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Habilitationsschrift

Komplementäre und Integrative Medizin in der Behandlung chronischer muskuloskelettaler Schmerzen in der Allgemeinbevölkerung und bei Musizierenden

zur Erlangung der Lehrbefähigung
für das Fach Epidemiologie und Orthopädie

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Abkürzungsverzeichnis

ANCOVA	*Analysis of covariance*
CHBQ	*Complementary and Alternative Medicine Health Belief Questionnaire*
CKP	*Chronic knee pain*
CLBP	*Chronic unspecific low back pain*
CNP	*Chronic unspecific neck pain*
CSP	*Chronic shoulder pain*
DASH	*Disabilities of the Arm, Shoulder and Hand questionnaire*
DOI	*Digital Object Identifier*
EP	Endpunkt
FFbH-R	Funktionsfragebogen Hannover Rücken
HWS	Halswirbelsäule
HSA NHK	Hochschulambulanz für Naturheilkunde, Charité – Universitätsmedizin Berlin, Campus Mitte, Institut für Sozialmedizin, Epidemiologie und Gesundheitsökonomie
ICD-10	*International Statistical Classification of Diseases and Related Health Problems, 10th revision*
KI	Konfidenzintervall
KIM	Komplementäre und Integrative Medizin
LWS	Lendenwirbelsäule
MBSR	*mindfulness-based stress reduction*
MCID	*Minimal clinically important difference*
MCS	*Mental component scale*
MD	Mittelwertdifferenz
MW	Mittelwert
NCCIH	*National Center for Complementary and Integrative Health*
NDI	*Neck Disability Index*
NPDS	*Neck Pain and Disability Scale*
NRS	Numerische Ratingskala
PCS	*Physical component scale*
PROM	*Patient-reported outcome measure*
RCT	*Randomized controlled trial*
SD	*Standard deviation*
SF-12, SF-36	*Short Form 12, Short Form 36*
SUE	Schweres unerwünschtes Ereignis
UE	Unerwünschtes Ereignis
VAS	Visuelle Analogskala
WHO	*World Health Organization*

1. Einleitung

1.1 Chronische muskuloskelettale Schmerzen

Chronische Schmerzen im Bereich der Lendenwirbelsäule (LWS), der Halswirbelsäule (HWS) und Schmerzen an den großen Gelenken der Extremitäten gehören zu den führenden Erkrankungen und sie stellen eine starke globale Herausforderung dar.[1, 2] Sie führen teilweise zu erheblichen persönlichen Beeinträchtigungen mit Einschränkung der Lebensqualität, hohen Krankenständen und hohen gesamtgesellschaftlichen Kosten.[3-5] Nach einer Analyse der *Global Burden of Disease Study 2019* leiden etwa 1,7 Milliarden Menschen an muskuloskelettalen Erkrankungen, am häufigsten an LWS-Schmerzen.[6] Zudem haben muskuloskelettale Erkrankungen den größten Anteil am Rehabilitationsbedarf.[6]

In Deutschland wurde entsprechend der Krankheitslast-Studie BURDEN 2020 (n = 5.009 Erwachsene) eine 12-Monatsprävalenz für LWS-Schmerzen von 52,9% (55,0% der befragten Frauen und 48,6% der befragten Männer) und für HWS-Schmerzen von 45,7% (54,9% der befragten Frauen und 36,2% der befragten Männer) berichtet.[7] Chronische Rückenschmerzen (Brustwirbelsäulen-Schmerzen und LWS-Schmerzen zusammen) wurden von 18,5% der Teilnehmenden angegeben, mit zunehmender Prävalenz nach Lebensalter von 4,5% bei 18- bis 29-jährigen bis zu 23,4% bei über 70-jährigen.[7] In einer deutschen repräsentativen Querschnittsstudie zur Prävalenz chronischer Schmerzen (n = 2.510 Teilnehmende) betrug die 3-Monats-Prävalenz für LWS-Schmerzen 25%, für HWS-Schmerzen 18% und für Schulterschmerzen 9-11%.[8] Eine britische Querschnittsstudie berichtete zudem eine 12-Monats-Prävalenz von Kniegelenksschmerzen von 25,3% bei über 50-jährigen.[9] Eine besondere Häufung von muskuloskelettalen Beschwerden tritt bei Personengruppen auf, die aufgrund ihrer beruflichen Tätigkeit spezifisch lokalisierten repetitiven Überlastungen einzelner Gelenke oder Muskelgruppen ausgesetzt sind. Dies betrifft insbesondere auch die in dieser Habilitationsschrift mituntersuchten beruflich Musizierenden, insbesondere die hohen Streicher und Streicherinnen. Ungefähr 80% der beruflich Musizierenden, Musikstudierende eingeschlossen, erleben während ihrer Karriere leistungsbeeinträchtigende gesundheitliche Probleme, insbesondere HWS- und LWS-Schmerzen.[10-16] In professionellen Orchestern in Deutschland (n = 408 Musizierende, Rücklaufquote 57%) wurden mit dem Instrumentalspiel assoziierte, spielbezogene muskuloskelettale Beschwerden (*playing-related musculoskeletal disorders*) mit einer 3-Monats-Prävelenz von 62,7% und einer Punktprävalenz von 8,6% angegeben.[17]

Chronische Schmerzen sind definiert als anhaltende oder wiederkehrende Schmerzen, die länger als 3 Monate andauern.[18] Chronische muskuloskelettale Schmerzen betreffen Knochen, Gelenke, das dazugehörige Gewebe einschließlich der Muskulatur, der Faszien- und Bandstrukturen. Als Ursache von muskuloskelettalen Schmerzen werden verschiedene Faktoren berichtet. Hierzu zählen

insbesondere unphysiologischen Belastungen („Fehlbelastungen“), Schädigungen oder Erkrankungen der Knochen, Gelenke, des Bindegewebes, der Muskeln, der Nerven und Nervenhüllstrukturen.[19] Zusätzlich zu nozizeptiven und radikulären Schmerzen sind auch somatisch übertragene Schmerzen (*somatic referred pain*), übertragene Schmerzen durch segmentbezogene Reflexmechanismen sowie viszeral übertragene Schmerzen bedeutsam.[20-26] Übertragene Schmerzen könnten im medizinischen Alltag bei lediglich lokaler klinischer Untersuchung am Schmerzort unerkannt bleiben. Zudem können funktionelle Störungen wie beispielsweise muskuläre Hypertonien (Muskelverspannungen) bei myostatischen Dysbalancen zu den sogenannten unspezifischen muskuloskelettalen Schmerzen beitragen.

Definitionsgemäß liegen den häufigsten unspezifischen muskuloskelettalen Schmerzen keine spezifisch verursachenden Pathologien (z.B. Bandscheibenvorfall, Spinalkanalstenose, Fraktur, Infektion) zugrunde.[27-29] Bei Patienten mit Schmerzen im Bereich der Wirbelsäule gibt es Hinweise für eine gute bis sehr gute Reliabilität manualmedizinischer Untersuchungstechniken.[30] Allgemein können Methoden der strukturierten manuellen Differentialdiagnostik muskulärer und gelenkbezogener Strukturen noch nicht zufriedenstellend empfohlen werden, da deren Trennschärfe und Reliabilität noch nicht ausreichend belegt sind.[27] Die „Nationale Versorgungsleitlinie Nicht-spezifischer Kreuzschmerz“ empfiehlt daher den Einsatz bestimmter Techniken zum Monitoring des Krankheitsverlaufes.[27] Zudem sind beispielsweise bei unspezifischen LWS-Schmerzen nach dem Verständnis eines biopsychosozialen Krankheitsmodells auch psychische (z. B. Problemlösekompetenz, Selbstwirksamkeitserwartung) und soziale Faktoren (z. B. soziale Integration und Unterstützung, berufliche Situation) bei Krankheitsentstehung und -aufrechterhaltung relevant.[27, 31, 32] Chronische unspezifische LWS-Schmerzen haben eine besondere Bedeutung. Definiert werden sie als Schmerzen im Bereich des unteren Rückens, in der anatomischen Region unterhalb des Rippenbogens und oberhalb der Gesäßfalte, einschließlich der LWS, des Kreuzbeines und des Steißbeins.[19, 27, 28, 33] Die Begriffe chronische unspezifische Kreuzschmerzen, chronische unspezifische LWS-Schmerzen, chronisches Lumbalsyndrom, (englisch *chronic unspecific low back pain* (CLBP)) werden synonym verwendet. Weiterhin von hoher Bedeutung sind chronische unspezifische Schmerzen im Schulter-Nacken Bereich. Dieser Bereich wird definitionsgemäß kranial durch die obere Nackenlinie, kaudal durch den ersten Brustwirbel und lateral durch die Schultergelenkansätze des Musculus trapezius begrenzt.[29] Synonym werden die Begriffe chronische unspezifische Nackenschmerzen, chronische unspezifische HWS-Schmerzen, chronisches Zervikalsyndrom, (englisch *chronic unspecific neck pain* (CNP)) verwendet. Weiterhin bedeutend sind chronische Schmerzen insbesondere an den großen Gelenken der Extremitäten. Zu diesen zählen auch die in dieser Habilitationsschrift in einer Beobachtungsstudie behandelten chronischen Schmerzen an Schultergelenken und Kniegelenken.

Für chronische unspezifische Schmerzen im Bereich der LWS respektive der HWS wird zur Verbesserung der Lesbarkeit im Folgenden die jeweilige englische Abkürzung „CLBP“ respektive „CNP“

verwendet, für nicht-chronische und/oder nicht sicher als unspezifisch definierte Beschwerden werden die Begriffe „LWS-Schmerzen“ respektive „HWS-Schmerzen“ verwendet.

Die Therapie chronischer muskuloskelettaler Schmerzen sollte nach aktuellen Leitlinien innerhalb eines multimodalen Konzeptes erfolgen.[27, 34-41] Eine Langzeitmedikation mit Analgetika (beispielsweise nichtsteroidale Antirheumatika, Opioide, Paracetamol) kann zu unerwünschten Ereignissen (UEs) und schweren unerwünschten Ereignissen (SUEs) führen.[42, 43] Dies wurde insbesondere in den Vereinigten Staaten von Amerika (USA) im Rahmen der Opioid-Krise deutlich, bei welcher es im Zusammenhang mit einem Missbrauch von Opioid-Analgetika zu einem krisenhaft häufigen Anstieg von Drogenabhängigen und Todesfällen kam.[42, 43] Zudem wird nach aktuellen Erkenntnissen Paracetamol nicht mehr zur Behandlung von LWS-Schmerzen empfohlen.[44, 45] Eine nicht-medikamentöse Behandlung von muskuloskelettalen Schmerzen erscheint wünschenswert und wird in Leitlinien empfohlen. Die Qualität der Leitlinien-Empfehlungen zu komplementären Therapieverfahren in der Behandlung von Patienten und Patientinnen mit LWS-Schmerzen einschließlich CLBP wurde jedoch im Jahr 2020 noch als gering beschrieben.[46] Dennoch gewinnen gesamtgesellschaftlich und nach Leitlinien nichtpharmakologische, körperbasierte Präventions- und Behandlungsansätze wie dosierte sportliche Bewegung, manuelle Therapieverfahren, edukative Maßnahmen, berufsspezifische Ansätze, Selbstmanagementstrategien und achtsamkeitsbasierte Interventionen an Bedeutung.[27, 36, 37, 42, 43, 45, 47-53] Diese nichtpharmakologischen Präventions- und Behandlungsansätze können anteilig, teils überlappend, sowohl der konventionellen („biomedizinischen“, „klassischen“) Hochschulmedizin als auch der komplementären beziehungsweise der Komplementären und der Integrativen Medizin (KIM, wird in Abschnitt 1.2.1 erläutert) zugeordnet werden. Ein Beispiel[54] für Komponenten eines multimodalen Behandlungskonzeptes bei chronischen muskuloskelettalen Schmerzen ist in Abbildung 1 dargestellt.

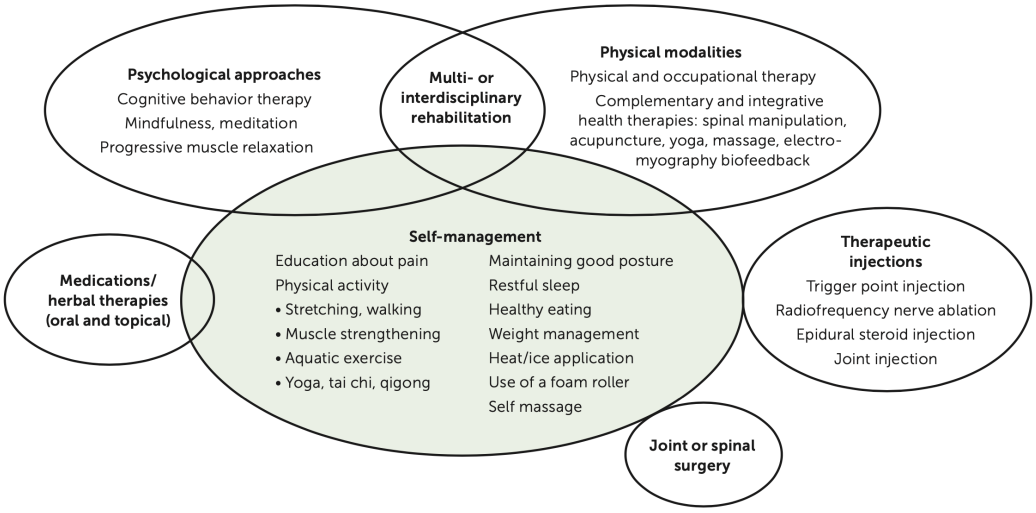

Abbildung 1. Mögliche Komponenten eines multimodalen Behandlungskonzeptes bei chronischen muskuloskelettalen Schmerzen. Aus: Flynn DM (2020)[54]

Entsprechend der Astana Deklaration (*Global Conference on Primary Health Care 2018*) der *World Health Organization* (WHO) sollte eine qualitativ hochwertige, sichere, umfassende, integrierte, zugängliche, verfügbare und erschwingliche medizinische Grundversorgung unter Einbeziehen von Gesundheitsdiensten für alle und überall, von gut ausgebildeten, qualifizierten, motivierten und engagierten Angehörigen der Gesundheitsberufe mit Mitgefühl, Respekt und Würde erbracht werden.[55] Hierbei wird explizit auch auf die integrierte Gesundheitsversorgung, welche auch körperbasierte Behandlungsansätze der KIM einschließt, abgezielt.

1.2 Körperbasierte Behandlungsansätze in der Komplementären und Integrativen Medizin

1.2.1 Komplementäre und Integrative Medizin (KIM)

Die komplementäre Medizin beinhaltet eine heterogene Gruppe von diagnostischen und therapeutischen Verfahren,[56] welche nicht der konventionellen (biomedizinischen beziehungsweise klassischen) Hochschulmedizin angehören, für die es zumindest Hinweise auf eine mögliche Wirksamkeit gibt. Eine große Vielfalt an Verfahren und die sich stetig entwickelnden und teils überlappenden Begrifflichkeiten erschweren auch heute noch eine eindeutige Definition. Kontextabhängig, sich geographisch, kulturell und zeitlich entwickelnd, werden Begriffe wie komplementär, integrativ, alternativ, ganzheitlich und erfahrungsbasiert mit Begriffen wie Gesundheit und Medizin kombiniert. Verwendet werden zusätzlich auch Begriffe wie Naturheilverfahren, besondere Therapierichtungen (Sozialgesetzbuch V), unkonventionelle Verfahren oder sanfte Medizin.[57-60] Im angloamerikanischen Sprachraum wurde bis vor etwa 10 Jahren der Begriff komplementäre Medizin häufig mit Alternativmedizin zu dem Begriff *Complementary and Alternative Medicine* zusammengefasst. Komplementäre Medizin und Alternativmedizin beinhalten oft dieselben Methoden, die gemäß dem Verständnis der komplementären Medizin den Therapieverfahren der konventionellen Hochschulmedizin[61] kombinierbar sind. Seit etwa 10 Jahren wird im angloamerikanischen Sprachraum eher der neuere Begriff *Complementary and Integrative Medicine* beziehungsweise *Complementary and Integrative Heath* benutzt. In den USA steht hierfür beispielhaft das durch das *National Center for Complementary and Integrative Health (NCCIH).*[62] Es gibt mehrere Definitionen von Integrativer Medizin und Gesundheit.[57] Es wurde beispielsweise definiert, dass in der Integrativen Medizin im Sinne eines ganzheitlichen und ressourcenorientierten Ansatzes, neben einer pathogenetischen Sichtweise, die salutogene und gesundheitsförderliche Perspektive ergänzt beziehungsweise in das bestehende Paradigma integriert wird.[57] Dieses Zusammengehen sollte nicht auf dem Verständnis einer Polarisierung beruhen, welche annähme, dass die konventionelle Hochschulmedizin auf die Pathogenese, dagegen die komplementäre Medizin auf Ganzheitlichkeit und Salutogenese alleinig abzielen würden. Die konventionelle Hochschulmedizin basiert zu großen Anteilen auf dem pathogenetischen Ansatz, enthält jedoch ebenfalls salutogene Ansätze beispielsweise im Bereich der Gesundheitsförderung. In der komplementären Medizin werden häufig salutogenetische Sichtweisen der Autoregulation, Gesundheitsförderung und ebenfalls der Selbstheilung verwendet. Zudem wird ebenso das

Entfernen von potentiell schädlich („pathogen“) verstandenen Agentien („Blockaden lösen“, „Entgiften“, „Ausleiten“) beabsichtigt. Dies einbeziehend und zusammenfassend ist ein wesentliches Merkmal der KIM die Integration von pathogenetischen und salutogenetischen Aspekten unter Zusammenführen von Methoden der konventionellen und der komplementären Medizin. Neuere Definitionen beziehen die Gesundheit, sowie alle therapeutischen, präventiven, gesundheitsfördernden und Lebensstilfaktoren ein.[57] Der Begriff KIM wird in dieser Habilitationsschrift im Folgenden durchgehend verwendet sofern nicht ausdrücklich Einzelkomponenten betont werden sollen.

KIM wird in Europa zunehmend und mit einer Spannweite von 0,3% bis 86%[63-65] in der Allgemeinbevölkerung in Anspruch genommen. In einer eigenen Querschnittsstudie fanden wir im Jahr 2019 unter Medizinstudierenden an der Charité – Universitätsmedizin Berlin unter 277 Antwortenden eine KIM Lebenszeitnutzung von 48,4%.[66] In einer Population von 334 Leistungssportlern und Leistungssportlerinnen (Alter (MW ± SD) 20,2 ± 6,6 Jahre, 25% weiblich), welche eine sportmedizinische Ambulanz in München besuchten, fand sich in einer Querschnittstudie, welche in Kooperation mit unserem Institut publiziert wurde, eine 12-Monats Prävalenz der KIM-Nutzung von 69%.[67]

In der europäischen und israelischen Allgemeinbevölkerung ist laut des siebenten *European Social Survey* (33.371 Teilnehmende) eine höhere KIM-Nutzung mit weiblichem Geschlecht, einem höheren Bildungsstatus, dem Vorliegen von chronischen Erkrankungen, höherer Inanspruchnahme des Gesundheitswesens, nicht erfüllten medizinischen Bedürfnissen, sowie einer negativen Meinung über den Zustand des Gesundheitswesens assoziiert.[68] Eine Datenanalyse aus der Schweizerischen Gesundheitsbefragung 2017 (18.832 Teilnehmende) ergab, dass unter anderem das weibliche Geschlecht, regelmäßiger Verzehr von Obst und/oder Gemüse und regelmäßige körperliche Aktivität Determinanten für die Verwendung von KIM waren. Derzeitiges Rauchen und Übergewicht/ Fettleibigkeit waren nach der Schweizerischen Gesundheitsbefragung 2017 Determinanten für die Nichtverwendung von KIM durch Patienten und Patientinnen.[65]

In Deutschland implementieren etwa 60% bis 85% der befragten Ärzte und Ärztinnen Verfahren der KIM in ihr klinisches Behandlungskonzept.[69, 70] Zu dieser Implementierung wird der Erwerb einer Zusatzbezeichnung empfohlen. Im Jahr 2021 waren in Deutschland 416,1 Tausend Ärzte beziehungsweise Ärztinnen berufstätig.[71] Hiervon praktizierten aktiv 17.891 Ärzte und Ärztinnen mit der Zusatzbezeichnung Manuelle Medizin/Chirotherapie, 13.044 Ärzte und Ärztinnen mit der Zusatzbezeichnung Akupunktur sowie 12.615 Ärzte und Ärztinnen mit der Zusatzbezeichnung Naturheilverfahren.[71]

Seit 2007 werden an der Hochschulambulanz für Naturheilkunde, Charité – Universitätsmedizin Berlin, Campus Mitte, Institut für Sozialmedizin, Epidemiologie und Gesundheitsökonomie (HSA NHK) Verfahren der KIM in die hochschulmedizinische Versorgung integriert und Forschungsprojekte zu

ausgewählten Verfahren durchgeführt. Die HSA NHK basiert auf der Charité Ambulanz für Prävention und Integrative Medizin, die von 2007-2012 bestand und im Innovationswettbewerb als "Ort im Land der Ideen 2008" ausgezeichnet wurde. Die HSA NHK versorgt interdisziplinär Patientinnen und Patienten mit überwiegend chronischen Erkrankungen und ermöglicht eine wechselseitige Translation von Wissenschaft und Praxis unter Einbeziehen von hochqualitativen Forschungsprojekten.[72-74]

1.2.2 Körperbasierte Behandlungsansätze

Verfahren und Bestandteile der KIM werden international noch uneinheitlich klassifiziert. Das NCCIH[58] schlägt für komplementäre Ansätze eine Klassifikation nach ihrem primären therapeutischen Einsatz, beziehungsweise der Art der Aufnahme oder Verabreichung der Therapie vor:

(1) Ernährungsbasierte Therapieansätze (z. B. spezielle Diäten, Nahrungsergänzungsmittel, Kräuter und Probiotika)

(2) Psychologisch basierte Therapieansätze (z. B. *mindfulness*)

(3) Physikalisch basierte Therapieansätze (z. B. Massagen, Wirbelsäulenmanipulation wie in der Osteopathischen Medizin und Chiropraktik)

(4) Kombinationen wie der von psychologisch und physisch basierten Therapieansätzen (z. B. Yoga, Tai Chi, Akupunktur, Tanztherapien, einige Formen der Kunsttherapie) oder psychologischen und Ernährungstherapien (z. B. achtsame Ernährung).

Anteilig hierauf basierend wurden Modifikationen von Barnes et al.[75] benutzt:

(1) Alternative medizinische Systeme (z. B. Akupunktur, Naturheilkunde, traditionelle Heiler)

(2) Biologisch basierte Therapien (z.B. auf Diät basierte Therapien)

(3) Manipulative und körperbasierte Therapien (z. B. Osteopathische Medizin, Chiropraktik, Bewegungstherapien wie Alexandertechnik oder Feldenkrais)

(4) Mind-Body Therapien (z.B. Meditation, Tai Chi, Qi Gong, Yoga) und

(5) Energetische Heiltherapien (z.B. Reiki).

In Kenntnis dessen verwendeten Fjær et al.[68] für eine Datenanalyse zur KIM-Nutzung (n = 33.371 Teilnehmende) eine dichotome Einteilung:

(1) Physikalische Therapien (z.B. Osteopathische Medizin, Chiropraktik, Akupunktur, Akupressur) und

(2) Konsumierbare Therapien (z.B. Pflanzliche Arzneimittel).

Basierend auf den genannten Klassifikationen[58, 68, 75] werden in dieser Habilitationsschrift nichtpharmakologische (und nichtkonsumierbare) physikalische Therapien in Form von:

(a) Körperbasierten Behandlungsansätzen und einer

(b) Kombination aus einem körperbasierten und einem psychologischen Behandlungsansatz untersucht. In dieser Habilitationsschrift wird schwerpunktmäßig auf den körperbasierten Anteil fokussiert.

Zu den (a) körperbasierten Behandlungsansätzen werden in dieser Habilitationsschrift Verfahren der Osteopathischen Medizin, die Tuina und das Schröpfen gezählt. Als eine Kombination aus einem körperbasierten und psychologischen Behandlungsansatz (b) wird das Achtsame Gehen (*Mindful Walking,* im Folgenden wird dieser Anglizismus verwendet) eingeordnet.

Nach vorausgegangener hochschulmedizinischer Diagnostik können körperbasierte Behandlungsansätze in das konventionell-hochschulmedizinische Therapiekonzept integriert werden. Körperbasierte Behandlungsansätze beachten psychosomatische Wechselwirkungen, sind jedoch gegensätzlich zur Körperpsychotherapie nicht notwendigerweise in ein Konzept der Psychotherapie eingebettet.[76] Körperbasierte Behandlungsansätze der KIM haben sich zumeist empirisch entwickelt und werden von Patienten und Patientinnen häufig genutzt. In dieser Habilitationsschrift werden klinische Studien zur wissenschaftlichen Untersuchung der Wirksamkeit und Sicherheit von körperbasierten Behandlungsansätzen bei Patienten und Patientinnen mit chronischen muskuloskelettalen Schmerzen einbezogen. Hierfür übergreifende Wirktheorien und mögliche Wirkmechanismen werden im Folgenden exemplarisch dargestellt. Körperbasierte Behandlungsansätze beabsichtigen unter anderem einen Ausgleich von myofaszialen und myostatischen Dysbalancen. Weiterhin wird die Anregung von körperlichen Regulationsprozessen beabsichtigt, unter anderem über Reflexmechanismen durch Setzen eines mechanischen Behandlungsreizes. Hierzu werden drei mögliche Wirkmechanismen diskutiert: 1) Schmerzreduktion durch mechanische Stimuli, so dass nozizeptive C-Fasern, Aδ-Fasern und mechanozeptive Aβ-Fasern stimuliert werden, 2) mechanische Einflüsse stimulieren hemmende rezeptive Felder der multirezeptiven Dorsalhornneuronen und 3) das Behandlungssetting könnte mental entspannend und beruhigend wirken.[77-79]

Segmentbezogene Reflexmechanismen könnten somatische und viszeral übertragene Phänomene unterhalten.[20-26, 77-81] Segmentale Störfaktoren können hierbei sowohl funktionelle (z.B. muskuläre Hypertonien) als auch pathologische Ursachen (z.B. Verletzung anatomischer Strukturen) sein. Durch segmentbezogene Reflexmechanismen erscheinen anatomisch-segmentale Verbindungen durch deren wechselseitige Beeinflussbarkeit diagnostisch und therapeutisch zugänglich.[21-23] Diese anatomisch-segmentalen Verbindungen umfassen die Haut/ Unterhaut (Dermatom), die Muskulatur (Myotom), das Nervengewebe (Neurotom), das Skelett/Periost (Sklerotom)[82, 83] in Überlappung zum vegetativen Nervensystem (sympathischer und parasympathischer Anteil) mit deren Innervation der Gefäße (Angiotom) sowie der Viszera.[21-23] Diagnostisch und therapeutisch wird dies beispielsweise in der KIM, wie beispielsweise in der Osteopathischen Medizin, der Manuellen Medizin, der Akupunktur, der Tuina, dem Schröpfen, der Bindegewebsmassage und der Neuraltherapie genutzt, beispielsweise unter Verwendung der diagnostischen Kiblerschen Hautfalte.[84-97] In der konventionellen Hochschulmedizin werden ebenfalls viszerokutane Reflexmechanismen nach Head[98] zu diagnostischen Zwecken berücksichtigt, beispielsweise können in den linken Arm ausstrahlende Schmerzen auf einen Myokardinfarkt hinweisen. Neben viszerokutanen Reflexmechanismen nach Head sind

die ebenfalls Anfangs des 20. Jahrhunderts beschriebenen myoviszeralen Reflexmechanismen nach Mackenzie[99] von besonderer Bedeutung. Hiernach können viszerale Pathologien beispielsweise mit muskulären Hypertonien und Schmerzen wie CNP oder CLBP in Verbindung stehen. Beispielhaft kann demnach eine Cholezystitis muskuläre Hypertonien und Schmerzen im Bereich des Thorax, der Brustwirbelsäule und der HWS auslösen. Eine integrierende Zusammenarbeit von Orthopädie, Innerer Medizin, Chirurgie und KIM könnte demnach eine zielgerichtete Diagnostik und Therapie von chronischen muskuloskelettalen Schmerzen unterstützen.

Allgemeine körperliche Regulationsprozesse können durch Kombination von gering-intensiver aerober Bewegung wie dem Gehen *(Walking)* und Selbstmanagementstrategien angeregt werden. Dies lässt sich als kombinierten körperbasierten und psychologischen Behandlungsansatz durch eine Verbindung von Walking und leicht zugänglich-niederschwelligen Achtsamkeits- (*Mindfulness*) Übungen realisieren. Im Folgenden werden in dieser Habilitationsschrift verwendete körperbasierte Behandlungsansätze übersichtsartig vorgestellt.

1.2.3 Osteopathische Medizin

Osteopathie (altgriechisch ‚ostéon' Knochen; ‚páthos' Leiden) und Osteopathische Medizin (beide in der Habilitationsschrift unter dem Begriff Osteopathische Medizin zusammengefasst) sind in Deutschland Teil der KIM. Die Osteopathische Medizin versteht sich als medizinischer Ansatz und basiert in Diagnostik und Therapie grundsätzlich auf der konventionellen Hochschulmedizin. In deren Ergänzung nutzt sie manuelle Diagnostik- und Therapieverfahren unter besonderer Berücksichtigung der strukturellen und funktionellen Integrität des Körpers, einschließlich seiner skelettalen, arthrodialen und myofaszialen Strukturen, sowie der damit verbundenen vaskulären, lymphatischen und neuralen Elemente.[84] Es werden das muskuloskelettale („parietale"), das viszerale[100] und das neurovegetative System mit den „kranial und sakral" verorteten anatomischen Strukturen einbezogen. Die Behandlungstechniken umfassen Manipulationen (Techniken unter Einsatz einer hohen Geschwindigkeit und geringen Amplitude) und allgemein Bewegungen von Gelenken (Mobilisationen), sowie Druck-, Zug- und Lagerungstechniken auf anatomische Körperstrukturen. Hierdurch werden auch unter Einbeziehen von segmentbezogenen Reflexmechanismen, übertragenen Schmerzen und myostatischen Dysbalancen funktionelle Störungen, wie muskuläre Hypertonien, Myogelosen, Triggerpunkte, Jones Punkte, somatische Dysfunktionen etc. behandelt, also Muskelverspannungen reduziert und „Blockaden gelöst". Unterstützend werden Eigenübungen beispielsweise mit dem Ziel der Verbesserung der Körperhaltung (Posturologie), dem Abbau myostatischer, myofaszialer und arthromuskulärer Dysbalancen angeleitet und zu es wird zu Lebensstilfaktoren (z.B. körperliche Bewegung, Ernährung) beraten.[101]

Im Allgemeinen werden manuelle Therapieverfahren seit Jahrtausenden angewandt. Aufzeichnungen zu manuellen Behandlungen des Rückens lassen sich nach Arno Sollmann auf etwa 2900 vor

unserer Zeitrechnung in Ägypten mittels des Edwin Smith *Surgical Papyrus* (mittelägyptische Abschrift aus etwa 1550 vor unserer Zeitrechnung) sowie auf etwa 2100 vor unserer Zeitrechnung in Mesopotamien zurückführen.[102] Die Osteopathische Medizin beruht auf den Theorien des Arztes Andrew Taylor Still Mitte bis Ende des 19. Jahrhunderts in den Vereinigten Staaten von Amerika.[84]

Die Ausübung von Osteopathischer Medizin ist international sehr unterschiedlich beziehungsweise nicht geregelt. In den USA wird die Osteopathische Medizin heute durch speziell hierfür voll approbierte Ärzte und Ärztinnen (*osteopathic physicians, Doctors of Osteopathic Medicine),* die gleichberechtigt zu den *Medical Doctors* sind, ausgeübt.[103, 104] Die Osteopathische Medizin wird von den *Doctors of Osteopathic Medicine* in den USA als Teil der konventionellen Medizin gesehen. Als zweites Land weltweit werden auch in Russland medizinisch ausgebildete osteopathische Ärzte und Ärztinnen als *osteopathic physician* anerkannt.[101] Weltweit wird die Osteopathische Medizin heute in 46 Ländern durch etwa 197.000 Behandelnde, davon durch etwa 118.000 registrierte osteopathische Ärzte und Ärztinnen (*osteopathic physicians* in den USA und Russland) oder Ärzte und Ärztinnen mit zusätzlicher osteopathischer Ausbildung (*medical physicians with osteopathic training)* angewandt.[101] In Deutschland gibt es, im Gegensatz zu einigen europäischen Ländern, keine formelle Regelung und keinen definierten Beruf "Osteopath".[101, 105] Die Ausbildung in Deutschland erfolgt zumeist in privaten Einrichtungen als nicht staatlich anerkannte Teilzeitausbildung für Ärzte und Ärztinnen[106] sowie andere Gesundheitsberufe (z.B. der Physiotherapie) beziehungsweise als nicht staatlich anerkannte Vollausbildung nach dem Abitur mit späterer Heilpraktiker-Qualifikation. Die strukturierte curriculare Fortbildung „Osteopathische Verfahren“ der Bundesärztekammer von 2013,[107] sieht eine Ausbildung von 160 Stunden in Ergänzung zur bereits bestehenden Zertifizierung (Beispiel Berliner Ärztekammer) in Manueller Medizin/Chirotherapie[108] vor. Aktuell können Ärzte und Ärztinnen noch nicht deutschlandweit eine umfängliche Zusatzweiterbildung für die Osteopathische Medizin erwerben. Beispielsweise ist keine Zusatzweiterbildung für osteopathische Verfahren oder Osteopathische Medizin in der Weiterbildungsordnung der Ärztekammer Berlin[108] gelistet. Gesetzliche Krankenkassen erstatten ihren Versicherten derzeit maximal einen Teilbetrag der Behandlungskosten zurück. Hierdurch erscheint es wahrscheinlich, dass die Osteopathische Medizin vermehrt durch Menschen mit höheren finanziellen Mitteln in Anspruch genommen wird.

1.2.4 Tuina

Tuina (Chinesisch ‚Tui‘ Schieben; ‚Na‘ Greifen) ist Teil der Chinesischen Medizin und der KIM.[91, 92, 109, 110] Tuina ist ein manuelles Therapieverfahren, das darauf abzielt, die Gesundheit zu fördern und verschiedenartige Beschwerden und Erkrankungen zu behandeln.[91, 92, 109] In den westlichen Ländern orientiert sich Tuina diagnostisch an der Hochschulmedizin sowie der Chinesischen Medizin, berücksichtigt anatomische sowie physiologische Prinzipien und fokussiert therapeutisch vorwiegend auf Akupunkturpunkte sowie Meridiane der Chinesischen Medizin.[91] Tuina umfasst spezifische manuelle Behandlungstechniken des Schiebens, Greifens, Ein-Finger-Drückens, Rollens, Knetens,

Reibens sowie des Pressens von Weichteilen.[91] Zudem werden an Wirbelsäule und Gelenken Manipulationen durchgeführt.[109] Durch Tuina-Techniken sollen energetische Ungleichgewichte („Leber Qi Stagnation“, „Blockaden des Qi und Xue“) behoben werden und „Blockaden gelöst“ werden. Die WHO zitiert in den *Benchmarks for training in Tuina*, dass Tuina in China seit über 2000 Jahren verwendet wird.[91]

Die Tuina-Ausbildung erfolgt in Deutschland in privaten Einrichtungen/Verbänden als nicht staatlich anerkannte Zusatzausbildung beispielsweise für Ärzte und Ärztinnen sowie andere Gesundheitsberufe. Im Gegensatz zur Akupunktur, welche ebenfalls Teil der Chinesischen Medizin ist, gibt es aktuell für die Tuina keine bei den zuständigen Ärztekammern (beispielsweise Berlin) anerkannte Zusatzweiterbildung.[108] Die Kosten von Tuina-Behandlungen werden derzeit nicht von den deutschen gesetzlichen Krankenkassen erstattet.

1.2.5 Schröpfen

Schröpfen ist Teil der KIM (und hierin sowohl Teil der Chinesischen Medizin und der Naturheilkunde) sowie der traditionellen westlichen Medizin. Beim Schröpfen werden auf lokal palpable Bindegewebsbefunde (z.B. muskuläre Hypertonien, Myogelosen) Glocken, (z.B. aus Glas, Plastik oder Bambus) mit einem in ihnen erzeugten Unterdruck auf zu behandelnde Regionen statisch platziert. Alternativ können die Glocken massageartig bewegt werden. Der Unterdruck kann thermisch mittels einer Hitzequelle sowie mechanisch mittels eines Gummiballons oder eines Unterdruck-erzeugenden Apparates erzeugt werden.[96] Das Schröpfen wird auch zu den sogenannten ausleitenden Verfahren („Entgiftung“) gezählt. Allgemein unterscheidet man drei Arten des Schröpfens: (1) das trockene Schröpfen, (2) das blutige Schröpfen bei dem zusätzlich die Haut vor Aufsetzen des Schröpfkopfes inzidiert wird und wonach sich der Schröpfkopf teilweise mit Blut füllt, sowie (3) die Schröpfkopfmassage bei welcher die Haut eingeölt und anschließend mit der Schröpfglocke massiert wird.[96]

Schröpfen wurde traditionell sowohl in der asiatischen (unter anderem in der Chinesischen Medizin), der nahöstlichen und in der europäischen Medizin[94, 109, 111] genutzt. Die ältesten Beschreibungen gehen auf den ägyptischen Ebers-Papyrus (etwa 1550 vor unserer Zeitrechnung) und die antike griechische Medizin zurück.[94] In Europa wurde das Schröpfen seit dem Mittelalter in Klöstern gelehrt und bis in das 19. Jahrhundert von Ärzten und Ärztinnen sowie von Laien angewandt. Im Zuge der pharmakologischen Entwicklung im 20. Jahrhundert verlor das Schröpfen in der hochschulmedizinischen Lehre und Praxis an Bedeutung. Aktuell wird das Schröpfen vorwiegend zur Behandlung von unspezifischen muskuloskelettalen Schmerzen unter Nutzung segmentaler Reflexmechanismen eingesetzt.[94, 96, 111] Kenntnisse und Fertigkeiten hinsichtlich des Schröpfens sind in Deutschland Bestandteil staatlich anerkannter Ausbildungscurricula zur Physiotherapie, zum Masseur und medizinischen Bademeister beziehungsweise Masseurin und medizinischen Bademeisterin, sowie Teil der ärztlichen Zusatzweiterbildungen Akupunktur und Naturheilkunde.[108] Ärztlich erbrachte Leistungen

des Schröpfens können in Deutschland über Leistungsziffern der Gebührenordnung für Ärzte[112] für privat Krankenversicherte, jedoch nicht für gesetzlich Krankenversicherte erstattet werden.

1.2.6 Mindful Walking

Mindful Walking kombiniert einen körperbasierten Behandlungsansatz, das Gehen als Form einer gering intensiven aeroben Bewegung[49, 50] mit einem psychologischen Behandlungsansatz, dem Achtsamkeitstraining. Beim Mindful Walking steht die Achtsamkeit im Vordergrund und wird im Folgenden kurz beschrieben. Achtsamkeitstraining *(mindfulness training*) ist Teil der KIM und ist eine aus der buddhistischen Meditation abgeleitete Strategie zur mentalen Stressreduzierung. Achtsamkeit wird definiert als die Tendenz, Erfahrungen von Augenblick zu Augenblick zu begegnen, ohne sich in nicht hilfreichen oder belastenden Gedanken zu verlieren.[113] Achtsamkeit nach Karbat-Zinn[114] ist absichtsvoll, bezieht sich auf den gegenwärtigen Moment und ist nicht wertend. Achtsamkeit wird oft auch mit Offenheit, Urteilslosigkeit, Neugier, Akzeptanz, Mitgefühl und Freundlichkeit in Verbindung gebracht.[115]

Achtsamkeitsbasierte Interventionen können als Selbstmanagementstrategien im Rahmen eines multimodalen Therapiekonzeptes eingesetzt werden und Schmerzen lindern.[116] So können entsprechend des biopsychosozialen Krankheitsmodells von Schmerzen die wichtigen psychologischen Faktoren wie Angst, Stress und Katastrophisieren adressiert werden.[116-118]

Beim Mindful Walking können gleichzeitig zwei mit der Schmerzwahrnehmung verbundene Mechanismen angesprochen werden: Körperliche Aktivität sowie Achtsamkeitstraining und Stressreduktion. Dies kann insbesondere für Menschen mit muskuloskelettalen Schmerzen und mit konkurrierenden Anforderungen an ihre Freizeit attraktiv sein, da hierdurch gleichzeitig Vorteile körperlicher Aktivität und mentaler Stressreduktion zur Schmerzlinderung nutzbar werden. Die Ausbildung in Achtsamkeitstraining, insbesondere der Richtung der Achtsamkeitsbasierten Stressreduktion (*mindfulness-based stress reduction*, MBSR) nach Kabat-Zinn[114] erfolgt in Deutschland in privaten Einrichtungen/Verbänden als nicht staatlich anerkannte Zusatzausbildung beispielsweise für Ärzte und Ärztinnen sowie andere Gesundheitsberufe. Achtsamkeitsbasierte Interventionen sind keine anerkannte Zusatzweiterbildung der Berliner Ärztekammer.[108] Gesetzliche Krankenkassen bezuschussen mit anteiligen finanziellen Beiträgen Achtsamkeitskurse zum MBSR als Gesundheitskurse.[119]

Im Folgenden Abschnitt wird, da im Rahmen dieser Habilitationsschrift relevant, zudem ein sich entwickelndes medizinisches Fachgebiet vorgestellt.

