2nd Annual Cedars-Sinai
Intracranial Hypotension Symposium
SATURDAY, OCTOBER 13, 2018
MARINA DEL REY MARRIOTT

SIH: CSF outflow resistance and other objective measurements

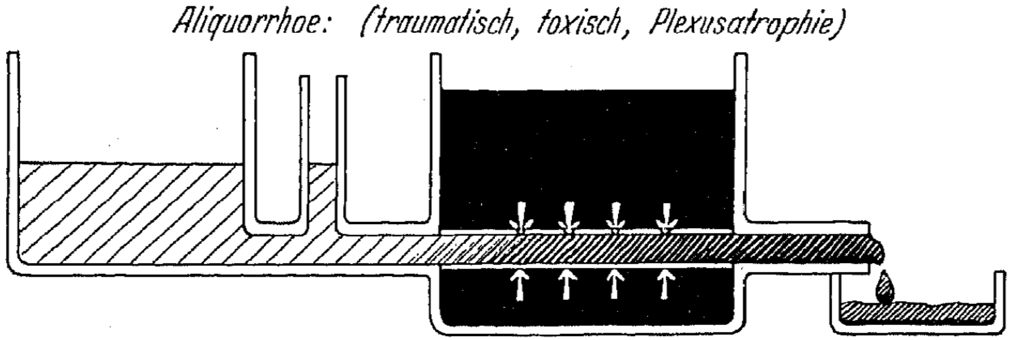
Prof. Dr. J. Beck

Chairman, Dept. of Neurosurgery
Medical Center – University of Freiburg, Germany

Neuere Anschauungen zur Pathophysiologie der Liquorzirkulation

Von G. Schaltenbrand[1]

Zentralblatt für Neurochirurgie 1938 Nr. 5



«Aliquorrhoe»

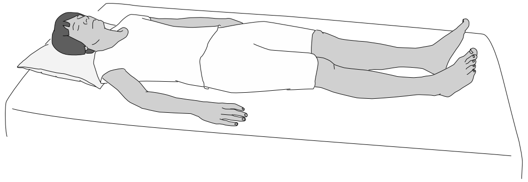
Spontaneous Idiopathic Hypotension

- (orthostatic) headache

+

or

- Low CSF pressure < 6 cm H_2O
- Evidence of CSF leaking on imaging



Cephalalgia An International Journal of Headache

International Headache Society

International Classification of Headache Disorders, 2018

Spontaneous Idiopathic Hypotension

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+

or

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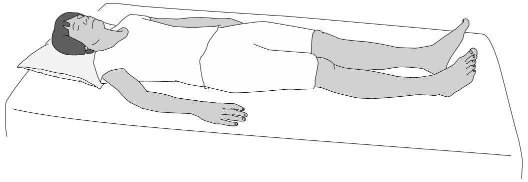


Cephalalgia · International Headache Society

International Classification of Headache Disorders, 2018

Spontaneous Idiopathic Hypotension

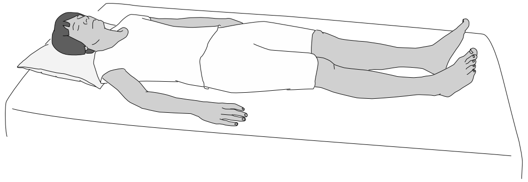
modified: • (orthostatic) *symptoms*

\+

or <

• Low CSF pressure < 6 cm H_2O

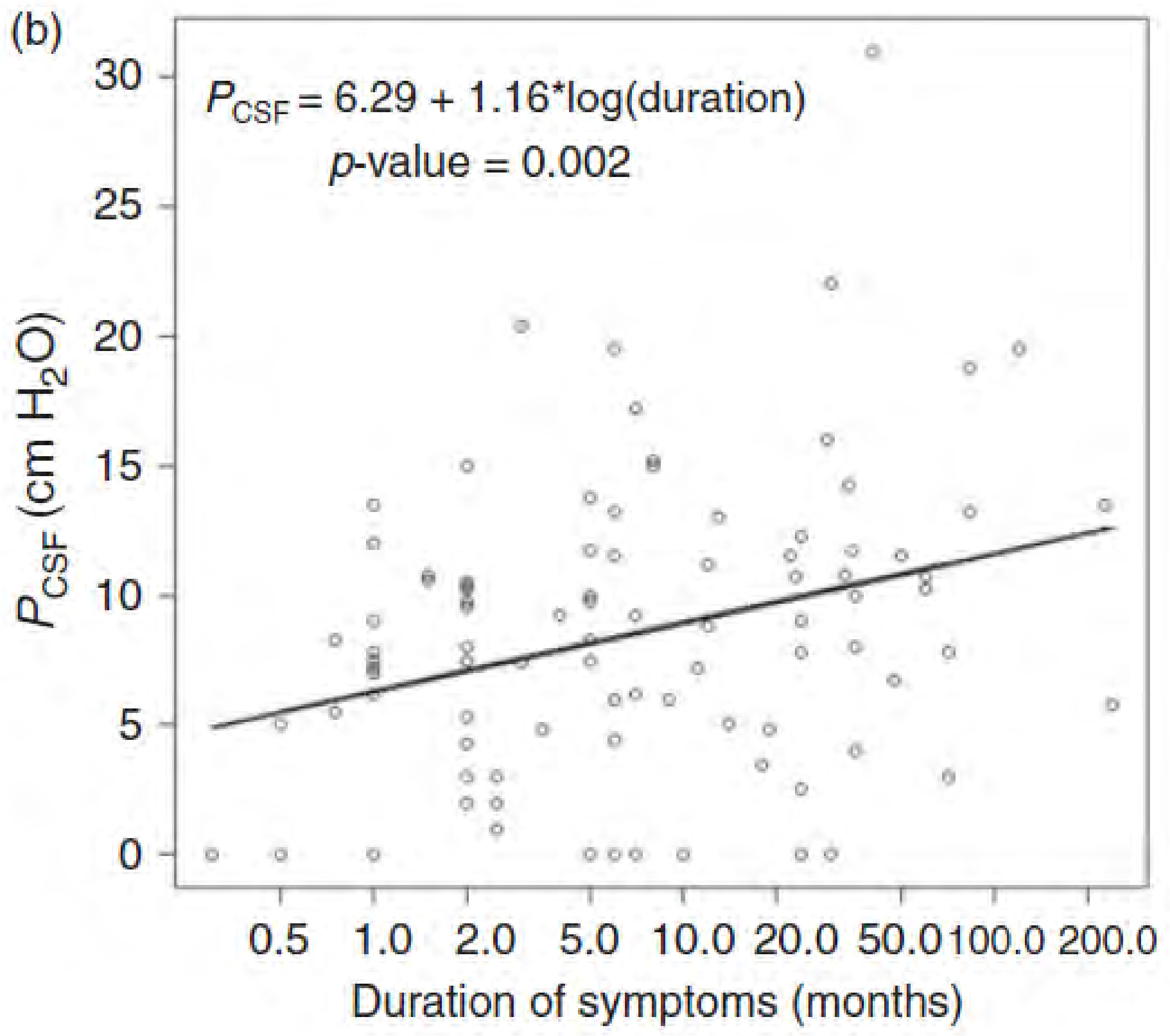
• Evidence of CSF leaking on imaging



Cephalalgia
An International Journal of Headache
International Headache Society

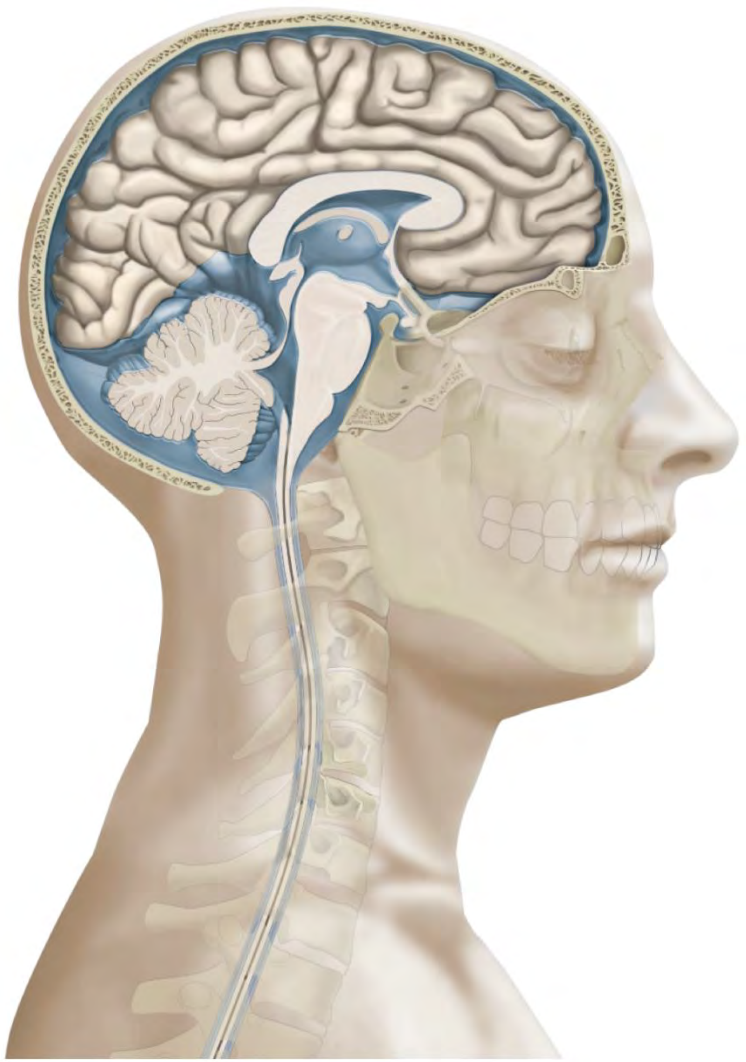
International Classification of Headache Disorders, 2018

Schievink et al. Neurology. 2016 Aug 16;87(7):673-9

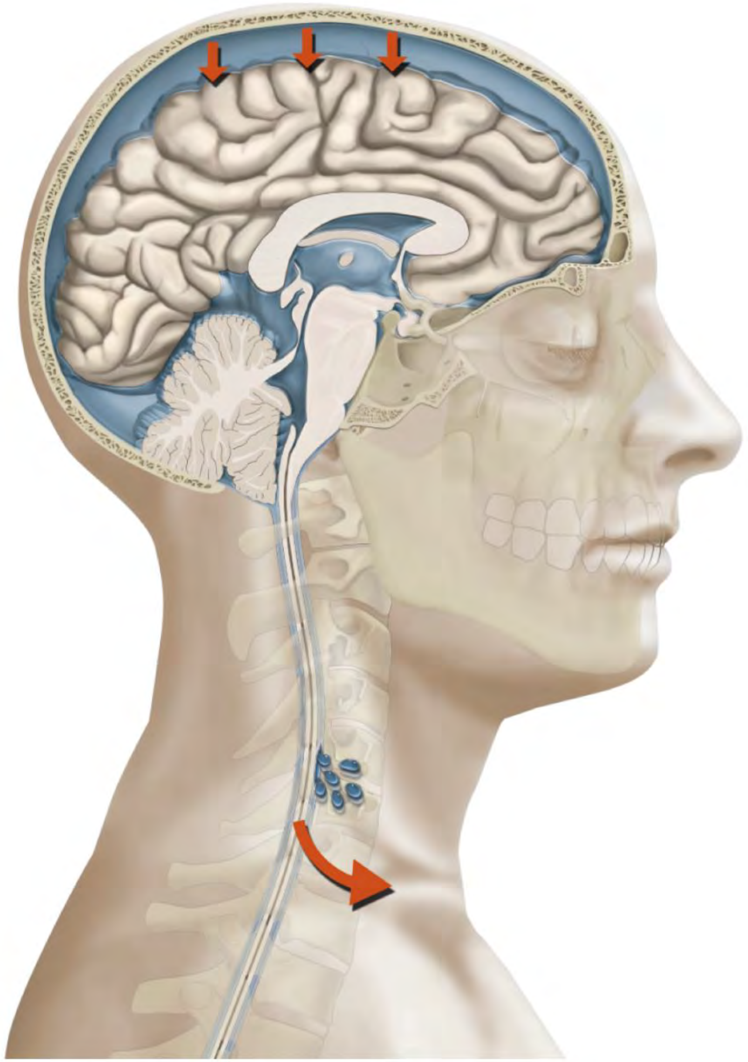


Kranz, Cephalgia 2015

Spontaneous Intracranial Hypotension



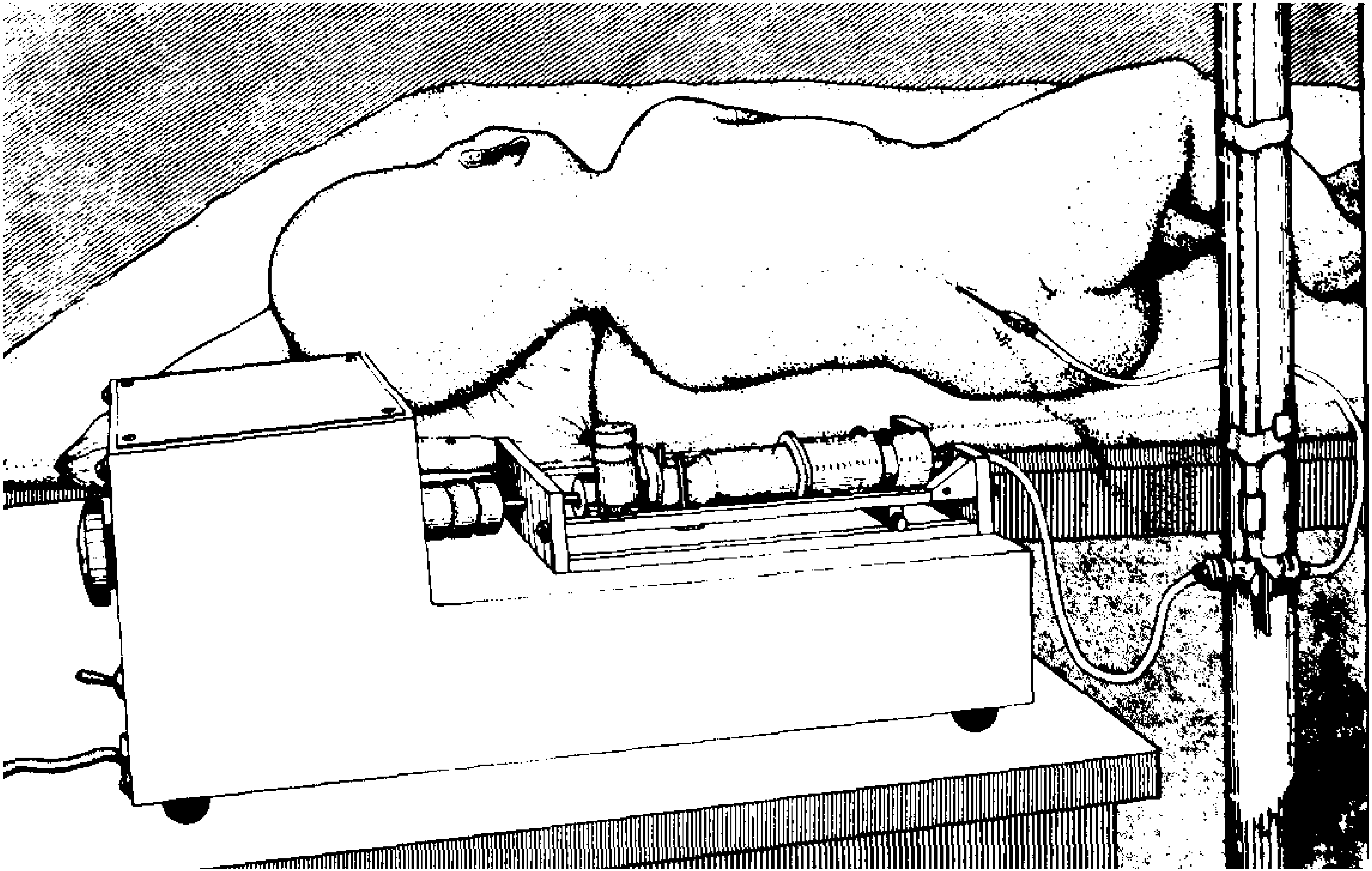
Spontaneous Intracranial Hypotension



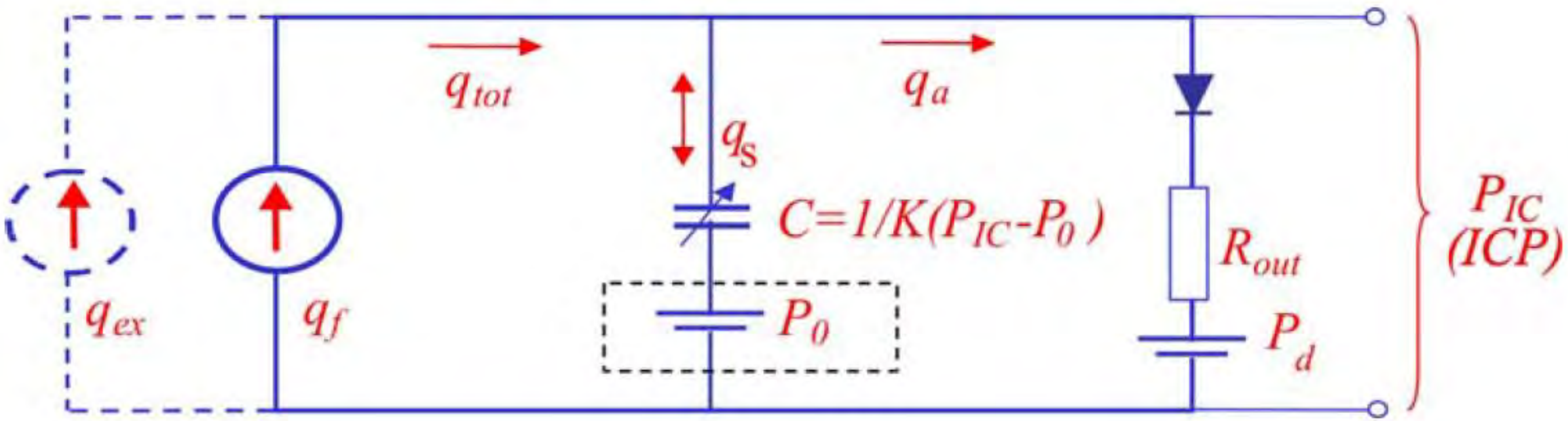
Lumbar infusion test

Rationale

- A CSF leak should alter normal CSF parameters
- A CSF leak implies a low resistance to CSF outflow



Katzmann and Hussey Neurology 1970



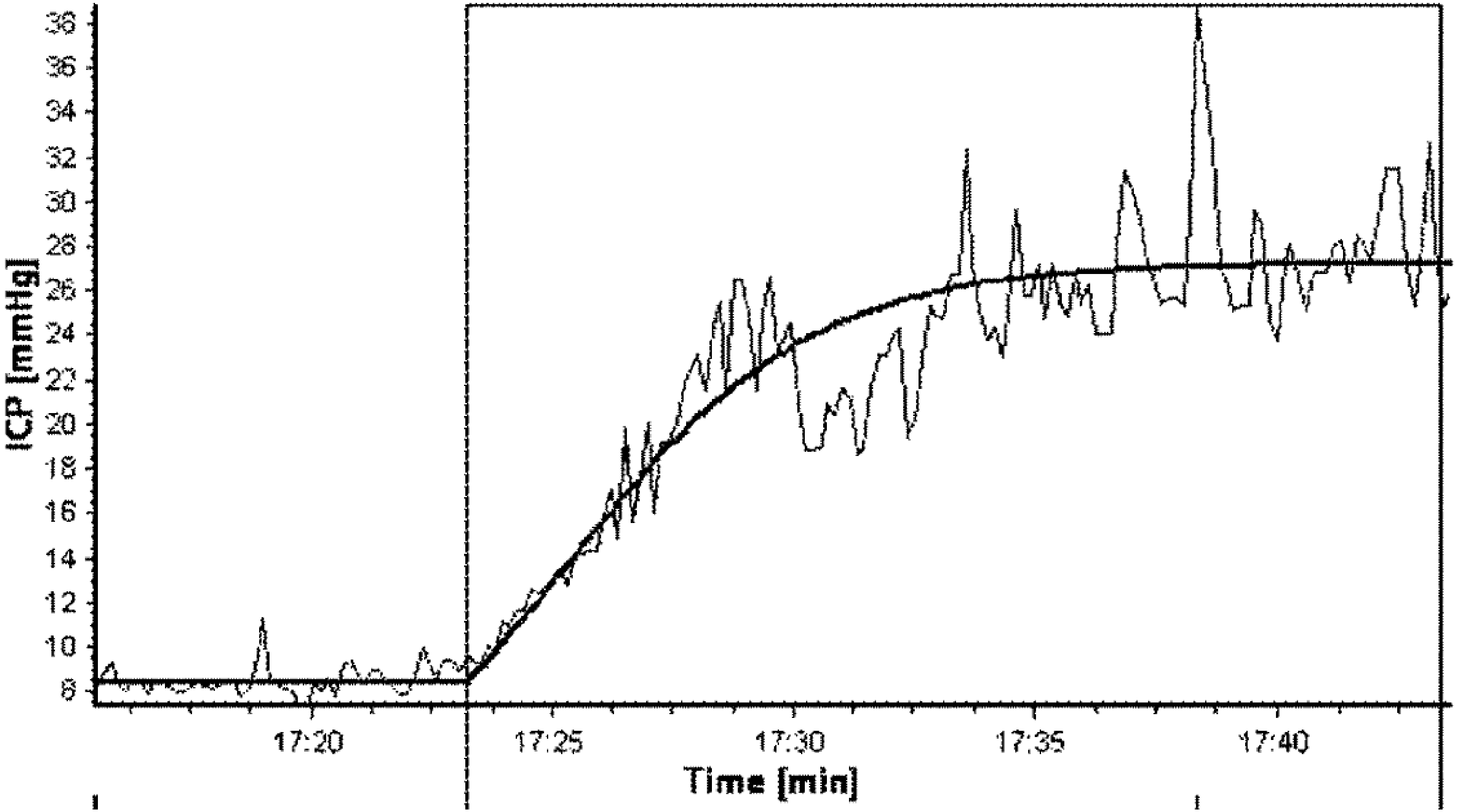
A computer system for the identification of the cerebrospinal compensatory model.

