



Die Perioperative Analgesie im Wandel: präoperative Herausforderungen für ein besseres postoperatives Langzeit-Outcome

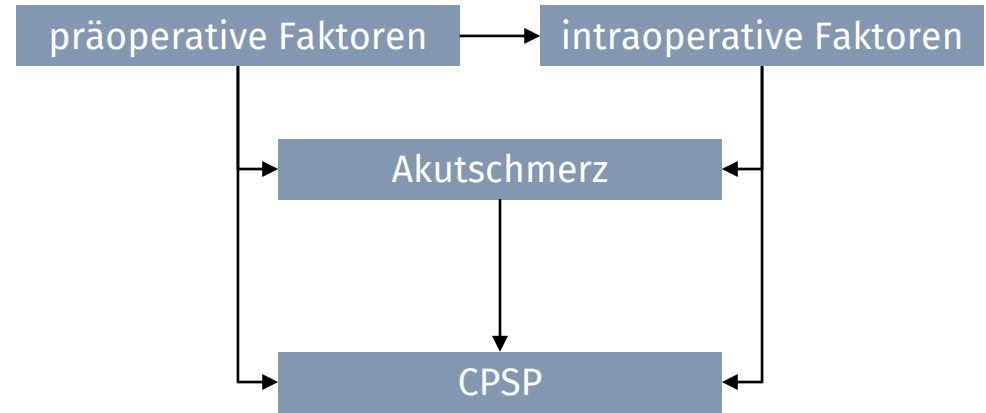
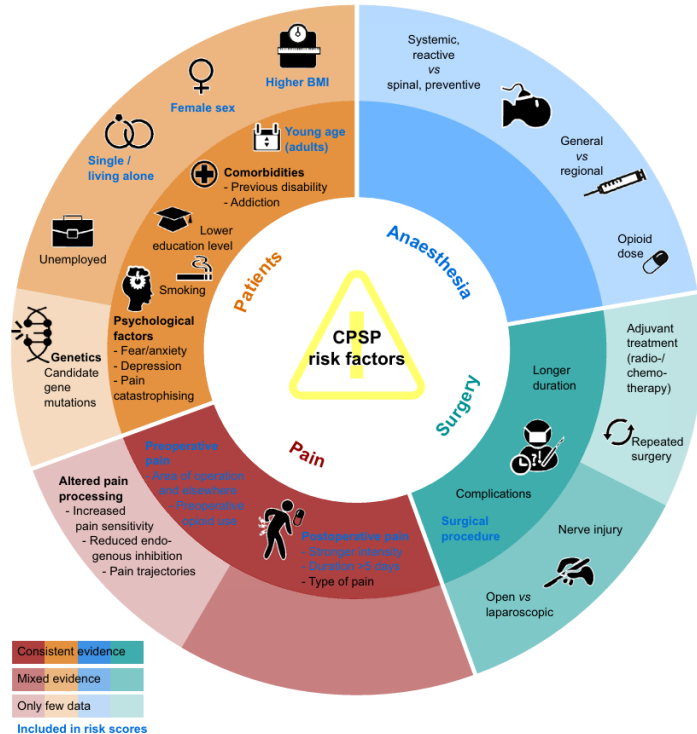
- Präoperatives Screening und intraoperative Messverfahren -

Deutscher Schmerzkongress | 22.10.2026 | Dr. phil. Dipl.-Psych. Philipp Baumbach

Das Langzeitoutcome wird perioperativ mitbestimmt

- **chronische postoperative Schmerzen** betreffen einen relevanten Anteil der Operierten
 - Inzidenz im Median 20-30%^[1-3]
- **persistierende funktionelle Einschränkungen und anhaltender Analgetikabedarf** sind klinisch relevant
 - Einschränkungen der Lebensqualität^[4,5]
 - persistierender Opioidgebrauch (D: 1,4%, USA/CAN: 3,5-6,5%)^[6-9]

Das Langzeitoutcome wird perioperativ mitbestimmt



- Risikopatient:innen früh erkennen
- nozizeptive Belastung besser steuern
- Analgesie individualisieren

Roadmap

1

Präoperatives Screening

Was erfassen wir?

Praxisbeispiel: *Preoperative blood pressure cuff-induced pain may support risk stratification for postoperative pain: a multicenter observational study*

2

Intraoperative Messverfahren

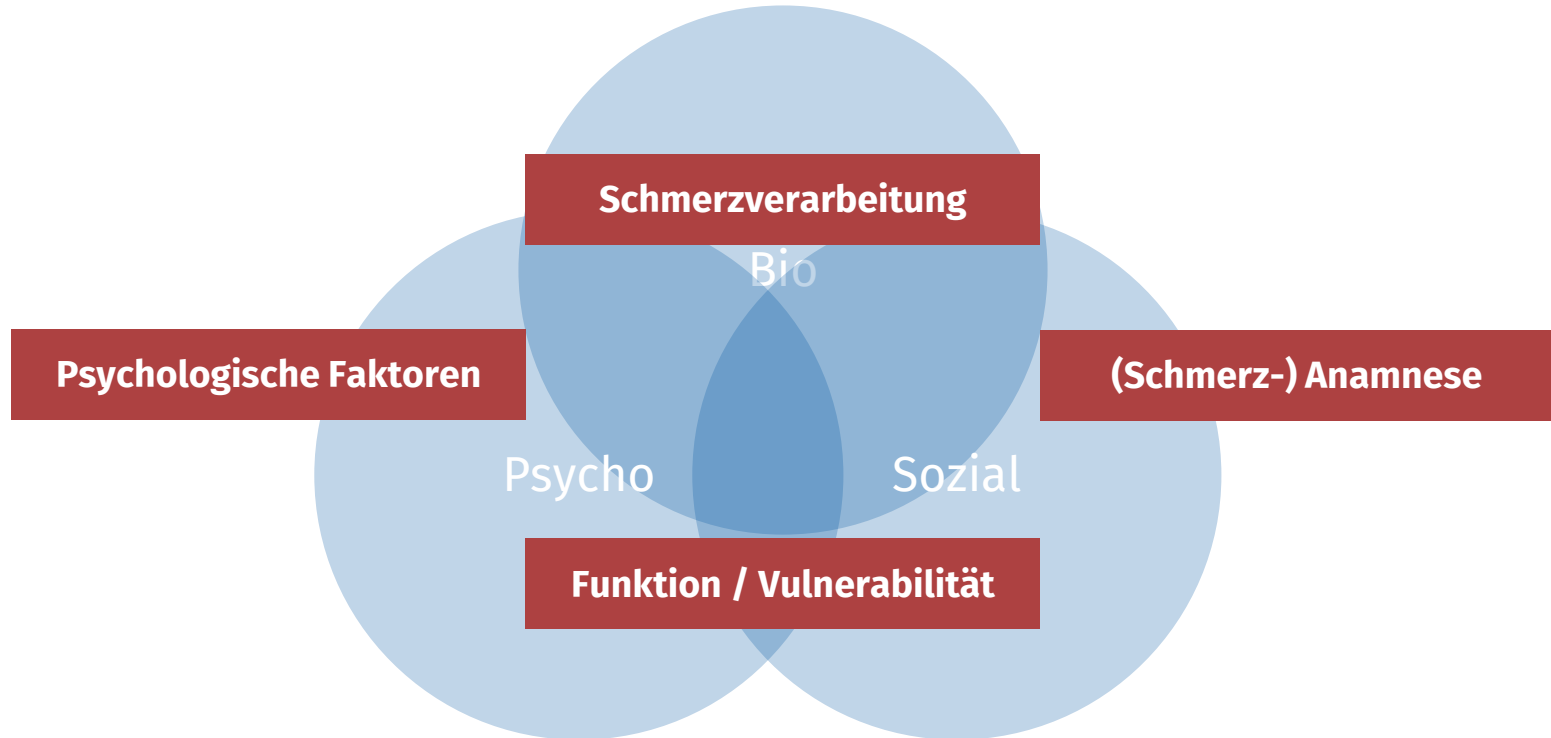
Was messen wir?

Praxisbeispiel: *Predicting acute postoperative pain: the role of intraoperative nociception level*

3

Fazit

Welche Risikodomänen sind relevant?



Was lässt sich in der Routine erfassen?

