Das Eyeness Team

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Factors influencing retinal venous pressure

A biomedical approach to a medical paradigm

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Was haben Diabetes und Glaukom Patienten mit toten Bergsteigern am Mt. Everest zu tun ?

† Mount Everest 20. May 2013

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Einführung

Bekannt und allgemein akzeptiert ist, dass der okuläre Kreislauf:

1. ein Indikator für den systemischen Kreislauf ist
2. vermutlich relevant für die Pathogenese bei Glaukom und diabetischen Augenerkrankungen ist

Golzan, S.M. et al., Dynamic association between intraocular pressure and spontaneous pulsations of retinal veins. Curr Eye Res, 2011. ***36****(1): p. 53-9.*

Einführung

Die Rolle des okulären Perfussionsdruckes:

"Inadequate ocular perfusion of the retina can cause ischemia leading to decreased oxygen supply (hypoxia) in tissues, which may result in deleterious sight-threatening effects."

Arjamaa, O. and M. Nikinmaa, Oxygen-dependent diseases in the retina: role of hypoxia-inducible factors. Exp Eye Res, 2006. 83(3): p. 473-83.

Klinische Evidenz

Erhöhter retinaler Venendruck ist publiziert für:

- Glaukom *(Pillunat et al. 2014; Fang et al. 2014; Morgan et al. 2009; Jonas, Harder 2003)*
- Venenverschluss *(Mozaffarie et al. 2014; Yasuda et al. 2010; Jonas et al. 2007)*
- Diabetes mellitus *(Cybulska et al. 2015)*
- Flammer Syndrome *(Fang et al. 2014)*
- Hypoxie - Höhen induziert (Baertschi et al. 2016)
    - potentiell für temporäre Amaurosis *(Baertschi, ISMM 2014)*
    - Retinablutungen und ONH Ödem *(multiple 1975-2009)*

Risk Factors for Incident Open-angle Glaucoma

The Barbados Eye Studies 2008

M. Cristina Leske, MD, MPH,[1,2] Suh-Yuh Wu, MA,[1,2] Anselm Hennis, FRCP(UK), PhD,[1,3,4] Robert Honkanen, MD,[2] Barbara Nemesure, PhD,[1,2] BESs Study Group

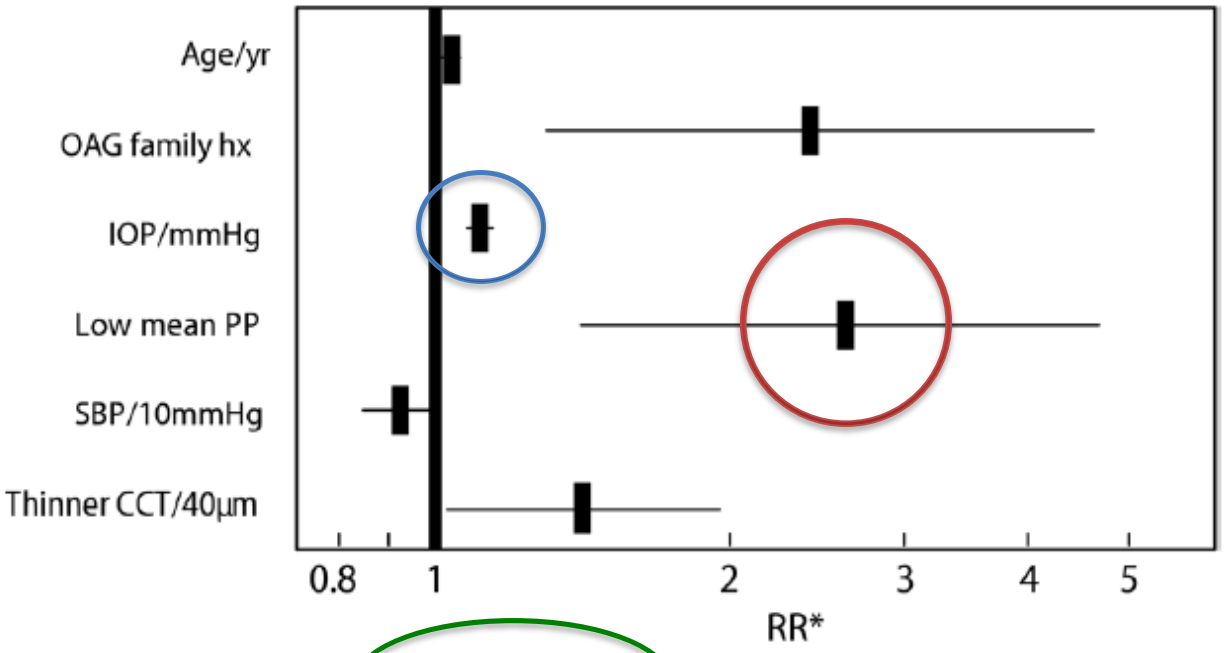
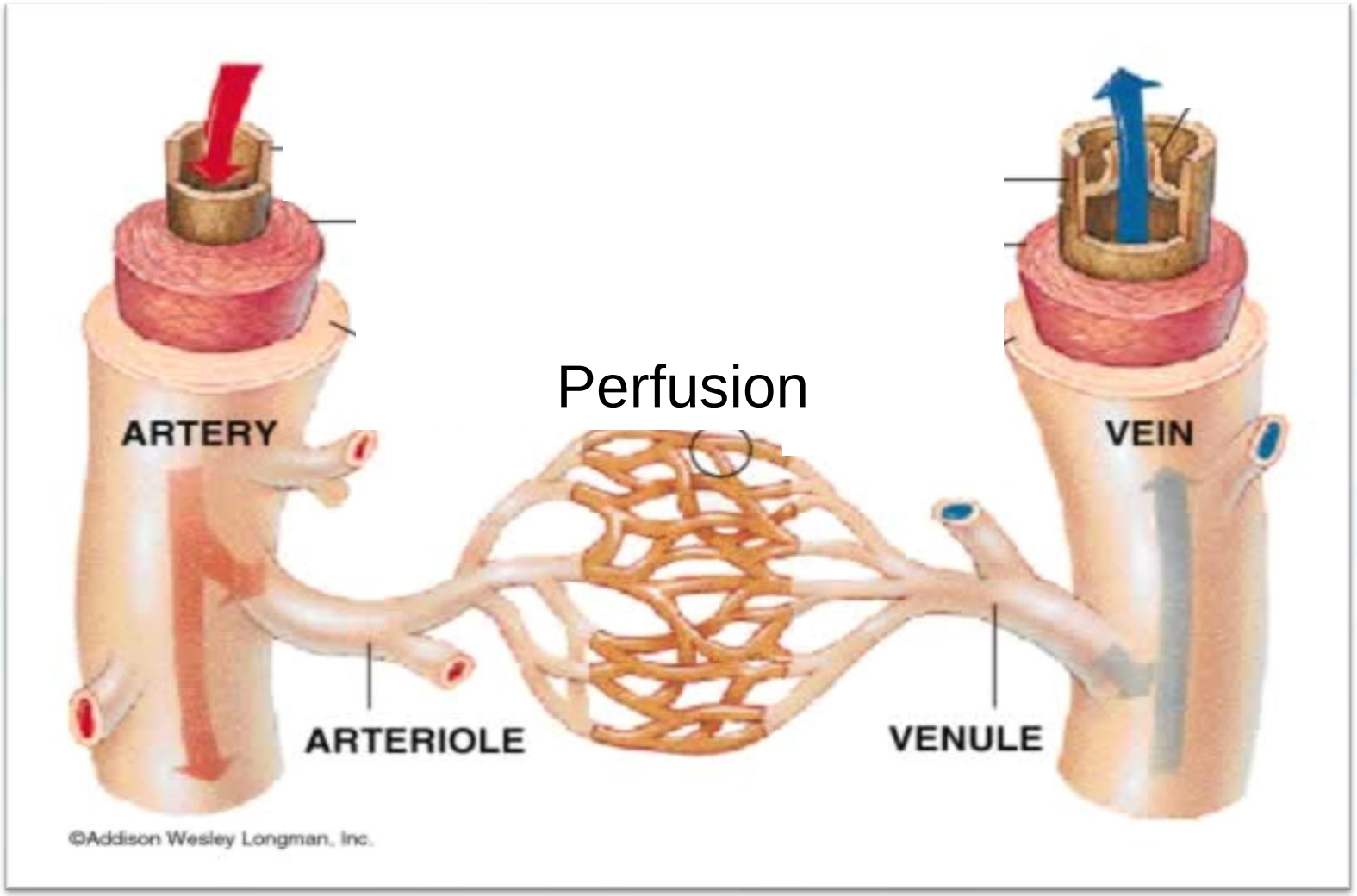