Czosnyka M[1], Batorski L, Laniewski P, Maksymowicz W, Koszewski W, Zaworski W.

Acta Neurochir (Wien). 1990;105(3-4):112-6

Assessment of cerebrospinal fluid outflow resistance

Anders Eklund · Peter Smielewski · Iain Chambers · Noam Alperin · Jan Malm · Marek Czosnyka · Anthony Marmarou



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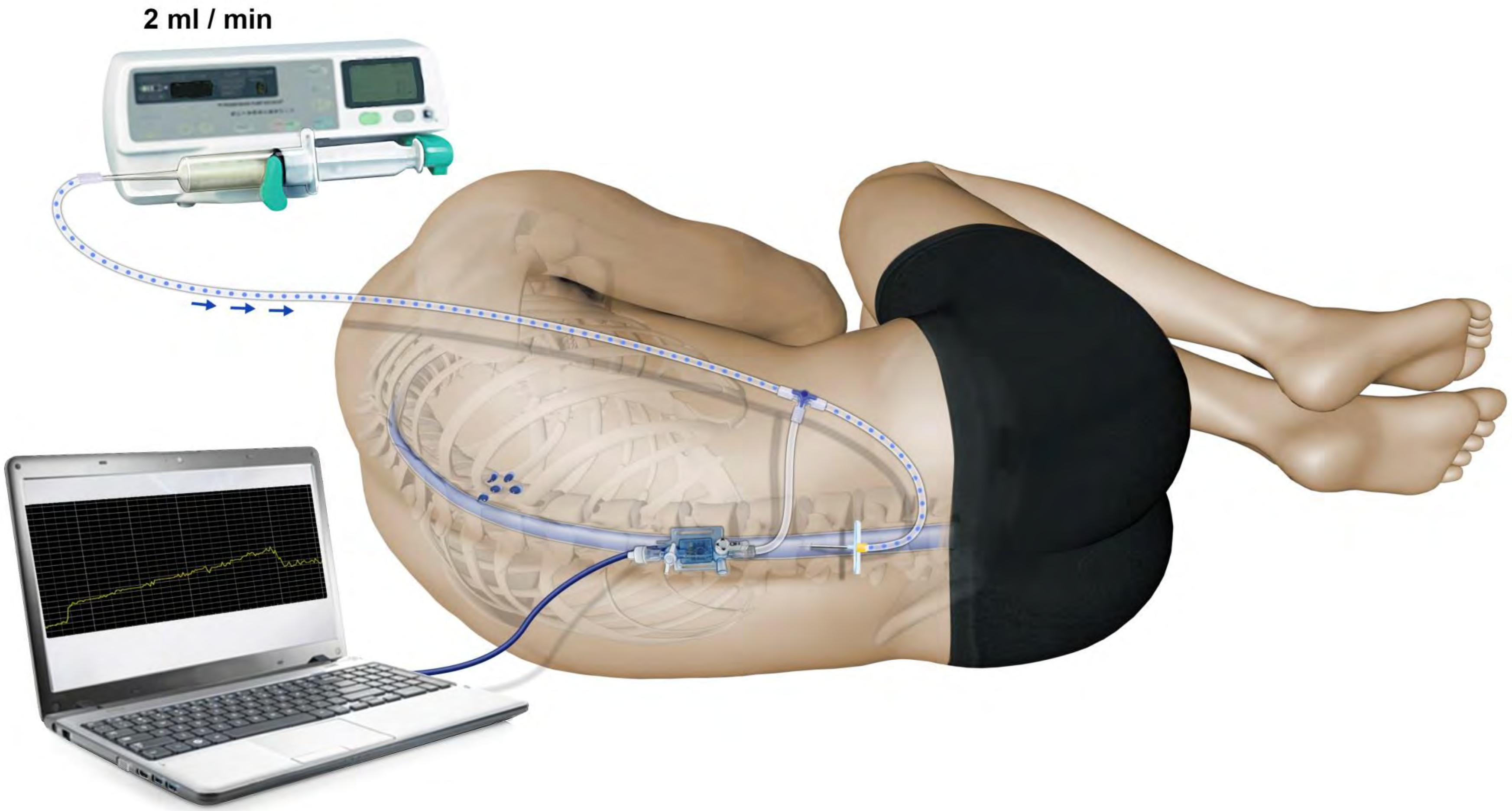
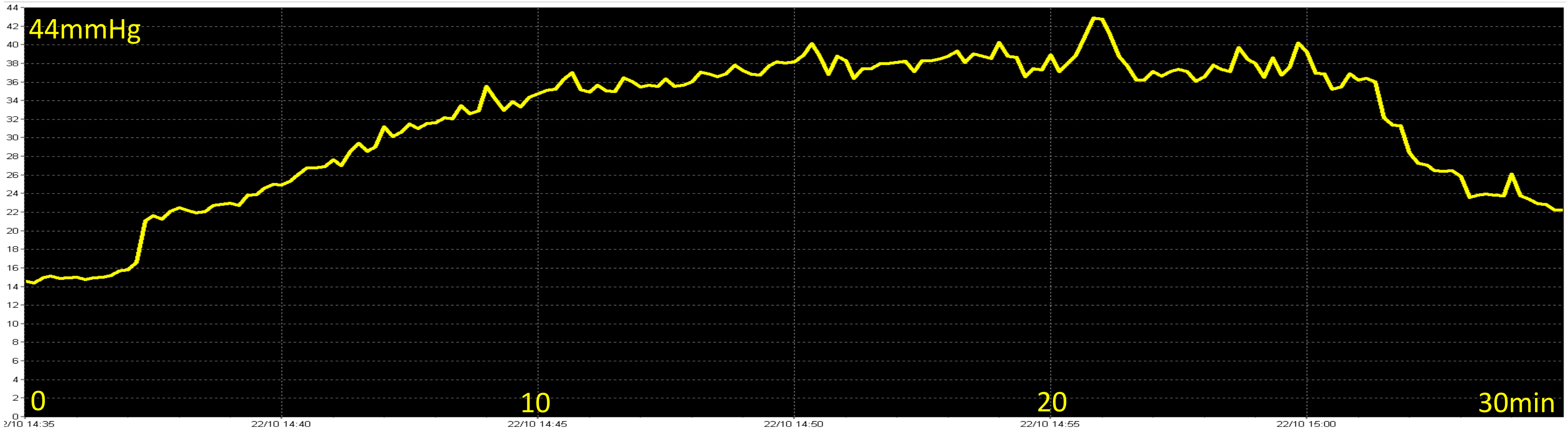
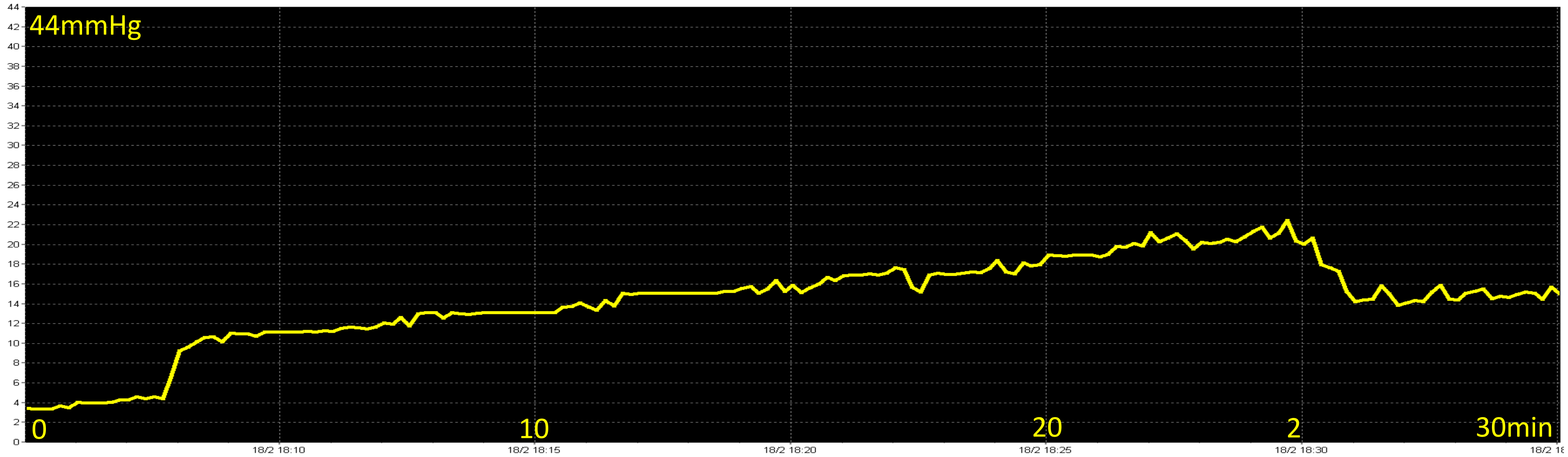
Lumbar infusion test



Beck et al. J Neurosurg Spine 2017

Lumbar infusion test – computerized *ICM+®*

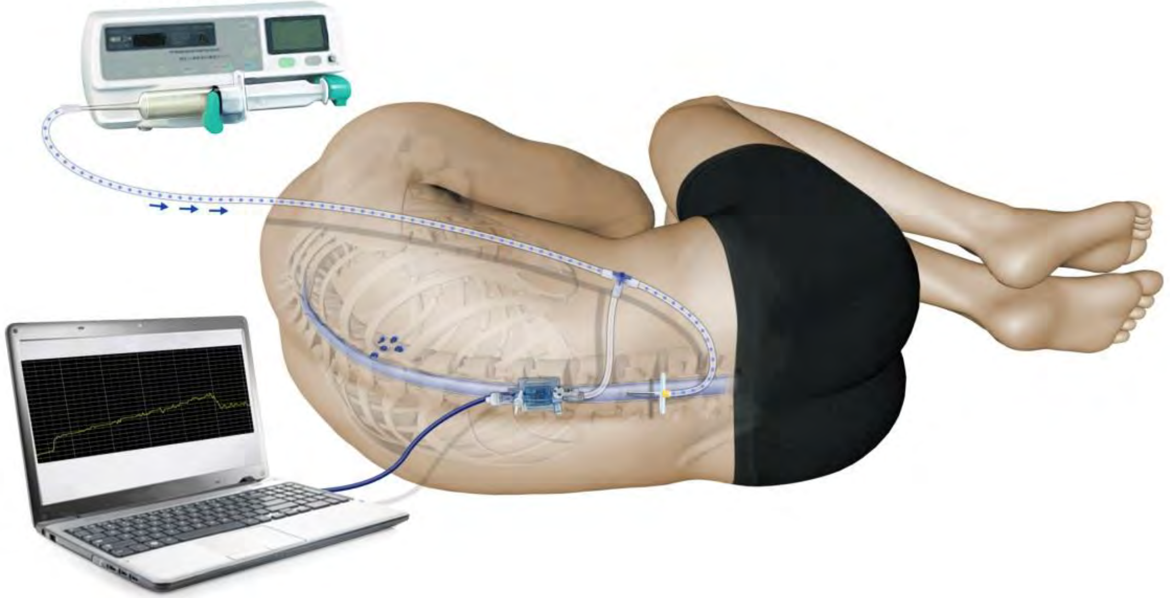




JNS SPINE
CLINICAL ARTICLE
J Neurosurg Spine 27:227–234, 2017

Cerebrospinal fluid outflow resistance as a diagnostic marker of spontaneous cerebrospinal fluid leakage

*Jürgen Beck, MD,[1] Christian Fung, MD,[1] Christian T. Ulrich, MD,[1] Michael Fiechter, MD,[1] Jens Fichtner, MD,[1] Heinrich P. Mattle, MD,[2] Marie-Luise Mono, MD,[2] Niklaus Meier, MD,[2] Pasquale Mordasini, MD,[3] Werner J. Z'Graggen, MD,[1] Jan Gralla, MD,[3] and Andreas Raabe, MD[1]



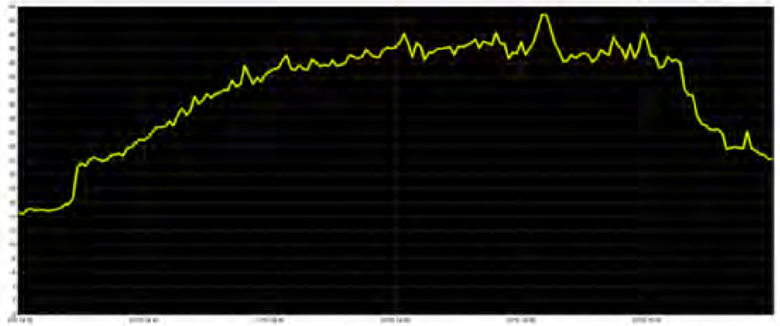


FIG. 4. Graph showing the pressure response of a computerized lumbar infusion test in a patient without a spinal CSF leak. Note the high opening pressure (about 14 mm Hg), with steep incline of pressure, which corresponds to the resistance of the needle after the start of the infusion. Thereafter, the graph shows a rather quick increase in pressure up to a plateau at about 38 mm Hg.

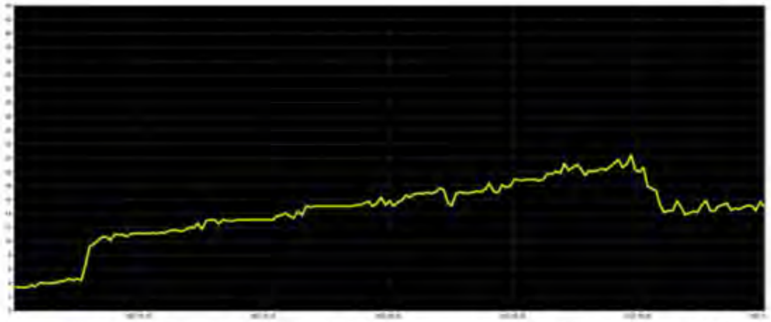


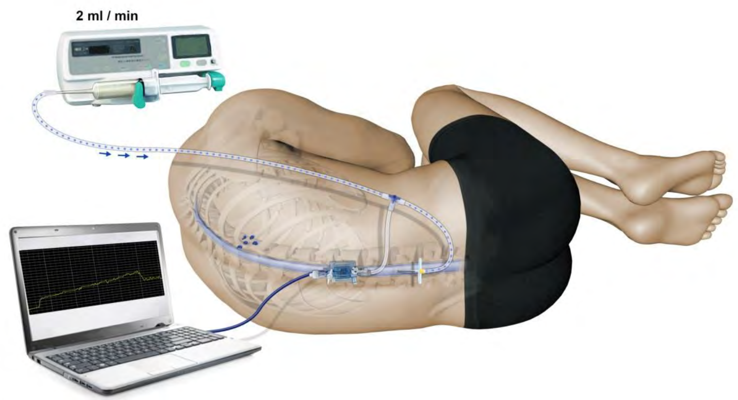
FIG. 5. Graph showing a pressure response of a computerized lumbar infusion test in a patient with a spinal CSF leak. Note the low opening pressure (about 4 mm Hg), with a steep incline of pressure, which corresponds to the resistance of the needle after start of the infusion. Thereafter, the graph shows a slow increase in pressure, without reaching a plateau. The maximum pressure is about 22 mm Hg.

The gold standard for a CSF leak

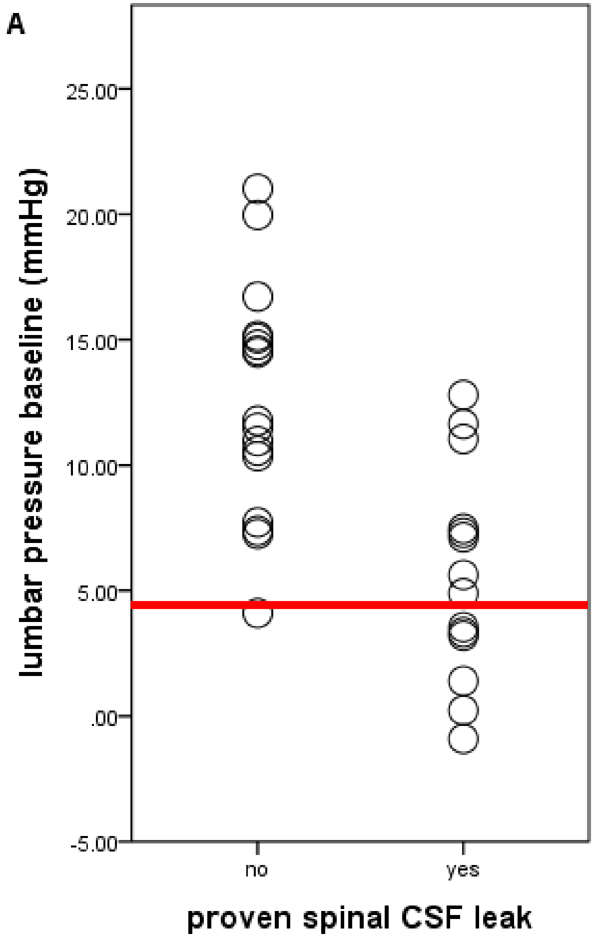
- extrathecal contrast after intrathecal application or
- visualization during microsurgery

Lumbar infusion test – *ICM+*

- 31 patients
- 17 females
- median 55 years
- 14 had proven spinal CSF leak



Lumbar pressure at baseline – *ICM+®*



57 % > 6 cm H_2O

4.4 mmHg ≈ 6 cm H_2O

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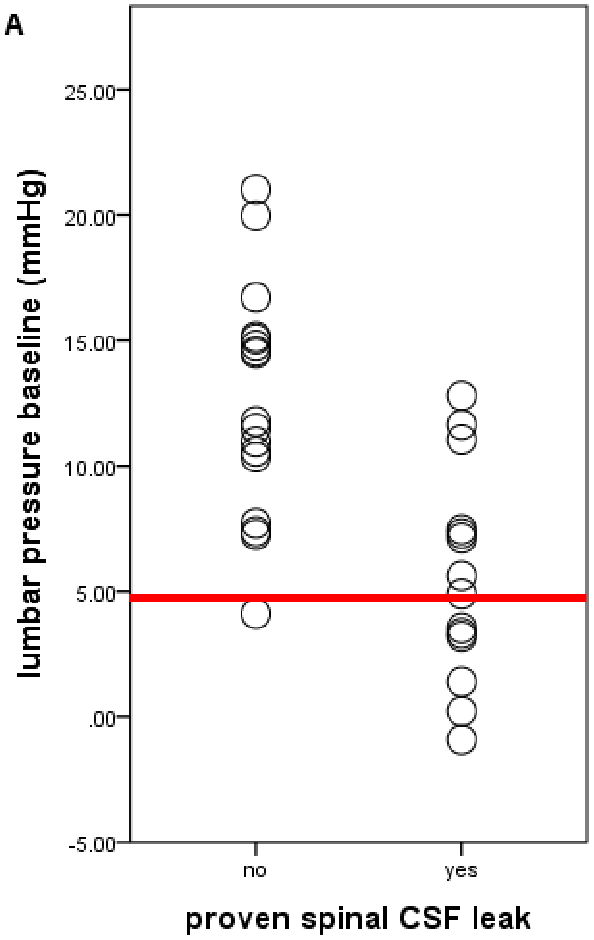
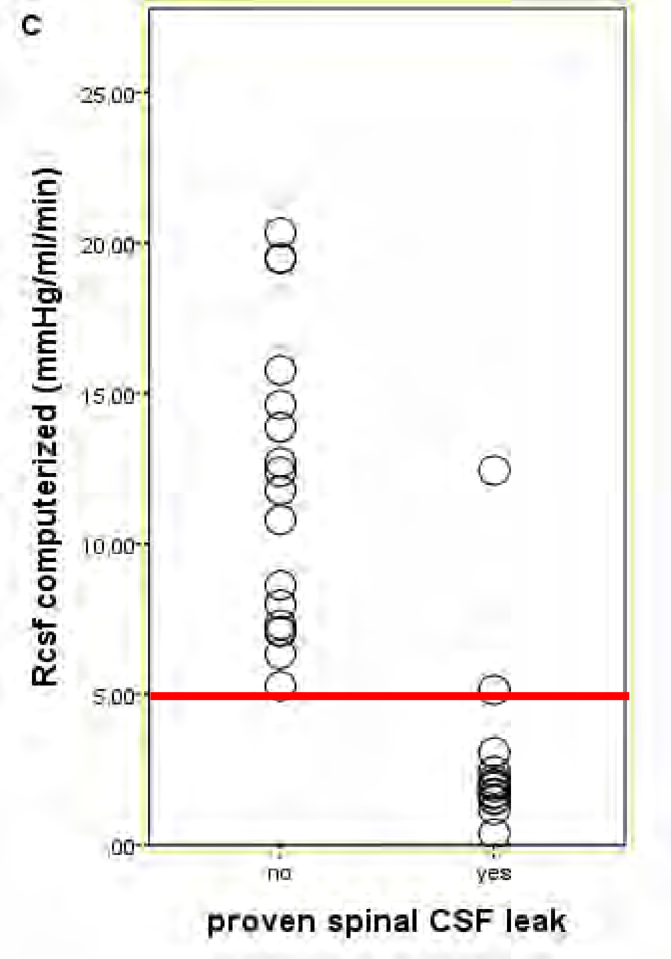
LP-baseline-P