1.3 Musikermedizin

Die Musikermedizin (der Begriff wird in dieser Habilitationsschrift für Musikermedizin und Musikerinnenmedizin verwendet) sieht sich als ein auch in Universitäten vertretenes Fachgebiet, dass sich der Prävention, Diagnostik und Therapie von Beschwerden widmet, welche durch das Musizieren entstehen oder sich auf das Musizieren auswirken können.[120] Die Musikermedizin geht auf Ramazzini im frühen 18. Jahrhundert zurück.[121] Der deutsche Musikwissenschaftler Kurt Singer beschrieb zu Beginn des 20. Jahrhunderts erstmals systematisch Symptomatik und Therapie beruflicher Erkrankungen durch das Musizieren.[122, 123] Zur Jahrtausendwende wurde aufgrund empirischer Beobachtungen von häufigen muskuloskelettalen Beschwerden und Erkrankungen im Zusammenhang mit dem beruflichen Instrumentalspiel eine Reihe von zumeist Querschnittstudien zu deren Erfassung publiziert. Hierbei wurden unterschiedliche Definitionen benutzt, beziehungsweise es wurde auf das "Überlastungssyndrom" verwiesen.[124, 125] Im Jahr 1998 wurde von Zaza et al.[126] der Terminus der spielbezogenen muskuloskelettalen Beschwerden eingeführt, der verschiedene muskuloskelettale Beschwerden und Erkrankungen zusammenfasst. Unter anderem in Deutschland haben sich im späten 20. und frühen 21. Jahrhundert zunehmend musikermedizinische Sprechstunden sowie Präventionsprogramme an Musikhochschulen und Universitäten unter Nominierung von Professuren etabliert.[127]

Da beruflich Musizierenden bereits in früher Kindheit mit Ihrer Karriere beginnen und Musikhochschulen sehr hohe spieltechnische und musikalische Anforderungen bereits in den Aufnahmeprüfungen zum Musikstudium stellen, werden in unserer Arbeitsgruppe auch Musikstudierende zu den beruflich Musizierenden gezählt. Allein in den klassischen 129 Berufsorchestern erfasst die Deutsche Orchestervereinigung e.V. 9.749 Planstellen (Jahresbericht vom Januar 2022), hiervon 8.513 Planstellen in 110 staatlichen, städtischen, öffentlich finanzierten Orchester, 141 Planstellen in 8 öffentlich finanzierten Kammerorchestern und 1.095 Planstellen in 11 Rundfunkorchestern (ohne Tanzorchester, Big Bands).[128] Hinzu kommen frei schaffende Musizierende sowie etwa 26.500 Studierende der Musik und Musikwissenschaft (Wintersemester 2021/2022) an 24 Musikhochschulen in Deutschland, welche vorwiegend in klassischen Musikgenres studieren.[129-131]

Insbesondere Violinisten, Violinistinnen, Violisten und Violistinnen (im Weiteren als hohe Streicherinnen und Streicher benannt) leiden im Zusammenhang mit den speziellen Spielanforderungen häufig unter muskuloskelettalen Schmerzen, insbesondere unter CNP.[14] In diese Habilitationsschrift werden hohe Streicher und Streicherinnen mit CNP einbezogen. Bei hohem Notenaufkommen in der Musikliteratur erfordert ihr Spiel eine hohe Frequenz wiederholter Bewegungen sowie komplexe Wiederholungsbewegungen mit langen statischen und dynamischen muskulären Belastungen. Dies erfolgt unter asymmetrischer Körperhaltung in Bezug auf beide Arme und die HWS. In der Regel hält die linke Hand die Violine oder Viola zusammen mit dem Druck des Kinns gegen die Schulter. Die linke Hand wird somit zeitweilig von der Haltearbeit befreit und schnelle sowie weite

Lagenwechsel sind möglich.[132] Durch Kinnhalter und Schulterstütze müssen die Instrumente angepasst werden.[133] Hierbei entsteht eine für das spezifische Instrumentalspiel typische, punktuelle Überlastung betroffener muskuloskelettaler Strukturen. Die Behandlung von hohen Streichern und Streicherinnen erfordert daher eine spezielle musikermedizinische Anamnese, Beratung und Behandlung. Dies beinhaltet individuelle Therapie- und Präventionsempfehlungen wie Haltungskorrektur, angepasste Bewegungsschulungen, Optimierung der Übungsgewohnheiten nach musikpädagogischen und musikphysiologischen Erkenntnissen, körperbasierte Behandlungsansätze, Strukturierung von Spielpausen und Wiederbeginn, Thermotherapie, Optimierung ergonomischer Hilfen wie Kinnhalter und Schulterstützen, analgetisch-antiphlogistische Therapie, physiotherapeutische Verfahren, manuelle Therapien und psychotherapeutische Maßnahmen.[132, 134] Die Musikermedizin stellt keine eigene Facharztbezeichnung oder Zusatzbezeichnung beispielsweise bei der Berliner Ärztekammer.[108] Musikermedizinische Sprechstunden können lediglich für die erbrachten ärztlichen Leistungen abrechnen.

1.4 Forschungsstand

1.4.1 Osteopathische Medizin

Osteopathische Medizin wird in Deutschland und international häufig in Anspruch genommen, insbesondere in der Behandlung von muskuloskelettalen Erkrankungen und Schmerzen.[135] Unter Erwachsenen wurde eine Inanspruchnahme während 12 Monaten von 4,6% (n = 1.067 Interviews, Australien) berichtet.[136] Entsprechend der Schweizerischen Gesundheitsbefragung 2017 (18.832 Teilnehmende) ist die Osteopathische Medizin unter den 5654 (30,3%) KIM-Nutzenden mit 1.930 (10,3%) der am häufigsten genutzte Bereich.[65] Nach Schätzungen nutzen weltweit jährlich etwa 37,8 Millionen Patienten und Patientinnen Osteopathische Medizin, insbesondere gegen muskuloskelettale Beschwerden.[101] Nutzer von Osteopathischer Medizin nehmen diese besonders häufig bei LWS-Schmerzen (36,0%), HWS-Schmerzen (15,0%), jedoch auch bei Schulterschmerzen (6,8%) in Anspruch.[135]

Insgesamt ist die Studienlage zur Osteopathischen Medizin bei chronischen muskuloskelettalen Schmerzen derzeit nicht ausreichend. Erste Studien weisen auf eine mögliche Wirksamkeit von Osteopathischer Medizin bei chronischen muskuloskelettalen Schmerzen in der Allgemeinbevölkerung hin. Eine im Jahr 2015 publizierte Meta-Analyse schloss drei randomisiert kontrollierte Studien (RCTs) mit insgesamt 123 Patienten und Patientinnen ein und fand Hinweise moderater Qualität für signifikante und klinisch relevante Wirksamkeit auf die Schmerzlinderung bei Patienten und Patientinnen mit CNP.[137] Eine in 2014 publizierte Meta-Analyse[138] fand bei etwa 770 Patienten und Patientinnen mit CLBP eine wissenschaftliche Evidenz von moderater Qualität für eine Wirksamkeit Osteopathischer Medizin hinsichtlich Schmerzlinderung und Funktionsverbesserung. In der Folge durchgeführte Meta-Analysen von Verhaeghe et al. (2018)[139] und Dal Farra et al. (2021)[140] sowie

eine Zusammenfassung von systematischen Reviews mit Meta-Analysen von Bagagiolo et al. (2022)[141] bestätigten Hinweise für die Wirksamkeit von Osteopathischer Medizin bei CNP, CLBP und allgemein muskuloskelettalen Schmerzen; es fehlen jedoch insgesamt hochqualitative Primärstudien wie beispielsweise randomisiert kontrollierte klinische Studien.[141] Hinsichtlich der Wirksamkeit von Osteopathischer Medizin bei Patienten und Patientinnen mit Schulterschmerzen und Knieschmerzen ist die wissenschaftliche Evidenzlage noch sehr gering. Drei randomisiert kontrollierte Studien: (1) eine US-amerikanische Studie aus dem Jahr 2002 an 29 Studienteilnehmenden im Alter von mehr 65 Jahren,[142] (2) eine im Studienregister retrospektiv registrierte deutsche Studie[143] von nicht-ärztlichen Osteopathen und Osteopathinnen sowie (3) eine nicht peer-reviewed veröffentlichte RCT in Deutschland[144] legen nahe, dass Osteopathische Medizin in der Linderung von Schulterschmerzen wirksam sein kann. Auf eine Wirksamkeit von Osteopathischer Medizin bei Knieschmerzen weist eine als Abschlussarbeit und nicht im Peerreview-Verfahren veröffentlichte RCT[145] hin. Insgesamt besteht trotz hoher Inanspruchnahme der Osteopathischen Medizin ein Mangel an hochqualitativen RCTs zur Wirksamkeit der Osteopathischen Medizin bei chronischen muskuloskelettalen Schmerzen. Weiterhin besteht ein Mangel an prospektiven Beobachtungsstudien, welche die osteopathische Behandlungsrealität von Patientinnen und Patienten mit chronischen muskuloskelettalen Schmerzen abbilden. Hinsichtlich gesundheitsökonomischer Aspekte wurden für die Behandlung von Patienten und Patientinnen der Allgemeinbevölkerung mit HWS-Schmerzen erste Hinweise einer Kosteneffektivität der Osteopathischen Medizin berichtet, jedoch waren die Studien von unzureichender Qualität und Quantität, um weiter reichende Schlussfolgerungen ziehen zu können.[146-149]

1.4.2 Tuina

Tuina ist international eine der am häufigsten angewandten Methoden der Chinesischen Medizin.[91] Die wissenschaftliche Evidenz zur Wirksamkeit und Effektivität von Tuina bei Patientinnen und Patienten mit CNP ist insgesamt sehr gering. Eine 2015 publizierte Meta-Analyse zur Wirksamkeit von Chinesischer Medizin bei Patientinnen und Patienten mit HWS-Schmerzen und LWS-Schmerzen schloss 75 RCTs (n = 11.077) ein, konnte jedoch keine Studien zu Tuina einschließen.[109] Eine Meta-Analyse von Cheng et al. (2014)[150] schloss 14 RCTs zu Massagetherapien (davon 7 RCTs zur Tuina) Patienten und Patientinnen mit CNP ein und fand moderate wissenschaftliche Evidenz für eine kurzfristige Schmerzlinderung. Insgesamt fehlen RCTs von hoher wissenschaftlicher Qualität zur Untersuchung der Wirksamkeit (*effectiveness*) von Tuina.[150, 151] Wissenschaftliche Untersuchungen zu Kosten oder zur Kosteneffektivität von Tuina bei Patienten und Patientinnen mit CNP oder muskulären Schmerzen konnten nicht ermittelt werden. In einer nicht kontrollierten retrospektiven Analyse[152] wurde bei Patienten und Patientinnen, die KIM erhalten haben, eine Schmerzreduktion und Verminderung der Versorgungskosten aus Krankenhausperspektive berichtet.

1.4.3 Schröpfen

Schröpfen wird von Patienten und Patientinnen mit chronischen Schmerzen häufig in Anspruch genommen. In einer Querschnittsstudie aus der Türkei[153] an 120 Patienten und Patientinnen mit primären Kopfschmerzen in gaben 27,5% an, Schröpfen zu verwenden. In einer Querschnittsstudie in China (n = 9.357)[154] berichteten 31,5% über chronische Schmerzen, hiervon nutzten 66.8% physiotherapeutische Verfahren wie Massage oder Schröpfen. Ein 2011 veröffentlichter systematischer Review ohne Meta-Analyse zum Schröpfen bei Schmerzen[155] schloss zwei RCTs zum Schröpfen bei Patienten und Patientinnen mit unspezifischen LWS-Schmerzen ein und fand einen begrenzten Nachweis der Wirksamkeit im Vergleich zur Regelversorgung (*usual care)* beziehungsweise Analgetika (nichtsteroidales Antirheumatikum Dexibuprofen). Eine im Jahr 2015 publizierte Meta-Analyse[109] zur Wirksamkeit von Verfahren der Chinesischen Medizin schloss 75 RCTs (n = 11.077) ein. Beinahe sämtliche Studien untersuchten Personen, die an CNP oder CLBP litten und es fanden sich jeweils Hinweise auf eine wirksame Schmerzlinderung durch Schröpfen. Eine im Jahr 2020 erschienene Meta-Analyse von Wood et al.[156] untersuchte die Wirksamkeit, Wirkung und Sicherheit westlicher Methoden des trockenen Schröpfens in der Behandlung von muskuloskelettalen Schmerzen und schloss 21 RCTs (n = 1.049) ein. Die Autoren fanden Evidenz von geringer Qualität für einen signifikanten Effekt bei Patienten und Patientinnen mit CNP und LWS-Schmerzen sowie wissenschaftliche Evidenz von moderater Qualität für eine Verbesserung des Funktionsstatus bei CNP. Ein systematischer Review aus dem Jahr 2022 bestätigte diese Erkenntnisse bei Ergänzung einer geringen Inzidenz von UEs durch das Schröpfen.[157]

1.4.4 Mindful Walking

Die Prävalenz der Nutzung von kombinierten Verfahren körperbasierter und psychologischer Behandlungsansätze (wie Yoga oder Tai Chi) betrug entsprechend der Längsschnittstudie *Midlife in the United States Survey* (MIDUS, n = 2.262 Teilnehmende) in den USA in den Jahren 1995, 2005 und 2015 respektive 20%, 17% und 18%.[158] Achtsamkeitsbasierte Interventionen können helfen, Schmerzen zu lindern.[116] Die für CLBP in der Schmerzverarbeitung wichtigen psychologischen Faktoren wie Stress und Ängste können durch Achtsamkeitsbasierte Interventionen adressiert werden, wie Übersichtsarbeiten berichten.[116-118] Achtsamkeitstrainings wie das Mindful Walking[159] und das MBSR[160-162] können Stress reduzieren, Schmerzen lindern und wertvolle Selbstmanagementstrategien darstellen. Eine Meta-Analyse schloss 30 RCTs zu chronischen Schmerzen ein und fand eine Linderung chronischer Schmerzen nach Achtsamkeitsmeditation.[117] Weiterhin ist für Patienten und Patientinnen mit CLBP die Wirksamkeit von niedrig-intensiver Bewegung wie des Walking gut belegt.[47, 163] Eine Meta-Analyse umfasste 17 Studien, die das Walking bei Patienten und Patientinnen mit chronischen muskuloskelettalen Schmerzen untersuchten, darunter fünf Studien zu CLBP, und kam zu dem Ergebnis, dass Gehen eine wirksame Form der Bewegung oder Aktivität für Personen mit CLBP sein kann.[163] Der Ansatz des Mindful Walking ist von großem Interesse, die

Teilnehmenden einer kürzlich veröffentlichten qualitativen Studie berichteten über ein breites Spektrum an wahrgenommenen Vorteilen.[164] Behandlungen in einer Gruppe sind im Mindful Walking umsetzbar, diese könnten therapeutische Gruppeneffekte nutzen, die Lebensqualität verbessern und Kosten senken.[165]

1.4.5 Musikermedizin

Gesundheitliche Probleme, und hier insbesondere muskuloskelettale Beschwerden und Erkrankungen, können die musikalische Karriere erheblich beeinträchtigen oder sogar beenden. Beruflich Musizierende und Musikstudierende leiden besonders häufig an muskuloskelettalen Beschwerden (bis 80%).[10, 14-16, 166, 167] Insbesondere die in professionellen Orchestern zahlenstark vertretende Gruppe der hohen Streicherinnen und Streicher weist eine erhöhte Prävalenz für HWS-Schmerzen auf.[14] Empirisch werden chronische muskuloskelettale Schmerzen bei Musizierenden unter anderem auf Mängel in den Bereichen Körperhaltung mit Fehlbelastungen, Stressbewältigung und Spielhygiene[14, 168-171] zurückgeführt. In einem systematischen Review wurde in unserem Institut die Wirksamkeit von therapeutischen Interventionen für muskuloskelettale Beschwerden und Erkrankungen von beruflich Musizierenden evaluiert und es fand sich eine unzureichende Studienlage um Wirksamkeitsaussagen geben zu können.[172] Die wissenschaftliche Evidenz zur Wirksamkeit von körperbasierten Behandlungsansätzen bei hohen Streichern und Streicherinnen mit muskuloskelettalen Schmerzen ist sehr gering und basiert auf nur wenigen RCTs und episodisch publizierten Fallberichten.[171-175]

Insgesamt ist die wissenschaftliche Evidenz für die Wirksamkeit, Sicherheit und Kosteneffektivität der Osteopathischen Medizin, Tuina, Schröpfen und Mindful Walking bei Patientinnen und Patienten der Allgemeinbevölkerung und speziell bei Musizierenden mit chronischen muskuloskelettalen Schmerzen, insbesondere mit CNP und CLBP, unzureichend.

1.4.6 Evidenzbasierte Medizin und wesentliche Endpunkte

Im Rahmen der Evidenzbasierten Medizin[176] werden drei Komponenten beschrieben: (1) Patient/Patientin: die Präferenz des Patienten oder der Patientin, (2) Klinik: die individuelle klinische Erfahrung des Arztes oder der Ärztin und (3) Forschung: der Forschungsstand mit der aktuell besten verfügbaren wissenschaftlichen Evidenz. In der KIM werden therapeutische Methoden oft auf der Basis von tradierter, empirischer klinischer Erfahrung und der Patienten- und Patientinnenpräferenz angewandt, noch ehe deren Wirksamkeit wissenschaftlich untersucht ist. Auf dieser Grundlage beginnt die Forschung in KIM (KIM Forschung) häufig mit Untersuchungen der Wirksamkeit (*effectiveness*) von Methoden im Vergleich zur Nicht-Anwendung der untersuchten Methode oder zur jeweils aktuellen Regelversorgung. Bei und nach einem Wirksamkeitsnachweis wird anschließend die spezifische Wirkung (*efficacy*) mittels Vergleichs zu einer adäquaten Scheinbehandlung (analog dem

Placebo der pharmakologischen Forschung) untersucht. Nach Darstellung einer spezifischen Wirkung werden wissenschaftliche Untersuchungen der Wirkmechanismen (Grundlagenforschung) durchgeführt. Dies steht im Gegensatz zur heute üblichen Reihenfolge in anderen medizinischen Bereichen wie insbesondere der pharmakologischen Forschung.[177-179] In der KIM Forschung werden auch für Patienten und Patientinnen subjektiv relevante und durch sie berichtete Endpunkte angewandt. Eine für diese Habilitationsschrift relevante Auswahl wird im Folgenden vorgestellt.

Patient-reported outcome measures (PROMs) messen für Patientinnen und Patienten subjektiv relevante Endpunkte durch diese selbst. In der Einschätzung von Effekten der wissenschaftlich untersuchten Studieninterventionen ist neben der Bestimmung der statistischen Signifikanz für den jeweiligen primären Endpunkt die Einschätzung der klinischen Relevanz bemerkter Gruppenunterschiede beziehungsweise Verlaufsunterschiede eine wichtige Größe. Hierzu eignet sich der minimale klinisch relevante Unterschied (*minimal clinically important difference*, MCID), welcher für den jeweiligen PROM und, nach Möglichkeit, spezifisch für die jeweilige Patientenpopulation und Erkrankung verwendet wird. Für diese Habilitationsschrift wichtige PROMs mit MCID werden im Folgenden kurz charakterisiert.

In der Behandlung von chronischen muskuloskelettalen Schmerzen sind unter anderem die Schmerzintensität und die Funktionsfähigkeit beziehungsweise Funktionsbeeinträchtigung im Alltag wichtige Endpunkte. In sämtlichen in dieser Habilitationsschrift vorgestellten klinischen Studien sowie in der vorgestellten Beobachtungsstudie wurde gleichermaßen die in den letzten sieben Tagen subjektiv empfundene mittlere Schmerzintensität auf einer horizontalen visuellen Analogskala (VAS, 0-100 mm, 0 = kein Schmerz, 100 = schlimmster vorstellbarer Schmerz) verwendet. Dieser validierte und auch häufig verwendete Endpunkt ist gut im Verlauf beziehungsweise zwischen Gruppen vergleichbar und einfach auszufüllen.[180, 181] Für diesen Endpunkt wurde bei HWS-Schmerzen eine MCID zwischen 4,6 und 21,4 mm berichtet.[182] Für die in dieser Habilitationsschrift vorgestellten Arbeiten wurde jeweils ein MCID 15 mm auf der VAS für die chronischen muskuloskelettalen Schmerzen zugrunde gelegt.[183, 184] Die Beeinträchtigung durch HWS-Schmerzen im täglichen Leben kann mittels des weit verbreiteten sowie auch in deutscher Sprache validierten *Neck Disability Index* (NDI)[185-190] gemessen werden. Die MCID des NDI wird je nach Skala angegeben: 3,0 bis 9,5 Punkte (0-50 Punkte Skala)[191-193] oder bei 9,8% (0-100% Skala).[193] Der NDI ist zudem vorteilhaft, da er für die Patienten und Patientinnen leicht auszufüllen ist. Die Funktionsbeeinträchtigung durch LWS-Schmerzen kann mittels des Funktionsfragebogens Hannover Rücken (FFbH-R, 0% = minimale Funktionsfähigkeit, 100% = maximale Funktionsfähigkeit; angenommene MCID: 12%)[194] erfasst werden. Weiterhin ist für Patienten und Patientinnen mit chronischen muskuloskelettalen Schmerzen die gesundheitsbezogene (allgemeine) Lebensqualität bedeutend. Diese kann mittels des weit verbreiteten und ebenfalls in deutscher Sprache validierten *Short Form 12* (SF-12, 0-100, MCID: 5 Punkte)[195-198] oder dem *Short-Form 36* (SF-36, 0-100 MCID: 5 Punkte)[195, 196] ermittelt werden.

Vor dem Hintergrund der steigenden Notwendigkeit des ökonomischen Einsatzes von Ressourcen ist die Kosteneffektivität von Therapieverfahren der KIM von zunehmender Bedeutung. In diese Habilitationsschrift werden zwei RCTs einbezogen, welche als sekundären Endpunkt Kosten und Kosteneffektivität von Osteopathischer Medizin beziehungsweise Tuina in der Behandlung von CNP untersuchten.

1.5 Forschungsziele

Das übergeordnete gemeinsame Forschungsziel war die wissenschaftliche Untersuchung der Wirksamkeit und Therapiesicherheit von ausgewählten körperbasierten Behandlungsansätzen der KIM bei Patienten und Patientinnen aus der Allgemeinbevölkerung beziehungsweise musikerspezifisch bei hohen Streichern und Streicherinnen mit chronischen muskuloskelettalen Schmerzen.
Die vorgestellten Studien hatten folgende Ziele:

- Bei erwachsenen hohen Streichern und Streicherinnen mit CNP wurden die Wirksamkeit und Sicherheit der Osteopathischen Medizin untersucht.
- Bei Patienten und Patientinnen mit chronischen muskuloskelettalen Schmerzen wurden Veränderungen auf Schmerzen und Funktionsbeeinträchtigungen während und nach der Osteopathischen Medizin beobachtet.
- Bei Patienten und Patientinnen mit CNP wurden zudem die Wirksamkeit und Sicherheit von Tuina untersucht.
- Bei Patienten und Patientinnen mit CLBP wurden die Wirksamkeit und Sicherheit von zwei verschiedenen Formen des trockenen, pulsierenden Schröpfens sowie eines Mindful Walking Programmes untersucht.

2. Eigene Arbeiten

2.1 The effect of osteopathic medicine on pain in musicians with nonspecific chronic neck pain: a randomized controlled trial

Rotter G, Fernholz I, Binting S, Keller T, Roll S, Kass B, Reinhold T, Willich SN, Schmidt A, Brinkhaus B. The effect of osteopathic medicine on pain in musicians with nonspecific chronic neck pain: a randomized controlled trial. Ther Adv Musculoskelet Dis. Dec 10 2020;12:1759720X20979853. DOI: 10.1177/1759720x20979853.

Der nachfolgende Text basiert auf dem Abstrakt und dem Inhalt des Artikels, übersetzt durch die Autorin:

Insbesondere die hohen Streicher und Streicherinnen leiden häufig unter CNP, wodurch das Musizieren und die berufliche Karriere erheblich beeinträchtigt werden können. Musizierende nutzen häufig die Osteopathische Medizin. Die wissenschaftliche Evidenz zur Wirksamkeit, Sicherheit und Kosteneffektivität ist noch unzureichend.

Ziel dieser monozentrischen zweiarmigen randomisiert kontrollierten klinischen Studie war die Untersuchung der Wirksamkeit, Sicherheit und Kosteneffektivität der Osteopathischen Medizin bei erwachsenen hohen Streichern und Streicherinnen mit CNP. Ein wesentliches Einschlusskriterium war eine in den letzten sieben Tagen subjektiv empfundene mittlere Stärke der HWS-Schmerzen von mehr als 40 mm auf einer VAS (0-100 mm, 0 = kein Schmerz, 100 = schlimmster vorstellbarer Schmerz). Zur Berücksichtigung der berufsspezifischen musikermedizinischen Komponente erhielten alle Teilnehmenden gleichermaßen nach Studieneinschluss und vor Randomisation eine semistandardisierte musikermedizinische Beratung, unterstützt durch ein Handout. Weiterhin erhielten alle Teilnehmenden eine Bedarfsmedikation mit Paracetamol. Anschließend wurden die Teilnehmenden zu entweder fünf individualisierten Behandlungen der Osteopathischen Medizin oder keiner studienspezifischen Intervention (Kontrolle, Wartelisten-Design) randomisiert. Der primäre Endpunkt war die in den letzten sieben Tagen subjektiv empfundene mittlere Intensität der HWS-Schmerzen gemessen an einer horizontalen VAS (0-100 mm) nach 12 Wochen. Ein sekundärer Endpunkt war die Funktionsbeeinträchtigung durch HWS-Schmerzen mittels NDI (0-100%) nach 12 Wochen. Die statistische Analyse beinhaltete die Kovarianzanalyse (ANCOVA), adjustiert für den jeweiligen Baselinewert. Weiterhin wurden gesundheitsökonomische Analysen durchgeführt. Insgesamt wurden 62 hohe Streicherinnen und Streicher (Osteopathische Medizin n = 28, Kontrolle n = 34), Alter Mittelwert ± Standardabweichung (MW ± SD) 41,6 ± 11,1 Jahre, 81% weiblich, in die Studie eingeschlossen. Die mittlere Intensität der HWS-Schmerzen betrug zu Baseline auf der VAS 55,9 ± 11,6 mm. Nach 12 Wochen zeigte sich zugunsten der Osteopathischen Medizin im Vergleich zur Kontrolle eine Verminderung der HWS-Schmerzen, Mittelwertdifferenz (MD) (95% Konfidenzintervall, 95% KI) von -26,2 mm (-35,2; -17,2), $p < 0,001$ sowie der Funktionsbeeinträchtigung durch HWS-Schmerzen. Es wurden keine SUEs beobachtet. Es konnten keine Gruppenunterschiede hinsichtlich qualitätsadjustierter Lebensjahre oder der Kosteneffektivität nachgewiesen werden.

Zusammenfassend deuten die Studienergebnisse darauf hin, dass die Osteopathische Medizin bei erwachsenen hohen Streichern und Streicherinnen mit CNP die Schmerzintensität wirksam reduzieren kann.

2.2 Osteopathic Medicine in Four Chronic Musculoskeletal Pain Diseases: An Observational Trial with Follow-Up

Rotter G, Binting S, Tissen-Diabaté T, Ortiz M, Brinkhaus B. Osteopathic Medicine in Four Chronic Musculoskeletal Pain Diseases: An Observational Trial with Follow-Up. Complement Med Res. 2022;29(1):53-66. DOI: 10.1159/000518311.

Der nachfolgende Text basiert auf dem Abstrakt und dem Inhalt des Artikels, übersetzt durch die Autorin:

Patienten und Patientinnen mit chronischen muskuloskelettalen Schmerzen nutzen im ambulanten Sektor die Osteopathische Medizin häufig. Die wissenschaftliche Evidenz zu Veränderungen von subjektiv für Betroffene relevanten Parametern ist noch unzureichend.

Ziel dieser prospektiven Beobachtungsstudie war es, Veränderungen unter Osteopathischer Medizin, in Ergänzung zur Regelversorgung, bei Patienten und Patientinnen mit chronischen muskuloskelettalen Schmerzen hinsichtlich der Schmerzintensität und erkrankungsspezifischer Funktionen, zu beobachten. Eingeschlossen wurden jeweils 10 Erwachsene mit den Diagnosen CNP, CLBP, chronische Schulterschmerzen (CSP) und chronische Knieschmerzen (CKP) von einer in den letzten sieben Tagen subjektiv empfundenen mittleren Stärke der jeweiligen Schmerzen von mehr als 40 mm auf einer VAS (0-100 mm). Die Teilnehmenden erhielten zusätzlich zur Regelversorgung bis zu sechs ärztlich durchgeführte Behandlungen in der Osteopathischen Medizin über einen Zeitraum von 26 Wochen. Die in der Beobachtungsstudie sämtlich als sekundär zu betrachtenden Endpunkte beinhalteten die in den letzten sieben Tagen subjektiv empfundene mittlere Intensität der jeweiligen diagnosespezifisch lokalisierten Schmerzen gemessen auf einer horizontalen VAS (0-100 mm) und PROMs zu diagnosespezifischen Funktionsbeeinträchtigungen. Die statistische Analyse war deskriptiv. Insgesamt wurden 40 Patienten und Patientinnen im Alter von (MW ± SD) 47,7 ± 8,3 Jahren, 73% weiblich, mit einer Schmerzintensität auf einer VAS von 59,4 ± 12,5 mm eingeschlossen. Nach 26 Wochen wurden eine klinisch relevante Verminderung der jeweiligen muskuloskelettalen Schmerzen, insgesamt MD (95% KI) -33.1 mm (-40,5; -25,7), sowie eine klinisch relevante Verbesserung der erkrankungsspezifischen Funktion im Vorher-Nachher-Vergleich beobachtet. Diese Verbesserungen hielten anteilig bis Woche 52 an. Es wurden keine SUEs beobachtet.

In der Zusammenfassung wurden in dieser Beobachtungsstudie positive Veränderungen während und nach Behandlung mit Osteopathischer Medizin, zusätzlich zur Regelversorgung, bei Patienten und Patientinnen mit vier verschiedenen chronischen muskuloskelettalen Schmerzerkrankungen beobachtet.

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The effect of osteopathic medicine on pain in musicians with nonspecific chronic neck pain: a randomized controlled trial

Gabriele Rotter, Isabel Fernholz, Sylvia Binting, Theresa Keller, Stephanie Roll, Benjamin Kass, Thomas Reinhold, Stefan N. Willich, Alexander Schmidt and Benno Brinkhaus

Abstract

Background: Nonspecific chronic neck pain (cNP) is common in adult violinists and violists and is often treated with osteopathic medicine (OM), although the effectiveness of this treatment has not been determined to date. This study aimed to evaluate the effectiveness and safety of OM in adult violinists and violists with cNP.

Methods: In a two-armed randomized controlled single-center open trial, adult violinists and violists, including music students, with cNP (⩾12 weeks) were randomized to either five individualized OM sessions (OM group) or to no intervention (control group, CG) in the outpatient clinic for integrative medicine, Charité - Universitätsmedizin Berlin, Germany. All patients received a musicians' medicine consultation and paracetamol on demand. The primary outcome parameter was the neck pain intensity on a visual analog scale (VAS, 0–100 mm, 0 = no pain, 100 = worst imaginable pain) after 12 weeks. Secondary outcomes included neck pain disability (Neck Disability Index, NDI, 0–100%) after 12 weeks. The last follow-up visit was after 52 weeks. Statistical analysis included analysis of covariance adjusted for respective baseline value.

Results: Altogether, 62 outpatients were included [OM group ($n = 28$), CG ($n = 34$); 81% female; mean age, 41.6 ± 11.1 years; mean baseline neck pain, 55.9 ± 11.6 mm]. After 12 weeks, OM was associated with an improvement in the OM group *versus* the CG in neck pain on the VAS [14.6 mm (95% confidence interval 8.0; 21.2) *versus* 40.8 mm (34.7; 46.9), $p < 0.001$, Cohen's $d = 1.4$], and neck pain disability as determined by the NDI [8.8% (6.7; 10.8) *versus* 17.2% (15.3; 19.1), $p < 0.001$]. Some improvements were maintained until 52 weeks of follow-up. No serious adverse events were observed.

Conclusions: The results of this study suggest that OM might be effective in reducing pain intensity in adult violinists and violists with nonspecific cNP. Further studies should investigate the efficacy of OM in comparison with a sham procedure and with other effective therapy methods in high-quality multicenter trials.

Trial registration: WHO Trial Registration https://apps.who.int/trialsearch/NoAccess.aspx?aspxerrorpath=/trialsearch/Trial2.aspx by German Clinical Trials Register DRKS00009258, Universal Trial Number (UTN): U1111-1173-5943.

Keywords: complementary medicine, musicians, neck pain, osteopathic medicine, randomized controlled trial

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Introduction

Neck pain is a global burden and is reported to be a leading cause of ill health.[1] For the purpose of the study, nonspecific chronic neck pain (cNP) was defined as pain in the anatomic region limited cranially by the superior nuchal line, caudally by the first thoracic vertebra, and laterally by the shoulder joint approaches of the trapezius muscle,[2] not caused by pathologic findings, and with a symptom duration of at least 12 weeks. A multimodal approach, including manual treatments, advice, muscular stretching and exercise can be used to address cNP.[3–9] Approximately 80% of professional musicians, including music students, experience health problems during their career that affect their performance, particularly neck pain and low back pain.[10–17] For the purpose of the study, adult violinists and violists are professional musicians who perform in orchestras or as soloists and earn their living by making music or are music students playing the violin or viola. The high prevalence of neck pain[18] in adult violists and violinists is attributed to the special playing demands, including frequent complex repetitive movements with long static and dynamic loads on the muscles in an asymmetric playing posture.[19] Violists and violinists hold their instrument between the chin and shoulder, often using a shoulder rest and/or a chin rest to support this position. The left hand holds the instrument, the left fingers need to move freely to precisely pinch the note, performing fast and repetitive movements between a high position and a low position, while the right arm engages in repetitive bowing.[19,20] Further risk factors include excess muscle tension, muscle fatigue, insufficient rest, long practice sessions, repertoire scheduling, poor posture, stress, poor injury management, performance anxiety, lack of fitness and insufficient warm-up.[14,21] These risk factors can be addressed by prevention as practiced in musicians' medicine.[22] In adult musicians, only a few controlled intervention studies addressing musculoskeletal pain relief can be found.[16,23] However, in musicians with cNP, trigger point therapy has been reported to be effective in pain reduction and functional improvement.[24] In violists and violinists, manual treatments combined with musicians' medicine have, to the best of the knowledge of the authors, been published only in case reports.[25,26]

Osteopathy and osteopathic medicine (both summarized in this paper under OM) are part of complementary and integrative medicine. OM is used by musicians for musculoskeletal symptoms.[23] OM relies on manual contact for diagnosis and treatment and focuses on the structural and functional integrity of the body, including skeletal, arthrodial and myofascial structures and related vascular, lymphatic and neural elements[27] in the so-called musculoskeletal, visceral and craniosacral systems. OM is commonly administered as a diagnosis-related and individualized treatment and additionally offers advice on self-training for postural improvement,[28] as is performed in this study. A previous systematic review and meta-analysis in the general population indicated effectiveness for pain reduction with OM compared with heterogeneous comparison interventions, including physiotherapy, sham manipulation or no specific intervention, in patients with cNP.[29]

For patients receiving complementary and integrative medicine, pain reduction and lower costs have been reported from a hospital perspective in a noncontrolled retrospective analysis.[30] Previous studies have indicated that OM may be cost effective for the management of neck pain in the general population; however, the published comparative effectiveness and health economics studies are of insufficient quality and quantity to draw further conclusions.[31–34] To our knowledge, studies investigating the effectiveness, safety, costs, or cost effectiveness of OM in musicians with cNP are not available.[35] The primary study aim was to evaluate the effect of five OM treatments in comparison with no OM treatment during 12 weeks on the subjectively perceived neck pain intensity in adult violinists and violists, including music students, with cNP. Further aims were to explore the impact of such therapy on the neck pain disability, stress intensity, quality of life, intake of analgesics, days of inability to work, days with restrictions in daily routine safety and cost effectiveness.

Methods

Study design

In a two-armed randomized controlled single-center open clinical trial, adult violinists and violists, including music students, with cNP were randomized to either five individualized OM sessions within 10 weeks (OM group) or to no OM intervention (control group, CG). All patients equally received a musicians' medicine consultation addressing playing-related problems and paracetamol on demand.

Setting

The study was performed at the outpatient clinic for integrative medicine of the Charité – Universitätsmedizin in Berlin, Germany, between September 2015 (first patient in) and May 2018 (last patient out after 52 weeks of follow-up).

This study was registered at the German Clinical Trials Register before enrollment of the first patient (DRKS00009258) and followed the standards of the Declaration of Helsinki[36] and the ICH-GCP guidelines.[37] It was approved by the Ethics Committee, Charité – Universitätsmedizin Berlin (approval number EA 1/198/15, with no amendments or any changes made to the study design). All patients gave oral and written informed consent before inclusion in the study.

Patients

Patients were recruited from various professional orchestras in Berlin and nearby federal states (Brandenburg, Mecklenburg-Western Pomerania, Saxony, Saxony-Anhalt, and Thuringia) and Berlin music schools/universities. We used posters, flyers, newspapers, electronic listings and digital media for recruiting. Violinists and violists who were active professional orchestral musicians, soloists, or music students of both sexes aged 18–65 years with a clinical diagnosis of cNP for at least 12 weeks prior to study onset and an average pain intensity within the last 7 days of at least 40 mm on a 100-mm horizontal visual analog scale (VAS, 0 = no pain, 100 = worst imaginable pain, Supplement 1) were included in the study. A 40-mm cutoff point for study inclusion was selected by the study team based on the literature, including a randomized controlled trial (RCT) investigating OM in patients with cNP[38] and earlier pain studies in our group.[39,40] A 40-mm cutoff point allows defining a population with at least medium pain severity to provide some homogeneity in pain intensity and to make recruitment of the study population feasible. Within the last 4 weeks before the start of the study, patients had used no therapy or only drug therapy for cNP. The exclusion criteria were defined as follows: peripheral or central neurological symptoms; known vascular anomaly, such as aneurysm; known or suspected primary or secondary bone tumor; neck pain caused by recent trauma; rheumatic disease; prior surgery on the cervical column; suspected osteoporosis; OM treatment within the last 6 months before the beginning of the study; neck pain treated by complementary medicine or physical therapy within the last 3 months before inclusion; obesity (body mass index $> 30\,kg/m^2$); current intake of centrally acting analgesics; pregnancy; presence of other acute or chronic disease impairing participation in the study intervention; presence of other psychic or somatic condition impairing participation in the study intervention; alcohol or substance abuse; planned or actual use of therapy with possible impact on cNP, such as physiotherapy, acupuncture, massage, neuroreflex therapy, or the Feldenkrais method, during study participation; insufficient German language skills; current application for a benefit; and participation in another clinical trial during the 6 months before the study or parallel to the study.

Patients were randomized to one of the two treatment groups (1:1 ratio) by a computer-generated block randomization process in the study center with variable block length. The allocation was performed in the study center by a study nurse and was concealed.