Figure 1. Risk factors for definite open-angle glaucoma (OAG; n = 3222). hx = history; PP = perfusion pressure; RR = risk ratio; SBP = systolic blood pressure. *Based on Cox regression models, adjusting for age, gender, intraocular pressure (IOP), and IOP- and blood pressure–lowering treatment; central corneal thickness (CCT) is presented as an odds ratio, based on logistic regression model in a subsample (n = 1023).

Rolle des Perfusionsdruckes



Interconnection between Arteries, Arterioles, Capillaries and Venules
(Reproduction with Permission of Pearson Education)

Rolle des Perfusionsdruckes

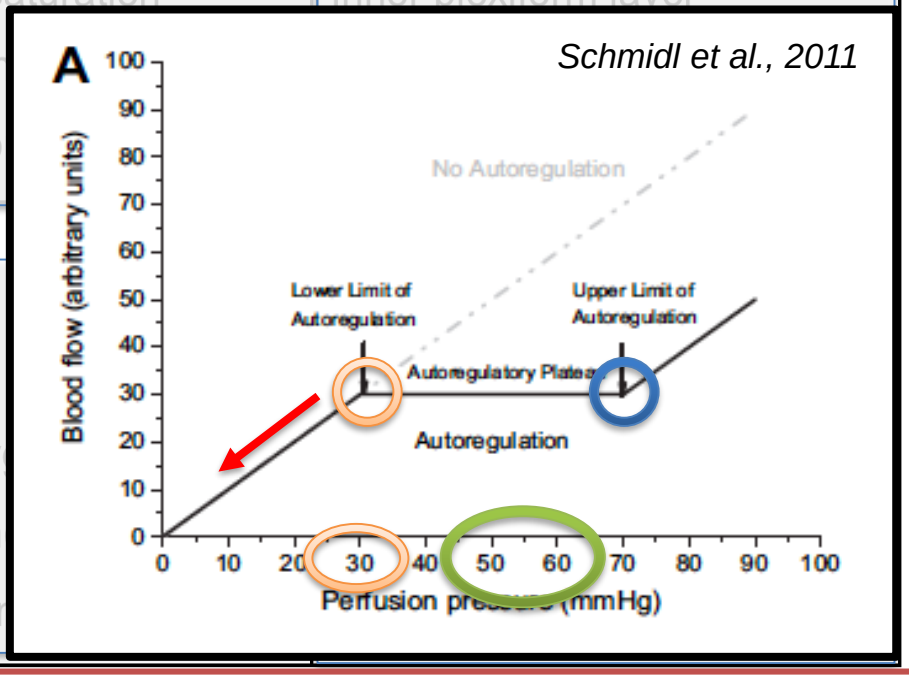
“Perfusion Pressure is defined as the difference between arterial and venous blood pressure and is the driving force of blood flow.”

Schmidl, D., G. Garhofer, and L. Schmetterer, The complex interaction between ocular perfusion pressure and ocular blood flow - relevance for glaucoma. Exp Eye Res, 2011. 93(2): p. 141-55.

Retinaler vs choroidaler Blutfluss

Tissue	Function and characteristics	Involved cell or fiber layer
Retina	Autoregulation	Inner limiting membrane
	Low flow rate	Optic nerve fibers
	Low perfusion rate	Ganglion layer
	Low venous oxygen saturation	Inner plexiform layer
	High vascular resistan	
	High oxygen extractio	
Choroidea	No Autoregulation	
	Very high flow rate	
	High perfusion rate	
	Very high venous oxy	
	Low vascular resistan	
	Low oxygen extractio	

e.g. Flicker, IOP/ICP, Endothelin-1



In POAG ist der Blutfluss am ONH um 20% reduziert !

(Dr. med. Claudia Lommatzsch, Lecture at DOG 2016 in Berlin/Germany)

Methode und Instrumente

Spontaner retinaler Venenpuls (SVP) ist nur sichtbar wenn der umgebende IOP identisch mit dem Venendruck im Gefäss ist.

Prevalenz von SVP ? (% of Px)

