profile such as higher total cholesterol, higher LDL, higher triglycerides and lower HDL, while AHI correlated positively with triglycerides and negatively with HDL levels only.[43] Several studies have also shown that OSA was associated with atherosclerosis and hence cardiovascular disease [44;45] such as an increased risk of acute myocardial infarction overnight.[46] Prospective observational studies (3–10 years of follow-up) showed that OSA predicts the development of incident cardiovascular disease.[47-52]

The Look AHEAD study of patients with T2D has shown as association between the AHI and self-reported history of stroke (adjusted OR 2.57, 95% CI 1.03-6.42), but not with coronary artery disease in a cross-sectional analysis.[53] In another study of 132 consecutive patients with T2D and normal exercise echocardiography at baseline after a median of 4.9 years follow up, OSA was associated with an increased risk of incident coronary artery disease (adjusted HR 2.2, 95% CI 1.2-3.9, p = 0.01) and heart failure (adjusted HR 3.5, 95% CI 1.4-9.0, p <0.01).[54]

4. OSA and diabetic retinopathy

As discussed above, OSA is associated with hyperglycaemia, hypertension, hyperlipidaemia, obesity and cardiovascular disease, all of which are risk factors for DR. In addition, our group and others have shown that OSA is associated with increased oxidative stress, inflammation, protein kinase C activation, increase advanced glycation end-product, and many other molecular pathways that are involved in the pathogenesis of DR.[9;17;39;55;56] Hence it is not surprising that many investigators have hypothesised that OSA might be associated with DR. In addition, retinal abnormalities have been described in patients with OSA who do not have diabetes, these include: retinal arteriolar narrowing and venular widening or branch retinal vein occlusion.[5;58]

4.1 OSA and DR in patients with T2D

Several studies examine the relationship between OSA and DR in patients with T2D, but all these studies but one were cross-sectional in nature which means that they describe associations and causation cannot be proven. Indeed, the studies vary considerably in terms of OSA and DR assessments and the populations included, which makes it difficult to confirm a consistent picture. In addition, while some studies focused on DR in general others have focused on more advanced disease such as pre-proliferative or proliferative DR or sight threatening retinopathy (STR).

In a study of 195 patients with clinically significant diabetes macular oedema, 54% had an oxygen desaturation index ≥ 10, and 31% had an AHI ≥ 15 (based on portable home sleep study). This suggests a high prevalence of OSA in patients with macular oedema; however, the relationship between the OSA severity and macular thickness (based on OCT) was not significant.[59]

In a large multi-centre cross-sectional study that included 880 hospitalised patients with T2D from 12 hospitals in China; OSA was assessed using overnight portable monitor and DR was assessed using the medical records. The lowest nocturnal oxygen saturation was associated with proliferative DR but this association was lost following adjustment for multiple confounders.[60] This study had limitations of population selection bias and unreliable method of assessing retinal status.

In a recent small cross-sectional study from Tunisia, 20 patients with T2D and OSA were age and diabetes duration matched to 40 patients with T2D but without OSA.[61] The assessment of DR in this study was based on ophthalmic examination.[61] The study participants had mean age of 59 years, diabetes duration of 10 years and poor glycaemic control with average HbA1c of 10%.[61] The prevalence of DR was greater in the OSA group vs. those without OSA (55% vs. 15%, P=0.03).[61] Non-proliferative DR (35% vs. 7.5%, p= 0.03) and proliferative DR (20% vs. 7.5%, p=0.042) were more common in the OSA group vs no OSA.[61] In addition, macular oedema was also more common in patients with OSA compared to those without (20% vs. 5%, p=0.04).[61] However, this study has limitations of a small number of patients and poor glycaemic control.

In a larger cross-sectional study of a 136 patients with T2D who underwent a sleep test and DR status determined by indirect ophthalmoscope or retinal photographs; 37 patients had DR and following adjusting for confounding variables, nadir nocturnal oxygen saturation was associated with the presence of DR.[62] Again this study included a small number of patients and is likely to have a selection bias.

