EXPUNERE DE MOTIVE

Secţiunea 1-a **Titlul proiectului de act normativ** Lege pentru modificarea şi completarea Legii nr. 153/2017 privind salarizarea personalului plătit din fonduri publice	
Secţiunea a 2-a **Motivul emiterii actului normativ**	
1. Descrierea situaţiei actuale	Prin intrarea în vigoare a Legii nr. 229/2016, profesiile existente în România, prin care se furnizează servicii de fizioterapie, conexe actului medical, s-a dorit cumularea sub denumirea unică de fizioterapeut, astfel încât să fie eliminate confuziile majore în ceea ce priveşte adresabilitatea pacienţilor, dificultăţile de intregrare pe piaţa muncii naţionale, inadvertenţele şi conflictele existente între specialiştii care, deşi au titluri profesionale diferite, competenţe diferite şi sunt încadraţi neunitar, desfăşoară aceeaşi activitate în scopul îmbunătăţirii şi restabilirii capacităţii de mişcare şi a abilităţii funcţionale a pacientului. Ocupaţiile de fiziokinetoterapeut, kinetoterapeut şi profesor CFM, existente în structura Clasificării Ocupaţiilor din România – nivel grupă de bază, conform Clasificării internaţionale standard a ocupaţiilor ISCO 08, care au corespondent în Legea nr. 153/2017, se exercită în baza următoarelor titluri profesionale: **1. Absolvenţi ai unui program de studii de licenţă (diplomă de licenţă) în următoarele specializări (prevăzute în art. 11 din Legea nr. 229/2016, ca titlu oficial de calificare în fizioterapie):** • fiziokinetoterapie; • kinetoterapie, cu durată de studii de 3-4 ani; • kinetoterapie şi motricitate specială, cu durată de studii de 3 ani; • cultură fizică medicală; • educaţie fizică şi sport, absolvenţi care au fost înscrişi sau şi-au finalizat studiile înainte de înfiinţarea primului program de studii/specializării de kinetoterapie; • balneofiziokinetoterapie şi recuperare. **2. Absolvenţi ai unui program de studii de licenţă (diplomă de licenţă) în următoarele specializări (care nu se regăsesc în art. 11**

din Legea nr. 229/2016):

- educație fizică și sport, absolvenți care au fost înscriși după înființarea primului program de studii/specializării de kinetoterapie;
- diferite ramuri sportive, (ex. baschet, handbal, tenis etc.), absolvenți care au fost înscriși după înființarea primului program de studii/specializării de kinetoterapie;

3. Absolvenți ai unui program de studii superioare de scurtă durată (diplomă de absolvire) în următoarele specializări (care nu se regăsesc în art. 11 din Legea nr. 229/2016):

- balneofizioterapie și recuperare;
- balneofiziokinetoterapie și recuperare;
- educație fizică și sport;
- educație fizică;
- cultură fizică;
- cultură fizică medicală.

Titurile profesionale menționate la punctele 2 și 3 au fost identificate după apariția Legii nr. 229/2016, respectiv după constituirea Colegiului Fizioterapeuților din România și se vor întreprinde măsurile necesare pentru ca aceste persoane să își păstreze în continuare locurile de muncă.

O parte din specialiștii mai sus menționați sunt angajați în sistemul public, iar postul pe care îl ocupă nu corespunde cu programul de studii/specializarea studiate. Spre exemplu, există absolvenți ai unui program de studii de licență cu specializarea în kinetoterapie, angajați pe posturi de fiziokinetoterapeut sau profesor CFM, precum și absolvenți ai unui program de studii de licență cu specializarea în fiziokinetoterapie sau balneofiziokinetoterapie și recuperare angajați pe posturi de kinetoterapeut.

În acest moment, specialiștii angajați în sistemul public de sănătate, pe funcțiile fiziokinetoterapeut, kinetoterapeut și profesor CFM, sunt personalul cu studii superioare cu cel mai scăzut nivel de salarizare.

De asemenea, având în vedere faptul că profesia de fizioterapeut (ocupațiile de fizioterapeut, fiziokinetoterapeut, kinetoterapeut și profesor CFM) se poate exercita atât ca profesie liberală, cât și prin prestarea serviciilor de fizioterapie în instituțiile finanțate din fonduri publice, din cauza nivelului foarte scăzut de salarizare din sistemul public există riscul ca aceste servicii să nu mai poată fi oferite în

	instituţiile medicale publice. Mai mult decât atat, profesia de fizioterapeut este foarte apreciată în statele membre ale Uniunii Europene, ale Spaţiului Economic European şi ale Confederaţiei Elveţiene, nivelul de salarizare al acestor specialişti fiind ridicat, ceea ce va determina un deficit de personal din ce în ce mai mare pentru acordarea serviciilor de fizioterapie pentru pacienţii români, în special pentru pacienţii din sistemul public de sănătate, prin exodul acestora. Având în vedere faptul că, şi la aceasta dată, personalul plătit din fonduri publice care ocupă funcţii în specialitatea fizioterapie este insuficient, menţinerea nivelului actual de salarizare va conduce la imposibilitatea asigurării acestor servicii în sistemul public de sănătate, astfel încât este absolut necesară modificarea Legii nr.153/2017 atât pentru a se corela cu Legea nr. 229/2016, precum şi pentru modificarea nivelului de salarizare a specialiştilor fizioterapeuţi care au calitatea de angajaţi plătiţi din fonduri publice.
2. Schimbări preconizate	*Iniţiativa legislativă de modificare a Legii nr. 153/2017 privind salarizarea personalului plătit din fonduri publice este imperios necesară pentru:* - *corelarea cu Legea nr. 229/2016 pentru organizarea şi exercitarea profesiei de fizioterapeut precum şi pentru înfiinţarea, organizarea şi funcţionarea Colegiului Fizioterapeuţilor din România, în scopul asigurării exercitării profesiei de fizioterapeut în sistemul de sănătate, în staţiunile medico-balneare şi în sistemul de asistenţă socială, de către angajaţii care deţin un titlu oficial de calificare în fizioterapie, conform art. 11 din Legea nr. 229/2016, precum şi de către cei care nu intră sub incidenţa legii dar care sunt angajaţi, în prezent, în sistemul public, pe posturi de fiziokinetoterapeut, kinetoterapeut şi profesor CFM;* - *eliminării discriminărilor existente pentru situaţiile în care aceleaşi servicii sunt prestate de specialişti angajaţi în funcţii cu denumiri diferite şi cu nivel de salarizare diferit;* - *reducerea exodului specialiştilor din domeniul fizioterapiei, în special către statele membre ale Uniunii Europene, ale Spaţiului Economic European şi ale Confederaţiei Elveţiene, unde nivelul de salarizare este cu mult mai mare decât cel din România;* - *responsabilirea specialiştilor privind asigurarea unor servicii de fizioterapie de înaltă calitate pentru pacienţii din România.* *Creşterea nivelul de salarizare va contribui astfel la creşterea posibilităţilor financiare ale beneficiarilor, în vederea participării la mai multe cursuri de perfecţionare; prin urmare, va creşte calitatea*

	serviciilor de fizioterapie furnizate pacienților România. *Având în vedere apariția Legii nr. 229/2016 care reglementează profesia de fizioterapeut, a existenței în structura Clasificării Ocupațiilor din România – nivel grupă de bază, conform Clasificării internaționale standard a ocupațiilor ISCO 08, a ocupației de fizioterapeut (grupa de bază 2264 – Fizioterapeuți, cod COR 226402 – fizioterapeut), precum și a existenței în desfășurare a contractelor de muncă pentru ocupația de fizioterapeut în sistemul privat,* ***este imperativ necesară introducerea unui nivel de salarizare și pentru această ocupație.*** Aspecte care necesită modificări și completări: 1. Introducerea funcției de fizioterapeut. 2. Gradele profesionale pentru fizioterapeuți, fiziokinetoterapeuți, kinetoterapeuți, profesori CFM, absolvenți de studii superioare – diplomă de licență - (S), în sensul păstrării celor 3 grade (debutant, specialist și principal) care ar presupune o creștere salarială gradată pe decursul a 9 ani de vechime în specialitate. 3. Gradele profesionale pentru fizioterapeuți, fiziokinetoterapeuți, profesori CFM, absolvenți de studii superioare de scurtă durată – diplomă de absolvire - (SSD), în sensul păstrării celor 2 grade (debutant, principal) care ar presupune o creștere salarială gradată pe decursul a 5 ani de vechime în specialitate. 4. Majorarea și stabilirea coeficientul de salarizare pentru fizioterapeuți, fiziokinetoterapeuți, kinetoterapeuți, profesori CFM absolvenți de studii superioare – diplomă de licență - (S). 5. Majorarea și stabilirea coeficientul de salarizare pentru fizioterapeuți, fiziokinetoterapeuți, profesori CFM absolvenți de studii superioare de scurtă durată – diplomă de absolvire - (SSD). 6. Creșterea nivelul salariului de bază – anul 2022 propus pentru fizioterapeuți, fiziokinetoterapeuți, kinetoterapeuți, profesori CFM absolvenți de studii superioare – diplomă de licență - (S). 7. Creșterea nivelul salariului de bază – anul 2022 propus pentru fizioterapeuți, fiziokinetoterapeuți, profesori CFM absolvenți de studii superioare de scurtă durată – diplomă de absolvire - (SSD). 8. Modificarea modalităților de încadrare pentru kinetoterapeuți și profesori CFM absolvenți de studii superioare – diplomă de licență - (S). 9. Modificarea modalităților de încadrare pentru fiziokinetoterapeuți, profesori CFM, absolvenți de studii superioare de scurtă durată – diplomă de absolvire - (SSD).
3. Alte informații	În prezent, la nivel mondial, Confederația Mondială de Fizioterapie (WCPT) recomandă spre utilizare termenul *Physical Therapy* sau *Physiotherapy* (traducere în limba română – fizioterapeut), în scopul protecției titlului profesional, ceea ce asigură că doar fizioterapeuții

	calificaţi au dreptul legal să practice ca fizioterapeuţi, dar şi protecţia populaţiei, prin limitarea utilizării acestui titlu de către persoanele necalificate. Conform clasificării europene a aptitudinilor, competenţelor, calificărilor şi ocupaţiilor (ESCO), la *Secţiunea Q Sănătate umană şi activitaţi de servicii sociale*, ocupaţia care se regăseşte la 2264 este de ***Fizioterapeut.*** Această clasificare a fost elaborată cu scopul de a: - crea un instrument european care să reflecte realitatea şi care poate avea valoare reală în ceea priveşte mobilitatea (migraţie europeană); - furniza un limbaj european comun pentru abilităţile/competenţele obţinute în contextul dezvoltării profesionale continue; - reactualizarea aptitudinilor şi competenţelor pentru ca profesioniştii care furnizează servicii de îngrijire a sănătăţii să fie capabili să desfăşoare activitatea în siguranţă, în legalitate şi cu eficienţă. Conform detalierii din CAEN REVIZUIT 2 - *Note explicative*, **Codul 8690** - *Alte activităţi referitoare la sănătatea umană* – cuprinde activităţi referitoare la sănătatea umană, ce nu sunt efectuate în spitale sau de către medici sau dentişti, cum sunt: activităţi ale infirmierelor, moaşelor, ***fizioterapeuţilor*** sau altor medici în domeniul optometriei, hidroterapiei, masajului medical, ergoterapiei, logopediei, homeopatiei, chiropracticii, acupuncturii, etc. Aceste activităţi se pot desfăţura în clinici medicale, de tipul celor ataşate întreprinderilor, şcolilor, azilelor de bătrâni, sindicatelor şi confederaţiilor sindicale şi in centre de sănătate, altele decât spitale, precum şi in cabinete particulare sau la domiciliul pacienţilor.

Secţiunea a 3-a

Impactul socio-economic al proiectului de act normativ

1. Impactul macroeconomic	Nu este cazul.
2. Impactul asupra mediului de afaceri	Diferenţele dintre retribuirea specialiştilor pentru activităţile de fizioterapie oferite în instituţiile medicale private faţă de retribuirea specialiştilor pentru activităţile de fizioterapie oferite în sistemul de sănătate publică sunt foarte mari, astfel încât nivelul de salarizare din sistemul public de stat nu poate asigura servicii de cea mai bună calitate.
3. Impactul social	Atragerea personalului în sectorul bugetar şi stoparea migraţiei în străinătate a practicienilor din domeniul fizioterapiei.
4. Impactul asupra mediului (***)	Nu este cazul.

5. Alte informaţii	Studii dovedite ştiinţific privind eficienţa clinică şi costurile reduse ale intervenţiei fizioterapeutice. Anexa nr. 1

Secţiunea a 4-a

Impactul financiar asupra bugetului general consolidat, atât pe termen scurt, pentru anul curent, cât şi pe termen lung (pe 5 ani)

- mii lei -

Indicatori	Anul curent	Următorii 4 ani				Media pe 5 ani
1	2	3	4	5	6	7
1. Modificări ale veniturilor bugetare, plus/minus, din care: a) buget de stat, din acesta: (i) impozit pe profit (ii) impozit pe venit b) bugete locale: (i) impozit pe profit c) bugetul asigurărilor sociale de stat: (i) contribuţii de asigurări	x	x	x	x	x	x
2. Modificări ale cheltuielilor bugetare, plus/minus, din care: a) buget de stat, din acesta: (i) cheltuieli de personal (ii) bunuri şi servicii b) bugete locale: (i) cheltuieli de personal (ii) bunuri şi servicii c) bugetul asigurărilor sociale de stat: (i) cheltuieli de personal (ii) bunuri şi servicii						

d) bugetul Fondului naţional unic de asigurări sociale de sănătate:e) bugetul Ministerului Sănătăţii Publice - venituri proprii						
3. Impact financiar, plus/minus, din care: a) buget de stat b) bugete locale						
4. Propuneri pentru acoperirea creşterii cheltuielilor bugetare						
5. Propuneri pentru a compensa reducerea veniturilor bugetare						
6. Calcule detaliate privind fundamentarea modificărilor veniturilor şi/sau cheltuielilor bugetare						
7. Alte informaţii	Anexa nr. 2					

Secţiunea a 5-a

Efectele proiectului de act normativ asupra legislaţiei în vigoare

1. Proiecte de acte normative suplimentare	Modificarea şi completarea Ordinul ministrului sănătăţii nr. 1470/2011 pentru aprobarea criteriilor privind angajarea şi promovarea în funcţii, grade şi trepte profesionale a personalului contractual din unităţile sanitare publice din sectorul sanitar, publicat în Monitorul Oficial cu numărul 796 din data de 10 noiembrie 2011.
2. Compatibilitatea proiectului de act normativ cu legislaţia comunitară în materie	Proiectul de act normativ nu se referă la acest subiect.
3. Decizii ale Curţii Europene de Justiţie şi alte documente	
4. Evaluarea conformităţii:	
Denumirea actului sau documentului comunitar, numărul, data adoptării şi data	

publicării.		
5. Alte acte normative şi/sau documente internaţionale din care decurg angajamente		
6. Alte informaţii		