99 % 75 % 50 %

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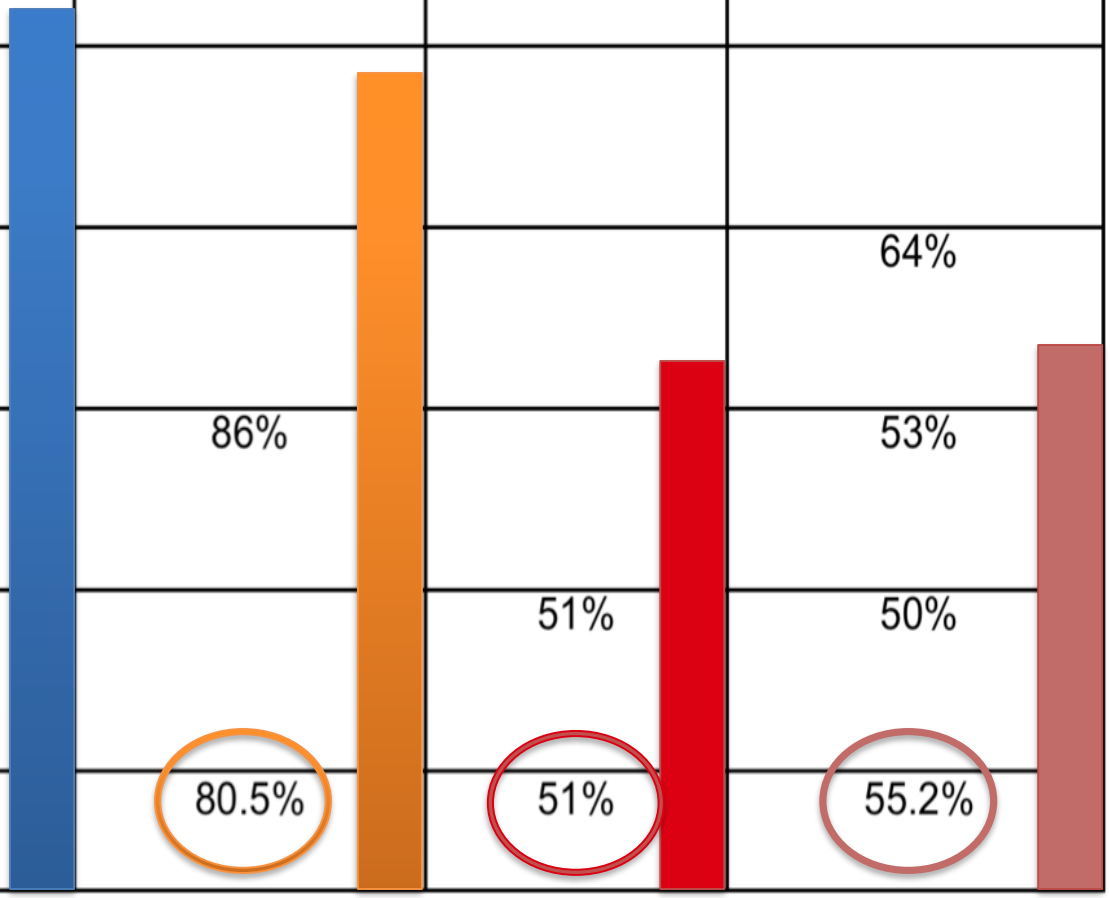
Epidemiologie

Prevalenz von spontanem retinalem Venenpuls aus fünf aktuellen Studien

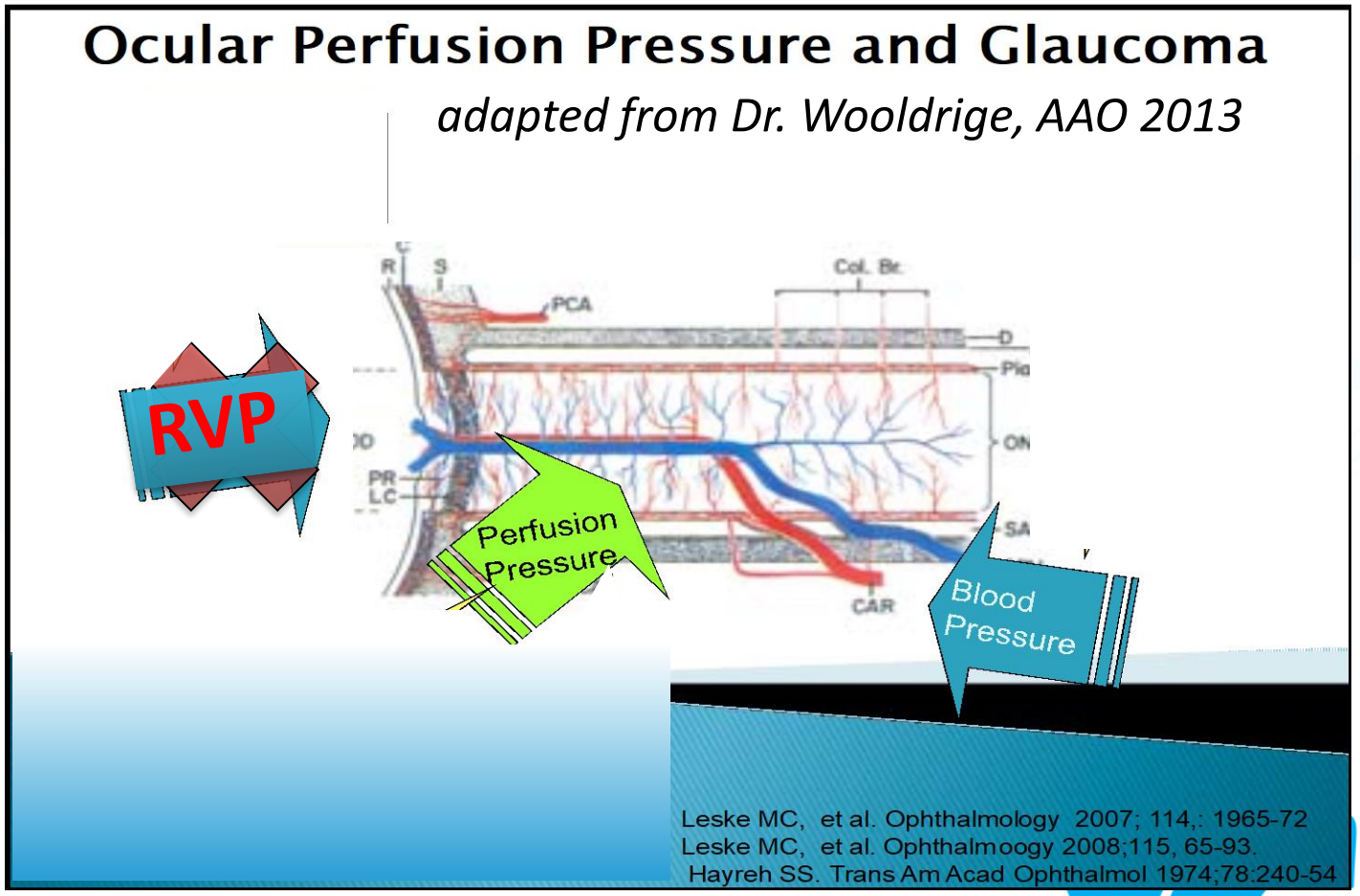
	Healthy controls	POAG suspects	NTG	POAG
Morgan et al., Ophthalmology, 2004; 111(8): 1489-94	98%	75%		54%
Harder and Jonas. Br J Ophthamol, 2007; 91(3): 401-02	89%			
Legler and Jonas. Glaucoma, 2009; 18(3): 210-12	75%			64%
Seo et al., Ophthalmology, 2012; 119: 2254-60		86%		53%
Abegao Pinto et al., Acta Ophthalmol, 2013; 91(6): 514-20	82%		51%	50%
Mean	86.0%	80.5%	51%	55.2%



