SVEUČILIŠTE U SPLITU

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PROCJENA OPORAVKA PACIJENATA S TRZAJNOM OZLJEDOM VRATA NAKON FIZIKALNE TERAPIJE KORIŠTENJEM ELASTOGRAFIJE POSMIČNIM VALOM I INDEKSA ONESPOSOBLJENOSTI VRATNE KRALJEŽNICE ŠEST MJESECI NAKON PROMETNE NEZGODE

DOKTORSKI RAD

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SADRŽAJ

1. POPIS OZNAKA I KRATICA

AIC	Akaike informacijski kriterij (engl. Akaike Information Criterion)
HRQoL	kvaliteta života povezana sa zdravstvenim stanjem (engl. Health-Related Quality of Life)
ICC	interklasni koeficijenti korelacije (engl. intraclass correlation coefficient)
kPa	kilopaskal
NDI	Indeks onesposobljenosti vratne kralježnice (engl. Neck Disability Index)
PCS	Upitnik o katastrofiziranju boli (engl. Pain Catastrophizing Scale)
PHQ-9	Upitnik o zdravlju pacijenta-9 (engl. Patient Health Questinnaire-9)
PROM	engl. patient reported outcome measure
RCT	randomizirano kontrolirani pokus (engl. randomized controlled trial)
SF-12	upitnik o kvaliteti života kratkog oblika (engl. Short Form 12)
SWE	elastografija posmičnim valom (engl. shear wave elastography)
TENS	transkutana električna živčana stimulacija (engl. transcutenous electrical nerve stimulation)
VAS	vizualno-analogna skala

2. POPIS RADOVA NA KOJIMA SE TEMELJI DOKTORSKI RAD

1. Neck Disability Index Is Better in Classification of Recovery after Whiplash Injury in Comparison with Ultrasound Shear Wave Elastography of Trapezius Muscle. Diagnostics (Basel). 2021;11(11):2077. doi: 10.3390/diagnostics11112077 (2021 JIF = 3,992).
2. Lack of Objective Measurement in the Initial Screening and Follow-Up of Patients Who Report Whiplash Injury—Is Elastography of the Trapezius Muscle an Answer? Journal of Clinical Medicine. 2022; 11(13):3851. doi: 10.3390/jcm11133851 (2022 JIF = 3,9).
3. Mobile App Intervention Increases Adherence to Home Exercise Program After Whiplash Injury—A Randomized Controlled Trial (RCT). Diagnostics. 2024; 14(23):2729. doi: 10.3390/diagnostics14232729 (2023 JIF = 3,0).

3. UVOD

Trzajna ozljeda vrata najčešća je ozljeda povezana s prometnim nesrećama (1) te podrazumijeva mekotkivnu ili koštanu ozljedu koja je nastala naglim naprijed-natrag pokretom glave i vrata (2). Do trzajne ozljede vrata uglavnom dolazi u prometnim nesrećama i to najčešće udarcem prednjeg dijela jednog vozila u stražnji dio drugog, ali se može zadobiti i prilikom pada (npr. pad s bicikla), sportskih ozljeda i ostalih nesreća. U razvijenim zemljama procijenjena godišnja incidencija trzajne ozljede vrata iznosi barem 300 na 100 000 stanovnika (3) s višom incidencijom kod adolescenata i odraslih od 15. do 64. godine života (4). Godišnji troškovi zbog liječenja i smanjene produktivnosti nakon ozljede su visoki i iznose oko 10 milijardi eura u SAD-u i Europi (5). S biomehaničkog gledišta, do ozljede dolazi u inicijalnoj fazi kada se glava i gornji vratni segment flektiraju, a donji dio vrata ekstendira te se stvara tzv. „S“ oblik vratne kralježnice (6). Simptomi nakon ozljede su raznoliki, a većina ozlijeđenih inicijalno pati zbog vratobolje praćene ograničenjem kretnji vrata i ramena, boli u ramenima, glavoboljom, poteškoćama sa spavanjem, ukočenošću vrata, trnjenjem ruku, anksioznosti, vrtoglavicom (2, 7). Nadalje, više od trećine ozlijeđenih razvije kroničnu bol i onesposobljenost, ima ograničenja u radu, socijalnim interakcijama i, posljedično svemu, ima lošiju kvalitetu života (8, 9). Sve navedeno pokazuje kako trzajna ozljeda stvara značajan socioekonomski problem (3).

Kao zlatni standard u procjeni trzajne ozljede, kao i u prognoziranju i praćenju oporavka, koristimo subjektivne mjere- upitnike za procjenu ishoda koje ispunjavaju bolesnici (engl. patient-reported outcome measures, skr. PROMs). Kako bi se ujednačili ishodi istraživanja i omogućilo njihovo uspoređivanje, 2019. godine napravljen je sržni set ishoda za procjenu trzajne ozljede vrata koji uključuje fizičko i psihičko funkcioniranje, subjektivni osjećaj oporavka, radnu sposobnost i socijalno funkcioniranje, kvalitetu života povezanu sa zdravstvenim stanjem (engl. Health-related quality of life, skr. HRQoL) i bol (10). Od svih ishoda mjerenih upitnicima, izdvaja se Indeks onesposobljenosti vratne kralježnice (engl. Neck Disability Index, skr. NDI) koji se pokazao pouzdanim, točnim i osjetljivim na promjenu kod osoba nakon trzajne ozljede vrata (11, 12) te ga sustavni pregledni rad Griffin, Leaver (13) i sur. iz 2021. godine izdvaja kao najprikladniji za procjenu onesposobljenosti nakon trzajne ozljede vrata. NDI se sastoji od deset kategorija kojima se ispituju različiti aspekti zdravlja. Dobivenim rezultatom osoba se kategorizira u jednu od pet razina onesposobljenosti (bez onesposobljenosti, blaga, umjerena, teška ili potpuna onesposobljenost).

Objektivne metode, kao što su slikovne metode vratne kralježnice (klasična radiografija, kompjutorizirana tomografija i magnetska rezonancija), istraživale su se u svrhu procjene težine ozljede, prognoze te procjene oporavka, međutim nisu se pokazale kao primjenjive (14).

Ultrazvučna elastografija posmičnim valom (engl. shear wave elastography, skr. SWE) je relativno nova radiološka metoda kojom se mogu analizirati strukturne promjene različitih tkiva, uključujući mišiće (15). Ultrazvuk je široko dostupan, omogućava brzu procjenu te nije štetan za ispitanika. Zbog ovih prednosti ultrazvuka mogućnosti primjene ultrazvučne SWE se u kliničkoj praksi naširoko istražuju (16). SWE-om se procjenjuju elastična svojstva mekih tkiva, a dobivene vrijednosti se izražavaju u jedinicama tlaka (kilopaskali, skr. kPa) (17).

Naša grupa autora procjenjivala je mogućnost primjene SWE nakon trzajne ozljede vrata na različitim mišićima vrata (m. splenius capitis, m. sternocleidomastoideus, m. trapezius). Od ispitivanih mišića, jedino se trapezni mišić izdvojio s pravilnom distribucijom napetosti uz nađenu značajnu razliku u napetosti trapeznog mišića između osoba s trzajnom ozljedom vrata i opće populacije (18). Međutim, ostalo je nepoznato je li SWE trapeznih mišića reproducibilna metoda, kako se elastrografske vrijednosti mijenjaju nakon fizikalne terapije, može li se koristiti u prognoziranju ili u praćenju oporavka nakon trzajne ozljede vrata.

Konzervativno liječenje je osnova liječenja trzajne ozljede vrata te uključuje edukaciju, terapijske vježbe, pasivne terapijske procedure kao što su transkutana električna živčana stimulacija (engl. transcutaneous electrical nerve stimulation, skr. TENS), terapijski ultrazvuk, laser, magnetoterapija (19), dok se u akutnoj fazi simptomi umanjuju uzimanjem analgetika i miorelaksansa. Do nedavno su se naširoko propisivali meki ovratnici i preporučalo mirovanje, što se pokazalo neučinkovitim. Danas se potiče rani povratak aktivnostima uz primjenu analgetika kod izraženih bolova (20).

Edukacija i terapijske vježbe su se pokazale učinkovitima u smanjenju dugotrajne onesposobljenosti i boli nakon trzajne ozljede (21, 22). Ako pogledamo učinkovitost vježbi, Himler, Lee (23) i sur. su u svom radu pokazali kako je utjecaj vježbi na ishod vratobolje izravno povezan s razinom adherencije. Međutim, dobro je poznat problem adheriranja bolesnika na dugotrajnu terapiju. Taj problem je prisutan i kod trzajne ozljede vrata, gdje je osnova liječenja provođenje terapijskih vježbi kroz duži vremenski period (24).

Kako bi pokušali poboljšati adherenciju na terapiju i tako poboljšati ishode liječenja, na polju fizikalne medicine i rehabilitacije postoji sve veći broj istraživanja u kojima se ispituje korisnost digitalnih tehnologija pa tako i mobilnih aplikacija. Tako je sustavni pregledni rad Lang, McLelland (25) i sur. pokazao kako se digitalnim intervencijama može povećati adherencija na provođenje vježbi kod kuće. Isto tako, Armfield, Elphinston (26) i sur. su u svom radu prezentirali kako se poticanjem putem mobilnih aplikacija može poboljšati adherencija na terapiju. Nije bilo poznato može li se korištenjem mobilnih aplikacija, putem push notifikacija, povećati adherencija bolesnika u provođenju terapijskih vježbi te smanjiti broj onesposobljenih osoba i težina onesposobljenosti nakon trzajne ozljede vrata.

4. PREGLED METODOLOGIJE OBJEDINJENIH RADOVA

4.1 Prvo istraživanje: Indeks onesposobljenosti vratne kralježnice je bolji u klasifikaciji oporavka nakon trzajne ozljede vrata u usporedbi s ultrazvučnom elastografijom trapeznog mišića posmičnim valom

Proveli smo prospektivno opažajno istraživanje od siječnja 2020. do veljače 2021. u Zavodu za fizikalnu medicinu i rehabilitaciju s reumatologijom KBC-a Split. U istraživanje smo uključili odrasle osobe s trzajnom ozljedom vrata koje su ozljedu zadobile unutar 90 dana u automobilskoj nesreći u kojoj su sudjelovali kao vozači ili suvozači. Dijagnoza je potvrđena od strane specijalista fizikalne medicine i rehabilitacije. Isključeni su svi koji su u nesreći zadobili kostolom, ozljedu kralježničke moždine, koji su liječili ili liječe malignu bolesti u posljednjih pet godina od ozljede te oni koji liječe tešku mentalnu bolest. Svi ispitanici potpisali su informirani pristanak prije uključivanja u istraživanje.

Svi sudionici su proveli standardni program fizikalne terapije koji je uključivao terapijske vježbe, terapijski ultrazvuk i TENS. Program je uključivao dva ciklusa fizikalne terapije, svaki trajanja 2 tjedna, 5x tjedno, uz 3 tjedna pauze između ciklusa. Po završetku programa fizikalne terapije ispitanici su dobili pisane i slikovne upute o vježbama koje je potrebno provoditi kod kuće.

Ishodi su mjereni u dvije vremenske točke, inicijalno i šest mjeseci od ozljede. Primarni ishod bila je napetost trapeznih mišića izmjerena sa SWE. Sekundarni ishodi bili su fizičko funkcioniranje, psihološko funkcioniranje i oporavak procijenjen od strane ispitanika.

Dva radiologa izvodila su SWE trapeznih mišića pri čemu su koristili linearnu multifrekvencijsku sondu (2-10 MHz, Aixplorer Supersonic Ultrasound system, Aix en Provence, France). Napetost trapeznog mišića izražena je u kPa. Radiolozi su mjerenja izvodili neovisno jedan od drugoga i nepoznavajući status ispitanika. Za svaki trapezni mišić mjerenje je ponovljeno tri puta. Hrvatska verzija NDI-a korištena je u procjeni fizičkog funkcioniranja, a Upitnik o zdravlju pacijenta-9 (engl. Patient Health Questinnaire-9, skr. PHQ-9) za procjenu psihološkog funkcioniranja, u procjeni subjektivnog osjećaja oporavka korištena je trostupanjska Likertova skala (1-potpuni oporavak, 2-parcijalni oporavak, 3-bez ikakvog oporavka).

Temeljem pilot studije (n=14 parova) izračunata je potrebna veličina uzorka (n=20 parova). Konačni broj sudionika izračunat je kao 50% veći od dobivenog analizom snage (n=30). Za

procjenu pouzdanosti elastografskih mjerenja korišteni su intraklasni koeficijenti korelacije (engl. intraclass correlation coefficient, skr. ICC). Prediktivni model oporavka izračunat je korišenjem ordinalne logističke regresije.

4.2 Drugo istraživanje: Nedostatak objektivnog mjerenja u početnom pregledu i praćenju pacijenata koji prijavljuju trzajnu ozljedu – je li elastografija trapeznog mišića rješenje?

Napravili smo sekundarnu analizu podataka dobivenih iz naša dva prethodna istraživanja koja se odnose na korištenje SWE trapeznih mišića kod trzajne ozljede vrata. Sudionici su bili osobe nakon trzajne ozljede vrata te kontrolna skupina iz opće populacije. Kriteriji uključivanja i isključivanja sudionika nakon trzajne ozljede vrata opisani su u metodama prvog istraživanja.

Napetost trapeznih mišića bila je primarni ishod, mjerena sa SWE. Učinjena je osobama s trzajnom ozljedom vrata u dvije vremenske točke, inicijalno i šest mjeseci nakon ozljede. Kontrolnoj skupini mjerenje je učinjeno u jednoj vremenskoj točki. Drugi ishodi bili su fizička onesposobljenost mjerena NDI-om i oporavak procijenjen od strane ispitanika.

Za izračun povezanosti kontinuiranih varijabli korišten je t-test. Za izračun klasifikacijskih modela vjerojatnosti pojave trzajne ozljede vrata te izračun granične napetosti trapeznih mišića korištena je logistička regresija.

4.3 Treće istraživanje: Intervencija putem mobilne aplikacije povećava adherenciju na provođenje programa vježbi kod kuće nakon trzajne ozljede vrata – randomizirano kontrolirani pokus (RCT)

Proveli smo randomizirano kontrolirani pokus (engl. randomized controlled trial, skr. RCT) s ciljem procjene učinka dodavanja mobilne aplikacije standardnoj terapiji na adherenciju u provođenju vježbi kod kuće te na oporavak nakon trzajne ozljede vrata. Istraživanje je provedeno od siječnja 2023. do kolovoza 2024. godine u Zavodu za Fizikalnu medicinu i rehabilitaciju s reumatologijom KBC-a Split. Prije početka studije protokol istraživanja je objavljen na platformi za prijavu protokola kliničkih istraživanja – clinicaltrials.gov (NCT05704023).

Ispitanici su bili osobe nakon trzajne ozljede vrata. Kriteriji uključivanja i isključivanja opisani su u metodama prvog istraživanja uz dodatni kriterij isključivanja – nemogućnost korištenja mobilnih aplikacija. Svi ispitanici su potpisali informirani pristanak prije uključivanja u istraživanje.