Studies of more advanced disease have been undertaken in Japanese patients undergoing vitreous surgery for advanced diabetic retinopathy (DR), lower oxygen saturations were associated with proliferative DR after adjustment for age, HbA1c and hypertension.[63] The investigators found that the oxygen desaturation index was associated with iris or angle neovascularisation in patients with proliferative DR.[64] In a further study by the same group included 124 consecutive patients who had polysomnography [65] and OCT measurement of the peripapillary retinal nerve fibre layer (RNFL), foveal thickness, and total macular volume. The AHI correlated significantly and negatively with the nasal RNFL thickness (right eye, r = -0.31, p = 0.0004; left eye, r = -0.39, p < 0.0001), while there was no relationship between the AHI and the foveal thickness and total macular volume.[65]

In a study from primary and secondary care in the UK, 198 men had retinal photographs and overnight oximetry.[66] The prevalence of OSA in this population was 24%.[66] Multiple regression analysis showed that OSA was associated with DR and maculopathy after adjusting for age, BMI, diabetes duration and hypertension in men with T2D.[66]

4.2. OSA treatment and DR and the impact of OSA on DR treatment in patients with Type 2 diabetes

In an uncontrolled, hypothesis generating study, CPAP treatment for 6 months was associated with improvement in visual acuity without an impact on macular oedema/thickness. This suggests improved functionality rather than actual change in the oedema.[67]

One interesting study in diabetic macular oedema and age-related macular degeneration showed that a poor response to anti-VEGF therapy with bevacizumab (Avastin) was associated with higher prevalence of OSA;[68] whether treating OSA would improve the response to treatment is currently unknown.

Similar to the previous studies, a UK study has reaffirmed that patients with OSA were 3-4 times more likely to have sight threatening DR, pre-proliferative/proliferative DR or maculopathy after adjustment for a wide range of confounders including gender and ethnicity.[69] In addition, in a longitudinal follow up of this study patients with OSA were more likely to develop pre-proliferative/proliferative DR (adjusted OR 6.6, 95% CI, 1.2-35.1, p=0.03); and patients who were compliant with CPAP treatment had lower progression to pre-proliferative/proliferative DR compared to non-complaint patients.[69] These important observations on the long term effects of OSA and the impact of OSA treatment on DR and its treatment are still unclear.

4.3. OSA and DR in patients with T1D

Data in patients with T1D are very limited; mainly because the relationship between OSA and T2D attracted much more attention as obesity is a common risk factor for both conditions.

In a cross-sectional study of 67 patients with T1D (BMI of 25.8 ± 4.7 kg/m^2), OSA (diagnosed by polysomnography and defined as AHI > 10) was common (46%) with 19% of patients having severe OSA (AHI > 30/h). Patients with T1D with and without OSA had similar age, sex, BMI, HbA1c and the Epworth sleepiness scale (as a marker of excessive daytime sleepiness). OSA was associated with DR (based on medical records) following adjustment for confounders (OR 4.54; 95% CI, 1.09-18.82; P=0.04).[70] It is important to note that the OSA prevalence was high in this study population despite that the study population was not obese, which suggests other possible mechanisms for OSA other than obesity; this is supported further by the fact that there was no difference in BMI between those who had OSA and those who did not. In another small study of 37 patients in which OSA diagnosis was based on oximetry, DR was more common in patients with OSA (73% vs. 23%) but there was no adjustment for DR risk factors in this analysis.[71]

Summary and conclusions

OSA is very common in patients with T2D and more recent studies suggest that OSA is also common in patients with T1D. Several studies in patients with T2D and T1D showed a high prevalence of OSA in patients with DR (including maculopathy), but whether OSA causes DR/maculopathy or result in worsening DR remains unclear. Cross-sectional studies have shown conflicting results regarding the association between OSA and DR but the consensus is that OSA was associated with more advanced DR (such as pre-proliferative and proliferative DR and maculopathy). The pilot study that showed improved visual acuity in patients with diabetic maculopathy following CPAP might also suggest causation if proven in ongoing RCT.