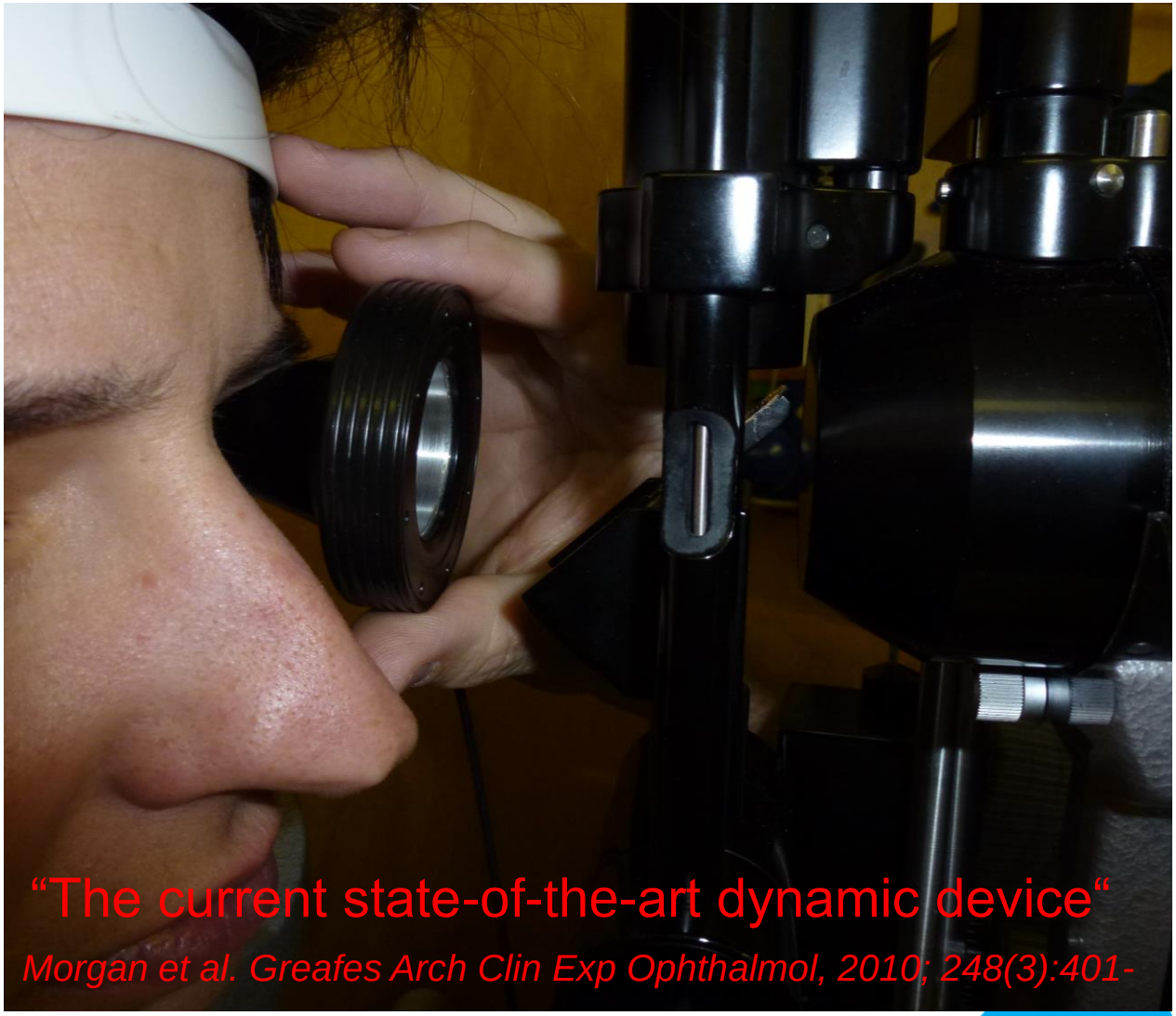
Korrekte Kalkulation des Perfusionsdruckes