Ispitanici su nakon uključivanja u istraživanje započeli program standardne fizikalne terapije čiji je protokol opisan u metodama prvog istraživanja. Po završetku prvog ciklusa fizikalne terapije, ispitanici su randomizirani u dvije skupine – intervencijsku i kontrolnu skupinu. Ispitanici u intervencijskoj skupini su na svoj pametni telefon preuzeli mobilnu aplikaciju koja je posebno razvijena u ovu svrhu. Svakodnevno su putem push notifikacije u 19:00 sati dobili podsjetnik na vježbanje. Također, unutar aplikacije dostupne su bile upute o vježbama. Kontrolna skupina je po završetku prvog ciklusa fizikalne terapije dobila pisane i usmene upute o nastavku provođenja vježbi kod kuće.

Primarni ishod bila je adherencija na vježbanje. Sekundarni ishodi bili su fizička i psihička onesposobljenost, informacije o radnoj sposobnosti, intenzitet boli, HRQoL te subjektivni osjećaj oporavka.

Adherenciju na vježbanje mjerili smo šest mjeseci od ozljede Likertovom skalom od 4 stupnja koja se odnosila na tjedno provođenje vježbi (od 1-ne vježbam uopće do 4-vježbam pet ili više puta tjedno). Sekundarni ishodi bili su fizičko funkcioniranje mjereno NDI-om, psihološko funkcioniranje mjereno pomoću Upitnika o katastrofiziranju boli (engl. Pain Catastrophizing Scale, skr. PCS), intenzitet boli mjeren vizualno-analognom skalom (VAS), kvaliteta života korištenjem Upitnika o kvaliteti života kratkog oblika (engl. Short Form 12, skr. SF-12), socijalno funkcioniranje (Likertova skala, od 1-neprestano ograničenje do 5-nema ograničenja), radna sposobnost (status zaposlenja, izostanak s posla, ograničenja u radu). Subjektivni osjećaj oporavka mjerili smo šest mjeseci od ozljede Likertovom skalom od 3 stupnja (1-potpuni oporavak, 2-parcijalni oporavak, 3-bez ikakvog oporavka).

Za veličinu uzorka korišten je uvriježeni način procjene kako je potrebno 10 do 30 sudionika po skupini za ovakvu vrstu istraživanja. Stoga smo planirali u svaku od skupina uključiti 30 sudionika.

Sudionici su randomizirani u intervencijsku ili kontrolnu skupinu korištenjem on-line randomizacijskog alata (randomizer.org) u omjeru 1:1. Kako bi se osiguralo prikrivanje, jedan ispitivač je kreirao randomizacijsku listu, a drugi je alocirao ispitanike u skupine.

S obzirom na narav ispitivanja, zaslijepljivanje ispitanika i osoba koje su ocjenjivale ishode nije bilo moguće. Fizioterapeuti i osoba koja je analizirala podatke bili zaslijepljeni.

Razlike u kontinuiranim varijablama testirane su Moodovim testom, Mann-Whitney testom i t-testom. Mjere pouzdanosti prikazane su kao veličina učinka i standardna pogreška, p-vrijednost, R^2, omjer dokaza baziran na korigiranom Akaike informacijskom kriteriju (engl. Akaike information criterion, skr. AIC). Linearni model je korišten za multivarijatnu analizu i korelacije.

5. SAŽETI PREGLED REZULTATA OBJEDINJENIH RADOVA

5.1 Prvo istraživanje: Indeks onesposobljenosti vratne kralježnice je bolji u klasifikaciji oporavka nakon trzajne ozljede vrata u usporedbi s ultrazvučnom elastografijom trapeznog mišića posmičnim valom

U prvom istraživanju analizirali smo podatke dobivene od 24 ispitanika. Prvo smo procijenili objektivnost elastografije analizom pouzdanosti svakog ispitivača zasebno (engl. intra-observer reliability) i međusobnim uspoređivanjem ispitivača (engl. inter-observer reliability), uspoređujući početna mjerenja (n=24) i završna mjerenja (n=22). Analizom je utvrđena odlična pouzdanost za svakog pojedinog ispitivača i među ispitivačima u obje mjerene točke i za sve mjerene mišiće. Nadalje, nije nađena značajna razlika u napetosti između lijevog i desnog trapeznog mišića kod prvog mjerenja (Δ=4.84 kPa; p=0.34; Δ=7.84 kPa; p=0.053) niti šest mjeseci nakon ozljede (Δ=1.2 kPa; p=0.72; Δ=0.4 kPa; p=0.89) za oba ispitivača. Mjerenja oba ispitivača pokazala su smanjenje napetosti trapeznih mišića šest mjeseci od ozljede, ali uz značajnost samo kod drugog ispitivača (Δ8.63 kPa; p=0.07 vs. Δ=10.1 kPa; p=0.04).

Klasifikacijski model za prognoziranje oporavka korištenjem različitih varijabli (NDI, PHQ-9 i SWE) pokazao je da je relativna promjena NDI-a kao pojedinačna varijabla najbolja u procjeni oporavka. Njome se sa točnošću od 73,9% može svrstati osobu u neku od kategorija oporavka (potpuni oporavak, parcijalni oporavak, bez ikakvog oporavka). Ipak, kada se za prognozu oporavka koriste dvije varijable, konkretno NDI i SWE trapeznih mišića šest mjeseci od ozljede, točnost svrstavanja povećava se na 77,3%.

Elastografske vrijednosti trapeznih mišića mjerene šest mjeseci od ozljede nisu se razlikovale ovisno o percipiranom statusu oporavka osobe (Δ=1.45, p=0.81). Za razliku od elastografije, vrijednosti NDI-a su bile povezane sa statusom oporavka kreirajući značajni kvadratni trend (R^2=62.5%; p<0.001).

5.2 Drugo istraživanje: Nedostatak objektivnog mjerenja u početnom pregledu i praćenju pacijenata koji prijavljuju trzajnu ozljedu – je li elastografija trapeznog mišića rješenje?

U drugom istraživanju analizirane su elastografske vrijednosti trapeznog mišića kod pacijenata inicijalno nakon trzajne ozljede vrata (n=99) i u kontrolnoj skupini (n=75). Određena je prosječna napetost trapeznog mišića osoba nakon trzajne ozljede vrata (82.24±21.11 kPa) i u

kontrolnoj populaciji (57.47±13.82 kPa). Utvrđena je granična vrijednost od 75,8kPa, kojom se osobu može svrstati u jednu od dvije skupine s točnošću od 77% (specifičnost 94.7%, osjetljivost 63.6%, p<0.0001) Kada se u obzir uzmu još i dob i spol osobe, točnost se povećava na 82,7% uz osjetljivost od 74,7% i specifičnost od 93,3%.

Nadalje, pokazali smo da svako povećanje napetosti trapeznog mišića od 1 kPa znači 1,12 puta veću vjerojatnost da osoba ima trzajnu ozljedu vrata. S druge strane, vjerojatnost da osoba ima trzajnu ozljedu smanjuje se za 0,93 puta sa svakim povećanjem dobi od jedne godine.

5.3 Treće istraživanje: Intervencija putem mobilne aplikacije povećava adherenciju na provođenje programa vježbi kod kuće nakon trzajne ozljede vrata – randomizirano kontrolirani pokus

U trećem istraživanju proveli smo RCT gdje je 60 osoba nakon trzajne ozljede vrata podijeljeno u dvije skupine, intervencijsku (n=30) i kontrolnu (n=30). Analizom smo pokazali kako se dnevnim korištenjem *push* notifikacija povećava adherencija na provođenje vježbi kod kuće u odnosu na kontrolnu skupinu šest mjeseci nakon trzajne ozljede vrata. Osobe iz intervencijske skupine prijavile su da vježbaju 2-4 puta tjedno dok je kontrolna populacija vježbe provodila povremeno (median[IQR]; 3 [2–4] vs. 2 [2–4];p=0,005). Također, multivarijatnom analizom varijabli (inicijalni NDI%, inicijalni VAS boli, inicijalni PCS, intervencija mobilnom aplikacijom) napravljeni su modeli utjecaja pojedinih varijabli na adherenciju. Model koji uključuje intervenciju mobilnom aplikacijom opisuje dobivene podatke 17 puta bolje, nego onaj bez intervencije.

Kada se pratilo smanjenje fizičke onesposobljenosti (ΔNDI%; median, IQR), nije nađena značajna razlika između skupina (20 [10–27] vs. 17 [6–25]; p=0.516). Također, nije nađena razlika u prosječnom smanjenju boli (ΔVAS) među skupinama (1.45 ± 2.4 vs. 1.45 ± 1.95; p=0.9). Ipak, u intervencijskoj grupi broj osoba koje katastrofiziraju bol (PCS) značajno se smanjio šest mjeseci od ozljede u odnosu na inicijalni broj (12 [41%] vs. 3 [10%]; p=0.01), za razliku od kontrolne skupine gdje je inicijalno katastrofiziralo 9 osoba (31%), a nakon šest mjeseci 4 osobe (13%, p=0.12). U obje skupine se kvaliteta života značajno poboljšala šest

mjeseci nakon ozljede (ΔSF-12), ali, uspoređujući skupine, značajno više u skupini s mobilnom aplikacijom (20 [6–36] vs. 15 [9–23]; p=0.038).

6. DISKUSIJA

U okviru ovog doktorskog rada objavljena su tri znanstvena rada koja se odnose na mogućnost objektivne inicijalne procjene i procjene oporavka nakon trzajne ozljede vrata korištenjem elastografije trapeznog mišića posmičnim valom te mogućnost utjecaja na oporavak učestalijim provođenjem terapijskih vježbi.

Inicijalna evaluacija, prognoza i procjena oporavka nakon trzajne ozljede vrata subjektivne su, a kao zlatni standard koristi se NDI. U tu svrhu smo u prva dva rada ispitali mogućnost primjene SWE trapeznog mišića uspoređujući ga s NDI-om. U trećem radu istraživali smo kako učestalost vježbanja kod kuće utječe na oporavak nakon trzajne ozljede vrata mjeren NDI-om.

Dijagnoza trzajne ozljede vrata bazira se na mehanizmu ozljede uz prisutne raznolike simptome i znakove. Procjena upitnicima koje bolesnici ispunjavaju otvara prostor za osobe koje prvenstveno žele izvući financijsku dobit. One tako mogu agravirati simptome i prijavljivati veću onesposobljenost (27).

S obzirom da je jedan od najučestalije prijavljivanih simptoma osoba nakon trzajne ozljede zatezanje mišića vrata, započeli smo ispitivati mogućnost primjene elastografije kako bi objektivizirali njihovu napetost. Ispitivanje Aljinović, Barišić (18) i sur. pokazalo je kako je od različitih mišića vrata trapezni mišić najpogodniji za procjenu napetosti zbog njezine uniformne distribucije.

Trapezni mišić širok je i veliki mišić koji pokriva gornji dio leđa, vrat i rame. Sva tri dijela trapeznog mišića izuzetno su važna za funkciju ramena (28). Poznato je da trzajna ozljeda može dovesti do oštećenja trapeznog mišića (29). Bolesnici tako navode bol, zatezanje, osjetljivost i ukočenost u području vrata i ramena te glavobolju. Nadalje, poremećena funkcija trapeznog mišića uzrokovana trzajnom ozljedom vrata može dovesti do promjene u funkciji drugih mišića u tzv. kinetičkom lancu uz stvaranje kompenzacija prilikom pokretanja vrata i ramena (30).

S obzirom da je ultrazvučna SWE relativno nova metoda, u prvom radu smo morali procijeniti objektivnost same metode. Poznato je kako je u primjeni ultrazvuka izuzetno važna krivulja učenja te se s iskustvom smanjuju greške (31). Stoga je SWE radilo dvoje radiologa s višegodišnjim iskustvom, neovisno jedan o drugome. Nismo pronašli razliku u mjerenjima svakog pojedinog ispitivača niti među ispitivačima te smo pokazali kako je SWE trapeznog mišića pouzdana metoda.

Uspoređujući napetost trapeznog mišića elastografijom kod osoba inicijalno nakon trzajne ozljede vrata i onih iz opće populacije, nađeno je kako je napetost trapeznog mišića u skupini nakon trzajne ozljede vrata u prosjeku veća za oko 25 kPa. Potom smo odredili graničnu vrijednost od 75,8kPa kojom se u gotovo 8 od 10 slučajeva može odrediti je li osoba pretrpila trzajnu ozljedu vrata ili nije. Kada smo u klasifikacijski model poznatim elastografskim vrijednostima nadodali dob i spol, značajno smo povećali osjetljivost klasifikacije, sa 63,9% na 74,9%. Tako je elastografijom objektivno pokazano ono što bolesnici često prijavljuju kao simptom nakon trzajne ozljede, a to je zatezanje mišića vrata.

Nadalje, povećanjem dobi smanjivala se vjerojatnost za trzajnu ozljedu vrata i to za svaku godinu 0,93 puta. Starenjem se pojačavaju degenerativne promjene vratne kralježnice, a one dovode do smanjene pokretljivosti uz povećanje stabilnosti vratnog segmenta što može biti razlog za manje ozljeda. Za razliku od dobi, spol se nije pokazao relevatnim za pojavnost trzajne ozljede.

Naši rezultati su pokazali da elastografija trapeznog mišića posmičnim valom ima potencijal u inicijalnoj diskriminaciji osoba nakon trzajne ozljede vrata. Ipak, kako bi mogli bolje interpretirati elastografske vrijednosti u okviru ozljede, potrebno je ispitati čimbenike koji utječu na normalnu distribuciju napetosti trapeznog mišića. Stoga su potrebna daljnja ispitivanja i veći uzorak, posebice ispitanika iz opće populacije.

Osobe nakon trzajne ozljede vrata često prijavljuju unilateralne simptome. Naši rezultati nisu pokazali razlike u napetosti između lijevog i desnog trapeznog mišića. Ozljedom dolazi do povećanja napetosti oba trapezna mišića neovisno o prijavljivanju simptoma. To znači da je u elastografskoj procjeni vjerojatno dostatno određivanje napetosti jednog trapeznog mišića. Ipak, jedino procjenom napetosti trapeznih mišića kod većeg uzorka, i to u osoba koje prijavljuju unilateralne simptome, bismo mogli doći do konačnog zaključka.

U više sustavnih preglednih radova i metaanaliza mogućih prognostičkih faktora oporavka (14, 32) pokazano je kako je u tu svrhu najbolje koristiti NDI. U našem prvom istraživanju smo korištenjem klasifikacijskog modela oporavka ispitali kako su pojedine varijable (NDI, SWE, PHQ-9) povezane sa subjektivnim osjećajem oporavka šest mjeseci nakon trzajne ozljede. Tako se NDI pokazao boljim od elastografije jer je s većom točnošću i manjom greškom klasificirao osobe u kategorije oporavka. Korištenjem relativne promjene NDI-a se najtočnije, u tri od četiri

slučaja, moglo procijeniti je li se osoba oporavila ili nije. Korištenjem elastografskih vrijednosti, bilo inicijalnih ili onih nakon šest mjeseci od ozljede, dobili smo visoku razinu pogreške u klasifikaciji oporavka te se one ne mogu koristiti u tu svrhu. Ipak, koristeći NDI i napetost trapeznog mišića šest mjeseci od ozljede, podiže se točnost klasificiranja na 77%, uz smanjenje moguće pogreške. Kada se u obzir uzme sve što je potrebno za izvođenje elastografije šest mjeseci nakon trzajne ozljede vrata (iskusni radiolog, validirani uređaj za elastografiju, dostupnost vjerojatno radno aktivne osobe), i povećanje točnosti klasifikacije oporavka od svega 3%, upitna je klinička relevantnost iste.