Taking into consideration that studies in non-diabetic patients with OSA did not show retinal changes similar to DR in patients with OSA and diabetes; it seems reasonable to postulate that the presence of hyperglycaemia and diabetes is essential for the development of DR but OSA might worsen the DR resulting into a quicker progression towards STDR. Hence, studies that examined DR without focussing on its severity found conflicting results as having OSA may not result in the development of background DR but might quicken the progression to more advanced disease. Future carefully designed RCTs should answer the crucial question of the relationship between OSA and DR and the impact of OSA on DR progression.

However, due to the proven high prevalence of OSA in patients with DR and STDR it is imperative that these patients are screened for OSA, which is also associated with several comorbidities other than DR, many of which might respond to treatment with CPAP even if the impact of CPAP on DR is unclear as yet. How to screen for OSA is a matter of resources and expertise but simple questions regarding snoring, tiredness, sleepiness, witness apnoea's and nocturia might identify many individuals. There are several validated questionnaires that can also be used and in more advanced settings, portable devices can be used to perform home-based sleep studies.

We suspect that the recognition and importance of OSA as a clinical entity need to be highlighted to clinicians and staff involved in the ophthalmological care of patients with DR.

Reference List

(1) Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. The Lancet 2010 July 10;376(9735):124-36.

(2) Congdon NG, Friedman DS, Lietman T. Important Causes of Visual Impairment in the World Today. JAMA: The Journal of the American Medical Association 2003 October 15;290(15):2057-60.

(3) Abhary S, Hewitt AW, Burdon KP, Craig JE. A systematic meta-analysis of genetic association studies for diabetic retinopathy. Diabetes 2009 July 8.

(4) Wirostko B, Wong TY, Simo R. Vascular endothelial growth factor and diabetic complications. Prog Retin Eye Res 2008 November;27(6):608-21.

(5) Prevent blindness America. Vision Problems in the US. *http://www.visionproblemsus.org/introduction.html . 2012. 2017.* Ref Type: Online Source

(6) Young T, Peppard PE, Gottlieb DJ. Epidemiology of Obstructive Sleep Apnea: A Population Health Perspective. Am J Respir Crit Care Med 2002 May 1;165(9):1217-39.

(7) McNicholas WT. Diagnosis of Obstructive Sleep Apnea in Adults. Proceedings of the American Thoracic Society 2008 February 15;5(2):154-60.

(8) Epstein LJ, Kristo D, Strollo PJ, Jr., Friedman N, Malhotra A, Patil SP et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med 2009 June 15;5(3):263-76.

(9) Tahrani AA. Diabetes and sleep apnea. International Textbook of Diabetes Mellitus. John Wiley & Sons, Ltd; 2015. p. 316-36.

(10) Bixler EO, Vgontzas AN, Lin HM, Calhoun SL, Vela-Bueno A, Kales A. Excessive Daytime Sleepiness in a General Population Sample: The Role of Sleep Apnea, Age, Obesity, Diabetes, and Depression. The Journal of Clinical Endocrinology & Metabolism 2005 August 1;90(8):4510-5.

(11) Martin SA, Atlantis E, Lange K, Taylor AW, O'Loughlin P, Wittert GA et al. Predictors of Sexual Dysfunction Incidence and Remission in Men. J Sex Med 2014 May 1;11(5):1136-47.

(12) Punjabi NM. The Epidemiology of Adult Obstructive Sleep Apnea. Proc Am Thorac Soc 2008 February 15;5(2):136-43.

(13) Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The Occurrence of Sleep-Disordered Breathing among Middle-Aged Adults. N Engl J Med 1993 April 29;328(17):1230-5.

(14) Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal Study of Moderate Weight Change and Sleep-Disordered Breathing. JAMA 2000 December 20;284(23):3015-21.