Verfahren	Beispiele	Einordnung
Klinische Anamnese ^[10, 11]	präoperativer Schmerz, Analgetika-/Opioidgebrauch, Schmerzerfahrungen, Alter, Geschlecht, Art der Operation	• hoch praktikabel • klinisch zentral
Selbstauskunft ^[10]	Erwartungshaltung, Stress, Schlafqualität	• einfach und vielversprechend • nicht standardisiert
Fragebögen ^[10]	Angst/Depression: <i>STAI, HADS</i> Katastrophisieren/Selbstwirksamkeit: <i>PCS, PSEQ</i> Schlaf: <i>PSQI</i> Schmerzsensitivität: <i>CSI, PSQ</i>	• teilweise assoziiert • insgesamt heterogene Evidenz
QST / experimentelle Tests ^[10, 12-14]	Temperatur (HPT, CPT, inkl. Toleranz), Druck (PPT, Cuff-Algometrie), elektrisch (EPT), dynamisch/komplex (TSP, CPM)	• z. T. klinisch/apparativ aufwendig • Evidenz heterogen bzw. kleine-moderate Assoziationen
Einfache Bedside-Tests ^[10]	Kanülierungsschmerz, LA-Infiltrationsschmerz	• vielversprechend, pragmatisch
Biomarker / Genetik ^[10]	Entzündungsmarker, SNPs, mRNA, u.v.m.	• derzeit keine Routineanwendung
Kombinierte Risiko-Scores ^[11]	multivariable Modelle aus Schmerz, Angst, OP-Typ etc.	• bessere Diskrimination als Einzelmarker • studienbedingtes Bias-Risiko [PROBAST]

CPM = Conditioned pain modulation; CSI = Central Sensitization Inventory; EPT = electrical pain threshold; HADS = Hospital Anxiety and Depression Scale; mRNA = messenger ribonucleic acid; PCS = Pain Catastrophizing Scale; PPT = Druckschmerzschwelle; PSEQ = Pain Self-Efficacy Questionnaire; PSQ = Pain Sensitivity Questionnaire; PSQI = Pittsburgh Schlafqualitätsindex; QST = Quantitative Sensorische Testung; SNPs = Single nucleotide polymorphisms; STAI = State-Trait Anxiety Inventory; TSP = Temporal summation of pain

Is the patient female?	Yes = 1 point	No = 0 points
Does the patient have persistent pain of NRS intensity over 3?	Yes = 1 points	No = 0 points
Did the patient receive opioids before admission?	Yes = 1 point	No = 0 points
Is the patient		
<30 years?	Yes = 2 point	
30–49 years?	Yes = 1 point	
50–70 years?	Yes = 0 point	
>70 years?	Yes = -1 point	

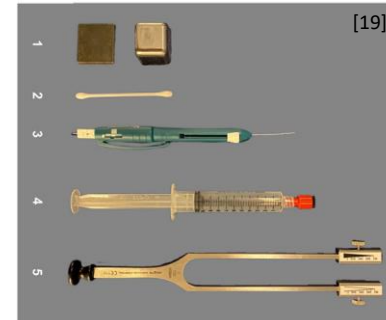
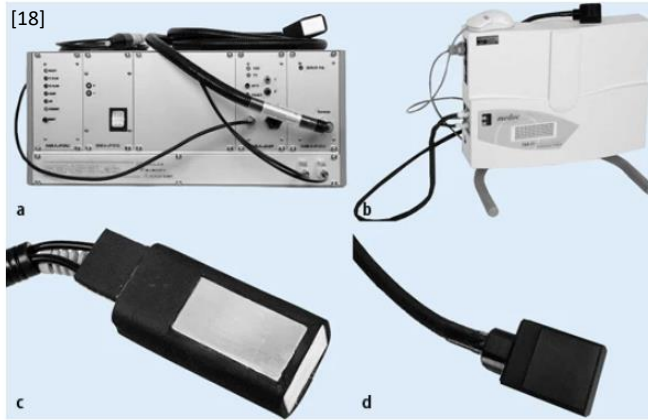
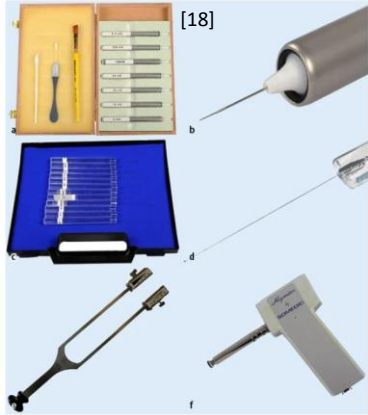
AUC: 0.607, 95% CI: 0.601–0.613, $P < 0.001$

ARTICLE OPEN

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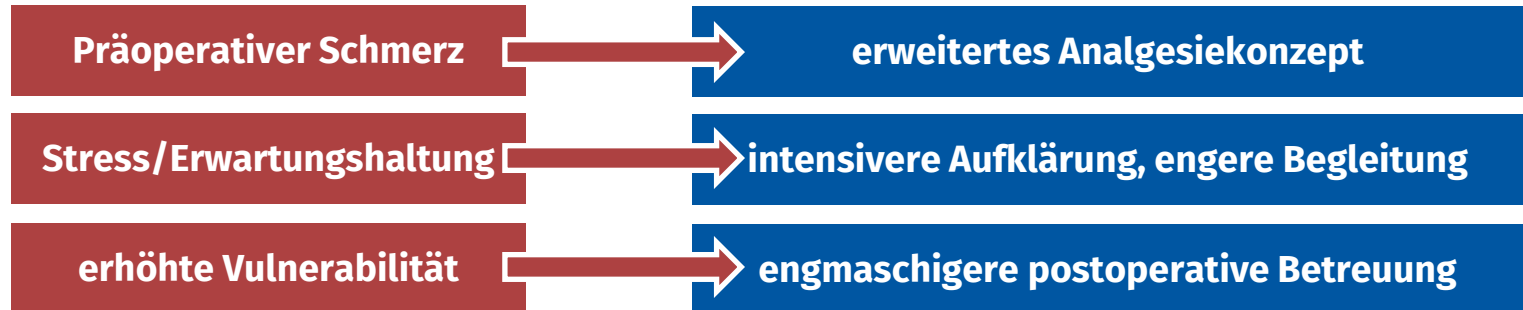
Schnabel, A., et al. 2020 [15]

Was lässt sich in der Routine erfassen?



Risikoprofil statt Einzelmarker

- nicht der beste Einzelmarker entscheidet, sondern das Gesamtrisiko
- pragmatische klinische Informationen sind oft nützlicher als komplexe Spezialtests
- der Wert des Screenings liegt in der **Risikostratifizierung** und **Therapieplanung**



Die Idee

- Erfassung der präoperativen Schmerzsensitivität mithilfe eines einfachen *Bedside*-Tests bzw. einer nicht-invasiven Routinemaßnahme



Methoden

- Schmerzzrating in Bezug auf „Blutdruckmessung“
 - **Prämedikationsambulanz**
 - 260 mmHg für 10 Sekunden
 - *Cuff-induced pain rating* (CIPR, 0-10 NRS)
 - CIPR_{hoch}: > 4/10 NRS
 - CIPR_{niedrig}: ≤ 4/10 NRS



Methoden



- QUIPS
 - standardisierte Erfassung von *Patient-Reported Outcomes* (PROs) und Prozessparametern
 - **postoperativer Tag 1** (POT₁)
 - Schmerzintensität (3 Items)
 - Schmerzbeeinträchtigung (4 Items)
 - Nebenwirkungen (3 Items)

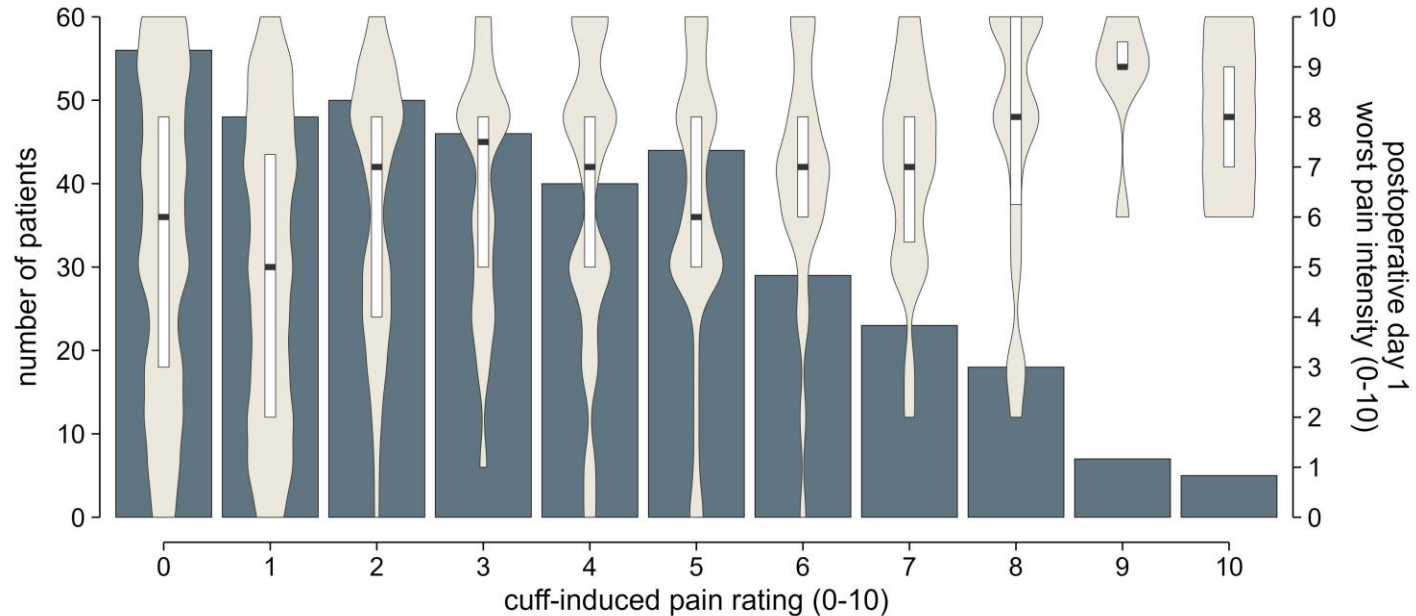
Ergebnisse

- Analysestichprobe: n = 366/383 Patient:innen
 - Ortho/Trauma (n=232), Gyn/Geburt (n=26), MKG (n=26), ACH (n=20), Uro (n=19), Auge (n=18), Gefäß (n=17), HNO (n=8)

Variable	Total
N = 366	
Age (> 60 years)	223 (64.5%); 346
≤ 30 years	13 (3.8%); 346
31 – 50 years	52 (15.0%); 346
51 – 70 years	158 (45.7%); 346
> 70 years	123 (35.5%); 346
Sex (female)	193 (53.0%); 364
Chronic preoperative pain (yes)	213 (58.7%); 363
Pain intensity > 3/10 NRS	199 (54.8%); 363
Opioid use	50 (13.9%); 360
Preoperative risk score (-1 – 5)	1 [0-2]; 335
Surgical specialty (orthopedics/traumatology)	232 (63.4%); 366
Duration of surgery	
Duration (minutes)	67 [50-95]; 356
Duration > 90 minutes (yes)	98 (27.5%); 356
Intraoperative anesthesia	
General anesthesia (GA)	219 (60.7%); 361
Regional anesthesia (RA)	42 (11.6%); 361
GA+RA	89 (24.7%); 361
Local anesthesia (solo)	11 (3.0%); 361