Secţiunea a 6-a

Consultările efectuate în vederea elaborării prezentului act normativ

1. Informaţii privind procesul de consultare cu organizaţii neguvernamentale, institute de cercetare şi alte organisme implicate.	Proiectul de act normativ a fost publicat în dezbatere publică pe site-ul Colegiului Fizioterapeuţilor din România, începând cu data 19.02.2019. Au fost consultaţi membrii CFZRO, reprezenaţi ai CFZRO, reprezenanţi ai asociaţiilor profesionale şi persoanele fizice interesate. S-a organizat o şedinţă pubică privind dezbaterea proiectului de act normativ în data de 17.03.2019, fiind prezenţi membri ai Consiliului naţional, organ de conducere al CFZRO şi reprezentanţi ai asociaţiilor profesionale. Au înaintat propuneri prin reprezenanţi următoarele asociaţii profesionale: APF Muntenia, APK Transilvania.
2. Fundamentarea alegerii organizaţiilor cu care a avut loc consultarea, precum şi a modului în care activitatea acestor organizaţii este legată de obiectul proiectului de act normativ	Colegiul Fizioterapeuţilor din România este organizaţie profesională, cu personalitate juridică, neguvernamentală, de interes public, apolitică, fără scop patrimonial, cu responsabilităţi delegate de autoritatea de stat, având ca obiect de activitate autorizarea, controlul şi supravegherea exercitării profesiei de fizioterapeut, ca profesie liberală de practică publică autorizată. Asociaţiile profesionale care au participat la dezbaterea proiectului normativ au obiective şi scopuri privind dezvolatrea profesiei de fizioterapeut (fiziokinetoterapeut, kinetoterapeut şi profesor CFM).
3. Consultările organizate cu autorităţile administraţiei publice locale, în situaţia în care proiectul de act normativ are ca obiect activităţi ale acestor autorităţi, în condiţiile Hotărârii Guvernului nr. 521/2005 privind procedura de consultare a structurilor asociative ale autorităţilor	

administraţiei publice locale la elaborarea proiectelor de acte normative	
4. Consultările desfăşurate în cadrul consiliilor interministeriale, în conformitate cu prevederile Hotărârii Guvernului nr. 750/2005 privind constituirea consiliilor interministeriale permanente	
5. Informaţii privind avizarea de către: **a) Consiliul Legislativ** **b) Consiliul Suprem de Apărare a Ţării** **c) Consiliul Economic şi Social** **d) Consiliul Concurenţei** **e) Curtea de Conturi**	Este necesar avizul Consiliului Legislativ.
6. Alte informaţii	

Secţiunea a 7-a

Activităţi de informare publică privind elaborarea şi implementarea proiectului de act normativ

1. Informarea societăţii civile cu privire la necesitatea elaborării proiectului de act normativ	
2. Informarea societăţii civile cu privire la eventualul impact asupra mediului în urma implementării proiectului de act normativ, precum şi efectele asupra sănătăţii şi securităţii cetăţenilor sau diversităţii biologice	
3. Alte informaţii	

Secţiunea a 8-a **Măsuri de implementare**	
1. Măsurile de punere în aplicare a proiectului de act normativ de către autorităţile administraţiei publice centrale şi/sau locale - înfiinţarea unor noi organisme sau extinderea competenţelor instituţiilor existente	
2. Alte informaţii	

ANEXA NR. 1
LA EXPUNEREA DE MOTIVE

Gradul de satisfacție al pacientului privind serviciile de fizioterapie pentru durerea musculoscheletală/
Patient Satisfaction with private Physiotherapy for musculoskeletal Pain

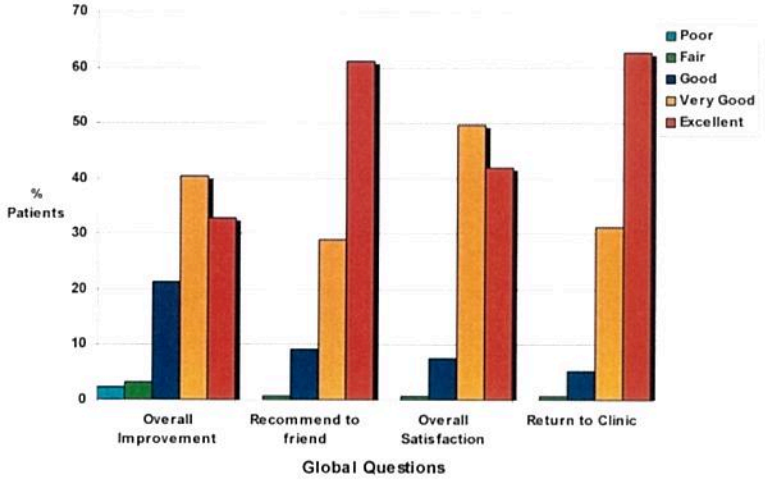
Sarah N Casserley-Feeney, Martin Phelan, Fionnuala Duffy, Susan Roush, Melinda C Cairns and Deirdre A Hurley[1]

BMC Musculoskeletal Disorders, 2008, **9**:50

Scopul acestui studiu este de a măsura gradul de satisfacție al pacienților referitor la serviciile de fizioterapie în Irlanda, pentru pacienții cu dureri musculoscheletale, folosind un chestionar specific pentru fizioterapie, privind gradul de satisfacție al pacenților, validat anterior.

Rezultatele demonstrează un grad ridicat de satisfacție a pacienților privind serviciile private de fizioterapie în Irlanda, dar ridică unele probleme cu privire la costurile tratamentelor private de fizioterapie.

Figure 1:Global ratings of Patient Satisfaction with overall experience of physiotherapy



[1] http://bmcmusculoskeletdisord.biomedcentral.com/articles/10.1186/1471-2474-9-50

Recuperarea prin exercițiu fizic a pacienților cu boală coronariană: recenzie și metaanaliză a studiilor randomizate/
Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials

Rod S Taylor, Allan Brown, Shah Ebrahim, Judith Jolliffe, Hussein Noorani, Karen Rees, Becky Skidmore, James A Stone, David R Thompson, Neil Oldridge[1]

Autorii au desfășurat o recenzie și o metaanaliză a unor lucrări de specialitate privind eficiența programelor de recuperare prin exercițiu fizic a pacienților cu boală coronariană. Au fost accesate baze de date precum MEDLINE, EMBASE și Cochrane Library. Au fost incluse 48 de studii desfășurate pe o perioadă de minim 6 luni, care au evaluat efectul antrenamentului prin exercițiu fizic, singur sau combinat cu intervenții psihologice sau educaționale, pe un număr total de 8940 pacienți.

Comparativ cu serviciile de îngrijire obișnuite, reabilitarea cardiacă a fost asociată cu reducerea ratei mortalității (odds ratio [OR] = 0.80; interval de confidență de 95% [IC]: 0.68 la 0.93); reducerea semnificativă a nivelului de colesterol total (diferența medie de –0.37 mmol/L [–14.3 mg/dL]; 95% IC: –0.63 la – 0.11 mmol/L [–24.3 la–4.2 mg/dL]), reducerea nivelului de triglilceride (diferența medie de –0.23 mmol/L [–20.4 mg/dL]; 95% IC: –0.39 LA –0.07 mmol/L [–34.5 to –6.2 mg/dL]), reducerea tensiunii arteriale sistolice (diferență medie de –3.2 mm Hg; 95% IC: –5.4 la –0.9 mm Hg); și reducerea numărului de persoane fumătoare autodeclarate (OR = 0.64; 95% CI: 0.50 to 0.83).

În concluzie, acesastă recenzie confirmă beneficiile recuperării cardiace bazate pe exercițiul fizic în contextul serviciilor de asistență de sănătate pentru bolnavii cardio-vasculari.

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[1] http://www.sciencedirect.com/science/article/pii/S0002934304001238

Fizioterapia pulmonară la copiii între 0 și 24 de luni, cu bronșiolită acută (recenzie Cochrane)/ Chest physiotherapy for acute bronchiolitis in paediatric patients between 0 and 24 months old (Cochrane review)

Roque i Figuls M, Gine-Garriga M, Granados Rugeles C, Perrotta C, Vilaro J
Cochrane Database of Systematic Reviews 2016; Issue 2, systematic review

Această recenzie Cochrane a fost publicată pentru prima dată în 2005 și îmbunătățită în 2007, 2012 și 2015.

Bronșiolita acută este una dintre cauzele majore ale urgențelor medicale pe perioada iernii, la copiii mai mici de doi ani. Fizioterapia pulmonară este uneori folosită pentru a asista nou-născuții la eliberarea căilor respiratorii de secreții, pentru a reduce efortul ventilator pulmonar.

Obiectivul studiului este de a determina eficiența fizioterapiei pulmonare la copiii mai mici de 24 de luni, cu bronșiolită acută. Un alt obiectiv a fost de a determina eficiența unor tehnici diferite de fizioterapie pulmonară (de exemplu, vibrația și percuția și expirul pasiv forțat).

S-a constatat că tehnicile resiratorii pasive lente asigură o ușurare imediată și tranzitorie la pacienții moderați, fără impact asupra duratei.

Fizioterapia prin presiune expiratorie pozitivă pentru eliberarea căilor respiratorii la pacienții cu fibroză chistică (recenzie Cochrane)/ Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis (Cochrane review)

McIlwaine M, Button B, Dwan K[1]
Cochrane Database of Systematic Reviews 2015;Issue 6

Fiziotarepia pulmonară este prescrisă pe scară largă pentru a asista eliberarea secrețiilor din căile respiratorii, la persoanele cu fibroză chistică.

Dispozitivul pentru presiune expiratorie pozitivă (PEP) asigură presiunea necesară căilor respiratorii, în timpul expirului. Astfel se poate îmbunătăți gradul de eliberare a căilor respiratorii, prin acumularea de gaz în spatele mucusului, prin ventilația colaterală, și prin creșterea temporară a capacității reziduale funcționale. Această recenzie Cochrane a demonstrat că există o reducere semnificativă a exacerbărilor pulmonare la persoanele care folosesc PEP, comparativ cu persoanele care folosesc alte mijloace, în studiile care au evaluat în primul rând rata exacerbărilor pulmonare.

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[1] http://search.pedro.org.au/search-results/record-detail/9959

Este important de notat faptul că există preferințe individuale cu privire la tehnicile de clearance pulmonar și că se va ține cont de fiecare pacient în parte în alegerea tratamentului optim pe termen scurt și lung, pe perioada vieții, având în vedere faptul că anumite circumstanțe precum stadiile de dezvoltare, simptomele pulmonare și funcția pulmonară, se schimbă în timp.

Abordarea fizioterapeutică pentru recuperarea funcției și mobilității, după accident vascular cerebral (recenzie Cochrane)
Physical rehabilitation approaches for the recovery of function and mobility following stroke (Cochrane review)

Pollock A, Baer G, Campbell P, Choo PL, Forster A, Morris J, Pomeroy VM, Langhorne P[1]

Diferite abordări fizioterapeutice pot fi folosite după un accident vascular cerebral (AVC), și există controverse și dezbateri considerabile privind eficiența acestor abordări.

Unii fizioterapeuți își bazează tratamentul pe o singură abordare; alții folosesc un mixaj de componente aparținând unor metode diferite.

Scopul acestei lucrări este de a determina care abordări fizioterapeutice sunt eficiente în recuperarea funcției și mobilității persoanelor cu AVC, și de a stabili dacă una dintre acestea este mai eficientă decât celelalte.

Recuperarea fizică, cuprinzând o selecție de componente aparținând diferitelor metode și mijloace de recuperare neurologică, este eficientă în îmbunătățirea funcției și mobilității pacienților cu AVC.

Fizioterapia în prevenția căzăturilor la vârstnici
Physiotherapy in the prevention of falls in older people

Catherine Sherrington, Anne Tiedemann[2]

Căzăturile sunt foarte frecvente la vârstnici și reprezintă o problemă importantă care poate avea consecințe importante la aceste persoane.

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[1] http://search.pedro.org.au/search-results/record-detail/10544, Cochrane Database of Systematic Reviews 2014; Issue 4

[2] http://dx.doi.org/10.1016/j.jphys.2015.02.011, Sherrington C, Tiedemann A (2015) Physiotherapy in the prevention of falls in older people. *Journal of Physiotherapy* 61: 54–60]
http://www.sciencedirect.com/science/article/pii/S1836955315000120

Căzăturile sunt de asemenea importante pentru sistemul de sănătate, datorită încărcării sistemului de servicii de sănătate. Fizioterapeuții pot juca un rol crucial în prevenirea căzăturilor la vârstnici. Există un nivel ridicat de dovezi științifice care demonstrează că prescrierea unei intervenții corespunzătoare poate preveni căzăturile.

Dovezile științifice curente demonstrează că: exercițiile de grup, intervențiile multifactoriale și pentru siguranța la domiciliu previn căzăturile la persoanele vârstnice cu risc crescut de cădere; și exercițiile individuuale și de grup precum și intervențile multifactoriale previn de asemenea căzăturile la grupurile de persoane evaluate în acest sens.

Prin urmare, instrumentele de evaluare a căzăturilor pot fi utilizate pentru a depista persoanele cu risc de cădere și pentru a stabili strategia terapeutică, dar nu sunt napărat necesare pentru a stabili cine va face gimnastică de grup sau individuală, deoarece se pare că toate persoanele vârstnice au beneficii în urma acestor intervenții fizioterapeutice.

Fizioterapia precoce în secțiile de terapie intensivă respiratorie
Early physiotherapy in the respiratory intensive care unit

Enrico Clini, Nicolino Ambrosino[1]

Fizioterapia este o parte integrantă a managementului pacienților din secțiile de terapie intensivă respiratorie (STIR). Cel mai important obiectiv în acest tip de unitate este de a îmbunătăți capacitatea funcțională generală a pacienților și de a restaura independența respiratorie și fizică a pacientului, reducând astfel riscul de imobilizare relungită la pat și riscul de apariție a complicațiilor asociate.

Acest articol este o recenzie a exemplelor științifice bazate pe dovezi cu privire la eficiența tratamentului fizioterapeutic la pacienții cu insuficiență respiratorie din STIR.

Cu cât mai repede se începe intervenția fizioterapeutică, cu atât crește posibilitatea de a inversa efectele imobilizării prelungite la pat. Aceste programe sunt foarte importante mai ales datorită faptului că numărul pacienților din secțiile de terapie intensivă respiratorie este în creștere peste tot în lume.

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[1] http://dx.doi.org/10.1016/j.rmed.2005.02.024

Efectul fizioterapiei la domiciliu și a supervizării, la pacienții cu spondilită anchilozantă – studiu randomizat

The effects of comprehensive home physiotherapy and supervision on patients with ankylosing spondylitis--a randomized controlled trial

Kraag G, Stokes B, Groh J, Helewa A, Goldsmith C[1]

În acest studiu randomizat au fost alocați cincizeci și trei de subiecți cu spondilită anchilozantă (SA); 26 dintre aceştia fac parte din grupul experimental, beneficiind de fizioterapie și educație cu privire la afecțiunea de care suferă, 27 subiecți fac parte din grupul de control, ei nebeneficiind de niciun fel de intervenție terapeutică.