S obzirom na elastografski povišenu napetost trapeznih mišića nakon trzajne ozljede vrata, mjerenja smo ponovili i šest mjeseci od ozljede. Željeli smo ispitati hoće li s oporavkom doći i do smanjenja napetosti trapeznog mišića i je li eventualno smanjenje napetosti povezano sa statusom oporavka. Premda su oba ispitivača mjerila manju napetost trapeznih mišića u odnosu na inicijalne vrijednosti, značajnost je postignuta samo za drugog ispitivača. Kada smo elastografske vrijednosti usporedili s percipiranim oporavkom, napetost trapeznog mišića se nije razlikovala između onih koji su se oporavili i onih koji se nisu oporavili. Za razliku od napetosti trapeznog mišića, razina onesposobljenosti mjerena NDI-om pokazala je povezanost sa statusom oporavka bolesnika šest mjeseci od ozljede. Tako smo ispitali mogućnost korištenja elastografije u praćenju osoba nakon trzajne ozljede vrata i pokazali kako SWE nije dobra metoda u praćenju osoba nakon trzajne ozljede vrata u usporedbi s NDI-om.

Važno je naglasiti da smo praćenje završili šest mjeseci od ozljede. Bol u vratu se prema vremenu trajanja klasificira kao akutna, subakutna i kronična. Naše praćenje od šest mjeseci od ozljede dostatno je da kažemo je li neka osoba razvila kroničnu bol i onesposobljenost. S druge strane, nije poznato koliko je dugo potrebno za promjenu napetosti trapeznog mišića. Moguće je da je za povratak napetosti trapeznog mišića na razinu prije ozljede potreban duži period, npr. godinu ili dvije dana.

Kada govorimo o oporavku, on uključuje više aspekata zdravlja. Oporavak nakon trzajne ozljede vrata podrazumijeva razinu fizičkog, psihičkog i socijalnog funkcioniranja. Još uvijek se u klasificiranju jačine ozljede i oporavka učestalo koristi klasifikacija koju je izradila grupa *Quebec Task Force* prije tridesetak godina, a koja uključuje različite simptome i znakove kao što su bol u vratu i limitiranost pokreta vratne kralježnice, iako se nije pokazala vrijednom u procjeni

oporavka (33). Simptomi kao što su bol ili zatezanje u vratu osciliraju u vremenu i ovisno o aktivnostima, a isto vrijedi i za opseg pokreta vratne kralježnice. Nadalje, opseg pokreta vratne kralježnice razlikuje se ovisno o dobi te u starijoj dobi očekujemo njegovo smanjenje s obzirom na razvoj degenerativnih promjena. Naša je grupa autora 2023. godine utvrđivala prisutnost boli u vratu i razinu onesposobljenosti kod stomatologa, liječnika obiteljske medicine i fizioterapeuta. Podjednaka prevalencija boli u vratu nađena je kod stomatologa i fizioterapeuta. Međutim, stomatolozi su od svih imali najmanje ograničenja u aktivnostima svakodnevnog života. Za razliku od njih, fizioterapeuti su prijavljivali puno veći nivo onesposobljenosti. Kod fizioterapeuta je svakodnevni rad fizički zahtjevan. Često se svakodnevno radi sa slabo pokretnim bolesnicima gdje je neophodna pomoć u transferima uz zadržavanje prisilnih položaja vrata što doprinosi razvoju onesposobljenosti (34). Iz toga je vidljivo da su simptomi kao što je bol samo dio onoga što nazivamo oporavak te nisu dovoljni kako bi se objasnio teret bolest, nego se trebaju promatrati u kontekstu onesposobljenosti. Isto vrijedi i za napetost trapeznog mišića kao komponentu koja utječe na oporavak te zbog toga nije dobra u prognozi i praćenju oporavka osoba nakon trzajne ozljede vrata, a NDI ostaje najbolji alat u te svrhe.

U trećem istraživanju smo ispitivali kako učestalost provođenja vježbi utječe na oporavak šest mjeseci nakon trzajne ozljede vrata. Sve osobe su provele standardnu fizikalnu terapiju uz preporuku nastavka provođenja vježbi kod kuće. Poznat je pozitivan učinak terapijskih vježbi na smanjenje onesposobljenosti. Međutim, ako osoba ne provodi vježbe redovito, možemo očekivati značajno smanjenje učinka terapije. McLean, Burton (35) i sur. su ustvrdili da ne postoji efikasna strategija za poboljšanje dugoročnog adheriranja na terapijske vježbe. Ipak, u našem istraživanju, osobe koje su dobivale dnevni podsjetnik na vježbanje putem mobilne aplikacije značajno su učestalije provodile vježbe kod kuće u odnosu na one koji su dobili standardne usmene i papirnate preporuke kroz šest mjeseci praćenja. Modelom koji je uključivao incijalnu razinu boli, razinu fizičke i psihičke onesposobljenosti, utvrdili smo kako je od svih varijabli intervencija mobilnom aplikacijom bila ključna u podizanju razine adherencije.

U želji da se bolje razumiju razlozi neadheriranja i kako bi se moglo na njih utjecati, opisani su razni čimbenici. Od opisanih negativnih čimbenika osobe često navode zaboravljivost i nedostatak vremena za provođenje terapijskih vježbi. Uz to, motiviranost za provođenje terapije smanjuje se kroz vrijeme jer se učinak vježbi ne vidi odmah (36). U novije vrijeme, velika dostupnost i jednostavna primjena mobilnih aplikacija uz mogućnost interveniranja u realnom

vremenu učinio ih je pogodnima kako bi utjecale na poboljšanje adheriranja na terapiju (26). U našem istraživanju, dnevnim podsjećanjem na provođenje vježbi vjerojatno smo utjecali na gore navedene uzroke neadheriranja.

Kao što je navedeno ranije, terapijske vježbe osnova su liječenja trzajne ozljede vrata te mogu utjecati na razinu boli i onesposobljenosti (21). Za očekivati bi bilo da će učestalije vježbanje dovesti do manje onesposobljenosti i boljeg oporavka, što nije bio slučaj u našem istraživanju. Rezultati su pokazali da je učestalost provođenja vježbi kod osoba koje su imale inicijalno višu razinu onesposobljenosti bila visoka u obje skupine, dok je u intervencijskoj skupini povećana adherencija kod osoba s nižom inicijalnom razinom onesposobljenosti koje su ionako imale dobru prognozu oporavka.

Međutim, iako NDI pojedinačno najbolje opisuje oporavak osoba nakon trzajne ozljede vrata, ispitivanjem ostalih domena života našli smo pozitivne učinke intervencije. Tako su značajnije poboljšani psihičko funkcioniranje i HRQoL.

Različiti psihološki faktori povezuju se s učinkom na oporavak nakon trzajne ozljede vrata. Katastrofiziranje boli poznat je faktor koji utječe na lošiji oporavak nakon trzajne ozljede vrata. Iako se u upitniku katastrofiziranja boli očekuje od ispitanika da sve svoje izjave ispunjava kao da ga boli tog trenutka te se navodi:“Kad me boli...“, naše istraživanje je pokazalo da katastrofiziranje izravno ovisi o aktualnoj razini boli te se katastrofiziranje smanjilo u obje skupine šest mjeseci nakon ozljede. Opisivani su i drugi faktori koji utječu na lošiji oporavak od kojih je zanimljiv model straha od izvođenja pokreta nakon ozljede. Generalno, češće izvođenje vježbi u intervencijskoj skupini moglo je utjecati i na ovaj model gdje strah od pokreta generira bol, a bol generira strah od pokreta. Ovaj koncept generiranja boli isprepliće se i s konceptom katastrofiziranja boli gdje osoba koju boli pretjerano razmišlja o boli, a to dovodi do straha i paralize funkcije.

Kada pogledamo ukupan broj ispitivanih osoba šest mjeseci od ozljede, fizičko funkcioniranje mjereno NDI-om najbolje oslikava oporavak. Manji dio smanjenog oporavka uzrokovan je smanjenim psihološkim ili socijalnim funkcioniranjem. Nakon šest mjeseci tek je jedna od deset osoba katastrofizirala bol, a većina osoba je prijavila kako nema ili rijetko ima ograničenja u socijalnom funkcioniranju. S druge strane, 70% ispitanika imalo je nekakvu razinu fizičke onesposobljenosti, a potpuni percipirani oporavak prijavilo je 40% osoba. Simptomi kao što su

bol u vratu, čak i ako su blagi, mogu se pojačavati u aktivnostima te ograničavati provođenje aktivnosti svakodnevnog života. Tako i blaga fizička onesposobljenost govori u prilog nepotpunog oporavka.

Ipak, potpuni oporavak šest mjeseci nakon ozljede prijavljivali su neki koji su imali fizičku onesposobljenost. Prilikom validacije NDI-a na hrvatski jezik (11) pronašli smo kako je trećina osoba iz opće populacije prijavljivala blagu ili, rijetko, umjerenu onesposobljenost. Stoga je vjerojatno određeni broj ispitanika u našem istraživanju i prije trzajne ozljede vrata imao neku razinu fizičke onesposobljenosti zbog tegoba od strane vratne kralježnice. Za njih je potpuni oporavak značio povratak na prvotnu razinu onesposobljenosti.

Fizičko, psihološko i socijalno funkcioniranje osobe zajednički generiraju ono što nazivamo kvaliteta života. Nakon trzajne ozljede vrata, ako gledamo pojedinačno, narušeni su svi gore navedeni aspekti zdravlja pa tako u konačnici i kvaliteta života. U obje skupine došlo je do značajnog poboljšanja kvalitete života. Ipak, intervencijska skupina imala je značajnije povećanje kvalitete života u odnosu na kontrolnu skupinu što možemo pripisati aktivnijem suočavanju s tegobama nakon ozljede u intervencijskoj skupini.

Većina osoba koje dožive trzajnu ozljedu radno je aktivna te nakon šest mjeseci u većine zaostaju neka ograničenja u svakodnevnom poslu. Kada se tome doda da je tek 30% osoba bilo bez ikakve fizičke onesposobljenosti nakon šest mjeseci, vidljivo je kako su potrebni novi pristupi u liječenju i praćenju trzajne ozljede vrata. Fokus trećeg istraživanja bio je utjecaj učestalosti provođenja terapijskih vježbi na ishode nakon trzajne ozljede vrata. Budući da povećanjem učestalosti provođenja vježbi nismo poboljšali oporavak, potrebno se usredotočiti na individualiziranje terapijskih vježbi kako bi se pokušalo poboljšati ishode.

Mobilne aplikacije su već u nekim zemljama prepoznate kao one koje mogu poboljšati ishode (engl. digital therapeutics) (37). Osim velike dostupnosti i jednostavne primjene, prednosti mobilnih aplikacija su što mogu uključivati veliki broj sadržaja te se mogu koristiti za praćenje u realnom vremenu. Primjerice, nakon trzajne ozljede vrata mobilnim aplikacijama mogao bi se u realnom vremenu pratiti one koji su rizični za razvoj kronične onesposobljenosti te pokušati poboljšati oporavak individualiziranjem terapije.

7. ZAKLJUČAK

U svrhu inicijalne procjene, prognoziranja i praćenja oporavka nakon trzajne ozljede vrata koriste se subjektivni upitnici kojima se procjenjuju različiti aspekti zdravlja. Kao najčešće korišten i najpouzdaniji upitnik izdvaja se NDI. Liječenje se bazira na kontinuiranom provođenju terapijskih vježbi kroz duži vremenski period. Veliki broj osoba dugoročno prijavljuje bol i onesposobljenost.

U sklopu ove disertacije napravljena su tri istraživanja. U prva dva istraživanja ispitivana je elastografija trapeznog mišića posmičnim valom kao metoda u procjeni i praćenju trzajne ozljede vrata. Utvrđeno je da je elastografija trapeznog mišića posmičnim valom objektivna metoda te se njome u četiri od pet slučajeva može odrediti ima li osoba trzajnu ozljedu ili nema. Također, utvrđeno je kako je praćenje od šest mjeseci nedostatno za potpuno smanjenje elastografskih vrijednosti trapeznog mišića. Uspoređujući elastografiju i NDI, utvrđeno je da je NDI bolji alat u prognoziranju i praćenju oporavka šest mjeseci od ozljede.

U trećem istraživanju pokazano je da se dnevnim podsjećanjem na vježbanje putem mobilne aplikacije povećava adherencija na vježbanje šest mjeseci nakon trzajne ozljede vrata. Međutim, povećana adherencija ne dovodi do smanjenja fizičke onesposobljenosti mjerene NDI-om niti subjektivnog osjećaja oporavka bolesnika. Ipak, smanjeno katastrofiziranje boli i povećana kvaliteta života prijavljene su u intervencijskoj skupini.

Elastografija trapeznog mišića posmičnim valom mogla bi se u koristiti u inicijalnom probiru osoba s trzajnom ozljedom vrata, ali nije dobra za procjenu oporavka šest mjeseci nakon ozljede. Nepoznato ostaje kako se elastografske vrijednosti mijenjaju kroz duži vremenski period nakon ozljede. Korištenjem mobilnih aplikacija može se povećati adherencija na terapijske vježbe. U budućnosti se mobilne aplikacije mogu koristiti za procjenu i individualiziranje terapije u realnom vremenu kod osoba rizičnih za lošiji oporavak nakon trzajne ozljede vrata.

8. SAŽETAK

Uvod: U procjeni i praćenju osoba nakon trzajne ozljede vrata koriste se subjektivne mjere od kojih se kao pouzdan i najčešće korišten izdvaja NDI. S obzirom da do ozljede najčešće dolazi u prometnim nesrećama, česta su potraživanja odšteta. Nedostatak objektivnih mjera stvara prostor za simuliranje, a često se rade dijagnostičke pretrage koje nemaju prognostičku vrijednost niti se pomoću njih može procijeniti oporavak. Osnova liječenja su terapijske vježbe koje su se uz edukaciju jedine pokazale učinkovite u smanjenju onesposobljenosti. Liječenje nije optimalno tako da veliki postotak osoba nakon ozljede pati od kronične boli i onesposobljenosti. U prvom dijelu ove doktorske disertacije cilj je bio ispitati mogućnost korištenja elastografije trapeznog mišića posmičnim valom kao objektivne metode u inicijalnoj evaluaciji i praćenju oporavka šest mjeseci nakon trzajne ozljede vrata. U drugom dijelu cilj je bio ispitati mogućnost poboljšanja oporavka utjecajem na adherenciju u provođenju terapijskih vježbi dnevnim podsjećanjem na vježbanje putem mobilne aplikacije.

Metode: Prvo smo prospektivnim opažajnim istraživanjem pratili osobe nakon trzajne ozljede vrata kroz šest mjeseci. Svi ispitanici su proveli standardnu fizikalnu terapiju (2 ciklusa fizikalne terapije, 10 terapija po ciklusu, 5x tjedno s pauzom od 3 tjedna između terapija). Elastografija posmičnim valom i NDI rezultat napravljeni su inicijalno i nakon šest mjeseci. Elastografija je učinjena od strane dvoje radiologa. Napravljen je prediktivni model statusa oporavka šest mjeseci nakon ozljede te usporedba elastografije i NDI rezultata šest mjeseci od ozljede sa subjektivnim osjećajem oporavka bolesnika. U drugom istraživanju napravili smo sekundardnu analizu podataka koje su uključivale elastografiju trapeznog mišića osoba nakon trzajne ozljede i onih iz opće populacije. U trećem istraživanju randomizirano-kontroliranim pokusom smo ispitivali kako kod osoba koje su pretrpile trzajnu ozljedu vrata i provele standardnu fizikalnu terapiju svakodnevno podsjećanje na provođenje vježbi utječe na adherenciju i oporavak mjeren NDI-om šest mjeseci od ozljede u odnosu na one koji su nakon fizikalne terapije dobili pisane i usmene preporuke o nastavku provođenja vježbi kod kuće.