Study intervention

Both groups

Before randomization, all patients received a 45-minute semi-standardized musicians' medicine consultation addressing playing-related problems with one of two experts in musicians' medicine (IF, AS), supported by a handout. The musicians' medicine consultation and handout were established by a consensus of experts, which included a review of the literature.[16] The musicians' medicine consultation and handout addressed risk factors for cNP in violinists and violists, especially excess muscle tension, muscle fatigue, insufficient rest, long practice sessions, repertoire scheduling, poor posture, stress, poor injury management, performance anxiety, lack of fitness and insufficient warm-up.[14] The consultation included behavioral advice regarding playing practice, lifestyle recommendations, instrument-specific ergonomics and occupational environment and advice for the work organization, which included the number of working hours and sufficient breaks. The details of the handout are provided in the supplemental material online (Supplement 2).

All patients were allowed to take 500 mg of paracetamol on demand up to four times daily during the first 12 weeks. Twelve weeks after randomization, patients in both groups were allowed to use any additional physical or psychological treatment.

OM group

Within the first 12 weeks after randomization, patients in the OM group received five individualized diagnosis-related OM treatment sessions that were 45 min long each at an approximately 2-week interval. Each session started with a short interview and physical examination of the musculoskeletal, visceral and craniosacral systems according to medical and OM principles. Based on the interview and physical examination, the actual treatment strategy following OM principles was determined for each session. According to the individually necessary treatment techniques in the musculoskeletal, visceral and craniosacral systems, patients were treated in a sitting or lying position with or without active participation of the patient. We chose an individualized diagnosis-related OM treatment approach, as is commonly administered in OM. Advice for postural improvement during instrument playing was included in the OM treatment. Therefore, all musicians were examined during one of the five OM treatment sessions while playing the instrument. The study intervention was applied by one medical doctor (and osteopath) with special expertise in musicians' medicine (GR).

Control group

Patients in the CG received no OM treatment within the first 12 weeks. After 12 weeks, patients of the CG could receive five OM treatments free of charge, if desired.

Outcome parameters and data collection

Parameters were measured at baseline and after 6, 12, 26, and 52 weeks using standardized patients' questionnaires. The primary outcome was neck pain; patients rated their average perceived neck pain within the last 7 days on a horizontal VAS (0–100 mm, 0 = no pain, 100 = worst imaginable pain, Supplement 1) after 12 weeks.[41] We used the VAS for pain measurement because it is validated, widely used, easy to use and takes less than 1 min to complete.[41,42] Recently, the minimal clinically important difference (MCID) on the VAS for neck pain was reported to be within a range between 4.6 mm and 21.4 mm.[43] During the planning of the study, we considered publications with an MCID of 13.7 mm on a 100-mm VAS for pain measurement,[42] of 8 mm on a 100-mm VAS for neck pain,[44] and of 1.5 points (range, 1–10) on a numeric rating scale for neck pain.[45] Based on the literature and our expectations for our study population, we decided to select an MCID of 15 mm on a 100-mm VAS to measure neck pain. The criterion for a substantial clinical benefit (SCB) was reported to be 26.5 mm.[44]

VAS neck pain levels after 6, 26, and 52 weeks were considered secondary outcomes. A further secondary outcome after 6, 12, 26 and 52 weeks was neck pain disability assessed by the Neck Disability Index (NDI, 0–100%) in a validated German version.[46,47] The NDI[46] measures neck pain disability in everyday life. The NDI is widely used and well validated.[48–52] The NDI is easy for the patient to fill out and easy for the investigator to evaluate. For the NDI, the MCID is given between 3.0 and 9.5 points (0–50 point scale)[44,53,54] or 9.8% (0–100% scale,[44] used in the present study) with an SCB of 29%.[44] Further secondary outcomes were stress intensity as determined by a horizontal VAS for stress. We used the VAS for stress measurement because it is validated,[55] easy to use and takes less than 1 min to complete. Patients rated their average perceived stress within the last 7 days on a horizontal VAS (0–100 mm, 0 = no stress, 100 = worst imaginable stress),[55] with no MCID for VAS stress determined, and health-related quality of life measured by the 12-item Short Form Health Survey (SF-12, MCID: 5 points).[56–59] We used the SF-12[58,59] because it is a short form of the well-accepted SF-36[56,57] and is commonly used.

Furthermore, we assessed the intake of analgesics in a diary, which we applied despite reported tendencies toward inaccuracy regarding the time and reliability of entries,[60] the days of inability to work due to cNP within the last 12 weeks (baseline) and within the last 6 weeks (all other measurement points), and the days with restriction in daily routine due to cNP within the last 12 weeks for baseline and within the last 6 weeks (all other measurement time points) by the (not validated) question: "On how many days in the last 12 (respective 6) weeks have you been restricted in your daily routine due to cervical spine pain?" Safety (adverse events and serious adverse events) was assessed by the study physician during the interviews in the OM group; additionally, patients were encouraged to contact the study center in the case of any adverse events. Patients also rated the changes in their complaints due to musculoskeletal pain within the last 6 weeks, and patients receiving OM rated the effectiveness of the OM treatment with reference to the last 6 weeks ("highly effective," "effective," "slightly

effective," "not effective"). Sociodemographic data, including age, sex, and education, were also assessed at baseline.

We decided to apply patient-relevant outcomes by using patient-reported outcome measures and not to add objective parameters. Therefore, blinding of outcome assessors (patients) was not feasible.

Statistical analysis

Sample size: For the primary outcome (VAS score of neck pain after 12 weeks), the sample size was calculated based on a consensus considering a previous German RCT in OM for cNP,[38] a Berlin RCT investigating Tui Na in cNP,[61] and an older pre–post pilot study investigating OM in patients with cNP and subchronic neck pain,[62] including literature about the MCID for the VAS for pain, ranging from at 8 mm in patients with cNP[44] to 13.7 mm for pain,[42] and including the MCID of 1.5 points (0–10) on a numeric rating scale.[45] As a result, a mean difference between the OM group and the CG of 15 mm was considered,[38] and the common standard deviation was assumed to be 25 mm. Thus, with 45 patients per group (90 in total), a two-sided *t*-test with a significance level of 5% would have a power of 80%. To compensate for potential dropouts, 100 patients were intended to be randomized (50 patients per group).

The primary analysis of the primary outcome was performed using an analysis of covariance (ANCOVA) with a fixed-factor treatment group adjusted for the baseline value of the VAS score for neck pain. The assumptions for normal distribution were both tested with reviewing histograms and Q–Qplots. The assumptions of equal regression slopes, outliers and linearity were checked with scatter plots, the assumption of variance homogeneity was tested with the Levene's test. The significance level was established as $<5\%$ ($p<0.05$). Post hoc Cohen's *d* was calculated for the VAS score of neck pain after 12 weeks. Cohen's *d* and all following analyses were considered explorative. The secondary outcomes for the VAS score of neck pain (after 6 weeks), neck pain disability as determined by the NDI, VAS score for stress, SF-12, quality-adjusted life years (QALYs), and total costs over the first 12 weeks were analyzed similar to the analysis of the primary outcome, that is, by ANCOVA adjusted for the respective baseline values. The results are reported as adjusted group means with 95% confidence intervals (CIs) and the *p*-value for the treatment group comparison. The *p*-values are only reported for the first 12 weeks as participants in the CG also received OM after week 12. All tests and CIs were two sided. All data were analyzed based on the intention-to-treat-principle using the full analysis set (FAS) with all available data without imputing missing data. All analyses were performed according to the original assigned groups. Adverse events are presented descriptively by frequency for each treatment group. In addition, a number of sensitivity analyses were performed. A per-protocol (PP) analysis was performed for the primary outcome, excluding patients if at least one of the following criteria was met: no complete data available for the primary endpoint, namely, the VAS score for neck pain at 12 weeks; not treated according to the allocated group; fewer than five interventions in the first 12 weeks (OM group only); and OM treatment (elsewhere) during the first 12 weeks (CG only).

Further, a sensitivity analysis of the VAS score for neck pain, neck pain disability as determined by the NDI, VAS score for stress and SF-12 was performed by ANCOVA adjusted for respective baseline values and for sex, education and the VAS score for stress. A responder criterion in a range of 30–50% pain reduction has been used in trials[40,63] and is recommended for research.[64] Furthermore, a pain reduction of 50% was reported to be meaningful.[65] Based on this literature, a responder was defined by at least 50% pain reduction as determined the VAS score for neck pain, and a post hoc responder analysis was performed. Statistical analyses, including health economics analyses, were performed using the software package SAS 9.4.[66]

Health economics analysis

In addition, a cost-effectiveness analysis was carried out for the period 12 weeks after baseline. Therefore, the achieved QALYs were linked to cNP-related total costs from a societal perspective (including direct and indirect costs). Data on utilization of medical resources, sick leave days and working hour reductions related to cNP were systematically collected using patient questionnaires and valued by using standardized German national unit cost assumptions. Costs arising due to the OM intervention were considered to be 85.80 Euro per session, according to a notification from the study center financial department. An algorithm developed by Brazier and Roberts[67] was

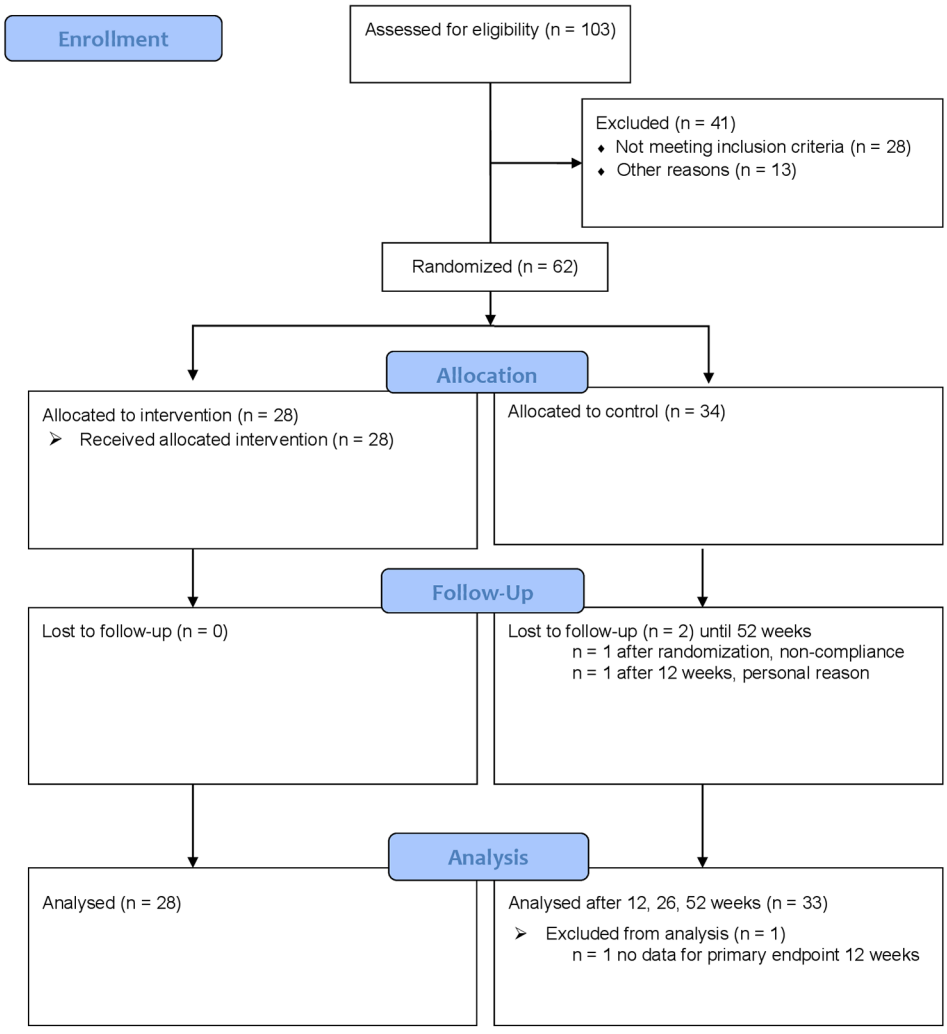

Figure 1. Recruitment, treatment and follow-up of patients with chronic neck pain.

applied to convert the data of the SF-12 into the SF-6D health state utility values. QALYs were measured based on these utility values by calculating the area under the curve, assuming linear changes between the longitudinal utility values. In the case of a significant QALY gain and significant additional costs in the OM group, it was planned to calculate the incremental cost-effectiveness ratio (ICER), reflecting the add-on costs for realizing one QALY gained.

Results

Patients and treatment

From 103 eligible patients, 62 were enrolled between September 2015 and May 2017 and were randomized into the two treatment groups (OM group, $n = 28$; CG, $n = 34$). Despite strong efforts, it was not possible to include more patients in the study, and the targeted sample size of $n = 100$ was not reached. After randomization, one patient in the CG dropped out due to noncompliance; after 12 weeks, another patient in the CG dropped out due to personal reasons. All other patients remained completed 52 weeks of follow-up and returned the questionnaires (Figure 1). After 12 weeks, 28 (82.3%) patients in the CG received at least one session of OM (anytime within the 52 weeks of follow-up and without restrictions regarding the treatment interval).

At baseline, the mean age was 41.6 ± 11.1 years (mean $\pm$ standard deviation). Fifty patients (80.7%) were female. The mean duration of cNP symptoms was 14.0 ± 10.9 years in the OM group and 13.8 ± 9.5 years in the CG (Table 1). At baseline, there were relevant differences between

Table 1. Baseline characteristics of patients.

	Osteopathic medicine group *n* = 28 Mean ± SD/*n* (%)	**Control group *n* = 34 Mean ± SD/*n* (%)**	**Total *n* = 62 Mean ± SD/*n* (%)**
Age (years)	42.8 ± 11.5	40.6 ± 10.8	41.6 ± 11.1
Range	21–63	21–63	21–63
Sex (female)	23 (82.1)	27 (79.4)	50 (80.7)
BMI (kg/m^2)	23.2 ± 3.3	22.0 ± 2.5	22.6 ± 2.9
Physically active	20 (71.4)	25 (73.5)	45 (72.6)
German university entrance qualification (Abitur)***	19 (67.9)	31 (91.2)	50 (80.7)
Employed (in students: in addition to study) (yes)	26 (92.9)	33 (97.1)	59 (95.2)
If employed (*n* = 59), incapacity for work last 12 weeks (days)	1.0 ± 3.1	0.7 ± 1.6	0.8 ± 2.3
Min–Max	0–14	0–7	0–14
Background[a]			
Professional musician	26 (92.9)	32 (94.1)	58 (93.6)
Student	2 (7.1)	3 (8.8)	5 (8.1)
Main instrument			
Violin	19 (67.9)	26 (76.5)	45 (72.6)
Viola	8 (28.6)	8 (23.5)	16 (25.8)
Both	1 (3.6)	0	1 (1.6)
Orchestra part			
Solo	4 (15.4)	4 (12.5)	8 (13.8)
Tutti	23 (88.5)	30 (93.8)	53 (91.4)
Time of playing last 6 weeks (average hours/day)	3.3 ± 1.9	3.5 ± 1.6	3.4 ± 1.7
Time of practice last 6 weeks (average hours/day) (*n* = 61[b])	1.7 ± 1.2	2.0 ± 2.0	1.9 ± 1.6
Duration of cNP (years)	14.0 ± 10.9	13.8 ± 9.5	13.9 ± 10.1
Min–Max	1.0–40.0	0.3–40.0	0.3–40.0
Pathologic findings in musculoskeletal system	11 (39.3)	9 (26.5)	20 (32.3)
Osteopathic treatment earlier	13 (46.4)	17 (50.0)	30 (48.4)
Osteopathic treatment earlier because of cNP	12 (42.9)	9 (26.5)	21 (33.9)
VAS neck pain (0–100 mm)*	56.9 ± 11.6	55.0 ± 11.7	55.9 ± 11.6
Neck pain disability by NDI (0–100%)*	20.6 ± 7.9	20.6 ± 7.6	20.6 ± 7.7
VAS stress (0–100 mm)*, ***	44.4 ± 22.9	57.8 ± 18.3	51.7 ± 21.4
SF-12 Physical Component Scale (0–100)** (*n* = 60[b])	47.0 ± 8.0	46.7 ± 7.6	46.8 ± 7.7

(Continued)

Table 1. (Continued)

	Osteopathic medicine group *n* = 28 Mean ± SD/*n* (%)	**Control group *n* = 34 Mean ± SD/*n* (%)**	**Total *n* = 62 Mean ± SD/*n* (%)**
SF-12 Mental Component Scale (0–100)** (*n* = 60[b])	46.3 ± 11.1	44.7 ± 9.2	45.4 ± 10.0
Days with restriction in activities of daily living last 12 weeks	21.4 ± 25.3	22.7 ± 27.2	22.1 ± 26.1
Min–Max	0–90	0–92	0–92
Restriction in making music due to cNP last 6 weeks (*n* = 61[b])	11 (39.3)	19 (57.6)	30 (49.2)
Days	20.0 ± 13.7	29.8 ± 14.4	26.4 ± 14.7
Min–Max (*n* = 29)	4–42	7–42	4–42
Satisfaction with working atmosphere			
Very satisfied	5 (17.9)	5 (15.6)	10 (16.7)
Satisfied	18 (64.3)	14 (43.8)	32 (53.3)
Neutral	4 (14.3)	12 (37.5)	16 (26.7)
Dissatisfied	1 (3.6)	1 (3.1)	2 (3.3)
Very dissatisfied	0	0	0
Study physician expectation of OM intervention			
Cure	0	0	0
Significant recovery	16 (57.1)	14 (41.2)	30 (48.4)
Slight recovery	12 (42.9)	20 (58.8)	32 (51.6)
No recovery	0	0	0
Patients expectation of OM intervention			
Cure	0	6 (17.7)	6 (9.7)
Significant recovery	26 (92.9)	25 (73.5)	51 (82.3)
Slight recovery	2 (7.1)	3 (8.8)	5 (8.1)
No recovery	0	0	0
Direct costs of cNP last 12 weeks (EUR)	67.69 ± 221.49	72.22 ± 177.24	70.17 ± 196.76
Indirect costs of cNP last 12 weeks (EUR)	682.36 ± 1,967.04	297.80 ± 614.38	471.48 ± 1,397.87
Total costs of cNP last 12 weeks (EUR)***	750.05 ± 2,013.18	370.03 ± 673.19	541.65 ± 1,440.63

[a]more than one answer possible: student and professional musician.
[b]baseline data only for *n* = respective value available.
*lower values indicate better status.
**higher values indicate better status.
***relevant differences between groups.
BMI, Body Mass Index; cNP, chronic neck pain; Max, maximum; Min, minimum; *n*, number; NDI, Neck Disability Index; OM, osteopathic medicine; SD, standard deviation; SF-12, 12-item Short Form Health Survey; VAS, visual analog scale.

the OM group and the CG regarding education level (German university entrance qualification: OM group, 67.9%; CG, 91.2%), VAS scores for stress (OM group, 44.4 mm ± 22.9; CG, 57.8 mm ± 18.3) and total costs over the 12 weeks prior to baseline (OM group, 750.05 ± 2,013.18 EUR; CG, 370.03 ± 673.19 EUR). The mean VAS score for neck pain was 56.9 ± 11.6 mm in the OM group and 55.0 ± 11.7 mm in the CG. Thirty (48.4%) patients had received osteopathic treatment (mostly by nonphysician osteopaths) in their life before, including 12 (42.9%) patients in the OM group and nine (26.5%) patients in the CG, because of cNP. Apart from cNP, further self-perceived health problems were reported by 24 (85.7%) patients in the OM group and 32 (94.1%) patients in the CG; the most frequently reported issue was shoulder pain [$n = 20$ (83.3%) patients in the OM group, $n = 26$ (81.3%) patients in the CG]. The physical examination at baseline revealed pathologic findings in the musculoskeletal system in 11 (39.3%) patients in the OM group and 9 (26.5%) patients in the CG.

Outcomes

After 12 weeks, the primary outcome, the VAS score for neck pain, was significantly and relevantly lower in the OM group [OM group-adjusted mean, 14.6 mm, 95% CI (8.0; 21.2); CG, 40.8 mm, (34.7; 46.9)] with an adjusted group difference of −26.2 mm [(−35.2; −17.2), $p < 0.001$] (Table 2). The effect size (Cohen's d) for the VAS score for neck pain after 12 weeks was $d = 1.4$ ($d = 1.5$, if adjusted for the baseline VAS score for neck pain). The sensitivity analyses for baseline differences and PP analyses for the VAS score for neck pain, neck pain disability as determined by the NDI, VAS score for stress, and SF-12 were also similar to the above-reported FAS analyses. The responder analysis for 50% pain reduction after 12 weeks revealed a point estimate (odds ratio) of 13.8 [95% Wald CI (3.8−50.3), $p < 0.001$].

The VAS score for neck pain after 6 weeks (secondary outcome) showed a clinically relevant difference favoring the OM group [−20.9, (−30.7; −11.1), $p < 0.001$]. Furthermore, we observed (not clinically relevant) differences in the baseline value-adjusted mean neck pain disability as determined by the NDI in favor of the OM group after 6 weeks [−4.5%, (−7.7; −1.4), $p = 0.006$] and 12 weeks [−8.4%, (−11.2; −5.6), $p < 0.001$]. The baseline value-adjusted mean VAS score for stress was lower in the OM group after 12 weeks [−15.7 mm, (−27.9; −3.4), $p = 0.013$] but not after 6 weeks [−10.8 (−22.4; 0.8), $p = 0.067$]. Regarding the SF-12, although better results in favor of OM were found for the baseline-adjusted mean difference for the physical component scale after 6 [3.0, (0.1; 5.8), $p = 0.044$] and 12 weeks [4.0, (1.5; 6.6), $p = 0.003$], the differences were not clinically relevant. There were no relevant effects on the mental component scale of the SF-12 in the OM group in comparison to the CG after 6 [1.3 95% CI (−3.1; 5.6), $p = 0.5632$] or 12 weeks [2.0 95% CI (−1.4; 5.5), $p = 0.3351$] (Table 2, Figures 2−5). For some outcomes, not all assumptions for ANCOVA were met. However, repeating the analysis correcting for the respective violation, the results from ANCOVA were robust (data not shown) and did not alter the interpretations.

After 12 weeks, 28 patients (82.4%) in the CG also received OM within the 52 weeks of follow-up. Among them, 24 patients (70.6%) received all five OM treatment sessions, and 27 patients (79.4%) received at least four OM treatment sessions within 52 weeks after baseline. After 52 weeks, patients in the OM group reported a VAS score for neck pain of 19.7 mm (12.2; 27.7), while patients in the CG reported a VAS score for neck pain of 30.6 mm (23.8; 37.5) (Table 2).

Analgesic use within the first 12 weeks was low overall and comparable between the two groups. In the OM group, only five patients (17.9%) took 24 pills of paracetamol in total, and in the CG, four patients (11.8%) took 23 pills of paracetamol in total. Regarding analgesics other than paracetamol, one patient in the OM group used arnica pain ointment, and others used 400−600 mg of ibuprofen or did not specify the dose of ibuprofen. In the OM group, two patients (7.1%) took a total of 16 analgesic doses (arnica pain ointment, ibuprofen). In the CG, four patients (11.8%) took 43 analgesic doses (ibuprofen) altogether.

Furthermore, we found a decrease in the days with inability to work due to cNP in the OM group within the first 12 weeks, which could not be observed in the CG. Days of inability to work due to cNP were measured at baseline (for the last 12 weeks) in the OM group and CG, with a mean of 1.0 (−0.2; 2.3), and 0.7 (0.1; 1.2), respectively; after 6 weeks (for the last 6 weeks) in the OM group and CG, the mean was 0.1 (−0.1; 0.3) and 0.3 (−0.1; 0.7), respectively; and after

Table 2. Primary and main secondary outcomes until 12 weeks (intergroup comparison), and until 52 weeks, patients of the control group started to receive OM treatment after week 12.

	n	Osteopathic medicine group-adjusted mean, (95% CI)[a]	Control group-adjusted mean, (95% CI)[a]	Differences (osteopathic medicine group – control group) adjusted mean, (95% CI)[a]	*p*
VAS neck pain (0–100 mm)* (average neck pain during the previous 7 days), MCID 15 mm, SBC 26.5 mm					
6 weeks	57	21.9 (14.7; 29.1)	42.8 (36.2; 49.4)	−20.9 (−30.7; −11.1)	<0.001
12 weeks (primary outcome)	61	14.6 (8.0; 21.2)	40.8 (34.7; 46.9)	−26.2 (−35.2; −17.2)	<0.001
26 weeks***	58	20.5 (12.0; 29.0)	35.8 (28.2; 43.5)	***	***
52 weeks***	56	19.7 (12.2; 27.7)	30.6 (23.8; 37.5)	***	***
Neck pain disability by NDI (0–100%)*, MCID 9.8%					
6 weeks	61	14.1 (11.8; 16.4)	18.6 (16.4; 20.7)	−4.5 (−7.7; −1.4)	0.006
12 weeks	61	8.8 (6.7; 10.8)	17.2 (15.3; 19.1)	−8.4 (−11.2; −5.6)	<0.001
26 weeks***	58	10.8 (8.0; 13.7)	15.1 (12.5; 17.6)	***	***
52 weeks***	57	10.3 (7.6; 13.0)	14.0 (11.5; 16.6)	***	***
VAS stress (0–100 mm)*					
6 weeks	61	40.7 (32.3; 49.0)	51.5 (43.8; 59.2)	−10.8 (−22.4; 0.8)	0.067
12 weeks	61	30.4 (21.6; 39.2)	46.1 (38.0; 54.2)	−15.7 (−27.9; −3.4)	0.013
26 weeks***	58	39.8 (28.6; 50.9)	44.2 (34.2; 54.2)	***	***
52 weeks***	57	35.0 (25.2; 44.8)	41.8 (32.4; 51.0)	***	***
SF-12 physical component scale (0–100)**, MCID 5 points					
6 weeks	59	51.2 (49.1; 53.3)	48.2 (46.3; 50.2)	3.0 (0.1; 5.8)	0.044
12 weeks	59	53.1 (51.2; 54.9)	49.1 (47.3; 50.8)	4.0 (1.5; 6.6)	0.003
26 weeks***	55	52.9 (50.6; 55.2)	49.7 (47.7; 51.8)	***	***
52 weeks***	54	51.7 (49.2; 54.1)	49.6 (47.2; 52.0)	***	***
SF-12 mental component scale (0–100)**, MCID 5 points					
6 weeks	59	48.0 (44.6; 51.2)	46.7 (43.7; 49.7)	1.3 (−3.1; 5.7)	0.563
12 weeks	59	49.8 (46.3; 53.3)	47.5 (44.4; 50.7)	2.0 (−1.4; 5.5)	0.335
26 weeks***	55	47.9 (44.3; 51.5)	47.6 (44.4; 50.8)	***	***
52 weeks***	54	49.3 (45.3; 53.3)	44.3 (40.5; 48.2)	***	***

[a]Results adjusted for respective baseline value.
*lower values indicate better status.
**higher values indicate better status.
***no comparison and no *p*-values, because after 12 weeks *n* = 28 (82.4%) participants of the control group started to receive OM treatment.
CI, confidence interval; MCID, minimal clinically important difference; *n*, number for respective available data from *n* = 61 patients; NDI, Neck Disability Index; SBC, substantial clinical benefit; SF-12, 12-item Short Form Health Survey; VAS, visual analog scale.

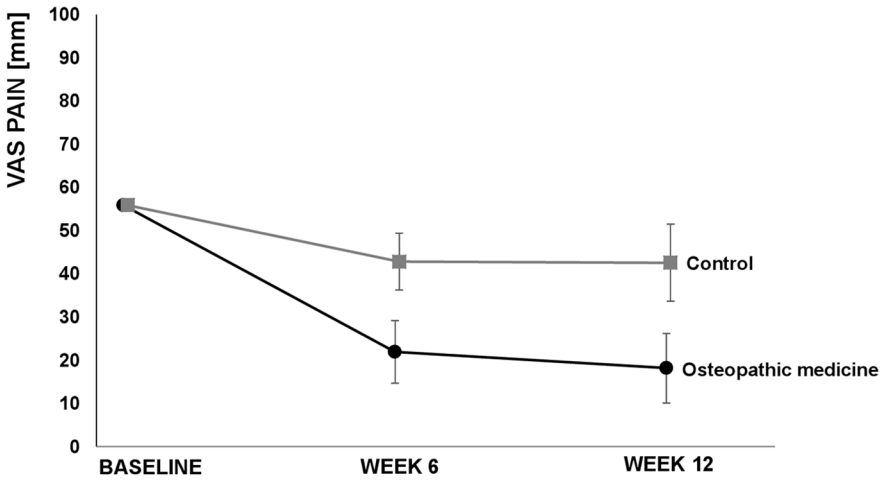

Figure 2. Primary outcome visual analog scale (VAS) pain over 12 weeks. Values are adjusted means and 95% confidence intervals.

Table 3. Days with restriction in daily routine due to chronic neck pain.

Days with restriction in daily routine due to chronic neck pain	*n*	Osteopathic medicine group, adjusted mean, (95% CI)[a]	Control group, adjusted mean, (95% CI)[a]	Differences (osteopathic medicine group – control group), adjusted mean, [95% CI][a]	*p*
After 6 weeks (last 6 weeks)	61	4.0 (0.3; 7.6)	11.2 (7.8; 14.6)	–7.3 (–12.3; –2.2)	0.005
After 12 weeks (last 6 weeks)	60	1.8 (–1.2; 4.9)	8.0 (5.2; 10.7)	–6.1 (–10.2; –2.1)	0.004
After 26 weeks (last 6 weeks)*	57	1.4 (–1.8; 4.5)	7.0 (4.2; 9.8)	*	*
After 52 weeks (last 6 weeks)*	57	2.5 (–0.7; 5.7)	4.9 (1.9; 8.0)	*	*

[a]Results adjusted for respective baseline value.
*no comparison and no *p*-values, because after 12 weeks 28 (82.4%) participants of the control group started to receive OM treatment.
CI, confidence interval; *n*, number for respective available data from 61 patients.

12 weeks (for the last 6 weeks), in the OM group and CG, the mean was 0.0 (0.4; 3.2) and 0.5 (−0.2; 1.2), respectively.

Days with restrictions in daily routine due to cNP improved in the OM group *versus* the CG [difference, −6.1 (−10.2; −2.1), $p = 0.004$] within the first 12 weeks (Table 3). Patients further evaluated their complaints due to musculoskeletal pain. Patients in the OM group reported a better improvement than patients in the CG (Table, Supplement 3). Most patients in the OM group rated the intervention as very effective after 12 weeks.

No serious adverse events were observed. Two patients reported transient mild adverse events after OM (tiredness and dizziness).

During the first 12 weeks after baseline, the OM group experienced 0.1789 adjusted QALYs (0.1734; 0.1845) compared with patients in the CG, with 0.1734 QALYs (0.1682; 0.1785). The adjusted mean QALY difference was 0.0055 (−0.0020; 0.0132) ($p = 0.147$), in favor of the OM group. For the same time period, a mean adjusted cost of 497.54 EUR (2.56; 992.52) and 704.54 EUR (242.94; 1166.14) occurred in the OM group in the CG, resulting in an adjusted mean difference of −207.00 EUR [(−887.43; 473.43), $p = 0.545$], in favor of the OM group. The additional direct costs due to the OM intervention seemed to be mainly compensated for by lower indirect costs due to work absenteeism in the OM group. An ICER was not calculated since the differences in QALYs and total costs were not statistically significant between the groups.

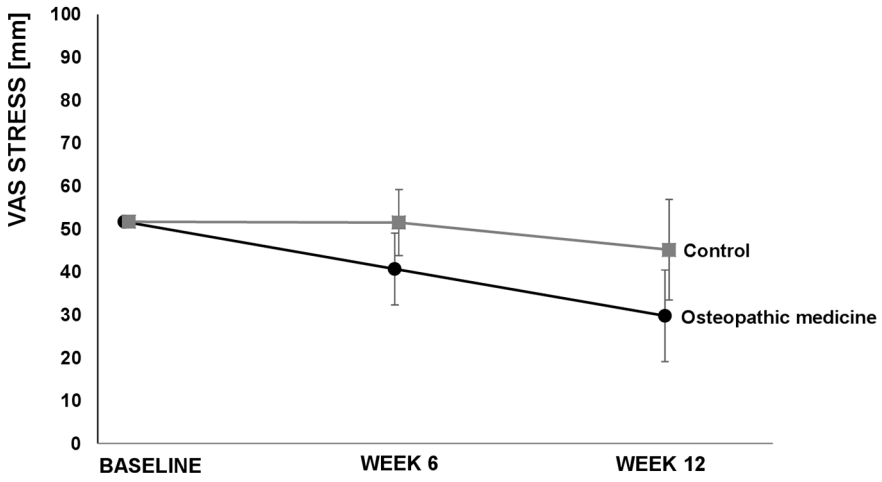

Figure 3. Visual analog scale (VAS) stress over 12 weeks. Values are adjusted means and 95% confidence intervals.

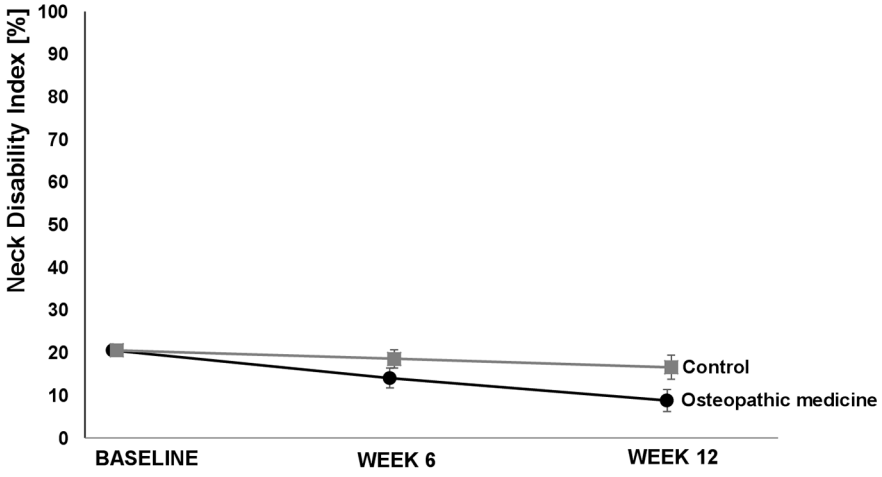

Figure 4. Neck disability index over 12 weeks. Values are adjusted means and 95% confidence intervals.

Discussion

Five OM sessions were associated with a clinically relevant and statistically significant reduction in the mean neck pain intensity in comparison to patients receiving no OM treatment. All further outcomes were exploratory and must be investigated in further confirmatory studies. Patients in the OM group tended to show improvements in neck pain disability and the SF-12 physical component compared with patients in the no-intervention CG, although the improvement was not clinically relevant. Furthermore, a tendency toward a reduction in the VAS score for stress was found in the OM group compared with the CG. Positive effects in the OM group were maintained, to some degree, for the mean neck pain intensity, neck pain disability and the SF-12 physical component scale within the 52 weeks of follow-up. The OM treatment was safe but not superior in terms of cost effectiveness.

We considered the adjusted group difference for the VAS score for neck pain, with –26.2 mm (with a large effect size, Cohen's *d*) indicating a good clinical result, even if the criterion for an SCB at −26.5 mm[44] was missed. The failure to meet the SCB criterion might be due to various factors: First, patients in the CG improved as well, which could be due to study effects and to the semi-standardized musicians' medicine consultation, which was provided equally for both groups. The musicians' medicine consultation

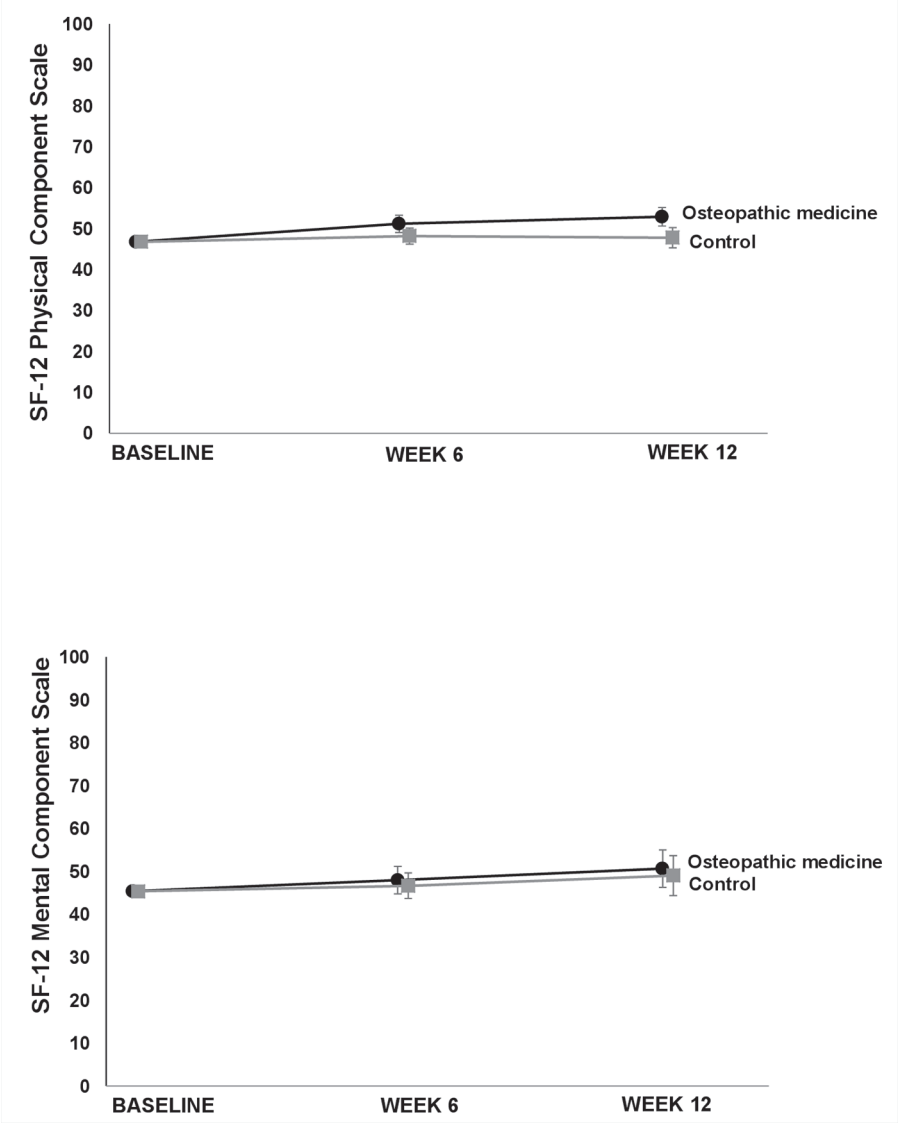

Figure 5. 12-item Short Form Health Survey (SF-12) Physical Component Scale and Mental Component Scale over 12 weeks. Values are adjusted means and 95% confidence intervals.

included a variety of playing and performance-related information. In particular, posture, optimization of shoulder rest/chin holder, and practice scheduling were determined to be important factors of cNP among violinists and violists and can be addressed by musicians' medicine.[14,19,22,68–72] Overall, the improvement in pain in the CG during the first 12 weeks also indicates (in addition to study effects) that a musicians' medicine consultation might be helpful.

We used a computer-generated block randomization method as it helps to prevent accidental bias and to achieve balance between groups.[73] However, within trials with a smaller study population, there can be baseline differences despite randomization by chance. In order to adjust for the risk of baseline differences between the groups regarding educational level and the VAS score for stress, we performed sensitivity analyses with adjustments for these factors and additionally for sex regarding the primary outcome of the VAS score for neck pain. The results of the analyses were robust.

The main strengths of this trial are the randomized study design, the relatively large sample size for a single-center interventional trial on OM, the implementation of musicians' medicine, including a job-specific subjective assessment,

treatment and outcome measurements, the high patient adherence rate, the long follow-up, and the comprehensive range of patient-reported outcomes, including neck pain, neck pain disability, quality of life, perceived stress, medication intake, and job-specific parameters. Furthermore, we considered health economics parameters. Additionally, validated and widely accepted clinical outcome measures were used, including the VAS for pain,[41] NDI,[46,47] VAS for stress[55] and SF-12.[56–59] In this RCT, we aimed to answer a research question with high personal relevance for adult musicians, as cNP is common in adult violinists and violists, including music students. The OM treatment was performed by an osteopath, who was also a medical doctor and orthopedic surgeon, by applying the usually performed individualized diagnosis-related osteopathic treatment.