Ocular Perfusion Pressure (OPP) = 2/3 [MAP*] – **RVP**

**MAP = Mean Arterial Pressure = BPdias + 1/3 (BPsyst – BPdias)*



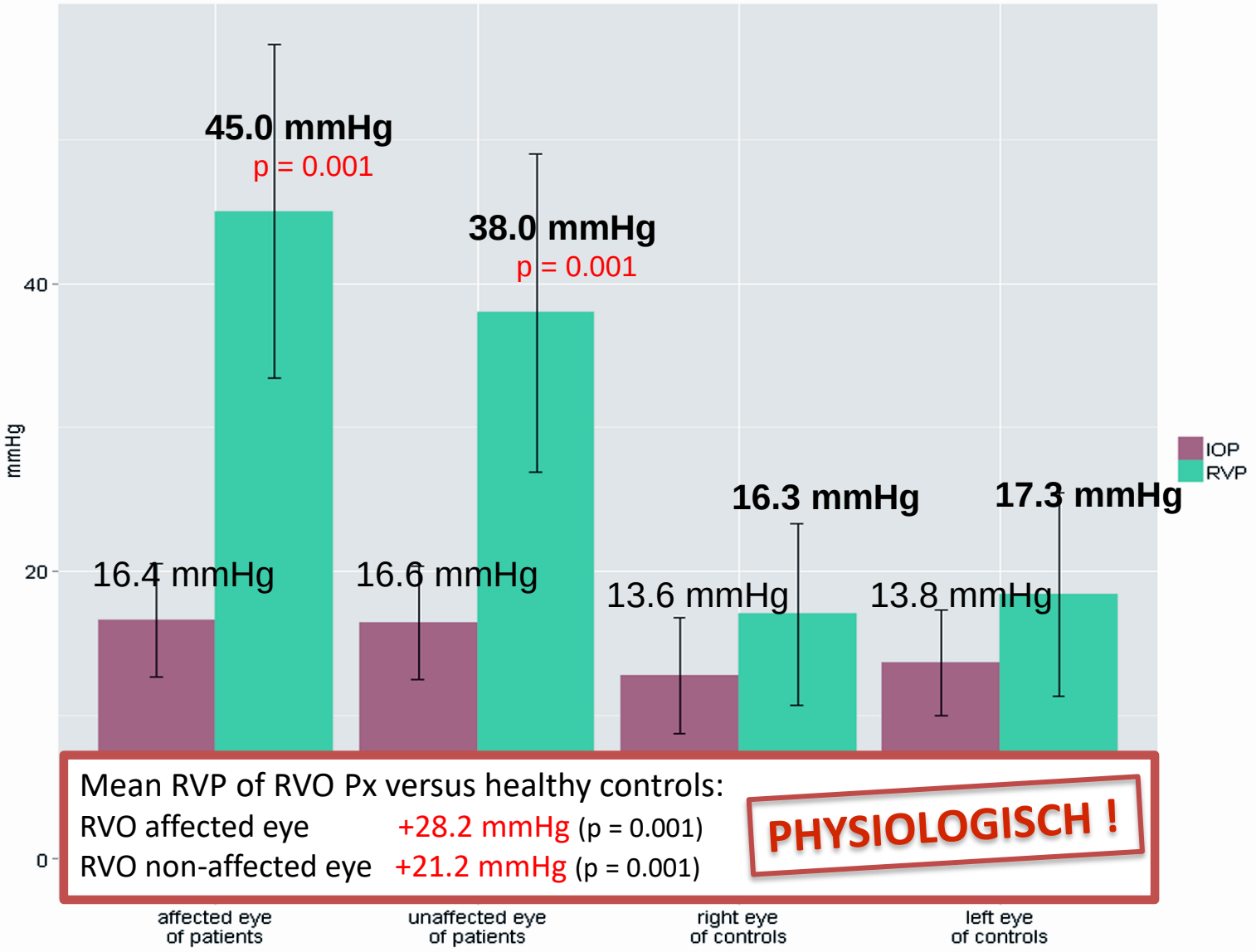
Methode und Instrumente



Ophthalmo-Dynamometry by Dr. Bernhard Loew, Germany

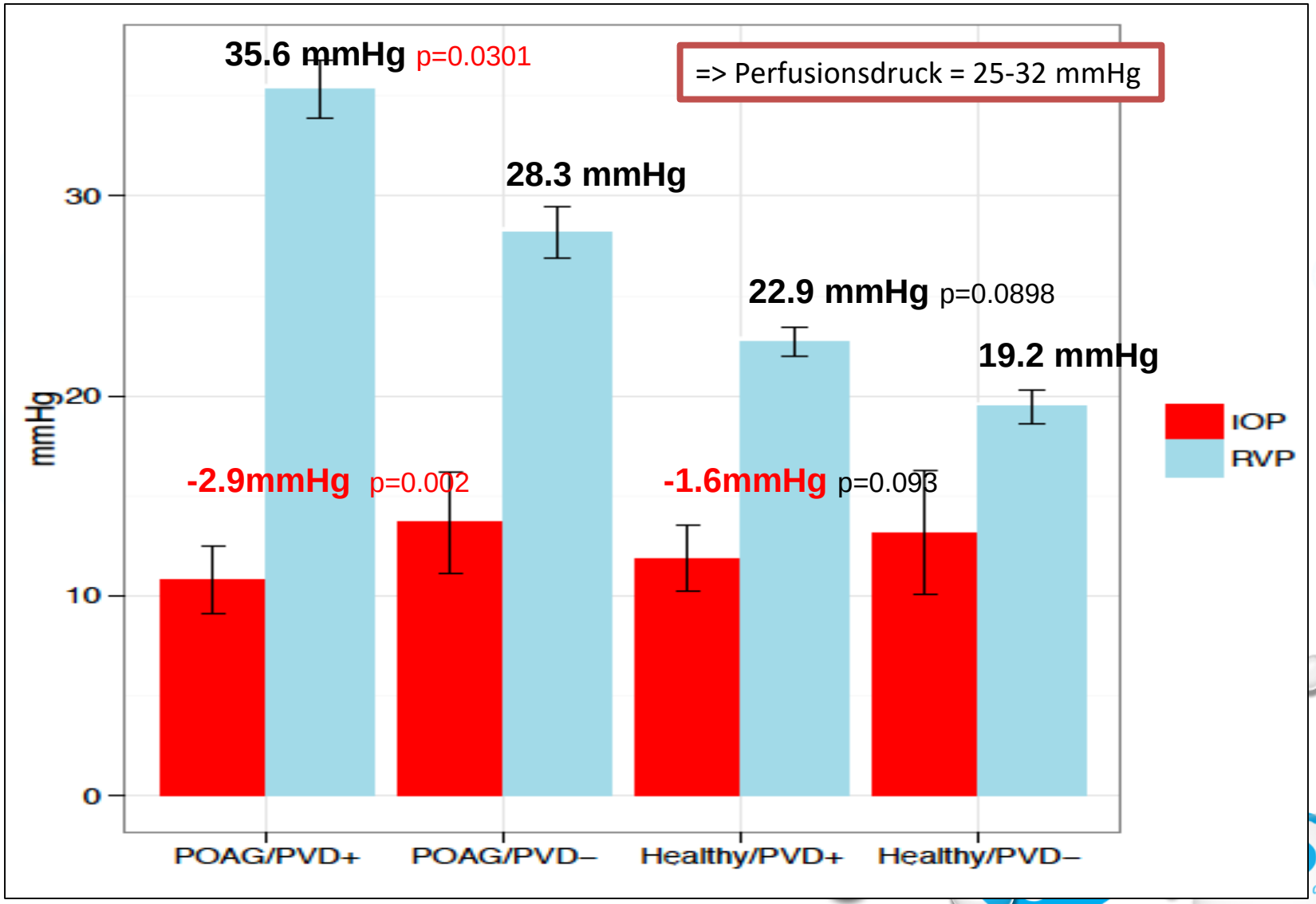
Resultate Venenverschluss

IOP and RVP in Patients and Controls (n = 31/31)