Rezultati: Prvo istraživanje: 24 osobe su napravile inicijalna mjerenja, 22 osobe su završile istraživanje. Elastografska mjerenja su pokazala odličnu pouzdanost unutar (ICC 0.75-0.94) i između ispitivača (ICC 0.78-0.88). Nakon šest mjeseci umanjila se napetost trapeznog mišića, ali statistički značajno samo za drugog radiologa (Δ8.63 kPa; p=0.07 vs. Δ10.1 kPa; p=0.04). Nakon šest mjeseci elastografske vrijednosti nisu se razlikovale s obzirom na status oporavka (55.6±9.7 vs. 57±15.8, Δ1.45; p=0.82) dok su osobe koje su prijavljivale potpuni oporavak imale značajno

niži NDI rezultat u odnosu na neoporavljene ili parcijalno oporavljene (Δ22.98; p<0.001). Pojedinačno se, poznavajući relativnu promjenu NDI-a najtočnije (73.9%) i sa niskim Akaike informacijskim kriterijom (AIC=39.2) može klasificirati osobu u neku od kategorija percipiranog oporavka. Uvrštavajući zajedno NDI rezultat i napetost trapeznog mišića šest mjeseci od ozljede točnost klasifikacije se povećala na 77.3% sa smanjenjem moguće greške (AIC=32.8). Drugo istraživanje: Analizirana je elastografija trapeznog mišića kod 99 osoba nakon trzajne ozljede i 75 osoba iz opće populacije. Prosječna napetost trapeznog mišića nakon ozljede bila je 82.24±21.11 kPa dok je za one iz opće populacije bila 57.47±13.82 kPa. Granična vrijednost elastografije od 75.8 kPa pokazala je 77% točnost u kategoriziranju osobe u jednu od skupina. Treće istraživanje: Analizirano je 29 osoba iz intervencijske i 30 iz kontrolne skupine. Šest mjeseci od ozljede uspoređujući skupine, intervencijska skupina pokazala je značajnije adheriranje (median [IQR]) u provođenju terapijskih vježbi kod kuće (3 [2–4] vs. 2 [2–4]; p=0.005) te poboljšanu HRQoL (20 [6–36] vs. 15 [9–23]; p=0.038). U intervencijskoj skupini je za razliku od kontrolne opaženo značajno smanjenje osoba koje katastrofiziraju zbog boli u dvije mjerene točke (31%; p=0.01). Nije nađena razlika u NDI rezultatu, intenzitetu boli te percipiranom oporavku.

Zaključak: U prva dva istraživanja pokazali smo kako je elastografija trapeznog mišića posmičnim valom objektivna metoda koja se može koristiti u inicijalnom probiru osoba nakon trzajne ozljede vrata, ali se ne može koristiti u prognoziranju niti praćenju oporavka šest mjeseci od ozljede. U te svrhe zlatni standard ostaje NDI. Povećanje adherencije na terapijske vježbe nakon trzajne ozljede vrata može se postići korištenjem dnevnih podsjetnika putem mobilne aplikacije. S obzirom da učestalije vježbanje nije rezultiralo boljim oporavkom šest mjeseci nakon ozljede, potrebno je individualizirati pristup u liječenju te modificirati vježbe u osoba rizičnih za razvoj kronične onesposobljenosti.

9. SUMMARY

TITLE OF THE DOCTORAL THESIS: RECOVERY EVALUATION IN PATIENTS AFTER WHIPLASH INJURY OF THE NECK AFTER PHYSICAL THERAPY USING SHEAR WAVE ELASTOGRAPHY AND NECK DISABILITY INDEX SIX MONTHS AFTER A TRAFFIC ACCIDENT

Background: In evaluation and follow-up after a whiplash injury of the neck, subjective measurements are used, among which the most reliable and the most used one is NDI. Considering the injury usually happens in car accidents, there are often requests for financial compensation. Lack of objective measurements leaves room for malingering, and diagnostic tests that are without prognostic value and can't predict recovery are often performed. The basic treatment consists of physical exercise and educational measures which are the only ones proven to be effective in reducing disability. The treatment is not yet optimized, and a large percentage of patients suffer from chronic pain and disability. The aim of the first part of this doctoral dissertation was to evaluate the possibility of using shear wave elastography as an objective method in initial evaluation and follow-up six months after a whiplash injury of the neck. In the second part, we aimed to evaluate the possibility of improving outcomes by increasing adherence to exercise using daily reminders sent via a mobile application.

Methods: An observational study of patients after whiplash injury over a period of six months was conducted. All subjects did standard physical therapy (2 cycles of 10 therapy sessions, 5x a week with a break of 3 weeks in between cycles). Shear wave elastography and NDI scores were obtained initially and after six months. Elastography was performed by two radiologists. A predictive model of recovery status six months after injury was made, along with a comparison of elastography and NDI score six months after injury with subjectively perceived recovery. In the second study, a secondary analysis of data was made comparing the elastography of trapezius muscle in patients six months after whiplash injury and those from the general population. The third study was a randomized-controlled study which evaluated the effect of daily mobile application reminders to exercise on adherence and recovery measured by NDI six months after physical therapy. Patients with whiplash injury of the neck had standard physical therapy and were then given either oral and written instructions on how to exercise at home or a mobile application. The two groups were compared.

Results: First study: 24 people had initial measurements made, and 22 finished follow-up. Elastography measurements showed excellent intraobserver (ICC 0.75-0.94) and interobserver

(ICC 0.78-0.88) reliability. After six months, there was a decrease in trapezius muscle stiffness, though statistically significant only in the second radiologist (Δ8.63 kPa; p=0.07 vs. Δ10.1 kPa; p=0.04). Also, elastography values after six months did not differ according to recovery status (55.6±9.7 vs. 57±15.8, Δ1.45; p=0.82), while patients who reported full recovery had significantly lower NDI scores compared to the partially recovered or not recovered group (Δ22.98; p<0.001). Knowing relative change in NDI, an individual person can be categorized by recovery status most precisely (73.9%) and with low Akaike information criteria (AIC=39.2). Second study: Elastography of the trapezius muscle in 99 patients after whiplash injury and 75 people from the general population was analyzed. Average trapezius muscle stiffness after injury was 82.24±21.11 kPa, and in the general population was 57.47±13.82 kPa. Cut off value of 75.8 kPa showed 77% accuracy in categorizing a person into one of the groups. Third study: 29 people from the intervention group and 30 people from the control group were analyzed. When comparing groups six months after injury, the intervention group showed significantly higher adherence (median [IQR]) to a home exercise program (3 [2–4] vs. 2 [2–4]; p=0.005) with improved HRQoL (20 [6–36] vs. 15 [9–23]; p=0.038). In the intervention group, unlike the control group, there were significantly fewer people pain catastrophizing between two time points (31%; p=0.01). There was no difference in NDI score, pain intensity, or perceived recovery.

Conclusion: The first two studies show shear wave elastography of the trapezius muscle to be an objective method that can be used in the initial screening of people after a whiplash injury of the neck but can’t be used in follow-up and predicting recovery six months after injury, where NDI remains the golden standard. Adherence to physical exercise after a whiplash injury of the neck can be increased using daily reminders via mobile application. Considering that more frequent exercise did not lead to better recovery six months after injury, there is a need for a more personalized approach, and modifications to exercise should be made for patients with a higher risk for chronic disability.

10. ŽIVOTOPIS

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Stručno usavršavanje:

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2. Interventional Musculoskeletal Ultrasound Cadaver Course, Fribourg, Switzerland, 9/2023.
3. MSK US guided injections in clinical practice - Observership with Dr. Kamal Mezian, Rehabilitace MUDr. Hassan Mezian, s.r.o., Litoměřice, Czech Republic, 9/2022.
4. Xeomin: for more quality daily functioning of patients with neurological disorders, Department of Neurology, Split, CRO, 3/2022.
5. Musculoskeletal Ultrasound, Department of Musculoskeletal Radiology, Clinical Hospital Center Sestre Milosrdnice, Zagreb, CRO, 10/2021.
6. Role of Xeomin in patients with cervical dystonia and upper limb spasticity, Special Hospital for Medical Rehabilitation Krapinske Toplice, CRO 11/2019.

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12. RADOVI OBJEDINJENI U DISERTACIJI

12.1 Prvi rad

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Neck Disability Index Is Better in Classification of Recovery after Whiplash Injury in Comparison with Ultrasound Shear Wave Elastography of Trapezius Muscle

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Abstract: A prospective observational study comparing shear wave elastography (SWE) of trapezius muscle with Neck Disability Index (NDI) in a prediction model of health status six months after a whiplash injury. Both SWE values, measured by two radiologists, and NDI scores were obtained at baseline and after physical therapy (PT) (6-month period). Those values were compared with a 3-point Likert scale (no, partial or full recovery). Twenty-two subjects completed the study. A decrease in trapezius stiffness was detected by both radiologists, statistically significant for one (Δ10.1 kPa; $p = 0.04$) but not for the second radiologist (Δ8.63 kPa; $p = 0.07$). The measurements showed excellent intra-observer (ICC 0.75–0.94) and inter-observer (ICC 0.78–0.88) reliability. After six months, fully recovered patients showed lower NDI scores than partially recovered patients (Δ22.98; $p < 0.001$). SWE values did not differ with the recovery status (55.6 ± 9.7 vs. 57 ± 15.8, Δ1.45; $p = 0.82$). The single most accurate variable in classifying health status six months after whiplash injury was the relative change of NDI, and it showed the highest accuracy (73.9%) and low Akaike information criterion (AIC = 39.2). Overall, the most accurate classification was obtained when combining NDI and SWE after physical therapy with an accuracy of 77.3% and a decrease in AIC (32.8).

Keywords: car accident; stiffness; depression; neck pain; recovery

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1. Introduction

Whiplash injury is the most common injury related to traffic accidents [1,2]. Approximately 30–50% of people experience chronic pain and disability following a whiplash injury, and 13–50% do not return to work six months after the injury; therefore, it becomes a great socioeconomic problem [2–4]. Although whiplash injury is common in modern society, and its incidence is increasing, the pathophysiological mechanism that leads to chronic disability and optimal treatment remains unclear [5]. Clinical guidelines identify the acute whiplash injury phase (90 days from the accident) as a critical period to classify patients according to the risk of developing chronic pain and disability. Patients at greater risk should be monitored more often, and their rehabilitation plans should be tailored individually [6,7].

Currently, subjective methods are used to assess the severity of the injury, prognosis, and recovery, with Neck Disability Index (NDI) being one of the most reliable and most commonly used ones [8–11].

There are no objective measurements used for the assessment of recovery following a whiplash injury of the neck. Data from previous studies showed that changes in cervical radiographs found after a car accident (straightening of cervical lordosis, kyphosis, or degenerative changes) are not suitable for estimating the severity of the injury and recovery prognosis [12,13]. The range of movement in the cervical spine, which can easily be measured, can vary up to 50% even on the same day, depending on the current pain level and patient's compliance when performing tests [14].

Ultrasound shear wave elastography (SWE) is another research method of evaluating the severity of whiplash injury by measuring the muscle stiffness in the cervical region. It is used to analyze structural changes in different tissues, including muscles. This method allows both qualitative and quantitative evaluation of the elasticity characteristics of soft tissues and their alteration in traumatic lesions and degenerative pathology. Tissue stiffness is measured by the shear modulus and expressed in pressure units (kilopascals; kPa) [15].

It was previously published that SWE values of the trapezius muscle are increased in the first 90 days after a whiplash injury compared to the healthy control group (75 vs. 50 kPa), with a sensitivity of 90% and specificity of 72%. That study was conducted on 75 participants in each group, with the intra-observer reliability of SWE values of stiffness of the trapezius muscle being 0.8. The authors suggested that more participants were needed to have more precise results, and inter-observer reliability was not calculated [16]. We were unable to find published reports on how SWE values change after physical therapy (PT) and studies investigating SWE as a potential prognostic factor of recovery after a whiplash injury.

The objective of this study was to analyze the feasibility of the usage of baseline or follow-up SWE values or their change in the classification of recovery six months after the whiplash injury and compare it with NDI.

2. Methods

2.1. Study Design

This prospective observational study was conducted from January 2020 to February 2021 at the Institute of Physical Medicine and Rehabilitation, University Hospital Split in Croatia and was approved by the Ethical Committee of the University Hospital Split. All participants were informed about the study design, and informed consent was obtained in written form.

2.2. Participants

Participants in this study were all symptomatic whiplash injury patients referred to a physiatrist that complied with inclusion and exclusion criteria and were willing to participate in the study. Enrolled subjects met the following inclusion criteria: patients older than 18 who sustained whiplash injury of the neck in a car accident as drivers or co-drivers, examined by physical medicine and rehabilitation (PMR) specialist within 90 days from the accident, and diagnosed with whiplash injury of the neck. Participants were excluded if they sustained bone fractures or spinal cord injury in an accident, had an accident in any vehicle other than a car, were treated with malignant disease in the last 5 years, or were treated with a severe mental illness (psychosis or major depressive disorder).

2.3. Variables

Patients following whiplash injury undertook the standardized physical therapy program individually at the outpatient clinic guided by a physiotherapist. It included supervised exercise, transcutaneous electrical nerve stimulation (TENS), therapeutic ultrasound, advice on posture, pain relief methods, and early return to daily activities.

The physical therapy program consisted of two parts: a 2-week program with therapies 5 times a week, followed by a 3-week break, and then another 2 weeks of therapies.

TENS and ultrasound were applied before starting the exercise. TENS (100 Hz) was administered for 20 min on the paravertebral musculature of the neck. Pulsed ultrasound (0.8 W/cm^2 with 1 MHz ultrasound probe) was applied for 5 min on trapezius muscles.

Initially, the exercise program focused on breathing exercises, gentle range of motion exercises, deep neck flexor activation, and stretching exercises. The importance of good posture was emphasized to facilitate deep cervical muscle function. Toward the end of the 2-week exercise period, participants were encouraged to continue exercise at home. The physician gave them written and illustrated material explaining the home exercise program. After three weeks, they came back for another 2-week program. Exercise then progressed with low isometric resistance, endurance training of shoulders, and an increase in the number of repetitions. Progressions were adjusted to each patient according to their symptoms and capability. After completing the entire program, participants were encouraged to continue exercising at home, avoid the aggravation of pain, and avoid any other physical treatments for their neck disorder during the six months of participating in this study.

2.4. Outcomes

The primary outcome measure of this study was the stiffness of the trapezius muscle obtained with SWE.

Secondary outcome measures included physical functioning assessed with NDI and depression level before the PT assessed with Patient Health Questionnaire 9 (PHQ-9). A three-point Likert scale with the values of no, partial, or full recovery was used for health assessment as a patient-perceived recovery scale (PPR).