R-CSF$_{out}$



57 %



14 %

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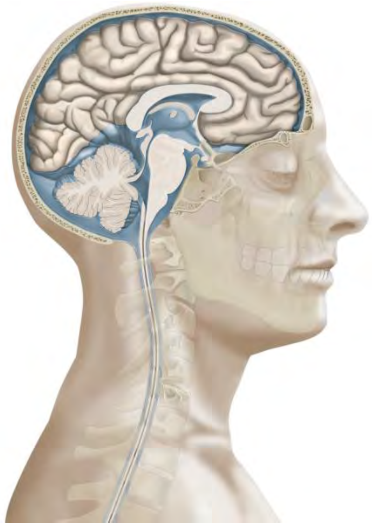
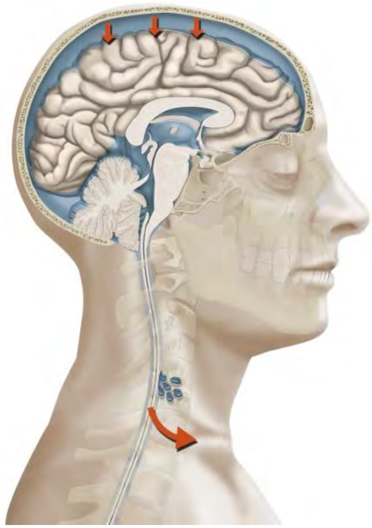
Lumbar pressure at baseline



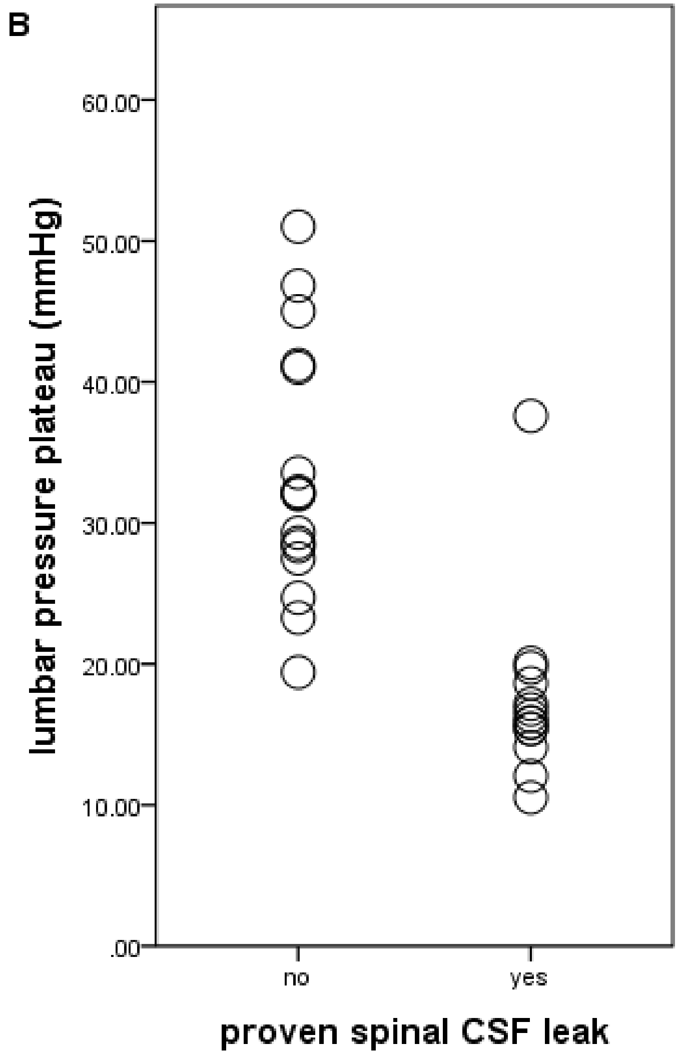
No spinal CSF leak: **11.77mmHg**

P<0.001



Proven spinal CSF leak: **5.26mmHg**

Lumbar pressure at plateau



No spinal CSF leak: **32.06mmHg**

P<0.001

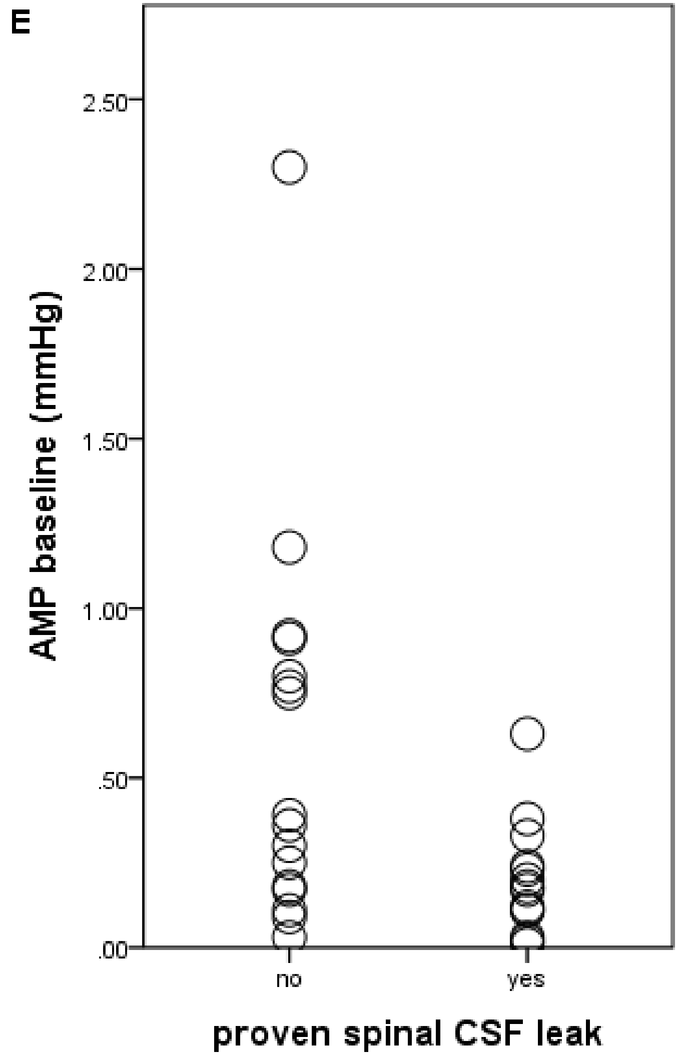
Proven spinal CSF leak: **16.11mmHg**

Pulse amplitude at baseline

Pulse amplitude (mmHg):

- The pulse amplitude is a pressure response (ΔP) to the transient increase in intracranial blood volume during a cardiac cycle (ΔV).
- Due to the exponential shape of the pressure–volume curve, pulse amplitude increases with increasing pressure.

Pulse amplitude at baseline



No spinal CSF leak: **0.38mmHg**

P<0.017

Proven spinal CSF leak: **0.18mmHg**

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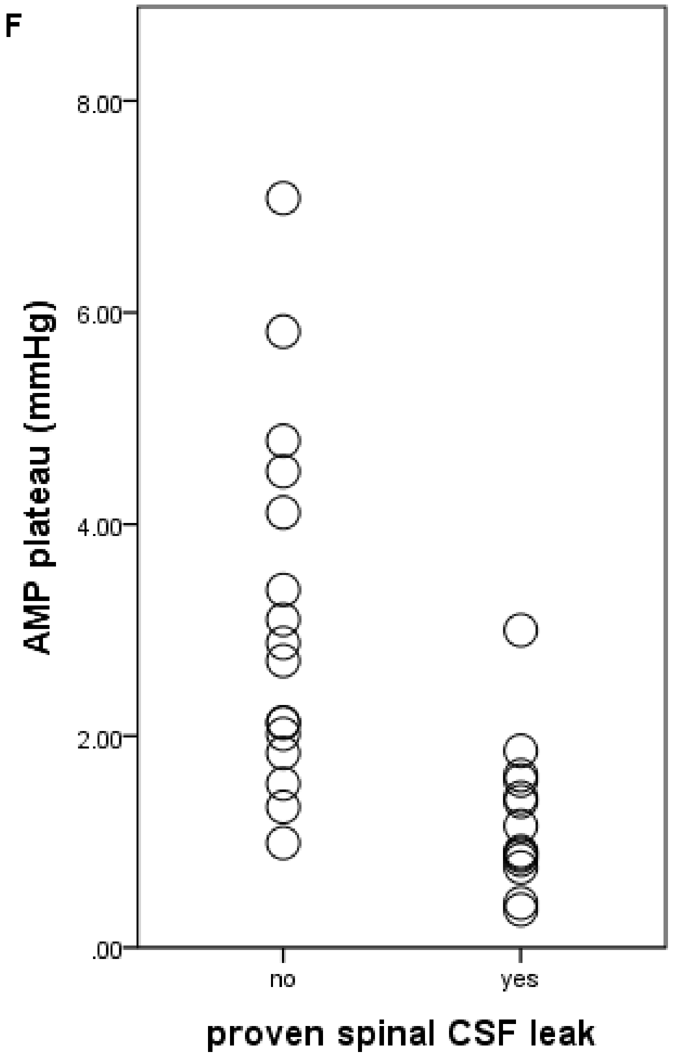
Pulse amplitude at plateau



No spinal CSF leak: **2.80mmHg**

P<0.001

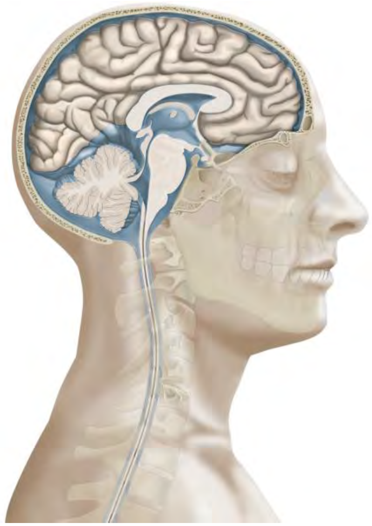
Proven spinal CSF leak: **1.03mmHg**

Resistance to CSF outflow computerized

Resistance to CSF outflow (mmHg/(ml/min):

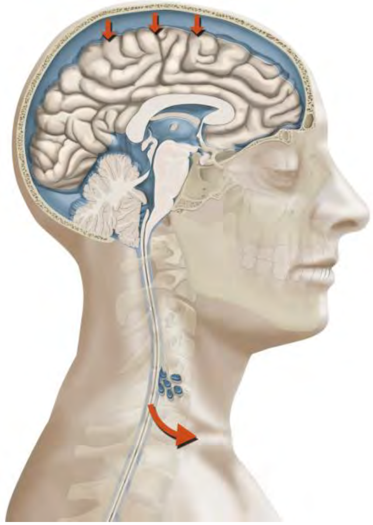
- The resistance to outflow measures the impedance to CSF drainage.
- It is equal to the effective pressure increase (ICP plateau - ICP baseline) divided by the rate of infusion.

Resistance to CSF outflow computerized



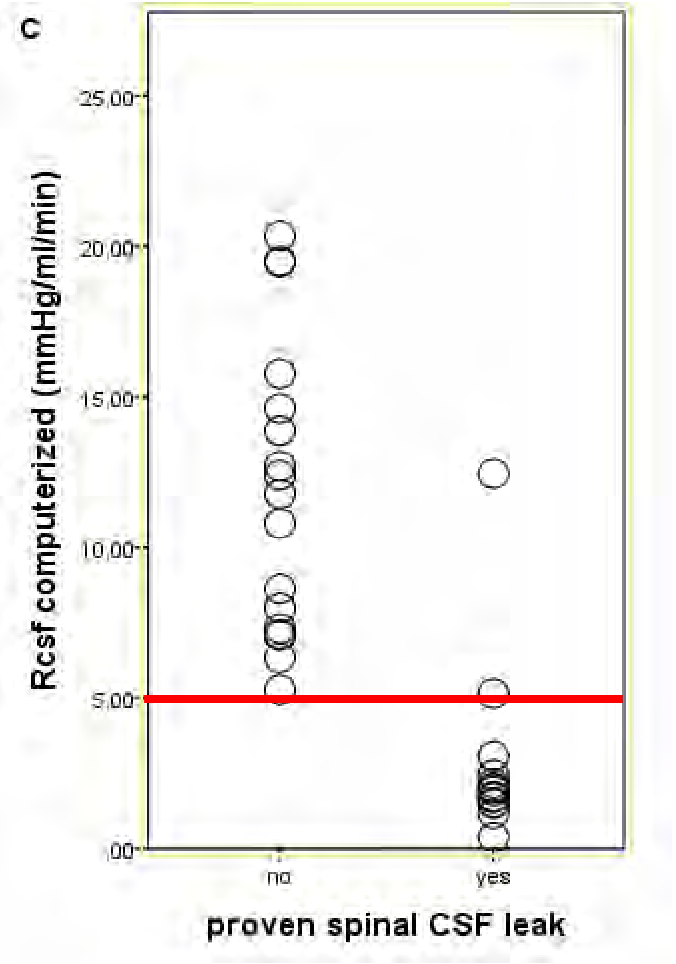
No spinal CSF leak: **11.78mmHg/ml/min**

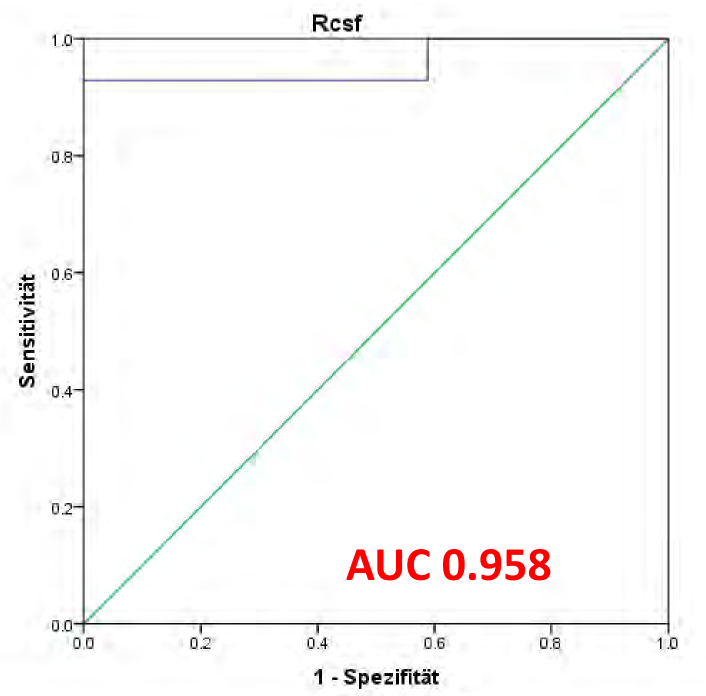
P<0.001



Proven spinal CSF leak: **1.97mmHg/ml/min**

Resistance to CSF outflow (Rcsf)



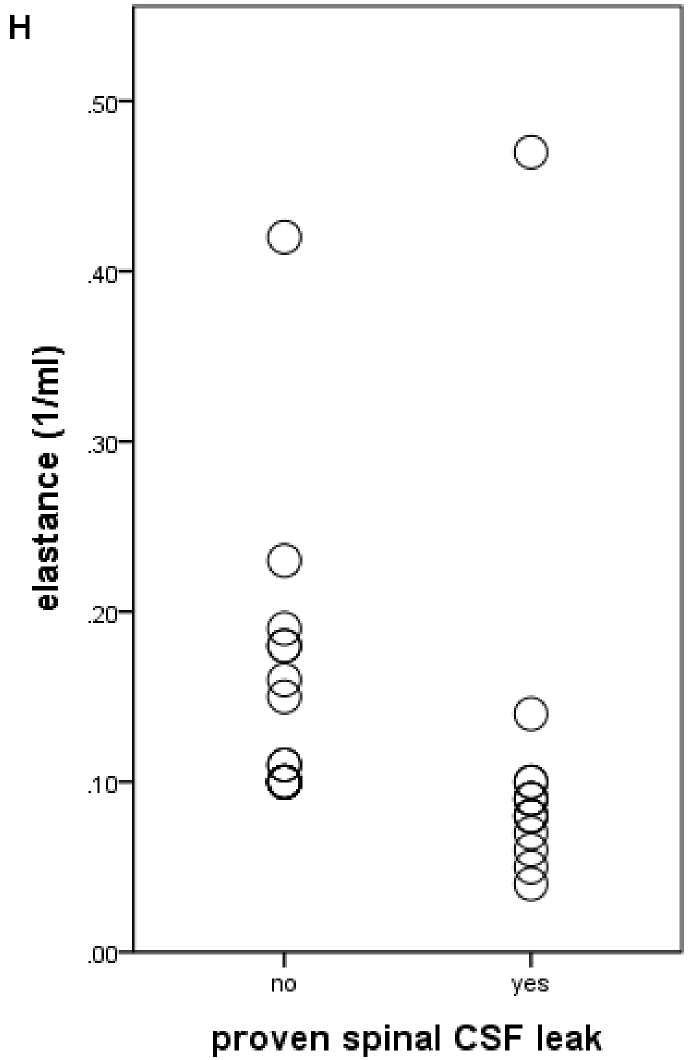


Elastance

Elastance:

The elastance coefficient describes the **stiffness** of the cerebrospinal system, e.g. the ability to compensate for a cerebrospinal volume increase.

Elastance



No spinal CSF leak: **0.11mmHg**

P<0.237

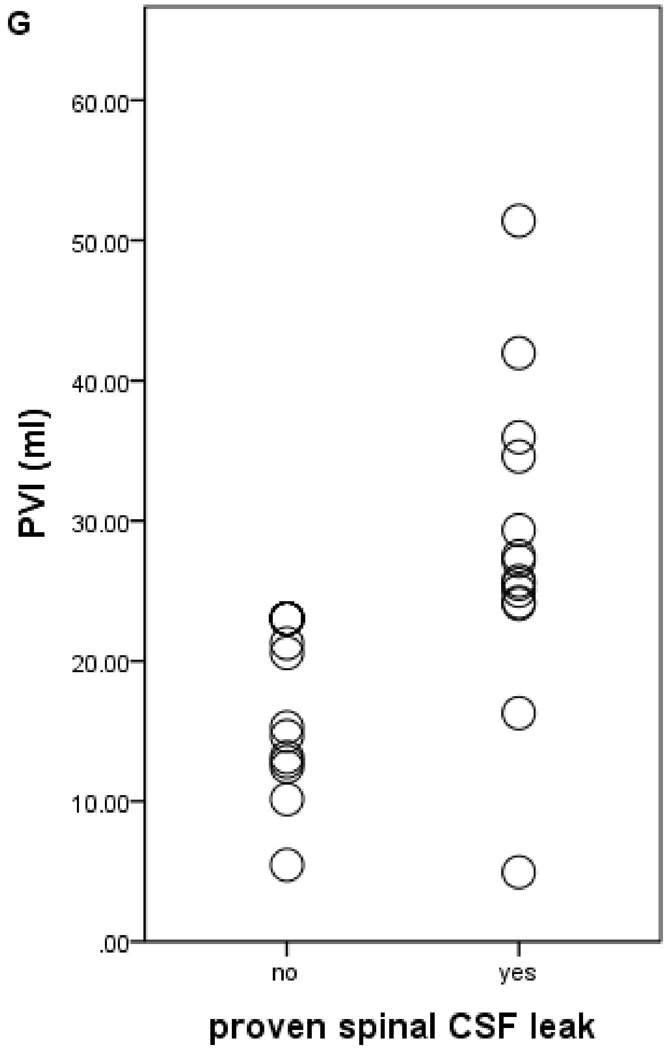
Proven spinal CSF leak: **0.09mmHg**

Pressure volume index

Pressure volume index (ml):

- The pressure volume index is the volume that has to be added to raise the pressure 10-fold.