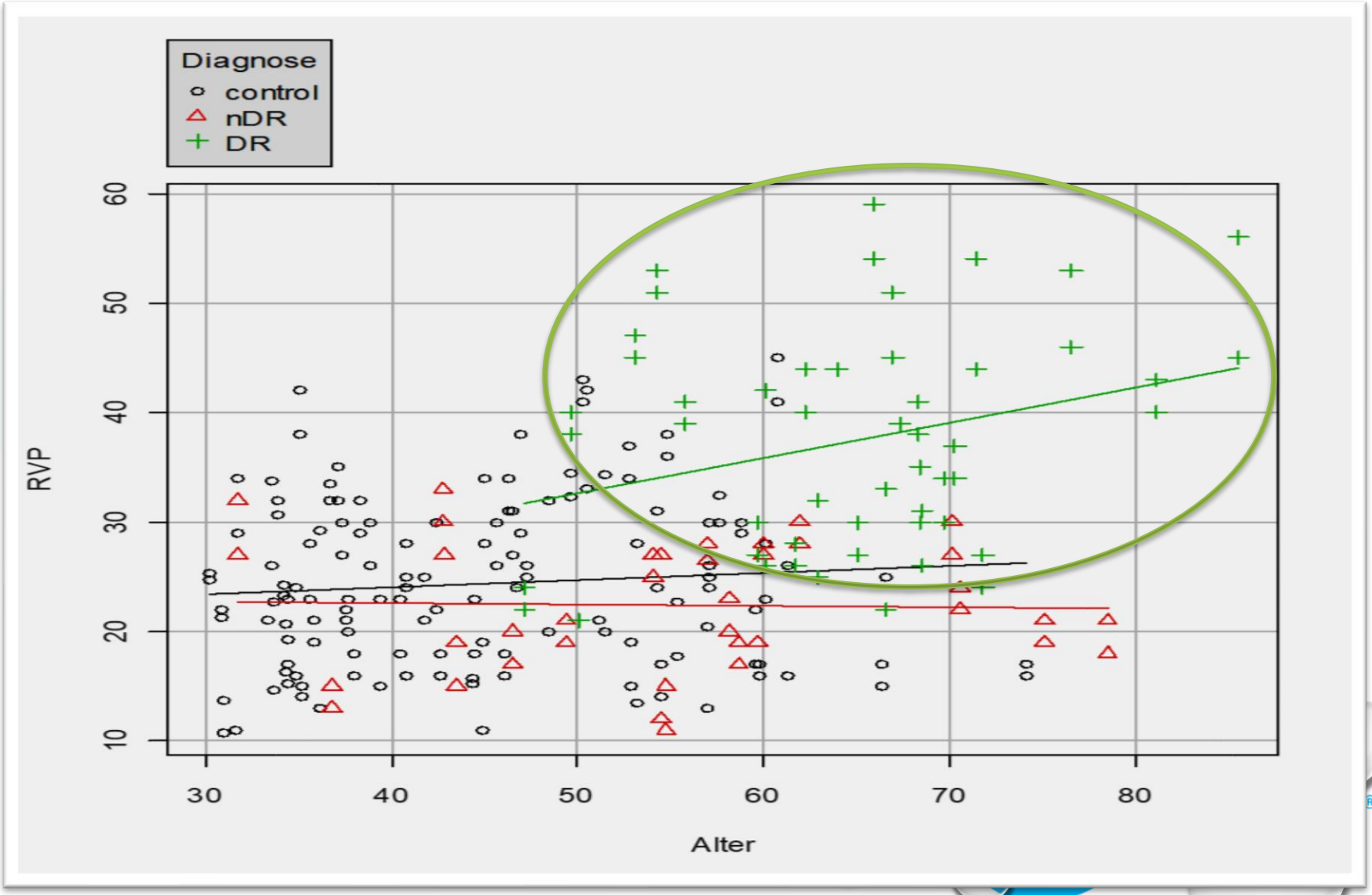
Resultate POAG und FS

IOP and RVP for POAG FS+/FS- and Healthy FS+/FS- (n=30/30)



Resultate Diabetes

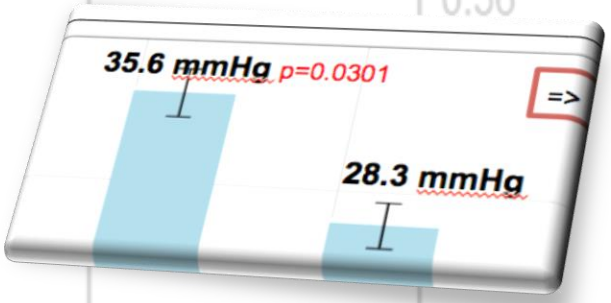
RVP versus Age for each study group (all subjects)



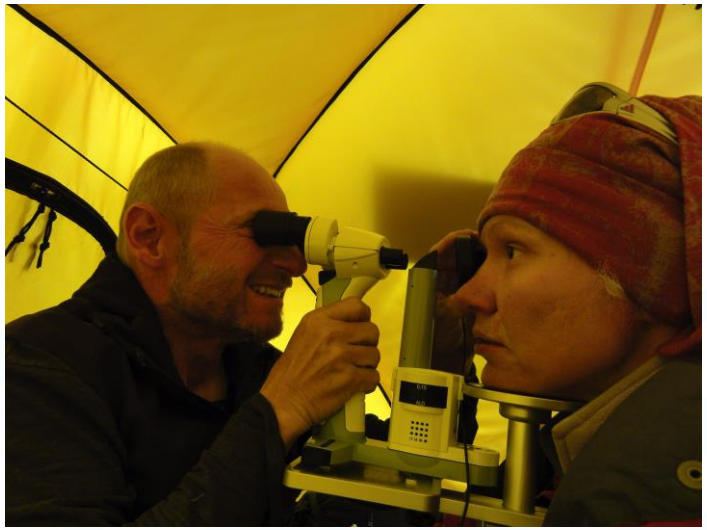
Resultate Diabetes

Deskriptive Statistik Alters-matched Data

	control N = 28	nonDR N = 40	DR N = 28	p overall
Age	58.5 (7.28)	55.3 (12.3)	58.6 (7.02)	0.55
IOP	14.9 (3.18)	15.3 (3.27)	15.9 (2.27)	0.319
RVP	25.2 (9.11)	22.5 (5.78)	33.8 (9.81)	0.0076
Gender				0.56
- female	14 (50%)	12 (30.0%)		
- male	14 (50%)	28 (70.0%)		



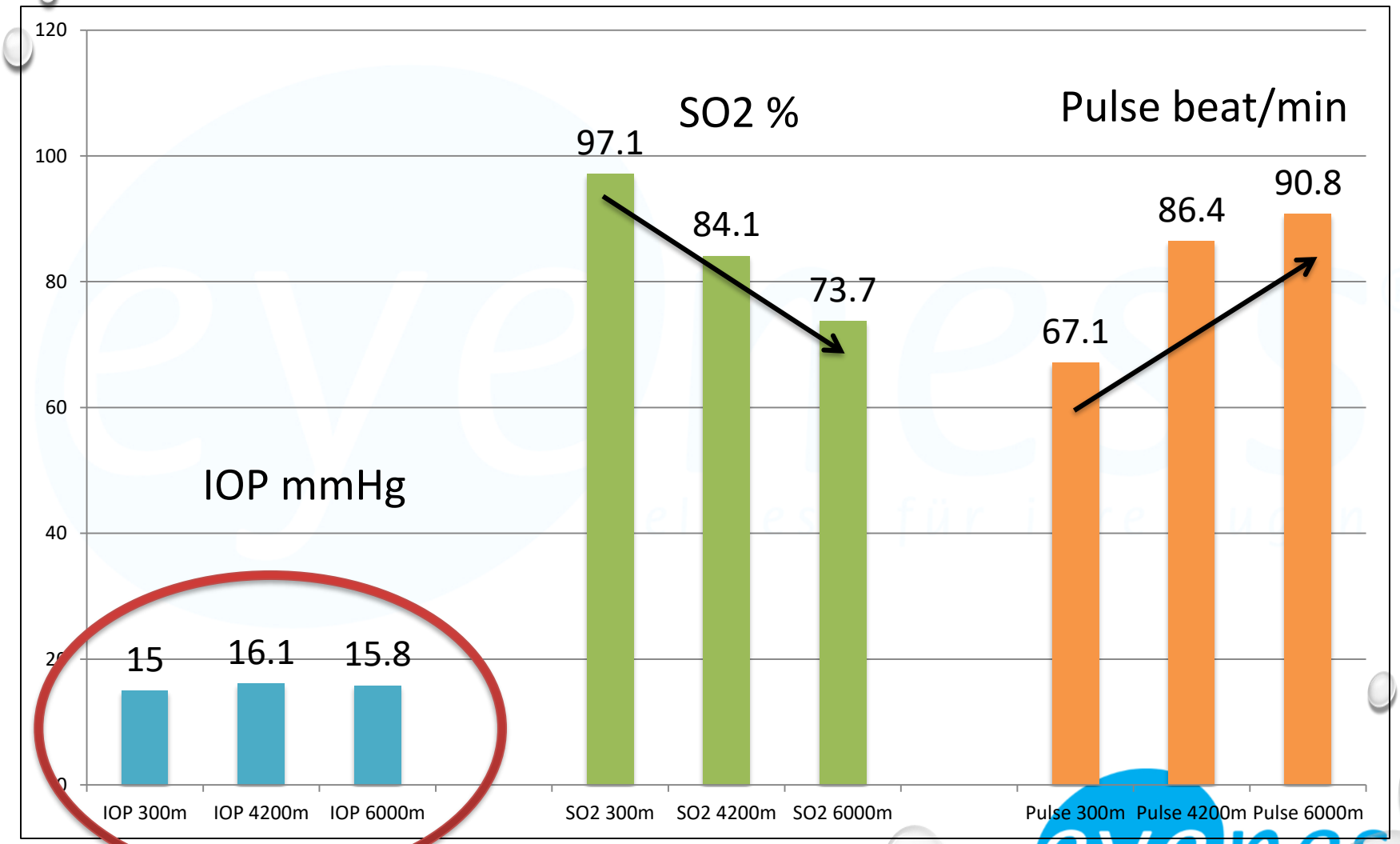
Einfluss von Höhe und Hypoxie auf den Venen- und Perfusionsdruck