2.5. Data Measurement

Two radiologists blinded to the status of the patient and blinded from each other performed ultrasound (US) SWE of the trapezius muscle. We used a multi-frequency linear probe (2–10 MHz, Aixplorer Multiwave™ System, Supersonic Imagine, Aix-en-Provence, France), and the level of muscle stiffness was measured by shear modulus and expressed in pressure units (kPa) with absolute elasticity values ranging from 0–300 kPa.

The patient sat on a chair with the relaxed shoulder girdle and arms in supination, resting on thighs. The radiology specialist put the US probe longitudinally to the muscle belly of the upper portion of the trapezius muscle in the shoulder region using minimal pressure of the US probe against the skin, identified the size of the circular regions of interest (ROIs) as the thickness of the upper trapezius, and measured mean stiffness. Measurement was repeated 3 times for each muscle. Separately, within 30 min, another radiology specialist performed the same procedure. The difference between left and right trapezius muscle was calculated for both radiologists with no significant difference. The mean of all 6 measurements (left and right trapezius) was calculated. The difference between measures obtained at baseline and 6-month follow-up was determined for each radiology specialist separately.

NDI-CRO, previously validated in Croatian, was used to quantify disability [17]. The total NDI score was divided by the maximal possible score and expressed in percentages (NDI%). Values from 0–8% are regarded as no disability, 10–28% mild disability, 30–48% moderate disability, 50–68% severe disability, and 70–100% total disability.

The level of depression was determined by the Patient Health Questionnaire 9 (PHQ-9) index: scores of 5–10, 11–15, 16–20, and >21 representing mild, moderate, moderately severe, and severe depression, respectively.

2.6. Study Size

The sample size was calculated based on the pilot study (n = 14 pairs). Given the observed differences in the pilot study, we calculated the needed sample size (n = 20 pairs) to obtain the power of 80% at the $\alpha = 0.05$. The sample size was calculated based on

paired *t*-test in G*Power Software Version 3.1.9.6 [18]. The final number of participants was calculated as 50% more than the power analyses required (n = 30).

2.7. Statistical Methods

Continuous data are presented as average and standard deviation. Intra-observer reliability was assessed by interclass correlation (ICC) with model 3.1 and inter-observer reliability with model 2.1 of Shrout and Fleiss and interpreted according to Cicchetti [19]. The differences in continuous variables were assessed by *t*-test for paired samples. Statistical measures of evidence are presented as effect size and its 95% confidence interval (CI) or its standard deviation (SD), *p*-values, R^2, and corrected Akaike information criteria (AIC). For building of the classification model, we used ordinal logistic regression in Gretl software [20]. Model accuracy is defined as ratio of correct predictions and all predictions made by model. All other statistical analyses were done in Past3 Software (Hammer, O. et al., 2001. PAST).

3. Results

A flowchart of the 45 whiplash injury patients that were assessed for eligibility is shown in Figure 1. The baseline characteristics of the participants are shown in Table 1.

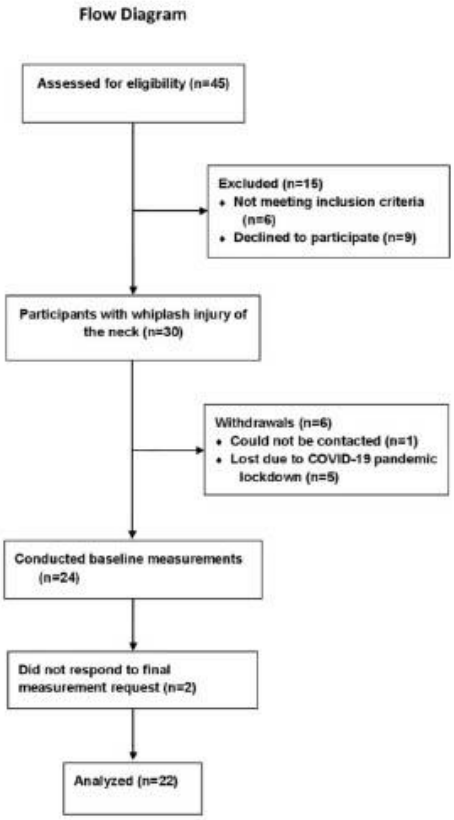

Figure 1. Flow of participants through the study.

Table 1. Demographic and baseline characteristics of whiplash injury patients that met eligibility criteria.

Patients (n = 30)	
Age, Median (IQR)	37.5 (31–52)
Female, n (%)	17 (57)
Time from accident, Mean ± SD	30.3 ± 12.8
Drivers, n (%)	26 (87)
Doctor's office visits, Mean ± SD	3.9 ± 1.2
Absence from work, n (%)	20 (67)
VAS of pain, Mean ± SD	5.1 ± 2.7
Analgesic drugs use, n (%)	
Occasionally 1 time/day 2 or more times/day	5 (17) 24 (80) 1 (3)
Myorelaxant drugs use, n (%)	18 (60)

IQR, interquartile range.

A complete follow-up examination six months after whiplash injury was obtained in 22 participants (12 women and 10 men; from 23 to 58 years of age; the mean age was 38.6 ± 11 years). Another two participants did not obtain SWE after six months, and three did not fill out NDI at six-month follow-up. All patients were drivers or co-drivers and used a seatbelt in a car accident. All subjects obtained radiographs of the cervical spine; thirteen were reported as normal, fourteen as cervical spine straightening, and three as a segmental kyphosis.

The difference in muscle stiffness between left and right trapezius before physical therapy and the difference in muscle stiffness between left and right trapezius after physical therapy was calculated for both radiologists. There was no statistical difference between left and right trapezius muscle stiffness for the first examiner at baseline (Δ = 4.84 kPa; p = 0.34) and six-month follow-up (Δ = 1.2 kPa; p = 0.72) nor for the second examiner at baseline (Δ = 7.84 kPa; p = 0.053) and six-month follow-up (Δ = 0.4 kPa; p = 0.89). Since there was no difference between the left and the right trapezius muscle's stiffness in the same person at the analyzed time points, for further statistical analyses, the mean of six measurements was used (three measurements of the right trapezius and three measurements of the left trapezius).

The difference in trapezius muscle stiffness measured at baseline and six-month follow-up was analyzed. Unlike measurements obtained by the first radiologist, which did not reach statistical significance (Δ = 8.63 kPa; p = 0.07), measurement differences obtained by the second radiologist were statistically significant (Δ = 10.1 kPa; p = 0.04)(Figure 2).

Furthermore, post-hoc power analysis was calculated on n = 22 (pairs), with an α = 0.05 and power of 0.8. Given the observed differences between timepoints, the second examiner needed 21 pairs of measurements to reach statistical significance, while the first examiner was underpowered (24 pairs needed). However, if the SWE differences between timepoints for each patient are compared between radiologists, then practically no differences can be found (Δ = 1.47 kPa; p = 0.65).

Intra-observer reliability at baseline and at six-month follow-up showed ICC between 0.75 and 0.94, which indicates excellent reliability for both radiologists and all muscles (Table 2).

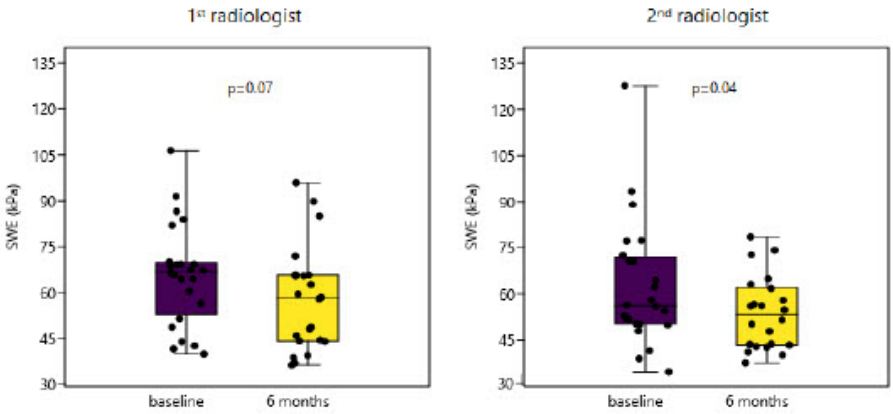

Figure 2. The difference of shear wave elastography (SWE) at baseline and 6-month follow-up measured by two radiologists. kPa, kilopascals.

Table 2. Intra-observer reliability of elastography measurements in trapezius muscles before and after physical therapy.

Elastography of Muscle	Radiologist No1		Radiologist No2	
	ICC Coefficient	95% CI	ICC Coefficient	95% CI
Before PT				
Trapezius R	0.79	(0.636, 0.8946)	0.75	(0.6779, 0.9091)
Trapezius L	0.75	(0.5839, 0.8755)	0.85	(0.7388, 0.9289)
After PT				
Trapezius R	0.94	(0.9001, 0.9768)	0.93	[0.8716, 0.9698)
Trapezius L	0.88	(0.782, 0.9459)	0.88	[0.7888, 0.9478)

Legend: R, right; L, left; ICC, inter-class correlation; PT, physical therapy.

Inter-observer reliability of SWE measurements of left and right trapezius muscle at baseline and six-month follow-up indicates excellent reliability by inter-class correlation (ICC varied from 0.78 to 0.88) (Table 3). Given the excellent inter-observer reliability and the finding that there are no practical differences between radiologists in measuring the individual patient difference in SWE between baseline and six-month follow-up, we decided to include in further analyses SWE values that are arithmetic average of values measured by two radiologists.

Table 3. Inter-observer reliability of elastography measurements in trapezius muscles before and after physical therapy.

Elastography of Muscle	ICC Coefficient	95% CI
Before PT		
Trapezius R	0.8787	(0.7211, 0.9474)
Trapezius L	0.7828	(0.4955, 0.9062)
After PT		
Trapezius R	0.795	(0.5131, 0.9144)
Trapezius L	0.7839	(0.4857, 0.9099)

Legend: R, right; L, left; ICC, inter-class correlation; PT, physical therapy.

NDI at baseline and at six-month follow-up was calculated. Mean NDI score (in percentages) was significantly lower at six-month follow-up in contrast to the baseline measurement when analyzing all the patients together (Δ = 15.28%, CI (8.6332%, 21.927%), $p < 0.0001$), (Figure 3).

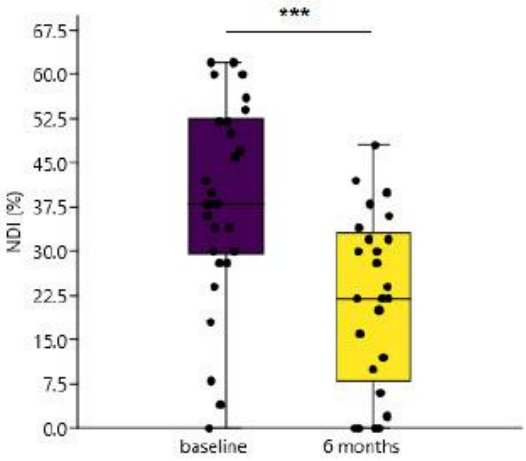

Figure 3. Statistically significant differences in NDI measured at baseline and 6-month follow-up, *** $p < 0.0001$, *t*-test (mean ± 95% CI), NDI showed in percentages of the maximum score.

Using PPR, total recovery was reported by 42% (n = 10) of patients, while 46% (n = 11) said that they were partially recovered and 12% (n = 3) that they were not recovered.

Upon further subdivision of patients regarding PPR, NDI scores at six-month follow-up differed between groups: fully recovered (mean 8.4 ± 8.9), partially recovered (mean 30.5 ± 9.67), and not recovered group (mean 34.7 ± 9.45). The correlation between the NDI score obtained at six-month follow-up, and perceived recovery type formed a significant quadratic trend (R^2 = 62.5%; $p < 0.001$). Furthermore, when no recovery and partial recovery groups were merged, together, they significantly differed from the fully recovered group (Δ = 22.98; $p < 0.001$) (Figure 4).

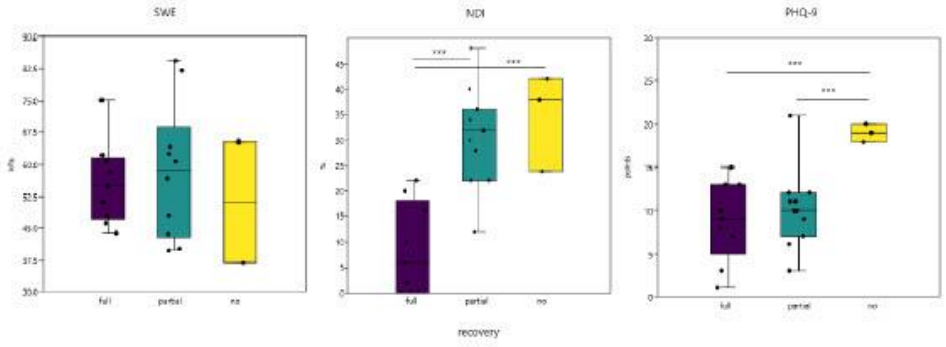

Figure 4. Differences in endpoint shear wave elastography measured as an average of both radiologists, Neck Disability index after 6 months, and initial PHQ-9 in comparison to patient perceived recovery status, *** $p < 0.0001$, *t*-test (mean ± 95% CI).

SWE values obtained at six-month follow-up stratified by PPR groups were calculated for both radiologists and as the average of latter (Figure 4). Measured by the first examiner, SWE values did not differ in relation to recovery status (49.1 ± 8.3 vs. 57.6 ± 13.09, Δ = 8.5; $p = 0.08$). In contrast, fully recovered patients had lower SWE values compared to those who recovered partially and did not recover at all when measured by the second radiologist (48.1 ± 10.7 vs. 65.7 ± 17.64, Δ = 17.55; $p = 0.01$). On the other hand, when the same groups were compared in terms of pooled SWE from both radiologists, no difference could be found (Δ = 1.45, $p = 0.81$).

Initial PHQ-9 scores were compared between PPR groups, and significantly higher PHQ-9 scores were found in participants who answered that they did not recover than those who reported complete or partial recovery (mean 9.3 ± 4.69 and 10.2 ± 4.69 vs. 19 ± 1; $p < 0.001$) (Figure 4).

Models classifying patient-perceived recovery were calculated (Table 4). Between all measures (NDI, PHQ-9, and SWE) obtained before and after physical therapy, the relative change of NDI $\frac{NDI_{after\ PT} - NDI_{baseline}}{NDI_{baseline}} \cdot 100$ showed to be the most accurate classifier of recovery (accuracy 73.9%, AIC 39.21), followed by NDI measured after the therapy (accuracy 69.6%, AIC 33.74). SWE before and after physical therapy and its change showed accuracy from 40–64% but with higher AIC values (≈46), which limits their usage (Table 4). When a combination of potential classifiers was calculated, SWE obtained after the therapy combined with NDI after physical therapy raised accuracy to 77.3% with AIC 32.85 (Table 4).

Table 4. Models predicting patient-perceived recovery.