Primul rezultat al tratamentului, evaluat după 4 luni, a fost modificarea mobilității coloanei vertebrale, măsurând distanța degete-sol.

Subiecții din grupul experimental au prezentat o reducere semnificativă a distanței degete-sol ($p \leq 0.004$) și o îmbunătățire a funcției ($p \leq 0.001$) comparativ cu subiecții din grupul de control.

Fizioterapia complectată cu educația privind afecțiunea este eficientă în tratamentul persoanelor cu SA.

Sănătatea posturală la femei: rolul fizioterapiei

Postural health in women: the role of physiotherapy

Britnell SJ, Cole JV, Isherwood L, Sran MM, Britnell N, Burgi S, Candido G, Watson L[2]

Acest studiu dorește să scoată în evidență rolul managementului fizioterapeutic în modificări posturale, condiții obstetricale, osteoporoză și incontinență urinară la femei și de a identifica situațiile femeii care constituie recomadări pentru ședințele de fizioterapie.

S-au studiat lucrări științifice din următoarele baze de date: MEDLINE, PEDro și Librăria Cochrane, având ca temă de studiu postura și condițiile referitoare la sănătatea femeii care puteu fi gestionate de un fizioterapeut.

S-a constata că:

1. Exercițiile musculaturii planșeului pelvin, executate sub îndrumarea unui fizioterapeut sunt recomandate pentru prevenția incontinenței urinare în timpul sarcinii și după naștere

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[1] The Journal of Rheumatology [1990, 17(2):228-233], http://europepmc.org/abstract/med/2181127

[2] Canadian Physiotherapy Association; Society of Obstetricians and Gynaecologists of Canada. https://www.ncbi.nlm.nih.gov/pubmed/16100646

2. Antrenarea musculaturii posturale sub îndrumarea unui fizioterapeut este recomadată pentru prevenirea și tratarea durerilor pelvine și de spate, în timpul sarcinii și după naștere.
3. Exercițiile prescrise de un fizioterapeut sunt recomandate la femei pentru a stimula modificările pozitive ale masei osoase și pentru a reduce riscul de fracturi.

BMJ Open

Finnish Subacromial Impingement Arthroscopy Controlled Trial (FIMPACT): a protocol for a randomised trial comparing arthroscopic subacromial decompression and diagnostic arthroscopy (placebo control), with an exercise therapy control, in the treatment of shoulder impingement syndrome

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ABSTRACT

Introduction Arthroscopic subacromial decompression (ASD) is the most commonly performed surgical intervention for shoulder pain, yet evidence on its efficacy is limited. The rationale for the surgery rests on the tenet that symptom relief is achieved through decompression of the rotator cuff tendon passage. The primary objective of this superiority trial is to compare the efficacy of ASD versus diagnostic arthroscopy (DA) in patients with shoulder impingement syndrome (SIS), where DA differs only by the lack of subacromial decompression. A third group of supervised progressive exercise therapy (ET) will allow for pragmatic assessment of the relative benefits of surgical versus non-operative treatment strategies.

Methods and Analysis Finnish Subacromial Impingement Arthroscopy Controlled Trial is an ongoing multicentre, three-group randomised controlled study. We performed two-fold concealed allocation, first by randomising patients to surgical (ASD or DA) or conservative (ET) treatment in 2:1 ratio and then those allocated to surgery further to ASD or DA in 1:1 ratio. Our two primary outcomes are pain at rest and at arm activity, assessed using visual analogue scale (VAS). We will quantify the treatment effect as the difference between the groups in the change in the VAS scales with the associated 95% CI at 24 months. Our secondary outcomes are functional assessment (Constant score and Simple shoulder test), quality of life (15D and SF-36), patient satisfaction, proportions of responders and non-responders, reoperations/treatment conversions, all at 2 years post-randomisation, as well as adverse effects and complications. We recruited a total of 210 patients from three tertiary referral centres. We will conduct the primary analysis on the intention-to-treat basis.

Ethics and Dissemination The study was approved by the Institutional Review Board of the Pirkanmaa Hospital District and duly registered at ClinicalTrials.gov. The findings of this study will be disseminated widely through peer-reviewed publications and conference presentations.

Trial registration number NCT00428870; Pre-results.

Strengths and limitations of this study

- Efficacy design: Strict eligibility criteria
- Placebo-surgery controlled trial: Blinding of both the participants and the outcome assessors in the comparison between index surgery and control (placebo surgery)
- Inclusion of a non-surgical treatment option to allow a pragmatic assessment of the relative benefits of surgical versus non-operative treatment strategies
- Potential confounding due to participants' knowledge of the treatment delivered in our secondary comparison between surgical and non-operative treatments

INTRODUCTION

Subacromial decompression is one of the most frequently performed procedures in orthopaedics.[1 2] It is carried out to treat patients with shoulder pain attributed to 'subacromial impingement syndrome' (SIS). Conventional wisdom dictates that SIS is caused by' impingement' of the rotator cuff (RC) between the humeral head and the

overlying acromion while lifting the arm. The appropriateness of this mechanistic explanation has been challenged lately where the generic label of 'subacromial pain syndrome' is currently advocated.[3 4] The aim of the subacromial decompression procedure, typically carried out arthroscopically, is to decompress the RC tendon passage through the subacromial space through resection and smoothening of the hypertrophied or prominent anterolateral undersurface of the acromion. Management of shoulder pain has been estimated to account for 4.5 million visits annually to physicians in the USA alone,[5] accounting for US$3 billion in costs each year.[6] Since 44%–65% of all shoulder complains are related to SIS, it is estimated that annual direct medical costs of SIS are over $1 billion in the USA.[7 8]

Since the introduction of subacromial decompression surgery in the early 1970s[9], the number of procedures has steadily increased across the entire western world. With the advent of arthroscopy, the number of these surgeries has increased dramatically—fivefold from the 1980s to 2005 in the USA[10] and 700% between 2000 and 2010 in the UK.[11] Remarkably, there is a stark absence of evidence from high-quality controlled trials to support the existing practice of performing subacromial decompression for patients with SIS. Two recent systematic reviews concluded that subacromial decompression provides no superior benefits in terms of pain relief, function or quality of life compared with non-surgical treatment.[12 13] There is even a placebo controlled trial to show the beneficial effect of exercise therapy (ET) over placebo physiotherapy.[14] However, the proponents of the procedure have argued that the evidence is skewed in favour of the therapeutic potential of surgery due to a significant crossover (5%–15%) from conservative treatment to surgery.[14–16] Although such concern is obviously warranted, it should also be recalled that surgeons' own perceptions on the success of any surgery might similarly be biased due to a considerable surgical placebo effect.

The outcome of any medical (surgical) intervention—particularly when treating primarily subjective symptoms—is a cumulative effect of three main elements: placebo effects, critical therapeutic (surgical) element and non-specific effects, most importantly, the normal variation in the course of the disease and the regression-to-the-mean phenomenon.[17 18] Conceding that the act of surgery per se produces a profound placebo response, a 'true' treatment effect is impossible to disentangle from the non-specific (placebo) effects—such as the patients' or researchers' expectations of benefit—without a placebo comparison group.[19] The critical therapeutic element is the component of the surgical procedure that is believed to provide the therapeutic effects (here, subacromial decompression), which are distinct from aspects of the procedures that are diagnostic or required to access the disease being treated (here, shoulder arthroscopy).

To the best of our knowledge, there is only one other ongoing study aiming to assess the true efficacy of subacromial decompression surgery in patients with SIS using a placebo controlled study design. According to the published protocol of this CSAW (Can Shoulder Arthroscopy Work?) trial,[20] the investigators have chosen a very similar approach to that of our Finnish Subacromial Impingement Arthroscopy Controlled Trial (FIMPACT). In brief, the CSAW trial is a three-group pragmatic randomised controlled trial comparing arthroscopic acromioplasty, active monitoring with specialist reassessment and investigational shoulder arthroscopy only. CSAW aims for recruitment of 300 patients with SIS to assess the efficacy of the surgery against no surgery, the need for a specific component of the surgery (acromioplasty) and the quantification of the possible placebo effect. As readily apparent, the two trials (FIMPACT vs CSAW) are very similar in design with the only notable differences being the primary outcome measure (pain at rest and after activity vs Oxford Shoulder Score, a score that assesses both pain and activities of daily living impairment), the primary outcome assessment point (24 months vs 6 months) and the intervention delivered for the third group (ET vs active monitoring with specialist reassessment), respectively.

The primary hypothesis of our FIMPACT trial is that arthroscopic subacromial decompression (ASD) is superior to diagnostic arthroscopy (DA) in patients with SIS. In addition, we will perform a pragmatic comparison of surgical and non-surgical treatment options (ASD vs ET). The relative benefits of ASD and ET will be assessed without a priori hypothesis of the superiority of one or the other.

MATERIALS AND METHODS

Overview of study design

The FIMPACT trial is an ongoing multicentre, three-group randomised controlled superiority study with a primary objective to assess the efficacy of ASD versus DA in patients diagnosed with SIS. Our design also enables the pragmatic comparison of surgical and non-surgical treatment strategies (ASD vs ET) (figure 1). To obtain three balanced study groups (of similar group size), we performed a twofold, sequential randomisation as follows: First, we randomised patients to surgical or conservative treatment in a 2:1 ratio and then randomised those allocated to surgery to ASD or DA in a 1:1 ratio. The initial patient screening for the trial began at one site (Tampere) on 1 February 2005 and was then expanded to two additional tertiary referral centres in March 2006 and December 2006 to improve recruitment and overall generalisability of the results. The recruitment was completed (all 210 required patients enrolled) in August 2013.

Ethical approval

Ethical approval was obtained on 28 December 2004 from the institutional review board of the Pirkanmaa Hospital District (R04200). Local research and development approvals were gained for each recruiting centre.

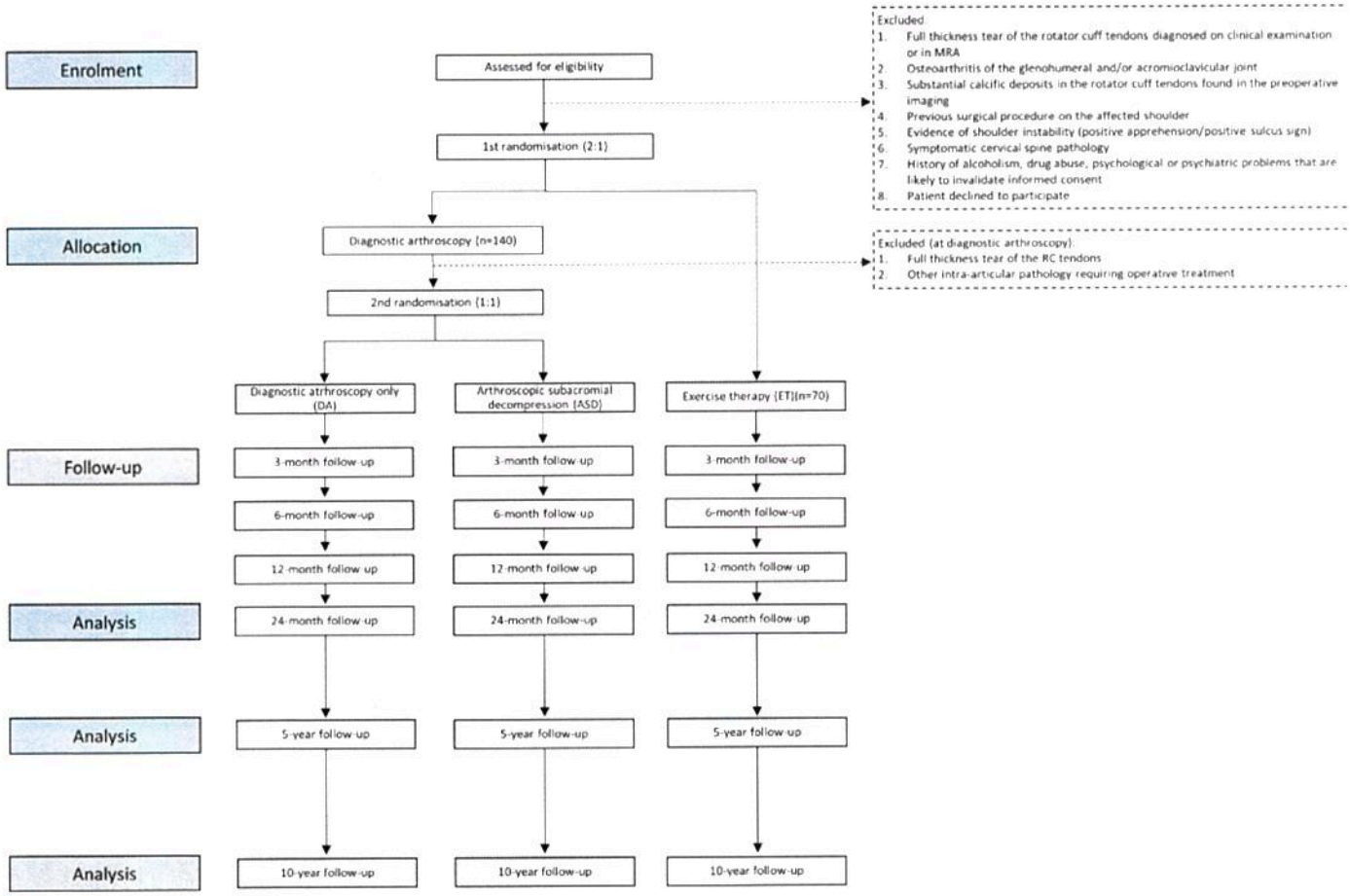


Figure 1 Flow chart of the trial: enrolment, assigned intervention and follow-up scheme. MRA, MRI with intra-articular contrast; RC, rotator cuff.

Participant selection

We assessed for eligibility all patients complaining of subacromial shoulder pain to any of the participating clinics. These participants were screened according to the inclusion and exclusion criteria and a recruitment surgeon confirmed the clinical diagnosis of SIS. To qualify as a recruitment surgeon, all trial surgeons had to have experience of more than 500 shoulder arthroscopies before the start of the trial. Detailed clinical examination of the shoulder was performed on all referred patients to rule out possible instability, clinical signs of RC rupture, frozen shoulder or other causes of symptoms. Standard X-rays and MRI were obtained from all potential participants and assessed by both a musculoskeletal radiologist and an orthopaedic surgeon. For patients found eligible for this study (fulfilling indications for ASD), we obtained written informed consent and randomised them into non-operative or operative groups (1:2) immediately after the baseline appointment. If patient had bilateral symptoms, only one shoulder was included in the study.

Eligibility criteria

We used specific eligibility criteria to ensure that recruited participants were only those with SIS. Accordingly, a standardised clinical examination was first performed, followed by a subacromial injection test. To exclude patients with concomitant pathology, particularly RC rupture, standard X-rays and MRI with intra-articular contrast injection (MRA) were carried out on all potential participants.