Ergebnisse

- Analysestichprobe: n = 366/383 Patient:innen



Ergebnisse

■ Unterschiede in PROs

Variable	CIPR: low [≤4/10 NRS] n=240 (65.6%)	CIPR: high [>4/10 NRS] n=126 (34.4%)	P	ES
CIPR (0–10)	2 [1–3]	6 [5–7]	<0.001^a	0.83
Postoperative day 1				
Pain intensity (0–10)				
Worst	6 [4–8]	7 [5–9]	0.004^a	0.15
Least	2 [0–3]	2 [1–3.8]	0.097 ^a	0.09
During activities	5 [3–7]	6 [4–8]	0.001^a	0.17
Pain interference				
Movement	182 (75.8%)	98 (77.8%)	0.774 ^b	0.02
Breathing/coughing	41 (17.1%)	31 (24.6%)	0.114 ^b	0.09
Sleep	139 (57.9%)	75 (59.5%)	0.853 ^b	0.02
Mood	63 (26.3%)	43 (34.1%)	0.145 ^b	0.08
Side effects				
Drowsiness	126 (52.5%)	79 (62.7%)	0.079 ^b	0.10
Nausea	42 (17.5%)	25 (19.8%)	0.683 ^b	0.03
Dizziness	58 (24.2%)	38 (30.2%)	0.266 ^b	0.06
Composite Pain Score (0–10)	4.1 [2.4–5.7]	4.8 [3.5–5.9]	0.004^a	0.15
Wish for more pain treatment	63 (26.5%); 238	26 (21.5%); 121	0.366 ^b	0.05

All data in n (%) or median [interquartile range]

Abbreviations: CIPR, cuff-induced pain rating; ES, effect size; N, total number of patients with available data (not indicated, if no patients with missing data); n, number of patients; %, percentage (denominator: N); NRS, numeric rating scale; RR, blood pressure cuff measurement

^a P value of the Mann-Whitney U tests comparing patients in the low vs. high CIPR group, r as corresponding effect size (values ≥ 0.1 small, ≥ 0.3 medium, ≥ 0.5 large effect)

^b P value of the chi-squared tests comparing patients in the low vs. high CIPR group, Cohen's w as corresponding effect size (values ≥ 0.1 small, ≥ 0.3 medium, ≥ 0.5 large effect)

P values < 0.05 are printed bold; all P values < 0.05 for patient-reported outcomes on postoperative day 1 were also < 0.05 after adjusting for multiple testing

Ergebnisse

■ logistische Regressionsmodelle

	Severe pain on postoperative day 1 (worst pain intensity $\geq 7/10$ NRS, n=326)	
	OR [95% CI]	P
Model 1		
Intercept	0.51 [0.35 – 0.76]	0.001
Surgical specialty: orthopedics/traumatology (vs. other)	3.76 [2.32 – 6.09]	<0.001
Model 2^a		
Intercept	0.39 [0.25 – 0.61]	<0.001
Surgical specialty: orthopedics/traumatology (vs. other)	3.41 [2.08 – 5.57]	<0.001
Preoperative risk score (–1 – 5),	1.36 [1.09 – 1.71]	0.007
Model 3^{b,c}		
Intercept	0.19 [0.10 – 0.34]	<0.001
Surgical specialty: orthopedics/traumatology (vs. other)	4.08 [2.42 – 6.87]	<0.001
Preoperative risk score (–1 – 5),	1.31 [1.04 – 1.66]	0.020
CIPR (0 – 10 NRS)	1.22 [1.10 – 1.34]	<0.001

Abbreviations: CIPR, cuff-induced pain rating; 95%CI, 95% confidence interval; AUC, area under the curve; NRS, numeric rating scale; OR, Odds ratio; P, P-value of OR (P-values <0.05 are printed in bold); RR, blood pressure cuff measurement

^a P DeLong test model 2 vs. model 1 = 0.058 (two-sided P value)

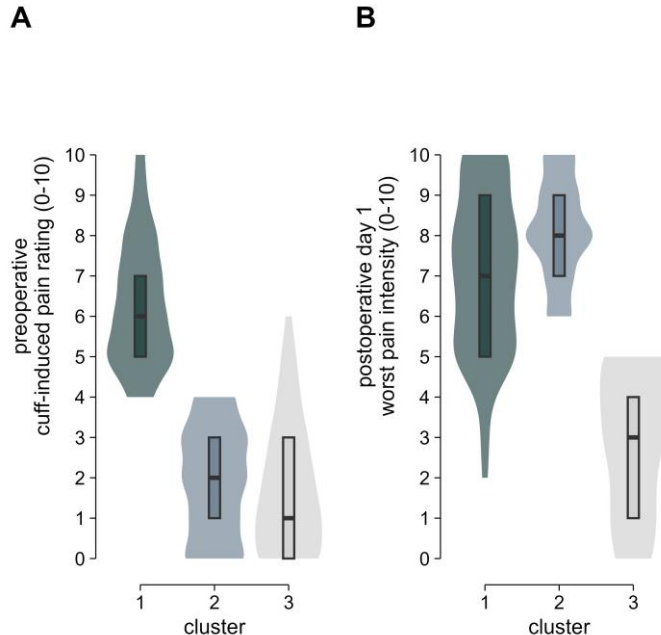
^b P DeLong test model 3 vs. model 1 < 0.001 (two-sided P value)

^c P DeLong test model 3 vs. model 2 = 0.006 (two-sided P value)

- **Model 1:** AUC: 0.65 [0.6–0.7], sensitivity: 0.79, specificity: 0.5
- **Model 2:** AUC: 0.68 [0.62–0.74], sensitivity: 0.83, specificity: 0.49
- **Model 3:** AUC: 0.73 [0.67–0.78], sensitivity: 0.64, specificity: 0.71

Ergebnisse

Explorative Clusteranalyse



Results of the partitioning around medoids cluster analysis. Violin plots and boxplots (median and interquartile range) for (A) preoperative cuff-induced pain rating (CIPR), (B) worst pain intensity on postoperative day 1, and (C) the Composite Pain Score on postoperative day 1. Differences between clusters 1 ($n = 130$), 2 ($n = 131$), and 3 ($n = 105$) were tested with Mann-Whitney U tests (* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$). Because CIPR and worst pain intensity on postoperative day 1 were used for cluster derivation, between-cluster differences for these variables are presented descriptively only.

max. Schmerzintensität: $\geq 7/10$ NRS

	Thresh	Spec	Sens
Combined decision rule			
Risk score ≥ 1 OR CIPR ≥ 5	rule	0.29	0.87
Risk score ≥ 1 AND CIPR ≥ 5	rule	0.81	0.31
Risk score ≥ 1 OR CIPR ≥ 6	rule	0.32	0.86
Risk score ≥ 1 AND CIPR ≥ 6	rule	0.91	0.23

Fazit

- ein einfacher nicht-invasiver *Bedside*-Test (CIPR) war mit stärkeren postoperativen Schmerzen an POT₁ assoziiert
- CIPR verbesserte die Vorhersage starker postoperativer Schmerzen über etablierte präoperative Risikofaktoren hinaus
- ABER: die Vorhersagegüte blieb insgesamt eher moderat

Hintergrund



<https://pixabay.com/de/photos/operation-krankenhaus-arzt-pflege-1822458/>

Was erfassen wir?

- Patient:innen unter Allgemeinanästhesie (AA) haben keine Schmerzen
- **Aber:** Schmerzen $\neq$ Nozizeption!
 - nozizeptive Aktivierung trotz AA vorhanden^[20, 21]

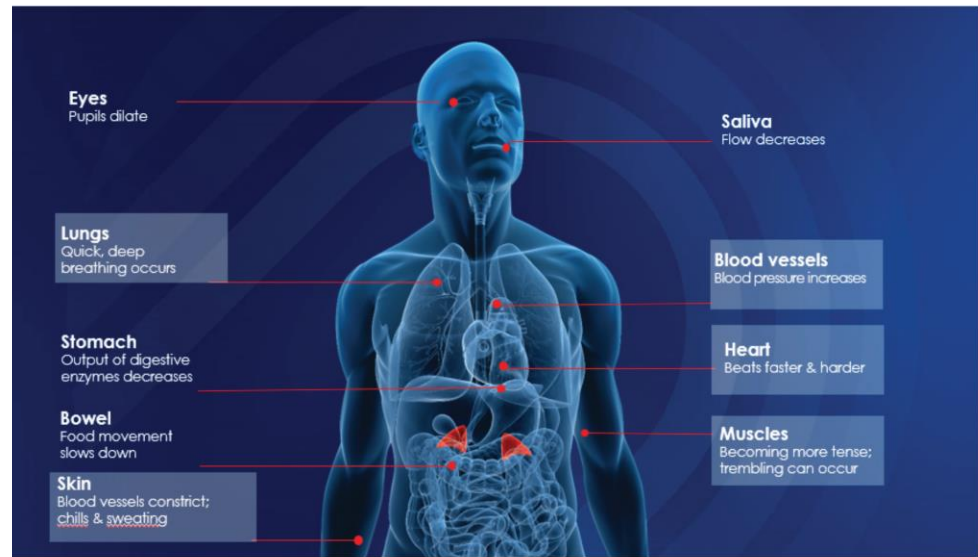
Was erfassen wir?