Pressure volume index



No spinal CSF leak: **20.93ml**

P=0.003

Proven spinal CSF leak: **26.43ml**

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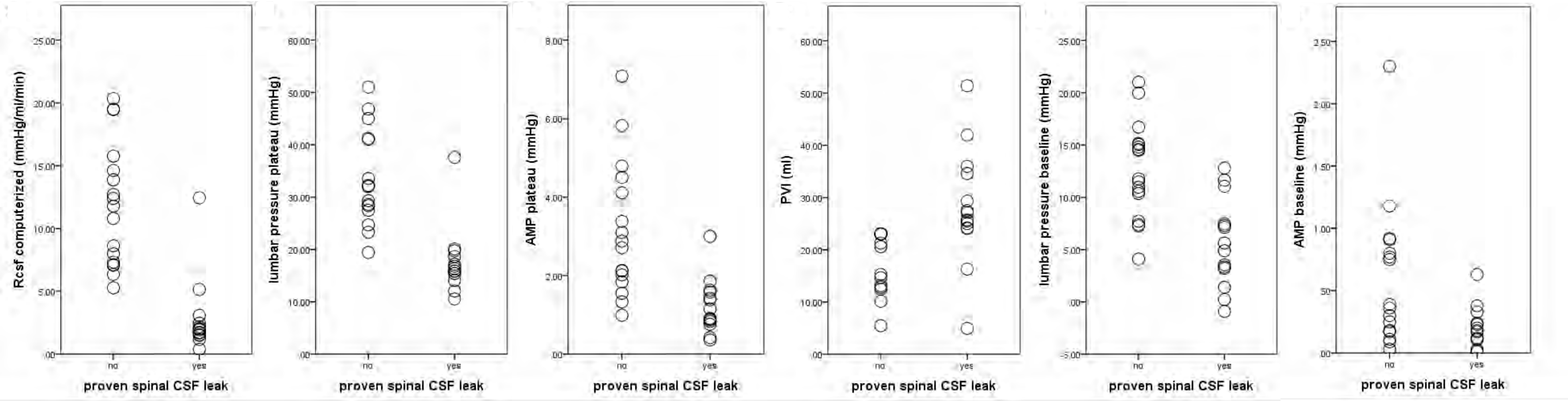
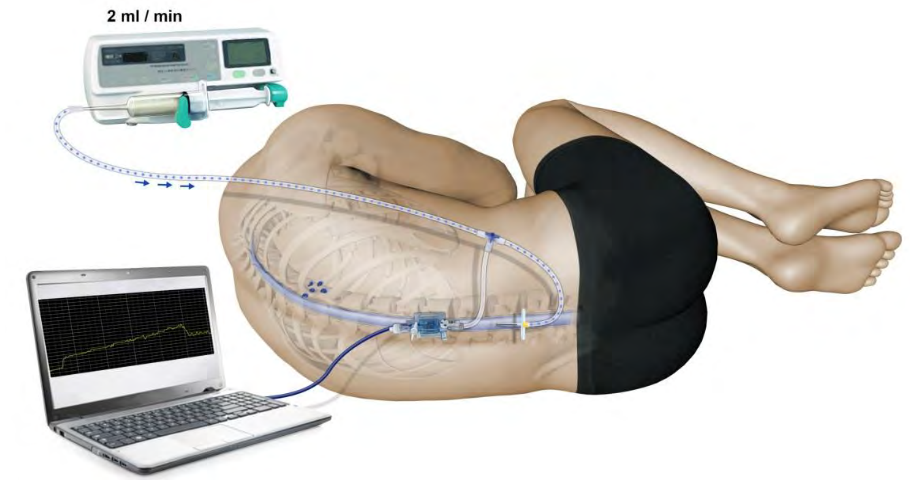
Results



	No leak		Proven leak			ROC
	Median	IQR	Median	IQR	P-value	AUC
R_{CSF} computerized	11·78	7·22–15·20	1·97	1·53–2·62	<0·001	0·958
Lumbar pressure plateau	32·06	27·71–41·15	16·11	15·08–18·91	<0·001	0·942
AMP plateau	2·80	1·89–4·40	1·03	0·81–1·59	<0·001	0·893
Pressure volume index	20·93	12·90–23·04	26·43	24·18–34·93	0·003	0·888
Lumbar pressure baseline	11·77	9·04–15·10	5·26	2·75–8·37	<0·001	0·866
AMP baseline	0·38	0·17–0·88	0·18	0·09–0·26	0·017	0·752

Lumbar infusion test – *ICM+®*



- Specific pattern of CSF dynamics
- Investigator independent
- **Rcsf out** may be the best CSK leak specific diagnostic parameter

Beck et al. J Neurosurg Spine 2017

Anatomy of the Optic Nerve Sheath

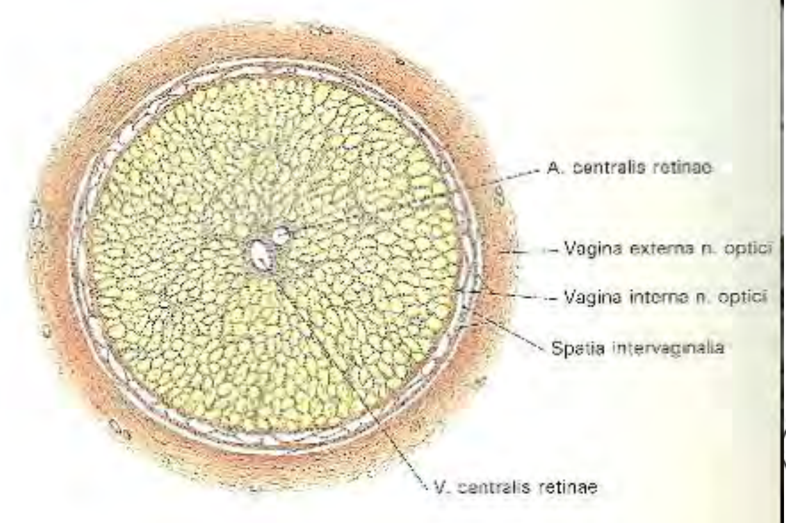
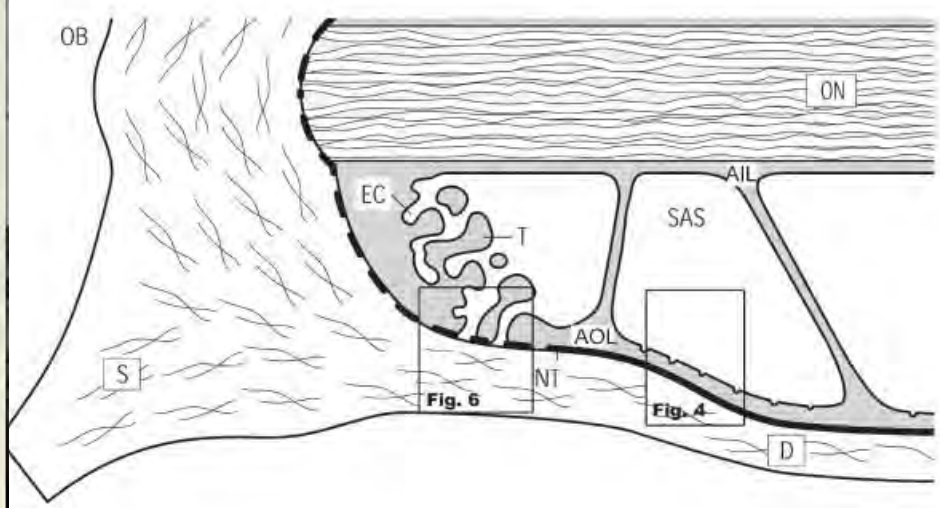
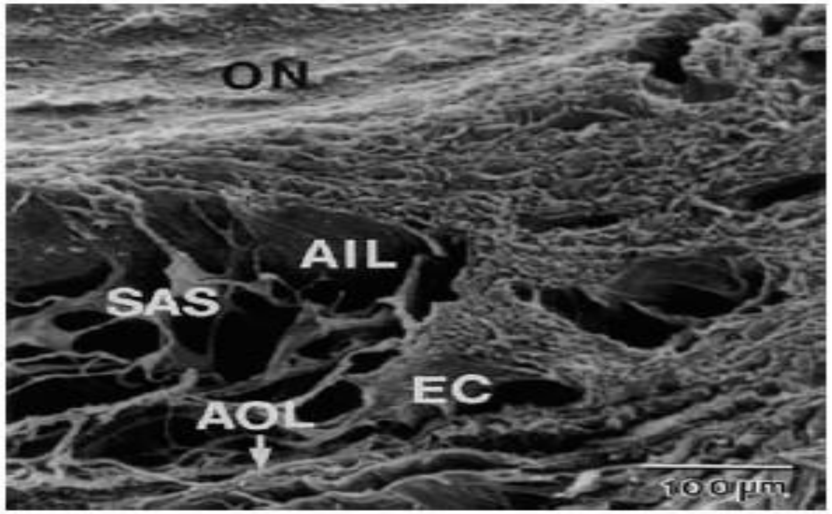


Abb. 128
Querschnitt durch den N. opticus nahe des Bulbus oculi.





- Lüdemann W, Berens von Rautenfeld D, Samii M, Brinker T: Ultrastructure of the cerebrospinal fluid outflow along the optic nerve into the lymphatic system. Child Nerv. Syst. 21, 96-103: 2005
- www.glaucoma.org

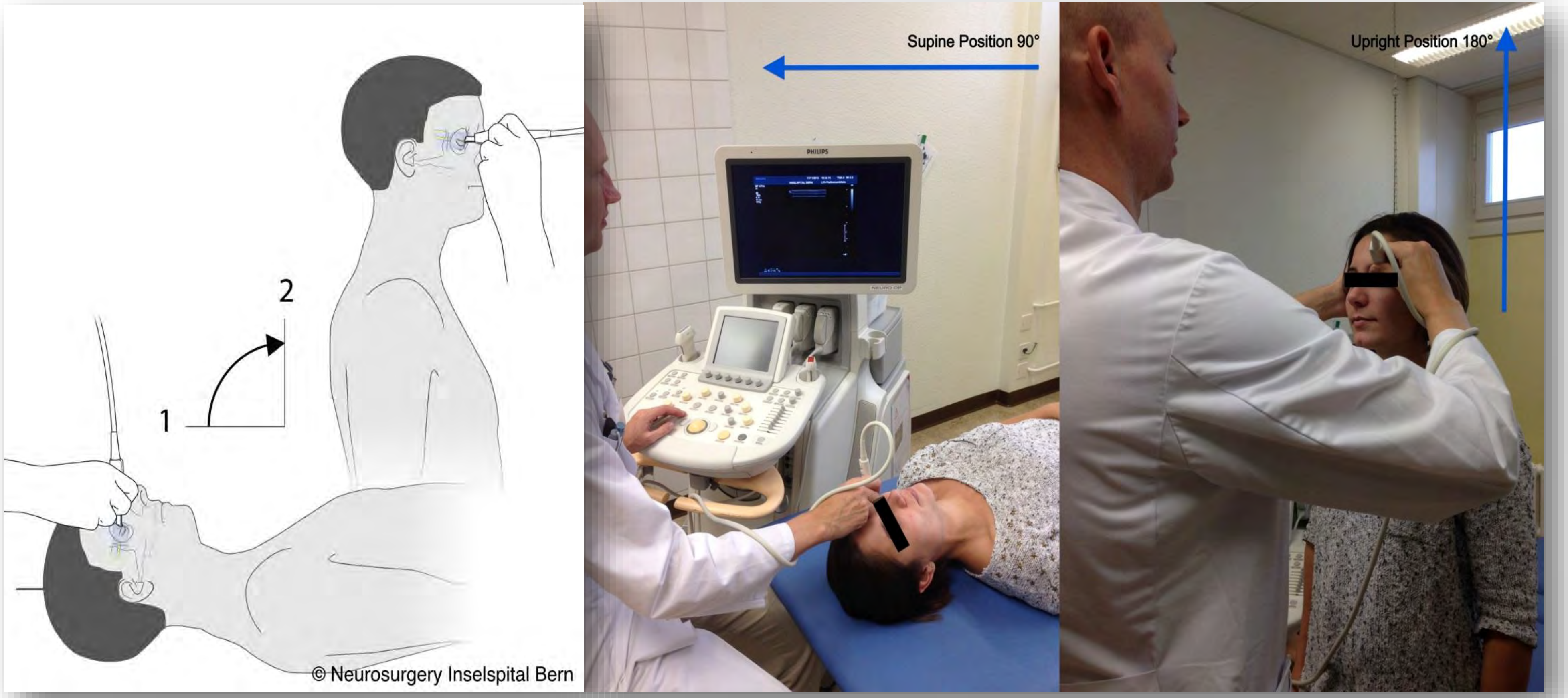
BF 75Hz
A1
2D
98%
K 51
M Aus
HAllg
ONSD RE SAG LI
Vitreous Body
AGC
S1
3mm
ON
SAS / T
ONS
3.7
Abstand 0.305 cm
Abstand 0.603 cm

Results – Diameter

No statistically significant difference of ONSD

0.538cm ± 0·091 vs. **0.539cm** ± 0.090; **p=0.957**

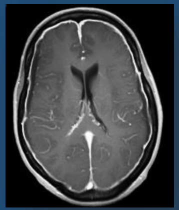
Diagnostic work-up CSF-leak-protocol



- **First in supine position -> secondary in upright position**

Diagnostic work-up CSF-leak-protocol

Patients with newly suspected SIH



n=44

Patients **with active/current** orthostatic headaches

n=18

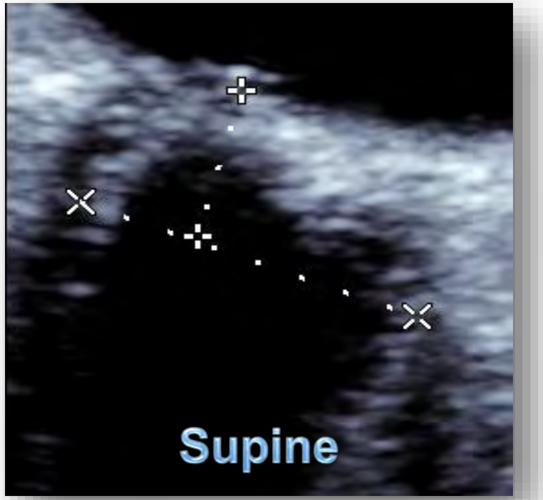
Patients **without active/current (or history) of** orthostatic headaches

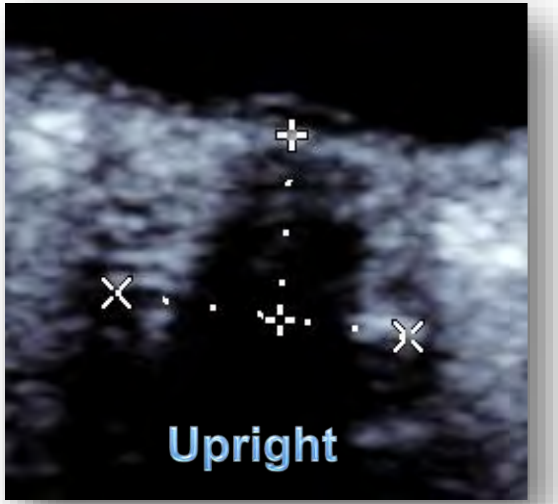
n=26

Results – Diameter

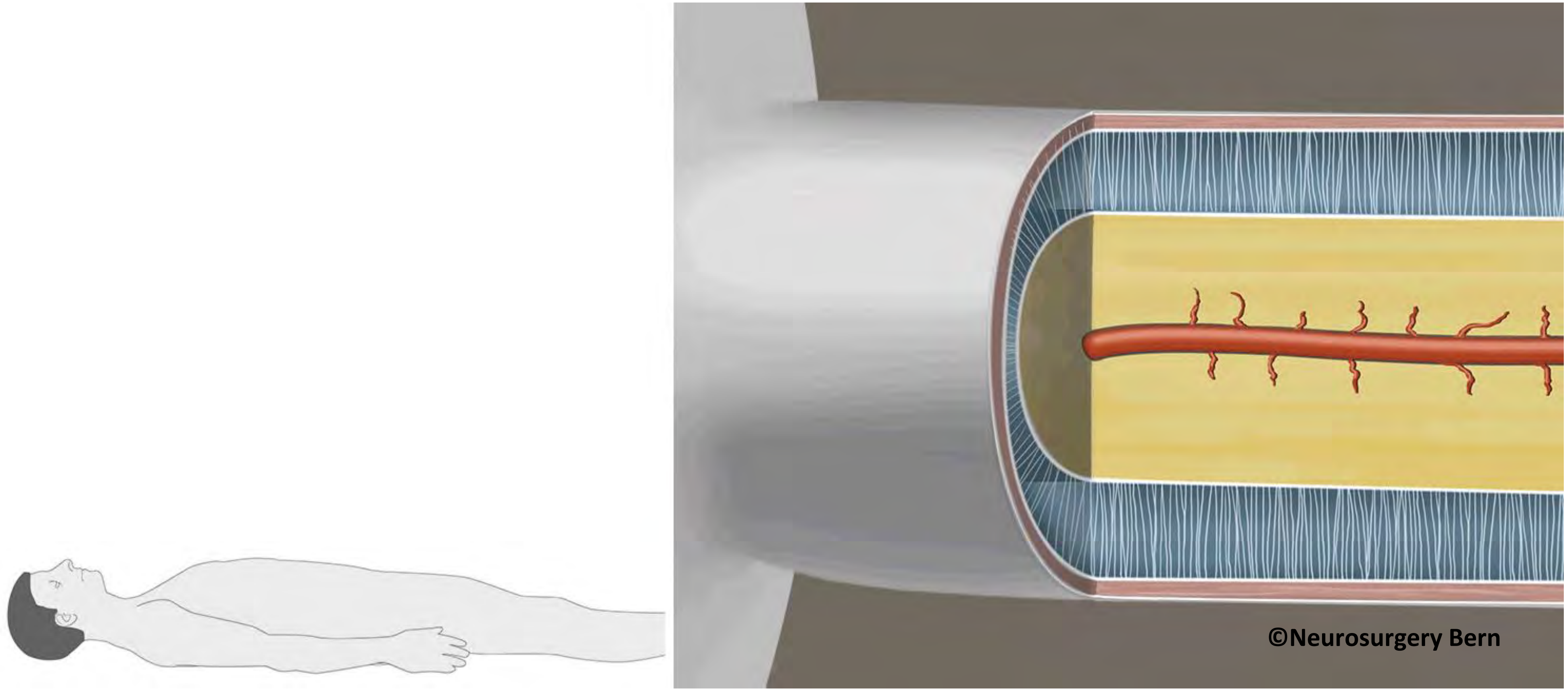
Significant difference between supine and upright position in patients with orthostatic headaches

ONSD Supine = **0.549cm** ± 0.097 vs. Upright = **0.484cm** ± 0·095; **p=0.036**





Ultrasound of the optic nerve sheath



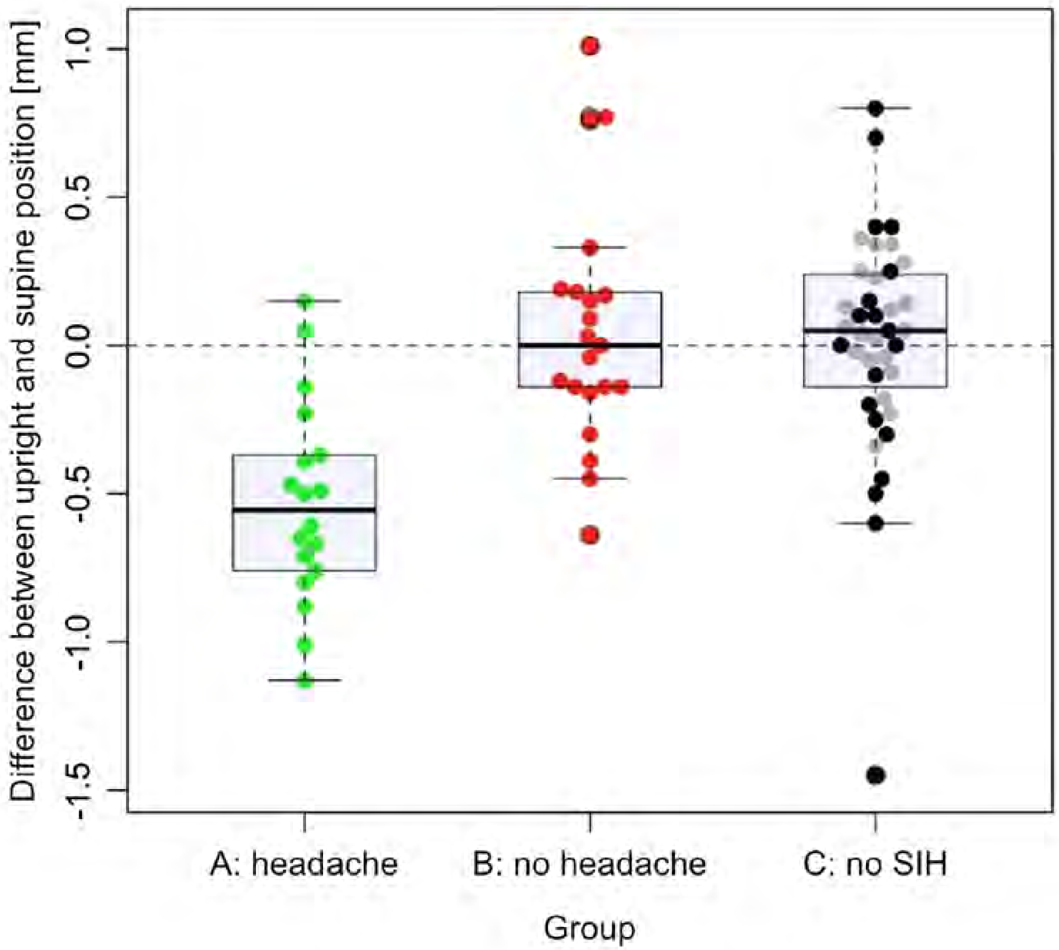
Fichtner et al. J Neurol Neurosurg Psychiatry August 2015

OPEN ACCESS

RESEARCH PAPER

Management of spontaneous intracranial hypotension – Transorbital ultrasound as discriminator