Inclusion criteria

1. Adult men or women ages 35 years to 65 years
2. Subacromial pain for greater than 3 months with no relief from non-operative means (physiotherapy, non-steroidal anti-inflammatory medication, corticosteroid injections and rest)
3. Pain provoked by abduction and positive painful arc sign
4. Positive impingement test (temporary relief of pain by subacromial injection of lidocaine)
5. Pain in at least two out of three of isometric tests (abduction 0° and 30° or external rotation)
6. Provision of informed consent from the participant
7. Ability to speak, understand and read in the language of the clinical site

Exclusion criteria

1. Full thickness tear of the RC tendons diagnosed on clinical examination (marked weakness in any of the examined muscles) or MRA

2. Osteoarthritis of the glenohumeral and/or acromioclavicular joint diagnosed on clinical examination and on X-rays
3. Substantial calcific deposits in the RC tendons found in the preoperative imaging
4. Previous surgical procedure on the affected shoulder
5. Evidence of shoulder instability (positive apprehension/positive sulcus sign)
6. Symptomatic cervical spine pathology
7. History of alcoholism, drug abuse, psychological or psychiatric problems that are likely to invalidate informed consent
8. Patient declined to participate

Recruitment process

Consultant orthopaedic surgeons carried out eligibility screening among patients referred to the study centres through standard clinical practice for shoulder pain. Patients meeting the eligibility criteria were introduced to the study. If patients expressed interest in participating, written information about the study was provided and they were asked to opt in. If the interest continued, arrangements were made for obtaining required imaging (X-rays and MRA) and for a separate baseline appointment.

Informed consent

At the first appointment, all participants were introduced to the detailed written information about the study and asked to sign a written informed consent form provided in the online supplementary appendix. At the baseline appointment (arranged within 45 days of initial contact), baseline data were completed and participant's willingness to participate in the study was confirmed. This procedure ensured that all potential participants had a reflection period for consent of at least 48 hours before giving their final consent to participate. Particular attention was paid to ensure that the participants realised that on entering the study they may receive only DA, in which case the subacromial decompression would not be performed. They were also informed that participation in the study is entirely voluntary and any decision they make would not affect their possible future care. In addition, every participant was informed of their right to withdraw from the trial whenever they desire without the need to supply any reason for such decision.

Baseline assessment

Baseline assessment included documentation of gender, birth date, education, employment, hand dominance, time from the onset of symptoms, recreational habits and employment status. We asked participants to assess their general heath and usage of pain medication. Modalities of any prior conservative treatment were also recorded (table 1).

Baseline clinical symptoms

The recruiting surgeon carried out a clinical history and a clinical examination related to shoulder pain. Shoulder complaints other than SIS, such as full-thickness RC tears, frozen shoulder, osteoarthritis of the acromioclavicular joint and instability were ruled out as much as clinical diagnosis allows.

Baseline imaging

Standard X-rays of the shoulder were obtained to assess possible glenohumeral or acromioclavicular osteoarthritis. An MRA was also obtained to rule out any other intra-articular or extra-articular pathologies. A musculoskeletal radiologist and an orthopaedic surgeon assessed all the images.

Randomisation and concealment

We used a two-phase sequential randomisation. In phase I, the participants were randomised into non-surgical or surgical treatment with allocation ratio 1:2. In phase II, those allocated to surgical treatment were further randomised to ASD or DA with 1:1 ratio (figure 1).

An independent statistician with no involvement in the execution of the trial prepared separate randomisation lists for each study centre using a computer-generated algorithm. Randomisation was carried out using sequentially numbered sealed opaque envelopes. The envelopes were kept in a secure, agreed location at each centre. To ensure concealment, block randomisation was applied using blocks varying in size randomly, the block size known only by the statistician.

To initially enter a participant into the study (phase I), an envelope containing the treatment assignment (non-surgical (ET) or surgery (ASD or DA), ratio 1:2) was opened during the baseline appointment. Participants randomised to ET started standardised physiotherapy within 2 weeks of the baseline appointment. Participants allocated to surgical treatment were scheduled for surgery aimed to be completed within 12 weeks of randomisation.

At the day of surgery, a DA was first carried out to confirm the eligibility of the participant (to rule out full-thickness RC tear and other obvious intra-articular pathology). Research/staff nurse then completed the randomisation procedure (phase II) by opening an envelope containing the surgical treatment allocation (ASD or DA, ratio 1:1). The allocation was revealed to the surgeon by showing the paper, but not expressed verbally.

Interventions

Diagnostic arthroscopy

All participants in the two operative groups first underwent arthroscopic examination of the shoulder with the use of standard posterior and lateral portals and a 4 mm arthroscope. To maintain concealment, the surgery was carried out under general anaesthesia. The orthopaedic surgeon evaluated and graded possible intra-articular pathological changes. The RC integrity was also evaluated from the subacromial space without performing routine bursectomy. If the integrity of the RC could not be assessed, bursal tissue was bluntly stretched with troachar or resected on the tendon side to allow visualisation.

Table 1 Baseline characteristics

	ASD	DA	ET
Age (years), mean (SD)			
Gender (female/male), n (%)			
Dominant hand affected, n (%)			
Socioeconomic status/workload			
Heavy manual labour (construction work, etc), n (%)			
Heavy manual labour (variable workload), n (%)			
Mostly manual labour including daily office work, n (%)			
Mostly office work with occasional manual assignments, n (%)			
Full-time office work, n (%)			
Unemployed, n (%)			
Pensioner/disability pensioner, n (%)			
Student, n (%)			
Home maker/housewife/other, n (%)			
Subjective health			
Duration of symptoms (months), mean (SD)			
Ability to work normally regardless of the shoulder symptoms? (yes/no), n (%)			
Recreational ability regardless of the shoulder symptoms? (yes/no), n (%)			
Prior treatments			
Rest, n (%)			
Pain medication, n (%)			
Topical pain medication, n (%)			
Corticosteroid injection, n (%)			
Ultrasound, laser or any other similar therapies, n (%)			
Physiotherapy including ET, n (%)			
Other, n (%)			
Generic health states			
15D			
SF-36			
Pain measurements/shoulder scores			
Pain at rest (0–100 VAS Scale), mean (SD)			
Pain during activity (0–100 VAS Scale), mean (SD)			
Constant-Murley Score (CS), mean (SD)			
The simple shoulder test (SST), mean (SD)			

ASD, arthroscopic subacromial decompression; DA, diagnostic arthroscopy; ET, exercise therapy; SF-36, Short Form 36; VAS, Visual Analogue Scale.

If arthroscopic examination revealed any unexpected pathology (such as capsular pathology, full-thickness RC tear or osteoarthritis), the patient was treated according to current clinical practice guidelines for the given pathology while under the same anaesthesia. In such a case, the participant was excluded from the trial. Patients with partial tears were included in the study, while patients with a full-thickness tear were excluded and RC repair was carried out.

After the arthroscopic examination of the glenohumeral joint and subacromial space, confirming the eligibility of the participant, the participants were randomly assigned to receive either ASD or DA only. If the patient was allocated to the DA group, the operation was terminated. To ensure concealment of the participants and the staff other than those in the operating theatre, the participants were kept in the operating theatre for the required time to perform subacromial decompression.

Arthroscopic subacromial decompression

Debridement of the subacromial bursa was performed with a shaver and/or electrocoagulation, followed by the resection of the bony spurs and projecting anterolateral

undersurface of the acromion by a shaver as described by Ellman.[21]

Postoperative care

In both the ASD and the DA groups, the postoperative rehabilitation was identical. All surgically treated participants received one visit to an independent physiotherapist for guidance and instructions for home exercises. Subsequent rehabilitation was carried out according to the standardised rehabilitation protocols of the participant centres. Since the initial rehabilitation after a surgery needs to be 'tempered' due to joint irritation, the rehabilitation protocol of the operatively treated groups (ASD and DA) was not identical to the ET group.

Exercise therapy

In the ET group, supervised progressive physiotherapy was started within 2 weeks of randomisation using a standardised protocol. The protocol was based on the same principles as the regimen shown effective for the treatment of SIS earlier,[14] but was updated—with the help of the principal investigator of the original study[14]—to conform with the state-of-the-art ET for SIS. The regimen was based on daily home exercises, and included 15 visits to an independent physiotherapist for guidance and monitoring of the progress, carried out approximately once a week. The aim of the supervised exercise treatment was to restore painless, normal mobility of the shoulder girdle, eliminate any capsular tightness and to increase the dynamic stability of the glenohumeral joint and the scapula.

Compliance to treatment allocation and possible crossover

Participants allocated to the ET group were told at the time of giving consent that they would be allowed to consider crossing over to the ASD group if they didn't get adequate relief of symptoms (preferably no sooner than 6 months post randomisation). Similarly, in the two surgical treatment groups, the participants were informed of the possibility of unblinding if debilitating symptoms persisted 6 months or more after operation. If the participant was allocated to the DA group, ASD was offered. If the participant had undergone ASD, he/she was offered extended physiotherapy. No prespecified criteria were used for determining 'inadequate relief of symptoms/debilitating symptoms', rather it was left to the participants and the study physicians to make the clinical judgement together.

Outcome measures

The outcomes used in this study and the timetable for follow-up assessments are summarised in table 2.

Primary outcome measure

Visual Analogue Scale

As the primary outcome measure, we used a Visual Analogue Scale (VAS) to measure the patient's perceived pain intensity at rest and at arm activity during the 24 hours preceding the assessment. Shoulder pain was assessed on a 100 mm scale ranging from 0 (no pain) to 100 (extreme pain). We considered 15 as the minimal clinically important difference (MCID) for VAS.[22]

Secondary outcome measures

Constant-Murley Score

The Constant-Murley Score (CS) is the most commonly used scoring system for evaluation of various disorders of the shoulder.[23] It consists of both objective (range of motion and strength) and subjective measurements (pain assessment, workload and leisure time activities), which are summarised in a score between 0 and 100. A higher score indicates better shoulder function. The minimal detectable change of the Constant Score is 17 for patients with SIS.[24]

In addition, as night pain is considered one of the hallmark symptoms in patients with SIS and our two primary outcome measures (patient's perceived pain intensity at rest and at arm activity in the last 24 hours) do not specifically address this issue, a specific question from the CS (unaffected sleep: 'Yes' or 'No') will be analysed separately.

Simple shoulder test

The simple shoulder test (SST) was developed to assess any impairment of the patient's activities of daily living.[25] The SST consists of 12 questions with yes (1) or no (0) response options. The maximum SST score is 12 indicating normal shoulder function, minimum score of 0 points refers severely diminished shoulder function. The SST has good reliability and responsiveness in patients with RC symptoms.[26] The MCID for the SST in RC disease is 2 points.[27]

15D

The 15D instrument (a health-related quality of life instrument with 15 dimensions) is a generic health-related quality of life (HRQoL) instrument comprising 15 dimensions.[28] For each dimension, the respondent must choose one of the five levels that best describes his/her state of health at that moment (the best level being 1 and the worst level being 5). A set of utility or preference weights is used in an addition aggregate formula to generate a single index number, the utility or 15D score. The maximum 15D score is 1 (no problems on any dimension) and the minimum score is 0 (being dead). The responsiveness, reliability and validity of 15D have been thoroughly established, and this instrument has been used extensively in clinical and healthcare research.[29 30]

Short form 36

The short form or SF-36 is a generic HRQoL instrument to quantify the physical, functional and psychological aspects of HRQoL. It consists of 36 questions in eight subscales that assess physical, functional, social and psychological well-being.[31] The score ranges from 0 to 100, where a higher score is associated with better health. The Physical and Mental Component Summary

Table 2 Outcomes and follow-up time points

Assessment	Screening	Enrolment (baseline)	Surgery	3 months	6 months	12 months	24 months	5 years	10 years
Screening form	X								
Informed consent		X							
Baseline characteristics form		X							
X-ray and MRI	X								X
Randomisation		X (first)	X (second)						
Arthroscopic findings form			X						
Follow-up form*				X		X			
Clinical examination		X			X		X	X	X
Complications/adverse effects form†			(X)	(X)	(X)	(X)	(X)	(X)	(X)
VAS, at rest		X		X	X	X	X	X	X
VAS, at arm activity		X		X	X	X	X	X	X
Constant- Murley Score (CS)		X			X		X	X	X
Simple shoulder test (SST)		X			X		X	X	X
SF-36		X		X	X	X	X	X	X
15D		X		X	X	X	X	X	X
Return to work				X	X	X	X	X	X
Return to previous leisure activities				X	X	X	X	X	X
Responder analysis				X	X	X	X	X	X
Patients' satisfaction to the treatment				X	X	X	X	X	X
Patients' assessment of the treatment allocation				X					
Health resource utilisation				X	X	X	X	X	X

*Letter/telephone interview
†If required
SF-36, Short Form 36; VAS, Visual Analogue Scale.

Scales are then calculated as composites of the related subscales. The SF-36 is one of most widely used measures of HRQoL.[32]

Patient satisfaction and responder analysis

We elicited patients' global assessment of satisfaction to the treatment with this question: 'Are you satisfied with the treatment you have received?' We used a VAS scale ranging from 0 (completely disappointed) to 100 (completely satisfied).

Additionally, we elicited patient satisfaction to the treatment outcome with the following question at each follow-up time point (table 2): 'How satisfied are you with the outcome of your treatment?' on a 5-item scale. The response options for this question are provided in the online supplementary appendix. Participants who reported very satisfied or satisfied will be categorised as 'Responders' and patients who responded very dissatisfied or dissatisfied as 'Non-responders'.

Return to previous leisure activities

Similarly, at each follow-up (table 2), participants were asked to respond to the following question: 'Have you been able to return to your previous leisure activities?' ('yes' or 'no').

Patients' perception of operative treatment-group assignment

At the 3-month follow-up point, the patients in the two operative groups were asked to guess whether they had undergone ASD or DA.

Health resource utilisation and costs

For the cost-effectiveness analysis, at each follow-up visit the participants were asked to fill in a questionnaire inquiring about the use of healthcare resources. The questionnaire contains a list of items of healthcare resources available and the participants were asked to fill in the number of visits per item during the recall period of each follow-up time point. The resource use will be calculated based on the number of visits times unit cost per item and expressed as mean costs by items of resource use, and the mean direct total healthcare resource costs. All costs will be discounted to the 2016 price level.

Time to return to work

Information about return to work was recorded at each follow-up time point (table 2).

Complications and adverse effects

Complications directly related to the interventions were registered. The participants were also encouraged to contact the participating hospitals if any adverse effects (AEs) occurred and contacts to the healthcare system were monitored at every follow-up visit. Potential AEs were categorised to serious adverse effects (SAEs) and minor adverse effects (MAEs) if the participants sought treatment. Death, cardiovascular or gastrointestinal effects, deep venous thrombosis, pulmonary embolism, systemic or local infection were categorised as SAEs and shoulder symptoms like pain, swelling and decreased range of motion were categorised as MAEs. The number and severity of complications and AEs will be assessed.