- klinische Zeichen
 - Tachykardie, Blutdruckanstieg, Schwitzen/Tränenfluss, Mydriasis, motorische Reaktionen, Atmung etc.)
- apparative Erfassung
 - Narkosetiefe (EEG-basierte Verfahren z. B. Bispektral Index, Narcotrend)
 - „Nozizeption“ (meist Reaktionen des autonomen Nervensystems)

Welche Verfahren stehen uns zur Verfügung?

■ Apparative Erfassung: Surrogatparameter Nozizeption^[22,23]

-  – Analgesia Nociception Index (ANI)
-  – Surgical Plethysmographic Index (SPI)
-  – CARDEAN
-  – Pupillometry (PPI, PDR)
-  – Skin Conductance
-  – NOL
-  – Nociceptive Flexion Reflex Threshold
-  – QNOx



<https://medasense.com/wp-content/uploads/The-NOL-Index-Algorithm-White-Paper.pdf>

Wie ist die aktuelle Evidenz?

BJA

British Journal of Anaesthesia, 134 (1): 180–191 (2025)

doi: [10.1016/j.bja.2024.09.020](https://doi.org/10.1016/j.bja.2024.09.020)

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Review Article

PAIN

Comparison of different monitors for measurement of nociception during general anaesthesia: a network meta-analysis of randomised controlled trials

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[23]

Wie ist die aktuelle Evidenz?

- Zielvariablen
 - intraoperativer Opioidkonsum
 - postoperativer Opioidkonsum
 - Zeit bis Entlassungsfähigkeit aus Aufwachraum
 - PONV
 - Extubationszeit
 - postoperative Schmerzen

Nur die Vergleiche zu standard of care vs. ANI, NOL, SPI, Pupillometrie und CARDEAN dargestellt [23]

Wie ist die aktuelle Evidenz?

- Zielvariablen
 - intraoperativer Opioidkonsum nur Pupillometrie ↓
 - postoperativer Opioidkonsum -
 - Zeit bis Entlassungsfähigkeit aus Aufwachraum nur Pupillometrie ↑
 - PONV -
 - Extubationszeit nur NOL ↓
 - postoperative Schmerzen -

Nur die Vergleiche zu standard of care vs. ANI, NOL, SPI, Pupillometrie und CARDEAN dargestellt [23]

Wie ist die aktuelle Evidenz?

- Spezifische Metaanalyse für NOL (Bornemann-Cimenti et al., 2023)^[24]

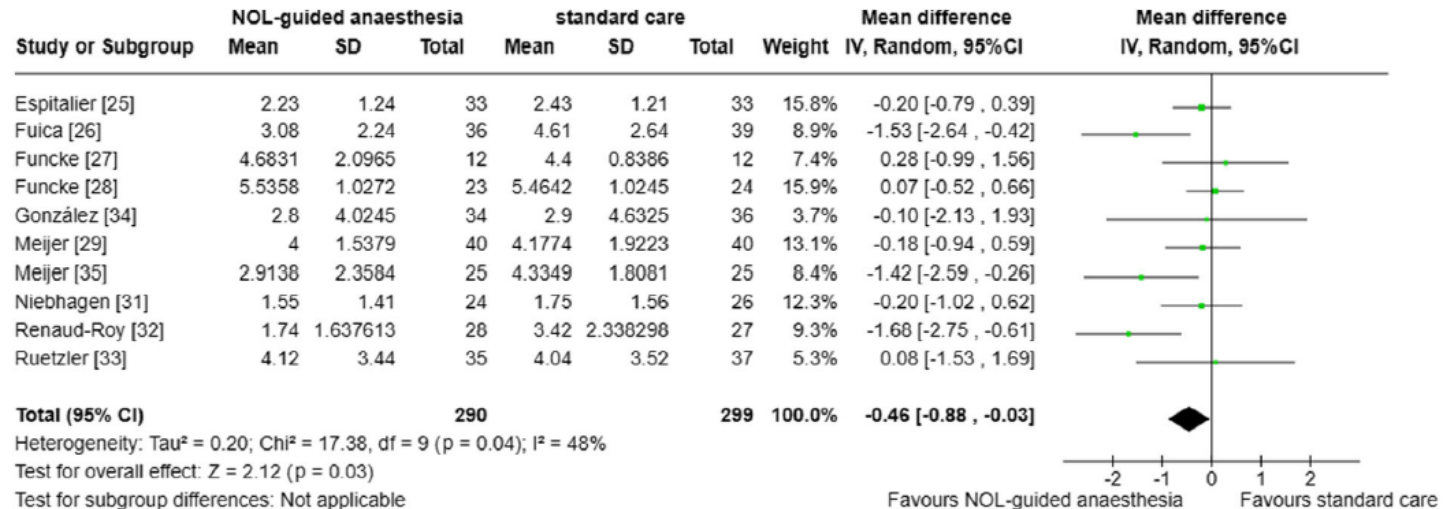


Figure 4 The effect of nociception level index-guided intra-operative analgesia on postoperative pain intensity compared with the effect of standard care in the first 60–120 min after surgery. IV, inverse variance; NOL, nociception level.

Wie ist die aktuelle Evidenz?

- aktuell ernüchternd^[23,24]
- **Aber ein Schritt zurück:** Nur vereinzelte Studien haben direkt den Zusammenhang zwischen Surrogatparametern intraoperativer Nozizeption – insbesondere NOL - und postoperativen Schmerzen untersucht!^[25-27]

Kooperation



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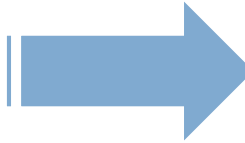
Medtronic

Fragestellung

- Assoziation intraoperativer nozizeptiver Einstrom vs. Schmerz POT₁



<https://medasense.com/wp-content/uploads/The-NOL-Index-Algorithm-White-Paper.pdf>



1. Wie stark waren Ihre Schmerzen seit der Operation, wenn Sie sich belastet haben, zum Beispiel bei **Mobilisierung, Bewegen, Waschen, Husten, Durchatmen**? Kreuzen Sie bitte die Zahl auf der Skala an, die für Ihren Belastungsschmerz zutrifft („0“ bedeutet Schmerzfreiheit und „10“ stärkster vorstellbarer Schmerz).

0	1	2	3	4	5	6	7	8	9	10
Kein Schmerz										Stärkster vorstellbarer Schmerz

2. Bitte kreuzen Sie hier den **stärksten Schmerz** an, den Sie seit Ihrer Operation hatten:

0	1	2	3	4	5	6	7	8	9	10
Kein Schmerz										Stärkster vorstellbarer Schmerz

3. Bitte kreuzen Sie hier den **geringsten Schmerz** an, den Sie seit Ihrer Operation hatten:

0	1	2	3	4	5	6	7	8	9	10
Kein Schmerz										Stärkster vorstellbarer Schmerz

Die nächsten vier Fragen beziehen sich darauf, ob bestimmte Tätigkeiten oder Ihre Stimmung seit der Operation **durch den Schmerz beeinträchtigt** sind. Mit „beeinträchtigt“ ist gemeint: die Tätigkeit ist **unmöglich** oder **nur unter großer Mühe möglich**.

Sind Sie durch die Schmerzen beeinträchtigt:

4. bei **Bewegung**?

☐ Ja ☐ Nein

5. beim **Husten oder tiefen Luftholen**?

☐ Ja ☐ Nein

6. beim **Schlafen**?

☐ Ja ☐ Nein

7. in Ihrer **Stimmung**?

☐ Ja ☐ Nein

8. Haben Sie sich seit der Operation sehr **müde** gefühlt?

☐ Ja ☐ Nein

9. Haben Sie seit der Operation unter **Übelkeit** gelitten?

☐ Ja ☐ Nein

10. Haben Sie seit der Operation unter **Schwindel** gelitten?

☐ Ja ☐ Nein

Methoden

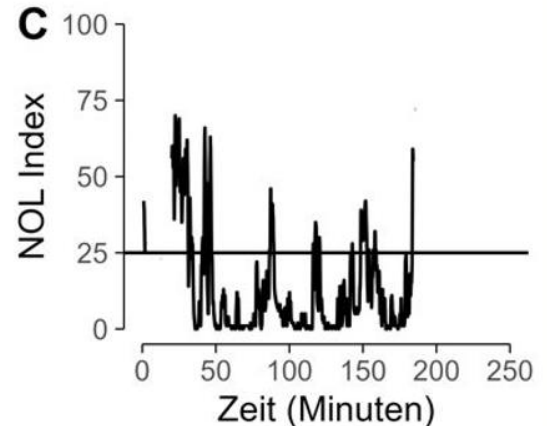
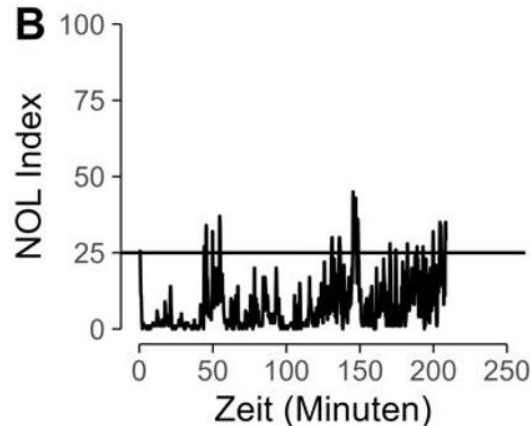
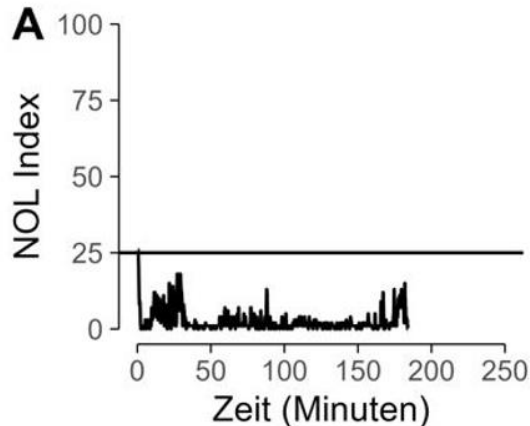
- PMD-200™ (Medasense, Ramat Gan, Isreal; Medtronic)
 - *Nociception Level (NOL): 0-100*