Jens Fichtner,[1] Christian T Ulrich,[1] Christian Fung,[1] Christin Knüppel,[2] Martina Veitweber,[2] Astrid Jilch,[1] Philippe Schucht,[1] Michael Ertl,[2] Beate Schömig,[2] Jan Gralla,[3] Werner J Z'Graggen,[1,4] Corrado Bernasconi,[5] Heinrich P Mattle,[4] Felix Schlachetzki,[2] Andreas Raabe,[1] Jürgen Beck[1]



JNNP 2015

Before and After Microsurgical Closure of a CSF leak

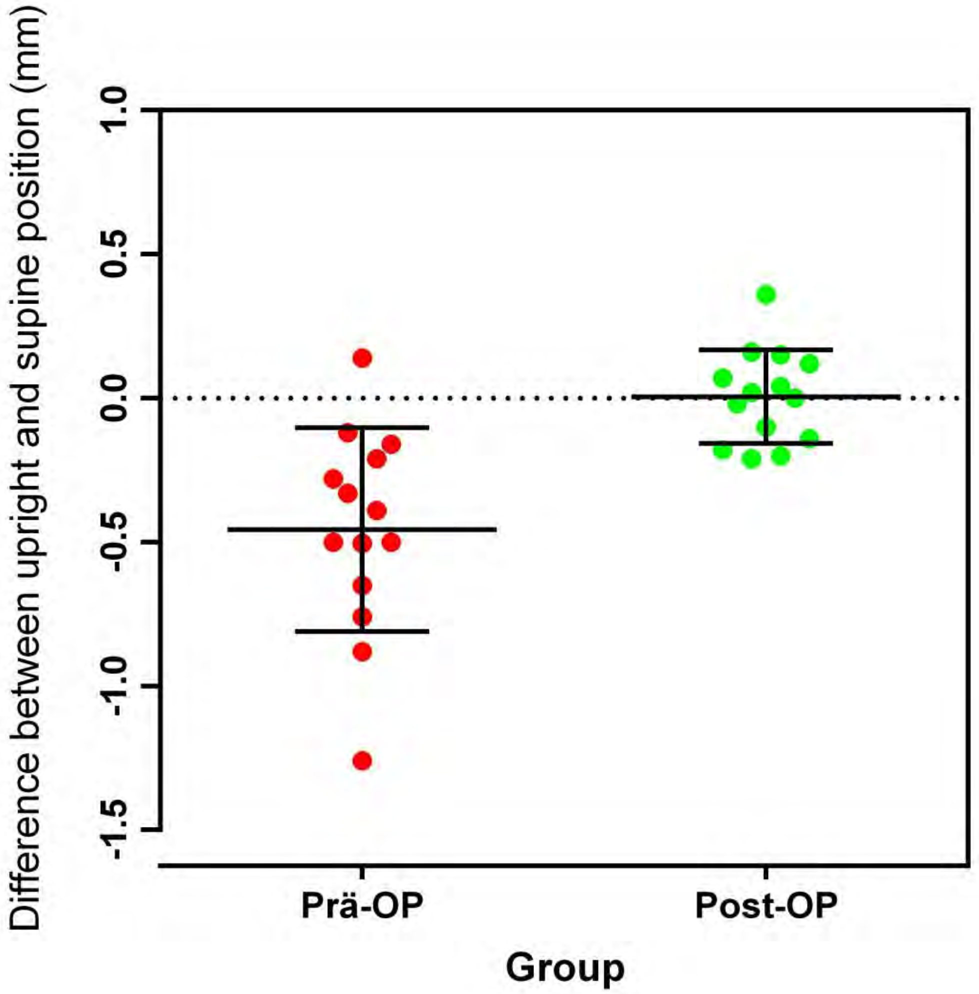
- assessment of the ONSD in Patients with spontaneous intracranial hypotension two times
- 14 Patients with proven fistula in myelography and surgery
- compared ONSD before and after surgery

Before and After Microsurgical Closure of a CSF leak

- Significantly different between supine and upright position before surgery
- 5.1mm vs. 4.7mm; p=0.002

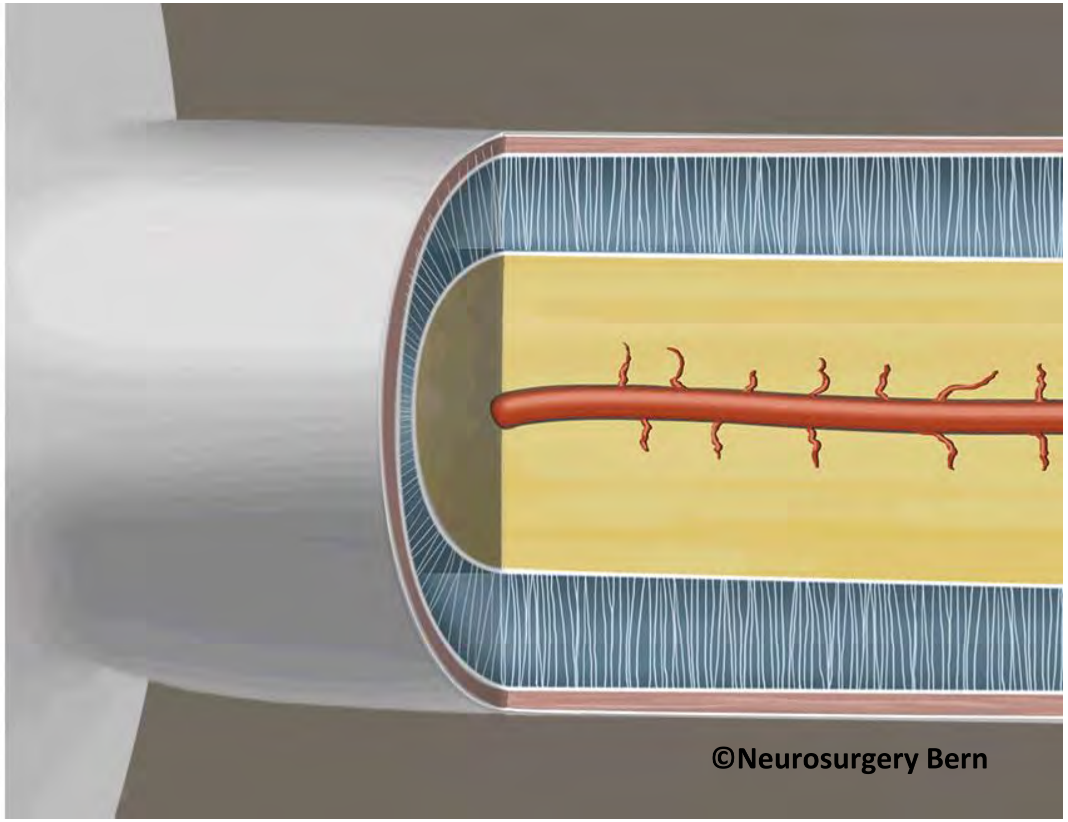
- No significant different between supine and upright position after surgery
- 5.3mm vs. 5.3mm; p=0.940

Transorbital ultrasound – before and after closure of the CSF leak



Δ = -0.5mm vs. 0.01mm;p=0.004

Ultrasound of the optic nerve sheath



Fichtner et al. J Neurol Neurosurg Psychiatry August 2015

Table 3 Magnetic resonance imaging findings

S Subdural fluid collection

E Enhancement of meninges

E Engorgement of veins

P Pituitary hyperaemia

S Sagging of brain

Schievink W, Cephalgia, Dez 2008

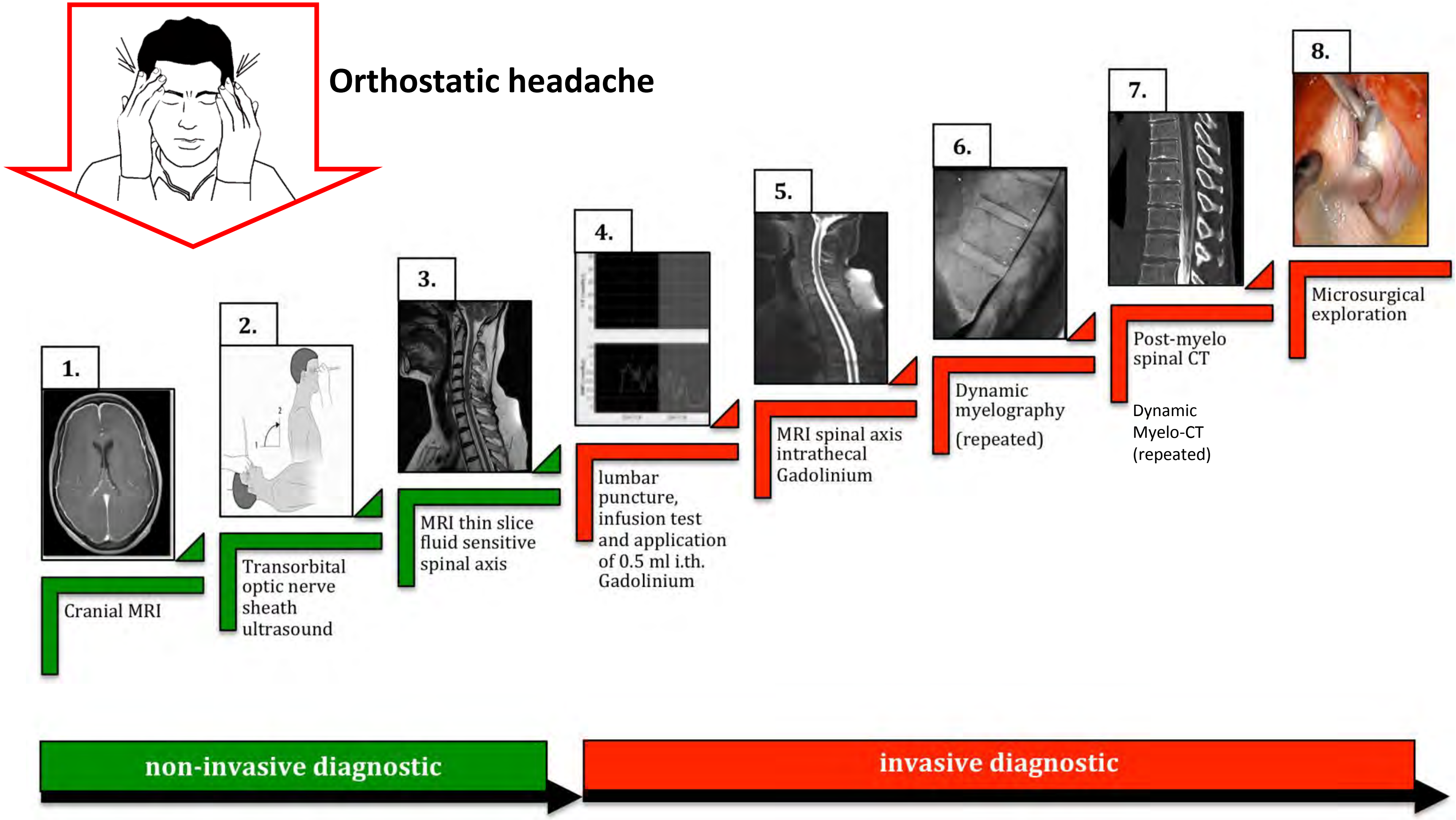
Predicting spinal CSF leaks in intracranial hypotension: a scoring system based on brain MRI findings

Tomas Dobrocky,[1] Lorenz Grunder,[1] Philipe S Breiding,[1] Mattia Branca,[2] Andreas Limacher, [2] Pascal J Mosimann,[1] Pasquale Mordasini,[1] Felix Zibold,[1] Levin Haeni,[3] Christopher M Jesse,[3] Christian Fung,[3,4] Andreas Raabe,[3] Christian T Ulrich,[3] Jan Gralla,[1] Jürgen Beck,[3,4*] Eike I Piechowiak[1*]

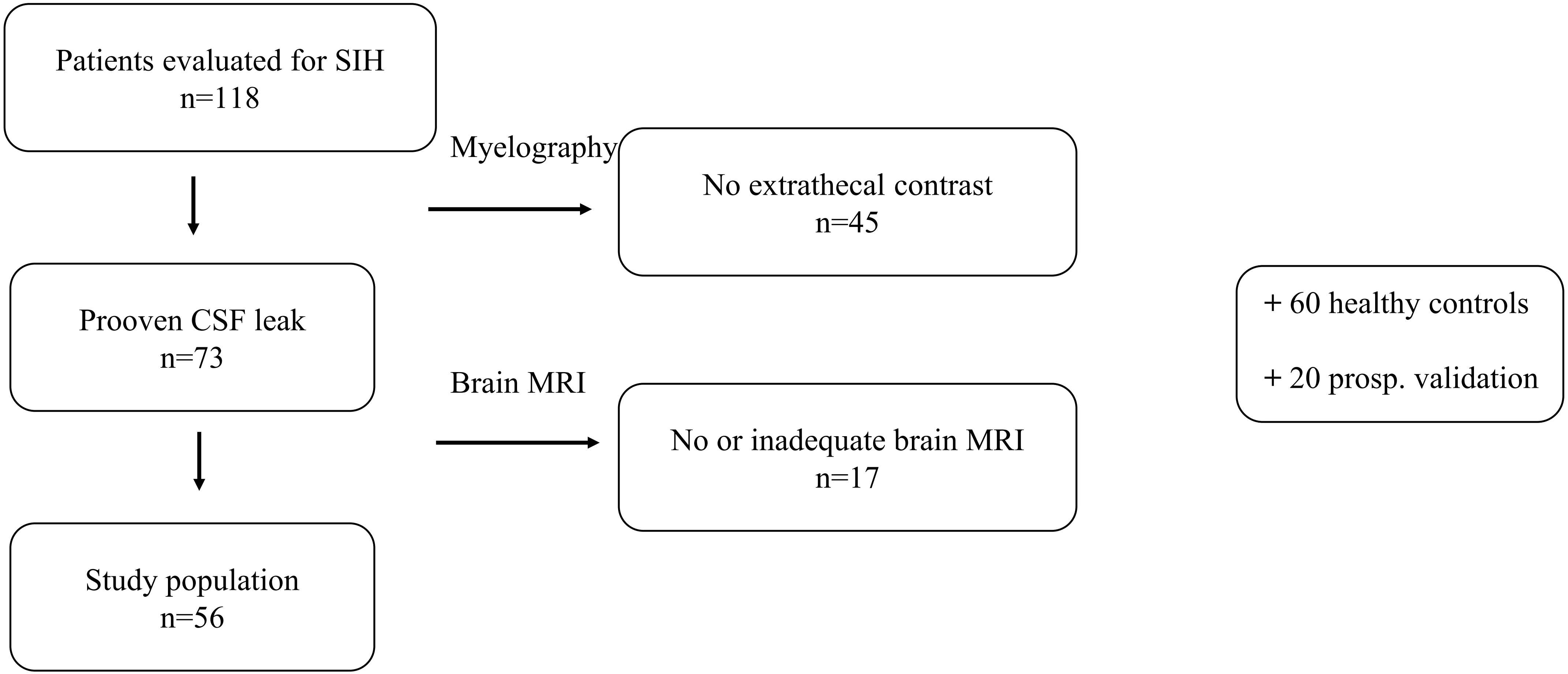
(1) University Institute of Diagnostic and Interventional Neuroradiology, University of Bern, Inselspital, Bern, Switzerland
(2) CTU Bern, and Institute of Social and Preventive Medicine (ISPM), University of Bern, Switzerland
(3) Department of Neurosurgery, University of Bern, Inselspital, Bern, Switzerland
(4) Department of Neurosurgery, Medical Center — University of Freiburg, Germany

Dobrocky... Piechowiak et al. submitted

Diagnostic work-up   Bern-Freiburg CSF-leak-protocol



Predicting spinal CSF leaks based on brain MRI findings



Dobrocky... Piechowiak et al. submitted

The gold standard for a CSF leak

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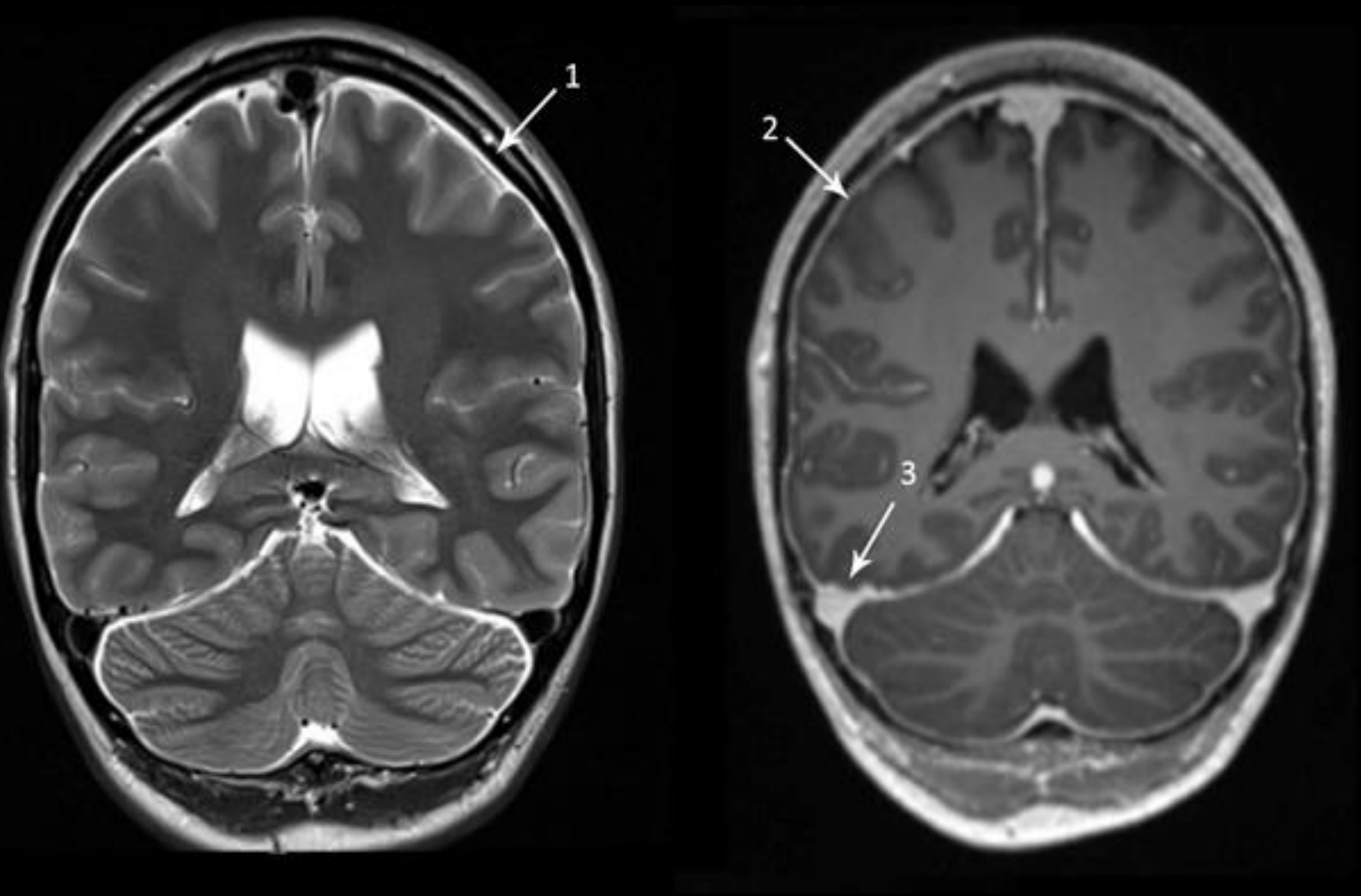
- visualization during microsurgery


1
2
3

Qualitative	Quantitative
Engorgement of venous sinus	Pontomesencephalic angle
Distended inferior intercavernous sinus	Suprasellar cistern
Pachymeningeal enhancement (smooth and diffuse)	Prepontine cistern
Midbrain descent (subjective)	Midbrain descent (iter to incisural line)
Superficial siderosis	Venous-hinge angle
Subdural fluid collection	Mamillopontine distance
Superior surface of pituitary (concave, flat, convex)	Pituitary height
	Tonsillar herniation (relating to McRae line)
	Area cavum veli interpositi

Qualitative	Quantitative
Engorgement of venous sinus	Pontomesencephalic angle
Distended inferior intercavernous sinus	**Suprasellar cistern**
Pachymeningeal enhancement (smooth and diffuse)	**Prepontine cistern**
Midbrain descent (subjective)	Midbrain descent (iter to incisural line)
Superficial siderosis	Venous-hinge angle
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Superior surface of pituitary (concave, flat, convex)	Pituitary height
	Tonsillar herniation (relating to McRae line)
	Area cavum veli interpositi