(15) Newman AB, Foster G, Givelber R, Nieto FJ, Redline S, Young T. Progression and Regression of Sleep-Disordered Breathing With Changes in Weight: The Sleep Heart Health Study. Arch Intern Med 2005 November 14;165(20):2408-13.

(16) Fogel RB, Malhotra A, White DP. Sleep -À 2: Pathophysiology of obstructive sleep apnoea/hypopnoea syndrome. Thorax 2004 February 1;59(2):159-63.

(17) Tahrani AA, Ali A, Stevens MJ. Obstructive sleep apnoea and diabetes: an update. Current Opinion in Pulmonary Medicine 2013;19(6):631-8.

(18) West SD, Nicoll DJ, Stradling JR. Prevalence of obstructive sleep apnoea in men with type 2 diabetes. Thorax 2006 November 1;61(11):945-50.

(19) Foster GD, Sanders MH, Millman R, Zammit G, Borradaile KE, Newman AB et al. Obstructive Sleep Apnea Among Obese Patients With Type 2 Diabetes. Diabetes Care 2009 June;32(6):1017-9.

(20) Lam DCL, Lui MMS, Lam JCM, Ong LHY, Lam KSL, Ip MSM. Prevalence and Recognition of Obstructive Sleep Apnea in Chinese Patients With Type 2 Diabetes Mellitus. Chest 2010 November 1;138(5):1101-7.

(21) Tahrani AA, Ali A, Raymond NT, Begum S, Dubb K, Mughal S et al. Obstructive Sleep Apnea and Diabetic Neuropathy: a Novel Association in Patients with Type 2 Diabetes. Am J Respir Crit Care Med 2012 June 21;186(5):434-41.

(22) Heffner JE, Rozenfeld Y, Kai M, Stephens EA, Brown LK. Prevalence of Diagnosed Sleep Apnea Among Patients With Type 2 Diabetes in Primary CareSleep Apnea in Diabetes Mellitus. Chest 2012 June 1;141(6):1414-21.

(23) Lecomte P, Criniere L, Fagot-Campagna A, Druet C, Fuhrman C. Underdiagnosis of obstructive sleep apnoea syndrome in patients with type 2 diabetes in France: ENTRED 2007. Diabetes Metab 2013 April;39(2):139-47.

(24) Shaw JE, Punjabi NM, Wilding JP, Alberti KG, Zimmet PZ. Sleep-disordered breathing and type 2 diabetes: A report from the International Diabetes Federation Taskforce on Epidemiology and Prevention. Diabetes Res Clin Pract 2008 July;81(1):2-12.

(25) Seetho IW, OΓÇÖBrien SV, Hardy KJ, Wilding JP. Obstructive sleep apnoea in diabetes-assessment and awareness. British Journal of Diabetes & Vascular Disease 2014;14(3):105-8.

(26) Hermans MP, Ahn SA, Rousseau MF. Cardiometabolic phenotype and UKPDS risk in male type 2 diabetic patients with obstructive sleep apnoea. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 2009 January;3(1):50-4.

(27) Hermans MP, Ahn SA, Mahadeb YP, Rousseau MF. Sleep apnoea syndrome and 10-year cardiovascular risk in females with type 2 diabetes: relationship with insulin secretion and insulin resistance. Diabetes Metab Res Rev 2013 March 1;29(3):227-34.

(28) Chen L, Pei JH, Chen HM. Effects of continuous positive airway pressure treatment on glycaemic control and insulin sensitivity in patients with obstructive sleep apnoea and type 2 diabetes: a meta-analysis. Arch Med Sci 2014 August 29;10(4):637-42.

(29) Harsch IA, Schahin SP, Br++ckner K, Radespiel-Tr+Âger M, Fuchs FS, Hahn EG et al. The effect of continuous positive airway pressure treatment on insulin sensitivity in patients with obstructive sleep apnoea syndrome and type 2 diabetes. Respiration 2004;71(3):252-9.