Follow-up

The full follow-up process is shown in figure 1. In brief, the participants filled in the above noted (mailed) outcome questionnaires at 3 months, 6 months, 12 months and 24 months postrandomisation, in addition to which they were also assessed clinically at 6 months and 24 months (and 5 years and 10 years) postrandomisation by a study physiotherapist unaware of treatment allocation, treatment given or possible unblinding. Outcome assessors were instructed not to inquire anything about prior treatment. Further, participants wore a T-shirt on all follow-up examinations.

Adherence and loss to follow-up

Several procedures were implemented to limit loss to follow-up, including excluding individuals likely to pose suboptimal adherence to study follow-up, obtaining verified contact information from each consented participant and having a local research nurse remind participants of upcoming follow-up/clinic visits. All attempts were made to make follow-up as convenient for the patients as possible. Participants were required to visit the outpatient clinic only at 6 months and 24 months (and 5 years and 10 years) postrandomisation, while the 3-month and 12-month follow-ups were carried out using mailed questionnaires to minimise inconvenience to the participants. The follow-up visits had no more discomfort for the participant than the routine clinical shoulder examinations. The follow-up schedule did not involve extra costs to the participants. Follow-up rate was monitored throughout the trial and patients who did not return follow-up questionnaires would receive reminder telephone calls. Using strategies highly similar to these in our previous placebo-surgery controlled trial,[33] a 99% follow-up rate was achieved.

The number and proportion of individuals eligible for and compliant with each follow-up was documented. Individuals who died during the study (from causes unrelated to the study or procedure) will be tabulated. An analysis of the demographic and prognostic characteristics will be carried out between the individuals who withdrew and those who remained in the study. For continuous variables, parametrical or non-parametrical analysis of variance will be used. For categorical variables, χ^2 or Fisher's exact test will be applied.

Missing items

We will use multiple imputation to handle missing data for those statistical analyses that cannot handle occasional missing values. All variables to be included in the final analyses will be included in the chained equations imputation model. The imputation algorithm, a fully conditional specification, uses a specific univariate model for each variable and, for each specific imputed data set,

iteratively imputes each variable with missing values and uses the imputed values in the imputation of other variables.

Sample size

The sample size calculation was based on the two primary outcome measures, VAS at rest and at arm activity, at 24 months postrandomisation. The FIMPACT trial was powered to detect a minimal clinically important improvement (MCII) in a VAS Pain Score (improvement of at least 15; assumed SD 25) between ASD and DA (or ET). To achieve a somewhat unconventional (stringent) 90% study power and using a two-sided type I error rate (5%), our trial requires 68 patients per study group to show clinically meaningful advantage of ASD over DA (or ET). Acknowledging the stringent power threshold, we reserved only 3% surplus for potential loss to follow-up/crossovers (3%), and accordingly, we set the recruitment target at 70 patients per treatment group.

Safety analysis

There are no anticipated safety issues with the FIMPACT Study. Identically to our previous placebo-surgery controlled trial,[33] an interim analysis, as requested by the ethics board, was carried out after the enrolment of 45 participants by an independent data and safety monitoring board (the National Institute for Health and Welfare) to ensure that the rates of complications or reoperations were within acceptable limits (within the normal rate of complications and/or reoperations related to shoulder arthroscopy). Since we found no marked discrepancy in our crude assessment of the incidence of complications/reoperations, no unsealing of group assignments (unblinding) was carried out. No other interim analysis was carried out.

Data management

Questionnaire forms on paper were the primary data collection tools for the study. On receipt of the questionnaire forms, a study nurse made a visual check of the responses and queried missing data when possible. Research assistants, blinded to the group allocation, stored the forms into an electronic database by double data entry to minimise typing errors. The researchers, blinded to the group allocation, perform a visual check of the data in the electronic database and then queried all missing, implausible and inconsistent data. Patient records in the participating hospitals were used when collecting missing data or interpreting inconsistent or implausible data. The final analysis was performed on data transferred to the file 'FIMPACT-full data_final', having been documented as meeting the cleaning and approval requirements of our independent statistician and after the finalisation and approval of the accompanying statistical analysis plan (SAP) document. Participant files will be maintained in storage (both in electronic and paper formats) at the coordinating centre for a period of 10 years after completion of the study (10-year follow-up visits).

STATISTICAL METHODS

Statistical analysis plan

Please refer to the online supplementary appendix for a more complete SAP, which we briefly summarise here. An independent statistician who is unaware of the group assignments will perform all the analyses.

We will summarise the baseline characteristics of the participants by group, reported as a mean (SD) or median (first quartile, third quartile) for continuous variables and count (per cent) for categorical variables.

We will analyse the data in a blinded manner. All p values will be reported to three decimal places with those less than 0.001 reported as $p<0.001$. The criterion for statistical significance will be set at $\alpha=0.05$.

Primary analysis

We will carry out the primary analysis according to the intention-to-treat principle: participants are retained in the groups to which they were initially randomised.

The primary comparison will be on the efficacy of ASD (ASD vs DA). We will perform the primary comparison on the efficacy of ASD (ASD vs DA) as a between-group comparison using a repeated measures mixed-effects model (RMMM). Study group and time of assessment (baseline, 3 months, 6 months, 12 months and 24 months) will be included as fixed factors and patient as a random factor. The model will include interactions between study group and time of assessment. The baseline value will be included as a covariate. The RMMM model will be used to quantify the treatment effect as the difference between the groups in pain scores (VAS) with the associated 95% CI and p -value at 24 months postprimary randomisation. To safeguard against potential multiplicity bias,[34] we will require a statistically significant treatment effect on both of our primary outcome variables, that is, pain at rest and pain at activity.

The same statistical model will also apply to the pragmatic comparison of the relative benefits of surgical versus non-operative treatment strategies on SIS (ASD vs ET).

Secondary analyses

We will also use the RMMM model to analyse secondary outcomes where applicable. The results will be reported as the differences between the groups with the associated 95% CI and p value at 24 months postprimary randomisation.

Categorical variables, reoperations or treatment conversions, and complications as well as AEs will be analysed using logistic regression analysis or Poisson regression dependent on whether subjects with complications or (multiple) complications (per subject) are analysed.

These secondary analyses will be supportive, explanatory and/or hypothesis-generating, which is why multiplicity is not a problem.[2]

Sensitivity analyses

We will carry out the following sensitivity analyses: (1) per-protocol analyses, in which the above noted primary and secondary analyses will be carried out again with patients who received the interventions as allocated; (2) and potential effects due to the treatment providing centres.

Subgroup analyses and hypothesised effects

We have identified three important subgroups. We will perform these three subgroup analyses with the primary end point as the outcome and the direction of hypothesised effect described[35]:

1. Duration of symptoms—Neer originally suggested that ASD should be considered for patients with persistent symptoms despite over 1 year of conservative treatment.[36] Recent randomised controlled trials failing to find efficacy on ASD (vs conservative treatment) have prompted arguments that ASD should be reserved to situations when long-term conservative treatment has failed.[37] Although a recent study specifically addressed this question and failed to support this hypothesis,[38] we still intend to compare the treatment effects of participants stratified based on the duration of symptoms. Accordingly, we will compare those with symptoms less than 12 months to those with symptoms longer than 12 months. We hypothesise that subacromial decompression will work better in patients with duration of symptoms longer than 12 months than for patients with symptoms less than12 months.
2. Severity of symptoms—A subgroup analysis will also be conducted comparing the treatment effects in patients with severe (VAS 70 or more), moderate (VAS 55 to 69) and mild (VAS less than 55) symptoms at baseline. We hypothesise that subacromial decompression will work better in patients with more severe (VAS 70 or more) than moderate (VAS 55 to 69) or mild (VAS less than 55) symptoms at baseline.
3. Acromial anatomy—A hook-type acromion has been suggested as an independent risk factor for subacromial impingement.[39] To assess the validity of this suggestion, a subgroup analysis will be conducted comparing the treatment effects in patients with flat (type I), curved (type II) or hooked (type III) acromion according to classification by Bigliani [illegible] We hypothesise that subacromial decompression will work better in patients with hooked (type III) than curved (type II) or flat (type I) acromion at baseline.

Effect modifying and mediating factors

Multiple regression models will be used to assess the potential effect modifying factors (eg, age, gender, psychological well-being, mental health, occupational shoulder load, education level and hand dominance) and effect mediating factors (eg, absence of complications and adherence to rehabilitation) on pain, functional disability and quality of life. These analyses are supportive, explanatory and/or hypothesis generating.

Blinded data interpretation

To safeguard against potential risk of bias during interpretation, we will use our recently introduced method of 'blinded data interpretation'.[41] So far, this method has been successfully applied to three previous trials.[33 42 43] Please refer to the online supplementary appendix for a more complete description of the process (blinded data interpretation plan), which we briefly summarise here. An independent statistician will provide the writing committee of the FIMPACT trial (authors of this protocol) with blinded results from the analyses with study groups labelled as group A, group B and group C. The writing committee will then contemplate on the interpretation of the results until a consensus is reached and agree in writing on all alternative interpretations of the findings. Once reaching a consensus, we will record the minutes of this meeting as a statement of interpretation document signed by all members of the writing committee. Only after reaching this common agreement will the data manager and independent statistician break the randomisation code.

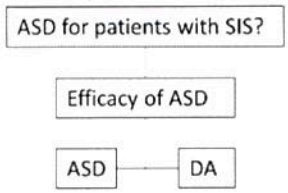
DISCUSSION

In this protocol paper, we describe the execution of a randomised, placebo-surgery controlled trial for the assessment of the efficacy of ASD in patients with SIS. Acknowledging the potential of surgery to produce powerful placebo effects,[44] our primary comparator is DA, differing from the ASD only by lacking the critical therapeutic element of the ASD (subacromial decompression). We will also conduct the pragmatic comparison of surgical and non-surgical treatment options of SIS by including a third group of progressive ET (figure 1, ASD vs ET).

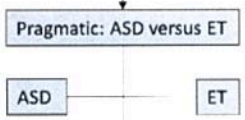
Interpretations and generalisability

Our interpretation scheme primarily rests on the tenet that the minimum requirement for the clinical viability of ASD is that it needs to show superiority to DA—a therapeutically inert and thus a clinically non-viable option. To test this, we have chosen a classic [illegible] or [illegible] design:[45–47] The recruited participants are those who—according to current evidence—should have an 'optimal response' to ASD and the participants and outcome assessors are blinded to the interventions given. This design should thus yield findings that are widely applicable to patients with characteristic clinical signs and symptoms of SIS. We will also compare ASD with a non-operative treatment option for SIS, the progressive ET, in a more pragmatic comparison, which is confounded by the lack of blinding of the participants (figure 2).

The generalisability of our primary (efficacy) comparison may be questioned as the patients are carefully



Comparison	Interpretation	Recommendation
ASD = DA	No relevant biological effect	Recommendation against surgery
ASD < DA	Detrimental biological effect	Recommendation against surgery
ASD > DA	Favourable biological effect	Comparison to non-operative treatment (ET)



Comparison	Interpretation	Recommendation
ASD = ET	Similar therapeutic effect	Recommend exercise (safety, costs)
ASD < ET	Exercise superior to surgery	Recommend exercise
ASD > ET	Surgery superior to exercise	Recommend surgery

Figure 2 Study design and interpretation of results. ASD, arthroscopic subacromial decompression; DA, diagnostic arthroscopy; ET, exercise therapy; SIS, subacromial impingement syndrome.

selected (strict eligibility criteria) and treated by experienced shoulder surgeons. Nevertheless, the eligibility criteria are in agreement with the existing treatment guidelines on SIS.[4] The results should thus be applicable to the specific populations currently receiving treatment for their SIS. As for the skill level of the surgeons, the index surgical procedure (ASD) is a relatively simple procedure and thus likely not very sensitive to individual surgeons' experience. For example, the amount of bone removed from the undersurface of the acromion seems to have at best a marginal effect on the outcome. Even bursectomy alone has been shown to produce the same therapeutic effect as standard acromioplasty.[48]

Rationale for outcome assessment and statistical analysis

Traditionally, the assessment of the treatment effects of two or more interventions has relied primarily on the statistical significance of the mean differences of the intervention groups. However, as described in a recent paper,[49] to truly assess the clinical relevance of a treatment, one also needs information about the distribution of individual responses. In essence, one needs to look at how many people on treatment and on comparator group(s) had a response at least as great as the MCID. Such individuals have been described as 'responders,' and this approach of comparing treatment groups as a 'responder analysis'.[50 51] The authors[49] suggested that '[redacted] The FIMPACT trial adheres to this suggested approach. Accordingly, we will elaborate several relevant and often interrelated issues, such as the study power, the primary outcomes and their interpretation, the MCID, as well as the approach we have chosen for carrying out a responder analysis.

Study power

Traditionally the sample size is calculated based on the MCID or MCII, that is, the smallest change in measurement that signifies an important/detectable improvement in a patient's symptom(s). MCII/MCID is not a static value even for one outcome instrument, but rather can have different values when assessed with different methods or [redacted] We chose VAS at rest and during arm activity as our primary outcomes, because shoulder pain is the primary complaint of patients with SIS. The FIMPACT trial was powered to detect an improvement of at least 15 on a 0–100 VAS scale[52] between ASD and ET. This yielded a sample size estimate of 70 participants per group. To safeguard against lack of study power, we chose a statistical threshold of 90% over the more conventional 80%. In this context, Norman [redacted] recently introduced a thought-provoking proposal arguing that a standard ('off-the-peg') sample size of 64 per group would be just as valid an estimate as one obtains by more traditional ('made-to-measure') sample size calculations.[53] Finally, although the statistical power is a vital step in the [redacted] of any clinical trial, the actual quality of evidence (certainty in the obtained estimates) can only be appropriately assessed from the CI of the data obtained.[54]

Responder analysis

As noted above, instead of focusing only on the statistical significance of the mean differences between treatment groups in the VAS (ie, the mean improvement from baseline to 24 months), we will also carry out 'a responder analysis'. In principle, this analysis allows physicians to inform a patient of his or her chance of experiencing a clinically meaningful improvement from the treatment, both in absolute terms and in comparison, to a control group. The difference between responders and non-responders can be considered the net benefit of the treatment. One proposed means to carry out a responder analysis relies on the assessment of the proportion of patients reaching the patient-acceptable symptom state (PASS) and the patient-disappointing symptoms state (PDSS). As no universal consensus exists on either the PASS or the PDSS in the context of SIS, we chose to anchor our responder analysis to the patient's assessment of satisfaction with the shoulder treatment outcome: Patients reporting very satisfied or satisfied will be categorised as 'Responders' and those reporting very dissatisfied or dissatisfied as 'Non-responders'. Given the obvious coarseness of this approach, we plan to evaluate the appropriate criteria for PASS and PDSS in more detail in the future, exploring the potential contribution of, for example, arm pain at rest and at activity, shoulder function, and night pain.

Ethics of placebo surgery

A recent systematic review of the use of surgical placebo shows that in more than half of these studies the treatment group that included critical surgical/therapeutic element had no greater effect than a placebo group.[18] The review also showed that risks of AEs were small and the placebo group was safer than the surgery under investigation. These findings make a compelling case for the use of surgical placebo controls when a placebo effect may be present. Regarding the ethics of surgical placebo controls, the authors of the review state '[redacted] They continue by concluding: '[redacted] Our views regarding the ethics of using a surgical placebo group are perfectly aligned with these notions.