Pik Lenin 6000m Juni 2012

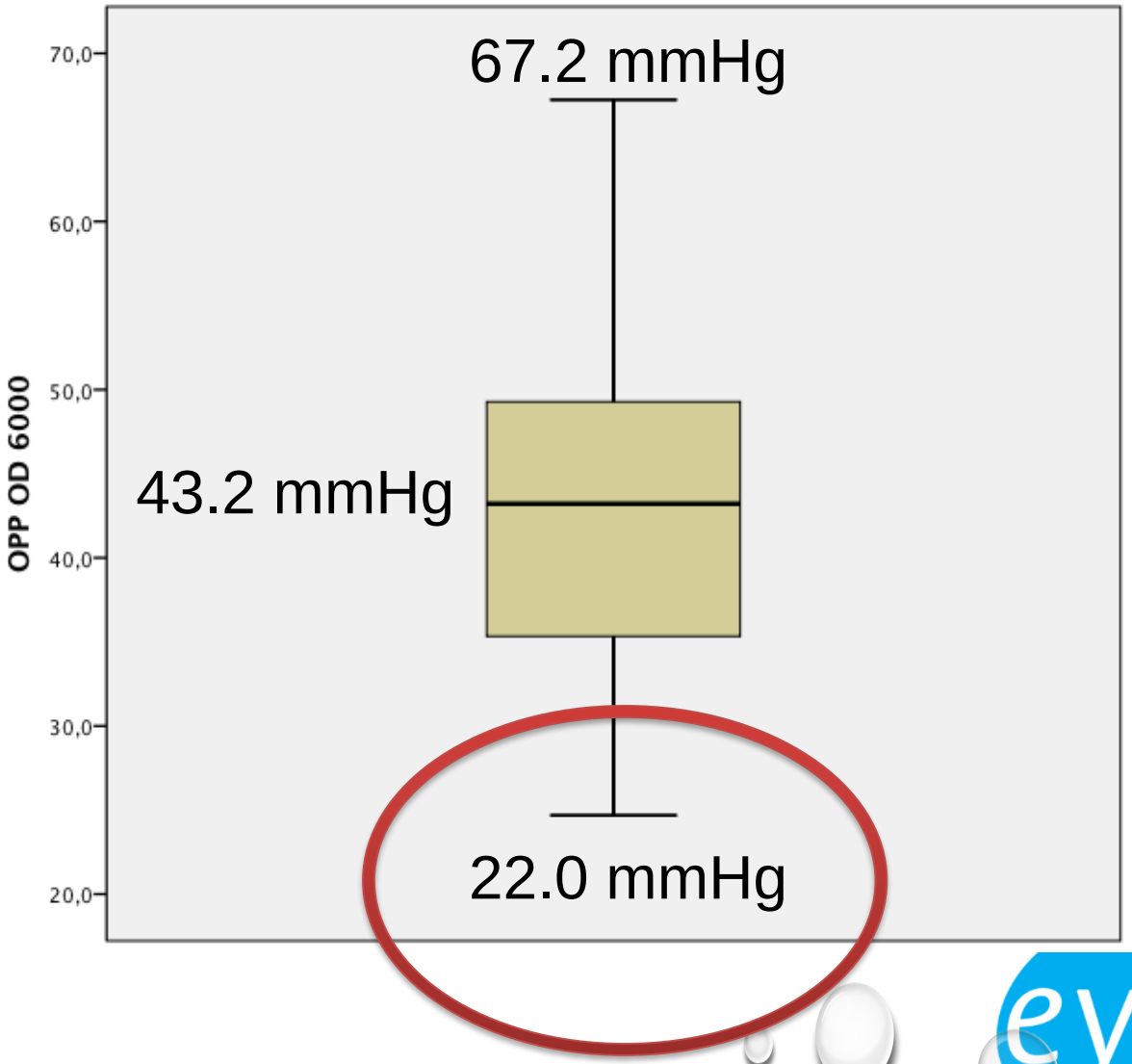
Resultate: IOP, SO2 und Puls

auf versch. Höhen (Hypoxie >24h) n=33/31)