(30) Brooks BELI, Cistulli PA, Borkman MARK, Ross GLYN, McGhee S, Grunstein RR et al. Obstructive sleep apnea in obese noninsulin-dependent diabetic patients: effect of continuous positive airway pressure treatment on insulin responsiveness. The Journal of Clinical Endocrinology & Metabolism 1994;79(6):1681-5.

(31) Papanas N, Steiropoulos P, Nena E, Tzouvelekis A, Maltezos E, Trakada G et al. HbA1c is associated with severity of obstructive sleep apnea hypopnea syndrome in nondiabetic men. Vasc Health Risk Manag 2009;5:751-6. Epub;%2009 Sep 18.:751-6.

(32) Pillai A, Warren G, Gunathilake W, Idris I. Effects of Sleep Apnea Severity on Glycemic Control in Patients with Type 2 Diabetes Prior to Continuous Positive Airway Pressure Treatment. Diabetes Technology & Therapeutics 2011 June 29;13(9):945-9.

(33) Aronsohn RS, Whitmore H, Van Cauter E, Tasali E. Impact of Untreated Obstructive Sleep Apnea on Glucose Control in Type 2 Diabetes. Am J Respir Crit Care Med 2010 March 1;181(5):507-13.

(34) Kent BD, Grote L, Ryan S, P+®pin JL, Bonsignore MR, Tkacova R et al. Diabetes mellitus prevalence and control in sleep-disordered breathing: The european sleep apnea cohort (esada) study. Chest 2014 October 1;146(4):982-90.

(35) Einhorn D, Stewart DA, Erman MK, Gordon N, Philis-Tsimikas A, Casal E. Prevalence of sleep apnea in a population of adults with type 2 diabetes mellitus. Endocr Pract 2007 July;13(4):355-62.

(36) Tamura A, Kawano Y, Watanabe T, Kadota J. Obstructive sleep apnea increases hemoglobin A1c levels regardless of glucose tolerance status. Sleep Medicine 2012 September;13(8):1050-5.

(37) Grimaldi D, Beccuti G, Touma C, Van Cauter E, Mokhlesi B. Association of obstructive sleep apnea in REM sleep with reduced glycemic control in type 2 diabetes: Therapeutic implications. Diabetes Care 2014;37(2):355-63.

(38) Tahrani AA, Ali A, Stevens MJ. Obstructive sleep apnoea and diabetes: an update. Current Opinion in Pulmonary Medicine 2013;19(6).

(39) Tahrani AA, Ali A. Obstructive Sleep Apnoea and Type 2 Diabetes. European Endocrinology 2014;10(1):43-50.

(40) Peppard PE, Young T, Palta M, Skatrud J. Prospective Study of the Association between Sleep-Disordered Breathing and Hypertension. N Engl J Med 2000 May 11;342(19):1378-84.

(41) Hla KM, Young T, Finn L, Peppard PE, Szklo-Coxe M, Stubbs M. Longitudinal association of sleep-disordered breathing and nondipping of nocturnal blood pressure in the Wisconsin Sleep Cohort Study. Sleep 2008 June 1;31(6):795-800.

(42) Ayala DE, Moyá A, Crespo JJ, Castiñeira C, Domínguez-Sardiña M, Gomara S et al. Circadian Pattern of Ambulatory Blood Pressure in Hypertensive Patients With and Without Type 2 Diabetes. Chronobiol Int 2012 October 25;30(1-2):99-115.

(43) Nadeem R, Singh M, Nida M, Waheed I, Khan A, Ahmed S et al. Effect of Obstructive Sleep Apnea Hypopnea Syndrome on Lipid Profile: A Meta-Regression Analysis. J Clin Sleep Med 2014 May 15;10(5):475-89.

(44) Turmel J, Sériès F, Boulet LP, Poirier P, Tardif JC, Rodés-Cabeau J et al. Relationship between atherosclerosis and the sleep apnea syndrome: An intravascular ultrasound study. Int J Cardiol 2009 February 20;132(2):203-9.