Limitations of the study

One possible confounder in our trial is that subacromial pain is also the hallmark symptom of a RC tear, although the latter patients usually also represent with muscle weakness. To exclude patients with a (clinically relevant) RC tear, our eligibility screening included two preoperative assessments: (A) clinical exams targeted at finding obvious weakness of the RC muscles and (B) MRA, an imaging modality with a shown 92 specificity and 94 sensitivity for 'full-thickness' RC tears.[55] In addition to these, we also carried out (C) a DA in the ASD and DA groups prior to randomisation. Despite the thorough [redacted] screening, 10% (14/136) of the participants allocated to the two surgical groups had to be excluded because of acromioclavicular arthrosis (n=1) or intra-articular pathology found at DA (n=13). Although this does not have any effect on our primary comparison (ASD vs DA), one could argue that the ET and operatively treated groups (ASD and DA) are not fully comparable. At the same time we don't know the clinical relevance of small RC tears or superior labrum anterior to posterior (SLAP) lesions, which don't result in obvious muscle weakness and/or are not apparent in MRA. In the end, if this bias proves clinically relevant in our analysis, it will skew our results by favouring the ASD group in the pragmatic comparison (ASD vs ET). Another concern related to the pragmatic comparison (ASD vs ET) is that the progressive ET regimen carried out in the ET group is different from the postoperative rehabilitation carried out by patients in the ET group, for obvious reasons; surgically treated patients need time to recover from the initial surgical trauma. Furthermore, patients with ASD are also subject to some degree of postoperative immobilisation, extended sick leave, and modifications in pain medication and activities, all of which potentially have an effect on the outcome of treatment.

Another obvious concern related to our study design is the discrepant timing of the start of the actual treatment between the ET and the two surgical groups due to the time required to arrange the surgery. Acknowledging this, the 2-year follow-up was chosen as our primary time point for assessing the benefits of treatment, as we assume that by this time the potential confounding effect of slightly different follow-up times should be diluted to a minimum. This is also the reason why we use data from the shorter-term follow-up visits (ie, visits performed at 3 months, 6 months and 12 months after randomisation) primarily to illustrate the trajectory of the treatment response in the three groups. Concerns over the varying time span from the randomisation of the patients to the trial to the actual induction of treatment (due to delay in surgery) also applies to the CSAW trial.[20] To compensate for the waiting list effects, the CSAW investigators have chosen a slightly different strategy: Although the primary outcome assessment is performed at 6 months after randomisation in the CSAW trial, they have introduced additional follow-up assessments, referenced from surgery, for patients waiting for longer than 4 months for their surgery after randomisation. They have also set a secondary outcome measurement point at 1 year postrandomisation

ETHICS AND DISSEMINATION

Ethics

FIMPACT trial is conducted in accordance with the principles of the Declaration of Helsinki. This trial has been approved by the Institutional Review Board of the Pirkanmaa Hospital District and each participating centre granted clinical trial authorisation prior to recruitment. The trial has been registered to ClinicalTrials.gov registry and any revisions about the protocol are documented in this registry. For each participant, informed consent is obtained prior to any study-related procedures.

Dissemination policy

We aim to produce high-impact publications of the results of the trial and present the findings to the clinicians who manage shoulder pain in the front line. The investigators will be involved in preparing drafts of the manuscripts, abstracts, press releases and any other publications arising from the trial. The final reporting will follow the Consolidated Standards of Reporting Trials (CONSORT) Statement guidelines. Authorship will be determined in accordance with the International Committee of Medical Journal Editors (ICMJE) guidelines and other contributors will be acknowledged. The funders will be acknowledged in all resulting publications. There is no intended use of professional writers.

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Competing interests ST reports personal fees from Evalua group of companies, personal fees from DBC group of companies, and personal fees from insurance companies, outside the submitted work.KK reports an honorarium for a lecture from Linvatec, outside the submitted work. TLNJ reports an honorarium for a lecture on osteoporosis from AMGEN (donated to AllTrials campaign). Authors not named here have disclosed no conflicts of interest.

Patient consent Obtained.

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Commentary

Consensus at last! Long-term results of all randomized controlled trials show that fusion is no better than non-operative care in improving pain and disability in chronic low back pain

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Chronic low back pain (LBP) represents an enormous challenge to our health-care systems, and trying to find the role, if any, for its surgical treatment is a major public health issue. Current guidelines advocate the use of multidisciplinary cognitive-behavioral and exercise rehabilitation programs as first-line treatments for chronic LBP, with fusion surgery being considered only if such non-operative treatments are unavailable or have failed to improve the condition [1]. The recently published long-term results of three randomized controlled trials (RCTs) carried out in the United Kingdom and Norway support these recommendations, having found no evidence for the superiority of surgery at the 11-year follow-up [2]. The long-term follow-up of the Swedish RCT is published in this edition [3].

Comparable treatment groups across the RCTs?

A systematic review of the midterm results of the RCTs from Sweden, Norway, and the United Kingdom highlighted the fact that the nature of the surgical treatments and their midterm outcomes were comparable across the trials [4]. However, the non-operative group in the Swedish study was not considered to have received contemporary evidence-based conservative treatment, suggesting that it was the poor results in this comparator group that accounted for the apparent superiority of fusion in the Swedish study. The non-operative group might hence be considered to represent "natural history" or, worse still, a nocebo group. As well as comparing non-operative and surgical treatment, the secondary aim of the Swedish study was to compare three different surgical techniques with one another. As a result, the two main groups (surgery and no surgery) were asymmetrical in size, and patients had a 3:1 chance of being randomized to surgery. Having already received conventional physiotherapy for years and failed to improve with it, randomization to one of the three surgical interventions was likely what the patient hoped for; possibly, assignment to "unstructured physiotherapy" [3] created harm and anger, precipitating a negative outcome [5]. This might have explained the 2-year results of the Swedish group. Previously, the authors of the Swedish Lumbar Spine Study claimed that their trial differed from the trials done in the United Kingdom and Norway in that the Swedish centers only included patients they were convinced were "good candidates for surgery" [6]. Interestingly, however, baseline characteristics in the four trials did not differ in any important aspect that would serve to substantiate their claim [4] (and unpublished data in connection with Mannion et al. [7]).

Group changers and dropouts

Trials of operative versus non-operative treatment are fraught with difficulties. The problems of numerous group changers and dropouts must be faced and dealt with. The intention to treat (ITT) principle, in which patients are analyzed in relation to the groups to which they were randomized [8], remains the best approach to the analysis of data from RCTs. It eliminates known or unknown prognostic factors from being

FDA device/drug status:

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associated with a given treatment [9]. ITT analyses may be supported by analyses in which cases are grouped as "per protocol" (those who underwent the treatment to which they were assigned and completed all the follow-ups) or "as treated" (the treatment actually received) or "worst case" (group crossovers considered as "failing" the treatment to which they were randomized). These subgroup analyses present their own problems. Patients moving from non-operative to surgical treatment can be tracked with relative ease, but not those having surgery, failing it, and then going on to have successful non-operative treatment. Any subgrouping based on group changes in one direction only and on the assertion that a group change from non-operative to surgery indicates failure of non-operative treatment but revision surgery does not count as failure of surgery will inevitably be biased.

Global assessment or serially measured outcomes?

An important issue in RCTs concerns the interpretation of results when differences arise between the primary and secondary outcomes, or between prospective and retrospective assessments of change. Retrospective assessments of "global outcome" are popular as an aggregate measure of all aspects of outcome of importance to the patient [10,11]. However, investigators using such scales should first ensure their validity by exploring the scale's relationships with pre- and post-values for corresponding domain scores [12,13]. If these global measures are truly measuring "change," their values should correlate as strongly with preoperative as with follow-up values of the outcomes they purport to reflect (eg, disability, pain, and quality of life) [12]. In many studies, these conditions are not fulfilled [10,14], suggesting recall bias or motivational bias (patients undergoing more cumbersome treatment overestimate their improvement [15]). In our own long-term data from the Norwegian and United Kingdom RCTs, the patients' "global assessment" correlated considerably more strongly with the Oswestry Disability Index (ODI) scores at long-term follow-up (r=0.70) than with the ODI values at baseline (r=0.17). It seems unlikely that, 11 to 13 years after treatment, patients can remember with any clarity their preoperative state, in order to quantify subsequent change. The longer the duration of follow-up, the less likely the "global assessment" is to be a reliable measure of change [14]. The changes derived by comparing serial measures on validated outcome instruments surely give a more truthful reflection of improvement or deterioration over time, without the concerns of recall or motivational bias.

The Swedish group's long-term results [3] now complement those of the combined Norwegian and United Kingdom studies with respect to the important, prospectively measured outcomes concerning pain and disability. Of interest, in the Swedish study, the mean ODI scores for the non-operative group appear to have improved since the 2-year follow-up [16], whereas those of the surgical group have remained stable. This has resulted in no significant group differences at the long-term follow-up [3].

In the Swedish study, only the "global assessment" showed any statistically significant differences favoring the surgical group, and only in the "as treated" or "per protocol" analyses: More of the surgical than the non-operative patients reported at long-term follow-up that they were better or much better [3]. In the ITT, even global assessment was not significantly different between the treatment groups. In their 2001 paper, the Swedish group states "pain, disability, global self-rating by the patient, and back-to-work were used as primary outcome measures in the study" [16]. We believe their follow-up report should have given equal emphasis to all these primary outcomes, rather than focusing on one singular retrospective rating of global outcome.

In "as treated" and "per protocol" analyses of the Swedish long-term data, the two treatment groups appeared to start with a similar ODI score and end with a similar ODI at follow-up, yet the surgery group had much superior ratings of improvement on "global assessment" [3]. This means a given reduction on the prospectively measured ODI was perceived as a "greater improvement" in the fusion group. This does not support the notion of the global assessment being a valid indicator of change over time and suggests possible motivational bias [15].

Deaths during the studies

The Swedish group was able to acquire more information than in our shared study [7] regarding patients who had died during follow-up. They were since able to establish that the deaths were "all unrelated to CLBP." In the United Kingdom and Norway combined study [2], we saw a higher rate of known deaths in the surgical group (10 of 242 patients) than in the non-operative group (1 of 231) (Fisher exact test p=.01). It would have been interesting to know whether the Swedish study found the same. The deaths per treatment group are not reported in the manuscript but are possibly important.

Interpretation of the results

We encourage the reader to consider carefully the use of the only statistically significant primary outcome as the focus of the long-term results in the Swedish study [3]. Comprehensive analyses and detailed results for the serial measures of pain and disability are found in the tables of their paper. We believe that the long-term results for all primary outcome measures have been under-communicated, particularly in the abstract. The abstract should have summarized the results for all the (original) primary outcomes, and for "global assessment" also using the ITT analysis. We disagree with the conclusion that "from the patient's perspective, reflected by the GA, lumbar fusion surgery is a valid treatment option in CLBP" [3]. This is a highly biased and selective interpretation; the ODI, pain, and quality of life measures also represent the patient's perspective. The abstract should have stated "on the other hand, the other primary outcome measures suggested no differences," not simply that "secondary outcome

measures suggested that there was still substantial disability at long-term after both treatments."

It is normal practice to look at a range of outcome measures to ensure that the overall data tell a consistent story. In all analyses other than the ITT (which did indeed deliver consistent findings with all outcome measures), the prospectively rated measures of pain, disability, and quality of life told the same story, with only the global assessment delivering different findings. Normally, one might go with the majority, but the Swedish group instead decided to focus on the global assessment. We consider this highly biased reporting and hope that there was no conflict of interest in this group of surgeon investigators (see Mannion et al. [17]).

We welcome the publication of the Swedish group's long-term outcomes, with a commendable follow-up rate [3]. Their data were originally analyzed in combination with those from the Norwegian and United Kingdom RCTs, but were then unexpectedly withdrawn, just before publication. It should now be possible to pool the findings in a mixed model analysis of the original data, or in a meta-analysis, to deliver an even stronger, evidence-based message to the spine community.

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REVIEW

Knee osteoarthritis: pathophysiology and current treatment modalities

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Abstract: For decades, multiple attempts to fully understand knee osteoarthritis pathophysiology and natural history have been attempted. Despite the extensive amount of research regarding this topic, there are still marked controversies. This multifactorial condition gets influenced by local, systemic, and external factors and its progression and/or response to treatments widely varies from patient to patient. Multiple therapies have been studied in the past, low impact physical activity seems to be supported by all the current medical societies while other interventions have shown conflicting findings. Newer therapies and routes of administration are under investigation and some of them have shown promising preliminary reports. This review intends to give an overview of the current knowledge of pathophysiology and non-surgical therapies available for knee osteoarthritis.

Keywords: knee osteoarthritis, cartilage degeneration, non-inflammatory arthritis, intra-articular injections, corticosteroids

Introduction

Osteoarthritis (OA) is the most common form of arthritis and one of the leading causes of disability. This degenerative and progressive joint disease affects around 250 million people worldwide[2] and more than 27 million people in the United States.[3,4] Elderly (approximately 35% of patients over 65 years old) females, patients with obesity and African Americans are the population with the highest risk of developing OA.[5,6] Given the trend of the population to live longer and the progressive increment of obesity in our country, the number of affected patients most likely will substantially increase within the upcoming years. This is concerning given the functional impairment and disability associated with this condition and its negative toll on the social and economic aspects of our society.

This review will discuss the current evidence regarding the pathophysiology of knee osteoarthritis, the current recommendations of treatment, with a special focus on intervention modalities including intra-articular steroids and the new extended-release (ER) presentations of these components.