<https://medasense.com/wp-content/uploads/The-NOL-Index-Algorithm-White-Paper.pdf>

Methoden

- PMD-200™ (Medasense, Ramat Gan, Isreal; Medtronic)
 - *Nociception Level (NOL): 0-100*
 - Werte ≥ 25 indizieren potentielle nozizeptiven Einstrom^[28] bzw. „Untertherapie“^[29,30]



Methoden

- standardisierte Erfassung von PROs
 - QUIPS (Schmerzintensität/-beeinträchtigung und Nebenwirkungen)
 - **Primäre Zielvariable:** Schmerz-Composite-Score (SCS, 0-10 Punkte)
 - **Sekundäre Zielvariablen:** einzelne Items



Ergebnisse

- Stichprobenbeschreibung
 - NOL-Aufzeichnung: 155 [118-210] Minuten
 - NOL-Mittelwert: 8.6 [5.6-11.5]
 - NOL-Standardabweichung: 8.6 [6.9-10.8]
 - SCS: 3.7 [2.5-5.1]
 - Maximalschmerz: 5 [3-7] NRS
 - Bewegung: 142/239 (59.4%)
 - Übelkeit: 58/240 (24.2%)

Table 1 | Sample characteristics.

	Total sample N=242
Study Center, n/N (%)	
center 1	190/242 (78.5%)
center 2	52/242 (21.5%)
Surgical discipline, n/N (%)	
urology	193/242 (79.8%)
obstetrics/gynecology	24/242 (9.9%)
general surgery	13/242 (5.4%)
traumatology/orthopedics	10/242 (4.1%)
otorhinolaryngology	1/242 (0.4%)
oral/maxillofacial/plastic surgery	1/242 (0.4%)
Age (years), n/N (%)	
< 31	1/239 (0.4%)
31-50	18/239 (7.5%)
51-70	150/239 (62.8%)
>70	70/239 (29.3%)
Sex (female), n/N (%)	58/241 (24.1%)
Pre-existing chronic pain (yes), n/N (%)	44/237 (18.6%)
pain intensity > 3/10 NRS	40/235 (17%)
opioid intake	7/238 (2.9%)
ASA (I-VI), n/N (%)	
I	7/239 (2.9%)
II	152/239 (63.6%)
III	78/239 (32.6%)
IV	2/239 (0.8%)

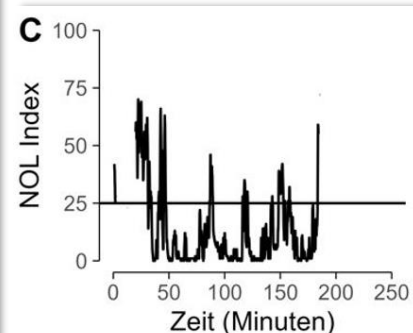
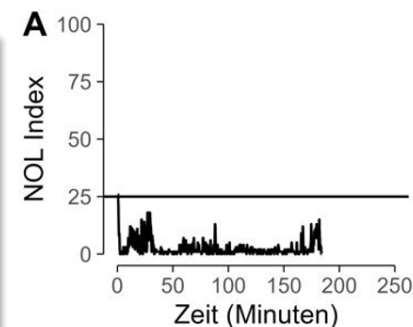
Ergebnisse

■ Primärer Endpunkt: SCS

Term	Risk-score model with medication: Full N=189 (R ² =0.26)		Backward deletion N=189 (R ² =0.26)	
	β_z [95% CI]	P	β_z [95% CI]	P
(Intercept)	-0.32 [-0.99 to 0.36]	0.360	-0.11 [-0.26 to 0.04]	0.144
NOL: standard deviation (z-score)	0.19 [0.06 to 0.33]	0.006	0.18 [0.05 to 0.32]	0.007
NOL-method: uncovered (vs covered)	-0.08 [-0.38 to 0.22]	0.590	n/a	
Pre-operative risk-score (-1 to 5 points) [†]	0.24 [0.09 to 0.39]	0.002	0.23 [0.09 to 0.37]	0.002
Type of surgery: others (vs urologic)	-0.53 [-0.95 to -0.1]	0.015	-0.53 [-0.9 to -0.17]	0.004
Type of anesthesia: GA+RA (vs GA only)	0.16 [-0.41 to 0.73]	0.587	n/a	
NOL: length of measurement (z-score)	0.04 [-0.11 to 0.19]	0.628	n/a	
Recovery room: non-opioid (vs none)	0.4 [0.01 to 0.78]	0.045	0.42 [0.04 to 0.8]	0.029
Ward: non-opioid (vs none)	0.18 [-0.47 to 0.84]	0.583	n/a	
Recovery room: Opioid (vs none)	0.11 [-0.16 to 0.37]	0.432	n/a	
Ward: Opioid (vs none)	0.87 [0.43 to 1.3]	<0.001	0.91 [0.49 to 1.33]	<0.001

β_z , standardized regression coefficient; GA, general anesthesia; NOL, NOL, nociception level monitor; P, p value of the regression coefficient; RA, regional anesthesia; R², coefficient of determination (0–1); 95% CI, 95% confidence interval

[†] Schnabel A, Yahiaoui-Doktor M, Meissner W, Zahn PK, Pogatzki-Zahn EM. Predicting poor postoperative acute pain outcome in adults: an international, multicentre database analysis of risk factors in 50,005 patients. *Pain Rep* 2020;5: e831.



Ergebnisse

- Sekundäre Endpunkte
 - NRS: Spearman's Korrelationskoeffizient
 - Dichotom: Mann-Whitney *U* Tests
 - Effektstärke (ES): *r*

Schmerzintensität (0-10 NRS)	Rho	P
Bewegung/Aktivität	0,20	0,002
Maximal	0,16	0,012
Minimal	0,14	0,027
Dichotome Variablen	ES	P
Beeinträchtigung		
Bewegung	0,12	0,08
Luftholen/Husten	0,10	0,11
Schlaf	0,10	0,14
Stimmung	0,05	0,45
Nebenwirkungen		
Müdigkeit	0,08	0,21
Übelkeit	0,25	<0,001
Schwindel	0,02	0,81
Behandlungswahrnehmung		
Wunsch nach mehr Schmerztherapie	0,04	0,57
Information über Schmerztherapie	-0,08	0,22

Fazit

- NOL ist signifikant mit SCS – primär der Schmerzintensität – am ersten postoperativen Tag assoziiert
- Aber: Zugewinn Varianzaufklärung „nur“ 3% bzw. Korrelationskoeffizienten im niedrigen Bereich

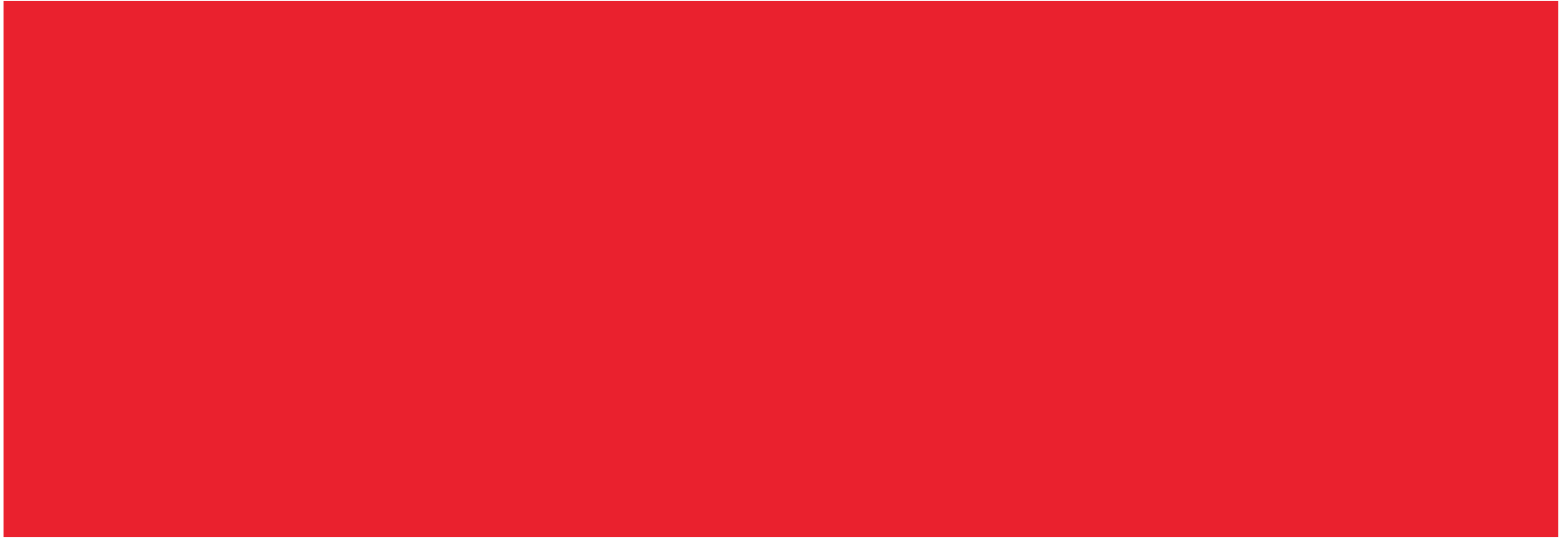
Take home message

- postoperative Schmerzen sind multifaktoriell und nur begrenzt durch Einzelmarker vorhersagbar
- **präoperativ** ist ein **multidimensionales Risikoprofil** am sinnvollsten
- **intraoperativ** erfassen wir Surrogate der Nozizeption, deren Bedeutung und Nutzen **noch nicht ausreichend geklärt** ist
- **Nutzen von Screening und Monitoring entsteht erst dann, wenn daraus konkrete therapeutische Entscheidungen folgen**