However, the study also has limitations. This study employed a single-center setting, with the involvement of only one therapist with very specific training, and there was a high percentage of women in our study population; these factors clearly limit the generalizability of our results. The calculated sample size for the primary outcome parameter was not achieved; however, the difference in the primary outcome between the treatment groups was larger than expected. The study design had more potential sources of bias: participants in the OM group received more time and attention than those in the CG, and the blinding of patients or the therapist with regard to group allocation was not feasible within the study design. The patients themselves assessed the outcomes with patient-reported outcome measures; therefore, blinding of outcome assessors was not feasible. The primary outcome, neck pain, was measured subjectively. The lack of additional blinded objective outcome parameters is a limitation of the study. However, recently, the importance of blinding in RCTs has been discussed, as a meta-epidemiological study found no evidence for an average difference in estimated treatment effects between trials with and without blinded patients, healthcare providers, or outcome assessors.[74] Nonetheless, the lack of blinding of outcome assessors could have led to an overestimation of the treatment effects. We used mostly validated measurement tools but also included nonvalidated tools, such as the assessment of the intake of analgesics in a diary, the assessment of days with restrictions in daily routine and the assessment of changes in complaints by patients and the rating of the effectiveness of OM treatment. These results must be considered orienting and hypothesis generating, and must be interpreted with caution. There is some discussion in the literature on how to best analyze the VAS. One analysis for example including more than 200 patients concluded that VAS might be nonlinear and thus ordinal and should be analyzed as such.[75] However, this can be specific to the data at hand and after checking the data in our study, we saw no reason to not use ANCOVA. It is considered to be a robust method, and many researchers such as Heller *et al.*[76] and Philip[77] recommend parametric analyses methods as the pragmatic choice with equal power. Further, in our study the ANCOVA was also the predefined analysis strategy, which should be followed as closely as possible to minimize the possibility of bias.

Another limitation is that a number of patients in both groups did not adhere to the study protocol and used additional treatments during the first 12 weeks. However, the results were robust with respect to the sensitivity analyses regarding the PP population.

We considered the relatively short period of 12 weeks for an intergroup comparison necessary to recruit patients and ensure compliance in the CG. If the period between treatments had been longer, approximately 3–4 weeks, as is often the case in OM, we would have expected a stronger improvement in pain and function.

From a health economics point of view, the relatively short period is a limitation. If the period of the intergroup comparison had been longer than 12 weeks, it might have been possible to obtain more robust results with respect to the cost-effectiveness analyses. Another limitation is that adverse events were not assessed by patients in diaries but by interviews and reports to the study center. This could have led to an underreporting of adverse events, especially mild adverse events, because patients might have forgotten to report these events at the time of the interviews.

To the best of our knowledge, this was the first study to compare OM with no treatment option in adult violinists and violists with cNP. We found only one nonrandomized clinical trial that was a thesis for a Bachelor's degree in the British College of Osteopathic Medicine treating 23 healthy violinists with one strain–counterstrain session, as a technique applied in OM, in comparison with positive visualization reporting

improved range of motion in the OM group. This thesis showed that nine musicians felt calmer and more relaxed after the strain–counterstrain treatment, and 19 musicians felt calmer and more relaxed after positive visualization.

Regarding other therapy options in adult violinists and violists, one pre–post study with a crossover design investigated scapula taping while playing the instrument in eight professional orchestra musicians.[78] The authors found no benefit of scapula taping regarding pain during violin playing. Other randomized trials investigating therapy options for musculoskeletal pain in a variety of adult musicians reported some improvement after exercise[79,80] or Tui Na treatment[81,82] but no clear benefit after yoga.[83]

To our knowledge, this was also the first study investigating the costs and cost effectiveness of OM in musicians with cNP. Our results tended to be in favor of OM but were not statistically significant. This conclusion is consistent with the literature. Steel *et al.*[32] stated that despite some positive findings, published comparative effectiveness and health economics studies of OM are of insufficient quality and quantity to inform policy and practice. However, OM was reported to be a cost-effective strategy in patients with neck pain when compared with usual care, although it involved additional costs.[31] In former publications,[33,34] the cost–utility analysis identified reported improvements in pain and quality of life in patients with neck or back pain at a cost of £3760 per QALY gained.[32]

Future studies should investigate efficacy by investigating specific therapeutic effects of OM in comparison with a sham procedure and with other effective therapy methods. Possible sham procedures could include nonspecific light touch procedures in patients naïve to osteopathic treatment. The nonspecific touch procedures should include the whole body and be applied by non-osteopaths. Regarding the comparison with other effective therapy methods, these could be single therapies, such as physiotherapy and analgesics, or could include multimodal approaches. Blinding of study patients, outcome assessors and statisticians should be considered in future trials, especially if a sham procedure is developed. A future trial on OM should include multiple centers, therapists with different levels of training, a comparison with other best care options, and a more balanced sample regarding sex. Adverse events should be reported by patients in diaries.

Conclusion

The results of this study suggest that OM might be effective in reducing the pain intensity in adult violinists and violists, including music students, with nonspecific cNP. Nevertheless, in terms of cost effectiveness, OM treatment was not superior to no OM treatment during a 12-week observation period. Further multicenter studies should investigate the efficacy of OM in comparison with an OM sham procedure and the effectiveness of OM in comparison with other therapy methods.

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Conflict of interest statement

Gabriele Rotter receives irregular lecture fees for teaching in osteopathic medicine and musicians' medicine. She is a board member of the European Register for Osteopathic Physicians (EROP). The other authors declare no conflicts of interest regarding this study.

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Conferences
The results were partially reported at the 12th European Congress of Integrative Medicine, Barcelona, Spain, 13–15.09.2019. Travel expenses were provided by the first affiliation.

Supplemental material
Supplemental material for this article is available online.

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Osteopathic Medicine in Four Chronic Musculoskeletal Pain Diseases: An Observational Trial with Follow-Up

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Keywords
Chronic neck pain · Chronic low back pain · Chronic shoulder pain · Chronic knee pain · Osteopathic medicine

Abstract
Background and Aim: Patients with chronic musculoskeletal pain diseases (CMPDs) often use osteopathic medicine (OM), although the changes in patients with pain diseases are still insufficiently investigated. This study aimed to observe changes along and after OM in addition to routine care on pain, functioning, and quality of life in patients with four CMPDs. ***Methods:*** In this observational trial with follow-up, patients suffering from chronic neck pain (CNP, $n = 10$), chronic low back pain (CLBP, $n = 10$), chronic shoulder pain (CSP, $n = 10$), or chronic knee pain (CKP, $n = 10$) received up to six OM sessions in addition to routine care. ***Results:*** A total of 40 patients (73% female, mean age 47.7 ± 8.3 years, mean pain intensity 59.4 ± 12.5 mm, measured by a visual analog scale [VAS] 0–100 mm) were included. After 26 weeks, there was an improvement in the VAS pain score in the whole population (mean difference to baseline –33.1 mm [95% CI –40.5 to –25.7]), as well in the patients with the four diseases: CNP (–33.7 mm [–54.7 to –12.6]), CLBP (–28.2 mm [–47.9 to –8.4]), CSP (–32.4 [–46.8 to –18.0]), and CKP (–38.1 mm [–49.1 to –27.0]). Regarding disease-specific outcomes, we found improvements in CNP, as measured by the neck disability index (scale 0–50; mean difference –3.6 [–9.0 to 1.9]), CLBP, as measured by the low back pain rating scale (scale 0–60; –3.4 [–12.5 to 5.7]), CSP, as measured by the disabilities of the arm, shoulder and hand score (scale 0–100; –13.4 [–23.1 to –3.7]), and CKP, as measured by the Western Ontario and McMaster Universities Osteoarthritis Index (scale 0–96; –13.0 [–23.5 to –2.5]). These improvements persisted through week 52. No adverse events were observed. ***Conclusion:*** The study observed beneficial changes along and after the OM treatment in addition to routine care in patients with four different CMPDs. High-quality, multicenter randomized controlled trials are strongly needed to compare the effectiveness of OM and standard care interventions in treating CMPDs in the future. We have provided sufficient data for sample size calculations for these trials.

Osteopathische Medizin in vier chronischen muskuloskeletalen Schmerzerkrankungen: Eine Beobachtungsstudie mit Follow-up

Schlüsselwörter
Chronische zervikale Schmerzen · Chronische lumbale Schmerzen · Chronische Schulterschmerzen · Chronische Knieschmerzen · Osteopathische Medizin

Trial registration: German Clinical Trials Register DRKS00008319, Universal Trial Number (UTN): U1111-1169-9945.

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Zusammenfassung

Hintergrund und Ziel: Patienten mit chronischen muskuloskeletalen Schmerzerkrankungen (CMPDs) nutzen oft osteopathische Medizin (OM), obwohl die Veränderungen bei Patienten mit Schmerzerkrankungen noch unzureichend untersucht sind. Ziel dieser Studie war es, Veränderungen während und nach der OM, in Ergänzung zur Routineversorgung, auf Schmerzen, Funktionsfähigkeit und Lebensqualität bei Patienten mit vier CMPDs zu beobachten. ***Methoden:*** In einer Beobachtungsstudie mit Follow-up erhielten Patienten, welche an chronischen zervikalen Schmerzen, (CNP, *n* = 10), chronischen lumbalen Schmerzen (CLBP, *n* = 10), chronischen Schulterschmerzen (CSP, *n* = 10), oder chronischen Knieschmerzen (CKP, *n* = 10) litten, bis zu sechs OM Behandlungen zusätzlich zur Routinebehandlung. ***Ergebnisse:*** Insgesamt wurden 40 Patienten (73% Frauen, mittleres Alter 47,7 ± 8,3 Jahre) mit einer mittleren Schmerzintensität von 59,4 ± 12,5 mm, gemessen auf einer Visuellen Analog Skala (VAS, 0–100 mm) eingeschlossen. Nach 26 Wochen bestand eine Verbesserung auf der VAS Schmerz in der Gesamtpopulation (mittlere Differenz zu Baseline –33,1 mm [95% KI –40,5; –25,7]), als auch bei den Patienten in allen vier Erkrankungen: CNP (–33,7 mm [–54,7; –12,6]), CLBP (–28,2 mm [–47,9; –8,4]), CSP (–32,4 [–46,8; –18,0]), und CKP (–38,1 mm [–49,1; –27,0]). Hinsichtlich krankheitsspezifischer Zielparameter fanden wir Verbesserungen im CNP, gemessen mittels Neck Disability Index (Skala 0–50; mittlere Differenz –3,6 [–9,0; 1,9]), CLBP, gemessen mittels Low Back Pain Rating Scale (Skala 0–60; –3,4 [–12,5; 5,7]), CSP, gemessen mittels Disabilities of the Arm, Shoulder and Hand Score (Skala 0–100; –13,4 [–23,1; –3,7]) und CKP, gemessen mittels Western Ontario and McMaster Universities Osteoarthritis Index (Skala 0–96; –13,0 [–23,5; –2,5]). Die Verbesserungen hielten bis zur Woche 52 an. Es wurden keine unerwünschten Ereignisse beobachtet. ***Schlussfolgerung:*** Die Studie beobachtete positive Veränderungen während und nach der OM-Behandlung, in Ergänzung zur Routineversorgung, bei Patienten mit vier verschiedenen CMPDs. Qualitativ hochwertige, multizentrische randomisierte kontrollierte Studien sind dringend erforderlich, um die Wirksamkeit von OM-Behandlungen und Standardbehandlungen bei der Behandlung von CMPDs in Zukunft zu vergleichen. Wir haben ausreichende Daten für die Berechnung der Stichprobengröße für diese Studien zur Verfügung gestellt.

Introduction

Low back pain, neck pain, and chronic musculoskeletal pain diseases (CMPDs) in general lead to a large disease burden globally, and CMPDs constitute one of the leading causes of ill health [1, 2]. The 12-month prevalence of chronic knee pain (CKP) among patients aged 50 years and older treated by general practitioners was reported to be 25.3% [3]. In a German cross-sectional study (*n* = 2,510 participants), the 3-month prevalence was 25% for chronic low back pain (CLBP), 18% for chronic neck pain (CNP), 11% for chronic shoulder pain (CSP) in the right shoulder, and 9% for CSP in the left shoulder [4]. These CMPDs are recommended to be treated by a multimodal regime, including analgesics, educational interventions, exercise, and manual treatments [5–13]. However, long-term medication with analgesics might result in adverse events, and there is growing interest in nonpharmacological treatment options, including treatments originating from complementary and integrative medicine [14–17].

Osteopathic medicine (OM) is a component of complementary and integrative medicine. In an Australian adult population, OM was reported to be used by 4.6% of the patients within the last 12 months (*n* = 1,067 interviews) [18]. Patients seek OM mostly for pain symptoms not only in the lower back (36%) and neck (15%) but also in the shoulder (7%) [19]. OM relies on manual contact for diagnosis and treatment and emphasizes the structural and functional integrity of the body, including skeletal, arthrodial, and myofascial structures and related vascular, lymphatic, and neural elements [20]. These structures include the musculoskeletal, visceral, and so-called craniosacral system. In Europe, OM is commonly administered by nonphysicians (in Germany, often physiotherapists and "Heilpraktiker" [healing practitioners]) or physicians as a diagnosis-related and individualized treatment (osteopathic manipulative treatment) and additionally offers self-training instructions for postural improvement. There is some evidence that OM might be effective in treating CMPDs. Previous studies have indicated that OM is effective in relieving pain in patients with CNP [21], relieving pain and improving function in patients with CLBP [22, 23], and relieving shoulder pain [24, 25]. Further, unpublished randomized controlled trials (RCTs) suggest beneficial effects of OM for shoulder pain [26] and knee pain [27].

However, until now, to the best of the authors' knowledge, a prospective observation of six routine OM treatments in patients with various CMPDs; outcomes for pain, quality of life, disease-specific function; restrictions in activities of daily living (ADL); and the utilization of additional therapies over a long follow-up period has not been published.

The aims of this observational trial with follow-up were to assess data on pain, functioning, and quality of life in patients suffering from CNP, CLBP, CSP, or CKP, who received OM in addition to German physician routine care setting, and to investigate the study feasibility. A further aim was to provide sufficient data for sample size calculations for future RCTs.

Methods

Study Design and Setting

The observational trial with follow-up included 40 adult patients, with 10 patients in each of the four groups of CMPDs (CNP, CLBP, CSP, or CKP). The outcomes were assessed after 12, 26, and 52 weeks. The study was performed at the outpatient clinic for Integrative Medicine of the Charité – Universitätsmedizin in Berlin, Germany.

Patients

Patients were recruited by the website of the outpatient department for integrative medicine and the intranet of Charité – Universitätsmedizin Berlin. Patients between 30 and 65 years of age with a clinical diagnosis of CNP, CLBP, CSP, or CKP (disease duration with the specific pain of at least 12 weeks) and an average visual analog scale (VAS) score for pain intensity (0–100 mm, 0 = no pain, 100 = worst imaginable pain) of at least 40 mm within the last 7 days with respect to the diagnosis were included. The main exclusion criteria were a history of OM treatment within the last 12 months; musculoskeletal pain due to known malignant diseases, infections, a previous accident, known or suspected primary or secondary bone tumor, known vascular anomaly, peripheral or central neurological symptoms, rheumatic diseases, or the presence of implants/endoprostheses in the respective body region; a body mass index higher than 30; the intake of centrally acting analgesics; and the presence of pregnancy or lactation.

Exposure

After inclusion, the patients received six individualized diagnosis-related OM treatment sessions that lasted 45 min each, with 3- to 4-week intervals (during 26 weeks), in addition to routine care. An on-demand dose of 500 mg paracetamol up to four times daily was provided in the first 26 weeks. The patients were discouraged from taking analgesics other than paracetamol. No changes were made to the other conventional or complementary therapy regimens received by the patients. The diagnostics method, treatment strategy, and treatment interval were intentionally made to be the same as those usually used in our outpatient clinic for integrative medicine. At the beginning of each session, a short anamnesis and physical examination were performed to determine the OM treatment strategy for the respective session. For the treatment techniques performed for the musculoskeletal, visceral, and craniosacral systems, the patients were treated in a standing, sitting, or lying position with or without active participation. Posturologic and ergonomic advice was included. The OM treatment was administered by a medical doctor who specialized in orthopedic surgery (G.R.), completed a 5-year part-time OM training program (1,350 h), holds an MSc degree in osteopathy, and had long-term experience in OM treatment.

Outcome Parameters

All parameters were measured at baseline and after 12, 26, and 52 weeks using standardized questionnaires, including validated patient-reported outcome measurements. Because this is an exploratory study, no primary outcome parameters were determined. All patients rated their average perceived pain in the respective body region within the last 7 days using a VAS [28]. For all CMPDs, the minimal clinically important difference (MCID) between baseline and 26 weeks (after 6 treatments) was considered to be 15 mm [29, 30]. The criteria for a substantial clinical benefit (SCB) was considered to be 26.5 mm [31]. Health-related quality of life was measured by the 12-item short form health survey (SF-12), with an MCID of 5 points [32–35].

In addition, for each diagnosis group, a disease-specific outcome parameter, listed below, was measured. In patients with CNP, neck function was assessed by the neck disability index (NDI, scores ranging from 0 to 50, MCID of 3.0 points, SCB of 8.4 points) [31, 36, 37]. In patients with CLBP, pain was evaluated with the pain subscale of the low back pain rating scale (scores ranging from 0 to 60, MCID of 1.2 points) [38–40]. In patients with CSP, upper extremity function was assessed by the disabilities of the arm, shoulder and hand questionnaire (DASH, scores ranging from 0 to 100, MCID of 8 points in the total score) [41–43]. In addition, the DASH includes an optional questionnaire module for sports/music that does not influence the DASH total score. In patients with CKP, knee function was evaluated by two outcome measurements, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC, total scores ranging from 0 to 96, MCID of 10 points in the total score) [44–47] and the Lequesne index (total scores ranging from 0 to 24, MCID of a 40% change in each score) [48–51].

Furthermore, the following parameters related to the respective CMPD with respect to the last 4 weeks were assessed: days with restrictions in activities of daily living (ADL), analgesic intake (reported as the number of patients taking analgesics), and the use of additional therapies. Furthermore, treatment expectations ("highly effective," "effective," "slightly effective," "not effective") and outcome expectations ("healing," "substantial improvement in symptoms," "modest improvement in symptoms," "no improvement") were rated by the study physician and by the patients. In addition, parameters related to the safety of OM, including therapy-related adverse events and serious adverse events, were evaluated.

Statistical Analysis

As this was an observational trial with follow-up, no sample size calculation was performed. A total of 10 patients per CMPD group was considered sufficient to achieve the objectives of the study. The collected data were evaluated descriptively: mean values, SDs, medians, and interquartile ranges, additionally in non-normally distributed data, and frequencies and percentages for the entire group and by CMPD group. The pre- and posttreatment outcome parameters were exploratively compared by mean differences. All confidence intervals were two-sided. The results are presented descriptively. The evaluation was carried out according to the intention-to-treat principle with the full analyses set and without the substitution of missing values. The statistical analysis was performed using SAS software, version 9.4 [52], and R, version 3.6.3 [53].

Results

Patients

Among the 91 eligible patients, 40 were enrolled (as planned, with 10 patients in each of the 4 CMPD groups, CNP, CLBP, CSP, and CKP) between June 2015 (first pa-

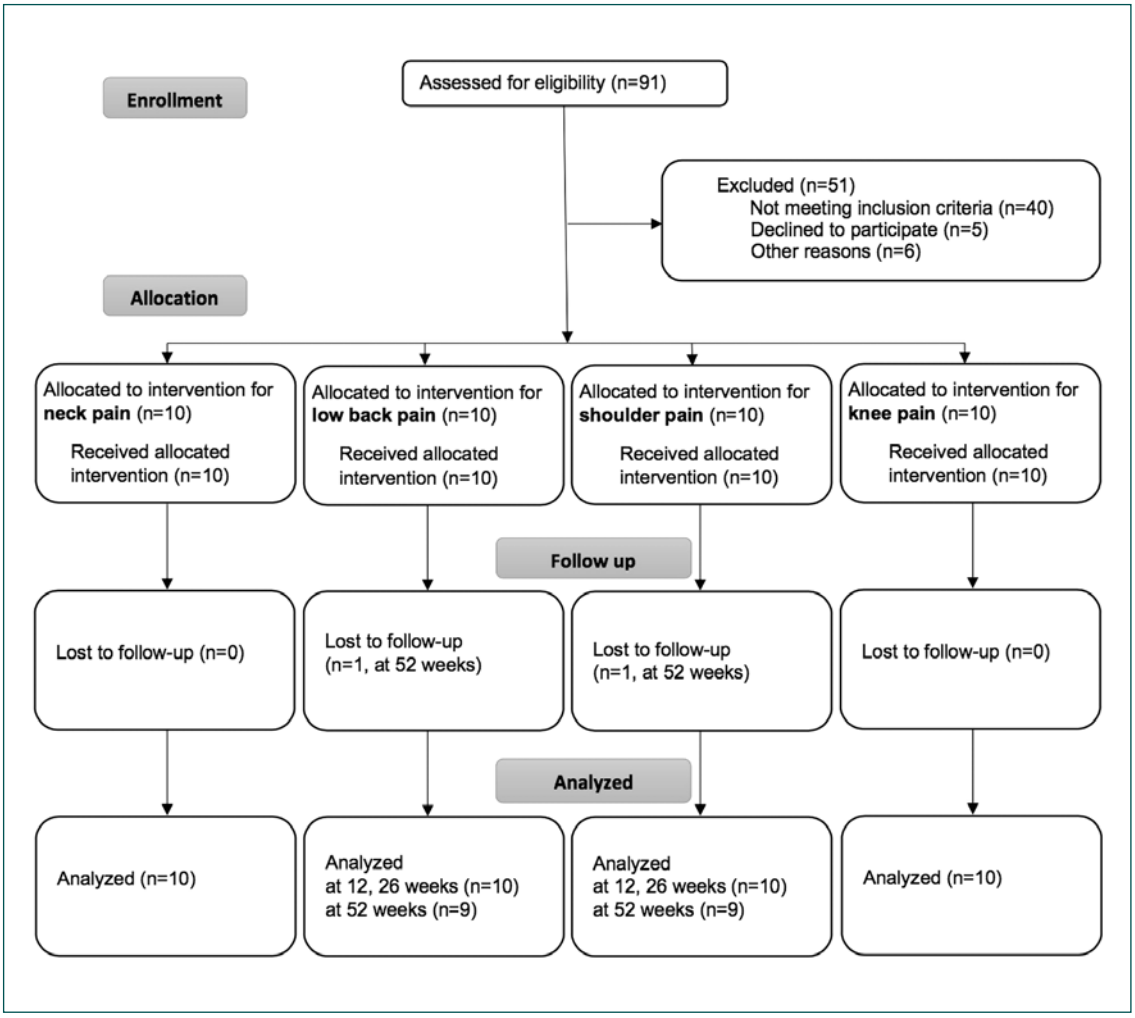

Fig. 1. Recruitment, treatment, and follow-up of patients with chronic neck pain, chronic low back pain, chronic shoulder pain, and chronic knee pain.

tient included) and January 2017 (last patient included) (Fig. 1). The group of patients with CLBP was complete first (January 2016), followed by the groups CNP (July 2016), CKP (October 2016), and finally CSP (January 2017). Two patients (one with CLBP and one with CSP) did not return the questionnaires after 52 weeks. There were no other patients lost to follow-up. To return the questionnaires one reminder had to be sent to 22 patients after 12 weeks, 19 patients after 26 weeks, and 21 patients after 52 weeks. During the entire study period, a total of 34 patients had to be reminded to return the questionnaires. Apart from that, the questionnaires were mostly well accepted and carefully completed.

At baseline, the mean age of all the patients (n = 40) was 47.7 ± 8.3 years (mean ± SD) (Table 1), with a range from 30 to 62 years. Twenty-nine patients (72.5%) were female, and the mean duration of the specific CMPD symptoms was 9.0 ± 10.3 years. At least one nondrug treatment for the respective CMPD within the last 6 weeks was reported by 26 patients (65%). In the past, 24 patients (60.0%) had received OM, 10 (25.0%) of whom received OM specifically for the respective CMPD. Analgesics for the respective CMPD were taken within the last 6 weeks by 20 patients (50.0%). The mean VAS score for pain was 59.4 ± 12.5 mm, the mean SF-12 physical component scale (SF-12 PCS) score was 39.2 ± 8.0, and the mean SF-12 mental component scale (SF-12 MCS) score was 48.6 ± 9.2. Regarding OM treatment expectations, the study physician mostly expected OM to be "effective" (55.0%) and "slightly effective" (40.0%), whereas the patients mostly expected it as "effective" (50.0%) and "highly effective" (47.5%). With respect to the outcome expectations, the study physician tended to report "substantial improvement in symptoms" (37.5%) or "modest improvement in symptoms" (62.5%), whereas the patients tended to report "substantial improvement in symptoms" (80.0%). For the duration of symptoms, restrictions in ADL, and pain intensity, as measured by the

Table 1. Baseline characteristics of study participants

	Total (n = 40)	Neck pain (n = 10)	Low back pain (n = 10)	Shoulder pain (n = 10)	Knee pain (n = 10)
Sex, female	29 (72.5)	7 (70.0)	7 (70.0)	7 (70.0)	8 (80.0)
Age, years	47.7±8.3	49.2±4.8	45.3±8.1	47.2±9.7	49.1±10.3
Profession, employed	30 (75.0)	8 (80.0)	8 (80.0)	7 (70.0)	7 (70.0)
Duration of the specific CMPD symptoms, years	9.0±10.3	11.4±11.7	6.8±6.1	5.7±4.5	12.2±15.1
	5.3 [8.0]	8.5 [5.0]	4.5 [7.8]	5.3 [7.1]	6.5 [11.3]
Restrictions in ADL, days	14.6±11.1	14.5±11.8	20.6±10.3	14.2±10.6	9.2±10.2
	15.0 [20.5]	9.0 [21.2]	22.5 [13.2]	12.5 [17.2]	4.5 [18.8]
Use of physical therapy last 4 weeks	13 (32.5)	4 (40.0)	3 (30.0)	6 (60.0)	0
Physical therapy in the past for the respective CMPD	33 (84.6)	9 (90.0)	7 (77.8)	10 (100)	7 (70.0)
Osteopathy in the past	24 (60.0)	8 (80.0)	4 (40.0)	6 (60.0)	6 (60.0)
For the respective CMPD	10 (25.0)	4 (40.0)	3 (30.0)	0	3 (30.0)
For other disease	17 (42.5)	5 (50.0)	2 (20.0)	6 (60.0)	4 (40.0)
CMPD-related analgesics intake (last 4 weeks)	20 (50.0)	5 (50.0)	4 (40.0)	8 (80.0)	3 (30.0)
Medications for other diagnoses	30 (75.0)	6 (60.0)	6 (60.0)	9 (90.0)	9 (90.0)
Visual analogue scale pain (0–100 mm)*	59.4±12.5	62.3±10.8	62.0±14.8	57.3±14.8	56.0±9.4
	57.2 [11.0]	60.0 [18.8]	57.5 [10.8]	55.2 [13.8]	57.0 [9.8]
SF-12					
Physical Component Scale (0–100)**	39.2±8.0	36.9±8.5	39.6±8.1	38.8±6.4	41.8±9.1
Mental Component Scale (0–100)**	48.6±9.2	42.9±10.3	51.7±9.0	47.2±7.4	52.5±7.7
	50.8 [14.7]	40.0 [17.9]	54.7 [7.4]	47.8 [10.6]	55.0 [8.2]
NDI (0–50)*	–	15.1±5.9	–	–	–
Low Back Pain Rating Scale (0–60)* (n = 9)		–	19.3±4.7	–	–
DASH (0–100)*	–	–	–	55.7±13.4	–
WOMAC total score (0–96)*	–	–	–	–	22.4±13.7
Lequesne index of severity (0–24)*	–	–	–	–	5.3±3.7

Data are presented as mean ± SD, median [IQR], or n (%). * Lower values indicate better status. ** Higher values indicate better status; in cases of non-normal distribution median and IQR are additionally reported. ADL, activities of daily living; CMPD, chronic musculoskeletal pain disease; DASH, Disabilities of Arm, Shoulder and Hand; NDI, Neck Disability Index Score; IQR, interquartile range; SF-12, 12-item Short Form Health Survey; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

VAS, we found distinct differences between the mean and median values.

Exposure

The interventions were performed as described in the Methods. Regarding adherence to the OM interventions, n = 39 patients underwent all 6 treatments. One patient with CNP underwent only one intervention because of personal reasons but did not drop out of the study and returned all questionnaires throughout the 52 weeks of follow-up.

Outcomes

VAS Pain

In the whole study population, pain intensity, as measured by the VAS, improved after 12 weeks and approximately three OM sessions (mean difference to baseline –29.3 mm [–35.7 to –23.0]) with a clinically stable improvement after 26 weeks and 6 treatments (mean difference to baseline –33.1 mm [–40.5 to –25.7]). The improvements had a substantial clinical benefit (SCB criteria change of 26.5 mm reached, Table 2). The largest improvement after 26 weeks was observed in CKP (mean difference to baseline –38.1 mm [–49.1 to –27.0]), and the lowest was observed in CLBP (–28.2 mm [–47.9 to –8.4]). Improvements persisted through the follow-up conducted at week 52 (mean difference to baseline –34.9 [–42.4 to –27.5]) (Fig. 2).

Health-Related Quality of Life with SF-12

After 12 weeks, there was a tendency to an overall improvement in the SF-12 PCS score, with a mean difference to baseline of 4.9 (1.9–7.9), but not in the SF-12 MCS score (0.08 [–2.2 to 3.8]). Similarly, after 26 weeks, the SF-12 PCS score mean difference to baseline (6.9 [4.2–9.5]) but not the SF-12 MCS score (–0.02 [–3.1 to 3.0]) improved (Table 2). The improvement in SF-12 PCS score after 26 weeks was clinically important (MCID 5 points) and persisted through week 52 (mean difference to baseline 6.7 [3.7–9.7]) (Fig. 3).

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Table 2. Subjective pain, health-related quality of life, and disease-specific outcomes, comparison baseline to 12 and 26 weeks

	N	Baseline, mean (95% CI)	*N*	At 12 weeks, mean (95% CI)	*N*	12 weeks vs. baseline, mean difference (95% CI)	*N*	At 26 weeks, mean (95% CI)	*N*	26 weeks vs. baseline, mean difference (95% CI)
Total population										
VAS pain (0–100 mm)*, MCID 15 mm	40	59.4 (55.4 to 63.4)	40	30.1 (23.7 to 36.4)	40	−29.3 (−35.7 to −23.0)	40	26.3 (18.8 to 33.8)	40	−33.1 (−40.5 to −25.7)
SF-12 PCS (0–100)**, MCID 5	40	39.2 (36.7 to 41.8)	39	44.2 (41.5 to 46.9)	39	4.9 (1.9 to 7.9)	40	46.1 (43.4 to 48.8)	40	6.9 (4.2 to 9.5)
SF-12 MCS (0–100)**	40	48.6 (45.7 to 51.5)	39	49.2 (45.6 to 52.7)	39	0.8 (−2.2 to 3.8)	40	48.6 (45.1 to 52.0)	40	−0.02 (−3.1 to 3.0)
By chronic musculoskeletal pain disease VAS pain, SF-12, and disease specific outcomes										
Chronic neck pain (CNP)										
VAS pain	10	62.3 (54.6 to 70.0)	10	27.7 (14.8 to 40.6)	10	−34.6 (−49.6 to −19.6)	10	28.7 (11.4 to 46.0)	10	−33.7 (−54.7 to −12.6)
SF-12 PCS	10	36.9 (30.8 to 42.9)	9	43.3 (35.0 to 51.6)	9	6.5 (−2.7 to 15.7)	9	43.9 (38.0 to 49.8)	9	7.0 (1.4 to 12.7)
SF-12 MCS	10	42.9 (35.6 to 50.3)	9	42.9 (31.7 to 54.1)	9	1.5 (−8.0 to 11.0)	9	43.5 (33.5 to 53.6)	9	0.6 (−5.7 to 6.9)
NDI (0–50)*, MCID 3.0	10	15.1 (10.9 to 19.3)	10	11.7 (7.3 to 16.1)	10	−3.4 (−7.2 to 0.4)	9	11.7 (5.2 to 18.2)	9	−3.6 (−9.0 to 1.9)
Chronic low back pain (CLBP)										
VAS pain	10	62.0 (51.4 to 72.6)	10	37.1 (18.7 to 55.5)	10	−24.9 (−43.6 to −6.3)	10	33.8 (12.3 to 55.3)	10	−28.2 (−47.9 to −8.4)
SF-12 PCS	10	39.6 (33.8 to 45.4)	10	43.3 (36.9 to 49.7)	10	3.7 (−3.0 to 10.4)	10	45.0 (37.8 to 52.1)	10	5.4 (−0.1 to 10.9)
SF-12 MCS	10	51.7 (45.3 to 58.2)	10	50.1 (41.5 to 58.6)	10	−1.7 (−6.0 to 2.6)	10	50.4 (42.7 to 58.1)	10	−1.4 (−8.7 to 6.0)
Low back pain rating scale (0–60)*, MCID 1.2	9	19.3 (15.7 to 22.9)	10	16.0 (7.4 to 24.6)	9	−1.9 (−9.6 to 5.8)	10	15.4 (6.5 to 24.3)	9	−3.4 (−12.5 to 5.7)
Chronic shoulder pain (CSP)										
VAS pain	10	57.3 (46.6 to 67.9)	10	31.6 (18.8 to 44.5)	10	−25.6 (−38.7 to −12.5)	10	24.9 (10.2 to 39.5)	10	−32.4 (−46.8 to −18.0)
SF-12 PCS	10	38.8 (34.2 to 43.3)	10	42.1 (37.6 to 46.6)	10	3.3 (−1.4 to 8.1)	10	47.9 (42.9 to 52.9)	10	9.1 (4.9 to 13.3)
SF-12 MCS	10	47.2 (41.9 to 52.5)	10	48.2 (42.5 to 53.8)	10	0.9 (−5.3 to 7.2)	10	47.5 (42.1 to 52.8)	10	0.2 (−4.3 to 4.8)
DASH disability/symptom (0–100)*, MCID 8	10	55.6 (46.1 to 65.2)	10	42.5 (32.5 to 52.5)	10	−13.2 (−20.2 to −6.1)	9	42.2 (33.3 to 51.1)	9	−13.4 (−23.1 to −3.7)
DASH sport/music (0–100)*	3	68.8 (6.6 to 130.9)	3	60.4 (36.7 to 84.1)	3	−8.3 (−47.4 to 30.7)	3	56.3 (25.2 to 87.3)	3	−12.5 (−105.7 to 80.7)
DASH work (0–100)*	10	48.8 (31.1 to 66.4)	10	48.8 (31.1 to 66.4)	10	0	9	41.0 (17.2 to 64.8)	9	−8.3 (−18.2 to 1.6)
Chronic knee pain (CNP)										
VAS pain	10	56.0 (49.3 to 62.8)	10	23.9 (11.8 to 36.1)	10	−32.1 (−41.6 to −22.5)	10	17.9 (5.1 to 30.8)	10	−38.1 (−49.1 to −27.0)
SF-12 PCS	10	41.8 (35.2 to 48.3)	10	47.9 (42.8 to 53.0)	10	6.2 (−1.0 to 13.4)	10	47.7 (41.4 to 54.0)	10	5.9 (−2.1 to 13.9)
SF-12 MCS	10	52.5 (47.0 to 58.0)	10	54.9 (50.7 to 59.2)	10	2.4 (−5.0 to 9.8)	10	53.0 (46.6 to 59.3)	10	0.5 (−8.8 to 9.7)
WOMAC, total score (0–96)*, MCID 10	9	22.4 (11.9 to 33.0)	10	12.5 (5.2 to 19.8)	9	−12.1 (−23.4 to −0.8)	10	10.7 (1.2 to 20.2)	9	−13.0 (−23.5 to −2.5)
WOMAC, pain (0–20)*	9	6.1 (4.0 to 8.2)	10	3.2 (1.4 to 5.0)	9	−3.3 (−5.4 to −1.2)	10	2.4 (0.2 to 4.6)	9	−4.1 (−6.2 to −2.0)
WOMAC, stiffness (0–8)*	9	2.2 (0.6 to 3.8)	10	1.9 (1.1 to 2.7)	9	−0.4 (−2.3 to 1.4)	10	1.7 (0.5 to 2.9)	9	−0.7 (−2.7 to 1.4)
WOMAC, physical function (0–68)*	9	14.1 (6.4 to 21.9)	10	7.4 (2.1 to 12.7)	9	−8.3 (−16.4 to −0.2)	10	6.6 (0.2 to 13.0)	9	−8.2 (−15.3 to −1.2)
Lequesne, index of severity (0–24)*, MCID 40%	9	5.3 (2.4 to 8.1)	10	3.2 (1.2 to 5.1)	9	−2.1 (−4.7 to 0.6)	10	3.2 (0.7 to 5.6)	9	−2.7 (−4.9 to −0.5)
Lequesne, pain (0–8)*	9	3.0 (1.3 to 4.7)	10	1.6 (0.5 to 2.7)	9	−1.4 (−3.0 to 0.1)	10	1.7 (0.3 to 3.1)	9	−1.7 (−3.1 to −0.3)
Lequesne, max. distance walked (0–8)*	9	0.4 (−0.1 to 1.0)	10	0.4 (−0.1 to 0.9)	9	0.0 (−0.4 to 0.4)	10	0.3 (−0.2 to 0.8)	9	−0.2 (−0.6 to 0.1)
Lequesne, ADL (0–8)*	9	1.8 (0.9 to 2.8)	10	1.2 (0.4 to 1.9)	9	−0.6 (−1.6 to 0.3)	10	1.2 (0.4 to 1.9)	9	−0.8 (−1.6 to 0.0)

* Lower values indicate better status. ** Higher values indicate better status. ADL, activities of daily living; DASH, Disabilities of Arm, Shoulder and Hand; Lequesne, Index of Severity for Osteoarthritis of the Knee; max., maximum; MCID, minimal clinically important difference (numbers without unit are given in points); NDI, Neck Disability Index Score; SF-12 MCS, 12-item Short Form Health Survey Mental Component Scale; SF-12 PCS, 12-item Short Form Health Survey Physical Component Scale; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

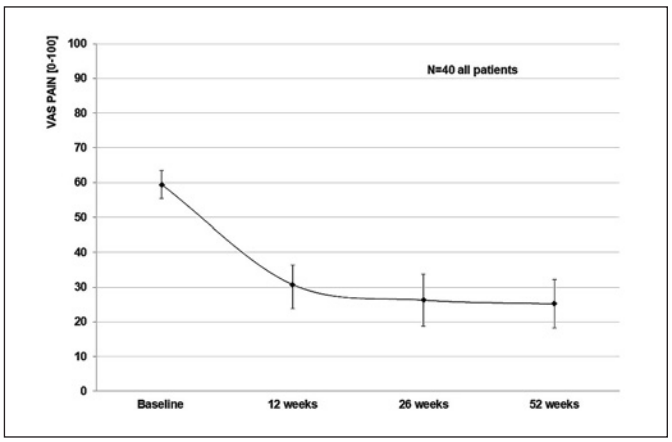

Fig. 2. Visual analog scale (VAS) pain through 52 weeks in all four chronic musculoskeletal pain diseases. Values are means and 95% CIs.

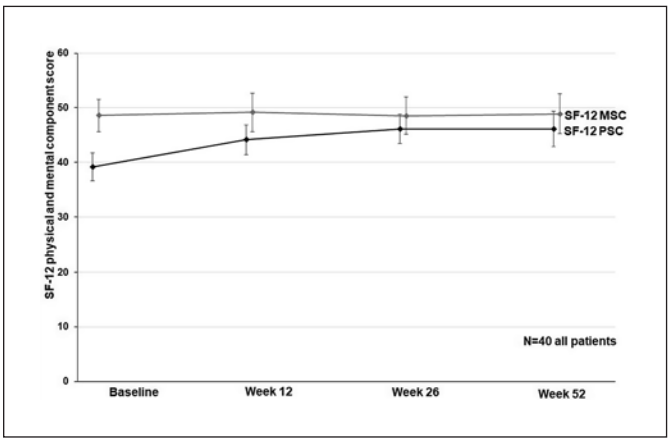

Fig. 3. Estimated mean scores of the 12-item Short Form Health Survey (SF-12) Physical Component Scale (PCS) and Mental Component Scale (MCS) over 52 weeks. Values are means and 95% CIs.