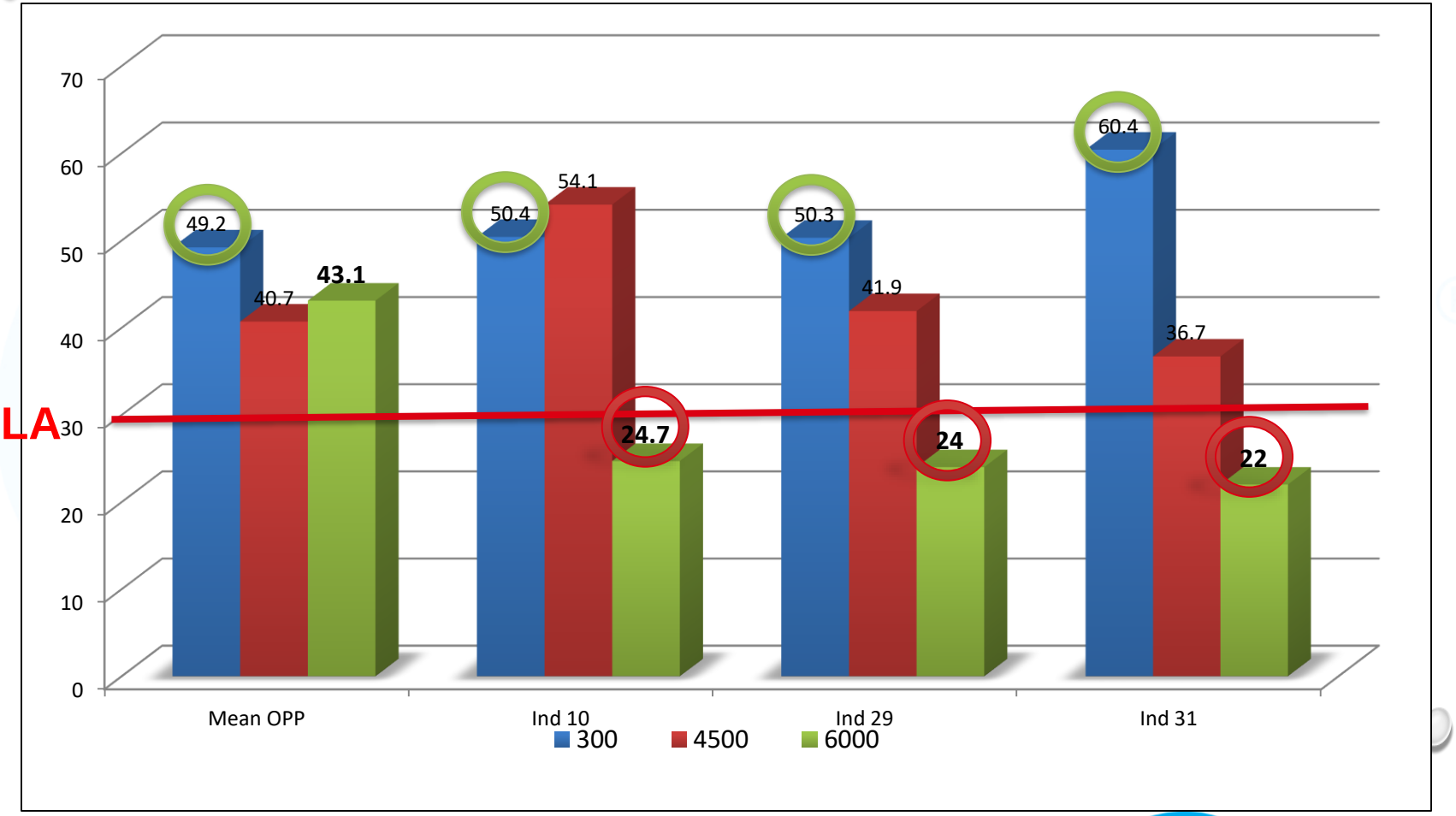
Resultate: Okulärer Perfusionsdruck

auf 6’000m n=31



Hypoxie und Perfusionsdruck

Teilweise tiefer als das “Lower Limit of Blood Flow Autoregulation” am ONH



Baertschi, M., et al.: "The effect of hypoxia on intra-ocular, mean arterial, retinal venous and ocular perfusion pressures." Clin Hemorheol Microcirc. Vol.63, no.3, pp 239-303, 2016

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Therapie Empfehlung 2013

Value of non-IOP lowering therapy for glaucoma:

Cybulska-Heinrich et al., Klin Monbl Augenheilk 2013: 230(2); 114-19

Resultate Nifedipine 2015

Graefe's Archive for Clinical and Experimental Ophthalmology
June 2015, Volume 253, Issue 6, pp 935–939

The effect of nifedipine on retinal venous pressure of glaucoma patients with the Flammer-Syndrome

L. Fang, S. Turtschi, Maneli Mozaffarieh

Results: **The RVP decreased significantly** after 3 weeks in both eyes of patients **treated with low-dosed Nifedipine** compared to the untreated group (mean **decrease of 12.5 mmHg** (SD 12.5), $P < 0.001$). A **larger response** to therapy was f**ents with the FS** compared to patients lacking th mmHg, confidence Interval (9). **No significant differences wer** the patients after treatment. In the untreated control grou significant differences were accounted for either in the RVP or the IOP after 3 weeks.

Suggestion: Nifedipine 5mg / Day (*Off-Label)

Conclusions: **Treatment with low-dosed Nifedipine decreases RVP in both eyes of glaucoma patients, particularly in those with the Flammer-Syndrome.** This effect may be due to the partial inhibition of **Endothelin-1 (ET-1)** by Nifedipine.

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Resultate ET-1 Blocker "Diavolezza-Studie"

Retinal vessel regulation at high altitudes[1]

Article type: Research Article

Authors: Neumann, Thomas[a,*] | Baertschi, Michael[b,c] | Vilser, Walthard[d] | Drinda, Stefan[e] | Franz, Marcus[f] | Brückmann, Andreas[g] | Wolf, Gunter[a] | Jung, Christian[h]

Clinical Hemorheology and Microcirculation, vol. 63, no. 3, pp. 281-292, 2016

CONCLUSIONS: Retinal arterial and venous vessels react to Normobaric Hypoxia and Hypobaric Hypoxia with a diameter increase and an impaired response to flicker light**.** Macitentan was capable to normalize the increased retinal venous pressure observed at high altitudes**.**

Zusammenfassung und Diskussion

- Der retinale Venendruck RVP ist ein essentieller Faktor zur korrekten Bestimmung des retinalen Perfusionsdruckes.
- RVP kann präzise, reproduzierbar, schnell und kosten-günstig mittels Ophthalmo-Dynamometrie bestimmt werden.
- RVP ist erhöht in verschiedenen Augenerkrankungen wie z.B. Glaukom, diabetischer Retinopathie und bei retinalem Venenverschluss.
- RVP ist ebenfalls erhöht in Personen mit Flammer-Syndrom und bei systemischer Hypoxie als Folge grosser Höhe.

Was haben Diabetes und Glaukom Patienten mit toten Bergsteigern am Mt. Everest zu tun ?

“Partial or total local circulatory collapse”

† Mount Everest 20. May 2013

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Take-Home !

- Der retinale Venen- und Perfusionsdruck sind **evident**.
- Ist kein spontaner retinaler Venenpuls sichtbar, ist der Venendruck **höher** als der intra-okular Druck und muss gemessen werden um ein **kompletteres klinisches Bild** zu erhalten.
- Ein erhöhter retinaler Venendruck kann mittels Kalzium Antagonist klinisch reduziert und mittels Endothelin-1 Blocker möglicherweise sogar normalisiert werden.

www.eyeness.ch/news/downloads