Knee osteoarthritis

The knee is the largest synovial joint in humans, it is composed by osseous structures (distal femur, proximal tibia, and patella), cartilage (meniscus and hyaline cartilage), ligaments and a synovial membrane. The latter is in charge of the production of the synovial fluid, which provides lubrication and nutrients to the avascular cartilage.[6]

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Unfortunately, given the high use and stress of this joint, it is a frequent site for painful conditions including OA.[7]

OA is classified into two groups according to its etiology: primary (idiopathic or non-traumatic) and secondary (usually due to trauma or mechanical misalignment). The severity of the disease can also be graded according to the radiographical findings by the Kellgren–Lawrence (KL) system described in 1957.[8] It was believed that OA was exclusively a degenerative disease of the cartilage, however, latest evidence has proven that OA is a multifactorial entity, involving multiple causative factors like trauma, mechanical forces, inflammation, biochemical reactions, and metabolic derangements.[9] It is also known that the cartilaginous tissue is not the only one involved. Given its lack of vasculature and innervation, the cartilage, by itself is not capable of producing inflammation or pain at least on early stages of the disease. Hence, the source of pain is mainly derived from changes to the non-cartilaginous components of the joint, like the joint capsule, synovium, subchondral bone, ligaments, and periarticular muscles.[6,9] As the disease advances, these structures are affected and changes including bone remodeling, osteophyte formation, weakening of periarticular muscles, laxity of ligaments, and synovial effusion can become evident.[10]

The role of inflammation is not well-understood and there is an ongoing debate to determine if the inflammatory reaction triggers the OA changes, or instead, the inflammation is secondary to the OA changes.[9] Different from inflammatory arthritis, inflammation in OA is chronic and low-grade inflammation, involving mainly innate immune mechanisms. Synovitis (infiltration of inflammatory cells into the synovium) is a common finding of OA and it can be present in early stages of the disease but is more prevalent towards the more advanced stages and can be related with severity.[1] In OA, the synovial fluid has been found to contain multiple inflammatory mediators including plasma proteins (C-reactive protein, proposed as a marker for development and progression of OA), prostaglandins (PGE2), leukotrienes (LKB4), cytokines (TNF, IL1β, IL6, IL15, IL17, IL18, IL21), growth factors (TGFβ, FGFs, VEGF, NGF), nitric oxide, and complement components.[1,11] Locally, all of these components can induce matrix metalloproteinases and other hydrolytic enzymes (including cyclooxygenase two and prostaglandin E) resulting in cartilage breakdown secondary to proteoglycan and collagen destruction.[12]

White blood cells are also involved, extracellular matrix breakdown releases certain molecules (damage-associated molecular patterns) that are recognized by the innate immune cells (macrophages and mast cells), usually as a protective mechanism. However, this prolonged and dysregulated degree of inflammation can lead to tissue destruction.[1] In animal studies, macrophages have been found to be involved in the development of osteophytes that are a pathological feature of OA.[1]

The body also has protective molecular mechanisms including various growth factors (insulin-like, platelet-derived, fibroblast 18, and transforming growth factor B), which, unfortunately, are altered in patients with knee OA and may become harmful to the joint.[1,11]

Treatment

OA is a progressive and degenerative condition, with unlikely regression and restoration of damaged structures. Thus, current management modalities are targeted towards symptom control unless the degree of severity dictates the necessity of surgical intervention with joint replacement.[1]

Currently, different guidelines have been developed by multiple academic and professional societies to standardize and recommend the available treatment options (Table 1). Among these, we can find the Osteoarthritis Research Society International (OARSI),[13] American College of Rheumatology (ACR)[14] and American Academy of Orthopedic Surgeons (AAOS)[15] publications.

Non-pharmacological management

The aim of the management of OA is to control the painful signals originated from these joints, but even more, to improve functionality and quality of life. Non-pharmacological therapies should always be attempted as the first line of treatment for knee OA.[3,6,13–15]

Inactivity and disuse are deleterious for the health of the knee joint, the absence of mechanical stimulation induces a more rapid cartilage degeneration due to cartilage softening/thinning, decrease of glycosaminoglycan content, impaired joint mechanics and flexibility.[16,17] Light-to-moderate physical activity provides multiple benefits to this patient population, besides the mechanical and functional improvements, they also offer a risk reduction of diabetes, cardiovascular events, falls, disability, and an improvement in mood, and self-efficacy.[16,18]

Exercise routines should be tailored to every patient's needs/tolerance and preferences, high impact activities should be avoided, and long-term adherence should be maximized to increase success.[18,19] There are different exercise modalities shown to have a favorable effect on patients with knee OA (Table 2), routines should be performed three times a week, and to assess response, the patient should complete at least 12 sessions.[6]

Table 1 Knee osteoarthritis management recommendations from societies

Societies recommendations			
Treatment	**OARSI**	**ACR**	**AAOS**
Exercise (land and water based)	Appropriate	Strong recommendation	Strong recommendation
Transcutaneous electrical nerve stimulation (TENS)	Uncertain	Conditional recommendation	Inconclusive
Weight control	Appropriate	Strong recommendation	Moderate recommendation
Chondroitin or Glucosamine	Not appropriate for disease modification, Uncertain	Recommended against use	Recommended against use
Acetaminophen	Without comorbidities: appropriate	Conditional recommendation	Inconclusive
Duloxetine	Appropriate	No recommendation	No recommendation
Oral NSAIDs	Without comorbidities: appropriate With comorbidities: not appropriate	Conditional recommendation	Strong recommendation
Topical NSAIDs	Appropriate	Conditional recommendation	Strong recommendation
Opioids	Uncertain	No recommendation	Recommended only tramadol
Intra-articular corticosteroids	Appropriate	Conditional recommendation	Inconclusive
Intra-articular viscosupplementation	Uncertain	No recommendation	Recommended against use

Note: Data from these studies.[13–15]

Abbreviations: OARSI, Osteoarthritis Research Society International; ACR, American College of Rheumatology; AAOS, American Academy of Orthopedic Surgeons; TENS, transcutaneous electrical nerve stimulation; NSAIDs, non steroidal antiinflamatory drug.

Table 2 Different exercise modalities for knee OA

Aerobic/endurance	Exercise modalities Resistance/strength training	Balance/proprioceptive	Stretching
Include activities like walking, climbing stairs, and cycling. They can decrease joint tenderness while improving functional status and respiratory capacity. Cycling is especially attractive to patients given the low impact profile.[16,18] One study showed a reduction of 10–12% on the physical disability and the knee pain questionnaires.[16]	Isometric, isotonic, isokinetic, and dynamic modalities have been studied. Most of them targeting quadriceps, hip abductors, hamstrings, and calf muscles. They improve strength, physical function, and pain levels, with similar efficacy and outcomes than aerobic exercises.	This includes modalities such as Tai Chi, using slow and gentle movements to adopt different weight baring postures while using breathing techniques.	This group will specifically help with patient's range of motion and flexibility.

Aquatic (water-based) therapies provide an alternative to patients who are hesitant to start land-based exercises, given the lesser joint impact. Some patients can better tolerate aquatic therapy and decrease the exacerbation of symptoms (sometimes experienced when starting weight bearing routines). Some physicians use this therapy as a bridge to get to land-based modalities once the patient has lost the fear of moving.[16,17]

Weight management plays an important role in symptom management, and it has been noted that the benefit of exercise is potentiated by the reduction of weight.[16] Obesity can predispose patients to suffer from knee OA, it has deleterious molecular and mechanical effects. The adipose tissue itself is a source of inflammatory factors. The cytokines adipokine, IL6, TNF alfa, and C-reactive protein are elevated in the plasma of obese patients and have been associated with alteration of cartilage homeostasis and degeneration.[1,9] During ambulation, the knee joint has to support 3–5 times the body weight, hence small changes in weight represent the high variation of forces to the joint.[20] Regardless of the used method (bariatric surgery vs lifestyles modifications), there is around 10% risk reduction of knee OA per kilogram of body-weight decreased (same proportion applies in the opposite direction for the increase in weight).[21] These findings were also noted in "The Framingham study", a weight loss of 12 lb resulted in a 50% risk reduction for knee OA.[22] Not only the total weight reduction is important, but studies have also taken into account the changes in body fat percentage; each point reduction represents a 28% increase in function and a 9.4% improvement in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score.[23]

Regarding other non-pharmacological interventions, patients might benefit from thermal modalities, but there is insufficient evidence to recommend the use of transcutaneous electrical nerve stimulation (TENS) or therapeutic ultrasound.[3]

Pharmacological management

The vast majority of OA patients are elderly and most of them will have multiple comorbidities. Hence, special attention should be paid to the possible interactions and adverse effects that systemic medications can induce in this population. Historically, cyclooxygenase inhibitors (acetaminophen and NSAIDs) have been the most commonly used medications. But given the gastrointestinal, renal, cardiac, and hematological adverse effects of these medications, their long-term use is limited. Acetaminophen has shown to be inferior to NSAIDs and not superior to placebo for pain control, leading to some guidelines to abstain to recommend it as an effective medical management strategy for moderate-to-severe OA.[15] Topical NSAIDs have shown to be safer, with a comparable, or slightly inferior efficacy than systemic NSAIDs.[13,24] On short follow-up studies, they have shown to be superior to placebo in controlling pain during the first week of treatment but failed to prove benefit after 2 weeks.[24]

Recently, more and more awareness has been raised regarding the consequences of the chronic use of opioids. Studies also keep providing evidence that opioids are not superior to NSAIDs to improve OA pain or WOMAC scores, and the risks of their use, clearly outweigh the benefits.[25,26] If a patient is refractory to other treatments and the use of an opioid is considered, Tramadol, a serotonin and norepinephrine reuptake inhibitor with weak μ opioid receptor agonist properties, has shown some benefit in the treatment of severe and moderate OA. This medication, compared to other opioids, has slightly less risk for abuse potential and respiratory depression.[27,28]

Duloxetine is a serotonin and norepinephrine reuptake inhibitor approved by the US Food and Drug Administration (FDA) for treatment of diabetic peripheral neuropathy and fibromyalgia. Recent studies have revealed that when used for more than 10 weeks, this medication is better than placebo controlling pain and improving function in patients with OA.[29,30]

Interventional management

Multiple substances delivered via intra-articular (IA) injections have been explored in the past. The idea behind this is that local treatments will have less systemic adverse effects and depositing the medication inside the joint will have a more direct effect. Studies have shown that in general IA therapies are more effective than NSAIDs and other systemic pharmacologic treatments, but they also disclosed that a percentage of that benefit might be secondary to IA placebo effect.[2]

Corticoid injections

Corticoids (CS), elicit their immunosuppressive and anti-inflammatory effects by acting directly on nuclear receptors, interrupting the inflammatory cascade at multiple levels. They decrease the action and production of IL-1, leukotrienes, prostaglandins, and metalloproteinases[9,11] and it is believed that these are some of the mechanisms of pain relief and increase joint mobility in knee OA.

Currently, the available FDA approved Immediate Release (IR) corticosteroids for IA usage are: Methylprednisolone Acetate (MA), Triamcinolone Acetate (TA), Triamcinolone Hexacetonide (TH), Betamethasone Acetate (BA), Betamethasone Sodium Phosphate (BSP), and Dexamethasone.[9] Attempts to define which is the best option have been done in the past. Dosages equivalent or higher than 50 mg of prednisone (equivalent to 40 mg of TA and MA) seems to be linked to a longer pain relief effect of 12–24 weeks compared to the short pain relief of 2–4 weeks reported with lower dosages.[31–36] There might be small differences between the approved IR corticosteroid preparations in terms of pain relief, but current evidence is equivocal. Yavuz et al mentioned that MA can provide superior pain relief in the first 6 weeks compared to the other corticosteroids used (TA, BDP), but all of them provide equivalent analgesia from week sixth to 12th.[36] Pyne et al also suggested that TA acts quicker and provides better pain relief for the first 3 weeks than MA, but the effect of the latter might not start immediately, thus it might provide better analgesia after the eighth week.[37] A recent comparative study by Buyuk et al showed that both MA and TH were equally effective until week 24th with a peak of action by the second week,[34] confirming similar findings by Lomonte et al.[38]

Multiple studies have tried to elucidate questions related to the use of IA CS, such as the specific mechanism of action, duration, CS of choice, indications, effect on cartilage structure/intra-articular space and adverse effects. Some of these studies have been highly variable in their design, showing contradictory results and hindering the creation of a strong consensus. This is reflected in the different association guidelines, the OARSI and ACR guidelines support their use,[13,14] while the AAOS considered that the available evidence was inconclusive to recommend for or against them.[15]

Identifying the adequate candidates has been attempted in the past. Due to the anti-inflammatory effects, one of the first hypothesis believed that patients with knee effusion, synovitis, and increased thickness of the synovial membrane (showed by ultrasound) would be the group of patients to have

the most benefit. A placebo-controlled trial showed promising correlation,[31] but other studies did not show a strong association.[39–41] Following this inflammatory trend, also cytological analyses of the synovial fluid were performed. Dieppe et al suggested that cell count was not related to the likelihood of response,[42] but recently McCabe et al revealed that patients with high synovial white blood count (ranging from 251/μL to 1000/μL) would have a better response than patients with lower counts.[43]

Other possible variables like the degree of knee tenderness, baseline pain, BMI, gender, and anxiety or depression, have failed to show reliable predictors of response.[40,44–47]

On the other hand, a low degree of radiographic changes on the KL system (0–1) seems to be related with a better response compared to patients with severe radiographical changes (3–4).[45]

In the past, multiple techniques of IA knee injection have been described, including the anterolateral and anteromedial (performed with the knee flexed 60–90 degrees), as well as the mid-lateral and superolateral approaches (performed with the knee extended).[35] Studies agree upon that using ultrasound guidance with the superolateral approach provides the best chance to inject the CS inside the knee joint accurately. On average using the ultrasound provides a 96.7% of accuracy, vs 81% with landmarks. Also, proper use of the ultrasound guidance can be reflected in better pain reduction, compared with other techniques.[48–50]

Although complications are rare (about 1 in 3000),[11] they are still a concern for the use of this therapy. Facial flush and transient pot-injection flares are self-limited and can be seen within the first 3 days.[35]

A study comparing radiographical changes of repeated, every 3 months injections of 40 mg of TA vs placebo for a 2-year period showed no difference,[46] but a recent randomized controlled trial using MRI, found evidence of cartilage volume loss.[51]

Research regarding CS and knee cartilage integrity has also provided equivocal results, some studies suggest that there is no alteration in the cartilage structure, while others suggest that CS can promote chondrocyte destruction and increase the necessity for joint replacement.[4,9,35,36,51] One of them found that the cartilage damage might be caused by oxidative stress which could be reduced by vitamin C supplement.[52]

A portion of the IA CS is absorbed systemically, with the possibility to produce hypoglycemia and transiently affect the hypothalamic-pituitary-adrenal (HPA) axis in up to 25% of the patients.[34,53] Cortisol levels might decrease after injection, but they return to baseline after 1–4 weeks.[34,53]

Extended-release triamcinolone acetonide

In an attempt to prolong the pain relief benefit, and also to decrease adverse effects, avoiding the high peak plasma concentrations seen with the IR use, a molecule called FX006 was developed and was approved by the FDA by the end of 2017. FX006 has TA contained inside microspheres (from 20 to 100 μm). These microspheres are composed of Poly-Lactic-Co-glycolic Acid (PLGA), a biocompatible compound, which ultimately degrades into carbon dioxide and water.[54–56]

The first animal study using this medication was published in 2014 by Kumar et al. They found that there was a prolongation of analgesic effect, improvement in inflammation, pannus formation, cartilage damage and bone resorption, these without evidence of the HPA axis function.[54]

A phase-2 double blind-multicenter study included 228 patients randomized to receive different concentrations of FX006 or 40 mg of IR TA for 12 weeks. They found that the analgesic effect of FX006 compared to that of the IR was prolonged and amplified with an optimal dose of 40 mg. The analgesic effect was found to be superior at 2 through 12 weeks and significantly superior at 5–10 weeks. Other measured outcomes like stiffness, function, WOMAC scores, and impression of change scales demonstrated the superiority of the FX006, especially until week eighth. Authors found a reduction by eightfold of CS peak plasma levels.[57]

A subsequent investigation attempted to determine the optimal dosage of FX006, they compared three groups (16 mg, 32 mg, and placebo) during 24 weeks and found that the average daily pain was significative improved by the 32 mg concentration for the first 11–13 weeks but only a small difference was found further than 13 weeks.[55]

There are currently ongoing studies on FX006, some of the preliminary results, suggest that this option might consistently provide 12 weeks of pain relief cost-effectively. But these should be analyzed with caution once the final reports are published.[58]

Some authors also suggest that PLGA might not be the optimal component for the microspheres and indicated that polyester amide (PEA) might have a safer profile and better release of the contained medication.[59]

Non-corticoid interventional therapies

As an alternative to the IA CS, in the recent years, new products and therapies have been used targeting different factors other than inflammation. Although these products

are promising, still some research is required to determine their efficacy, applicability, and safety profile.