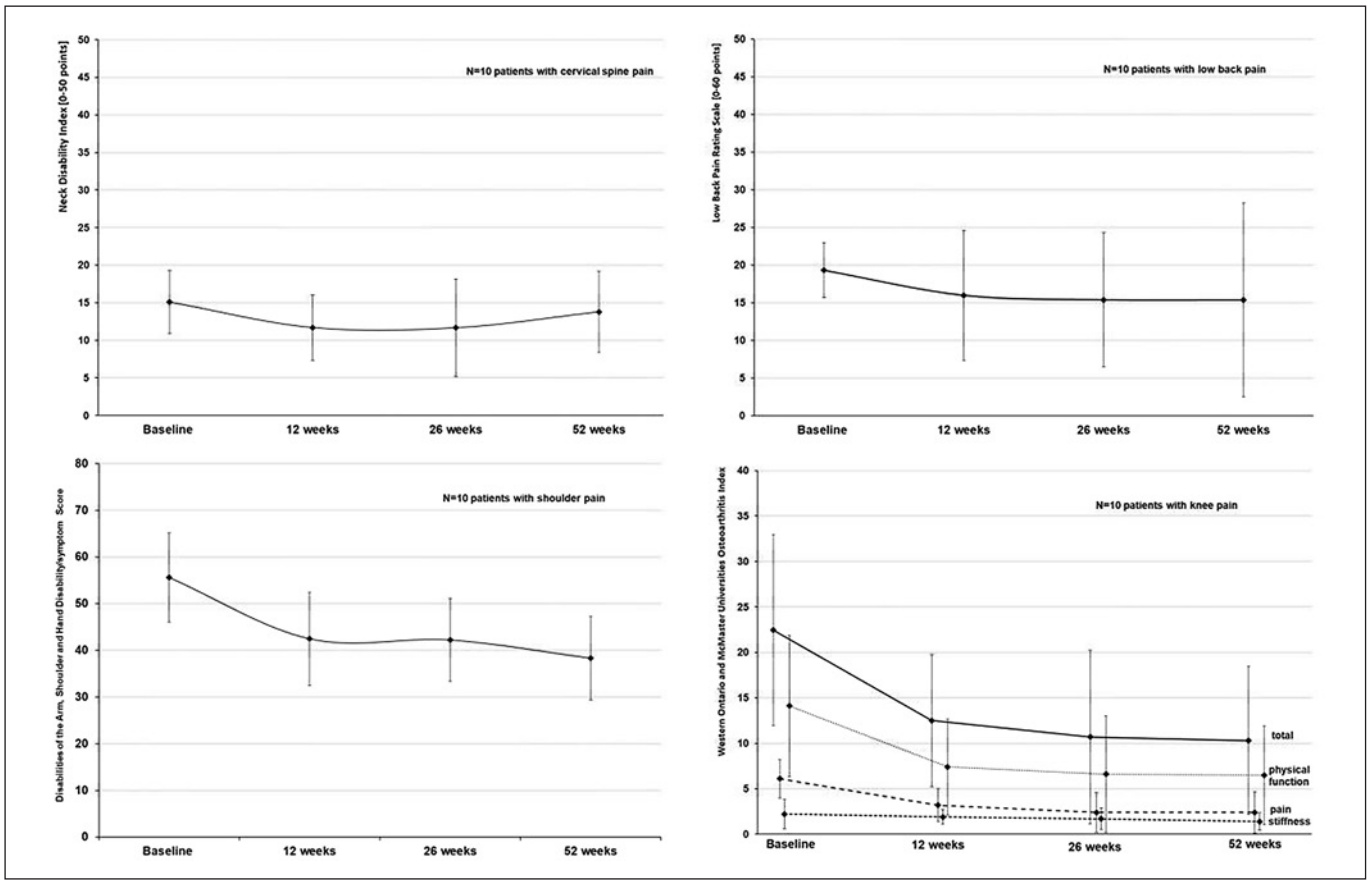

Fig. 4. Estimated mean scores for Neck Disability Index, Low Back Pain Rating Scale, Disabilities of Arm, Shoulder and Hand Score, and Western Ontario and McMaster Universities Osteoarthritis Index through 52 weeks in the according diagnosis group. Values are means and 95% CIs.

Disease-Specific Outcomes

All disease-specific outcomes showed at least a tendency toward improvement over time in the respective study populations of 10 patients (Table 2; Fig. 4).

Among the CNP patients, we found clinically relevant (MCID 3.0 points) improvements in the NDI score from baseline to 12 weeks (mean difference [95% CI] −3.4 [−7.2 to 0.4]) and versus 26 weeks (−3.6 [−9.0

Table 3. Number of days with restrictions in activities of daily living within the last 4 weeks, for total study population and for each chronic musculoskeletal pain disease

	N	Baseline, mean (95% CI)	*N*	At 12 weeks, mean (95% CI)	12 weeks vs. baseline, mean difference (95% CI)	*N*	At 26 weeks, mean (95% CI)	26 weeks vs. baseline, mean difference (95% CI)	*N*	At 52 weeks, mean (95% CI)	52 weeks vs. baseline, mean difference (95% CI)
Total study population	40	14.6 (11.1 to 18.2)	40	7.8 (5.3 to 10.3)	−6.8 (−10.1 to −3.5)	40	6.0 (3.3 to 8.7)	−8.6 (−11.8 to −5.5)	38	5.4 (2.7 to 8.0)	−8.8 (−12.1 to −5.4)
Neck pain	10	14.5 (6.1 to 22.9)	10	7.3 (0.5 to 14.1)	−7.2 (−16.5 to 2.1)	10	6.6 (−0.0 to 13.2)	−7.9 (−13.0 to −2.8)	10	7.8 (1.4 to 14.2)	−6.7 (−12.8 to −0.6)
Low back pain	10	20.6 (13.2 to 28.0)	10	9.6 (3.6 to 15.6)	−11.0 (−18.3 to −3.7)	10	8.6 (0.6 to 16.6)	−12.0 (−22.0 to −2.0)	9	4.8 (−2.0 to 11.6)	−15.9 (−25.6 to −6.2)
Shoulder pain	10	14.2 (6.6 to 21.8)	10	9.8 (4.3 to 15.3)	−4.4 (−10.1 to 1.3)	10	5.8 (0.0 to 11.6)	−8.4 (−15.4 to −1.4)	9	6.7 (−1.3 to 14.6)	−6.0 (−11.7 to −0.3)
Knee pain	10	9.2 (1.9 to 16.5)	10	4.5 (1.4 to 7.6)	−4.7 (−11.6 to 2.2)	10	2.9 (0.5 to 5.3)	−6.3 (−12.5 to −0.1)	10	2.3 (0.0 to 4.6)	−6.9 (−13.9 to 0.1)

to 1.9]). For patients with CLBP, a clinically relevant (MCID 1.2 points) improvement in the low back pain rating scale was observed after 12 weeks (–1.9 [–9.6 to 5.8]) and after 26 weeks (–3.4 [–12.5 to 5.7]). In the ten patients with CSP, a clinically relevant (MCID 8 points) functional improvement in the DASH disability/symptom score was found from baseline to 12 weeks (–13.2 [–20.2 to –6.1]) and to 26 weeks (–13.4 [–23.1 to –3.7]). Only $n = 3$ patients filled out the questionnaires for the optional sport/music score. In the patients with CKP, a clinically relevant improvement in function (MCID 10 points) according to the WOMAC total score was observed after 12 weeks (–12.1 [–23.4 to –0.8]), and additional improvement was observed after 26 weeks (–13.0 [–23.5 to –2.5]). After 26 weeks, we observed a tendency for improvements in the WOMAC subscale scores for pain (–4.1 [–6.2 to –2.0]), stiffness (–0.7 [–2.7 to 1.4]), and physical function (–8.2 [–15.3 to –1.2]). Some improvements were also observed in the Lequesne index of severity after 12 weeks (–2.1 [–4.7 to 0.6]) and 26 weeks (–2.7 [–4.9 to –0.5]). The observed improvement, 39.6%, did not reach the MCID (40%).

After 52 weeks, the improvements in the disease-specific parameters persisted in the CLBP (low back pain rating scale score mean [95% CI] 15.4 [2.5–28.2]), CSP (DASH disability/symptom score 38.3 [29.4–47.2]), and CKP groups (WOMAC total score 10.3 [2.1–18.5]) but not in the CNP group (NDI 13.8 [8.4–19.2]) (Fig. 4).

Restrictions in Activities of Daily Living, Analgesics Intake, and the Use of Additional Therapies for CMPDs over the Last 4 Weeks

The number of days with restrictions in ADL over the last 4 weeks decreased from baseline to 12 weeks (overall mean of 14.6 vs. 7.8 days) and decreased further to 26 weeks for the whole study population and within every CMPD group. Only the CNP and CSP groups did not show additional improvement after 52 weeks (Table 3). The number of patients taking analgesics decreased in the whole study population from baseline to 26 weeks (Table 4). In the patients with CNP and CLBP, the number of patients taking analgesics remained unchanged from baseline to 26 weeks. The reduction in analgesic intake remained fairly low (overall by 18.4 percentage points) through 52 weeks. With regard to the respective CMPD, in the whole population, the number of patients undergoing physical therapy decreased from $n = 13$ (32.5%) at baseline to $n = 7$ (17.5%) at 12 weeks but increased again to $n = 12$ (30.0%) at 26 weeks (Table 4). The number of patients who used additional complementary medicine decreased from baseline to 26 weeks from $n = 12$ (30.0%) to $n = 8$ (20.0%). Additionally, the

Table 4. Number of patients using additional medical aid for the respective musculoskeletal pain disease

	Baseline (n = 40)*	At 12 weeks (n = 40)*	At 26 weeks (n = 40)*	At 52 weeks (n = 38)*
Patients taking analgesics (n = 40, last week)**	20 (50.0)	13 (32.5)	10 (25.0)	12 (31.6)
Ibuprofen	15 (37.5)	9 (22.5)	6 (15.0)	7 (18.4)
Diclofenac	4 (10.0)	3 (7.5)	4 (10.0)	2 (5.2)
Metamizol	4 (10.0)	4 (10.0)	2 (5.0)	2 (5.2)
Paracetamol	0	1 (2.5)	0	1 (2.6)
Flupirtin	1 (2.5)	0	0	0
Indometacin	0	0	0	1 (2.6)
Patients taking analgesics per diagnosis group				
Neck pain (n = 10)	5 (50.0)	5 (50.0)	5 (50.0)	5 (50.0)
Low back pain (n = 10, n = 9 after 52 weeks)	4 (40.0)	3 (30.0)	4 (40.0)	1 (11.1)
Shoulder pain (n = 10, n = 9 after 52 weeks)	8 (80.0)	5 (50.0)	1 (10.0)	3 (30.3)
Knee pain (n = 10)	3 (30.0)	0	1 (10.0)	3 (30.0)
Patients using non-drug therapy (last 4 weeks)**				
Use of physical therapy**	13 (32.5)	7 (17.5)	12 (30.0)	10 (26.3)
Physiotherapy	10 (25.0)	4 (10.0)	5 (12.5)	4 (10.5)
Exercise	0	0	0	2 (5.3)
Massage	3 (7.5)	4 (10.0)	4 (10.0)	2 (5.3)
Thermotherapy	6 (15.0)	4 (10.0)	5 (12.5)	4 (10.5)
Other	6 (15.0)	1 (2.5)	5 (12.5)	5 (13.2)
Use of complementary medicine**	12 (30.0)	10 (25.0)	8 (20.0)	10 (26.3)
Homeopathy	1 (2.5)	1 (2.5)	1 (2.5)	0
Autogenic training	0	0	0	2 (5.3)
Yoga	7 (17.5)	3 (7.5)	1 (2.5)	5 (13.2)
Ayurveda	0	1 (2.5)	0	0
Herbal therapy	1 (2.5)	1 (2.5)	0	1 (2.6)
Biofeedback	0	0	0	0
Bioresonance	0	0	0	0
Feldenkrais	0	0	0	1 (2.6)
Hypnotherapy	0	0	0	0
Meditation	4 (10.0)	0	1 (2.5)	2 (5.3)
Cupping	1 (2.5)	0	1 (2.5)	0
Sessions with a healer	1 (2.5)	0	0	0
Tai Qi	1 (2.5)	0	0	0
Other	6 (15.0)	4 (10.0)	5 (12.5)	5 (13.2)
Visiting a physician**	24 (60.0)	9 (22.5)	9 (22.5)	9 (23.7)
General practitioner	10 (25.0)	4 (10.0)	3 (7.5)	4 (10.5)
Rheumatologist	0	0	0	1 (2.6)
Orthopedic surgeon	12 (30.0)	5 (12.5)	6 (15.0)	7 (18.4)
Neurologist	3 (7.5)	1 (2.5)	1 (2.5)	0
Surgeon	2 (5.0)	0	0	0
Other physician	6 (15.0)	2 (5.0)	3 (7.5)	2 (5.3)
Visiting a complementary medicine provider**	4 (10.0)	4 (10.0)	4 (10.0)	6 (15.8)
Physician for homeopathy	1 (2.5)	1 (2.5)	1 (2.5)	0
Physician for anthroposophical medicine	0	0	0	0
Chinese medicine physician	1 (2.5)	2 (5.0)	0	2 (5.3)
Physician for naturopathy	0	0	1 (2.5)	0
Osteopath	1 (2.5)	0	1 (2.5)	3 (7.9)
Healing practitioner	2 (5.0)	0	0	1 (2.6)

Data are presented as n (%). * Percent are reported as valid percent. ** More than one answer possible.

number of patients visiting another physician decreased from n = 24 (60.0%) at baseline to n = 9 at 12, 26, and 52 weeks. The number of patients visiting a complementary medicine provider remained at n = 4 (10.0%) from baseline to 26 weeks and increased to n = 6 at 52 weeks.

Safety

No adverse events were observed.

Discussion

In this observational trial with follow-up, we observed beneficial changes along and after the OM treatment in addition to Germans' physician routine care in patients with CMPDs. Furthermore, in a homogeneous research environment, the course of 4 CMPDs during and after OM treatments could be followed across diagnoses. Six OM sessions were associated with a substantial clinical

improvement in pain intensity in patients with CMPD. Moreover, we observed clinically relevant disease-specific improvements in all CMPD groups except for the CKP group. Furthermore, we observed fewer restrictions in ADL, lower rate of use of analgesics and of additional therapies, and a clinically relevant improvement in the SF-12 PCS score but not in the SF-12 MCS score. Improvements with substantial clinical benefits were observed after only 3 OM treatments over 12 weeks, but additional benefits were observed after 26 weeks and 6 OM treatments. At 52 weeks, the improvements remained, including those in overall pain, the SF-12 PCS score, restrictions in ADL, and disease-specific parameters for CLBP, CSP, and CKP, but not CNP. No adverse events were reported after OM treatment. Apart from the reminders to return the questionnaires, the study was straightforward to conduct, and patients with CLBP and CNP appeared to be the easiest to recruit into the study. Furthermore, patients showed high study adherence.

The study observed beneficial changes after OM in addition to routine care in patients with CMPDs. These results are supported by those of an observational study [54] from the United States of America (USA) focusing on the outcomes per OM office visit. In the prospective part of the study (299 office visits), patients' perceptions of the symptoms after the treatment were assessed. Immediately after 92% of the office visits for OM, patients reported feeling better or much better, and after <2% of the office visits, they reported feeling worse; after 7 days (last follow-up), 72% of the patients reported feeling better or much better, and 6% reported feeling worse. The authors observed a short-term symptom relief after OM. Our study results included several validated patient-reported measurements and observed pain and functional improvements in patients with CMPDs. Furthermore, after 52 weeks, we found indications for lasting improvements. For future research, long-term follow-ups should be considered. Further, the inclusion of patients with different CMPD provides the opportunity to compare the symptom development of patients with different diagnoses under OM treatment. We must be aware that the mode of application of OM might differ across settings in Germany and the USA in accordance with the different training systems. For future comparisons of study results between the two countries, uniform OM definitions and standards are indispensable.

Though we observed improvements in CMPDs, there is some conflicting evidence regarding OM for CMPDs. A systematic review [55] investigated OM for various types of musculoskeletal pain and found no convincing evidence that it is effective. A more recent meta-analysis [56] that included 19 RCTs found some evidence suggesting that OM may be effective in treating patients suffering from neck pain and low back pain. Regarding CNP, a meta-analysis [21] that included 3 RCTs (n = 123 patients) found moderate-quality evidence for significant and clinically relevant effectiveness of OM in relieving pain, as measured by a 100-point scale (mean difference –13.04 [95% CI –20.64 to –5.44]). A more recent RCT [57] reported that OM might be effective in reducing pain intensity in adult violinists and violists with CNP. For CLBP, a meta-analysis [21] that investigated the effectiveness of OM found moderate-quality evidence for a significant intergroup difference in favor of OM regarding pain, as measured by a 100-point scale (–14.93 [95% CI –25.18 to –4.68]) based on 7 studies (n = 769 patients), and functional status, as measured using the standard mean difference in a random-effects model (mean difference, –0.32 [95% CI –0.58 to –0.07]) based on 7 studies (n = 771 patients). The results of a recent meta-analysis [23] strengthen the evidence, and OM was more effective than control interventions in pain reduction (effect size –0.59 [95% CI –0.81 to –0.36], $p < 0.001$) and in improving functional status (effect size –0.42 [–0.68 to –0.15], $p = 0.002$). Further, two RCTs investigated OM in patients with CLBP. One RCT [58] (n = 66) compared 5 OM and 5 sham OM interventions and found a clinically relevant improvement in pain and function between groups, in favor of OM. Another RCT [59] (n = 39) investigated two different OM approaches in 10 sessions in addition to exercise and found improvements in pain, function, and general health in both groups.

To further interpret our results, we used the MCID and SCB with respect to baseline. For pain, after 26 weeks, we observed an SCB in the whole population and in each of the four CMPD groups for pain. For the NDI, we considered the MCID to be 3.0 points, as described previously [31]. Using this value, we observed an MCID after 12 and 26 weeks, but we have to consider that slightly older publications report a larger range of MCID for the NDI, varying between 3.5 and 9.5 points (scores ranging from 0 to 50) [60, 61]. On the basis of these references, we would not have observed an MCID in CNP. The same is true for the MCID of the low back pain rating scale, which we considered to have an MCID of 1.2 points [40], although another paper reported the overall MCID to be 6 points [62]. Furthermore, we considered the MCID for the DASH total score (range 0–100) to be 8 points [43]. This MCID was calculated [43] using data from a prospective cohort study conducted by a multicenter collaborative study group, the Surgery of the Ulnar Nerve group, including 38 patients (mean age 49.3 years, range 23–70 years), in the USA. However, a more recent publication reported the MCID to be 25.41 points on the same scale in a convenience sample of 200 younger patients (mean age 39.4 ± 12.6) recruited from 3 outpatient physiotherapy clinics located in Iran [63]. However, the patient characteristics, especially the age of the population,

in the first mentioned study [43] more closely resemble those of our study population.

In our study, no adverse events were reported in the 40 patients. However, the study population was too small to draw conclusions for treatment safety. In the United Kingdom, in private OM practices, a total of 1,630 complete datasets were collected [19]. Osteopaths performed OM treatments in addition to other treatments, including counselling, acupuncture and electrotherapy. In n = 969 (54%) patients, no adverse events after first treatment were experienced; in n = 1,260 (77%), no adverse events were observed after subsequent treatments. The authors stated that the treatment provided was safe and did not yield severe or moderately severe adverse events. A recent OM study in the USA [64] that recorded adverse events at 1,847 office visits in 884 patients (75% female, mean age 51.8 ± 15.8 years) found the incidence rate for adverse events to be 2.5% (95% CI 1.3–4.7%). The most common adverse event was pain/discomfort, with an incidence of 0.9% (0.5–1.6%). Within our study population (n = 40), this incidence suggests that one patient may have experienced an adverse event. An explanation for no adverse events being reported in this study might be that although the study physician asked patients about adverse events at each treatment session (as performed in routine care) and patients were encouraged to contact the study center if they experience adverse events, we did not provide a diary for the documentation of adverse events. For future research, patients should be provided with diaries to document adverse events in a timely manner. Adverse events, especially severe adverse events, might seldom occur in patients treated with OM. Therefore, to further investigate adverse events related to OM, we advise designing larger and multicenter studies.

The main strength of this trial is that we conducted the study in a university research environment. To the best of our knowledge, this is the first European OM study in patients with CMPDs conducted in a university research environment following the quality standards of the Declaration of Helsinki [65] and the ICH-GCP guidelines, including prospective trial registration and ethics approval. Another strength is the long follow-up of 52 weeks during which long-term changes in patients with CMPDs were observed. OM treatment was performed by a well-trained provider, an osteopath who was also an orthopedic physician, with the individualized diagnosis-related osteopathic treatment method that is typically used.

However, the study has various limitations. First, the study observed only a small number of patients in total and per diagnosis group. Furthermore, this study was a single-center study recruiting at one university and involving only one provider with good but very specific training, clearly limiting the generalizability of our results. In addition, it applied only subjective outcome parameters. However, we used a variety of standardized and validated patient-reported outcome measures. Another limitation is the study design. The absence of a control group follows the empirical approach of health care providers in routine care but limits the interpretation of the observed changes. The reported improvements may have been caused by known study effects, including observer effects [66, 67] and regression to the mean. Such study effects impact the results less in studies including a control group, and interventional trials like RCTs. However, this study was designed to observe changes along and after the OM treatment in addition to routine care. Furthermore, prior to the study, we empirically observed that patients seeking OM in addition to routine care often have a strong desire to undergo the desired treatment within a reasonable timeframe. By omitting an observed control group, we could immediately include all interested patients and provide them with OM treatment. Overall, the observed changes have to be interpreted with caution, and the results reported here have to be validated in RCTs.

The effectiveness of OM in the treatment of CMPDs should be further investigated in studies such as larger high-quality RCTs because it might be an effective and safe nonpharmacological treatment option. This is especially important because adverse events in analgesics include gastrointestinal bleeding, drug-induced headache [14, 15], and other severe adverse events caused by opioids [16].

The results presented here provide data for sample size calculations for future OM RCTs. Future studies should investigate the effectiveness and efficacy of OM in RCTs by investigating specific therapeutic effects of OM in comparison with a sham procedure and other effective therapeutic methods. Sham procedures should simulate OM diagnostics and therapies [68], or include single sham techniques that are compared with verum techniques [69]. However, a systematic review [70] comparing sham procedures with OM showed that 43 studies used very heterogeneously different types of manual sham procedures and provided little information about their application. The authors emphasized the need for guidelines to design sham procedures [70]. In our opinion, sham OM should simulate OM diagnostic and therapeutic procedures in studies investigating the specific therapeutic effects of OM. Regarding the comparison of OM with other effective therapy methods, these therapies could include single therapies, such as physiotherapy and analgesic intake, or could include multimodal therapeutic approaches. The blinding of study participants, outcome assessors, and statisticians should be considered in future trials, although blinding might not be necessary, as recently discussed [71]. Future trials conducted on OM should include multiple centers to investigate the external validity and transferability of our results. Adverse events should be reported by patients in diaries.

Conclusion

We observed beneficial changes along and after the OM treatment in addition to routine care in patients with four CMPDs. Moreover, the observational study was straightforward to conduct. Given the high rate of use of OM in CMPD patients, high-quality multicenter clinical RCTs are urgently needed. The data provided in this study are sufficient for sample size calculations.

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Statement of Ethics

The study was approved by the Ethics Committee, Charité – Universitätsmedizin Berlin (approval number EA1/068/15, no addendums, the study was performed without any changes during the trial). All patients gave oral and written informed consent before inclusion in the study. This study (German Clinical Trials Register DRKS00008319, Universal Trial Number, UTN: U1111-1169-9945) followed the standards of the Declaration of Helsinki [65] and the ICH-GCP guidelines. The study was an investigator-initiated trial with no external funding sources.

Conflict of Interest Statement

Gabriele Rotter receives irregular lecture fees for teaching osteopathic medicine and musicians' medicine. She is a board member of the European Register for Osteopathic Physicians (EROP). The other authors do not have any conflicts of interest regarding this study.

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Author Contributions

G.R. conceived, coordinated, and carried out the study, interpreted the data, and drafted the manuscript. S.B. managed the data, carried out the statistical analyses, interpreted the data, and revised the manuscript. T.T.-D. revised and carried out the statistical analyses and revised the manuscript. M.O. helped design the study and revised the manuscript. B.B. helped design the study and methodology, contributed to the interpretation of the data, and revised the manuscript. All authors have read and approved the final version of the manuscript and agree with the order in which the authors are listed.

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2.3 Effectiveness and Cost-Effectiveness of Tuina for Chronic Neck Pain: A Randomized Controlled Trial Comparing Tuina with a No-Intervention Waiting List

Pach D, Piper M, Lotz F, Reinhold T, Dombrowski M, Chang Y, Liu B, Blödt S, **Rotter G**, Icke K, Witt CM. Effectiveness and Cost-Effectiveness of Tuina for Chronic Neck Pain: A Randomized Controlled Trial Comparing Tuina with a No-Intervention Waiting List. Journal of alternative and complementary medicine (New York, N.Y.). Mar 2018;24(3):231-237. DOI: 10.1089/acm.2017.0209.

Der nachfolgende Text basiert auf dem Abstrakt und dem Inhalt des Artikels, übersetzt durch die Autorin:

Patienten und Patientinnen mit CNP wenden häufig körperbasierte Behandlungsansätze aus der Chinesischen Medizin wie zum Beispiel Tuina an. Die wissenschaftliche Evidenz zur Wirksamkeit, Sicherheit und Kosteneffektivität bei Patientinnen und Patienten mit CNP ist sehr gering.

Ziel der monozentrischen zweiarmigen randomisiert kontrollierten klinischen Studie bei Patienten und Patientinnen mit CNP war die Untersuchung der Wirksamkeit, Sicherheit und Kosteneffektivität von Tuina im im Vergleich zu keiner studienspezifischen Intervention. Erwachsene mit einer in den letzten sieben Tagen subjektiv empfundenen mittleren Schmerzintensität von mehr als 40 mm auf einer VAS (0-100 mm) erhielten entweder sechs Sitzungen mit Tuina innerhalb von drei Wochen oder zunächst keine Tuina. Teilnehmende beider Gruppen konnten zusätzliche Therapien weiterführen. Der primäre Endpunkt war die in den letzten sieben Tagen subjektiv empfundene mittlere Intensität der HWS-Schmerzen gemessen an einer horizontalen VAS (0-100 mm) nach vier Wochen. Sekundäre Endpunkte beinhalteten Funktionsbeeinträchtigung durch HWS-Schmerzen gemessen an dem NDI (0-100%). Die statistische Analyse beinhaltete die ANCOVA, adjustiert für den jeweiligen Baselinewert. Weiterhin wurden gesundheitsökonomische Analysen durchgeführt. Die 92 Teilnehmenden waren im Alter von (MW ± SD) 45,4 ± 9,7 Jahren, 87% von Ihnen waren Frauen. Die Tuina-Behandlung war mit einer klinisch relevanten und statistisch signifikanten Schmerzreduktion im Vergleich zur Kontrollgruppe nach vier Wochen assoziiert, MD (95% KI) -22,8 mm (-31,7; -13,8), $p < 0.001$. Zusätzlich fanden sich Hinweise auf eine Verminderung der Funktionsbeeinträchtigung durch HWS-Schmerzen. SUEs traten nicht auf. Es konnten keine Gruppenunterschiede hinsichtlich der qualitätsadjustierten Lebensjahre oder der Kosteneffektivität ermittelt werden.

Zusammenfassend deuten die Studienergebnisse darauf hin, dass sechs Tuina-Sitzungen über drei Wochen bei Erwachsenen mit CNP die Schmerzintensität wirksam reduzieren kann.

Pach D, Piper M, Lotz F, Reinhold T, Dombrowski M, Chang Y, Liu B, Blödt S, **Rotter G**, Icke K, Witt CM. Effectiveness and Cost-Effectiveness of Tuina for Chronic Neck Pain: A Randomized Controlled Trial Comparing Tuina with a No-Intervention Waiting List. Journal of alternative and complementary medicine (New York, N.Y.). Mar 2018;24(3):231-237. DOI: https://doi.org/10.1089/acm.2017.0209.

2.4 Pulsatile dry cupping in chronic low back pain - a randomized three-armed controlled clinical trial

Teut M, Ullmann A, Ortiz M, **Rotter G**, Binting S, Cree M, Lotz F, Roll S, Brinkhaus B. Pulsatile dry cupping in chronic low back pain - a randomized three-armed controlled clinical trial. BMC Complement Altern Med. Apr 2 2018;18(1):115. DOI: 10.1186/s12906-018-2187-8.

Der nachfolgende Text basiert auf dem Abstrakt und dem Inhalt des Artikels, übersetzt durch die Autorin:

Schröpfen wird traditionell in Asien, im Nahen Osten und der europäischen Medizin genutzt. Trotz dieser Verbreitung ist die wissenschaftliche Evidenz von Schröpfen noch unzureichend.

Ziel war die Untersuchung der Wirksamkeit von Schröpfen bei Patientinnen und Patienten mit chronischen muskuloskelettalen Schmerzen. Hierzu wurde eine monozentrische dreiarmige randomisiert kontrollierte Studie durchgeführt. Die Studie untersuchte bei Erwachsenen mit CLBP die Wirksamkeit und Sicherheit von zwei verschiedenen Formen des trockenen, pulsierenden Schröpfens im Vergleich zu einer reinen Bedarfsmedikation. Eingeschlossen wurden Teilnehmende mit CLBP von einer in den letzten sieben Tagen subjektiv empfundenen mittlere Schmerzintensität von mehr als 40 mm auf einer VAS (0-100 mm). Innerhalb von vier Wochen erhielten die Teilnehmenden entweder acht Behandlungen eines regulär dosierten pulsierendes Schröpfens, acht Behandlungen eines minimal dosierten Schröpfens oder kein Schröpfen. Weiterhin erhielten alle Teilnehmenden eine Bedarfsmedikation mit Paracetamol. Der primäre Endpunkt war die in den letzten sieben Tagen subjektiv empfundene mittlere Intensität der LWS-Schmerzen gemessen auf einer horizontalen VAS (0-100 mm) nach vier Wochen. Sekundäre Endpunkte beinhalteten die Schmerzintensität auf einer VAS nach 12 Wochen und die Rückenfunktion, gemessen mit dem Funktionsfragebogen Hannover Rücken (FFbH-R) nach vier und 12 Wochen. Die statistische Analyse beinhaltete die ANCOVA, adjustiert für den jeweiligen Baselinewert. Zu Baseline betrug das mittlere Alter in der Gruppe pulsierendes Schröpfen (n = 37, MW ± SD) 49,0 ± 13,7 Jahre, 43,2% männlich, in der Gruppe minimales Schröpfen (n = 36) 47,5 ± 13,8 Jahre, 36,1% männlich, und in der Kontrollgruppe (n = 37) 50,7 ± 10,7 Jahre, 32,4% männlich. Für den primären Endpunkt fand sich nach vier Wochen eine statistisch signifikante Schmerzreduktion im Gruppenvergleich zwischen dem pulsierenden Schröpfen und der Kontrolle (MD (95% KI) -21,2 mm (-12,2; -30,1), $p < 0,001$) als auch zwischen dem minimalen Schröpfen und der Kontrolle (MD (95% KI) -15,7 mm (-6,9; -24,4), $p = 0,001$). Es bestand kein signifikanter Unterschied zwischen den beiden Formen des Schröpfens (MD 95% KI) 5,5 mm (-3,5; 14.5), $p = 0,225$). Zugunsten des pulsierenden Schröpfens, jedoch nicht des minimalen Schröpfens, fanden sich im Vergleich zur Kontrolle in den sekundären Endpunkten Hinweise auf eine verbesserte Rückenfunktion. SUEs traten nicht auf.

Zusammenfassend waren beide Formen des Schröpfens bei Patienten und Patientinnen mit CLBP wirksam, ohne im direkten Vergleich nach vier Wochen signifikante Unterschiede zu zeigen.

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RESEARCH ARTICLE Open Access

Pulsatile dry cupping in chronic low back pain – a randomized three-armed controlled clinical trial

M. Teut*†, A. Ullmann†, M. Ortiz, G. Rotter, S. Binting, M. Cree, F. Lotz, S. Roll and B. Brinkhaus

Abstract

Background: We aimed to investigate the effectiveness of two different forms of dry pulsatile cupping in patients with chronic low back pain (cLBP) compared to medication on demand only in a three-armed randomized trial.

Methods: 110 cLBP patients were randomized to regular pulsatile cupping with 8 treatments plus paracetamol on demand ($n = 37$), minimal cupping with 8 treatments plus paracetamol on demand ($n = 36$) or the control group with paracetamol on demand only (n = 37). Primary outcome was the pain intensity on a visual analogue scale (VAS, 0–100 mm) after 4 weeks, secondary outcome parameter included VAS pain intensity after 12 weeks, back function as measured with the 'Funktionsfragebogen Hannover Rücken' (FFbH-R) and health related quality of life questionnaire Short form 36 (SF-36) after 4 and 12 weeks.

Results: The mean baseline-adjusted VAS after 4 weeks was 34.9 mm (95% CI: 28.7; 41.2) for pulsatile cupping, 40.4 (34.2; 46.7) for minimal cupping and 56.1 (49.8; 62.4) for control group, resulting in statistically significant differences between pulsatile cupping vs. control (21.2 (12.2; 30.1); $p < 0.001$) and minimal cupping vs. control (15.7 (6.9; 24.4); $p = 0.001$). After 12 weeks, mean adjusted VAS difference between pulsatile cupping vs. control was 15.1 ((3.1; 27.1); $p = 0.014$), and between minimal cupping vs. control 11.5 ((− 0.44; 23.4); $p = 0.059$). Differences of VAS between pulsatile cupping and minimal cupping showed no significant differences after 4 or 12 weeks. Pulsatile cupping was also better (− 5.8 (− 11.5;-0.1); $p = 0.045$) compared to control for back function after 4 weeks, but not after 12 weeks (− 5.4 (− 11.7;0.8); $p = 0.088$), pulsatile cupping also showed better improvements on SF-36 physical component scale compared to control at 4 and 12 weeks (− 5.6 (− 9.3;-2.0); $p = 0.003$; − 6.1 (− 9.9;-2.4); $p = 0.002$). For back function and quality of life minimal cupping group was not statistically different to control after 4 and 12 weeks. Paracetamol intake did not differ between the groups (cupping vs. control (7.3 (− 0.4;15.0); $p = 0.063$); minimal cupping vs. control (6.3 (− 2.0;14.5); $p = 0.133$).

Conclusions: Both forms of cupping were effective in cLBP without showing significant differences in direct comparison after four weeks, only pulsatile cupping showed effects compared to control after 12 weeks.

Trial registration: The study was registered at ClinicalTrials.gov (identifier: NCT02090686).

Keywords: Cupping, Pulsatile cupping, Minimal cupping, Low back pain, Chronic low back pain, RCT

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Background

Back pain is a very common complaint in Germany; the 12-month prevalence was reported to be 66% in women and 58% in men [1], the 1-day prevalence between 32 and 49% [2], and the prevalence over lifetime between 74 and 85% [3]. Between 5 and 10% of all patients with low back pain will develop chronic low back pain (cLBP), accompanied by high treatment costs, sick leave, and individual suffering. Low back pain is one of the main reasons that people seek health care services [4]. The prevalence increases from the third decade of life until 60 years of age and it is more prevalent in women [4]. The Global Burden of Disease 2010 study showed that globally low back pain causes more disability than any other condition, the global point prevalence was 9.4% (95% CI 9.0 to 9.8) [5].

Pharmacological treatments alone do often not lead to sufficient clinical responses, and the use of non-steroidal anti-inflammatory drugs (NSAIDs, in particular) may lead to negative side effects such as gastrointestinal or renal complications. The German National Disease Management Guideline 'Low Back Pain' recommends patient education, physical activity, relaxation therapy, behavioural therapy, and occupational therapy as interventions [4]. However, not all cLBP patients can be treated sufficiently and often continue to have clinically relevant symptoms. Therefore, cLPB patients often use complementary and integrative medicine (CIM) therapies like acupuncture, manual therapy, or cupping, but the effectiveness of many CIM treatments is unclear.

One of the oldest traditional therapies worldwide, and especially in the Asian, Middle-East and European medical traditions, cupping is very often used to treat musculoskeletal diseases [6, 7]. Cupping is based on a sucking traction of the skin: a cupping glass is applied to a predefined skin area and a negative pressure (compared to atmospheric pressure) is generated mechanically (pumping) or thermally (cooling heated air) withdrawing the trapped air from under the cup [7, 8]. This results in reddening and warming of the affected skin area due to increased perfusion. In "dry cupping", a negative pressure is applied, whereas in "wet cupping" the skin under the cup is pricked with a needle and the cupping is accompanied by bleeding. A modern technology is pulsatile cupping, in which a mechanical device generates a pulsatile negative pressure with a pump [8].

Huang et al. recently investigated the effectiveness of cupping in treating low back pain in a systematic review [9]. They identified only one randomized controlled trial (RCT) (10), six non-RCTs, 20 case reports, and two other studies, concluding that cupping "is promising for pain control and improvement of quality of life, and minimises the potential risks of pharmaceutical treatments but that further studies are needed to determine the potential role of cupping therapy in the treatment of low back pain."

Recently Wang et al. [10] published a meta-analysis on cupping in low back pain. They were able to include six RCTs and showed that cupping therapy was superior to the control therapies regarding Visual Aanalogue Scale scores (SMD: − 0.73, [95% CI: -1.42 to − 0.04]; $P = 0.04$), and ODI scores (SMD: − 3.64, [95% CI: -5.85 to − 1.42]; $P = 0.001$), but a high level heterogeneity and risk of bias limited the validity of the findings. Cupping for low back pain is also discussed in other up to date reviews [11–13].

To date, no clinical studies have been published about the effectiveness of dry cupping and especially pulsatile cupping in cLBP. The aim of our study was to investigate the effectiveness of dry pulsatile cupping in reducing pain and improving back function and quality of life in patients with nonspecific cLBP. We were additionally interested in the relationship between the strength of the applied pressure and outcomes, and whether a dose-response-relationship could be observed. We therefore designed a three-armed, randomized controlled trial comparing i) strong negative pressure pulsatile cupping plus paracetamol on demand (pulsatile cupping) vs. paracetamol on demand only (control, no cupping), and ii) weak negative pressure cupping plus paracetamol on demand (minimal cupping) vs. paracetamol on demand only (control, no cupping).

Methods

Design

This study was designed as a three-armed, parallel, participant blinded monocenter randomized controlled clinical trial. All study participants gave written informed consent before inclusion. The study was performed at the Charité Universitätsmedizin in Berlin, Germany, between March 2014 and February 2015. Patients who fulfilled the prescreening criteria were invited to meet the study physician for further information, at which time informed consent was obtained, inclusion and exclusion criteria were checked, and enrolled patients received a baseline assessment. The allocation to the three treatment groups followed a 1:1:1 block randomization process with a variable block length and was performed by a study nurse not being included in the recruitment by telephone. The randomization sequence was generated by SAS 9.2 Software (SAS Institute Inc. Cary. NC, USA). Allocation to treatment was concealed.

Patients

Participants were recruited through newspaper advertisements, the website of the outpatient department for integrative medicine, and the central email newsletter of the department. Interested patients were informed about the study, and an experienced study nurse pre-screened them on the phone for inclusion.

Inclusion criteria were patients of both gender of 18–65 years with the clinical diagnosis of nonspecific cLBP,

defined as pain duration of at least 3 months and an absence of specific pathological neurological symptoms. Further inclusion criteria were self-assessed subjective pain intensity ≥40 mm on the Visual Analogue Scale (0–100 mm; VAS) for the previous week, pharmacological treatment only with NSAIDs or no treatment in the last 4 weeks, and a signed informed consent. Exclusion criteria were the use of anticoagulants (e.g. Phenprocoumon, Heparin, Apixaban), a known coagulopathy, cupping treatments within the last 6 weeks, other complementary medicine therapies in the last 12 weeks (e.g. acupuncture, osteopathy), physical therapy in the last 12 weeks (including e.g. massage, chirotherapy), participation in another study in the last 3 months, allergy to or intolerance of paracetamol, pathological neurological symptoms such as muscular paralysis or paresthesia due to spinal disc herniation or other causes, known renal and / or hepatic diseases, intake of central nervous system-acting analgesics in the last 6 weeks (e.g. opioids), application for early retirement due to low back pain, and other severe disease states that disallow participation.