(45) Kent BD, Garvey JF, Ryan S, Nolan G, Dodd JD, McNicholas WT. Severity of obstructive sleep apnoea predicts coronary artery plaque burden: a coronary CT angiography study. Eur Respir J 2013 March 7;42(5):1263-70.

(46) Sert Kuniyoshi FH, Garcia-Touchard A, Gami AS, Romero-Corral A, van der Walt C, Pusalavidyasagar S et al. Day−Night Variation of Acute Myocardial Infarction in Obstructive Sleep Apnea. J Am Coll Cardiol 2008 July 29;52(5):343-6.

(47) Peker Y, Hedner J, Norum J, Kraiczi H, Carlson J. Increased Incidence of Cardiovascular Disease in Middle-aged Men with Obstructive Sleep Apnea: A 7-Year Follow-up. Am J Respir Crit Care Med 2002 July 15;166(2):159-65.

(48) Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. The Lancet 2005;365(9464):1046-53.

(49) Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive Sleep Apnea as a Risk Factor for Stroke and Death. New England Journal of Medicine 2005 November 10;353(19):2034-41.

(50) Ou Q, Chen YC, Zhuo SQ, Tian XT, He CH, Lu XL et al. Continuous Positive Airway Pressure Treatment Reduces Mortality in Elderly Patients with Moderate to Severe Obstructive Severe Sleep Apnea: A Cohort Study. PLoS ONE 2015 June 11;10(6):e0127775.

(51) Molnar MZ, Mucsi I, Novak M, Szabo Z, Freire AX, Huch KM et al. Association of incident obstructive sleep apnoea with outcomes in a large cohort of US veterans. Thorax 2015 June 2.

(52) Gottlieb DJ, Yenokyan G, Newman AB, O'Connor GT, Punjabi NM, Quan SF et al. Prospective Study of Obstructive Sleep Apnea and Incident Coronary Heart Disease and Heart Failure: The Sleep Heart Health Study. circulation 2010 July 27;122(4):352-60.

(53) Rice TB, Foster GD, Sanders MH, Unruh M, Reboussin D, Kuna ST et al. The relationship between obstructive sleep apnea and self-reported stroke or coronary heart disease in overweight and obese adults with type 2 diabetes mellitus. Sleep 2012 September;35(9):1293-8.

(54) Seicean S, Strohl KP, Seicean A, Gibby C, Marwick TH. Sleep Disordered Breathing as a Risk of Cardiac Events in Subjects With Diabetes Mellitus and Normal Exercise Echocardiographic Findings. Am J Cardiol 2013 April 15;111(8):1214-20.

(55) Tahrani A, Ali A. Oxidative Stress, Inflammation and Endothelial Dysfunction: The Link Between Obstructive Sleep Apnoea and Vascular Disease in Type 2 Diabetes. In: Obrosova I, Stevens MJ, Yorek MA, editors. Studies in Diabetes. Springer New York; 2014. p. 149-71.

(56) Altaf QaA, Ali A, Piya MK, Raymond NT, Tahrani AA. The relationship between obstructive sleep apnea and intra-epidermal nerve fiber density, PARP activation and foot ulceration in patients with type 2 diabetes. Journal of Diabetes and its Complications 2016 September;30(7):1315-20.

(57) Lin G-M, Redline S, Klein R, Colangelo LA, Cotch MF, Wong TY et al. Sex−Specific Association of Obstructive Sleep Apnea With Retinal Microvascular Signs: The Multi-Ethnic Study of Atherosclerosis. J Am Heart Assoc 2016 July 22;5(7):e003598.

(58) Kwon HJ, Kang EC, Lee J, Han J, Song WK. Obstructive Sleep Apnea in Patients with Branch Retinal Vein Occlusion: A Preliminary Study. Korean J Ophthalmol 2016 April 25;30(2):121-6.