Qualitative	Quantitative
2 **Engorgement of venous sinus**	Pontomesencephalic angle
Distended inferior intercavernous sinus	**Suprasellar cistern** 2
2 **Pachymeningeal enhancement (smooth and diffuse)**	**Prepontine cistern**
Midbrain descent (subjective)	Midbrain descent (iter to incisural line)
Superficial siderosis	Venous-hinge angle
Subdural fluid collection	**Mamillopontine distance**
Superior surface of pituitary (concave, flat, convex)	Pituitary height
	Tonsillar herniation (relating to McRae line)
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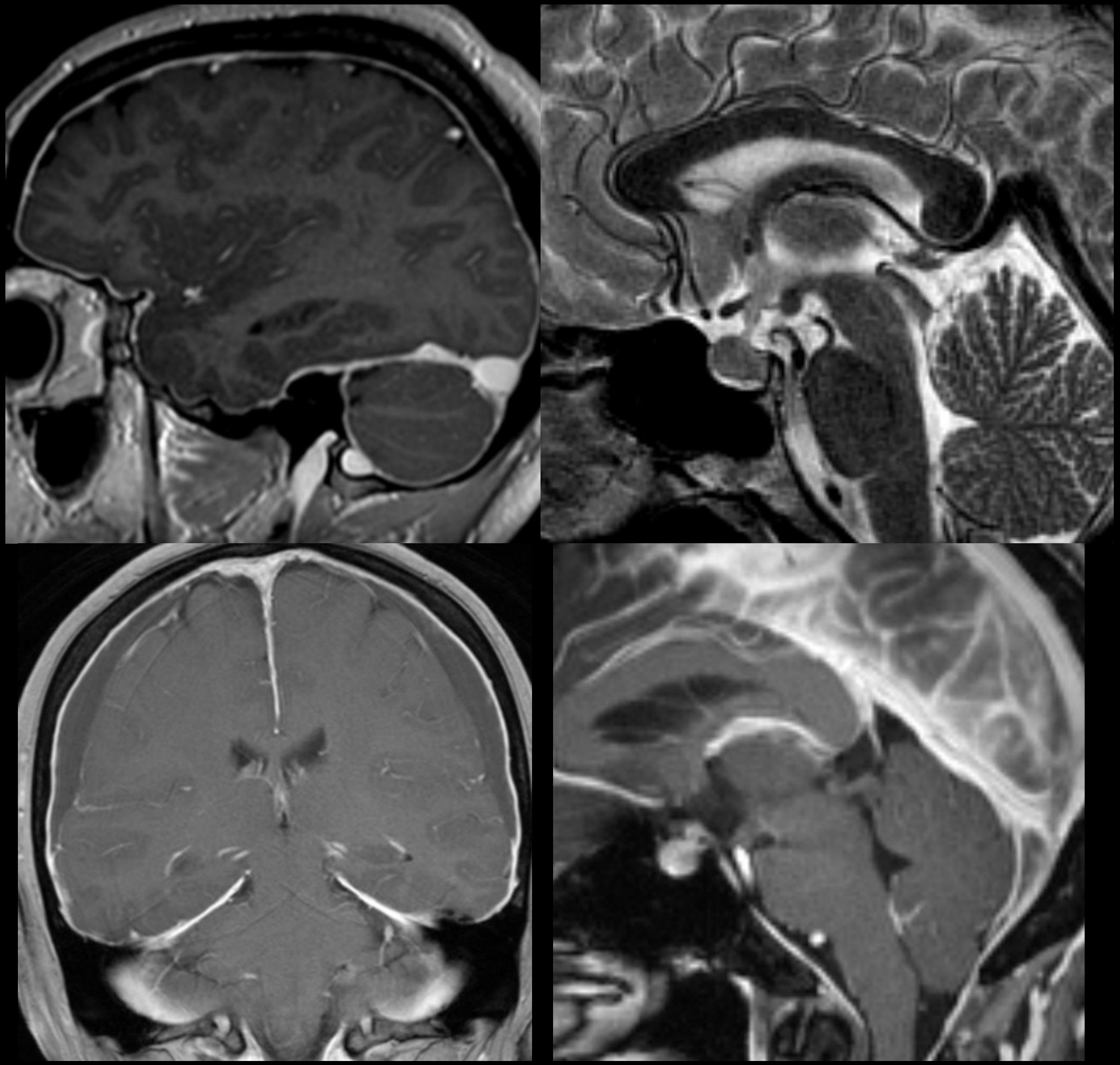
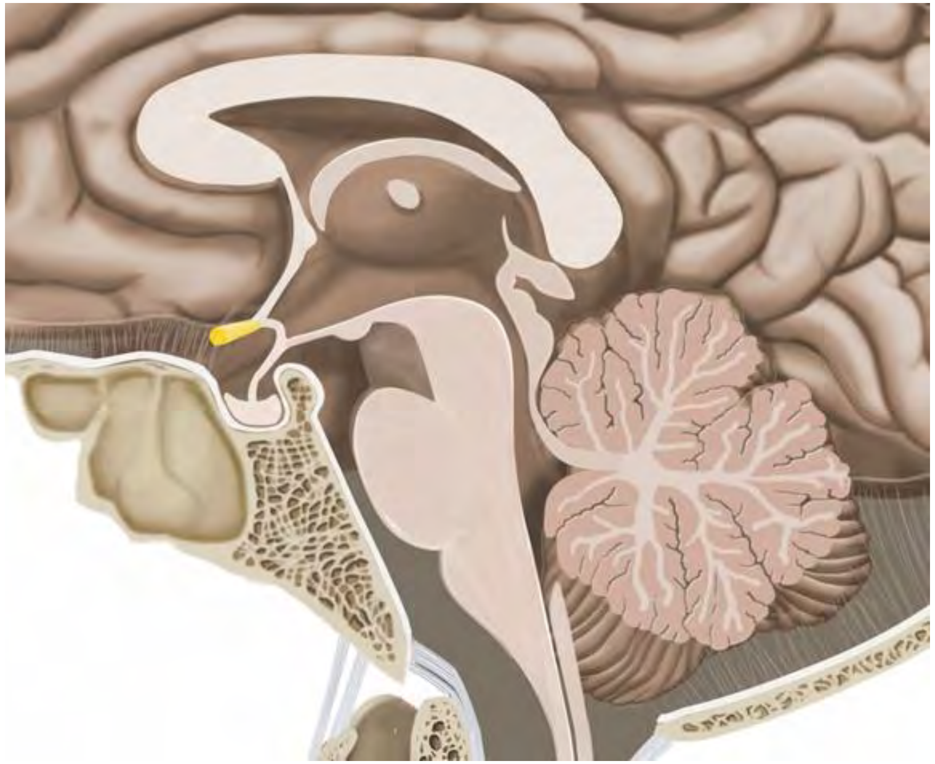
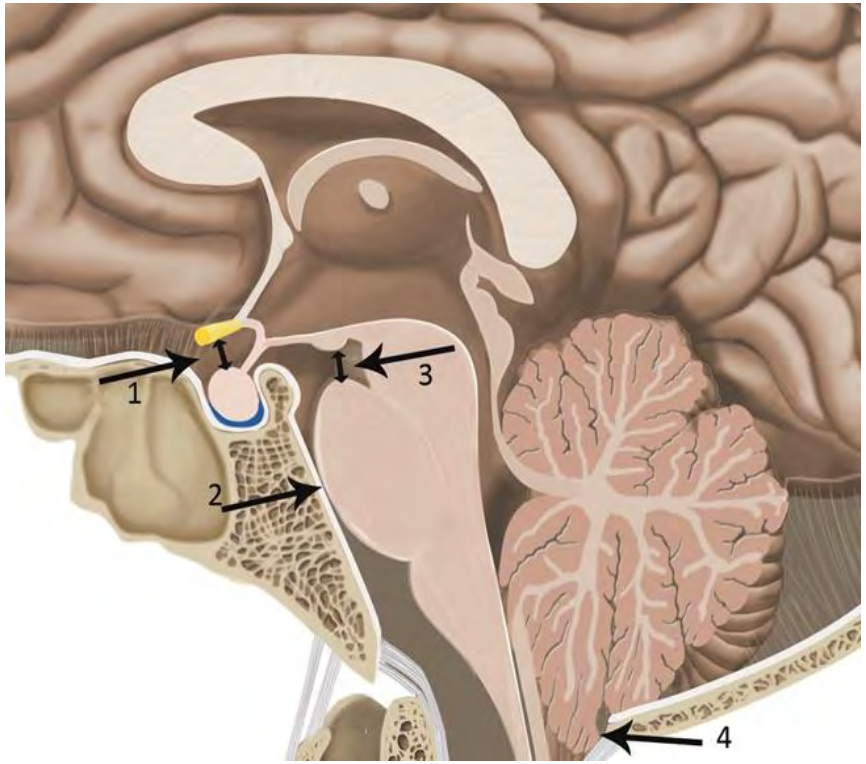






Dobrocky et al. submitted

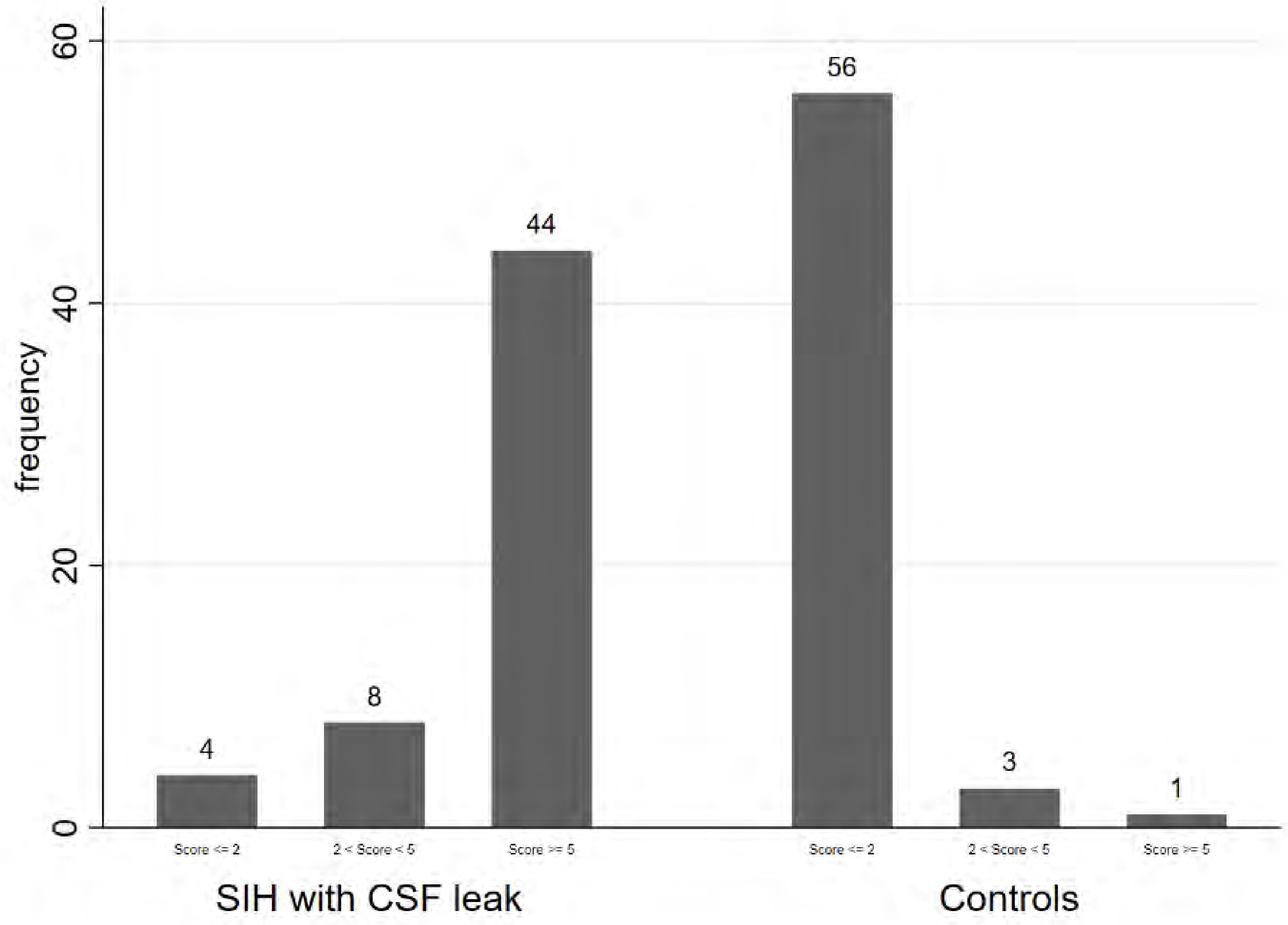
- 4 mm **Suprasellar cistern**
- 5 mm **Prepontine cistern**
- 6.5 mm **Mamillo-pontine distance**

1
2
3

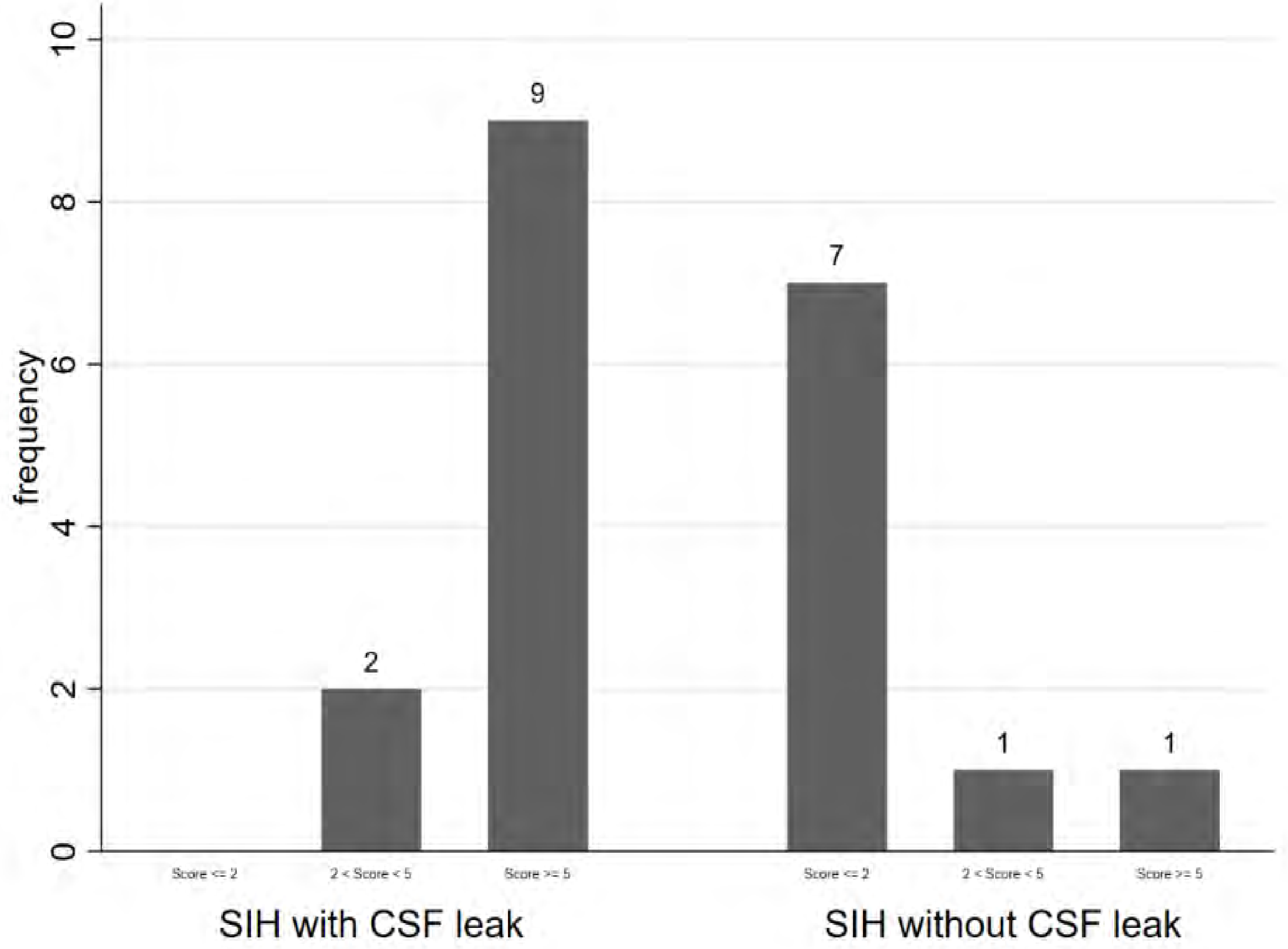
	Coefficient (95%-CI)	OR (95%-CI)	p-value	Score
Engorgement venous sinus	2·95 (1·18 to 4·72)	19·12 (3·26 to 112·30)	0·001	**2**
Pachymeningeal enhancement	4·04 (2·50 to 5·59)	57·01 (12·18 to 266·78)	<0·001	**2**
Subdural fluid collection	1·54 (-0·10 to 3·17)	4·65 (0·90 to 23·92)	0·066	**1**
Suprasellar cistern (≤4 mm)	3·48 (2·36 to 4·60)	32·32 (10·55 to 99·02)	<0·001	**2**
Prepontine cistern (≤5 mm)	1·47 (0·41 to 2·52)	4·34 (1·51 to 12·47)	0·007	**1**
Mamillopontine distance (≤ 6.5 mm)	1·13 (0·07 to 2·19)	3·08 (1·07 to 8·90)	0·037	**1**

	patients	dural enhance-ment	subdural collec-tion	venous engorge-ment	tonsillar ectopia (>5 mm)	pituitary enlarge-ment	inferior intercaver-nous sinus	Venous hinge	Mid brain descent	PMA (in °)	MPD (in mm)	Suprasellar cistern	Normal imaging
Alcaide[12]	26	100%	50%	77%	23%		50%	65 (35-98)	50%				
Aslan[17]	34	68%	41%	62 %	27 %	59%				50 ± 8·4	4·9 ± 0·99		
Tian[18]	26	88%	38%	28 %		54%			17%	47·8 ±8·7	5·4 ±1·6		
Shankar[15]	17	71%	65%			41%			71%				
Watanabe[19]	18	83%	72%		72%	67%			72%				
Farb[11]	15	95%											
Kranz[20]	99, 53% with leak	83%		75%					61%				7 %
Our study	56	83%	54%	65%	5%		47%	95 (±15)	27%	49 ± 11	5·7 ± 1·7	3·1 ± 1·9	0 %

Predicting spinal CSF leaks based on brain MRI findings



Predicting spinal CSF leaks based on brain MRI findings

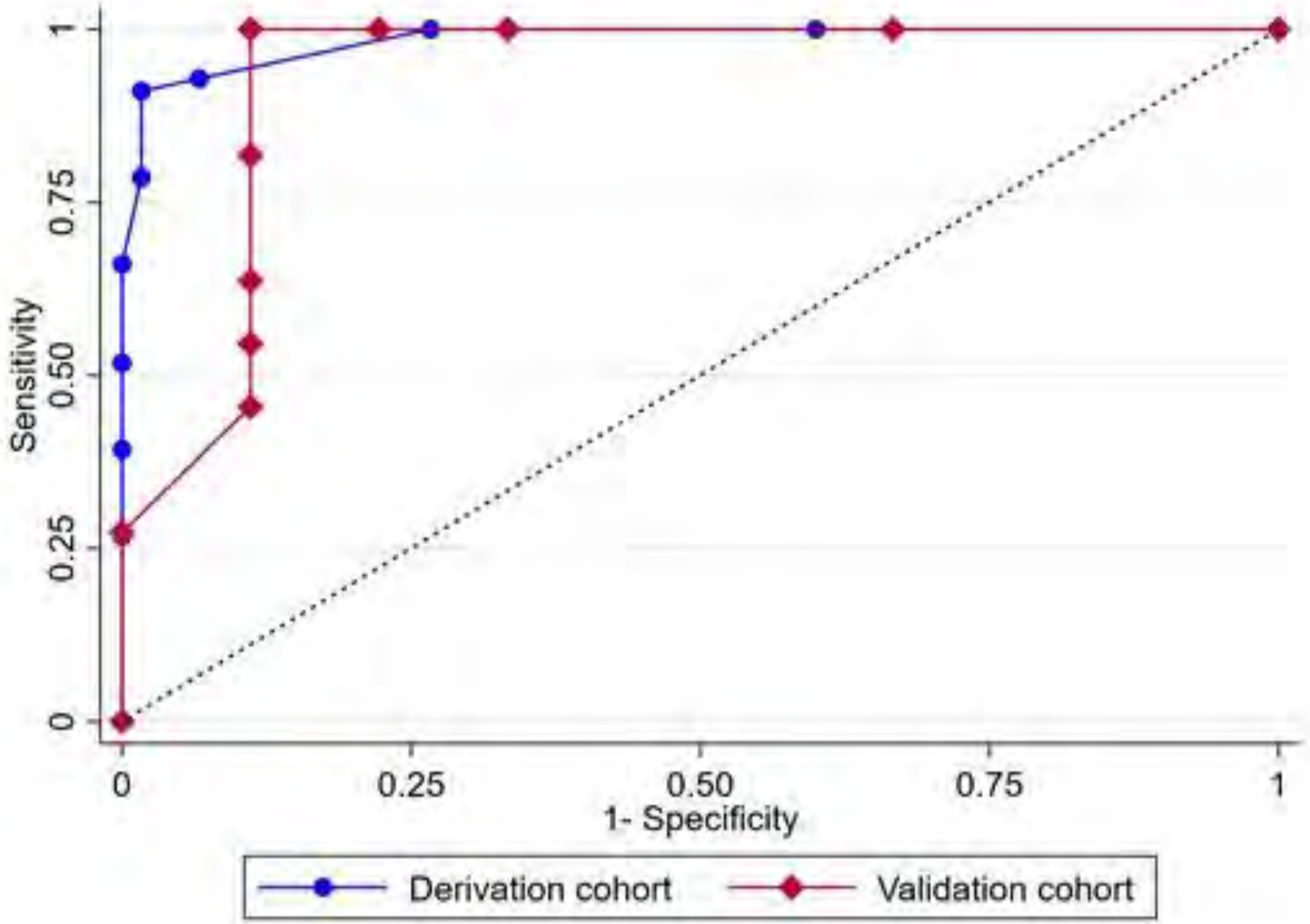


Derivation cohort

	Cutpoint	Sensitivity	Specificity	LR+	LR-
LOW	≥1	100·0%	40·0%	1·7	0·0
	≥2	100·0%	73·3%	3·8	0·0
INTER-MEDIATE	≥3	92·9%	93·3%	13·9	0·1
	≥4	91·1%	98·3%	54·7	0·1
HIGH	≥5	78·6%	98·3%	47·1	0·2
	≥6	66·1%	100·0%		0·3