Vielen Dank für die Aufmerksamkeit

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Ergänzende Informationen



Methoden

- Studiendesign
 - Prospektive Multicenter-Studie
 - Ethikvoten: 2722-12/09, 241/18-lk, 2696-2015/2696_1-2015
 - Einschlusskriterien:
 - Erwachsene mit elektiver Operation
 - schriftliche Einwilligung
 - Ausschlusskriterien:
 - (geplanter/absehbarer) Aufenthalt auf Intensivtherapiestation
 - Sprachbarriere / kognitive Einschränkungen



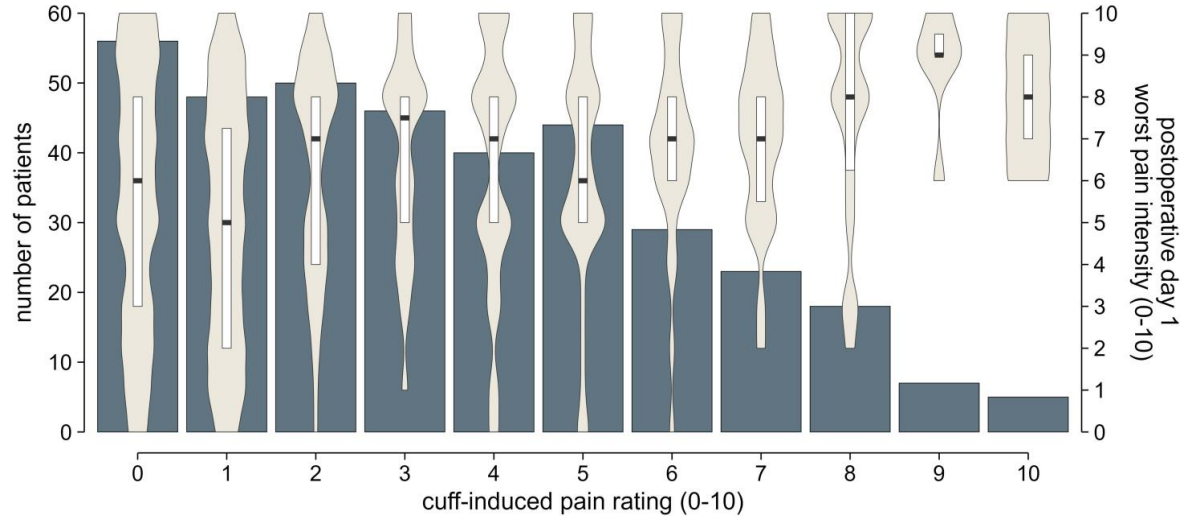
Methoden



- Endpunkte
 - Primär:
 - Unterschied in der maximalen Schmerzintensität (POT_1) zwischen $CIPR_{hoch}$ vs. $CIPR_{niedrig}$
 - Sekundär:
 - Unterschiede hinsichtlich weiterer PROs
 - Assoziation von CIPR (0-10 NRS), maximaler Schmerzintensität, Composite-Schmerz-Score (CSS) und starken postoperativen Schmerzen ($\geq 7/10$ NRS)
 - Explorativ:
 - ROC-Analysen
 - Clusteranalysen

Ergebnisse

- Patient:innen mit CIPR_{hoch}: n = 126/366 (34.4%)



- assoziierte Faktoren: weibliches Geschlecht (CIPR_{niedrig}: 42,4% vs. CIPR_{hoch}: 73%) und Alter > 60 Jahre (CIPR_{niedrig}: 60,4% vs. CIPR_{hoch}: 72,3%)

Ergebnisse

- multiple lineare Regressionsmodelle



	Worst pain intensity ^a (n=326, R ² =0.33 ^b)		CPS ^a (n=326, R ² =0.32 ^c)	
	β [95%CI]	P	β [95%CI]	P
(Intercept)	3.05 [2.43–3.67]	<0.001	1.91 [1.43–2.38]	<0.001
CIPR (0–10 NRS)	0.32 [0.22–0.41]	<0.001	0.20 [0.12–0.27]	<0.001
Surgical specialty: orthopedics/traumatology (vs. other)	1.58 [0.97–2.18]	<0.001	0.90 [0.45–1.34]	<0.001
Age: ≤60 years (vs. >60 years)	0.61 [0.09–1.13]	0.023	0.59 [0.20–0.98]	<0.001
Sex: female (vs. male)	dropped	–	0.45 [0.06–0.84]	0.023
Chronic preoperative pain: >3/10 NRS (vs. none or ≤3/10 NRS^d)	1.55 [0.95–2.15]	<0.001	1.30 [0.86–1.74]	<0.001
Chronic preoperative pain: Opioid use (vs. none)	0.78 [0.02–1.55]	0.045	0.48 [–0.09–1.05]	0.097

Abbreviations: CIPR, cuff-induced pain rating; 95%CI, 95% confidence interval; β, regression coefficient; NRS, numeric rating scale; P, P-value of the regression coefficient; R², coefficient of determination (0–1); RR, blood pressure cuff measurement

^a variable selection was based on the Akaike information criterion (AIC). The duration of surgery was not significantly associated with either outcome.

^b R² without CIPR: 0.24 (i.e., 8.7% additional variance explained)

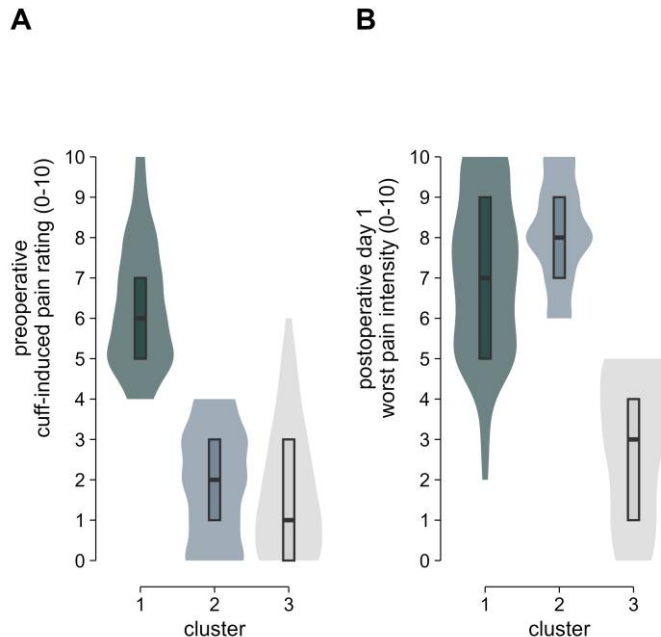
^c R² without CIPR: 0.27 (i.e., 5.6% additional variance explained)

^d only n = 14 patients with chronic pain and chronic pain intensity ≤ 3

P-values <0.05 are printed in bold.

Ergebnisse

■ Explorative Clusteranalyse



Domäne	Cluster 1 n=130	Cluster 2 n = 131	Cluster 3 n = 105
Präoperatives Risikoprofil	↑	↑↑	↓
CIPR	↑	↓	↓
Postoperative Opioidtherapie	↑	↑↑	↓
Patient-reported outcomes Tag 1	↑	↑↑	↓

	Thresh	Spec	Sens
Combined decision rule			
Risk score ≥ 1 OR CIPR ≥ 5	rule	0.29	0.87
Risk score ≥ 1 AND CIPR ≥ 5	rule	0.81	0.31
Risk score ≥ 1 OR CIPR ≥ 6	rule	0.32	0.86
Risk score ≥ 1 AND CIPR ≥ 6	rule	0.91	0.23

Ergebnisse

■ Explorative ROC-Analysen

	Thresh	Spec	Sens	Youden	PPV	NPV	LR+	LR-	TP	FN	TN	FP
Combined decision rule												
Risk score ≥ 1 OR CIPR ≥ 5	rule	0.29	0.87	0.165	0.59	0.66	1.23	0.43	158	23	45	109
Risk score ≥ 1 AND CIPR ≥ 5	rule	0.81	0.31	0.115	0.65	0.50	1.59	0.86	56	125	124	30
Risk score ≥ 1 OR CIPR ≥ 6	rule	0.32	0.86	0.187	0.60	0.67	1.28	0.43	156	25	50	104
Risk score ≥ 1 AND CIPR ≥ 6	rule	0.91	0.23	0.141	0.75	0.50	2.55	0.84	42	139	140	14

Abbreviations: CIPR, cuff-induced pain rating; AUC, area under the curve (95% confidence interval) of the receiver operating characteristic curve; **Thresh**, threshold for CIPR or the preoperative risk score; **Spec**, specificity; **Sens**, sensitivity; **Youden**, Youden index (the row with the maximum value is printed in bold); **PPV**, positive predictive value; **NPV**, negative predictive value; **LR+**, positive likelihood ratio; **LR-**, negative likelihood ratio; **TP**, true positives (n); **FN**, false negatives (n); **TN**, true negatives (n); **FP**, false positives (n)