(59) Mason RH, West SD, Kiire CA, Groves DC, Lipinski HJ, Jaycock A et al. HIGH PREVALENCE OF SLEEP DISORDERED BREATHING IN PATIENTS WITH DIABETIC MACULAR EDEMA. RETINA 2012;32(9).

(60) Zhang R, Zhang P, Zhao F, Han X, Ji L. Association of Diabetic Microvascular Complications and Parameters of Obstructive Sleep Apnea in Patients with Type 2 Diabetes. Diabetes Technology & Therapeutics 2016 March 31;18(7):415-20.

(61) Baba A, Zbiba W, Bouayed E, Korbi M, Ghrairi H. [Obstructive sleep apnea syndrome. Is it a risk factor for diabetic retinopathy?]. J Fr Ophtalmol 2016 February;39(2):139-42.

(62) Nishimura A, Kasai T, Tamura H, Yamato A, Yasuda D, Nagasawa K et al. Relationship between sleep disordered breathing and diabetic retinopathy: Analysis of 136 patients with diabetes. Diabetes Research and Clinical Practice109(2):306-11.

(63) Shiba T, Maeno T, Saishin Y, Hori Y, Takahashi M. Nocturnal Intermittent Serious Hypoxia and Reoxygenation in Proliferative Diabetic Retinopathy Cases. Am J Ophthalmol 2010 June 1;149(6):959-63.

(64) Shiba T, Takahashi M, Hori Y, Saishin Y, Sato Y, Maeno T. Relationship Between Sleep-Disordered Breathing and Iris and/or Angle Neovascularization in Proliferative Diabetic Retinopathy Cases. Am J Ophthalmol151(4):604-9.

(65) Shiba T, Takahashi M, Sato Y, Onoda Y, Hori Y, Sugiyama T et al. Relationship between Severity of Obstructive Sleep Apnea Syndrome and Retinal Nerve Fiber Layer Thickness. Am J Ophthalmol157(6):1202-8.

(66) West SD, Groves DC, Lipinski HJ, Nicoll DJ, Mason RH, Scanlon PH et al. The prevalence of retinopathy in men with Type 2 diabetes and obstructive sleep apnoea. Diabet Med 2010 April;27(4):423-30.

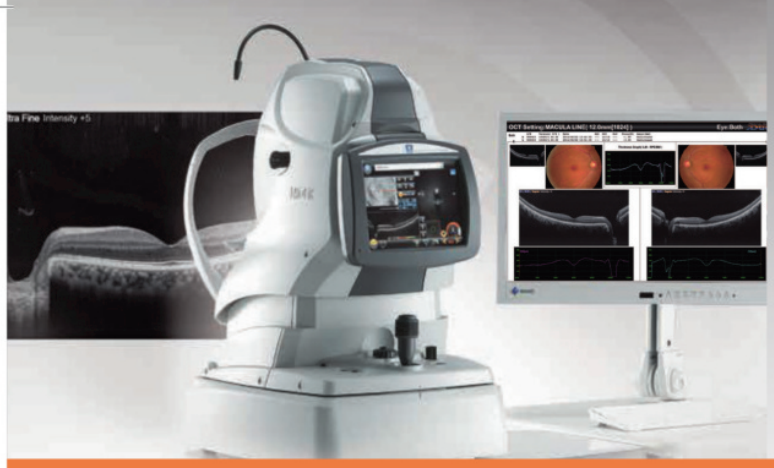
(67) Mason RH, Kiire CA, Groves DC, Lipinski HJ, Jaycock A, Winter BC et al. Visual Improvement following Continuous Positive Airway Pressure Therapy in Diabetic Subjects with Clinically Significant Macular Oedema and Obstructive Sleep Apnoea: Proof of Principle Study. Respiration 2012;84(4):275-82.