Viscosupplementation with hyaluronic acid

Hyaluronic acid (HA), is a natural glycosaminoglycan synthesized by type B synovial cells, chondrocytes, and fibroblasts and secreted into the synovial fluid. It provides viscous lubrication, has shocking absorbing properties and additionally, possible anti-inflammatory and anti-oxidant functions have been described.[6,9,11] In the osteoarthritic knee the concentration and the molecular weight of the HA decrease considerably,[9,11] and that is why some proposed to viscosupplement the joint in an attempt to restore the HA benefits. The current evidence regarding efficacy is conflicting[6,9,11,60] and in result, there is variation regarding recommendations from the societies. The AAOS does not recommend its use,[15] the ACR has no recommendations about it,[14] the OARSI has an "uncertain recommendation,"[13] and a recent European consensus stated that HA was well tolerated and effective for low and moderate grade OA.[61] Lastly, this treatment might be more effective in patients with higher levels of knee pain, younger and with lower KL score.[60]

Regenerative medicine

Aiming to stop and revert the degeneration associated with OA, IA injections of autologous conditioned serum (ACS), platelet rich plasma (PRP), and mesenchymal stem cell (MSC) have been tested.[9,11,62,63] Their mechanisms of action is reduction of inflammatory reactions mediated by cytokines, and the induction of anabolism and chondrocyte differentiation via growth factors and stem cells contained in it. These methods are promising and some studies have reported them to be safe, well tolerated and, in some cases, superior to IA placebo and HA in terms of pain relief and knee function.[9,11,62,63] This is still a developing field and more research is required in order to define and standardize the optimal retrieval, storage, and preparation methods of these products.

Discussion

Osteoarthritis is a complex and multifactorial condition of the joints, affecting mainly the knees. Multiple hypotheses have been proposed but still there is not a clear etiology or understanding of its natural course. Based on those hypotheses, a wide variety of treatments have been developed and tested, some more successful than others, but ultimately all of them are aimed to decrease pain, increase function, and delay the necessity for a surgical joint replacement. All the current guidelines agree that water or land-based exercise should be attempted first for symptom control, slowly escalating towards the other therapies such as topical or oral medications. If they are not effective, then a patient can receive IA therapies, which seem to have a certain degree of benefit over the oral therapies with some contribution of the placebo effect. Among those therapies, one of the most studied has been IA CS, but it seems that the current data might not be clear given that efforts to elucidate the exact mechanism of action, analgesic efficacy, indication, and safety profile are still ongoing. Recent papers have not been able to provide a robust and clear answer on using IR CS by patients. Some authors have mentioned that the presence of joint effusion, synovial membrane thickness, high BMI, psychological factors, and knee tenderness could be an indicator, but there is no conclusive data on this.[31,39–47] Perhaps white blood cells counts in the synovial fluid and low degree of radiographical changes on the KL score might be related to a better response, but it is not a definite answer. Part of the conflicting data is because of the high variability of the design of the studies that make them hard to be compared. Nowadays with the advancements in technology and ultrasound, we should aim to use this option whenever available to increase the rate of adequate IA placement of the injected substance. On October 2017, the FDA approved the extended-release presentation for TA contained in microspheres, called FX006, which theoretically, compared to IR CS, should provide a longer lasting pain relief and less adverse effects given the marked reduction on the serum levels of the CS.[64,65] Some animal models also showed to be protective of the cartilage structure, and also some first studies have shown some adequate safety profile, but there are still doubts regarding its duration beyond 13 weeks. The truth is that this new presentation of an old medication will require more research to clarify some doubts regarding the indications and magnitude of the benefits of the IR option. But it seems that it might play a role if there is a concern of HPA axis suppression and hyperglycemia given its pharmacodynamic properties.

The regenerative medicine field is developing other non-CS IA therapies, showing promising results, but more knowledge and standardization of their therapies will be required.

Conclusion

Despite being one of the most studied and more prevalent conditions of our population, knee osteoarthritis still does not have a clear pathophysiology or a single most efficacious intervention to treat the symptoms and degeneration associated. Exercises in early stages are a valuable therapy for these patients and it is recommended by all the medical societies.

Other non-surgical treatments have variable efficacy and their success will depend on multiple variables (provider, equipment, patient) and their use has to be selected judiciously according to the specific clinical situation.

Author contributions

All authors contributed to data analysis, drafting and revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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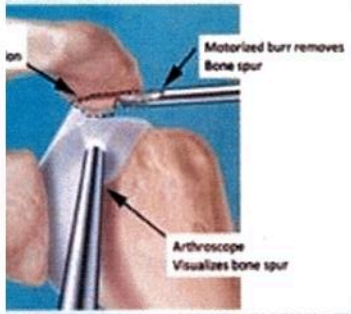
Subacromial Impingement Syndrome

Exercise is as effective as **Surgery**

..at 1, 2, 4 and 5 year follow-ups

...at a fraction of the cost of surgery



Haahr et al (2005) **1 year follow up**

Haahr & Andersen (2006) **4 year follow up**

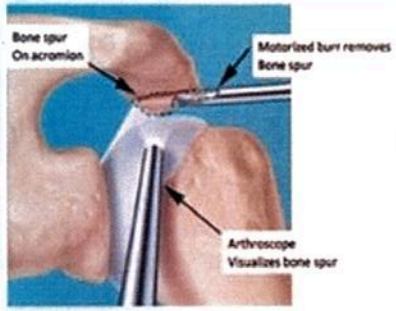
Ketola et al (2009) **2 year follow up**

Ketola et al (2013) **5 year follow up**

Subacromial Impingement Syndrome

Exercise significantly reduces the need for **Surgery**

...up to 80%

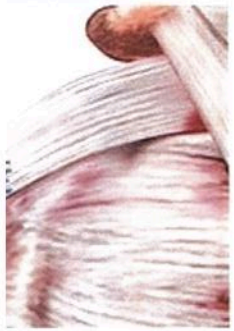


Holmgren et al (2012)
Effect of specific exercise strategy on need for surgery in patients with SIS: randomised controlled study. ***BMJ***

Rotator Cuff Partial Thickness Tears (< 75%)

Exercise is as effective as **Surgery**

...at a fraction of the cost of surgery



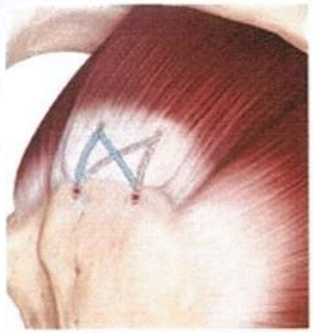
Treatment of non-traumatic RC tears.
n=180 shoulders

Group I Physiotherapy (n= 10 treatments)
Group II Aromioplasty & physiotherapy
Group III RC repair, acromioplasty & physiotherapy

Kukkonen et al (2014) ***B&J Journal***

(Atraumatic) Full Thickness Rotator Cuff Tears

Exercise significantly reduces the need for **Surgery (75%)** [@2 years]



Kuhn et al (2013) Effectiveness of PT in treating atraumatic FT RC tears: a multicentre prospective cohort study. ***JShElSurg.***

ANEXA NR. 2
LA EXPUNEREA DE MOTIVE

ANEXA nr. 2

Încadrare funcții în lege actuală	Denumirea funcțiilor în actuala lege	Nivelul studiilor	Salariu de bază în legea actuală -lei-Gradația 0-anul 2022	Taxe angajator	TOTAL	Încadrare funcții în proiectul de modificare a legii	Denumirea funcțiilor în proiectul de modificare a legii	Nivelul studiilor	Salariu de bază în proiectul de modificare a legii -lei-Gradația 0-anul 2022	Taxe angajator	TOTAL
Anexa nr. II Capitolul I, Subcapitolul 2, punctul 1, litera a), subpunctul a.1. nr. crt.: 22, 23, 24 și 25	fiziokinetoterapeut, principal	S	4819	108	4927	Anexa nr. II capitolul I, subcapitolul 2, punctul 1, litera a), subpunctul a.1. nr. crt. 25¹, 25², 25³ și 25⁴	fizioterapeut, fiziokinetoterapeut, kinetoterapeut, profesor CFM, principal	S	9250	208	9458
	fiziokinetoterapeut, specialist	S	4302	97	4399		fizioterapeut, fiziokinetoterapeut, kinetoterapeut, profesor CFM, specialist	S	8600	194	8794
	fiziokinetoterapeut	S	4087	92	4179		fizioterapeut, fiziokinetoterapeut, kinetoterapeut, profesor CFM	S	8175	184	8359
	fiziokinetoterapeut, debutant	S	3950	89	4039		fizioterapeut, fiziokinetoterapeut, kinetoterapeut, profesor CFM, debutant	S	4750	107	4857
Anexa nr. II Capitolul I, Subcapitolul 2, punctul 1, litera b), subpunctul b1. nr. crt. 5, 6 și 7	kinetoterapeut, profesor CFM, principal	S	4733	106	4839	Aceste categori sunt încadrate în Anexa nr. II Capitolul I, Subcapitolul 2, punctul 1, litera a), subpunctul a.1. nr. crt. 25¹, 25², 25³ și 25⁴					
	kinetoterapeut, profesor CFM	S	4259	96	4355						
	kinetoterapeut, profesor CFM, debutant	S	3950	89	4039						
Anexa nr. II Capitolul I, Subcapitolul 2, punctul 1, litera a), subpunctul a.1. nr. crt.: 32, 33 și 34	fiziokinetoterapeut, principal	SSD	4087	92	4179	Anexa nr. II Capitolul I, Subcapitolul 2, punctul 1, litera a), subpunctul a.1. nr. crt. 34¹, 34² și 34³	fizioterapeut, fiziokinetoterapeut, profesor CFM, principal	SSD	7925	178	8103
	fiziokinetoterapeut	SSD	3900	88	3988		fizioterapeut, fiziokinetoterapeut, profesor CFM	SSD	7100	160	7260
	fiziokinetoterapeut, debutant	SSD	3850	87	3937		fizioterapeut, fiziokinetoterapeut, profesor CFM, debutant	SSD	4130	93	4223
Anexa nr. II Capitolul I, Subcapitolul 2, punctul 1, litera b), subpunctul b1. nr.crt. 8, 9 și 10	profesor CFM, principal	SSD	4302	97	4399	Aceste categori sunt încadrate în Anexa nr. II Capitolul I, Subcapitolul 2, punctul 1, litera a), subpunctul a.1. nr. crt. 34¹, 34² și 34³					
	profesor CFM	SSD	3950	89	4039						
	profesor CFM, debutant	SSD	3850	87	3937						
Anexa nr. II Capitolul I, Subcapitolul 2, punctul 1, litera a), subpunctul a.3. nr.crt. 17, 18, 19 și 20	fiziokinetoterapeut, principal	S	5142	116	5258	Anexa nr. II Capitolul I, Subcapitolul 2, punctul 1, litera a), subpunctul a.3. se introduc nr.crt. 20¹, 20², 20³ și 20⁴	fizioterapeut, fiziokinetoterapeut, kinetoterapeut, profesor CFM; principal	S	9725	219	9944
	fiziokinetoterapeut, specialist	S	4591	103	4694		fizioterapeut, fiziokinetoterapeut, kinetoterapeut, profesor CFM; specialist	S	9025	203	9228
	fiziokinetoterapeut	S	4361	98	4459		fizioterapeut, fiziokinetoterapeut, kinetoterapeut, profesor CFM	S	8600	194	8794
	fiziokinetoterapeut, debutant	S	4215	95	4310		fizioterapeut, fiziokinetoterapeut, kinetoterapeut, profesor CFM; debutant	S	4750	107	4857
Anexa nr. II Capitolul I, Subcapitolul 2, punctul 1, litera b), subpunctul b3. nr.crt. 1, 2 și 3	kinetoterapeut, profesor CFM; principal	S	5050	114	5164	Aceste categori sunt încadrate în Anexa nr. II Capitolul I, Subcapitolul 2, punctul 1, litera a,) subpunctul a.3. nr.crt. 20¹, 20², 20³ și 20⁴					
	kinetoterapeut, profesor CFM	S	4545	102	4647						
	kinetoterapeut, profesor CFM, debutant	S	4215	95	4310						
Anexa nr. II Capitolul I, Subcapitolul 2, punctul 1, litera a), subpunctul a.3. nr.crt. 27, 28 și 29	fiziokinetoterapeut, principal	SSD	4361	98	4459	Anexa nr. II Capitolul I, Subcapitolul 2, punctul 1, litera a), subpunctul a.3. nr.crt. 29¹, 29² și 29³	fizioterapeut, fiziokinetoterapeut, profesor CFM; principal	SSD	8600	194	8794
	fiziokinetoterapeut	SSD	4161	94	4255		fizioterapeut, fiziokinetoterapeut, profesor CFM	SSD	8375	188	8563
	fiziokinetoterapeut, debutant	SSD	4108	92	4200		fizioterapeut, fiziokinetoterapeut, profesor CFM, debutant	SSD	3610	81	3691

Încadrare funcții în lege actuală	Denumirea funcțiilor în actuala lege	Nivelul studiilor	Salariu de bază în legea actuală -lei-Gradația 0-anul 2022	Taxe angajator	TOTAL	Încadrare funcții în proiectul de modificare a legii	Denumirea funcțiilor în proiectul de modificare a legii	Nivelul studiilor	Salariu de bază în proiectul de modificare a legii -lei-Gradația 0-anul 2022	Taxe angajator	TOTAL
Anexa nr. II Capitolul I, Subcapitolul 3, subpunctul 3.2 nr crt. 22, 23 și 24	profesor CFM, principal	SSD	3950	89	4039	Anexa nr. II Capitolul I, Subcapitolul 3, subpunctul 3.2. nr crt. 24^1, 24^2 și 24^3	fizioterapeut, fiziokinetoterapeut, profesor CFM, principal	SSD	7925	178	8103
	profesor CFM	SSD	3900	88	3988		fizioterapeut, fiziokinetoterapeut, profesor CFM	SSD	7100	160	7260
	profesor CFM, debutant	SSD	3850	87	3937		fizioterapeut, fiziokinetoterapeut, profesor CFM, debutant	SSD	4130	93	4223
		49 de poziții		TOTAL	210290			28 de poziții		TOTAL	205906
				MEDIA	4291,63					MEDIA	7353

MEDIA DE CREȘTERE SALARIALĂ/ANGAJAT/LUNĂ pentru anul 2022	3,062,155
membri ai CFZRO care lucrează în sistemul de stat	995
Nr. total preconizat angajați în sistemul de stat	1300