Variables in Model	AIC	Accuracy
SWE before PT	46.6	63.6%
SWE after PT	46.6	40.9%
ΔSWE	46.47	50%
Relative ΔSWE	46.62	50%
NDI (%) before PT	49.66	56.5%
NDI (%) after PT	33.74	69.6%
ΔNDI	47.37	60.9%
Relative ΔNDI	39.21	73.9%
PHQ9	44.54	47.8%
PHQ9 and SWE after PT	44.29	54.5%
NDI (%) after PT and PHQ9	34.02	69.6%
NDI (%) after PT and SWE after PT	32.85	77.3%
SWE after PT, NDI (%) after PT and PHQ9	34.2	72.7%

Legend: AIC, Akaike information criterion (AIC) is an estimator of prediction error; SWE, shear wave elastography; PT, physical therapy; NDI, Neck Disability Index; PHQ-9, Patient Health Questionnaire 9; ΔSWE, change from 6-month vs. baseline measurement; ΔNDI, change from 6-month vs. baseline measurement; Relative ΔNDI (%) = $\frac{NDI_{after\ PT} - NDI_{baseline}}{NDI_{baseline}} \cdot 100$; Relative ΔSWE (%) = $\frac{SWE_{after\ PT} - SWE_{baseline}}{SWE_{baseline}} \cdot 100$; analysis was done on pooled (averaged) SWE data from both radiologists.

Model coefficients for best predictive models (relative ΔNDI and combined SWE after PT with NDI after PT) with cut-off values for allocating into recovery groups are shown in Table 5.

Table 5. Model coefficients for most accurate models.

Model with Single Variable		
Variable (x)	*Coefficient* (β)	*Std. Error*
Relative ΔNDI	0.048	0.017
cut1	−2.72	1.08
cut2	1.59	0.83
Model with Combined Variables		
Variable (x)	*Coefficient* (β)	*Std. Error*
SWE after PT	−0.025	0.031
NDI (%) after PT	0.13	0.07
cut1	0.15	2.64
cut2	4.8	2.79

Legend: dependent variable (y) value less then cut1 implies full recovery, between cut1 and cut2 partial recovery, and above cut2 no recovery. Model equation is ordinal logistic regression equation $y = \beta_1 x_1 + \beta_2 x_2$. Thus, for model with single variable, the equation is $y = 0.048 \cdot$ relative ΔNDI, where relative $\Delta NDI = \frac{NDI_{after\ PT} - NDI_{before\ PT}}{NDI_{after\ PT}} \cdot 100$; for model with combined variables, the equation is $y = -0.025 \cdot SWE_{after\ Pt} + 0.013 \cdot NDI\ (\%)_{after\ Pt}$.

4. Discussion

Our study was the first to compare SWE values at baseline and after the follow-up period of six months. We also assessed the value of SWE as a prognostic or classification tool in the recovery of whiplash injury patients. In this study, lower SWE values were measured in patients after performing PT at a six-month follow-up. Excellent intra- and inter-observer reliability of SWE in measuring the trapezius muscle stiffness at baseline and six-month follow-up was found. These findings are consistent with those from the studies assessing intra- and inter-observer reliability of SWE of the upper trapezius muscle and other muscles both in healthy individuals and in pathological conditions, such as cerebral palsy [21–26].

We did not find a difference in stiffness between left and right trapezius muscles in whiplash injury patients before and after PT. This is in accordance with the results from our previous study [16] but differs from Zhang et al. [27], which reported a significant difference between dominant and non-dominant upper trapezius muscle. This difference could be due to different study populations. Zhang et al. obtained measurements on 20 healthy young male participants [27]. We assume that factors such as injury, age, gender, and work position could affect these results.

NDI has already been described in the literature as a good prognostic factor of recovery after the injury [28–31]. In this study, NDI has proven to be a better outcome classifier, with higher accuracy and lower possibility of error than SWE. The best health status classification can be made from the relative change of NDI (almost 74%) with an AIC value of 39.2.

However, six-month follow-up SWE values combined with NDI raised the accuracy of classifying outcomes with a further decrease in error risk (77.3%, AIC 34.21). Consequently, SWE after PT could be used with NDI after PT for estimating recovery after a whiplash injury, keeping in mind that SWE requires the work of an experienced operator with adequate equipment, which is expensive and not always available [32].

When analyzed individually, initial SWE values of upper trapezius muscle showed a high risk of error in predicting outcome and are unsuitable for being used as a prognostic tool. Due to the low accuracy and a high risk of error when classifying the patients in different recovery groups, SWE values obtained after six months and the change of SWE values showed to be inadequate for recovery status classification.

Postural changes in patients with neck and shoulder complaints lead to greater stiffness of the upper trapezius muscle [33,34]. Various therapies can lower trapezius stiffness

in the short term [35,36]. However, it is important to emphasize that muscle stiffness in healthy subjects does not vary in time, even after a long-term exercise program [37–39]. Although trapezius stiffness in whiplash injury patients decreased after PT at a six-month follow-up, it is difficult to determine the clinical implications of the observed changes in SWE values. We assume that the change in the trapezius stiffness addresses just one part of the recovery. Hence, it is not as sensitive as NDI, which engages more components involved in the recovery. This is supported by literature that affirms other factors influencing the outcome after the injury, such as psychological ones [40,41].

5. Limitations

This study requires consideration of a few limitations. First, a major limitation was a high dropout rate of 27%. The study was conducted during the unexpected COVID-19 lockdown, and patients were advised to attend only urgent medical examinations. Although we enrolled 50% more participants than proposed after performing power analysis, lowering of the trapezius stiffness did not reach statistical significance for the first radiologist. Post-hoc power analysis showed that three more participants were needed. Higher values of muscle stiffness can be measured if an individual intentionally contracts the trapezius muscle, so to minimize this error, all participants were instructed to relax, and SWE was performed after confirmation of no muscle contraction on the B-mode image. Additionally, the question of patients' home exercise adherence should be included in future studies and tested with patient recovery status.

6. Conclusions

We have found that SWE is not as good a classifier of recovery as NDI six months after a whiplash injury. Furthermore, NDI showed both better accuracy and a smaller margin of error. The most accurate variable in the classification of recovery was the relative change of NDI, and the overall best classification was obtained when combining NDI and SWE after physical therapy.

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Review

Lack of Objective Measurement in the Initial Screening and Follow-Up of Patients Who Report Whiplash Injury—Is Elastography of the Trapezius Muscle an Answer?

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Abstract: Background: Painfully decreased cervical range of motion accompanied by muscle spasm is a common presentation of whiplash injury of the neck. Stiffness of the cervical muscles can be assessed by ultrasound shear wave elastography (SWE), expressed in kilopascals (kPa). The hypothesis: SWE of the trapezius muscle is an objective measurement suitable for the initial screening and follow-up of patients who report whiplash injury. Methods and results: A total of 99 patients after whiplash injury were compared to 75 control participants. Mean trapezius stiffness was 82.24 ± 21.11 vs. 57.47 ± 13.82 for whiplash patients and controls, respectively. The cut-off value of SWE of 75.8 kPa showed 77% accuracy in correctly assigning patients to the whiplash or control group. To evaluate whether SWE can be used as a follow-up method of recovery after a whiplash injury, initial and endpoint SWE (after six months, $n = 24$) was carried out. Patients reporting no recovery showed similar SWE values as completely recovered patients. This finding refutes the second part of our hypothesis. Conclusions: SWE is a method that can be used for the initial screening of patients with whiplash injury, but we are still searching for an objective measurement that can be used in the follow-up of recovery.

Keywords: whiplash injury; elastography; ultrasound; stiffness; trapezius; shear wave

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1. Introduction

Whiplash injury of the neck is very common after "non-catastrophic" traffic accidents, with an incidence of more than 300 persons per 100,000 people [1], and it is defined as a bony or soft-tissue injury caused by sudden acceleration/deceleration of the head and neck [2]. The diagnosis is based on the mechanism of the injury. Patient-reported symptoms can be multiple and diverse (headache, paresthesia, pain, spasm, weakness, etc.) and are generally classified as whiplash-associated disorder (WAD) [3]. Painfully restricted cervical range of motion accompanied by muscle spasm is a common presentation in patients with whiplash injury [2]. Prolonged sick leaves and lower productivity after returning to work after the injury due to chronic pain and disability significantly impact the healthcare system [4].

In WAD, patients can report a wide variety of whiplash-related symptoms, and there are no standardized objective measurements to confirm or dismiss them. That creates the space for insurance claims seeking financial compensation [5]. The assessment of the severity and longevity of the disability after the injury is acquired by patient-reported indices and can add to potential malingering, estimated at 15% to 40% [6].

Three components of whiplash injury need to be analyzed for eventual objective measurement: pain, range of motion, and muscle spasm. Modern medicine does not possess a quantitative tool to measure other people's pain level. Pain levels are obtained through patient-reported indices, most commonly the visual analog scale (VAS) or numerical rating scale (NRS). Multidimensional pain questionnaires are rarely used in everyday practice.

Cervical range of motion (CROM) after the injury can be measured with a goniometer. It is an accurate and valid measurement often used by physiotherapists in everyday practice. CROM restriction is associated with pain level [7], and both correlate with the severity of the injury, but only to be dismissed as a method of follow-up [8]. The main reason is that their values can vary in a day. For example, if the patient wakes up with only slight pain in the neck, but tries to read newspapers, one can aggravate the pain for the whole day. In addition, both measurements are susceptible to potential malingering either by reporting worse possible pain or unwillingness to do the maximal possible movement of the cervical spine.

Increased stiffness or spasm of the cervical muscles is the third category that needs to be discussed. Increased muscle spasm of the cervical region is reported by almost all patients with a whiplash injury [3]. It can be a normal evolutionary mechanism for the prevention of further injuries, but its prolonged state can enhance disability after the injury. Palpation of the trapezius muscles is an integral part of the clinical examination to assess whether the affection is symmetrical or one side is more affected. When all of this is put into perspective, a need for objective measurement of muscle stiffness is crucial.

Ultrasound shear wave elastography (SWE) is a method that can assess the qualitative and quantitative elasticity properties of soft tissues, including the muscles. Tissue stiffness is measured by shear modulus and expressed in pressure units (kilopascals (kPa)). The SWE method uses a combination of the radiation force induced in tissue by an ultrasonic beam and the ultrafast imaging sequence capable of catching the propagation of the resulting shear waves in real time [9].

This procedure is safe, reproducible, and does not involve any radiation for the patient or examiner. It is also not time consuming when performed by an experienced radiologist. When using SWE, all participants are instructed to relax the shoulder girdle, and SWE is performed after confirmation of no muscle contraction in the B-mode image. Potential pitfalls of this method are that the standardization of the examination procedure is required, along with more radiologists versed in elastography measurement, more ultrasound machines with an elastography mode, and finally, the values of the stiffness of the cervical muscles in the general population subdivided by age and gender.

1.1. Hypothesis of This Review

Ultrasound shear wave elastography of the trapezius muscle is an objective measurement suitable for the initial screening and follow-up of patients who report a whiplash injury.

1.2. Evaluation of the Hypothesis

Our group of authors previously published the results for the stiffness of different muscles in the neck region after a whiplash injury. Seventy-five people with whiplash injuries were compared with 75 age- and gender-matched controls. The results showed that sternocleidomastoid and splenius capitis muscle SWE could not be used in diagnosing whiplash injury due to the highly asymmetrical data distribution and variance in tone of 300% between patients [10]. Trapezius muscle showed symmetrical data distribution with clinically relevant results described by higher stiffness in whiplash injury than in the control population group (87.84 ± 23.23 kPa vs. 57.47 ± 13.82 kPa, $n = 75$). There was no statistical difference between the left and right trapezius, which proved symmetrical affection of the neck.

To evaluate this hypothesis, we included an additional 24 patients after a whiplash injury (n = 99). The mean trapezius stiffness was 82.24 ± 21.11 kPa; the patients were aged 41.9 ± 13.

Knowing only the SWE value of the participant, a classification model using logistic regression was calculated (n-whiplash = 99, n-control = 75). The cut-off value of SWE of 75.8 kPa showed 77% accuracy in correctly assigning patients either to the whiplash or the control group (94.7% specificity; 63.6% sensitivity, $p < 0.0001$, ROC (AUC, area under curve) = 0.86).

When the classification model was calculated using SWE value, age, and gender, an accuracy of 82.7% was obtained (93.3% specificity; 74.7% sensitivity, $p < 0.0001$, AIC evidence ratio = 1108 when compared to SWE only model, ROC (AUC) = 0.89, probability cut-off of at 65%).

In Figure 1, the effects of age, gender, and SWE values on the occurrence of whiplash injury were calculated. An increase in SWE value by 1 kPa is associated with a 1.12-fold increase in the odds of whiplash injury (OR = 1.12, 95% confidence interval (CI) of 1.08–1.15). Older age lowered the odds of whiplash injury for each year 0.93-fold (OR = 0.93, 95% CI 0.9–0.96). No conclusion can be made regarding gender's effect on the occurrence of whiplash injury. The female gender showed an OR of 1.2 (95% CI 0.56–2.92), and further studies are needed to explain such width in an estimate of effect.

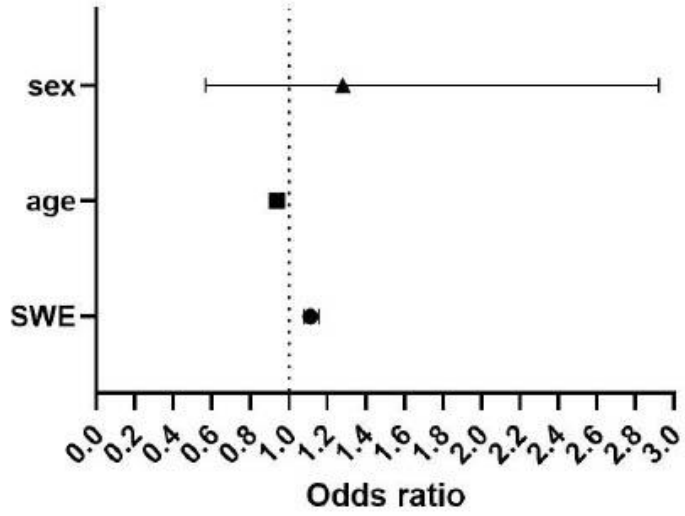

Figure 1. Likelihood of occurrence of whiplash injury in response to age, gender, and SWE. $probability\ of\ injury\ (\%) = \frac{1}{1+e^{4.326-0.015*SWE-0.248*sex+0.063*age}}$. Sex = 0 for male and 1 for female, SWE should be expressed in kPa and age in years.

This finding gives us positive evidence for the initial part of our hypothesis: SWE can be used in the screening of whiplash injury with the cut-off value of 75.8 kPa, which can be used to correctly assign three out of four patients in the control or whiplash group by knowing only the SWE.

To evaluate the second part of our hypothesis, that SWE can be used for the follow-up of whiplash injury patients, we carried out additional research.

Our group of authors reported SWE measurements after whiplash injury at baseline and after six months. The measurements were taken by two radiologists, and a decrease in stiffness was reported by both (first Δ10.1 kPa; $p = 0.04$; second Δ8.63 kPa; $p = 0.07$). In addition, excellent intra- and inter-observer reliability was reported [11].

However, when we compared the endpoint SWE values with the patient-perceived recovery values, we found no difference in the SWE values between the recovered and non-recovered patients after six months (55.6 ± 9.7 vs. 57 ± 15.8, Δ1.45; $p = 0.82$).

This finding refutes the second part of our hypothesis, that SWE can be used as a follow-up tool after a whiplash injury. Although a decrease in trapezius stiffness was detected, the correlation with patient-reported recovery was not found, so patients reporting no recovery showed similar SWE values as completely recovered patients.

The trapezius tone one year after a whiplash injury is still unknown.