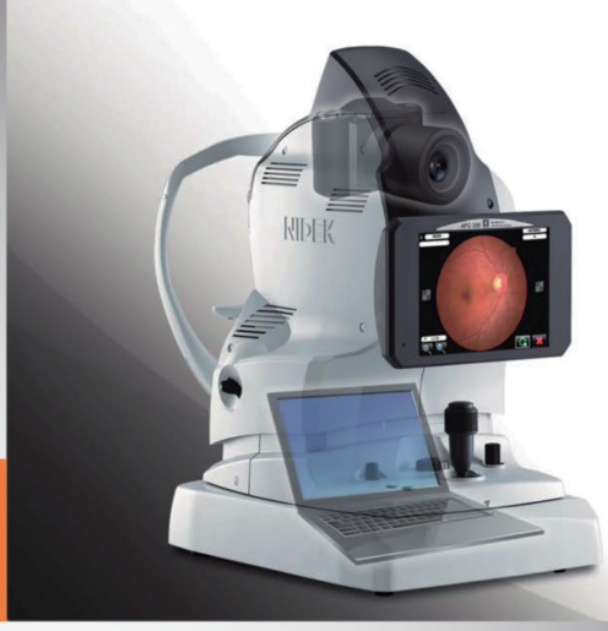
(68) Nesmith BL, Ihnen M, Schaal S. POOR RESPONDERS TO BEVACIZUMAB PHARMACOTHERAPY IN AGE-RELATED MACULAR DEGENERATION AND IN DIABETIC MACULAR EDEMA DEMONSTRATE INCREASED RISK FOR OBSTRUCTIVE SLEEP APNEA. RETINA 2014;34(12):2423-30.

(69) Tahrani AA, Dodson P, Ali A, Altaf Q, Wharton H, Raymond NT et al. Obstructive sleep apnoea is associated with sight threatening retinopathy and predicts the development of preproliferative and proliferative retinopathy in patients with type 2 diabetes: a longitudinal analysis. Eur J Ophthalmol 2013;23(3):449.

(70) Manin G, Pons A, Baltzinger P, Moreau F, Iamandi C, Wilhelm JM et al. Obstructive sleep apnoea in people with Type-á1 diabetes: prevalence and association with micro- and macrovascular complications. Diabet Med 2015 January 1;32(1):90-6.

(71) Borel AL, Benhamou PY, Baguet JP, Halimi S, Levy P, Mallion JM et al. High prevalence of obstructive sleep apnoea syndrome in a Type-á1 diabetic adult population: a pilot study. Diabet Med 2010 November 1;27(11):1328-9.





Imaging technology designed for your patients and you...

RS-330

High-Definition OCT & Fundus Imaging in One Compact System

- Based on AFC-330 non-mydriatic fundus camera
- 12 MPixel true colour fundus image
- High-resolution OCT
- Auto-mode
- Manual-mode
- Navis-Ex software platform
- DES programme approved camera

AFC-330

Non-Mydriatic Auto Fundus Camera

The AFC-330 has a built-in camera and computer, automated photography functions, multiple data management utilities, and easy-to-use operator assist functions. These smart features make fundus photography easier for screening and diagnosis.

- Automated non-mydriatic fundus camera
- Touch screen control
- Optional Navis-Ex software platform
- Manual-mode for difficult patients
- 12 MPixel true colour fundus image
- DES programme approved camera

Versacam™ α

Handheld Fundus Camera

- 5 MPixel
- Clearer details, better diagnosis
- Internal fixation ability
- Auto-focus, half press focus, fully press capture
- Foot pedal, carrying case
- Slit lamp adapter
- Wi-Fi SD card compatible

NIDEK

Member of Vision Ophthalmology Group

spectrum

Spectrum Fernbank House, Springwood Way, Macclesfield, Cheshire, SK10 2XA
Tel: 01625 618816 • **Fax:** 01625 619959 • **Email:** enquiries@spectrum-uk.co.uk

www.spectrum-uk.co.uk

AT THE FOREFRONT OF OPHTHALMIC TECHNOLOGY