Study interventions

The study protocol was developed by an expert panel experienced in cupping patients with LBP.

Participants randomized to the pulsatile cupping group received 8 cupping sessions (each 8 min) in 4 weeks with a HeVaTech PST 30 pulsatile cupping device and a negative pressure between − 150 to − 350 mbar) and suction intervals of 2 s (see Fig. 1). In addition, paracetamol (maximum dosage 4 × 500 mg/day) on demand as rescue medication was allowed. Figure 1 shows both silicone cups being applied to the low back area.

Participants randomized to the minimal cupping group received 8 cupping sessions (each 8 min) in 4 weeks with a HeVaTech PST 30 pulsatile cupping device, also with two silicone cups and a weaker negative pressure around -70 mbar and suction intervals of 2 s. In addition, paracetamol (maximum dosage 4 × 500 mg/day) on demand as rescue medication was allowed.

Fig. 1 Application of the silicone cups at the low back area

Participants randomized to the control group received no cupping intervention in the study period of 12 weeks, but were allowed to treat their back pain complaints with paracetamol (maximum dosage 4 × 500 mg/day) on demand. All patients in the control group were offered a cost-free cupping intervention after completing the trial after 12 weeks.

Specially trained medical doctors, nurses, and/or medical students applied the cupping treatments. Patients of both cupping groups were blinded to their study intervention.

Outcome parameters

Patients completed standardized questionnaires measuring outcomes at baseline, and after 4 and 12 weeks. The primary outcome parameter was the mean of the subjective pain intensity during the week prior to treatment and again after 4 weeks, using the Visual Analogue Scale (VAS, 0–100 mm; 0 = no pain, 100 mm = maximum intensity) [14]. Secondary parameters included the last week's pain intensity on the VAS after 12 weeks, the back function measured with the 'Funktionsfragebogen Hannover Rücken' (FFbH-R) [15] at 4 and 12 weeks, the health-related quality of life measured with the SF-36 questionnaire [16] at 4 and 12 weeks, the perceived effect measured with a 5-point Likert scale after 4 and 12 weeks, the intake of paracetamol within the 4 weeks intervention or waiting period (diary) and adverse events across the whole study period of 12 weeks. We also assessed patient perception about their group allocation.

Statistical analysis

The sample size calculation was performed for the primary comparison between the cupping and the control group. An adjusted difference of 15 mm on the VAS after 4 weeks with a common standard deviation of 20 mm, given a significance level of $\alpha = 0.05$, was assumed for a two-sided t-test. Based on these assumptions and a power of 85%, 33 patients per group were needed. To compensate for drop-outs, a total of 36 patients per group were included and randomized. Sample size calculation was done with nQuery Advisor 6.02.

The statistical analysis was performed using the software package SAS release 9.3 / 9.4 (SAS Institute Inc., Cary, NC, USA) and IBM SPSS Statistics Version 23. The analysis of the primary outcome was calculated using an analysis of covariance (ANCOVA) with the fixed factor treatment group adjusted for baseline value of VAS pain intensity (covariate). To adjust for three group comparisons, a hierarchical testing procedure with three steps was performed, ensuring an overall significance level of $\alpha = 0.05$ (two-sided). The first step was the comparison between the cupping and the control group. In case of a significant

difference, the next step was performed confirmatively; otherwise, all following steps were explorative. The second step was the comparison between the minimal cupping and the control group. Again, in the case of a significant difference the next step was confirmative, otherwise, the following step was considered explorative. The third step was the comparison between the cupping and the minimal cupping groups.

All following analyses were explorative. The analyses of the secondary endpoints and the secondary analyses of the primary endpoint were performed with a similar model, depending on the distribution and the scale of the variables, but without the hierarchical procedure.

Results were reported as adjusted means with 95% confidence intervals and the p value for the group comparison. All tests and confidence intervals were two-sided. All data were analyzed based on the intention-to-treat-principle (ITT) using the full analysis set (FAS) with all available data without imputing for missing values.

Adverse events are presented descriptively by frequency for each treatment group.

Results

Patients were recruited between March and September 2014. Study interventions and follow-up assessments were completed by February 2015. Figure 2 shows the recruitment and allocation process.

In total, 396 patients were screened for eligibility; 286 were excluded for not meeting the inclusion criteria (n = 160) or refusing to participate after being informed about the trial (n = 126). Altogether 110 patients were randomized and allocated to pulsatile cupping (n = 37), minimal cupping (n = 36), or control (n = 37). After 12 weeks, 11 patients (pulsatile cupping n = 4, minimal cupping n = 4, control n = 3) had dropped out of the trial. The main reasons for withdrawal from the study were identified as "personal" (n = 6). Other reasons for drop-outs were health problems (n = 3) and non-compliance (n = 2). Three patients discontinued the intervention because of health problems (cupping n = 1, minimal cupping n = 1) or for personal reasons (minimal cupping n = 1). The VAS data for 6 patients in the control group after 4 weeks were missing.

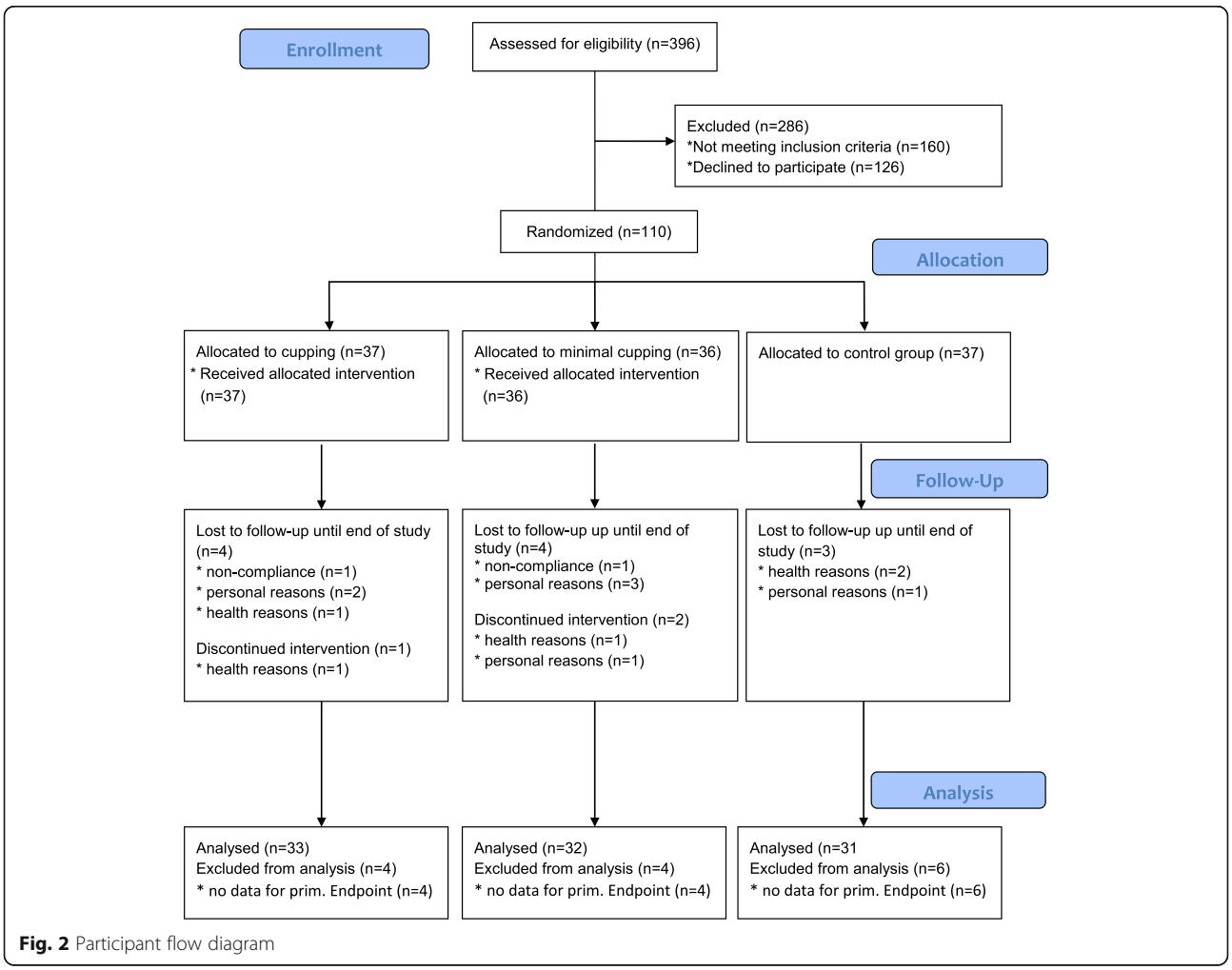

Fig. 2 Participant flow diagram

91.4% of the cupping group and 88.2% of the minimal cupping group had 8 cupping sessions as asked by the study protocol.

The mean age of patients was 49 years (pulsatile cupping group: 49 years, minimal cupping group: 48, control group: 51) at baseline (see Table 1); the mean Body Mass Indexes scored between 25 and 26 kg/m^2 (Table 1). There were more males in the pulsatile cupping group (43.2%) compared to minimal cupping (36.1%) and control (32.4%). The pain intensity measure by the VAS was higher in the minimal cupping 60.3 ± 12.3 and in the control group 59.9 ± 12.8 compared with the pulsatile cupping group (53.2 ± 7.4).

The mean adjusted VAS pain intensity after 4 weeks was 34.9 mm (95% CI: 28.7; 41.2) for the pulsatile cupping group, 40.4 (34.2; 46.7) for minimal cupping, and 56.1 (49.8; 62.4) for control (see Table 2 and Fig. 3), resulting in statistically significant differences between pulsatile cupping vs. control (21.2 (12.2;30.1), $p < 0.001$) and minimal cupping vs. control (15.7 (6.9;24.4), $p = 0.001$) (Table 2, Fig. 3).

After 12 weeks, mean adjusted VAS pain intensity was lower for pulsatile cupping vs. control (15.1 (3.1;27.1), $p = 0.014$), but not for minimal cupping vs. control (11.5 (− 0.44;23.4), $p = 0.059$). The group differences of pain intensity between minimal cupping and pulsatile cupping showed no significant differences after 4 and 12 weeks (VAS adjusted mean: 5.5 (− 3.5; 14.5); $p = 0.225$) and 12 weeks (3.7 (− 8.6;15.9); $p = 0.554$). (Table 3, Fig. 3).

The FFbH-R back function of the pulsatile cupping group showed better effects than control after 4 weeks, but not after 12 weeks; the minimal cupping group was not statistically different to control after 4 and 12 weeks. The pulsatile cupping group also showed improvements on the SF-36 Physical Component Summary compared to control at 4 and 12 weeks, but not in the comparisons between minimal cupping vs. control. Also, several SF-36 sub-scores showed improvements after 4 and 12 weeks in favour of pulsatile cupping, but not of minimal cupping compared to control (e.g., bodily pain, SF-36 physical role and vitality, SF-36 General Health Perception). No differences between groups were observed for the SF-36 Mental Component Summary after 4 and 12 weeks.

Paracetamol intake did not differ between the groups (cupping vs. control (7.3 (− 0.4;15.0); $p = 0.063$); minimal cupping vs. control (6.3 (− 2.0;14.5); $p = 0.133$) (Table 2).

After four weeks, 42% of the pulsatile cupping group and 44% of the minimal cupping group rated the cupping therapy as effective on the Likert Scale, whereas around 30% in both groups said that the cupping therapy was less effective. That assessment of treatment effect remained nearly the same after 12 weeks. Most of the participants in the minimal cupping group (84%) were able to identify their group allocation after 4 weeks, whereas in the cupping cupping group 55% identified their group allocation.

No serious adverse events were observed during the whole study period. Moderate adverse events were observed in two patients in the pulsatile cupping group who reported an aggravation of their low back pain after the cupping sessions for a few hours. One of those patients dropped out of the therapy but not the study. Other reported side effects in a 24-h time interval after cupping included light muscular backache in six patients in the pulsatile cupping group, and in two patients in the minimal cupping group.

Discussion

Both forms of cupping were effective in reducing cLBP after 4 weeks compared to the control group that only

Table 1 Baseline characteristics of patients

	Cupping High pulsatile vacuum *n* = 37 Mean ± SD / n (%)	Minimal Cupping Low pulsatile vacuum *n* = 36 Mean ± SD / n (%)	Control n = 37 Mean ± SD / n (%)
Age [years]	49.0 ± 13.7	47.5 ± 13.8	50.7 ± 10.7
Gender (Male)	16 (43.2)	13 (36.1)	12 (32.4)
BMI	26.3 ± 4.3	25.0 ± 4.1	25.3 ± 4.7
Exercise (yes)	28 (75.7)	29 (80.6)	29 (78.4)
Duration of low back pain [years]	13.1 ± 9.3	15.8 ± 12.9	13.2 ± 11.2
Current drug intake because of low back pain	11 (29.7)	14 (38.9)	14 (37.8)
Current consultations because of low back pain	35 (94.6)	36 (100)	36 (97.3)
VAS pain intensity [mm][a]	53.2 ± 7.4	60.3 ± 12.3	59.9 ± 12.8
FFbH-R[b]	75.9 ± 16.3	72.2 ± 12.9	70.2 ± 18.7
SF-36			
Physical Component Summary[b]	39.1 ± 8.4	38.2 ± 6.6	38.6 ± 8.5
Mental Component Summary[b]	50.9 ± 10.4	50.2 ± 9.1	50.1 ± 10.0

[a]Lower values indicate better status, [b]higher values indicate better status

Table 2 Primary and secondary outcomes at week 4: group means and mean group differences with 95% confidence interval (CI), adjusted for respective baseline value

	Cupping ($n = 33$)	Minimal Cupping ($n = 32$)	Control ($n = 31$)	Control vs. Cupping		Control vs. Minimal Cupping		Minimal Cupping vs. Cupping	
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean difference (95% CI)	*p*-value	Mean difference (95% CI)	*p*-value	Mean difference (95% CI)	*p*-value
VAS pain intensity[a] (primary outcome)	34.9 (28.7;41.2)	40.4 (34.2; 46.7)	56.1 (49.8;62.4)	21.2 (12.2;30.1)	< 0.001	15.7 (6.9;24.4)	0.001	5.5 (−3.5; 14.5)	0.225
FFbH-R[b]	76.0 (72.1;80.0)	74.2 (70.2;78.2)	70.2 (66.1;74.3)	-5.8 (−11.5;-0.1)	0.045	−4.0 (−9.7;1.7)	0.171	−1.8 (−7.5;3.8)	0.517
SF-36[b]									
Physical Component Summary	43.8 (41.3;46.4)	39.5 (37.0;42.1)	38.2;(35.6;40.9)	−5.6 (−9.3;-2.0)	0.003	−1.3 (−5.0;2.4)	0.478	−4.3 (−7.9;-0.7)	0.021
Mental Component Summary	50.1 (47.0;53.2)	47.1 (44.0;50.3)	47.6 (44.4;50.8)	−2.5 (−6.9;2.0)	0.270	0.5 (−4.0;5.0)	0.820	−3.0 (−7.4;1.4)	0.179
SF-36 subscales[b]									
General health	63.2 (58.8;67.6)	55.2 (50.6;59.8)	56.8 (52.2;61.4)	−6.4 (−12.7;0.02)	0.051	1.7 (−4.9;8.2)	0.617	−8.0 (− 14.4;-1.6)	0.015
Mental health	70.8 (66.3;75.2)	66.2 (61.7;70.8)	65.8 (61.2;70.4)	−5.0 (− 11.4;1.5)	0.128	− 0.4 (−6.9;6.0)	0.897	−4.5 (−10.9;1.8)	0.160
Bodily pain	56.1 (50.8;61.4)	48.9 (43.5;54.3)	42.3 (36.9;47.8)	−13.7 (−21.4;-6.1)	0.001	−6.5 (− 14.2;1.1)	0.093	−7.2 (− 14.7;0.4)	0.063
Physical functioning	74.7 (68.4;81.0)	69.3 (62.9;75.7)	68.8 (62.3;75.2)	−6.0 (−15.0;3.1)	0.192	−0.6 (−9.7;8.6)	0.905	−5.4 (− 14.4;3.6)	0.234
Role: Emotional	79.3 (67.6;91.0)	69.2 (57.3;81.1)	70.1 (57.8;82.4)	−9.2 (−26.2;7.8)	0.284	0.9 (−16.2;18.0)	0.918	−10.1 (−26.8;6.6)	0.233
Role: Physical	68.0 (56.4;79.6)	48.6 (36.8;60.3)	45.3 (33.3;57.2)	−22.7 (−39.4;-6.1)	0.008	−3.3 (− 20.1;13.5)	0.699	−19.4 (− 35.9;-3.0)	0.021
Social functioning	79.8 (73.1;86.5)	69.1 (62.3;76.0)	72.4 (65.5;79.3)	−7.4 (−17.0;2.2)	0.131	3.3 (−6.5;13.0)	0.510	−10.6 (−20.2;-1.0)	0.03
Vitality	53.8 (49.4;58.2)	46.5 (42.1;50.9)	44.4 (39.9;48.9)	−9.3 (−15.6;-3.0)	0.004	−2.0 (−8.4;4.3)	0.526	−7.3 (−13.5;-1.1)	0.022
Pain rescue medication (count of pills, Paracetamol)	4.6 (−1.0;12.0)	5.6 (−0.7;12.0)	11.9 (6.7;17.1)	7.3 (−0.4;15.0)	0.063	6.3 (−2.0;14.5)	0.133	1.0 (−7.5;9.5)	0.814

[a]Lower values indicate better status, [b]higher values indicate better status

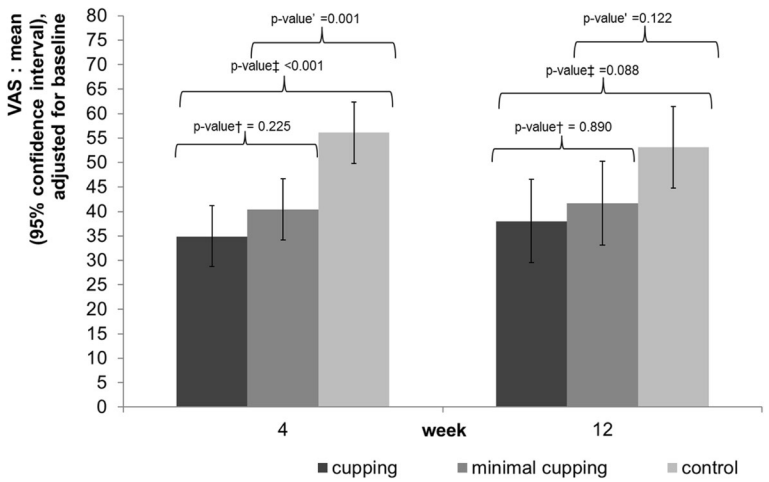

Fig. 3 Pain intensity measured by Visual Analogue Scale at 4 and 12 weeks. Legend Fig. 3: VAS, 0–100 mm; 0 = no pain, 100 mm = maximum intensity †low vacuum vs high vacuum, ‡ control vs high vacuum, 'control vs low vacuum

Table 3 Secondary outcomes at week 12: group means and mean group differences with 95% confidence interval (CI), adjusted for respective baseline value

	Cupping (n = 33)	Minimal Cupping (n = 32)	Control (n = 31)	Control vs. Cupping		Control vs. Minimal Cupping		Minimal Cupping vs. Cupping	
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean difference (95% CI)	*p*-value	Mean difference (95% CI)	*p*-value	Mean (95% CI)	*p*-value
VAS pain intensity[a]	38.0 (29.5;46.5)	41.7 (33.1;50.2)	53.1 (44.8;61.4)	15.1 (3.1;27.1)	0.014	11.5 (− 0.44;23.4)	0.059	3.7 (−8.6;15.9)	0.554
FFbH-R[b]	76.0 (71.6;80.4)	75.6 (71.1;80.1)	70.6 (66.2;75.0)	−5.4 (−11.7;0.8)	0.088	−5.0 (− 11.3;1.4)	0.122	−0.4 (−8.8;5.9)	0.890
SF-36[b]									
Physical Component Summary	44.9 (42.3;47.6)	41.1 (38.3;43.8)	38.8 (36.1;41.1)	−6.1 (−9.9;-2.4)	0.002	−2.3 (−6.1;1.5)	0.237	−3.8 (−7.7;-0.03)	0.048
Mental Component Summary	46.7 (43.2;50.1)	45.8 (42.2;49.3)	48.4 (45.0;51.8)	1.8 (−3.1;6.6)	0.477	2.6 (−2.3;7.6)	0.291	−0.9 (−5.8;4.0)	0.719
SF-36 subscales[b]									
General health	61.0 (56.5;65.5)	56.2 (51.5;60.9)	51.6 (47.1;56.1)	−9.4 (−15.8;-3.0)	0.004	−4.6 (−11.2;2.0)	0.167	−7.8 (− 11.3;1.8)	0.152
Mental health	68.6 (63.6;73.6)	64.8 (59.7;70.0)	67.4 (62.4;72.4)	−1.2 (−8.3;5.8)	0.732	2.4 (−4.6;9.7)	0.486	−3.7 (−10.9;3.4)	0.302
Bodily pain	58.1 (51.7;64.6)	48.9 (42.2;55.5)	46.0 (39.5;52.3)	−12.2 (−21.3;-3.1)	0.009	−2.9 (− 12.1;6.4)	0.539	−9.3 (− 18.5;-0.03)	0.049
Physical functioning	75.2 (68.3;82.1)	74.3 (67.2;81.4)	67.4 (60.5;74.3)	−7.8 (−17.5;1.9)	0.114	−6.9 (−16.9;3.0)	0.167	−0.9 (− 10.8;9.1)	0.863
Role: Emotional	69.0 (55.9;82.1)	68.5 (54.9;82.1)	73.0 (59.9;86.2)	4.1 (−14.5;22.6)	0.665	4.5 (−14.4;23.4)	0.634	−0.5 (−19.4;18.4)	0.959
Role: Physical	71.0 (58.8;83.3)	49.8 (37.2;62.5)	55.0 (42.7;67.2)	−16.1 (−33.4;1.3)	0.069	5.1 (−12.5;22.7)	0.563	−21.2 (− 38.8;-3.6)	0.019
Social functioning	75.0 (67.4;82.5)	70.4 (62.5;78.2)	74.7 (67.1;82.3)	−0.3 (−11.0;10.5)	0.960	4.3 (−6.7;15.4)	0.435	−4.6 (−15.5;6.3)	0.403
Vitality	50.9 (45.5;56.4)	47.8 (42.2;53.4)	46.8 (41.4;52.2)	−4.1 (−11.8;3.5)	0.286	−1.0 (−8.8;6.8)	0.799	−3.2 (− 10.9;4.6)	0.424

[a]Lower values indicate better status, [b]higher values indicate better status

took pain medication on demand. However, there were no significant differences between pulsatile cupping and minimal cupping after 4 weeks. After 12 weeks only the pulsatile cupping group showed effects compared to control in most of the outcome parameters. However, power and sample size calculations were based on the differences to the control group, not on changes between interventions. We also observed improvements in quality of life on the SF 36 Physical Component Summary in the pulsatile cupping group after 4 and 12 weeks. Those improvements can be mainly found in the bodily pain, physical role, general health perception, and vitality subscale aspects. After 12 weeks, differences were reported only for the aspects of general health perception and bodily pain.

To our knowledge, this was the first study that compared pulsatile cupping plus medication on demand and minimal cupping plus medication on demand with the control condition medication on demand only.

Strengths of the study were the inclusion of a control group to assess the overall effect of both forms of cupping and the strict randomization and allocation process.

A major limitation of our study, as in all other cupping studies, is the lack of blinding between cupping and control interventions, which may have had influence on the study results e.g. in better results of the verum treatment and worser results in the minimal cupping group. Patients sense the application of cups and also the generation of negative pressure involved. They do also have some sense of how strong the cupping pressure applied is. A sham cupping device would be highly useful to experimentally distinguish specific from nonspecific effects of cupping. Up to 2016, no trial on sham cupping was published [17]. Lauche et al. [18] introduced 2016 a sham cupping device consisting of conventional cupping glasses being fixed on the skin with elastic tape. The cups were prepared with small holes, through which the negative pressure was released during seconds after the

negative pressure was applied. This is a clever solution, but also this sham device relies on short period of cupping, as an application of negative pressure is involved. In our own preparation for this trial, we experimented with different systems and developed a special form of minimal cupping using a pulsatile cupping device and applied the weakest negative pressure being able to fix the silicone cups on the skin. However, our procedure yielded no sufficient blinding, especially in the minimal cupping group. Any minimal cupping procedure restricting cupping time or reducing the pressure involved may produce some specific effects and would therefore better be called "minimal cupping" instead of sham.

In our trial, the no cupping control group may be seen as a limitation, as no active intervention was undertaken. In our opinion, this limitation is debatable and ethically justifiable because all patients were allowed up to 2 g of paracetamol per day as pain medication on demand. In the waiting control there may have been an element of frustration of the participants about the allocation to no active intervention, which could have had a negative influence on the outcome assessments. We tried to minimize this possible element of bias by offering all control group patients a complete set of eight cost free cupping therapies after 12 weeks (after the end of the trial). However, theoretically, this potential bias could also explain differences between active therapy and control.

We based our sample size calculation on a small difference of 15 mm on the VAS because we assumed that this would make a clinically important change between both cupping groups compared to the control group. Based on our assumption, this would mean that there were clinically relevant changes for pulsatile cupping and minimal cupping after 4 weeks and for pulsatile cupping after 12 weeks. Other authors have described the minimal clinical important change of VAS in chronic low back pain higher around 20 mm [19, 20]. In this case, only pulsatile cupping would show a relevant improvement vs. control after 4 weeks, but not minimal cupping.

Only few studies have been published investigating the effects of cupping on low back pain: One RCT by Kim et al. [21] investigated the effectiveness of six wet cupping sessions compared to a no therapy (waiting list) control group in 32 Korean participants. Significant differences regarding pain intensity on the McGill Pain Questionnaire for pain intensity and reduction of acetaminophen intake were described after 2 weeks and 4 weeks, but there was no significant difference for pain intensity on a numeric rating scale and the Oswestry Disability Questionnaire.

Another RCT of Farhadi et al. (2009) [22] compared 3 sessions of wet (bloody) cupping in one week to usual care in 98 Iranian patients with nonspecific low back pain and observed significant group differences on the McGill Present Pain Index, the Owestry Pain Disability Index and on the Medication Quantification Scale after 3 months. Farhadi et al. included patients with a pain duration longer than 4 weeks, so their sample could have been different from ours. They also used a different (blood sucking) technique and used different areas of cupping.

The effects of both cupping interventions on VAS intensity of pain compared to waiting control group in our trial are very comparable to the effects we observed in a former trial of twelve sessions of acupuncture or minimal acupuncture compared to waiting control group in patients with chronic low back pain [23]. From the clinicians view dry cupping may be seen as a less invasive form of reflex therapy compared to acupuncture with needles. A mix of potential effectors of cupping was suggested by Musial et al. [24] who generally proposed three potential mechanisms of action for reflex therapies such as cupping: (1) pain reduction could be caused by deforming or even injuring the skin which may stimulate Aβ fibres in painful skin regions, (2) manipulations may stimulate inhibitory receptive fields of the multireceptive dorsal horn neurons, and (3) the setting may have a relaxing and socially comforting effect. Emerich et al. who did research on the local reactions in the cupped areas described a strong anaerob metabolism with high lactate concentrations in the regions being cupped [25]. Cupping induced a lasting anaerobe metabolism in the subcutaneous tissue and did increase immediate pressure pain thresholds in some areas.

Although we find evidence that cupping is effective in cLBP, our data does not allow conclusions about specific mechanisms or effectors of cupping. Also in the Lauche et al. trial, no specific effect of the verum cupping could be detected compared to the described sham cupping device in patients with chronic neck pain. The mechanism of cupping remains unclear, effects could as well be caused by unspecific effects and expectation, especially in a waiting group design trial. However, as dry cupping is a non-pharmacological and comparably safe therapy it may be of use in clinical care independent of mechanisms involved. Further research about mechanisms involved in cupping, specific effects but also real life effects in clinical care routine conditions are needed to further understand its mode of action and its usefulness.

Conclusion

Both forms of cupping were effective in patients with chronic low back pain after 4 weeks without showing significant differences in direct comparison. In addition, only pulsatile cupping showed effects compared to a non-treatment control in reducing pain after 12 weeks, but not minimal cupping.

Abbreviations
BMI: Body Mass Index; CIM: complementary and integrative medicine; cLBP: chronic low back pain; FAS: full analysis set; FFbH-R: Funktionsfragebogen Hannover zu Funktionsbeeinträchtigung durch Rückenschmerzen; ITT: intention-to-treat; NSAID: non-steroidal anti-inflammatory drugs; RCT: randomized controlled trial; SF-36: Short Form-36; VAS: Visual Analogue Scale

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Availability of data and materials
The datasets generated and analyzed during the current study are not publicly available as participants were not asked to provide consent regarding such use of their data.

Authors' contributions
Study concept and design: BB, MT, AU, SR. Data Management: SB, MC, AU. Interventions: AU, MC, MT, MT, MO, BB. Statistical analysis: FL, SR, SB, AU. Analyses and interpretation of data: MT, AU, BB, FL, SR, MO, GR, SB. Obtained funding: BB, MT. Drafting the manuscript: MT, AU, BB, SB, FL, SR. All authors read and approved the final manuscript.

Ethics approval and consent to participate
The Ethics Committee of Charité Universitätsmedizin Berlin reviewed the study protocol and approved the study (EA1/031/14; 20.02.2014). All participants gave written informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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2.5 Mindful walking in patients with chronic low back pain – a randomized controlled trial

Rotter G, Ortiz M, Binting S, Tomzik J, Reese F, Roll S, Brinkhaus B, Teut M. Mindful walking in patients with chronic low back pain – a randomized controlled trial. J Integr Complement Med. Jun 2022;28(6):474-483. DOI: 10.1089/jicm.2021.0361.

Der nachfolgende Text basiert auf dem Abstrakt und dem Inhalt des Artikels, übersetzt durch die Autorin:

In der Therapie chronischer muskuloskelettaler Schmerzen, insbesondere von CLBP, sind aktivierende körperbasierte Behandlungsansätze und das Erlernen von Selbstmanagementstrategien unter Einbeziehen psychologischer Therapieansätze von besonderer Bedeutung. Achtsamkeitsbasierte Interventionen wirken psychologisch und könnten bei bio-psychosozial beeinflussbaren Erkrankungen wie CLBP wirksam sein. Eine Kombination von niedrig intensiver Bewegung mit achtsamkeitsbasierten Übungen adressiert körperliche und psychische Faktoren. Die Entwicklung eines Programmes zum Mindful Walking könnte insbesondere für vielbeschäftigte Menschen eine wertvolle Therapieoption darstellen. Ein Therapieprogramm in einer Gruppe könnte therapeutisch Gruppeneffekte nutzen, hierbei die Lebensqualität verbessern und Kosten senken.

Mittels der vorgestellten monozentrischen zweiarmigen randomisiert kontrollierten Studie bei Erwachsenen mit CLBP von einer in den letzten sieben Tagen subjektiv empfundenen mittleren Schmerzintensität mehr als 40 mm auf einer VAS (0-100 mm) wurde die Wirksamkeit und Sicherheit eines Mindful Walking Programmes untersucht. Die Teilnehmenden wurden zu entweder acht wöchentlichen Behandlungseinheiten des Mindful Walking im Gruppensetting oder keiner studienspezifischen Therapie (Kontrolle) randomisiert. Weiterhin erhielten alle Teilnehmenden eine Bedarfsmedikation mit Paracetamol. Der primäre Endpunkt war die subjektiv empfundene Schmerzintensität (VAS 0-100 mm) nach acht Wochen. Sekundäre Endpunkte beinhalteten die Rückenfunktion, gemessen mit dem Funktionsfragebogen Hannover Rücken (FFbH-R). Die Ergebnisse wurden unter Einbeziehen der ANCOVA, adjustiert für den jeweiligen Baselinewert, statistisch ausgewertet. Zu Baseline betrug das mittlere Alter in der Gruppe, welche das Mindful Walking Programm durchführte (n = 29, MW ± SD) 52,5 ± 8,6 Jahre, 82,8% weiblich und in der Kontrollgruppe (n = 26) 54,8 ± 7,5 Jahre, 84,6% weiblich. Nach acht Wochen fand sich im Intergruppenvergleich kein statistisch signifikanter Unterschied hinsichtlich der subjektiv empfundenen Schmerzintensität (MD (95% KI) -9,6 mm (-22,3; 3,1), p = 0,136). Hinsichtlich der Rückenfunktion fand sich kein klinisch relevanter Gruppenunterschied. Es traten keine SUEs bezogen auf die Intervention auf.

Zusammenfassend fand sich in dieser Studie keine signifikante Schmerzreduktion und keine klinisch relevante Funktionsverbesserung durch Mindful Walking, die Intervention war sicher hinsichtlich UEs.

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ORIGINAL ARTICLES

Mindful Walking in Patients with Chronic Low Back Pain: A Randomized Controlled Trial

Gabriele Rotter, MD, MSc, Miriam Ortiz, MD, Sylvia Binting, Juliane Tomzik, MSc, Frauke Reese, Stephanie Roll, PhD, Benno Brinkhaus, MD,* and Michael Teut, MD*

Abstract

Aim: The objective of this study was to investigate the effectiveness of a mindful walking program (MWP) in patients with chronic low back pain (CLBP).

Methods: The trial was a two-armed, randomized, controlled single-center open clinical trial. The study was performed in the Outpatient Clinic for Integrative Medicine of the Charité–Universitätsmedizin Berlin. The participants were adults aged 18–65 years with CLBP (≥3 months) and an average low back pain within the past 7 days measured on a visual analog scale (VAS, 0 = no pain, 100 = worst imaginable pain) of at least 40 mm. The patients received either eight weekly MWP sessions or no intervention (control). The primary outcome was the perceived pain intensity assessed with a VAS (0–100 mm) after 8 weeks. The secondary outcomes included back function assessed by the Hannover Functional Questionnaire Backache (FFbH-R) and perceived stress assessed by the 14-item Cohen's Perceived Stress Scale (PSS-14). The results were obtained by analysis of covariance adjusted for the respective baseline values.

Results: In total, 55 patients were randomized (MWP: $n = 29$, 82.8% female, mean (±standard deviation) age: 52.5 ± 8.6 years, pain: 56.4 ± 14.1 mm; control: $n = 26$, 84.6% female, 54.8 ± 7.5 years, pain: 55.4 ± 13.1 mm). After 8 weeks, compared with the control conditions, the MWP was not associated with a statistically significant benefit for pain (VAS), adjusted mean − 9.6 [−22.3 to 3.1], $p = 0.136$, clinical benefits for back function (FFbH-R), adjusted mean 2.2 [−4.2 to 8.6], $p = 0.493$, or stress (PSS-14), adjusted mean − 1.6 [−4.8 to 1.6], $p = 0.326$.

Conclusion: In conclusion, compared with no intervention, mindful walking did not significantly improve pain, back function, or perceived stress in patients with CLBP.

Clinical Trial registration: ClinicalTrials.gov (NCT01893073).

Keywords: low back pain, complementary medicine, integrative medicine, randomized controlled trial

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Introduction

Low back pain is one of the leading causes of ill health globally and leads to a high disease burden.[1,2] In Germany, the 3-month prevalence was reported at 25%,[3] and the lifetime prevalence was between 74% and 85%.[4] Not all patients with low back pain are sufficiently treated and continue to have relevant symptoms. The prevalence of nonspecific chronic low back pain (CLBP) was internationally reported to be between 4% and 20%.[5]

The usual CLBP treatment consists of a multimodal regimen, including nonsteroidal analgesics, educational interventions, relaxation therapy, and exercises such as walking and mind–body interventions.[6–8] However, long-term treatment with analgesics might result in relevant adverse events, and there is growing interest in nonpharmacological simple and cost-effective therapies, including treatments originating from complementary and integrative medicine, such as mindful walking.[9–12]

Mindful walking combines walking as a low-intensity exercise with mindfulness training. The effectiveness of exercise and especially walking as a low-intensity exercise in the treatment of CLBP is well established.[7] A meta-analysis of 17 studies investigating walking in patients with chronic musculoskeletal pain, including five studies investigating CLBP, found that walking can be an effective form of exercise or activity for individuals with CLBP.[13]

Mindfulness training is a mental stress reduction strategy derived from Buddhist meditation. Mindfulness is defined as the tendency to encounter moment-to-moment experiences without being lost in unhelpful or distressing thoughts triggered by the experience.[14] Being mindful is also often related to be open, nonjudgmental, friendly, curious, accepting, compassionate, and kind.[15] Mindfulness-based interventions have been reported to be effective in alleviating various bio-psychosocially influenced conditions, including pain.[16]

The most commonly studied mindfulness training program is mindfulness-based stress reduction (MBSR). In various pain conditions, including low back pain, pain-relieving effects and strengthening of coping skills with MBSR have been reported.[17–19] Psychological factors, such as anxiety, stress, catastrophizing pain, and lack of coping strategies, play an important role in causing or aggravating CLBP. In therapy, it is important to also address the psychological sphere. Reviews and systematic reviews report mindful interventions' beneficial impact.[16,20,21]

A systematic review and meta-analysis of 30 randomized controlled trials (RCTs) investigating chronic pain showed improvement in chronic pain management after mindfulness meditation interventions.[20] The approach of mindful walking is of great interest, and patients reported a broad range of perceived benefits in a recently published qualitative study.[22]

The rationale for this trial was that a combination of mindfulness and mental stress reduction strategies with exercise would provide a useful treatment strategy for CLBP. Therefore, we developed an easy-to-follow training program that combines mindfulness training with walking exercise in a mindful walking program (MWP). An additional rationale for the development and testing of the MWP is that such a program can simultaneously address the following two mechanisms linked to pain perception: physical activity and stress/distress.

Individuals have competing demands for time (i.e., people are busy, and it can be difficult to meet both physical activity and mental health self-care recommendations with limited time); a program that may offer benefits for physical activity, stress, and pain simultaneously offers significant utility and future promise.

The aim of this RCT was to investigate the effectiveness of mindful walking in patients with CLBP.

Methods

Study design and setting

In a single-center open two-armed randomized controlled clinical trial, CLBP patients were randomized to either an MWP group or no study intervention (control group [CG]). The randomization (1:1 ratio, consecutive ID numbers) was generated by a data manager as a computer-generated randomization sequence by using SAS 9.3 software.[23] The sequence was concealed by use of a computer interface implemented in the electronic case report form and kept by the study nurse. The study physician contacted the study center (study nurse) by telephone and provided the participants' inclusion information.

After entering these data, the participants were assigned to the intervention or CG, and the results of the randomization were reported to the study physician. The study was performed at the Outpatient Clinic for Integrative Medicine of the Charité–Universitätsmedizin in Berlin, Germany. This study followed the standards of the Declaration of Helsinki[24] and the ICH-GCP guidelines.[25] All patients gave oral and written informed consent before study inclusion. The study was approved by the Ethics Committee of the Charité–Universitätsmedizin, Berlin, Germany (EA1/118/13) and was registered at ClinicalTrials.gov.

Patients

Patients were recruited by local daily newspapers and the website of the outpatient department for integrative medicine, Charité. Patients between 18 and 65 years of age with a clinical diagnosis of CLBP (disease duration of at least 3 months) and an average low back pain within the past 7 days measured on a visual analog scale (''VAS pain,'' 0–100 mm; 0 = no pain, 100 = worst imaginable pain)[26] of at least 40 mm were included.

The exclusion criteria were active walking or jogging (past 6 weeks, more than 60 min/week); regular meditation, relaxation exercise, or mindfulness exercises (past 6 weeks, more than 30 min/week); complementary medicine or use of other nonpharmacological therapies; participation in another clinical trial (past 3 months); neurological symptoms related to the spine; elevated risk of falls or inability to walk; angina pectoris (past 3 months); chronic respiratory disease with respiratory insufficiency; intake of central nervous system-acting analgesics (such as opioids, past 6 weeks); known renal and/or hepatic disease; severe organic, psychological, or psychiatric disorders not permitting study participation; and ongoing application for early retirement due to low back pain.

Study interventions

The MWP was based on our previous study in patients with stress symptoms,[27] with an adjustment toward more

physically active exercise. Over the course of 8 weeks, the patients allocated to the MWP group participated in eight group sessions, each restricted to 15 participants and lasting 50 to 60 min. The instructions regarding the mindful aspect included health education and an explanation of the term ''mindfulness'' and essential aspects of mindfulness awareness.