2. Discussion

Most patients, after a whiplash injury, have symptoms without radiologically apparent bony or soft tissue injury. Therefore, imaging (X-ray, CT, or MRI) initially used to evaluate patients cannot be used to determine the seriousness of the injury. However, the value of MRI as a prognostic factor for functional and neurological outcomes was described in cervical subaxial spinal cord injuries [12]. Even though the evidence is still inconclusive [13,14], some recent studies showed a correlation between preexisting facet joint degeneration or constitutional cervical sagittal alignment (low neck tilt and low thoracic inlet angle) on CT and worse recovery [15,16]. Further studies are needed to confirm the usefulness of those radiologic findings in predicting outcomes.

Our hypothesis focuses on a prolonged spasm of the cervical muscles as a possible reason for pain and disability after a whiplash injury. Painful muscle spasm is a symptom present in every patient with a whiplash injury of the neck. Although the literature does not support the effectiveness of muscle relaxants in whiplash, their short-term use is common in everyday practice [17]. Sometimes, in the interview with the patients, we find that using a muscle relaxant, like diazepam, has more effect on alleviating the symptoms than using analgesics or non-steroid anti-inflammatory drugs. Physical medicine interventions aimed at decreasing the spasm of the muscles, like electrotherapy or ultrasound therapy, are commonly used in clinical practice, but there is no evidence to support the benefit of their use [18].

SWE was used as a method for the evaluation of our hypothesis. It is a new diagnostic method for this purpose, and it requires standardization (e.g., positioning of the patient or number of measurements). Ultrasound examination can detect the voluntary contraction of the muscles in B-mode, which is an advantage of this method. If contraction is detected, the patient is advised to relax the muscles. We assume this can prevent people from voluntarily trying to increase muscle stiffness.

The initial part of the hypothesis, that SWE can be used to diagnose whiplash injury, was confirmed, since increased stiffness in the trapezius muscle was detected in the whiplash injury group compared to the control group. We also calculated the classification model that correctly assigns patients to the whiplash or control group in 77% of the cases only by knowing the SWE value (cut-off value 75.8 kPa).

Our data showed that six months after the whiplash injury, most patients had decreased trapezius muscle stiffness of around 10 kPa. However, similar values of muscle stiffness were found in both patients who reported complete recovery and no recovery. Therefore, this value is not clinically relevant and cannot support the second part of our hypothesis that SWE can be used as a follow-up method. We presume that physical therapy, which included medical exercise, transcutaneous electric nerve stimulation (TENS, as a form of analgesic electro procedure), and therapeutic ultrasound of cervical muscle groups, provided a decrease in muscle stiffness in all patients after the injury. However, when performing activities of daily living (ADL) such as reading, cooking, or driving, adequate strength of the neck muscle groups is required to maintain the neck in a fixed position for an extended period of time. These activities can induce pain and cannot be detected by one-dimensional diagnostics like stiffness evaluation by SWE. We assume that an increase in the adherence to exercise after the institutionalized PT and progressive strengthening of the neck muscle groups can provide more extended painless periods in ADLs and increase

the quality of life, and future studies could answer this hypothesis. The decrease in muscle stiffness after PT is only a component of recovery, which is influenced by other physical and psychological factors. Unlike SWE, patient-reported outcome measurements that assess all parts of human functioning through one-day, vocational, avocational, and everyday activity, like the Neck Disability Index (NDI), are used as follow-up tools of disability after a whiplash injury [19]. Given that the NDI is a subjective tool, patients can use it to aggravate the level of disability when seeking financial compensation. The NDI was previously validated and used by our group of authors and its superiority to SWE in the follow-up of whiplash injury patients has been confirmed [11,20].

To conclude, SWE is a method that can be used for the initial screening of patients who report whiplash injury, but we are still searching for an objective measurement that can be used in the follow-up of recovery after a whiplash injury.

Author Contributions: Conceptualization, B.B. (Blaž Barun) and J.A.; methodology B.B. (Blaž Barun), J.A. and B.B. (Benjamin Benzon); investigation, J.A., A.P., B.B. (Blaž Barun), and T.V.; writing—original draft preparation, J.A., B.B. (Blaž Barun); writing—review and editing A.P. and B.B. (Benjamin Benzon); supervision, T.V. and J.A. All authors have read and agreed to the published version of the manuscript.

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12.3 Treći rad

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Article

Mobile App Intervention Increases Adherence to Home Exercise Program After Whiplash Injury—A Randomized Controlled Trial (RCT)

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Abstract: Objective: Can mobile app intervention via push notifications increase adherence to exercise and reduce disability and pain after a whiplash injury? Methods: A randomized controlled trial was conducted with concealed allocation, blinding of some assessors, and an intention-to-treat analysis. Participants who sustained whiplash injury at most 3 months prior were divided into active and control groups. Both groups completed a two-part physiotherapist-supervised physical therapy program (3-week break in between, ten sessions each, 5x/week). The program included TENS, therapeutic ultrasound, and exercises (breathing, ROM, deep neck flexor activation, and stretching). Both groups were encouraged to exercise at home. The active group additionally received push notifications through the mobile app once a day as a reminder to exercise. Outcomes were adherence to exercise (four-point Likert scale), physical functioning (NDI), pain intensity (VAS), perceived recovery (three-point Likert scale), work information, psychological functioning (PCS), and HRQoL (SF-12) at baseline and 6-month follow-up. Results: At month 6, when comparing the groups, the intervention group showed higher adherence to home exercise (3 [2–4] vs. 2 [2–4]; $p = 0.005$, median [IQR]) and improved HRQoL (ΔSF-12) (20 [6–36] vs. 15 [9–23]; $p = 0.038$). Unlike the control group, the intervention group showed a significant decrease in pain catastrophizing (31%; $p = 0.01$). A multivariant analysis showed that mobile app intervention influenced adherence most (≈1 Likert point). The groups did not differ in NDI, pain VAS, perceived recovery, or work limitation. Conclusions: Mobile app intervention increased adherence to home exercise, reduced pain catastrophizing, and increased HRQoL six months after a whiplash injury. Trial registration: ClinicalTrials.gov NCT05704023.

Keywords: randomized controlled trial; whiplash injury; adherence to exercise; physical therapy; Neck Disability Index

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1. Introduction

Neck pain is one of the leading causes of disability [1]. Whiplash injury is the most common injury related to motor vehicle accidents, and up to 50% of injuries lead to chronic neck pain and disability [2,3]. Besides being a cause of chronic physical impairment, it harms mental health, leading to higher healthcare system use and lower productivity, resulting in an increased burden on society [4]. The initial level of disability measured by the Neck Disability Index (NDI) [5] is recognized as a critical risk factor for developing chronic disability [6–8]. High initial pain intensity, coping styles, depression, fear of movement, and catastrophizing are other contributing factors for higher disability levels [9–14]. Conservative

treatments following a whiplash injury usually include a variety of active (exercises) and passive (rest, ultrasound, transcutaneous electric nerve stimulation (TENS), and laser therapy) procedures. Although conservative treatments are the golden standard after a whiplash injury, their effectiveness is still not statistically proven [15]. However, a positive effect of education and exercise was reported to improve pain and disability levels after a whiplash injury [16,17].

With the widespread use of smartphones and the development of mobile apps, many studies are now investigating ways to utilize these technological advances in medicine. Mobile apps can be useful in monitoring health status and providing feedback and health information in real time. Papers describing the promotion of health by stimulating an increase in physical activity, improvements in dietary habits, a reduction in smoking, and the monitoring of diabetes can be found in the literature [18–21]. Likewise, research has been conducted in the physical and rehabilitation medicine field where mobile apps have been shown to have positive effects on functional and health outcomes (gait, mobility, pain, and quality of life) [22]. Furthermore, mobile apps are already proven to be effective in increasing adherence in cardiac rehabilitation and could also help in other conditions where adherence to intervention is an issue, such as neck pain, including whiplash injury of the neck [23,24].

No clinical trials or systematic reviews regarding increasing adherence to exercise through mobile apps after whiplash injury of the neck are found in medical databases. The effect of adherence to exercise and disability level, comparing standard written recommendations to mobile apps with push notifications, is not yet known.

The aim of this randomized controlled trial was to determine whether the mobile app "WIApp" can be effective in promoting adherence to exercise and consequently lead to better recovery of patients after whiplash injury of the neck.

2. Methods

2.1. Study Design

This is a randomized, active-controlled, parallel-group unmasked to intervention allocation trial, which primarily assessed the effects of adding a mobile app to standard treatments on the adherence and recovery of patients following a whiplash injury. Standard care supported by a mobile reminder app (Arm A) was compared to standard care alone (Arm B). A timeline of data collection is provided in Additional File 1: Supplementary Figure S1.

2.2. Participants

2.2.1. Eligibility Criteria

The enrolled participants met the following inclusion criteria: age $\geq$ 18 years, whiplash injury of the neck in a car accident as the driver or co-driver, whiplash injury of the neck diagnosed by a physical and rehabilitation medicine specialist within three months, an NDI score higher than 5 (10%), possession of and ability to use a smartphone and a mobile app, and signed written informed consent. Subjects were excluded if they had an accident in any other type of vehicle other than a car, sustained a bone fracture or spinal cord injury in the accident, treated a malignant disease in the last five years, or non-compliance was expected (it was not possible to use a smartphone because of severe mental or physical impairment).

2.2.2. Settings and Locations

This study was conducted at the Division of Physical Medicine and Rehabilitation with Rheumatology, University Hospital of Split, Croatia.

2.3. Intervention Description

This study comprised two groups: a "WIApp" intervention group and a control group. A physical therapy specialist examined all participants, referred them to the physical therapy program, and allocated them to either the intervention or control group. If needed,

pain medications were prescribed. In between and after the physical therapy program, patients exercised at home with or without mobile app support.

2.3.1. Physical Therapy

All participants undertook the standardized physical therapy program guided by a physiotherapist. The detailed physical therapy program was described in our previous paper [8].

A two-part physical therapy program was carried out: a 2-week program with therapy 5 times a week, followed by a 3-week break, and then another 2 weeks of therapy.

2.3.2. Mobile App (Intervention Group)

WIApp is a smartphone app that aims to improve patient adherence to exercise and help patients recover after a whiplash injury; it includes a daily reminder to exercise, photographs, and explanations of exercises. The app was developed by the professional Mateh software d.o.o. from Zagreb, Croatia, and was available for iOS and Android. The main feature of WIApp is exercise support. Daily, at 7 p.m., patients received a notification with a reminder to exercise. The app included photographs of the exercises, with instructions, that patients could look at and read if they forgot which exercises they needed to perform and how.

After the participants met the eligibility criteria and were included in the trial, the physician referred them to physical therapy. After completion of the first part of the physical therapy program and allocation to the intervention group, they were introduced to the WIApp by the physician who, also being the administrator of WIApp, created a user profile for the participant. The participant downloaded the WIApp to their mobile phone and accessed their profile using a QR code or 16-digit code. The physician explained to the patient how they need to use the app during the follow-up.

2.3.3. Control Group

After the participants completed the first and second parts of the physical therapy program, a physiotherapist determined whether one could continue performing exercises at home. After participants confirmed that they knew how to perform the exercises, the physician gave them written and illustrated material explaining the home exercise program (HEP). Participants were advised to continue the HEP and to record adherence on a weekly basis.

2.4. Outcomes

We used the core outcome set according to Recommendations For Core Outcome Domain Set For Whiplash-Associated Disorders (CATWAD) [25]. Measurements were undertaken at two time points in each group: at baseline and 6-month follow-up. The only discrepancy between the registered protocol and that described in this paper was a change of adherence to exercise from a secondary to primary outcome.

1. Adherence to exercise: assessed at the 6-month follow-up with a four-point Likert scale (EAS) regarding weekly exercise completion (classified as no sessions, occasional, 2–4 sessions/week, or $\geq$5 sessions/week);
2. Physical functioning: assessed before physical therapy and at the 6-month follow-up with an NDI (where values of 0–8% are regarded as no disability, 10–28% as mild disability, 30–48% as moderate disability, 50–68% as severe disability, and 70–100% as complete disability);
3. Perceived recovery: assessed before physical therapy and at the 6-month follow-up with a three-point Likert-scale (PRS) (where 1 indicates non-recovery and 3 indicates full recovery);
4. Work: assessed before physical therapy and at the 6-month follow-up with work status information, work-time loss, and a work limitation scale (WLS) (a six-point Likert scale where 1 indicates normal work capability and 6 indicates no working capability);

5. Psychological functioning: assessed before physical therapy and at the 6-month follow-up with a Pain Catastrophizing Scale (PCS) (score range from 0 to 50, a score of 30 or more represents a clinically significant level of catastrophizing);
6. Health-related quality of life (HRQoL) and social functioning: assessed before physical therapy and at the 6-month follow-up with a Short form-12 (SF-12) Health Survey version 1 (online scoring calculator: https://orthotoolkit.com/sf-12/) and Social Functioning Scale (SFS)—a five-point Likert scale where 1 indicates a constant limitation in social activities and 5 indicates none limitation;
7. Pain intensity (neck region and head): assessed before physical therapy and at the 6-month follow-up with a visual analog scale (VAS) (ranging from 0 = no pain to 10 = maximum pain).

2.5. Sample Size

For the sample size calculation, we used the usual rule of thumb, which states that 10 to 30 participants per variable are needed for modeling. Therefore, we planned to analyze 60 participants. Due to potential dropouts, we planned to enroll 68 participants.

2.6. Assignment of Interventions: Allocation

2.6.1. Sequence Generation

The patients were randomized with an online randomization tool (randomizer.org) in a 1:1 ratio to receive either standard care supported by a reminder app (Arm A) or standard care (Arm B) for treatment of whiplash injury.

2.6.2. Allocation Concealment

To ensure allocation concealment, one research team member created a randomization list and another allocated the participants to a group.

2.6.3. Implementation

Generation of the allocation sequence, enrolment of participants, and assignment of participants to interventions were performed by physicians registered as investigators for this trial.

2.7. Blinding

Due to the nature of interventions applied in this study, blinding of the participants and outcome assessors was not possible. However, the physiotherapists and data analysts were blinded.

2.8. Statistical Methods

Continuous data are presented as median ± interquartile range (IQR), or mean and SD, and proportions are presented as percentages. Differences in continuous variables were tested with Mood's median test, Mann–Whitney tests, and t-tests. Differences in proportions were tested by Fisher's exact test. Statistical measures of evidence are presented as an effect size and its standard error, p values, R^2, and evidence ratio based on differences in corrected Akaike information criteria (AIC). For the multivariate analysis and correlation, we used a linear model. Statistical analyses were performed in Past3 Software and GraphPad Prism 10.0 software.

3. Results

A total of 78 participants were screened for the study; 68 were enrolled, and 60 were randomized into 2 treatment groups. The screening, randomization, and follow-up are summarized in Figure 1. The participants were recruited between January 2023 and February 2024 with a 6-month follow-up period.

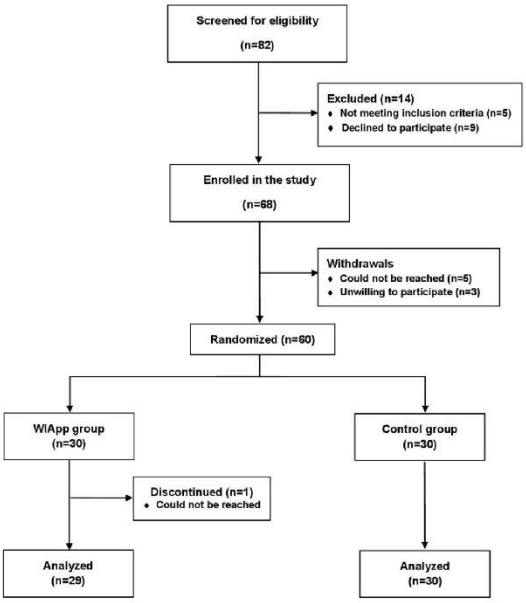

Figure 1. Flow of participants through the trial.