Methoden

- Ethikvotum (Ethikkommission UKJ: 2722-12/09)
- Einschlusskriterien
 - Schriftliche Einwilligung
 - Alter ≥ 18 Jahre
 - Postoperative Behandlung auf Normalstation
 - Mind. 75% gültige intraoperative NOL-Messungen
- Ausschlusskriterien
 - Ablehnung/nicht anwesend/kognitiv eingeschränkt
 - Sprachbarriere

Methoden

- Statistik
 - Deskriptive Statistik
 - Median [Interquartilabstand]
 - Absolute (n) und relative Häufigkeiten (%)
 - Assoziative Analysen
 - Spearman Korrelationskoeffizienten
 - Multiple (lineare) Regression
 - Abhängige Variable: Schmerz an POT₁ (primär: SCS)
 - Unabhängige Variablen: NOL, Demographie und Prozessparameter

Ergebnisse

■ Stichprobenbeschreibung

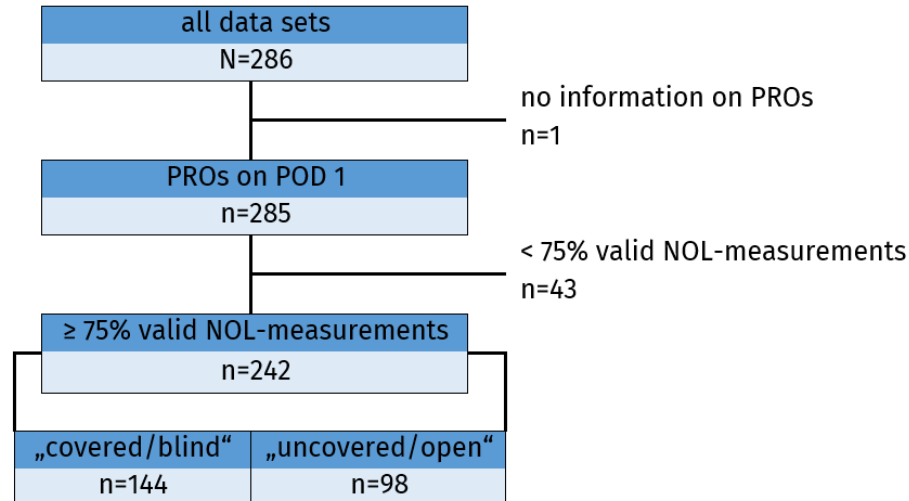
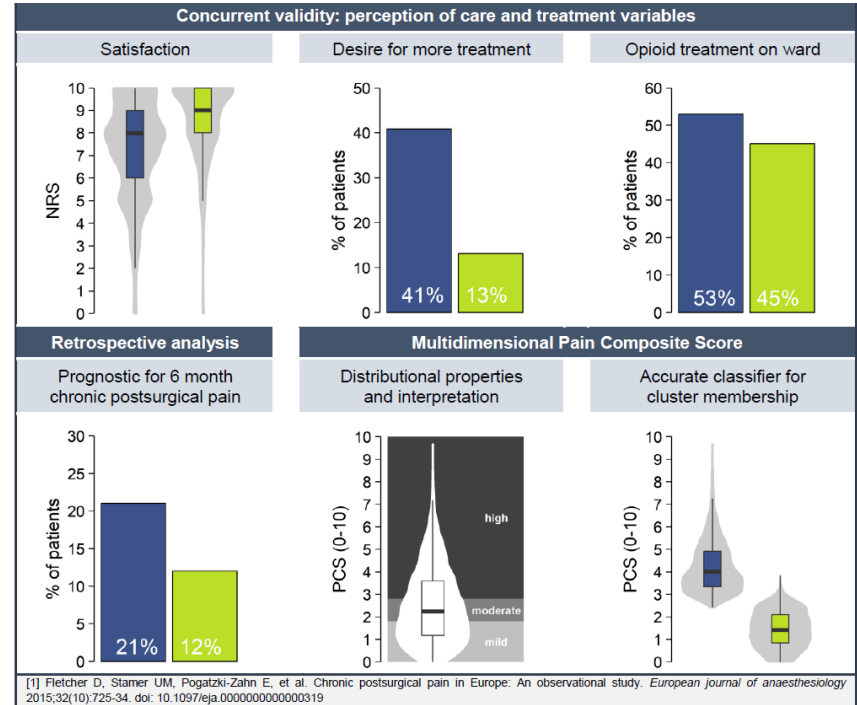
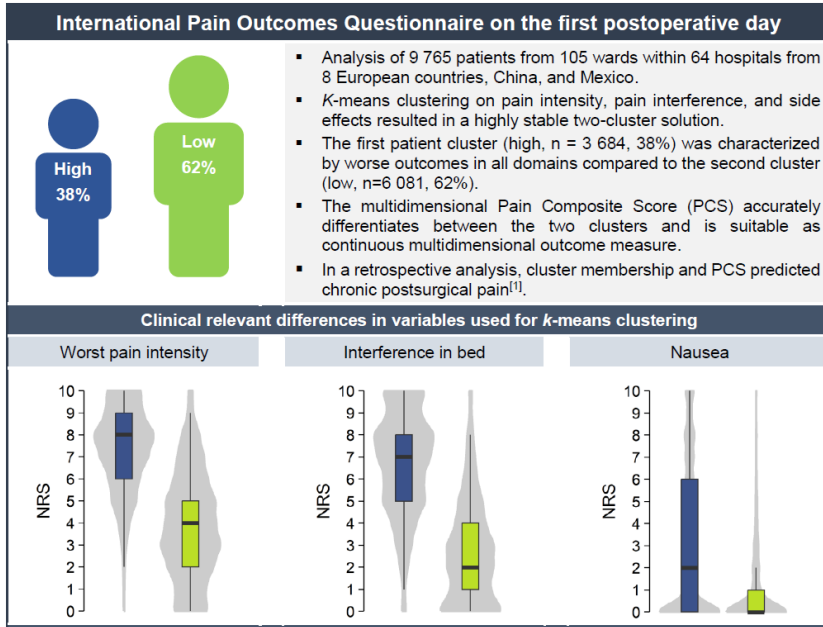


Figure 1 | Flow-Chart. NOL, Nociception Level monitor; POD1, postoperative day one; PROs, Patient-reported Outcomes

Ergänzende Informationen

- Zielvariablen
 - **Primär:** Schmerz Composite Score (SCS)
 - Mittelwert: Schmerzintensität (max., min. und bei Aktivitäten)
 - Summe: Schmerzbeeinträchtigung & Nebenwirkungen (nein: 0, ja: 1)
 - $SCS = (MW_{\text{Schmerzintensität}} + \text{Summe}_{\text{Beeinträchtigung \& Nebenwirkungen}}) / 1,7$
 - Wertebereich 0-10 (niedrige Werte indizieren bessere Outcomes)

Ergänzende Informationen



Ergänzende Informationen

Pre-operative risk score (-1 to 5)[†], median [IQR]	0 [0-1], n=227
Intraoperative anesthesia, n/N (%)	
general anesthesia (only)	211/239 (88.3%)
general and regional anesthesia	28/239 (11.7%)
Recovery room: non-opioid (any), n/N (%)	37/219 (16.9%)
Recovery room: opioid (any), n/N (%)	110/216 (50.9%)
Recovery room: PCA, n/N (%)	11/230 (4.8%)
Ward: non-opioid (any), n/N (%)	225/239 (94.1%)
Ward: opioid (any), n/N (%)	34/240 (14.2%)
Ward: PCA, n/N (%)	24/240 (10%)
Individual treatment plan (yes), n/N (%)	234/241 (97.1%)
Pain documentation (yes), n/N (%)	214/241 (88.8%)
Non-pharmaceutical treatment (any), n/N (%)	55/240 (22.9%)

ASA, American Society of Anesthesiologists risk classification; IQR, interquartile range; PCA, patient-controlled anesthesia

[†] Schnabel A, Yahiaoui-Doktor M, Meissner W, Zahn PK, Pogatzki-Zahn EM. Predicting poor postoperative acute pain outcome in adults: an international, multicentre database analysis of risk factors in 50,005 patients. *Pain/Rep* 2020;5: e831.

Ergänzende Informationen

Table 2 | Descriptive statistics for NOL-measurements.