Validation cohort

	Cutpoint	Sensitivity	Specificity	LR+	LR-
LOW	≥1	100.0%	33·3%	1·5	0·0
	≥2	100.0%	66·7%	3·0	0·0
INTER-MEDIATE	≥3	100.0%	77·8%	4·5	0·0
	≥4	100.0%	88·9%	9·0	0·0
HIGH	≥5	81.8%	88·9%	7·4	0·2
	≥6	63.6%	88·9%	5·7	0·4



1
0.75
0.50
0.25
0
Sensitivity
0
0.25
0.50
0.75
1
1- Specificity
Derivation cohort
Validation cohort

No patient with a proven spinal CSF leak had a normal brain MR score of 0 or 1

Timing

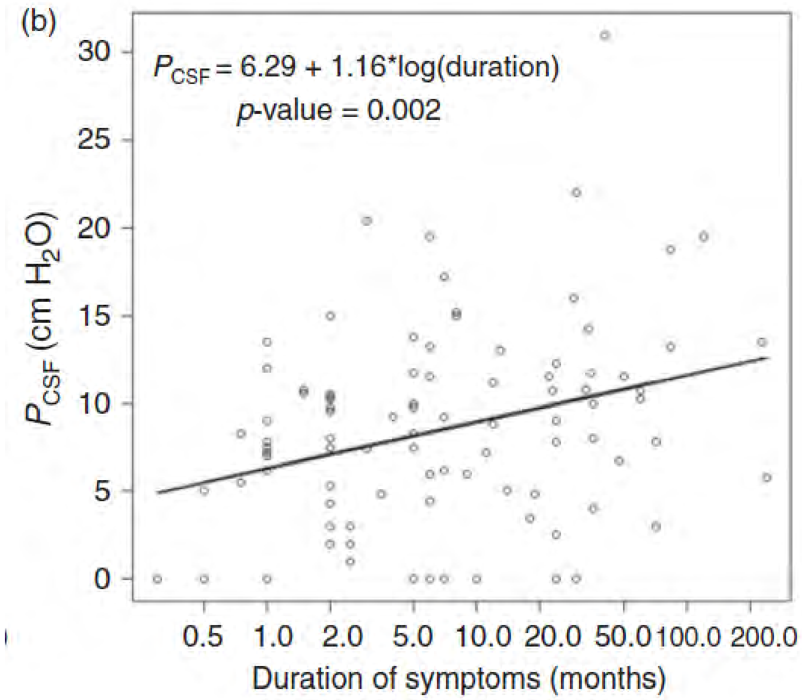
- Diagnostic criteria: Low CSF pressure (<60 mmCSF)
  (ICHD 3rd Version, Cephalgia 2018)

- Normal CSF pressure is common in up to 2/3 of patients
  (Kranz, Cephalgia 2015; Beck J Neurosurg Spine 2017)

- Lumbar infusion testing has proven to be a useful tool
  (Beck, J Neurosurg Spine 2017)

Natural history of SIH

- Symptoms most severe initially
- The orthostatic nature of the headache may become less obvious over time
  (ICHD 3rd Version, Cephalgia 2018; Ducros, Lancet 2015; Tyagi, Pract Neurol 2016; Lobo, BMJ Case Rep 2013; Mokri, Headache 2013; Schievink, Headache 2011)
- Opening pressure increases slowly with increasing symptom duration
  (Kranz, Cephalgia 2015)



Kranz, Cephalgia 2015

Natural history of SIH

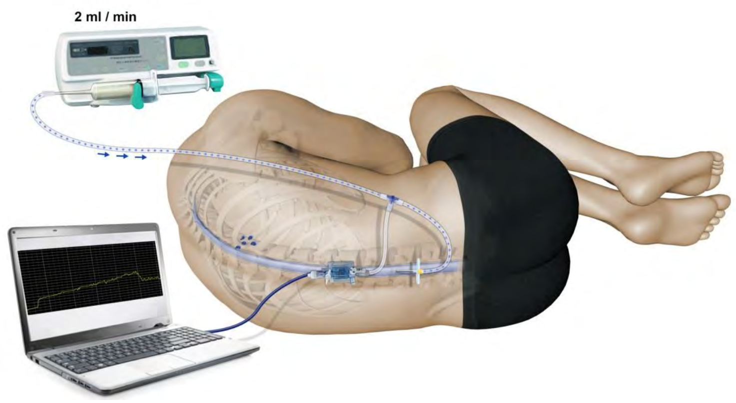
Acute
≤10 weeks

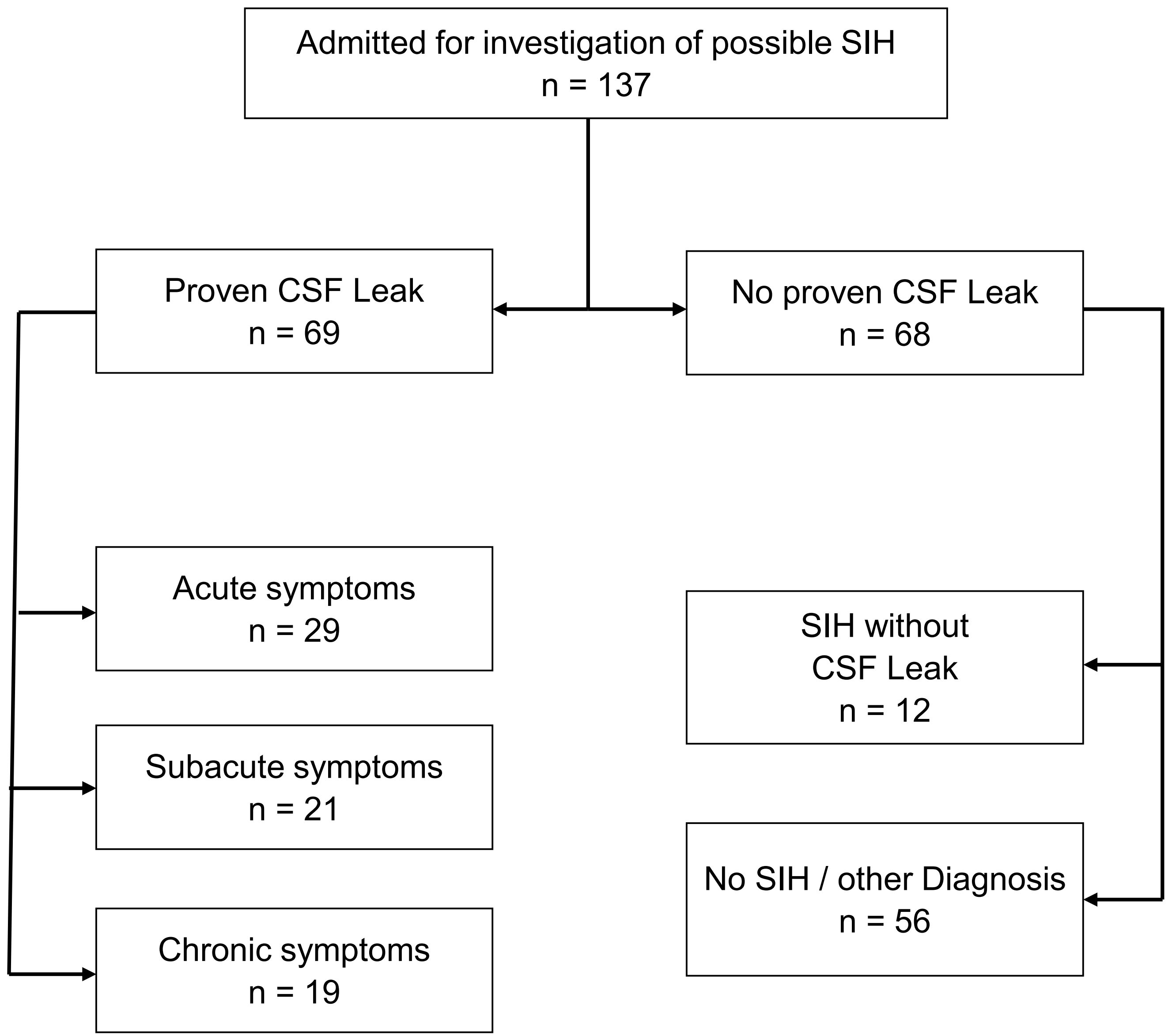
Subacute
11-52 weeks

Chronic
>52 weeks

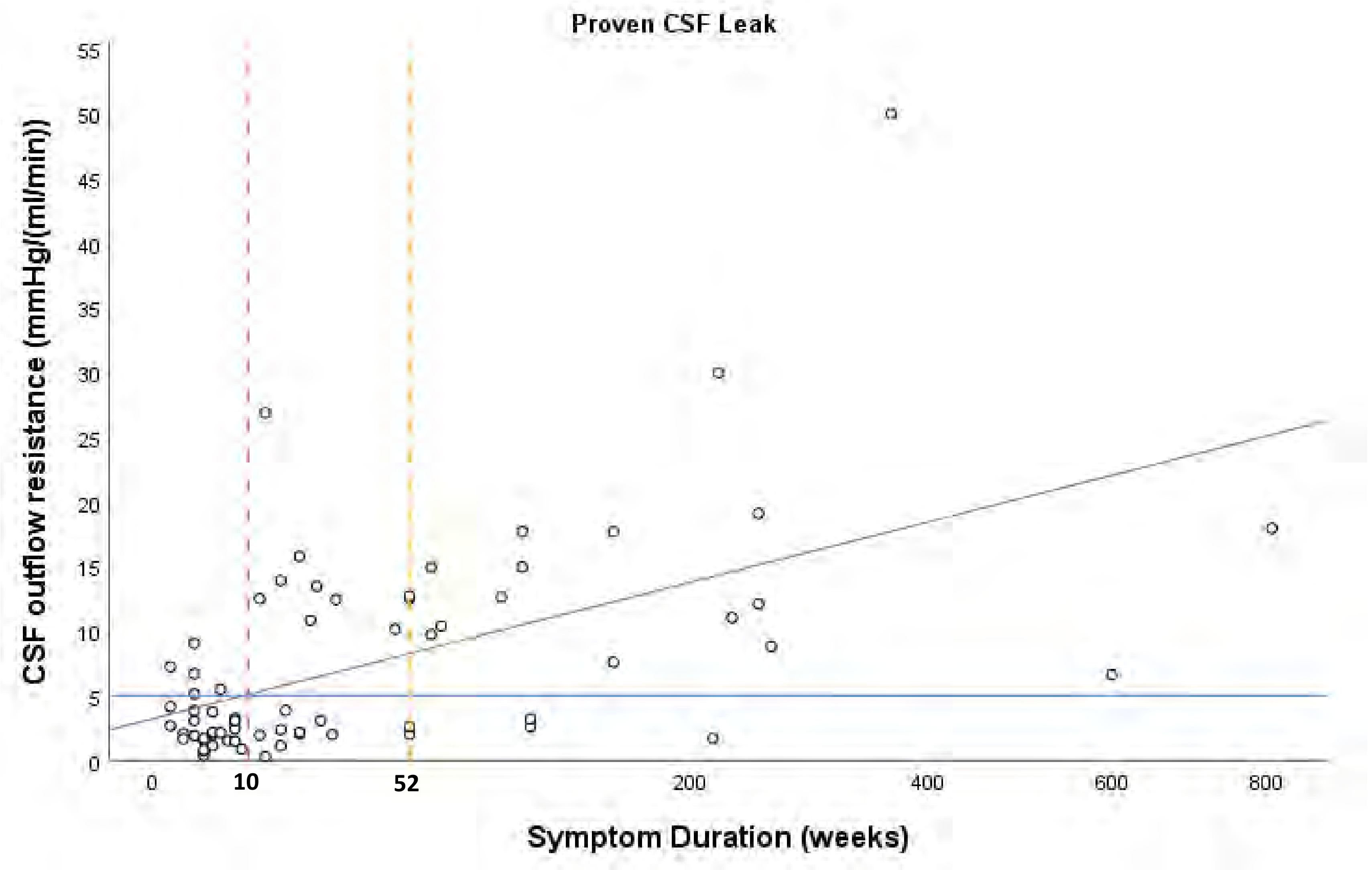
Update - lumbar infusion test – *ICM+*

137	**lumbar infusion tests**
53.3%	female
Mean age	49 years
69	**had proven spinal CSF leak**



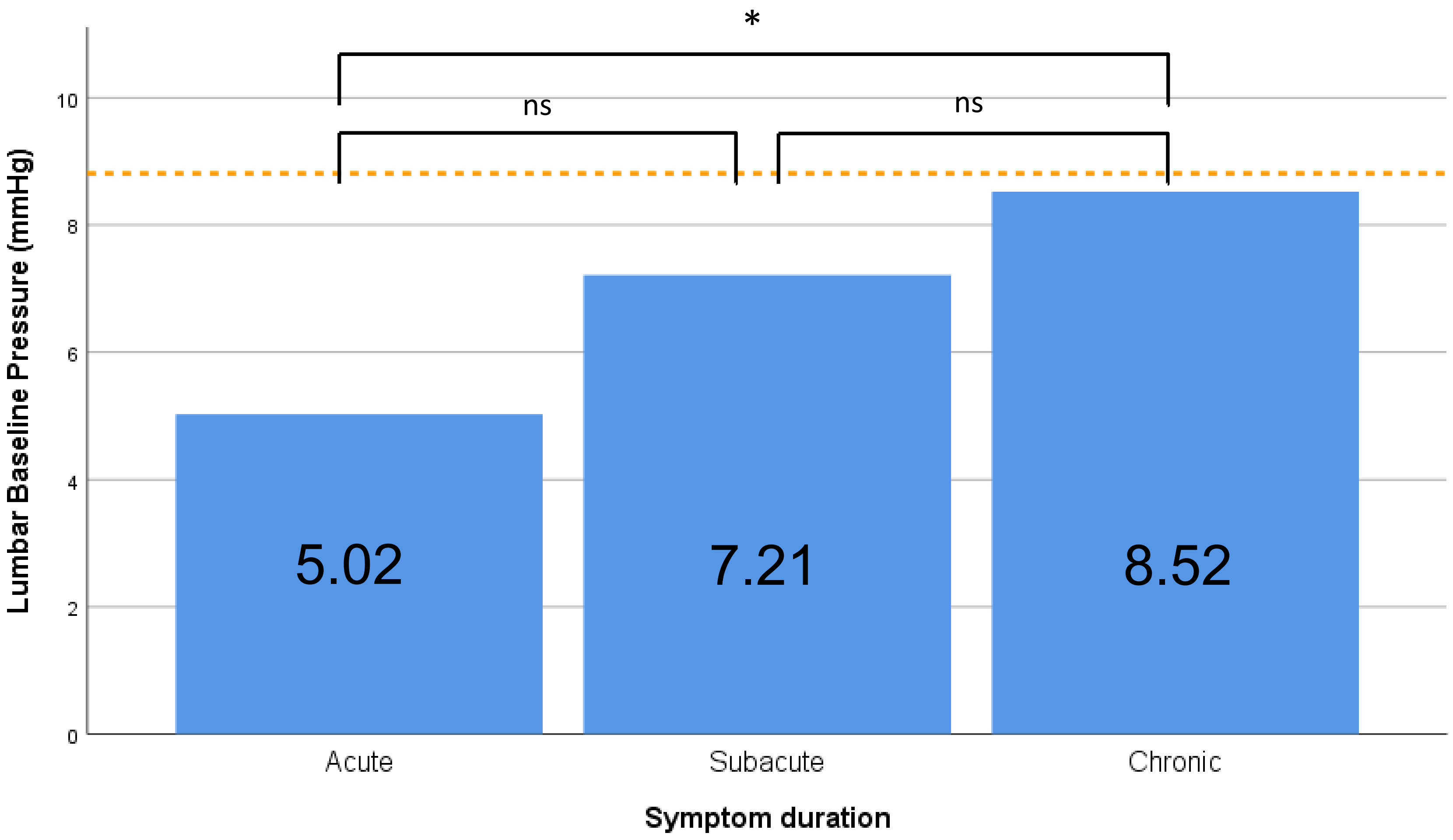


Admitted for investigation of possible SIH
n = 137
Proven CSF Leak
n = 69
No proven CSF Leak
n = 68
Acute symptoms
n = 29
Subacute symptoms
n = 21
Chronic symptoms
n = 19
SIH without
CSF Leak
n = 12
No SIH / other Diagnosis
n = 56