The instructions regarding the mindful aspect included an explanation of the term and essential aspects of mindfulness. At the beginning, the essential components of active walking in the sense of ''good mood walking'' were taught, and individual techniques of walking were instructed (rolling of the foot, arm–shoulder movement, and torso posture). In the following walking lessons, repetitions of the concept of mindfulness occurred, and the technique of mindful walking was practiced in the sense of a guided and feedback-controlled learning process.

In the first week, the focus was on the conscious rolling of the feet; in the second week, the swinging of the arms was additionally learned; and in the third week, the conscious torso posture was taught. The last week was dedicated to the complex implementation of all learned elements. In this intervention program, the main task was the conscious awareness of one's own body and thoughts. The participants were instructed to focus their awareness on the regions and movements introduced in each session. In addition, awareness of breathing while walking was taught. Strict adherence to the prescribed technique was not necessary, but the focus was on trying and adapting to individual physical conditions.

In addition, the participants were encouraged to be mindful of themselves and their environment, including the people in their surroundings, in their daily lives and were asked to report their experiences with practicing mindfulness in each session (Table 1). The patients in the MWP group were advised and instructed to self-exercise between group sessions. The MWP was carried out by a physiotherapist and physician and a sports therapist. All were trained in MBSR techniques, and the trainers received additional instructions from the principal investigator. Because the objective was to investigate the effectiveness,[28] the patients in the CG received no study intervention but could participate in eight, free-of-cost MWP sessions after study completion outside of the study.

The patients in both groups were allowed and instructed to use rescue medication on demand (paracetamol; maximum dosage, four times 500 mg/day).

Outcome parameters and data collection

Data were collected at baseline and after 8 and 12 weeks by using standardized patient questionnaires.

The primary outcome was perceived low back pain intensity after 8 weeks; the patients rated pain over the previous week on the VAS (0–100 mm).[26,29] The minimal clinically important difference (MCID) has been reported to be 15 mm.[30,31] Low back pain by VAS after 12 weeks and all other outcomes were considered secondary outcomes. Back function was measured with the Hannover Functional Questionnaire Backache (FFbH-R; 0% = minimal functional capacity, 100% = maximal functional capacity; assumed MCID: 12%).[32]

Perceived stress was measured by the 14-item Cohen's Perceived Stress Scale (PSS-14; range: 0–56, with lower scores indicating a lower stress level; no MCID determined).[33] Health-related quality of life was assessed by the Short-Form-36 Health Survey (SF-36)[34,35] (assumed MCID: 5 points). The patients also rated the treatment expectancy at baseline if randomized to the MWP group or CG (''cure,'' ''significant recovery,'' ''slight recovery,'' and ''no recovery''). After 12 weeks, the patients rated the changes in their low back pain (''slightly reduced,'' ''significantly reduced,'' ''completely reduced,'' ''not changed,'' and ''worsened''). Safety (adverse events and serious adverse events) was assessed across the whole study period. The intake of paracetamol and all other analgesics during the first 8 weeks was documented in the patient diaries.

Statistical analysis

The sample size calculation was based on the primary outcome (VAS pain after 8 weeks), with an assumed difference of 15 mm (MCID)[30,31] between the treatment groups and an assumed common standard deviation (SD) of 15 mm. A two-sided *t*-test would have a power of 80% with a significance level of 5% if 24 patients were enrolled in each group (total $n = 48$), including a dropout rate of $\sim 25\%$. nQuery Advisor 6.02 was used for this calculation.

The primary analysis of the primary outcome was performed by using an analysis of covariance (ANCOVA) with a fixed-factor treatment group adjusted for the baseline VAS pain value. The significance level was 5%. Secondary outcomes were analyzed in a similar manner as the primary outcome, that is, by ANCOVA adjusted for the respective baseline values and were considered exploratory. The results are reported as adjusted group means with 95% confidence

Table 1. Structure of a Mindful Walking Session (50 to 60 Min)

5 min	Group meets in a park surrounding; greetings (''Tiergarten, Berlin'')
10 min	Stretching exercises to warm up and short walking instructions.
15–25 min	An increasingly active pace of walking with a ''good mood walking'' attitude with individual step length and foot roll intensity emphasizing an actively moving forward movement of the foot.
10 min	Individual mindful walking. Participants were instructed to mindfully observe and focus on their bodily sensations (foot movement, trunk erection and movement, arm-shoulder movement, breathing) while walking and maintaining focus on their moment-to-moment experiences without being lost in unhelpful or distressing thoughts triggered by the experience. If this was experienced as a problem, the participants were instructed to focus their awareness on their breath while inhaling and exhaling.
5 min	Stretching exercises.
5 min	A feedback round was used to share and discuss the experiences, followed by farewells.

intervals (95% CI) and the *p*-value for the treatment group comparison. All tests and CIs were two sided. All data were analyzed based on the intention-to-treat principle by using the full analysis set with all available data without imputing missing data, based on the original assigned group. Adverse events are descriptively presented by frequency for each treatment group.

For the primary outcome, sensitivity analyses included the replacement of missing values using the last value carried forward method and ANCOVA adjusted for the baseline value, education, and duration of CLBP. In addition, an analysis for the primary outcome based on the per-protocol (PP) population excluded patients if at least one of the following criteria was met: not treated based on group allocation; fewer than six group sessions attended (MWP group only); and intake of analgesics other than paracetamol (MWP group and CG).

The analgesic costs were assessed by using the prices for daily defined dosages (DDD)[36] provided by the Drug Prescription Report 2014. The DDD was calculated for the first 8 weeks. The overall analgesic costs were calculated by multiplying the DDD prices by the number of days the drug was taken. The statistical analyses were performed by using the software packages SAS 9.3[23] and R, version 3.6.3.[37]

Results

Patients and study interventions

Between May 2013 and October 2013, of the 221 screened patients, 55 patients were randomized (MWP group, $n=29$; CG, $n=26$). After randomization and before the first intervention, five (17.2%) patients randomized to the MWP group refused to participate and dropped out, and three (11.5%) patients randomized to the CG dropped out (Fig. 1). Five patients in the MWP group attended the course less than six times. One trainer conducted 80% of the courses.

Most patients were female, and the mean age was older than 50 years (MWP group: 82.8% female, mean ± SD: 52.5 ± 8.6 years; CG: 84.6% female, 54.8 ± 7.5 years; Table 2). There were relevant baseline differences between the groups for the following parameters: Patients allocated to the MWP group more often had a university entrance qualification (58.6% vs. 38.5%, respectively), and they had a longer

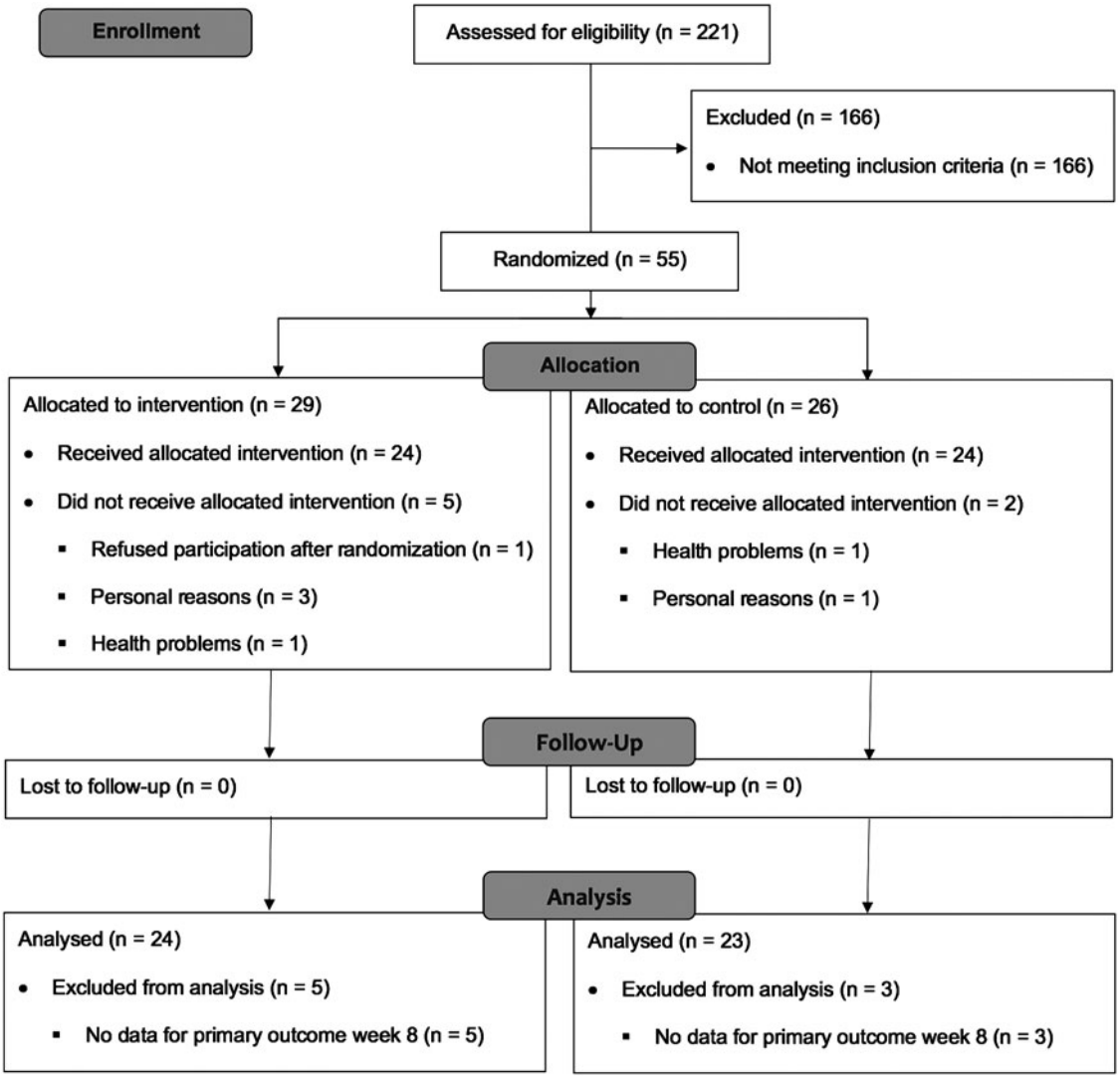

FIG. 1. Flow chart. Recruitment, treatment and follow-up of patients.

Table 2. Baseline Characteristics of Patients

	Mindful walking program n = *29* *Mean ± SD*/n *(%)*	*Control* n = *26* *Mean ± SD*/n *(%)*
Age, years	52.5 ± 8.7	54.8 ± 7.5
Sex, female	24 (82.8)	22 (84.6)
BMI, kg/m^2	25.7 ± 4.4	26.2 ± 5.3
German university entrance qualification (Abitur)	17 (58.6)	10 (38.5)
Employed	19 (65.5)	16 (61.5)
Two-person household	16 (55.2)	12 (46.2)
Physically active	22 (75.9)	16 (61.5)
Duration of CLBP, years	9.6 ± 10.1	7.6 ± 10.1
VAS pain (0–100 mm)[a]	56.4 ± 14.1	55.4 ± 13.1
FFbH-R (0%–100%)[b]	70.7 ± 13.7	73.6 ± 17.5
PSS-14 (0–56)[a]	31.0 ± 7.0	30.9 ± 8.5
SF-36 physical component scale (0–100)[b]	41.1 ± 6.9	40.9 ± 8.0
SF-36 mental component scale (0–100)[b]	46.5 ± 9.8	45.4 ± 11.9
Intake of analgesics (last 4 weeks)	10 (34.5)	9 (34.6)
Among them intake of >1 analgesic	0	2 (7.7)
Analgesics (last 4 weeks)		
Paracetamol	1 (3.5)	2 (7.7)
Ibuprofen	5 (17.2)	7 (26.9)
Acetylsalicylic acid	2 (6.9)	1 (3.9)
Metamizole	1 (3.5)	1 (3.9)
Diclofenac	1 (3.5)	4 (15.4)
Patients' expectation if randomized to intervention		
Cure	0	3 (11.5)
Significant recovery	23 (79.3)	18 (69.2)
Slight recovery	6 (20.7)	5 (19.2)
No recovery	0	0
Patients' expectation if randomized to control		
Cure	0	0
Significant recovery	1 (3.4)	0
Slight recovery	3 (10.3)	4 (15.4)
No recovery	25 (86.2)	22 (84.6)

[a]Lower values indicate better status.
[b]Higher values indicate better status.
BMI, body mass index; CLBP, chronic low back pain; FFbH-R, Hannover functional questionnaire backache; PSS-14, 14-item Cohens' Perceived Stress Scale; SF-36, Short-Form-36 Health Survey; VAS, visual analog scale.

duration of CLBP (8.4 ± 9.9 vs. 6.8 ± 6.2) years, than those allocated to the CG. The VAS scores for pain were comparable at 56.4 ± 14.1 versus 55.4 ± 13.1 mm in the two groups. Regarding treatment expectancy, most patients in both groups expected a ''significant recovery'' if randomized to the MWP (MWP group: 79.3%; CG: 69.2%) and ''no recovery'' if randomized to the control condition (MWP group: 86.2%; CG: 84.6%).

After 8 weeks, the between-group differences in the primary and all secondary outcomes tended to slightly favor the MWP group in comparison to the CG but failed to reach clinical relevance (Table 3). The primary outcome, low back pain assessed with the VAS, was not significantly different between the MWP group and the CG, with adjusted means [95% CI] of 35.9 [26.9–44.8] and 45.4 [36.3–54.5], respectively, and adjusted mean difference [95% CI] of –9.6 [–22.3 to 3.1], p-value = 0.136.

Neither imputation of missing endpoint values nor adjustment for additional baseline variables or repeating the analysis with the PP (n = 44) produced a relevant change in the results with the primary outcome. We found no significant or clinically relevant mean differences between the MWP group and the CG for back function (FFbH-R), 2.2 [–4.2 to 8.6], p-value = 0.493; for stress (PSS-14), –1.6 [–4.8 to 1.6], p-value = 0.326; for health-related quality of life (SF-36 physical component scale), 3.5 [–0.2 to 7.3], p-value = 0.066; and health-related quality of life (SF-36 mental component scale), –1.2 [–5.5 to 3.0], p-value = 0.567. After 8 weeks, out of 48 patients, 15 patients in the MWP group (62.5%) and one patient in the CG (4.2%) reported an improvement in low back pain (pain ''slightly reduced'' or ''significantly reduced'').

Within the first 8 weeks, the intake of rescue medication (paracetamol) was comparable between groups, with an MWP group mean ± SD of 5.4 ± 13.1 (range: 0–48) and a CG mean of 5.4 ± 8.7 (range: 0–30). During this time, 16 (55.2%) patients in the MWP group and 14 (53.9%) patients in the CG took no analgesic medication. Very few patients reported the use of analgesics other than the recommended rescue medication paracetamol. In the MWP group, the only additional analgesic was diclofenac taken by one patient in 1 week. In the CG, ibuprofen was taken by one patient in 4 weeks.

The total costs for analgesics used in the first 8 weeks were 78.66 (Euro, MWP group) versus 66.69 Euro (CG), with an average cost per week of 6.05 ± 9.01 Euro vs. 5.15 ± 4.46 Euro, respectively, p-value = 0.570.

During the first 8 weeks, no patient in the CG, but three patients in the MWP group, reported adverse events (n = 1

Table 3. Primary and Secondary Outcomes at Weeks 8 and 12

	n	*MWP Adjusted mean, [95% CI]*[a]	*Control Adjusted mean, [95% CI]*[a]	*Mean difference (MWP – control) Adjusted mean, [95% CI]*[a]	p[a]
VAS pain (0–100 mm),[b] MCID 15 mm (average neck pain during the previous 7 days)					
8 weeks (primary outcome)	47	35.9 [26.9 to 44.8]	45.4 [36.3 to 54.5]	−9.6 [−22.3 to 3.1]	0.136
12 weeks	47	34.8 [25.6 to 44.1]	47.4 [38.0 to 56.9]	−12.6 [−25.8 to 0.6]	0.061
FFbH-R (0–100%),[c] assumed MCID 12%					
8 weeks	48	75.1 [70.6 to 79.7]	72.9 [68.4 to 77.5]	2.2 [−4.2 to 8.6]	0.493
12 weeks	47	74.9 [70.1 to 79.8]	74.0 [69.1 to 79.0]	0.9 [−6.0 to 7.9]	0.792
PSS-14 (0–56)[b]					
8 weeks	48	29.0 [26.7 to 31.2]	30.5 [28.3 to 32.8]	−1.6 [−4.8 to 1.6]	0.326
12 weeks	47	28.1 [25.6 to 30.7]	31.2 [28.6 to 33.8]	−3.1 [−6.7 to 0.6]	0.096
SF-36 physical component scale (0–100),[c] assumed MCID 5 points					
8 weeks	48	43.4 [40.8 to 46.1]	39.9 [37.3 to 42.6]	3.5 [−0.2 to 7.3]	0.066
12 weeks	47	43.6 [40.9 to 46.3]	39.9 [37.1 to 42.6]	3.7 [−0.2 to 7.6]	0.059
SF-36 mental component scale (0–100),[c] assumed MCID 5 points					
8 weeks	48	45.7 [42.7 to 48.7]	46.9 [43.9 to 49.9]	−1.2 [−5.5 to 3.0]	0.567
12 weeks	47	46.7 [42.7 to 50.6]	44.5 [40.5 to 48.6]	2.1 [−3.5 to 7.7]	0.454
SF-36 subscales[c] after 8 weeks					
General health	48	58.3 [53.1 to 63.4]	51.5 [46.4 to 56.6]	6.8 [−0.6 to 14.1]	0.069
Mental health	48	65.1 [60.8 to 69.3]	64.1 [59.8 to 68.4]	1.0 [−5.1 to 7.0]	0.751
Bodily pain	48	49.3 [43.6 to 55.0]	45.6 [39.9 to 51.3]	3.6 [−4.4 to 11.7]	0.369
Physical functioning	48	74.7 [70.5 to 79.0]	74.2 [69.9 to 78.5]	0.5 [−5.5 to 6.6]	0.858
Role-emotional	48	69.4 [58.1 to 80.7]	73.7 [62.3 to 85.0]	−4.3 [−20.3 to 11.8]	0.593
Role-physical	48	68.6 [54.6 to 82.6]	51.2 [37.2 to 65.2]	17.4 [−2.4 to 37.2]	0.083
Social functioning	48	73.2 [66.4 to 79.9]	74.2 [67.5 to 81.0]	−1.1 [−10.7 to 8.5]	0.821
Vitality	48	47.8 [44.2 to 51.5]	46.7 [43.1 to 50.3]	1.1 [−4.0 to 6.2]	0.666
SF-36 subscales[c] after 12 weeks					
General health	47	61.0 [55.6 to 66.4]	51.0 [45.5 to 56.5]	10.0 [2.2 to 17.8]	0.013
Mental health	47	67.2 [61.0 to 73.3]	62.2 [56.0 to 68.5]	4.9 [−3.8 to 13.7]	0.263
Bodily pain	47	53.0 [45.5 to 60.4]	42.9 [35.3 to 50.5]	10.1 [−0.6 to 20.8]	0.063
Physical functioning	47	73.8 [69.2 to 78.4]	72.3 [67.6 to 77.0]	1.5 [−5.1 to 8.1]	0.644
Role-emotional	47	65.8 [51.4 to 80.2]	61.8 [47.1 to 76.5]	4.0 [−16.5 to 24.6]	0.696
Role-physical	47	63.4 [48.8 to 77.9]	50.2 [35.3 to 65.1]	13.2 [−7.7 to 34.0]	0.209
Social functioning	47	75.4 [67.0 to 83.7]	70.8 [62.3 to 79.4]	4.5 [−7.5 to 16.5]	0.450
Vitality	47	52.0 [47.3 to 56.7]	45.1 [40.3 to 49.9]	7.0 [0.2 to 13.7]	0.043

[a]Results adjusted for respective baseline value.
[b]Lower values indicate better status.
[c]Higher values indicate better status.
CI, confidence interval; FFbH-R, Hannover functional questionnaire backache; MWP, mindful walking program; n = number for respective available data; PSS-14, 14-item Cohens' perceived stress scale; SF-36, short-form-36 health survey; VAS, visual analog scale; MCID, minimal clinically important difference.

pneumonia with suspected pertussis, $n = 1$ toe injury (hemotoma) during a women's run competition, and $n = 1$ toe injury during weekend cycling), all not causally related to the intervention.

Between weeks 8 and 12, 19 (65.5%) patients in the MWP group continued to exercise for themselves. After 12 weeks, the intergroup difference in VAS pain increased to −12.6 [−25.8 to 0.6], p-value = 0.061 (Fig. 2). The between-group differences in back function assessed by the FFbH-R, stress assessed by the PSS-14, and health-related quality of life assessed by the SF-36 physical component scale (but not by the SF-36 mental component scale) tended to favor the MWP compared with the control conditions but failed to reach clinical relevance.

Discussion

In this single-center, open, two-armed randomized controlled clinical trial in CLBP patients, eight weekly MWP sessions did not result in statistically significant or clinically relevant group differences in the mean low back pain intensity in comparison to no mindful walking. In addition, secondary outcomes showed no clinically relevant differences between the study groups after 8 weeks. After 12 weeks, the intergroup difference in the VAS score for pain broadened, favoring mindful walking, but was still not clinically relevant. The analgesic intake was comparable in both groups; however, analgesic costs were slightly higher for patients in the MWP group than for controls. No adverse events were associated with the MWP.

The strengths of this RCT were the use of a previously tested intervention program, the comprehensive range of validated patient-reported outcomes, and the follow-up 4 weeks after the end of the therapy. The rather homogeneous study population regarding pain intensity due to the inclusion criteria and the standardized intervention program

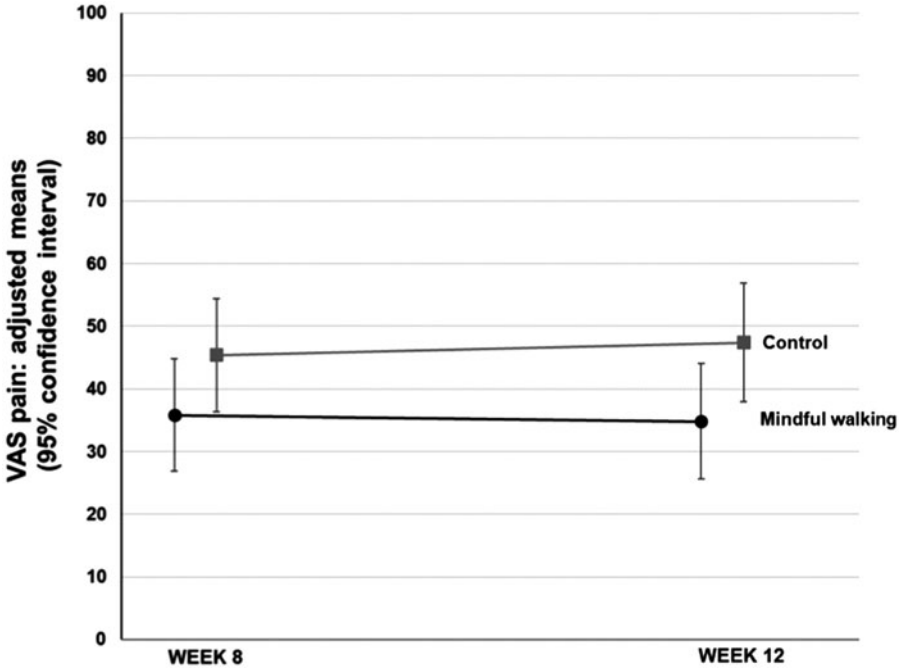

FIG. 2. Adjusted means and 95% confidence intervals of the last average pain intensity in the last week (VAS) at 8 and 12 weeks with *p*-values comparing mindful walking with no intervention (lower values indicating less pain). VAS, visual analog scale.

augment the internal validity of the study. The external validity was augmented by implementing three therapists deriving from three different professions.

This study has limitations. This RCT employed a single-center setting and included a high percentage of women. These factors limit the generalizability of our results. We excluded patients with severe organic, psychological, or psychiatric disorders. However, we did not systematically assess psychiatric comorbidities. Psychiatric comorbidities, such as depressive disorders, may have an impact on pain, stress, and function in patients with CLBP and may have influenced the results of our study.

The frequency of self-applications and non-drug adjunctive therapies was not determined, which may have contributed to a decrease in the group difference in the primary and secondary outcome parameters as the participants in the CG may also have started mindful self-applications. Despite giving instructions, mindfulness was not controlled in this study. Suitable instruments for measuring mindfulness are available.[38–42] The study design had several potential sources of bias: Patients in the MWP group received time and attention that patients in the CG did not receive, and we did not include blinded outcome assessments.

Considering these factors, tendencies for treatment effects may have been overestimated. However, recently, the relevance of blinding in RCTs has been discussed, as a meta-epidemiological study found no evidence for an average difference in estimated treatment effects between trials with and without blinded patients, health care providers, or outcome assessors.[43] However, the lack of blinding might have an impact on the results in our population, as the patients expected more positive results if randomized to the MWP group.

We used mostly validated outcomes. The assessment of analgesic use from patient diaries was not validated but standardized because analgesics might cause relevant life-threatening side effects,[9–12] and reduction in their use is highly relevant to the patients. In our opinion, the evaluation of analgesics is important for the interpretation of study results, and it was performed earlier in trials on CLBP and chronic neck pain.[44–50] However, the obtained results must be interpreted with caution.

To facilitate compliance in the MWP group, we chose to provide eight sessions of MWP, with a pragmatic duration of ~60 min each. Longer MWP treatments, such as eight weekly 1.5- to 2.5-h sessions, as performed in MBSR trials in patients with low back pain,[19] might have provided stronger effects on pain intensity. To maintain the pragmatic advantage of the shorter 60-min interventions, the time available for individual mindful walking could be progressively significantly increased. For example, mindful walking could last 30 min from week 5. Further, a more intensive exercise component could have had a stronger effect on pain intensity, as exercise is an important and potent component of the multimodal therapy regimen for CLBP.[6,7]

We instructed patients in the MWP group to self-exercise between sessions but did not assess adherence to the self-exercises. Such an assessment could have been a motivational factor and possibly resulted in a higher treatment effect.

We used the VAS for pain intensity measurement as the primary outcome, because pain is relevant to patients. The VAS assessments of pain have been validated, widely used, and established in our research groups; are easy to use; and require less than 1 min to complete.[26,29,44,47,51–56] However, recently, their validity has been questioned.[57] In patients with CLBP, the between-group difference was not statistically significant in our study. This might be due to various factors. First, we might have overestimated the treatment effects of our MWP, and in a larger study population, the treatment effects could have become more evident.

For low back pain (any duration), a meta-analysis included four RCTs comparing MBSR (171 patients) with routine care (155 patients)[19] and found a statistically significant but not clinically relevant improvement in pain intensity

(numeric rating scale, range: 0–10, MCID: 1.5) at short-term follow-up (mean difference: 0.96 [95% CI 1.64–0.34]). We found a comparable mean difference between groups after 8 weeks with −9.6 [−22.3 to 3.1] on a VAS (0–100 mm) with our rather easy-to-apply MWP. However, the mentioned meta-analysis[19] found no statistically significant or clinically important group differences (mean difference: 0.90 [7.66–5.86]) in pain intensity at long-term follow-up (6 months after randomization) in two RCTs.[19]

In contrast, we found an indication for a slightly larger intergroup difference at 12 weeks after randomization in our study. This might be partly due to the high percentage of patients who continued to walk after 8 weeks and to the shorter observation time compared with the mentioned meta-analysis. A previous systematic review on ''acceptance- and mindfulness-based interventions'' included 25 RCTs (1285 patients) with various chronic pain conditions. It reported smaller beneficial effects for pain intensity (range: 0–10) with a pooled standard mean difference of 0.24 [0.06–0.42].[17]

Michalsen et al. conducted an RCT involving 68 patients with CLBP and found no differences in the primary outcome of VAS pain in a focused meditation versus self-care exercise comparison.[58] Regarding back function, measured by the German tool FFbH-R, we found hints for a small non-clinically relevant effect in the MWP group compared with the CG after 8 weeks, but this difference diminished after 12 weeks. In contrast, the meta-analysis mentioned earlier[19] reported two studies that investigated MBSR compared with routine care in patients with low back pain with statistically significant but clinically irrelevant improvement in physical functioning, and these benefits were not observed at the follow-up.

Further, the authors[19] found no statistically significant or clinically relevant benefit of MBSR compared with active controls in short- or long-term analyses on health-related quality of life. This is in line with our results for health-related quality of life and stress. However, in our previous randomized clinical trial in patients with stress symptoms,[27] a less physically active MWP, compared with control conditions, resulted in a statistically significant reduction in perceived stress assessed with the PSS-14. Further, a more recent trial on MBSR in patients with CLBP (involving 17 sequentially sampled patients in the intervention condition and 11 patients in the waiting-list control condition) reported between-group medium-to-large effect sizes with a pre–post comparison of pain severity and quality of life.[59]

Conclusion

Practicing mindful walking in patients with low back pain did not result in relevant improvements in pain, stress, or back function compared with no intervention. Future studies should consider intensifying the mindful walking intervention and including long-term follow-up.

Authors' Contributions

G.R. helped design the study, interpreted the data, and drafted the article. M.O. helped design the study and revised the article. S.B. managed the data, carried out the statistical analyses, interpreted the data, and revised the article. J.T. carried out the statistical analyses. F.R. helped with the design and carried out the study interventions. S.R. was involved in the methodological design of the study, carried out the statistical analyses, and revised the article. B.B. was the study director who planned and designed the study along with M.T. and helped ensure successful study implementation, contributed to the interpretation of the data, and revised the article. M.T. planned and designed the study, coordinated the study, interpreted the data, and codrafted and revised the article.

All authors have read and approved the final version of the article and agree with the order in which the authors are listed.

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3. Diskussion

Chronische muskuloskelettale Schmerzen führen zu hohen persönlichen Beeinträchtigungen und Betroffene nutzen häufig körperbasierte Behandlungsansätze aus dem Bereich der KIM. Im Rahmen dieser Habilitationsschrift wurden die Wirksamkeit und Therapiesicherheit ausgewählter körperbasierter Behandlungsansätze bei Patienten und Patientinnen mit chronischen muskuloskelettalen Schmerzen wissenschaftlich untersucht.

3.1 Zusammenschau der Hauptergebnisse der hier präsentierten Studien

In insgesamt fünf Studien, vier klinischen Interventionsstudien und einer Beobachtungsstudie, wurden im hochschulambulanten Setting die Wirksamkeit und Therapiesicherheit von körperbasierten Behandlungsansätzen der KIM bei Patienten und Patientinnen der Allgemeinbevölkerung sowie selektiv bei hohen Streichern und Streicherinnen mit chronischen muskuloskelettalen Schmerzen untersucht beziehungsweise Veränderungen beobachtet.

Alle vier RCTs wurden in vergleichbarerem Forschungsdesign und vergleichbarer Forschungsmethodik an der HSA NHK durchgeführt. Eingeschlossen wurden Patienten und Patientinnen mit CNP[199, 200] beziehungsweise CLBP[201, 202] im Alter von 18 bis 65 (beziehungsweise 60[200]) Jahren mit einer in den letzten sieben Tagen subjektiv empfundenen mittleren Schmerzintensität von mindestens 40 mm auf einer VAS (0-100 mm). Dieser Trennwert für die Schmerzintensität wurde auf Basis der Literatur und früherer Schmerzstudien in unserem Institut gewählt.[203-205] Die Studienteilnehmenden erhielten entweder körperbasierte Behandlungen im Einzelsetting[199-201] beziehungsweise eine Kombination aus einem körperbasierten und psychologischen Behandlungsansatz im Gruppensetting[202] oder jeweils zunächst keine studienspezifischen körperbasierten Behandlungen (Kontrollen im Wartegruppendesign). Patienten und Patientinnen aller Studiengruppen konnten ihre bisherige Therapie weiterführen beziehungsweise erhielten zusätzlich eine Bedarfsmedikation mit Paracetamol. Der primäre Endpunkt war in allen RCTs die in den letzten sieben Tagen subjektiv empfundene mittlere Intensität der HWS- beziehungsweise LWS-Schmerzen auf einer horizontalen VAS zu einem definierten Zeitpunkt, nach Beendigung der jeweiligen Interventionsphasen. Sekundäre Endpunkte beinhalteten die Funktionsbeeinträchtigung durch HWS-Schmerzen mittels NDI[199, 200] beziehungsweise durch LWS-Schmerzen mittels FFbH-R.[201, 202] Weiterhin wurde in den Interventionsstudien als sekundärer Endpunkt die gesundheitsbezogene Lebensqualität mittels SF-12[199, 200] (CNP) beziehungsweise mittels SF-36[201, 202] (CLBP) gemessen. Zur Bestimmung der Therapiesicherheit wurden UEs und SUEs erfasst. Das mittlere Alter der Studienteilnehmenden betrug zwischen (MW ± SD) 41,6 ± 11,1[199] und 52,5 ± 8,6[201] Jahren. Die Studienteilnehmenden waren überwiegend weiblich. Weitere Studiencharakteristika sind in Tabelle 1 übersichtsartig zusammengestellt. Für sämtliche Studien wurden in Tabelle 1, auch wenn in der Originalpublikation nicht erwähnt, MCIDs der Endpunkte dargestellt.

Tabelle 1. Charakteristika der randomisiert kontrollierten Studien und der Beobachtungsstudie mit Darstellung ausgewählter Endpunkte

Studien	**Patienten und Patientinnen**	**Interventionen und Kontrollinterventionen**	**Endpunkte (EPs)** 1. Schmerzintensität 2. Funktion 3. Lebensqualität 4. Therapiesicherheit	**Ergebnisse** 1.-3. für den jeweiligen Baselinewert adjustierte Mittelwerte/ adjustierte Mittelwertdifferenz (95% Konfidenzintervall), berechnet mittels ANCOVA 4. Anzahl UE/SUE (n)
Rotter et al. 2020 RCT	- N = 62 (28:34) - Hohe Streicher/ Streicherinnen - CNP, ≥ 40 mm VAS Schmerz* - 81% Frauen - 41,6 ± 11,1 Jahre - Dropouts für primäre Analyse nach 12 Wochen: n = 1 (0:1) - Letztes Follow-up: 52 Wochen	**Osteopathische Medizin**: - 5 x Osteopathische Medizin (individualisiert diagnosegeleitet, je 45 Minuten), Abstand etwa 2 Wochen innerhalb von 12 Wochen - 45-minütige semi-standardisierte musikermedizinische Beratung vor Randomisierung - Paracetamol nach Bedarf (maximal 4 x 500mg) **Kontrolle:** - keine Osteopathische Medizin - 45-minütige semi-standardisierte musikermedizinische Beratung vor Randomisierung - Paracetamol nach Bedarf (maximal 4 x 500mg) - Wartelisten-Design	1. VAS Schmerz (primärer EP nach 12 Wochen, MCID 15 mm)*,** 2. NDI (0-100%, MCID 9,8%)** 3. SF-12 PCS (0-100, MCID 5) und SF-12 MCS (0-100, MCID 5)*** 4. UE, SUE**	Nach 12 Wochen: 1. VAS Schmerz: Osteopathische Medizin vs. Kontrolle MW (95% KI) 14,6 mm (8,0; 21,2) vs. 40,8 mm (34,7; 46,9), MD -26,2 mm^{+} (-35,2; -17,2), p < 0,001, Cohen's d = 1,4 2. NDI: 8,8% (6,7; 10,8) vs. 17,2% (15,3; 19,1), MD -8,4%$^{+}$ (-11,2; -5,6), p < 0,001 3. SF-12 PCS: 53,1 (51,2; 54,9) vs. 49,1 (47,3; 50,8), MD 4,0 (1,5; 6,6), p = 0,003 SF-12 MCS: 49,8 (46,3; 53,3) vs. 47,5 (44,4; 50,7), MD 2,0 (-1,4; 5,5), p = 0,335 4. Therapiesicherheit: Kein SUE Osteopathische Medizin (n = 2) milde vorübergehende UEs (Müdigkeit und Schwindel)
Rotter et al. 2022 Beobachtungsstudie	N = 40 - Diagnose entweder CNP (n = 10), CLBP, (n = 10), CSP (n = 10), CKP (n = 10), jeweils ≥ 40 mm VAS Schmerz* - 73% Frauen - 47,7 ± 8,3 Jahre - Dropouts nach 26 Wochen: n = 0 - Letztes Follow-up: 52 Wochen	**Osteopathische Medizin:** - 6 x Osteopathische Medizin (individualisiert diagnosegeleitet, je 45 Minuten), Abstand 3-4 Wochen innerhalb von 26 Wochen - Beibehalten einer eventuellen Therapie vor Studienbeginn **Keine Kontrolle**	1. VAS Schmerz (MCID 15 mm)*,** 2. - CNP: NDI (0-50, MCID 3.0)** - CLBP: low back pain rating scale (0-60, MCID 1.2)** - CSP: DASH (0-100, MCID 8)** - CNP: WOMAC (0-69, MCID 10); Lequesne (0-24, MCID 40%)** 3. SF-12 PCS (0-100, MCID 5) und SF-12 MCS (0-100, MCID 5)*** 4. UE, SUE**	Nach 26 Wochen, MD zu Baseline: A: Gesamtpopulation (N = 40): 1. -33.1 mm^{+} (-40,5; -25,7) 2. Siehe Diagnosegruppen 3. SF-12 PCS: 6,9 (4,2; 9,5); SF-12 MCS: -0,02 (-3,1; 3,0) 4. Kein UE, kein SUE B: Diagnosegruppen: CNP 1. -33,7 mm^{+} (-54,7; -12.6); 2. NDI -3,6^{+} (-9,0; 1,9) CLBP 1. -28,2 mm^{+} (-47,9; -8,4); 2. -3,4^{+} (-12,5; 5,7) CSP 1. -32,4 mm^{+} (-46,8; -18,0), 2. DASH -13,4^{+} (-23,1; -3,7) CKP 1. -38,1 mm^{+} (-49,1; -27,0); 2. WOMAC -13,0^{+} (-23,5; -2;5), Lequesne -2,7 (-4,9; -0,5) VAS Schmerz MD 12 Wochen zu Baseline: -29,3 mm^{+} (-35,7; -23,0)
Pach et al. 2018 RCT	N = 92 (46:46) CNP, ≥ 40 mm VAS Schmerz* - 87% Frauen - 45,4 ± 9,7 Jahre - Dropouts für primäre Analyse nach 4 Wochen: n = 3 (0:3) - Letztes Follow-up: 12 Wochen	**Tuina**: - 6 x Tuina (je 30 Minuten) innerhalb von 3 Wochen - Beibehalten einer eventuellen Therapie vor Studienbeginn **Kontrolle:** - Keine spezifische Studienintervention - Beibehalten einer eventuellen Therapie vor Studienbeginn - Wartelisten-Design	1. VAS Schmerz (primärer EP nach 4 Wochen, MCID 15 mm)*,** 2. NDI (0-100%, MCID 9,8%)** 3. SF-12 PCS (0-100, MCID 5) und SF-12 MCS (0-100, MCID 5)*** 4. UE, SUE**	Nach 4 Wochen: 1. VAS Schmerz: Tuina vs. Kontrolle MW (95% KI) 31,2 mm (25,0; 37,3) vs. 53,9 mm (47,6; 60,3), MD -22,8 mm^{+} (-31,7; -13,8); p < 0.001, Cohen's d = 1.16 2. NDI: 37,8% (34,8; 40,9) vs. 47,6% (44,4; 50,8), MD -9,8%$^{+}$ (-14,2; -5,3), p<0,001 3. SF-12 PCS: 47,9 (45,7; 50,0) vs. 42,9 (40,7; 45,1), MD 5,0^{+} (1,9; 8,1), p = 0,002 SF-12 MCS 47,2 (44,4; 50,0) vs. 45,7 (42,8; 48,7), MD 1,5 (-2,6; 5,5), p = 0,474 4. Kein SUE. VAS Schmerz MD nach 12 Wochen: -17,9 mm^{+} (-27,1; -8,8), p < 0,001

Tabelle 1. (Fortsetzung)