	Total sample N=242
Method (NOL covered), n/N (%)	144/242 (59.5%)
Duration of measurement, median [IQR]	
total (minutes)	155.4 [118-209.9], n=242
valid (minutes)	148.5 [112.4-206.8], n=242
valid (%)	98.8 [96.9-99.6], n=242
Mean (0-100), median [IQR]	8.6 [5.6-11.5], n=242
Standard deviation (0-100), median [IQR]	8.6 [6.9-10.8], n=242
Maximum (0-100), median [IQR]	53 [43-66], n=242
AUC (total), median [IQR]	14,975 [9659.5-21,913.2], n=242
AUC (≥ 25), median [IQR]	3341 [1525.8-7275.8], n=242
Ratio: log₁₀(AUC: ≥ 25) / log₁₀(AUC: < 25), median [IQR]	0.9 [0.8-0.9], n=242
Time with measurements ≥ 25 (minutes), median [IQR]	7.7 [3.9-17.2], n=242
Time with measurements ≥ 25 (% of total time), median [IQR]	5.3 [2.7-10.4], n=242
Mean of measurements ≥ 25 (0-100), median [IQR]	33 [30.5-36.1], n=237

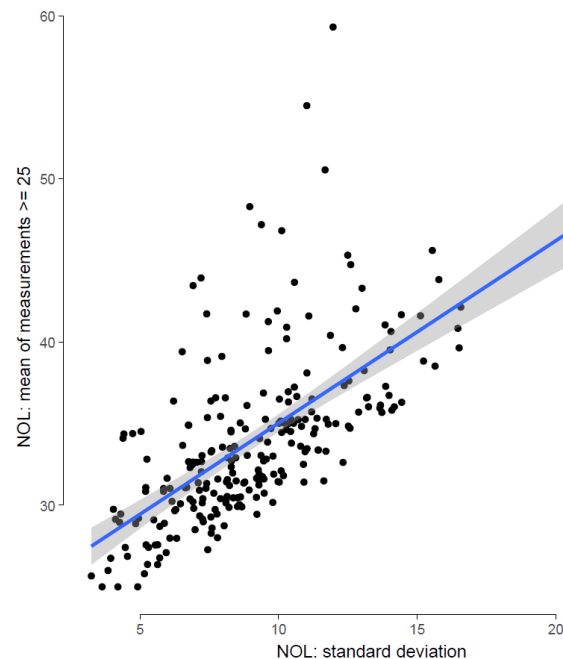
AUC, area under the curve (i.e., sum); IQR, interquartile range; NOL, nociception level monitor

Ergänzende Informationen

Table 3 | Example of Spearman correlation coefficients (ρ) between the standard deviation of NOL-measurements and other NOL-variables.

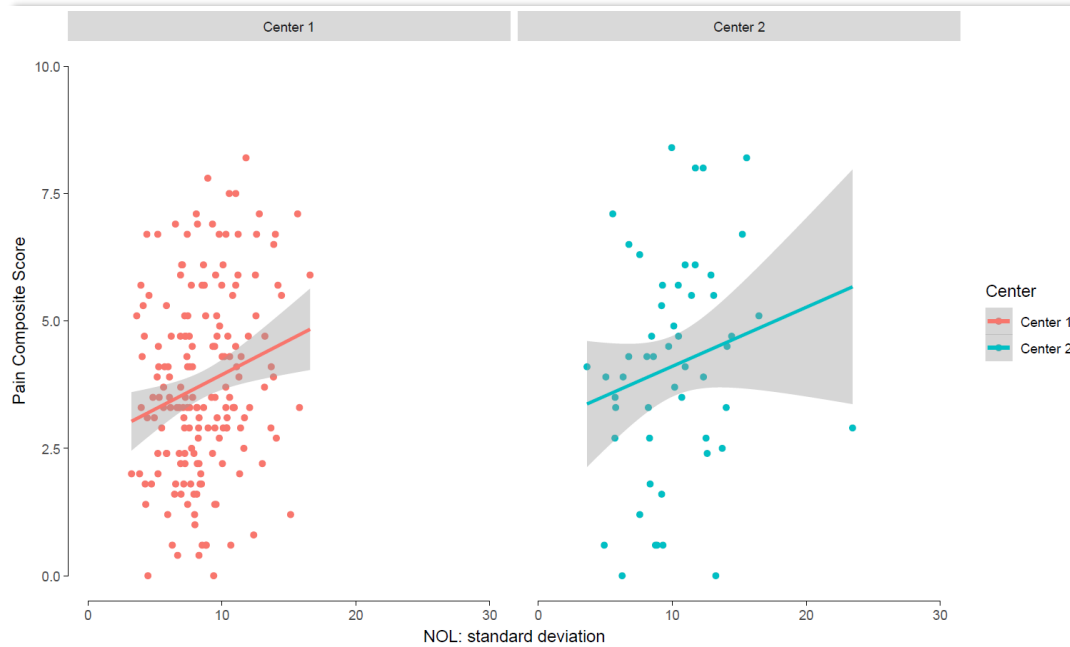
NOL: standard deviation (total) vs	ρ	P	N
Duration of measurement: valid (minutes)	-0.18	0.006	242
Duration of measurement: valid (%)	-0.15	0.016	242
Mean (total)	0.82	<0.001	242
Maximum	0.81	<0.001	242
AUC (total)	0.60	<0.001	242
Time with measurements ≥ 25 (minutes)	0.84	<0.001	242
Time with measurements ≥ 25 (% of total time)	0.89	<0.001	242
AUC ≥ 25	0.87	<0.001	242
Mean of measurements ≥ 25 (0-100),	0.70	<0.001	237
Ratio: $\log_{10}(\text{AUC: } \geq 25) / \log_{10}(\text{AUC: } < 25)$	0.92	<0.001	242

AUC, area under the curve (i.e., sum); NOL, nociception level monitor



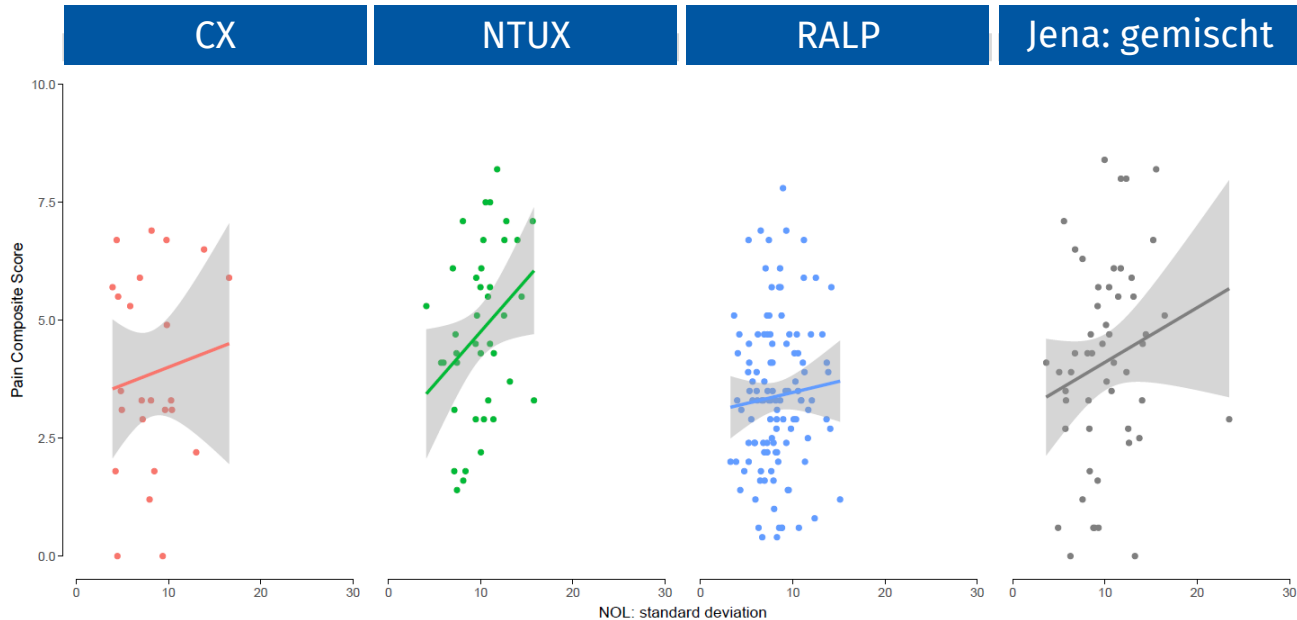
Ergänzende Informationen

- Zentrumseffekte



Ergänzende Informationen

- Unterschiede zwischen Operationen



Ergänzende Informationen

Variable 1	Variable 2	Category		p: MWU	es: r
NOL: Method	Duration of measurement: valid (minutes)	yes (covered)	135.6 [102.7-194.4], n=144	0,003	-0,19
		yes (uncovered)	160.7 [121.1-222.4], n=98		
	Duration of measurement: valid (%)	yes (covered)	98.8 [97.2-99.5], n=144	0,817	0,02
		yes (uncovered)	98.8 [96.4-99.6], n=98		
	NOL: mean (total)	yes (covered)	8.6 [5.4-12.4], n=144	0,705	0,02
		yes (uncovered)	8.6 [6.1-10.2], n=98		
	NOL: standard deviation (total)	yes (covered)	8.4 [6.6-10.6], n=144	0,436	-0,05
		yes (uncovered)	8.7 [7.2-10.9], n=98		
	NOL: max.	yes (covered)	52.5 [43-63], n=144	0,197	-0,08
		yes (uncovered)	53 [43.5-71.2], n=98		
	NOL: AUC (total)	yes (covered)	13822 [9100.5-20603.2], n=144	0,029	-0,14
		yes (uncovered)	16982.5 [10780-22993], n=98		
	NOL: time >=25 (total)	yes (covered)	6.5 [3.6-17.2], n=144	0,273	-0,07
		yes (uncovered)	9.9 [4.5-16.8], n=98		
	NOL: time >=25 (%)	yes (covered)	5.2 [2.7-12], n=144	0,806	0,02
		yes (uncovered)	5.8 [2.8-9.2], n=98		
	NOL: AUC >=25	yes (covered)	2562.5 [1406.2-7481.8], n=144	0,273	-0,07
		yes (uncovered)	3880.5 [1712.2-7193], n=98		
	NOL: mean (>=25)	yes (covered)	33.3 [30.4-35.4], n=141	0,357	-0,06
		yes (uncovered)	32.9 [30.7-37.2], n=96		
	NOL: sum (>=25)	yes (covered)	3.4 [3.1-3.9], n=144	0,273	-0,07
		yes (uncovered)	3.6 [3.2-3.9], n=98		
	NOL: sum (<25)	yes (covered)	4 [3.8-4.2], n=144	0,008	-0,17
		yes (uncovered)	4.1 [3.9-4.2], n=98		
	NOL: ratio	yes (covered)	0.9 [0.8-0.9], n=144	0,992	0,00