The baseline characteristics were similar between the groups (Table 1). The median age (IQR) in the WIApp group was 37 (24–51), and 19 participants (66%) were female.

Table 1. Baseline characteristics of participants.

	Total (n = 68)	WIApp (n = 29)	Control (n = 30)
Age, median [IQR]	38 [25–50]	37 [24–51]	35 [25–52]
Female, n [%]	43 [63]	19 [66]	17 [57]
Marital status, n [%]			
Single	34 [50]	12 [41]	15 [50]
Married	28 [41]	14 [48]	14 [47]
Divorced	5 [7]	3 [10]	0 [0]
Widowed	1 [2]	0 [0]	1 [3]
Education level, n [%]			
Elementary education	1 [1]	1 [3]	0 [0]
Secondary education	39 [57]	18 [62]	17 [57]
Bachelor's level	11 [16]	5 [17]	5 [17]
Master's/ Doctoral	17 [25]	5 [17]	8 [27]
Employed, n [%]	49 [72]	19 [66]	22 [73]
Initial absence from work, n [%]	42 [86] *	15 [79] *	20 [91] *
Time from accident, median [IQR]	29 [22–46]	36 [23–48.5]	27 [22–42.5]
Doctor's office visits, mean ± SD	3.6 ± 0.96	3.8 ± 1.13	3.5 ± 0.81
analgesics use, n [%]	52 [76]	23 [79]	25 [83]

* Percentage of employed participants. WIApp—Whiplash mobile application, Intervention group.

Fifty-nine participants completed the study and were analyzed: 29 in the WIApp group and 30 in the control group. Table 2 summarizes all measured outcomes at baseline and the 6-month follow-up for both groups.

Table 2. Primary and secondary outcomes at baseline and six-month follow-up for both groups.

	WIApp (n = 29)			Control (n = 30)			WIApp (n = 29)	Control (n = 30)	
	Initial	Final	*p*	Initial	Final	*p*	Δ = |Final − Initial|		*p*
Adherence, median [IQR]		3 [2–4]			2 [2–3]				0.005
NDI%, median [IQR]	38 [26–43]	16 [4–27]	<0.001	35 [26–47]	17 [9–27]	<0.001	20 [10–27]	17 [6–25]	0.516
Perceived recovery (full, partial, not), n [%]		11 [38], 16 [55], 2 [7]			12 [40], 16 [57], 1 [3]				0.823
PCS (significant/insignificant), n [%]	12 [41] vs 17 [59]	3 [10] vs. 26 [90]	0.010	* 9 [31] vs. 20 [69]	4 [13] vs. 26 [87]	0.120			
SF12, median [IQR]	40 [36–50]	60 [48–83]	<0.001	49 [36–57]	66 [45–78]	0.001	20 [6–36]	15 [9–23]	0.038
VAS pain, mean ± SD	5.4 ± 1.6	2.4 ± 2.6	<0.001	5.8 ± 1.7	2.9 ± 2.3	<0.001	1.45 ± 2.4	1.45 ± 1.95	0.900
SFS, median [IQR]	3 [3–4]	4 [3–4.5]	0.003	3 [2.75–4]	4 [3–4]	0.030	1 [0–1]	1 [0–1]	0.970
WLS, median [IQR]	3 [2–3.5]	2 [1–2.5]	0.003	3 [2–4]	2 [1–3]	0.004	1 [0–1.5]	1 [0–2]	0.770
Work time loss, median [IQR]		12 [0–58]			24 [10–70]				0.100

* Missing data for one participant who did not report PCS (valid percent reported). WIApp—Whiplash mobile application, Intervention group; NDI—Neck Disability Index; PCS—Pain Catastrophizing Scale; SF-12—Short Form Survey 12; SFS—Social Functioning Scale (1—constant limitation to 5—no limitation); WLS—Work Limitation Scale (1—no limitation to 6—complete limitation).

The WIApp group showed significantly higher adherence to HEP, with most participants reporting exercising 2–4 times/week, compared to the control group, who reported occasional exercise ($p = 0.005$). The level of adherence to exercise for both groups is shown in Table 3.

Table 3. Participants divided into outcome categories.

	Initially		After 6 Months	
	WIApp (n = 29)	**Control (n = 30)**	**WIApp (n = 29)**	**Control (n = 30)**
Adherence to exercise, n [%]				
Never			2 [7]	1 [3]
Occasionally			6 [21]	17 [57]
2–4 sessions/week			10 [34]	11 [37]
≥5 sessions/week			11 [38]	1 [5]
Neck Disability Index%, n [%]				
no disability (0–8%)			10 [34]	8 [27]
mild disability (10–28%)	8 [28]	10 [33]	14 [48]	16 [53]
moderate disability (30–48%)	15 [52]	13 [43]	4 [14]	3 [10]
severe disability (50–68%)	5 [17]	7 [23]	1 [3]	2 [7]
complete disability (>70%)	1 [3]			1 [3]
VAS pain (0–10), n [%]				
no pain (0)			9 [31]	5 [17]
mild pain (1–3)	2 [7]	4 [13]	13 [45]	15 [50]
moderate pain (4–6)	22 [76]	14 [47]	4 [14]	8 [27]
severe pain (7–10)	5 [17]	12 [40]	3 [10]	2 [7]
Social Functioning Scale (limitation), n [%]				
all of the time	1 [3]			
most of the time	5 [17]	7 [23]		1 [3]
some of the time	13 [45]	14 [47]	10 [34]	11 [37]
a little of the time	8 [28]	9 [30]	12 [41]	13 [43]
none of the time	2 [7]		7 [24]	5 [17]
Work Limitation Scale, n [%]				
No work limitation	1 [3]	1 [3]	11 [38]	9 [30]
I can do only my usual work	9 [31]	8 [27]	11 [38]	12 [40]
I can do most of my usual work, but no more	12 [41]	13 [43]	6 [21]	8 [27]
I can't do my usual work	5 [17]	7 [23]	1 [3]	1 [3]
I can hardly do any work at all	1 [3]	0 [0]		
I can't do any work at all	1 [3]	1 [3]		

WIApp—Whiplash mobile application, Intervention group.

Adherence correlated differently, i.e., oppositely, with initial NDI% in the intervention group ($r = -0.18$) and control group ($r = 0.26$) ($p < 0.001$). Using a multivariant analysis, we calculated how particular variables (initial NDI%, initial pain VAS, initial PCS, and intervention) influenced exercise adherence. The model that considers mobile app intervention describes data 17 times better ($\Delta AIC = 5.645$, $ER \approx 16.82$, $p = 0.007$, and $R^2 = 23\%$) than the one without it (Table 4).

Initially, 52% of patients in the WIApp and 43% in the control group reported moderate disability (Table 3), with no difference between the groups ($p = 0.6$). At the six-month follow-up, both groups had significantly lower NDI% scores, with 48% of participants in the intervention and 53% in the control group reporting mild disability. Furthermore, the median change in the NDI% was not statistically different between the groups (20 IQR 10–27 vs. 17 IQR 6–25; $p = 0.516$).

When analyzing PRS six months after the injury, most participants reported partial recovery (16, [55] vs. 17 [57]), followed by total recovery (11, [38] vs. 12, [40]) and no recovery (2, [7] vs. 1 [3]), with no significant difference between the groups ($p = 0.823$).

Table 4. Estimates of model variables' effects on adherence.

Variable	Effect Size (β)	Standard Error	*p* Value
Intercept	2.593	0.4156	<0.0001
NDI initially (%)	−0.006714	0.008337	0.4242
Pain (VAS) initially	−0.05571	0.06781	0.4150
PCS initially	0.01584	0.008822	0.0782
Intervention (app.)	0.5883	0.2082	0.0066

NDI—Neck Disability Index; PCS—Pain Catastrophizing Scale.

At baseline, significant pain catastrophizing was reported in 41% of participants in the WIApp and 31% in the control group ($p = 0.58$). Six months after the injury, pain catastrophizing was decreased by 31% in the WIApp group ($p = 0.01$) and by 18% in the control group ($p = 0.12$). Additionally, at baseline, we found that increased pain catastrophizing was connected to increased NDI% (OR = 1.071, 95%CI 1.025 to 1.127; $p = 0.002$), and a similar connection was found six months after the injury (OR = 1.111, 95%CI 1.049 to 1.2; $p < 0.001$).

Initially, 91% of participants in the WIApp and 87% in the control group reported moderate or severe pain intensity levels (Table 3), with no difference between the groups ($p = 0.369$). Both groups reported significantly lower average pain intensity levels six months after the injury, with 45% of participants in the intervention and 50% in the control group reporting mild pain. No difference in the average change of pain VAS was found between groups (1.45 ± 2.4 vs. 1.45 ± 1.95; $p = 0.9$).

After the injury, absenteeism was reported in 79% of participants in the WIApp and 91% in the control group ($p = 0.389$), with only 3% of participants from both groups having no work limitations (Table 3). Six months after the injury, participants had significantly fewer work limitations, with 38% of subjects in the intervention and 30% in the control group reporting no limitation. The median change in work limitation (ΔWLS) showed no difference between the groups (1 IQR 0–1.5 vs. 1 IQR 0–2; $p = 0.770$). Although there was a difference in the median workday loss between the groups, it was not statistically significant (12 IQR 0–58 vs. 24 IQR 10–70; $p = 0.1$).

After the injury, 45% of participants in the WIApp and 47% in the control group reported they sometimes have limitations in social activities (Table 3), with no difference between the groups ($p = 0.758$). Six months after the injury, both groups had limitations in social activities significantly less of the time, with 41% of participants in the intervention and 43% in the control group reporting only occasional limitations in social activities. There was no difference in the change in social limitation (ΔSFS) between the groups (1 IQR 0–1 vs. 1 IQR 0–1 $p = 0.970$).

There was no difference in the initial median SF-12 scores (40 IQR 36–50 vs. 49 IQR 36–57; $p = 0.12$). Both groups reported significantly higher SF-12 scores six months after the injury (60 IQR 48–83; $p < 0.001$ vs. 66 IQR 45–78; $p = 0.01$). When the change in the SF-12 was compared between groups, the intervention group showed a significantly greater increase (20 IQR 6–36 vs. 15 IQR 9–23; $p = 0.038$).

4. Discussion

This study compared the effectiveness of adding mobile app intervention to standard physical therapy in increasing adherence to exercise and lowering disability in a 6-month follow-up period in patients after whiplash injury of the neck. Mobile app use increased adherence to HEP. Both groups showed significant improvement in disability, pain, social functioning, and work capabilities, with no significant differences between them. Pain

catastrophizing was significantly decreased, and HRQoL improved more in the intervention group six months after the injury.

HEP for neck pain showed effectiveness in decreasing pain and disability [26]. Furthermore, adherence to HEP plays a key role in optimizing the benefits of exercise, and it is connected to better functional outcomes [27]. Adherence to HEP is challenging for patients, especially when it is needed for a prolonged period, as it is after a whiplash injury [28,29]. Digital interventions showed the ability to tackle that problem [30,31]. In this study, everyday reminders to exercise via push notifications increased adherence to exercise compared to the control group. In the control group, we showed a link between higher initial disability and higher adherence to HEP. This link was not found in the intervention group. So, participants with a higher initial disability and who are at risk for developing chronic pain and disability [32,33] were adherent in both groups. The intervention increased adherence in participants with a lower initial disability and who already had a good recovery trajectory [6]. This could explain why increased adherence in the intervention group did not lead to an additional decrease in disability.

Psychological factors are often described to negatively impact recovery after a whiplash injury [32,33]. However, our study did not show this connection. Moreover, our results showed that pain catastrophizing correlated with actual disability levels. In both groups, catastrophizing decreased six months after the injury when disability levels decreased. However, the change in pain catastrophizing was significant only in the WIApp group. This is in accordance with Campbell et al. 2018 [34], who did not find evidence of pain catastrophizing negatively impacting recovery after a whiplash injury.

A work limitation is largely prevalent after a whiplash injury [35], and many people with injuries have a lower ability to work six months after their injury [36]. In our study, 8 out of 10 participants in the intervention and 9 out of 10 in the control group reported initial absenteeism, with a lower rate of work-disabled participants in the intervention group. Also, the intervention group had a lower number of days of sick leave, but it was not statistically significant. This is in accordance with the paper by Brakenridge, et al. [37], which states that interventions following whiplash injury were not effective in decreasing days of sick leave. Although both groups showed significant improvements in presenteeism, almost one out of three were unable to perform their usual work six months after the injury.

Social functioning is also affected by the injury [38,39]. Both groups showed significant improvement in social functioning, and no difference was found between them. In both groups, three out of five participants reported rare or no limitations in social functioning six months after the injury.

Whiplash injury patients often sustain chronic pain and disability and do not fully recover [40]. Accordingly, three out of five participants reported partial recovery after six months, and no difference was found between groups.

It is known that whiplash injury negatively impacts a person's HRQoL [41,42]. When analyzing HRQoL, both groups showed significant improvement in a six-month period. As stated before, no difference was found between the groups when the outcomes were analyzed individually (physical health, mental health, work limitation, and social functioning). However, when united in HRQoL, the mobile app group showed a superior improvement. Similarly, in a study by Chen et al. [43], telerehabilitation increased HRQoL but did not affect physical functioning in patients with knee osteoarthritis.

5. Strengths and Limitations

The main strength of the study is the methodology—an RCT comparing the effectiveness of mobile app intervention in increasing adherence to HEP against written and illustrated material given to the whiplash injury participant. The methodology was guided by CONSORT recommendations, and all outcomes were reported according to CATWAD. Generally, a low dropout rate was observed (9/68, 13.2%), with only one participant dropping out after the allocation. Due to a low drop-out rate and increased adherence to HEP

in the WIApp group, we assume the app is suitable for every smartphone user who has sustained a whiplash injury. There are a few limitations that need reflecting upon. First, blinding of the patients and outcome investigators could not be achieved due to the nature of the intervention. Second, all outcome measures were patient-reported. Although they are the current golden standard for evaluation and follow-up of a whiplash injury, they can be subject to malingering [44]. Third, the follow-up period was six months. Therefore, further studies are needed to evaluate the long-term outcomes between the groups.

6. Conclusions

By adding mobile app intervention, we increased adherence to HEP, but that did not have an added impact on disability and pain. However, in the intervention group, lowered pain catastrophizing and increased HRQoL were observed. In this study, we focused on adherence, so there was no difference in exercise presentation between groups. In the future, content could be added to the app to be more interactive and to provide educational materials, videos of the exercises, and progression feedback. To maximize the apps' potential, further studies could investigate how more individualized exercise programs impact recovery in high-risk participants. These participants could be reassessed in real time, and treatment plans could be retailored as needed.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/diagnostics14232729/s1, Figure S1. Participant timeline and data collection method.

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Informed Consent Statement: All participants were informed about the study design, and informed consent was obtained in written form.

Data Availability Statement: Raw data can be provided upon request.

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