Teut et al. 2018 RCT	N = 110 (37:36:37) CLBP, ≥ 40 mm VAS Schmerz* Pulsierendes Schröpfen: - 57% Frauen - 49,0 ± 13,7 Jahre Minimales Schröpfen: 64% Frauen 47,5 ± 13,8 Jahre Kontrolle: 68% Frauen 50,7 ± 10,7 Jahre - Dropouts für primäre Analyse nach 4 Wochen: n = 14 (4:4:6) - Letztes Follow-up: 12 Wochen	**Pulsierendes Schröpfen**: - 8 x pulsierendes Schröpfen (je 8 Minuten) innerhalb von 4 Wochen - Paracetamol nach Bedarf (maximal 4 x 500mg) **Minimales Schröpfen:** - 8 x minimales Schröpfen (je 8 Minuten) innerhalb von 4 Wochen - Paracetamol nach Bedarf (maximal 4 x 500mg) **Kontrolle:** - Keine spezifische Studienintervention - Paracetamol nach Bedarf (maximal 4 x 500mg) - Wartelisten-Design	1. VAS Schmerz (primärer EP nach 4 Wochen, MCID 15 mm)*,** 2. FFbH-R (0-100%, MCID 12%)*** 3. SF-36 PCS (0-100, MCID 5) und SF-36 MCS (0-100, MCID 5)*** 4. UE, SUE**	Nach 4 Wochen: 1. VAS Schmerz: pulsierendes Schröpfen vs. minimales Schröpfen vs. Kontrolle: 34,9 mm (95% KI 28,7; 41,2) vs. 40,4 mm (34,2; 46,7) vs. 56,1 mm (49,8; 62,4) MD puls. Schröpfen vs. Kontrolle -21,2 mm^{+} (-12,2; -30,1), p < 0,001 MD min. Schröpfen vs. Kontrolle -15,7 mm^{+} (-6,9; -24,4), p = 0,001 MD min. Schröpfen vs. puls. Schröpfen 5,5 mm (-3,5; 14.5), p = 0,225 2. FFbH-R: 76,0% (72,1; 80,0) vs. 74,2% (70,2; 78,2) vs. 70,2% (66,1; 74,3) MD puls. Schröpfen vs. Kontrolle 5,8% (11,5; 0,1), p = 0,045 MD min. Schröpfen vs. Kontrolle 4,0% (9,7; -1,7), p = 0,171 MD min. Schröpfen vs. puls. Schröpfen -1,8% (-7,5; 3,8), p = 0,517 3. SF-36 PCS: 43,8 (41,3; 46,4) vs. 39,5 (37,0; 42,1) vs. 38,2 (35,6; 40,9) MD puls. Schröpfen vs. Kontrolle 5,6^{+} (9,3; 2,0), p = 0,003 MD min. Schröpfen vs. Kontrolle 1,3 (5,0; -2,4), p = 0,478 MD min. Schröpfen vs. puls. Schröpfen -4,3 (-7,9; -0,7), p = 0,021 SF-35 MCS: 50,1 (47,0; 53,2) vs. 47,1 (44,0; 50,3) vs. 47,6 (44,4; 50,8) MD puls. Schröpfen vs. Kontrolle 2,5 (6,9; -2,0), p = 0,270 MD min. Schröpfen vs. Kontrolle -0,5 (4,0; -5,0), p = 0,820 MD min. Schröpfen vs. puls. Schröpfen -3,0 (-7,4; 1,4), p = 0,179 4. Kein SUE. UEs Puls. Schröpfen: (n = 2) Verstärkung LWS-Schmerzen einige Stunden, (n = 6) leichte LWS-Schmerzen 24 Sunden UEs min. Schröpfen: (n = 2) leichte LWS-Schmerzen 24 Sunden VAS Schmerz MD nach 12 Wochen: MD puls. Schröpfen vs. Kontrolle -15,1 mm^{+} (-3,1; -27,1), p = 0,014) MD min. Schröpfen vs. Kontrolle -11,5 mm (0,44; -23,4), p = 0,059) MD min. Schröpfen vs. puls. Schröpfen 3,7 mm (-8,6; 15,9), p = 0,554
Rotter et al. 2022 RCT	- N = 55 (29:26) - CLBP, ≥ 40 mm VAS Schmerz* - 85% Frauen - 52,5 ± 8,6 Jahre - Dropouts für primäre Analyse nach 8 Wochen: n = 8 (5:3) - Letztes Follow-up: 12 Wochen	**Mindful Walking**: - 8 x Mindful Walking Programm wöchentlich im Gruppensetting, (maximal 15 Teilnehmende, Dauer 50-60 Minuten) innerhalb von 8 Wochen - Paracetamol nach Bedarf (maximal 4 x 500mg) **Kontrolle:** - Keine spezifische Studienintervention - Paracetamol nach Bedarf (maximal 4 x 500mg) - Wartelisten-Design	1. VAS Schmerz (primärer EP nach 8 Wochen, MCID 15 mm)*,** 2. FFbH-R (0-100%, MCID 12%)*** 3. SF-36 PCS (0-100, MCID 5) and SF-36 MCS (0-100, MCID 5)*** 4. UE, SUE**	Nach 12 Wochen: 1. VAS Schmerz*: Mindful Walking vs. Kontrolle 35,9 mm (95% KI 26,9; 44,8) vs. 45,4 mm (36,3; 54,5), MD -9,6 mm (-22,3; 3,1); p = 0,136 2. FFbH-R: 75,1% (70,6; 79,7) vs. 72,9% (68,4; 77,5), MD 2,2% (-4,2; 8,6), p = 0,493 3. SF-36 PCS: 43,4 (40,8; 46,1) vs. 39,9 (37,3; 42,6), MD 3,5 (-0,2; 7,3), p = 0,066 SF-36 MCS: 45,7 (42.7; 48,7) vs. 46,9 (43,9; 49,9), MD -1,2 (-5,5; 3,0), p = 0,567 4. Keine UE bezogen auf die Intervention VAS Schmerz MD nach 12 Wochen: -12,6 mm (-25,8; 0,6); p = 0,061

* VAS Schmerz: die in den letzten sieben Tagen subjektiv empfundenen mittleren Schmerzintensität auf einer visuellen Analogskala (VAS, 0-100 mm, 0 = kein Schmerz, 100 = schlimmster vorstellbarer Schmerz);
** geringere Werte bedeuten einen besseren Zustand; *** höhere Werte bedeuten einen besseren Zustand, $^{+}$die MD ist klinisch relevant
ANCOVA Kovarianzanalyse; CKP chronische Knieschmerzen; CLBP chronische unspezifische Lendenwirbelsäulenschmerzen; CNP chronische unspezifische Halswirbelsäulenschmerzen; CSP chronische Schulterschmerzen; DASH *Disabilities of the Arm, Shoulder and Hand questionnaire*; EP Endpunkt; FFbH-R Funktionsfragebogen Hannover Rücken; KI Konfidenzintervall; LWS Lendenwirbelsäule; MCID minimaler klinisch relevanter Unterschied; MCS *mental component scale* (psychische Summenskala); MD *mean difference*; NDI *Neck Disability Index*; MW Mittelwert; NPDS *Neck Pain and Disability Scale*; PCS *physical component scale* (körperliche Summenskala); RCT randomisiert kontrollierte Studie; SD Standardabweichung; SF-12 *Short Form 12*; SF-36 *Short Form 36*; SUE schweres unerwünschtes Ereignis; UE unerwünschtes Ereignis; VAS visuelle Analogskala; VAS Schmerz: die in den letzten sieben Tagen subjektiv empfundene mittlere Schmerzintensität gemessen an einer horizontalen VAS (0-100 mm, 0 = kein Schmerz, 100 = schlimmster vorstellbarer Schmerz)

Bei Patienten und Patientinnen mit CNP war nach fünf Behandlungen mit Osteopathischer Medizin beziehungsweise sechs Tuina Behandlungen und bei Patienten und Patientinnen CLBP war nach acht Sitzungen Schröpfen die subjektiv empfundene mittlere Schmerzintensität statistisch signifikant und klinisch relevant (MCID) im Vergleich zur Kontrolle vermindert. Dieser klinisch relevante Unterschied fand sich hingegen nicht in der vorgestellten RCT an Patienten und Patientinnen mit CLBP nach acht Gruppeninterventionen des Mindful Walking. Für die sekundären Endpunkte wird im Folgenden die Beurteilung der klinischen Relevanz von Gruppenunterschieden zum Hauptmesszeitpunkt nach Beendigung der Interventionsphasen benannt. Sämtliche Ergebnisse sekundärer Endpunkte sollten in konfirmatorischen RCTs weiter untersucht werden. Es fanden sich klinisch relevante Verminderungen der Funktionsbeeinträchtigungen nach Behandlungen mit der Osteopathischen Medizin beziehungsweise Tuina jeweils im Vergleich zur Kontrolle bei Patienten und Patientinnen mit CNP. Hinsichtlich der allgemeinen Lebensqualität im körperlichen Bereich wurde eine klinische relevante Verbesserung bei Patienten und Patientinnen mit CNP zugunsten von Tuina und bei Patienten und Patientinnen mit CLBP zugunsten des pulsierenden Schröpfens im Vergleich zur Kontrolle sichtbar. Es fanden sich jedoch keine klinisch relevanten Unterschiede bezüglich der allgemeinen Lebensqualität im psychischen Bereich zugunsten eines der untersuchten körperbasierten Behandlungsansätze im Vergleich zur Kontrolle. Alle untersuchten Interventionen waren sicher. Die Patienten- und Patientinnensicherheit bezüglich des Auftretens von UEs und SUEs war in allen untersuchten Interventionen gegeben.

In der Beobachtungsstudie konnten bei Patienten und Patientinnen mit chronischen muskuloskelettalen Schmerzen (CNP, CLBP, CSP, CNP) nach bis zu sechs Behandlungen mit Osteopathischer Medizin im Vergleich Baseline zu 26 Wochen eine klinisch relevante Schmerzreduktion, erkrankungsspezifische Funktionsverbesserungen und Verbesserungen der allgemeinen Lebensqualität im körperlichen Bereich beobachtet werden.

3.2 Stärken und Limitationen

Die in diese Habilitationsschrift einbezogenen vier konfirmatorischen RCTs weisen begünstigend für die Zusammenschau eine weitgehend homogene Forschungsmethodik auf. Dies betrifft die Studienpopulationen hinsichtlich Ein- und Ausschlusskriterien, einschließlich des Trennwertes *(Cut-off)* der Schmerzintensität, des Alters, und der Erkrankungen (CNP, CLBP), der homogenen Nutzung einer Kontrolle im Wartelisten-Design, desselben validierten primären Endpunktes jeweils nach Beendigung der Studieninterventionen, der überwiegend homogenen und validierten sekundären Endpunkte, der Vergleichbarkeit der statistischen Auswertungsmethodik im Intergruppenvergleich unter Einbeziehen der ANCOVA (adjustiert für die jeweiligen Baseline-Werte), der homogenen Forschungsumgebung und der homogenen praxisnahen Studiendurchführung an der HSA NHK. Die prospektive Beobachtungsstudie wurde, soweit angemessen, hinsichtlich der Einschlusskriterien, der Endpunkte, der Forschungsumgebung und des Studienortes analog durchgeführt. Hierdurch

konnte eine Zusammenschau der untersuchten körperbasierten Behandlungsansätze gegeben werden. Einschränkend wurden die Wirksamkeit und Sicherheit der Osteopathischen Medizin nicht in der Allgemeinbevölkerung, sondern der speziellen Population der hohen Streicher und Streicherinnen mit CNP[199] untersucht.

Die hier vorgestellten vier RCTs[199-202] und die Beobachtungsstudie[206] haben teils gemeinsame Schwächen. Hierzu zählen das monozentrische Design im universitären Umfeld und der vorherrschende Frauenanteil unter den Studienteilnehmenden, wodurch die Generalisierbarkeit der Studienergebnisse eingeschränkt ist. Zwar gaben beispielsweise in einer Befragung Frauen im Vergleich zu Männern häufiger LWS-Schmerzen (55,0% versus 48,6%) beziehungsweise HWS-Schmerzen (54,9% versus 36,2%)[7] an, jedoch war der Frauenanteil in den vier vorgestellten RCTs mit bis zu 87% erheblich höher. Andererseits weisen Frauen mit chronischen muskuloskelettalen Schmerzen sowohl eine höhere KIM-Nutzung als auch eine höhere Inanspruchnahme des Gesundheitssystems im Vergleich zu Männern auf. So waren die Diagnosen „Arthrose“ (*International Statistical Classification of Diseases and Related Health Problems, 10th revision*, ICD-10, M15-M19) und „Sonstige Krankheiten der Wirbelsäule und des Rückens“ (ICD-10 M50-M54) einschließlich LWS-Schmerzen bei Frauen Platz 4 und Platz 5 der häufigsten Diagnosen für Krankenhausbehandlungen.[207] Diese Erkrankungen fanden sich nicht unter den 10 häufigsten Diagnosen für Krankenhausbehandlungen bei Männern.[207] Zudem waren LWS-Schmerzen (ICD-10 M54) im Jahr 2018 die zweithäufigste hausärztliche Diagnose.[208] Die Studiendesigns hatten potentielle Verzerrungsfaktoren (Bias): (1) die den körperbasierten Behandlungen zugeteilten Studienteilnehmenden erfuhren im Vergleich zu den Kontrollen mehr Aufmerksamkeit und Zuwendung. Zur Beantwortung der Forschungsfragen zur Wirksamkeit (*effectiveness*) wurden körperbasierte Behandlungsansätze zumeist im Vergleich zu einer Kontrolle ohne studienspezifische Intervention untersucht, eine Verblindung (hinsichtlich Gruppenzugehörigkeit) der Studienteilnehmenden oder Therapierenden war in diesem gewählten Design nicht möglich. Eine Forschungsfrage zur Untersuchung spezifischer Wirkungen (*efficacy*) körperbasierter Behandlungen kann durch einen Vergleich der untersuchten Intervention mit Schein- oder Minimalbehandlungen bei Verblindung der Studienteilnehmenden hinsichtlich ihrer Gruppenzugehörigkeit beantwortet werden. Dies wurde in der Schröpfstudie[202] durch eine Verblindung zwischen zwei Formen des trockenen, pulsierenden Schröpfens realisiert. In allen hier vorgestellten RCTs und in der Beobachtungsstudie haben die Studienteilnehmenden selbst das Therapieergebnis mittels für Patienten und Patientinnen relevanter PROMs eingeschätzt. Das Fehlen von zusätzlichen verblindet erhobenen objektiven Endpunkten ist eine Limitation sämtlicher in diese Habilitationsschrift einbezogener RCTs und der Beobachtungsstudie. Hierdurch könnten die jeweiligen Behandlungseffekte überschätzt worden sein. Andererseits wurde kürzlich der Nutzen von Verblindungen in RCTs diskutiert. Eine Meta-Epidemiologische Studie fand keinen Nachweis für einen Unterschied in den geschätzten Behandlungseffekten zwischen Studien mit und ohne verblindete Studienteilnehmenden, Gesundheitsdienstleister oder Ergebnisbeurteilern.[209] Eine weitere

Limitation der in dieser Habilitationsschrift vorgestellten RCTs und der Beobachtungsstudie ist, dass die UEs nicht durch die Patienten und Patientinnen in Tagebüchern erfasst wurden, sondern während der Behandlungstermine oder – und hierzu wurden die Studienteilnehmenden explizit ermutigt – mittels Benachrichtigungen an das Studienzentrum. Die Erfassung von UEs während der Behandlungstermine entspricht einerseits der üblichen medizinischen Praxis außerhalb von Studien, andererseits könnte es hierdurch zu einer Untererfassung von UEs gekommen sein. Robustere Ergebnisse zu eher selten vorkommenden UEs können zudem wenig valide in kleinen Studien ermittelt werden, hierzu wären eher größere Studien mit höheren Fallzahlen notwendig.
In den zwei RCTs,[199, 200] welche die Wirksamkeit von körperbasierten Behandlungsansätzen bei Patienten und Patientinnen mit CNP untersucht haben, wurden gesundheitsökonomische Analysen einbezogen. Hier stellen aus gesundheitsökonomischer Sicht die relativ kurzen Studienzeiträume eine Limitation dar. Längere Zeiträume hätten möglicherweise robustere Ergebnisse in Bezug auf die Analysen der Kosteneffektivität erlaubt. Eine spezifische Limitation der prospektiven Beobachtungsstudie[206] ist das Fehlen einer Kontrollgruppe. Dieses einarmige Design war auch geeignet, weitestgehend die real praktizierte Versorgung mit Osteopathischer Medizin, zusätzlich zur Regelversorgung, an unserer Hochschulambulanz zu beobachten und allen Studieninteressierten mit chronischen muskuloskelettalen Schmerzen ohne Verzögerung eine Behandlung mit Osteopathischer Medizin anzubieten. Dennoch, durch das Fehlen einer Kontrollgruppe könnten die beobachten Effekte klinisch relevanter Verbesserungen auch auf Studieneffekte, einschließlich des Hawthorne-Effekts (*observer effects),*[210, 211] zurückzuführen sein. Diese Beobachtungen sollten in konfirmatorischen RCTs auf Basis der in dieser Studie generierten Daten, validiert werden.

3.3 Diskussion der Ergebnisse der Studien übergreifend

Körperbasierte Behandlungsansätze der KIM werden von und bei Patienten und Patientinnen mit chronischen muskuloskelettalen Schmerzen genutzt und angewandt, auch wenn die wissenschaftliche Evidenz teilweise noch sehr unzureichend ist.

3.3.1 Körperbasierte Behandlungsansätze bei Musizierenden sowie Patienten und Patientinnen der Allgemeinbevölkerung mit chronischen Halswirbelsäulenschmerzen

Die hier präsentierte RCT zur Untersuchung der Wirksamkeit der Osteopathischen Medizin bei hohen Streichern und Streicherinnen mit CNP[199] ist die erste, welche die Wirksamkeit von Osteopathischer Medizin, eingebettet in ein Behandlungskonzept von Musikermedizinischer Beratung und analgetischer Bedarfsmedikation, bei beruflich Musizierenden (Musikstudierende eingeschlossen) untersucht hat. Vorausgehende RCTs fanden Symptomlinderungen bei Musizierenden mit muskuloskelettalen Schmerzen nach körperlicher Bewegung[212, 213] und nach Tuina,[214, 215] jedoch nicht nach Yoga.[216] Für Musikstudierende im Fach Violine mit unspezifischen HWS-Schmerzen könnten Stabilisationsübungen an der Halswirbelsäule Beschwerden lindern. Hierauf deutet eine neuere

einarmige Studie hin.[217] In der Allgemeinbevölkerung fand eine Meta-Analyse zur Wirksamkeit (*effectiveness*) von Osteopathischer Medizin bei Patienten und Patientinnen mit CNP[137] anhand von drei RCTs (n = 123) Evidenz von moderater Qualität hinsichtlich einer signifikanten und klinisch relevanten Schmerzlinderung. Der mittlere Unterschied der Schmerzintensität auf einer VAS (0-100 mm) betrug MD (95% KI) -13,04 (-20,64; -5,44),[137] während die in dieser Habilitationsschrift dargestellte RCT an 62 hohen Streichern und Streicherinnen einen mittleren Unterschied auf der VAS (0-100 mm) von MD (95% KI) -26,2 mm (-35,2; -17,2), p < 0,001, Cohen's d = 1,4) ermittelt hatte.[199] Ein im April 2022 veröffentlichter Überblick systematischer Reviews und Meta-Analysen bestätigte die Hinweise für die Wirksamkeit von Osteopathischer Medizin bei muskuloskelettalen Schmerzen.[141] Eine kürzlich veröffentlichte Meta-Analyse fand bei Patienten und Patientinnen mit unspezifischen Schmerzen im Bereich der HWS, bei sehr geringer Qualität der Evidenz, eine statistisch signifikante Minderung der Schmerzstärke (*effect size* -1,57 (-2,50; -0,65), p < 0,001) und Verbesserung des funktionellen Status (*effect size* -1,71 (-3,12; -0,31), p = 0,02) zugunsten der Osteopathische Medizin im Vergleich zu keiner Intervention/ beziehungsweise Scheinbehandlungen.[218] Die in dieser Habilitationsschrift vorgestellte RCT[199] war in die besagte Meta-Analyse eingeschlossen worden.

Die wissenschaftliche Evidenz zur Wirksamkeit und Sicherheit von Tuina bei Patienten und Patientinnen mit CNP ist noch limitiert.[150] Eine Meta-Analyse von Cheng et al. (2014)[150] zur Wirksamkeit von Massagetherapien bei Patienten und Patientinnen mit CNP schloss 14 RCTs (davon 7 RCTs zur Tuina) ein und fand moderate Evidenz für eine kurzfristige Schmerzlinderung insbesondere im Vergleich zu inaktiven Therapien (n = 153, *standardized mean difference* (95% KI) -1,30 (-0,09; -2,50), p = 0,03) und limitierte Evidenz im Vergleich zur (übrigen) Chinesischen Medizin (n = 125, *standardized mean difference* (95% KI) -0,73 (-0,13; -1,33), p = 0,02). Mittels der in dieser Habilitationsschrift einbezogenen RCT an Patienten und Patientinnen mit CNP fanden wir nach sechs Tuina-Behandlungen zum Messzeitpunkt vier Wochen nach Baseline eine im Vergleich zu dieser Meta-Analyse[150] deutlichere Schmerzlinderung mit MD (95% KI) -22,8 mm (-31,7; -13,8), p < 0,001. Zudem blieb in unserer RCT die Wirkung zum Messzeitpunkt 12 Wochen nach Baseline erhalten.[200] Inwieweit sich diese Ergebnisse auch bei hohen Streichern und Streicherinnen analog der RCT zur Osteopathischen Medizin[199] hätten darstellen lassen, kann aufgrund der besonderen beruflichen Beanspruchung der Musizierenden nicht abgeleitet werden. Allerdings berichteten Sousa et al. bei Orchestermusikern und Orchestermusikerinnen mit muskuloskelettalen Schmerzen, welche entweder zu Tuina (n = 39) oder Sham-Tuina (n = 30) randomisiert wurden, über eine Wirksamkeit von Tuina.[214, 215]

In beiden in dieser Habilitationsschrift vorgestellten Studien an Patienten und Patientinnen mit CNP wurden die Kosten und die Kosteneffektivität untersucht. Es konnten weder für die Osteopathische

Medizin noch für die Tuina jeweils im Vergleich zur Kontrolle Gruppenunterschiede hinsichtlich der qualitätsadjustierten Lebensjahre oder der Kosteneffektivität ermittelt werden.

Beide RCTs tragen entscheidend zur wissenschaftlichen Evidenzlage der Medizin bei, da wenige Studien zur Osteopathischen Medizin oder Tuina bei CNP und bisher keine weiteren Studien zur Osteopathischen Medizin bei hohen Streichern und Streicherinnen mit CNP veröffentlicht wurden.

3.3.2 Körperbasierte Behandlungsansätze bei Patienten und Patientinnen mit chronischen Lendenwirbelsäulenschmerzen

Zwei in dieser Habilitationsschrift vorgestellte RCTs untersuchten bei Patienten und Patientinnen mit CLBP die Wirksamkeit von zwei Arten des trockenen Schröpfens[202] beziehungsweise eines Mindful Walking Programms, letztere als einzige in dieser Habilitationsschrift vorgestellte Intervention im Gruppensetting.[201]

Die RCT zur Wirksamkeit des trockenen Schröpfens bei Patienten und Patientinnen mit CLBP[202] war die erste, in welcher pulsierendes Schröpfen plus Bedarfsmedikation und minimales Schröpfen plus Bedarfsmedikation mit einer Kontrolle von Bedarfsmedikation alleinig verglichen wurde. Nach Interventionsende (vier Wochen) waren beide Schröpfarten bei Patienten und Patientinnen mit CLBP wirksam im Vergleich zur Kontrolle, jedoch nicht in direktem Vergleich miteinander. Rückschlüsse auf mögliche spezifische Wirkmechanismen des Schröpfens konnten nicht gezogen werden. Diese Schröpfstudie[202] wurde in eine Meta-Analyse[219] eingeschlossen, an welcher auch die Autorin dieser Habilitationsschrift mitgearbeitet hat. In dieser Meta-Analyse sollte die wissenschaftliche Evidenz zur Wirksamkeit und Sicherheit des Schröpfens als nichtpharmalogische Therapieoption für Patientinnen und Patienten mit chronischen Schmerzen zusammengefasst werden. Das Verzerrungsrisiko der bis November 2018 publizierten und eingeschlossenen RCTs wurde mittels des Cochrane *Risk of Bias Tool* bewertet. Es wurden 18 RCTs eingeschlossenen, welche zumeist Schröpftherapien an insgesamt 1.172 Patienten und Patientinnen mit chronischen muskuloskelettalen Schmerzen untersucht hatten. In dieser Meta-Analyse fanden wir trotz klinischer Heterogenität und Verzerrungsrisiken Hinweise darauf, dass Schröpfen für Patienten und Patientinnen mit chronischen muskuloskelettalen Schmerzen, einschließlich CLBP und CNP, eine körperbasierte Behandlungsoption darstellen könnte. Diese Ergebnisse gehen konform mit einer im selben Jahr publizierten Meta-Analyse von Wood et al.,[156] welche die Wirksamkeit und Sicherheit westlicher Methoden des trockenen Schröpfen bei muskuloskelettalen Schmerzen an 21 RCTs (n = 1.049) untersuchte. Die Autoren fanden Hinweise von geringer Qualität dafür, dass trockenes Schröpfen eine signifikante Verminderung der Schmerzintensität (VAS, 0-100 mm) bei CNP mit MD (95% KI) von -21,67 (-36,55; -6,80) und LWS-Scherzen mit MD (95% KI) -19,38 (-28,09; -10,66) hat. Weiterhin fanden Wood et al. Hinweise von mäßiger Qualität auf eine Verbesserung der Funktion bei CNP. Eine im Jahr 2015 publizierte Meta-Analyse[109] zur Wirksamkeit von Verfahren der Chinesischen Medizin

schloss 75 RCTs (n = 11.077) ein. Beinahe sämtliche Studien untersuchten Personen, die an CNP oder CLBP litten. Auch hier fanden sich vergleichbare Hinweise für eine Wirksamkeit des Schröpfens auf die Schmerzintensität (VAS, 0-100 mm) im Vergleich zu einer Kontrolle im Wartelisten-Design für CNP (MD (95% KI) -19,10 (-27,61; -10,58), p < 0,001) beziehungsweise im Vergleich zu Analgetika (z.B. nichtsteroidale Antirheumatika) für CLBP (MD (95% KI) -5,4 (-8,9; -0,19), p = 0,003).

Die in dieser Habilitationsschrift dargestellte RCT zur Wirksamkeit und Sicherheit eines Mindful Walking Programms[201] bei Patienten und Patientinnen mit CLBP fand im Vergleich zur Kontrolle keine signifikante oder klinisch relevante Verminderung der Schmerzintensität gemessen auf einer VAS (0-100 mm) mit MD (95% KI) -9,6 (-22,3; 3,1), p = 0,136. Dies könnte möglicherweise auch darauf zurückzuführen sein, dass der erwartete Behandlungseffekt bei der Fallzahlberechnung überschätzt wurde. Eine Meta-Analyse (2018)[162] schloss vier RCTs ein, in denen Interventionen der Achtsamkeit des MBSR (n = 171) mit der Regelversorgung (n = 155) verglichen wurden. Im Ergebnis fand sich eine kurzfristige, statistisch signifikante Verminderung der Schmerzintensität (numerische Ratingskala, NRS, 0-10) von MD (95% KI) -0,96 (-1,64; -0,34). Michalsen et al.[220] untersuchten in einer RCT an 68 Patienten und Patientinnen mit CLBP Meditation als mindful-basiertem Ansatz (gezielte Meditation versus Selbstfürsorgeübung) und fanden ebenso keinen Gruppenunterschied hinsichtlich des primären Endpunktes der Schmerzintensität, gemessen auf einer VAS. Zudem erhielten die Studienteilnehmenden im Mindful Walking keine direkte körperliche Behandlung, im Gegensatz zu den anderen im Rahmen dieser Habilitationsschrift untersuchten Behandlungsmodalitäten.

Insgesamt können die untersuchten körperbasierten Behandlungsansätze der KIM eine wertvolle Ergänzung der konventionell-hochschulmedizinischen, multimodalen Therapie bei Patienten und Patientinnen mit CNP, CLBP sowie potentiell mit weiteren chronischen muskuloskelettalen Schmerzen darstellen. Dies sollte jedoch in zukünftigen multizentrischen, hochqualitativen konfirmatorischen Studien mit beispielsweise aktiven Vergleichstherapien der konventionellen Hochschulmedizin weitergehend wissenschaftlich untersucht werden. Dazu könnte die *efficacy* einzelner Interventionen wie Osteopathischer Medizin, Tuina und Schröpfen im Vergleich zu sham-Interventionen wie osteopathische Schein-Behandlungen ohne therapeutische Intention, Scheinbehandlungen außerhalb der Meridiane der Chinesischen Medizin oder Schröpfen an unwirksam erachteten anatomischen Regionen untersucht werden.

Im Abschnitt 1.2.2 wurden mögliche übergreifende Wirktheorien und Wirkmechanismen für körperbasierte Behandlungsansätze beschrieben. Hierzu zählen die Anregung von nozizeptiven C-Fasern, von Aδ-Fasern und von mechanozeptiven Aβ-Fasern, die Hemmung rezeptiver Felder der multirezeptiven Dorsalhornneuronen durch mechanische Einflüsse.[77-79] Weiterhin wurden hierzu Theorien und verschiedenartige wissenschaftliche Untersuchungen zu somatischen und viszeral übertragenen Phänomen, als auch Illustrationen zum viszeral übertragenen Schmerz, auch aus der

Arbeitsgruppe um Beissner et al. publiziert.[20-26, 77-81] In diesen Bereichen könnten weiterführende wissenschaftliche Untersuchungen in enger Verbindung von Klinik und Grundlagenforschung wegweisend sein.

3.3.3 Ausblick in die Zukunft – Einstellung von Medizinstudierenden zur Komplementären und Integrativen Medizin

Eine Integrierte Gesundheitsversorgung wird entsprechend der Astana Deklaration von der WHO befürwortet.[55] International unterrichten bis zu 81% der medizinischen Hochschulen Verfahren der KIM in insgesamt sehr heterogenen Curricula mit zumeist unzureichender Lernerfolgsbewertung (Kirkpatrick's Level 1 und/ oder 2).[221, 222] Studierende haben wenig Wissen über KIM, daher wurde eine stärkere Integration in die universitäre Lehre befürwortet.[223, 224] An der Charité – Universitätsmedizin Berlin verfolgt das aktuelle Medizinische Curriculum im Modellstudiengang einen kompetenzbasierten Lehransatz.[225] Eine Kombination aus zusätzlich angebotener kritischer KIM-Lehre mit praktischer Erfahrung unter Vermittlung der jeweiligen wissenschaftlichen Evidenz könnte jedoch zur Entwicklung einer ganzheitlichen, patientenorientierten Einstellung bei Medizinstudierenden beitragen.[226] Das Wissen über die Einstellung der künftigen Medizinergeneration zur KIM in Deutschland ist unzureichend. Daher haben wir im Institut für Sozialmedizin, Epidemiologie und Gesundheitsökonomie, Charité – Universitätsmedizin Berlin mittels einer online-basierten explorativen Querschnittsstudie an der Charité – Universitätsmedizin Berlin die Einstellung von Medizinstudierenden zu KIM im Allgemeinen sowie ihre Einstellung zur KIM in der universitären Forschung und Lehre untersucht.[66] Die 349 Teilnehmenden (Rücklaufquote 27,8% aus dem ersten und fünften Studienjahr) waren (MW ± SD) 23,7 ± 4,3 Jahre alt und zu 69,0% weiblich. Die Einstellung zur KIM wurde mittels *Complementary and Alternative Medicine Health Belief Questionnaire* (CHBQ, Range 10-70, neutral 40; ein höherer Wert bedeutet eine positivere Einstellung) als eher neutral bei einem CHBQ von 44,2 ± 10,7 ermittelt. Die Ergebnisse weiterer Fragen (nicht validiert) deuteten jedoch darauf hin, dass Medizinstudierende Forschung und Lehre im Bereich der KIM befürworten.[66]

3.4 Empfehlungen für zukünftige Forschungen

Die Förderung der muskuloskelettalen Gesundheit ist ein wichtiges internationales Anliegen für die Zukunft.[227] Die Ergebnisse der hier dargestellten RCTs und der prospektiven Beobachtungsstudie sollten mittels multizentrischer hochqualitativer konfirmatorischer klinischer Studien weiter erforscht werden. Hierzu sollte auch die spezifische Wirkung (*efficacy*) von Osteopathischer Medizin, Tuina und Schröpfen im Vergleich zu Schein- (*sham*-)Interventionen und zur Regelversorgung beziehungsweise mit aktuell leitliniengerechten Standard-Interventionen (z.B. Analgetika jedoch nicht mehr Paracetamol bei CLBP,[44, 45] Physiotherapie, Psychotherapie) weiter untersucht werden. Im Rahmen der Versorgungsforschung sollte eine Implementierung von Osteopathischer Medizin, Tuina, Schröpfen und weiterer KIM Therapien in ein multimodales Behandlungskonzept für

ambulante Patienten und Patientinnen mit chronischen muskuloskelettalen Schmerzen erprobt und durch wissenschaftliche Untersuchungen begleitet werden. Hierzu sollten auch objektiv messbare Endpunkte einbezogen werden. Die Sicherheit, sowie die Kosten und Kosteneffektivität von körperbasierten Behandlungsansätzen der KIM sowie deren Implementierung in die Regelversorgung sollten zukünftig in größeren und längerfristigen klinischen Studien sowie im Rahmen der Versorgungsforschung wissenschaftlich untersucht werden. Weitergehend sollten bei wissenschaftlicher Evidenz für eine Wirksamkeit *(effectiveness)*, spezifische Wirkung *(efficacy),* Sicherheit und Kosteneffektivität für die betreffenden körperbasierten Behandlungsansätze die Reliabilität deren körperbasierter Diagnostikkonzepte als auch deren unterliegende Wirktheorien im Rahmen der Grundlagenforschung weitergehend wissenschaftlich untersucht werden.

4. Zusammenfassung

Chronische muskuloskelettale Schmerzen, insbesondere chronische Schmerzen im Bereich der Halswirbelsäule und der Lendenwirbelsäule, gehören global zu den führenden Erkrankungen und führen häufig zu hohen persönlichen Beeinträchtigungen, zu hohen Krankenständen sowie zu hohen gesellschaftlichen Kosten. In die Behandlung von chronischen muskuloskelettalen Schmerzen können körperbasierte Diagnostik- und Therapiekonzepte der Komplementären und Integrativen Medizin in das multimodale Behandlungskonzept einbezogen werden. Im Rahmen dieser Habilitationsschrift wurden in vier randomisiert kontrollierten Studien und einer Beobachtungsstudie körperbasierte Behandlungsansätze wissenschaftlich untersucht.

Bei Patienten und Patientinnen mit chronischen Schmerzen im Bereich der Halswirbelsäule wurden die Wirksamkeit und Therapiesicherheit von Osteopathischer Medizin beziehungsweise von Tuina, bei Patienten und Patientinnen mit chronischen Schmerzen im Bereich der Lendenwirbelsäule wurden die Wirksamkeit und Therapiesicherheit von Schröpfen beziehungsweise Mindful Walking untersucht. Der primäre Endpunkt war jeweils die in den letzten sieben Tagen subjektiv empfundene mittleren Schmerzintensität gemessen auf einer visuellen Analogskala (0-100 mm) nach Beendigung der Interventionsphase im Intergruppenvergleich. Bei hohen Streichern und Streicherinnen mit chronischen Schmerzen im Bereich der Halswirbelsäule fand sich nach fünf Behandlungen mit Osteopathischer Medizin im Vergleich zu einer Kontrollgruppe ohne Osteopathische Medizin eine statistisch signifikante und klinisch relevante Schmerzreduktion bei einer Mittelwertdifferenz (95% Konfidenzintervall) von -26,2 mm (-35,2; -17,2), $p < 0,001$. Patientinnen und Patienten mit chronischen Schmerzen im Bereich der Halswirbelsäule hatten nach sechs Sitzungen Tuina im Vergleich zu einer Kontrollgruppe ohne Tuina eine statistisch signifikante und klinisch relevante Schmerzreduktion bei einer Mittelwertdifferenz -22,8 mm (-31,7; -13,8), $p < 0.001$. Bei Patienten und Patientinnen mit chronischen Schmerzen im Bereich der Lendenwirbelsäule wurden nach acht Anwendungen des pulsierenden Schröpfens beziehungsweise des minimalen Schröpfens im Vergleich zu einer Kontrollgruppe ohne Schröpfen eine statistisch signifikante und klinisch relevante Schmerzlinderung bei einer Mittelwertdifferenz von -21,2 mm (-12,2; -30,1), $p < 0,001$ beziehungsweise -15,7 mm (-6,9; -24,4), $p = 0,001$ ermittelt. Nach acht Gruppenanwendungen Mindful Walking im Vergleich zu keiner studienspezifischen Therapie konnte bei Patienten und Patientinnen mit chronischen Lendenwirbelsäulenschmerzen keine signifikante oder klinisch relevante Schmerzreduktion, Mittelwertdifferenz (95% Konfidenzintervall) -9,6 mm (-22,3; 3,1), $p = 0,136$ ermittelt werden.

In Zusammenschau dieser Ergebnisse mit einer Beobachtungsstudie zu Effekten der Osteopathischen Medizin bei Patienten und Patientinnen mit chronischen Schmerzen im Bereich der Halswirbelsäule, chronischen Schmerzen im Bereich der Lendenwirbelsäule, chronischen Knie- und chronischen Schulterschmerzen fanden sich Hinweise, dass nichtpharmakologische körperbasierte

Behandlungsansätze der Komplementären und Integrativem Medizin eine wirksame und sichere Ergänzung der konventionell-hochschulmedizinischen (biomedizinischen) Therapie darstellen könnten. Diese Hinweise sollten in zukünftigen multizentrischen, konfirmatorischen Studien hinsichtlich Wirksamkeit *(effectiveness)* in der Regelversorgung und spezifischer Wirkung *(efficacy)* weitergehend wissenschaftlich untersucht werden. Die Kosten und Kosteneffektivität von körperbasierten Behandlungsansätzen der Komplementären und Integrativen Medizin sowie deren Implementierung in die Regelversorgung sollten zukünftig in multizentrischen klinischen Studien mit hohen Zahlen von Teilnehmenden (Fallzahlen) sowie im Rahmen der Versorgungsforschung wissenschaftlich untersucht werden. Für nachgewiesen wirksame *(effectiveness und efficacy),* sichere und kosteneffektive körperbasierte Behandlungsansätze sollte die Reliabilität von deren körperbasierten Diagnostikkonzepten und deren unterliegenden Wirktheorien im Rahmen der Grundlagenforschung weitergehend wissenschaftlich untersucht werden. Die wissenschaftliche Evidenz zu bestehendem und auch nicht bestehendem Wirknachweis, Therapiesicherheit und/oder Kosteneffektivität sollte für Medizinstudierende transparent gelehrt werden. Dabei gilt es auch die Grenzen der Behandlungsindikationen darzustellen. Betreffende körperbasierte Behandlungsansätze der Komplementären und Integrativem Medizin mit positiver wissenschaftlicher Evidenz für eine Wirksamkeit und/oder Kosteneffektivität könnten in die Hochschullehre integriert werden. Zur Versorgung von Patienten und Patientinnen mit chronischen muskuloskelettalen Schmerzen ist eine zukünftig wachsende wechselseitige Integration von klinischer Versorgung, praxisnaher Forschung und Lehre auch zu körperbasierten Behandlungsverfahren der Komplementären und Integrativem Medizin wegweisend. Dies unterstützt auch die Umsetzung der Visionen der Astana Deklaration der *World Health Organization* auf eine qualitativ hochwertige, sichere, umfassende, integrierte, zugängliche, verfügbare und finanziell erschwingliche medizinische Grundversorgung.

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Erklärung

§ 4 Abs. 3 (k) der HabOMed der Charité

Hiermit erkläre ich, dass

- weder früher noch gleichzeitig ein Habilitationsverfahren durchgeführt oder angemeldet wurde,
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- mir die geltende Habilitationsordnung bekannt ist.

Ich erkläre ferner, dass mir die Satzung der Charité – Universitätsmedizin Berlin zur Sicherung Guter Wissenschaftlicher Praxis bekannt ist und ich mich zur Einhaltung dieser Satzung verpflichte.

12.12.2022

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Dr. Gabriele Rotter