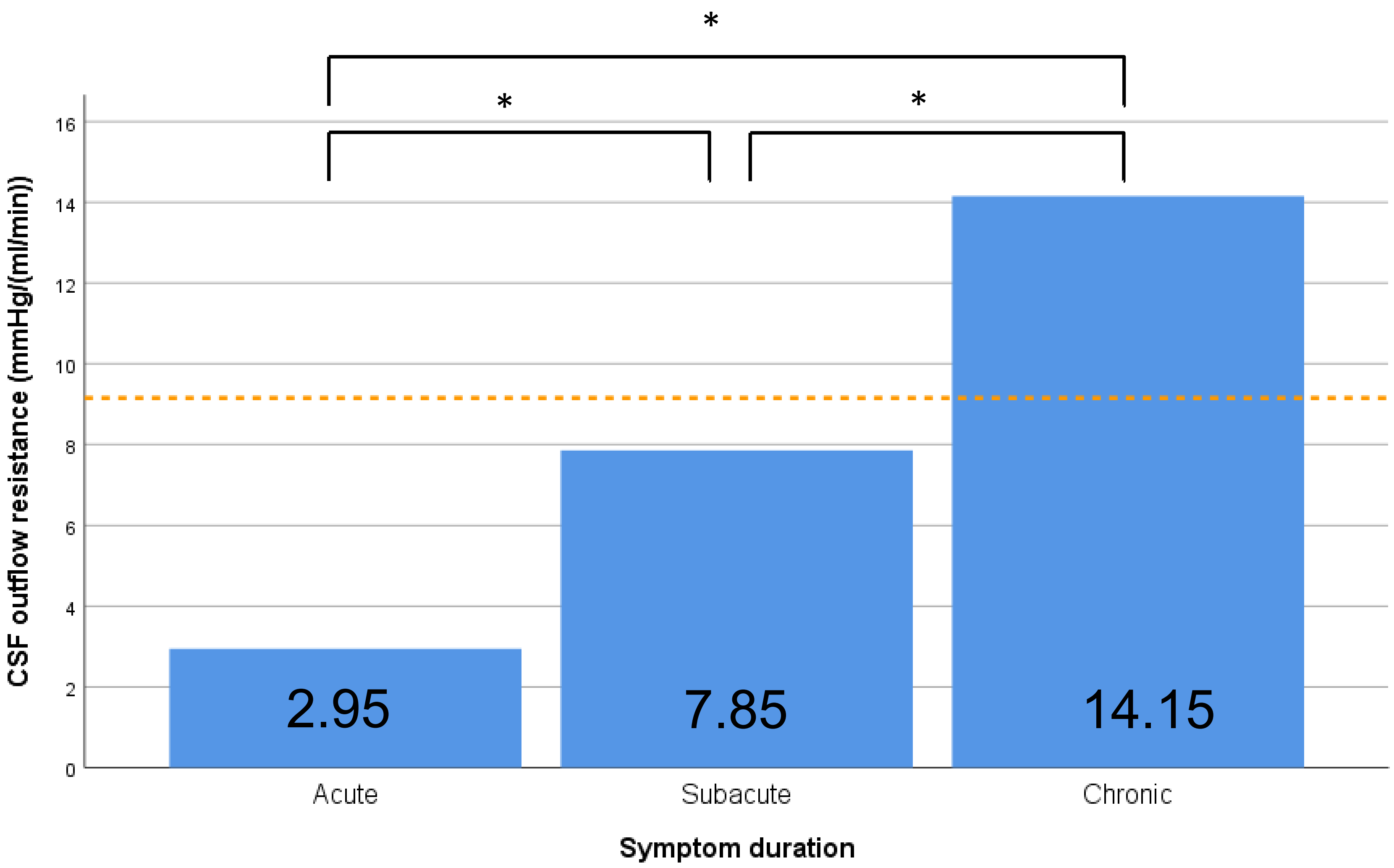


Correlation coefficient = 0.457 $p < 0.001$

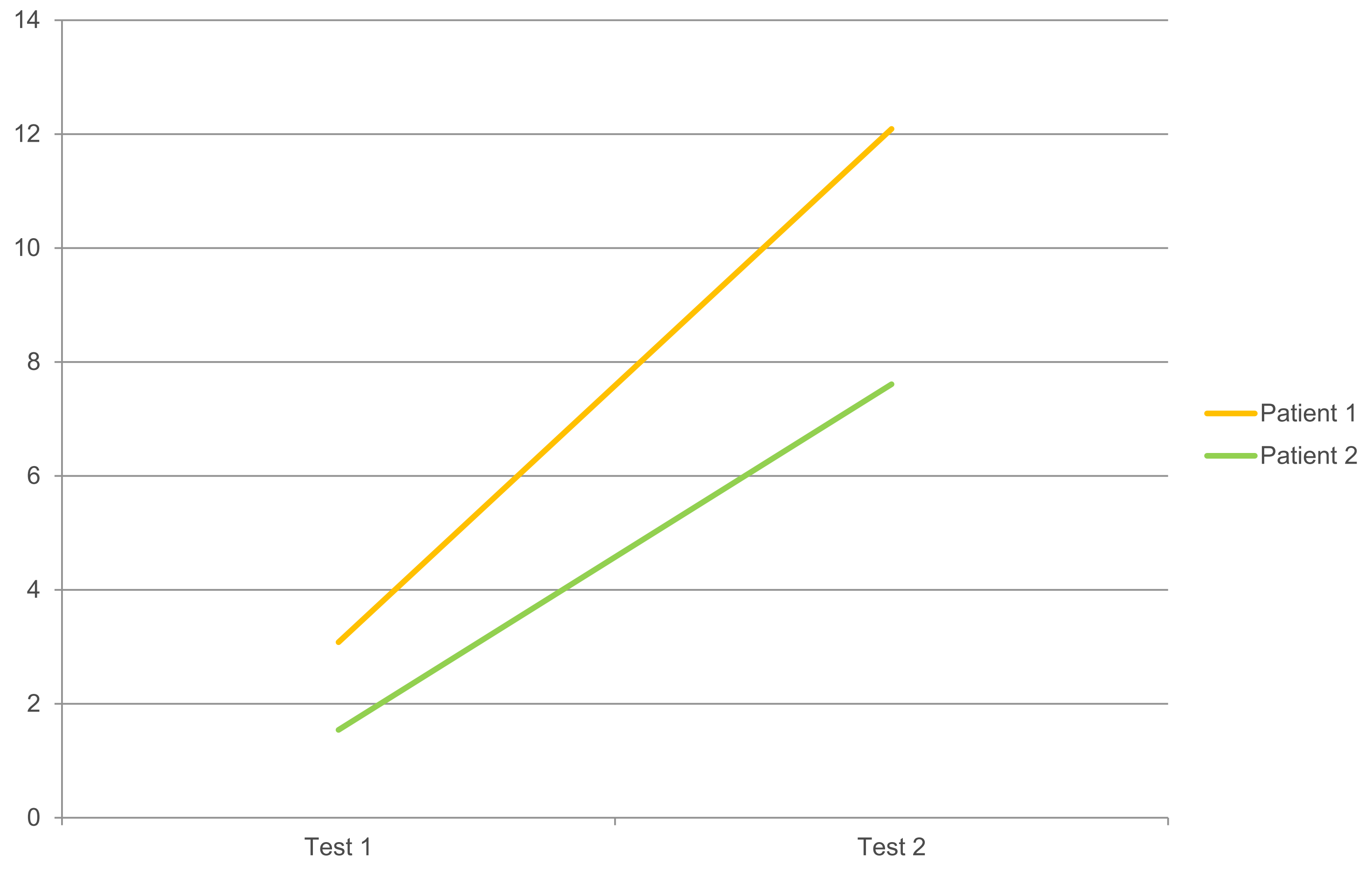
Update - lumbar infusion test – *ICM+*



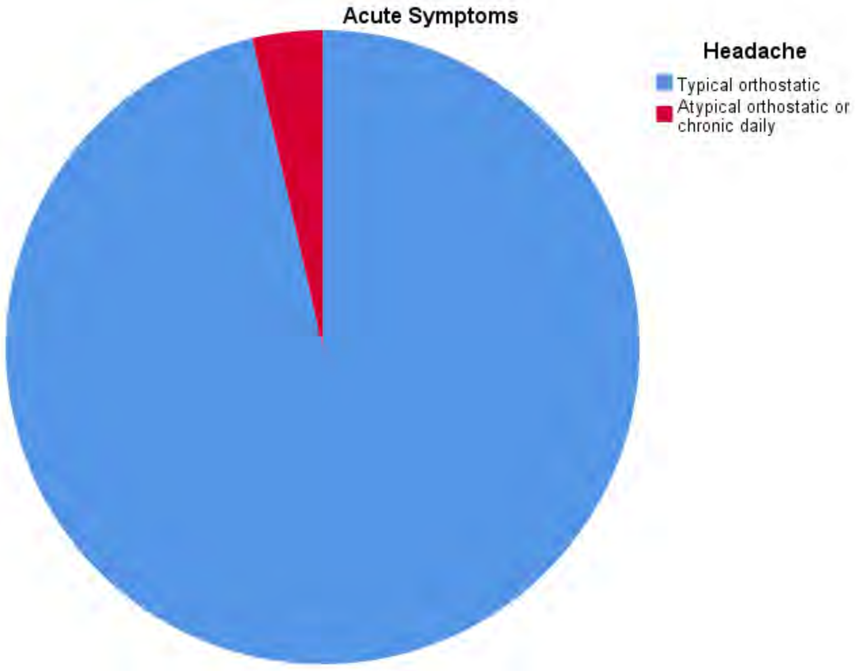
Update - lumbar infusion test – *ICM+*

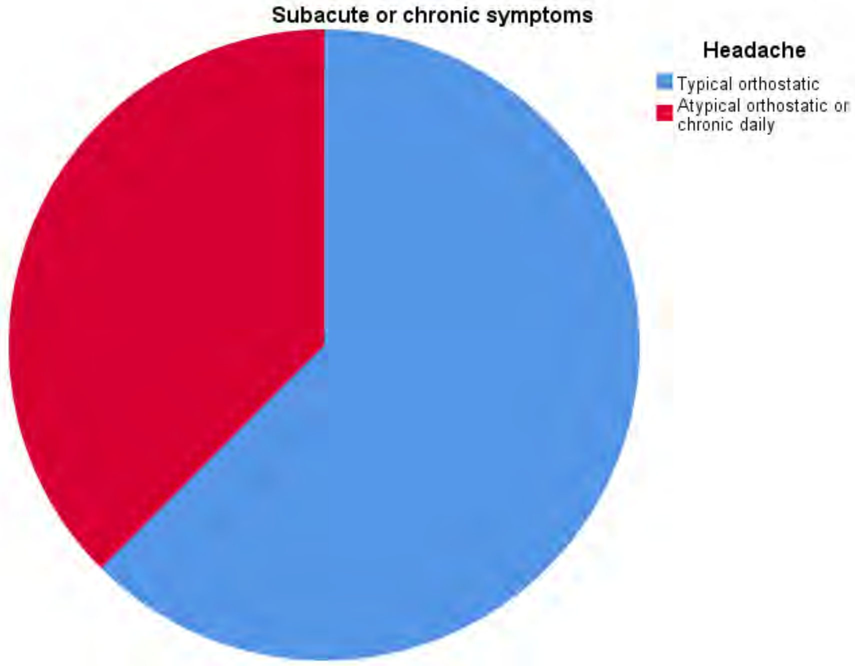


same patients over time

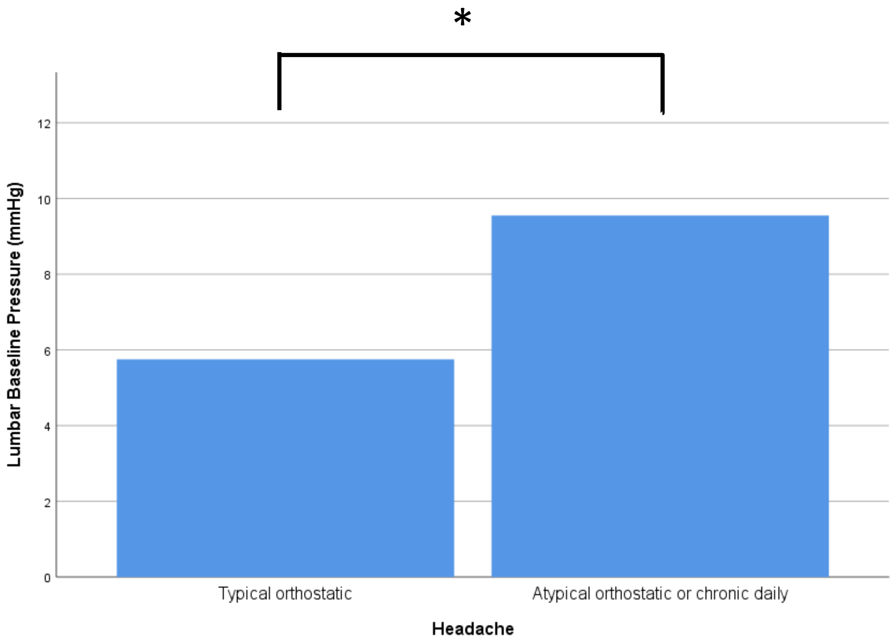


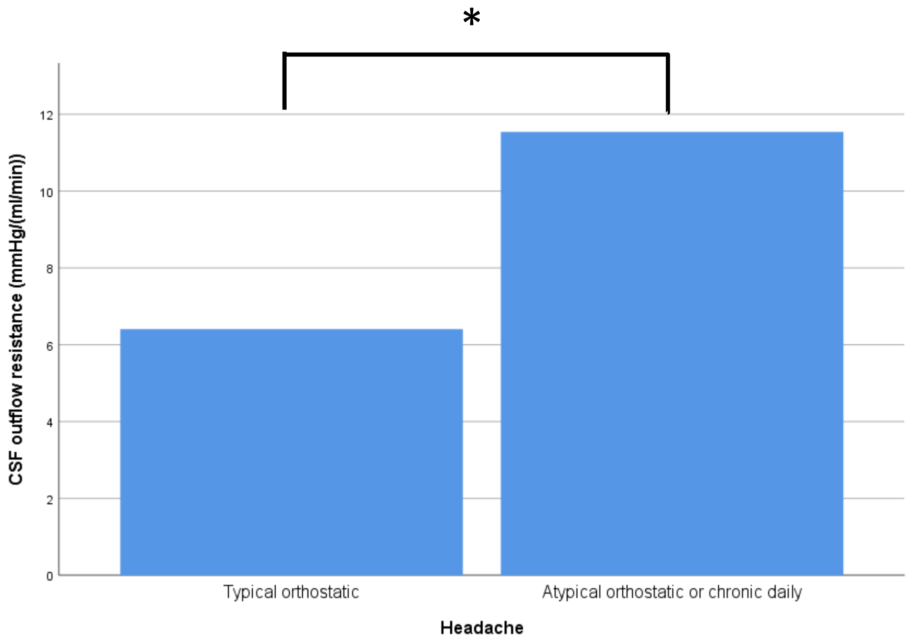
Type of headache acute vs. subacute and chronic



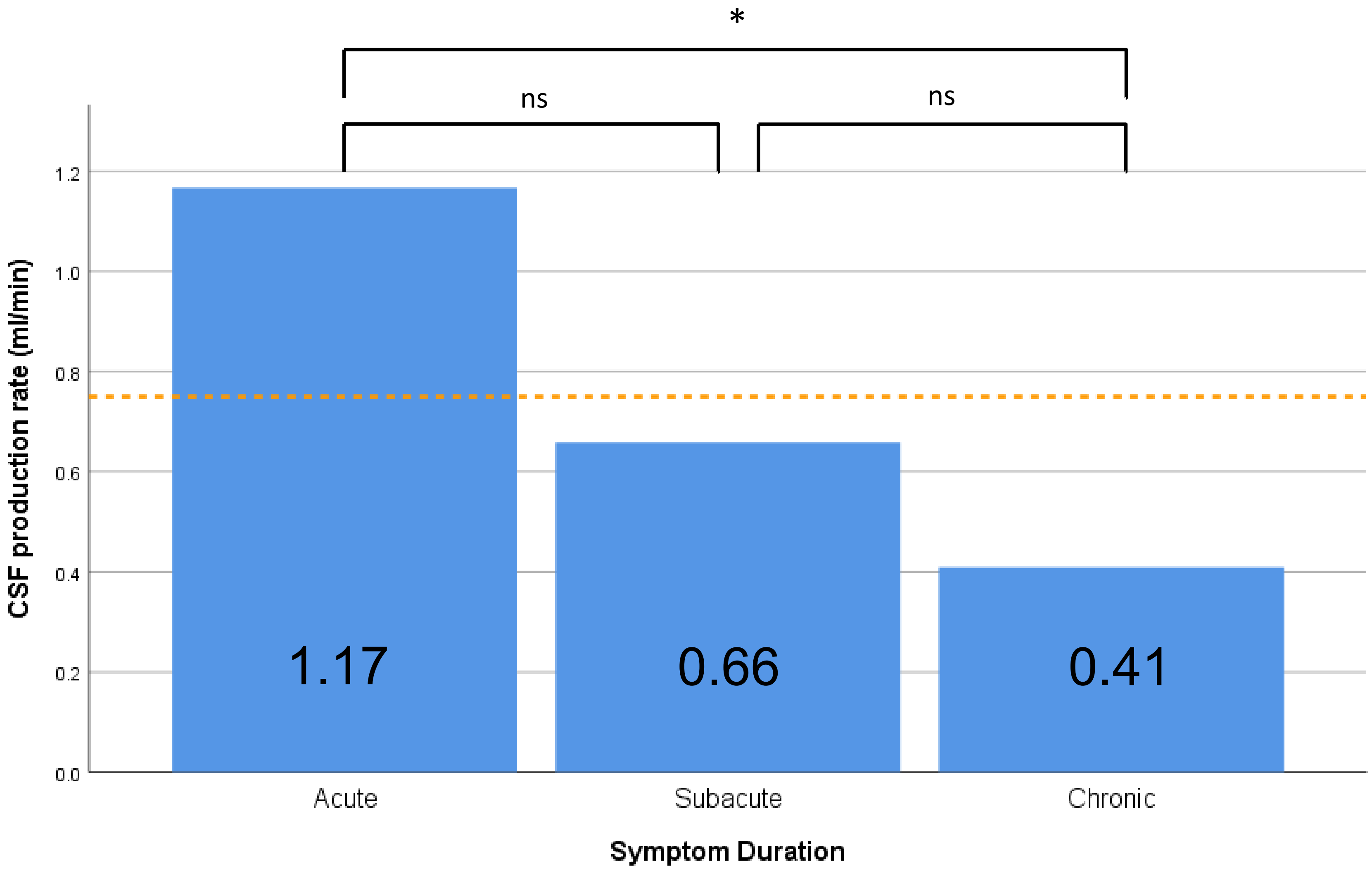


Type of headache and CSF paramter





Update - lumbar infusion test – *ICM+*



Lumbar infusion testing over the course of SIH

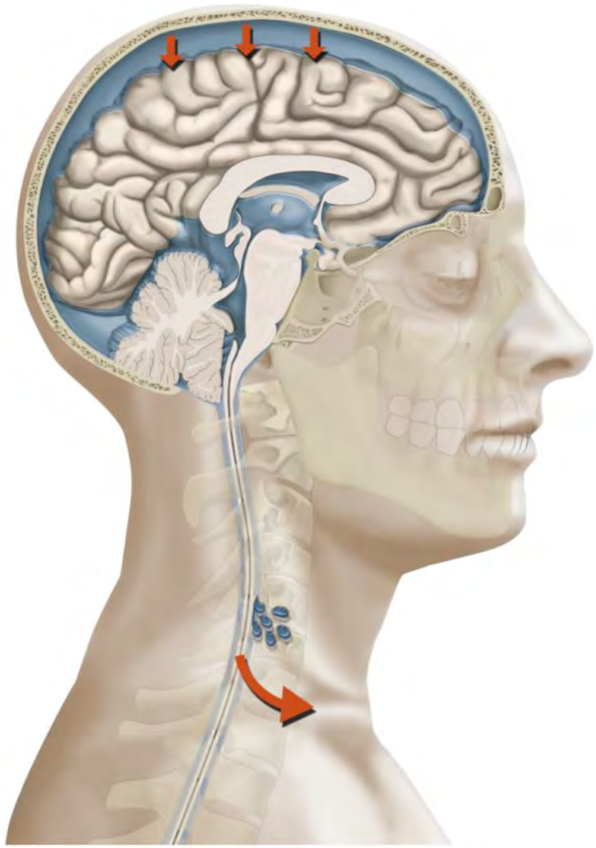
- **Patients with different symptom duration show clearly different profiles of CSF fluid dynamics**

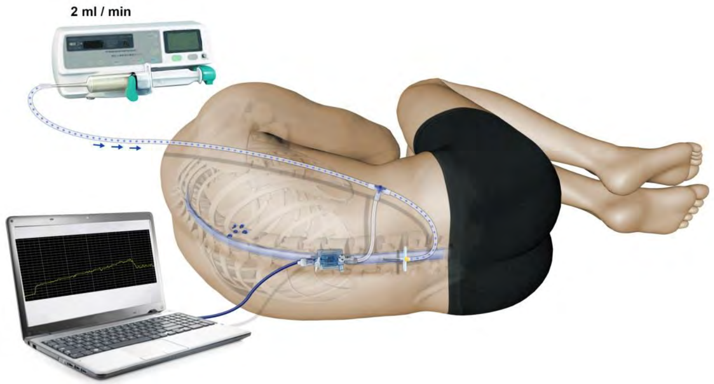
- **Longer symptom duration is associated with an altered CSF fluid dynamics (normalization?) and with atypical symptoms**

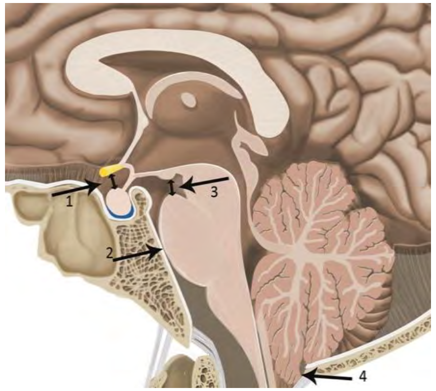
- **Natural history: what is the compensatory mechanism?**


1
2
3

Spontaneous Intracranial Hypotension







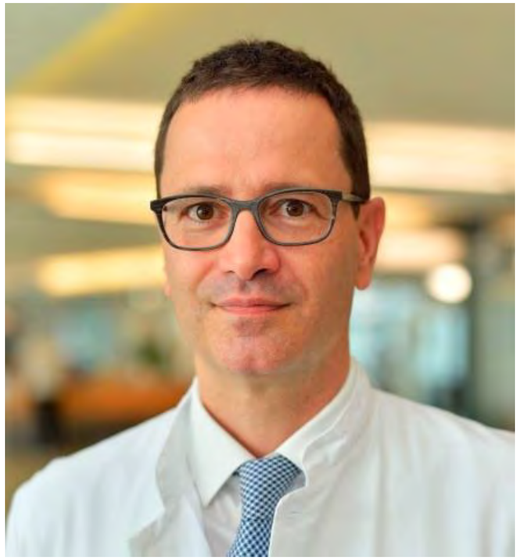










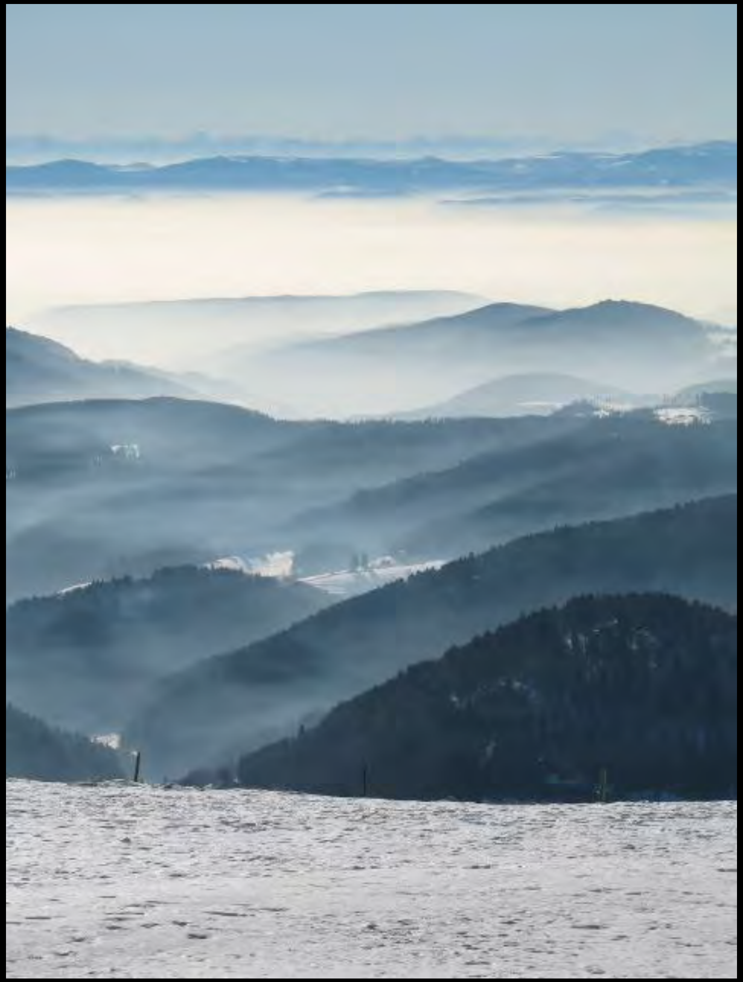







Thank you !

Freiburg im Breisgau


SIH
1st Bern Expert Meeting on Spontaneous Intracranial Hypotension & CSF Circulation Disorders
May 5-7, 2016