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ORIGINAL RESEARCH PAPER ORIGINALNI ZNANSTVENI RAD

OUTCOMES OF OSTEOARTHRITIS TREATMENT – RESULTS OF AN 8-YEAR FOLLOW-UP STUDY

ISHODI LIJEČENJA OSTEOARTRITISA – REZULTATI OSMOGODIŠNJEG PRAĆENJA

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ABSTRACT

Introduction: Osteoarthritis (OA) is the most common chronic joint disease. It is characterized by chronic pain, joint deformation and loss of function. The treatment of OA is complex and long-term, includes non-pharmacological, pharmacological and surgical methods, and for optimal results a combination of several forms of treatment is required. *Participants and methods:* The research was conducted as a prospective clinical observational cohort study in the period from 2008 to 2017 on 77 participants from Eastern Croatia suffering from OA who were treated at University Hospital Centre Osijek. All participants underwent screening, the initial inclusion round and the final round according to a pre-prepared protocol. During the follow-up, data were collected on any change in health status, medication therapy or surgical procedure. *The aim of the study* was to assess the OA treatment outcomes during long-term follow-up, and it was especially focused on comparing outcomes of combined conservative and surgical methods, and conservative treatment methods alone. *Results:* Out of the 77 participants who were included after screening, 55 completed the study, 22 died or refused further participation. Subjective assessment of the state of the disease in relation to the beginning of the study was: extremely worsened 10.9%, significantly worsened 36.36%, slightly worsened 25.45%, equal 10.9%, slightly improved 7.27%, significantly improved 9.09%. At the beginning of the study, the average HAQ score (Health Assessment Questionnaire) was 1.37 (0–2.25), the average chronic pain score on the visual-analogue scale (VAS) was 55.55 (0–100), the average overall health assessment was 43.45 (0–100). At the end of the study: 9 participants underwent total knee arthroplasty (16.36%), and 15 participants underwent total hip arthroplasty (27.27%), average HAQ score 1.53 (0–2.28), average chronic pain score on VAS 50.18 (0–100), average overall health assessment 40.38 (0–90). *Conclusion:* The effect of OA treatment in this study was unsatisfactory according to subjective and objective indicators, for both conservative and surgical treatment methods. The use of medications should be rationalized and complementary to physical therapy, while surgical treatment methods should be reserved as a method of last but timely choice of treatment.

KEY WORDS: osteoarthritis, treatment outcomes, conservative treatment, surgical procedures

SAŽETAK

Uvod: Osteoartritis (OA) je najčešća kronična bolest zglobova; karakterizirana je kroničnom boli, deformacijom i gubitkom funkcije zgloba. Liječenje OA je složeno i dugotrajno, obuhvaća nefarmakološki, medikamentozni i kirurški pristup, a za optimalni rezultat potrebno je kombinirati više oblika liječenja. *Ispitanici i metode:* Istraživanje je prospektivna klinička opservacijska kohortna studija provedena u razdoblju od 2008. do 2017. godine na 77 ispitanika oboljelih od OA s područja istočne Hrvatske, liječenih u Kliničkome bolničkom centru Osijek. Svi su ispitanici prošli probir, prvu vizitu i završnu vizitu prema unaprijed pripremljenom protokolu. Tijekom praćenja prikupljeni su podatci o svakoj promjeni zdravstvenog stanja, promjeni u medikamentoznoj terapiji ili operacijskom zahvatu. *Cilj istraživanja* je procjena ishoda liječenja OA tijekom dugotrajnog praćenja, osobito usporedba ishoda kod kombiniranih konzervativnih i operativnih metoda i samo konzervativnih metoda liječenja. *Rezultati:* Od 77 ispitanika koji su nakon probira uključeni, 55 je završilo istraživanje, 22 je preminulo ili odbilo daljnje sudjelovanje. Subjektivna ocjena stanja bolesti u odnosu na početak istraživanja bila je: izuzetno pogoršano 10,9%, značajno pogoršano 36,36%, blago pogoršano 25,45%, jednako 10,9%, blago poboljšano 7,27%, značajno poboljšano 9,09%. Na početku istraživanja prosječni HAQ skor (engl. *Health Assesment Questionare*) bio je 1,37 (0 – 2,25), prosječni skor kronične boli na vizualno-analognoj skali (VAS) 55,55 (0 – 100), prosječna ukupna procjena zdravstvenog stanja 43,45 (0 – 100). Na završetku istraživanja: devet ispitanika je imalo ugradnju totalne endoproteze koljena (16,36%) i petnaest ispitanika je imalo ugradnju totalne endoproteze kuka (27,27%), prosječni HAQ skor 1,53 (0 – 2,28), prosječni skor kronične boli na VAS 50,18 (0 – 100), prosječna ukupna procjena zdravstvenog stanja 40,38 (0 – 90). *Zaključak:* Učinak liječenja OA u ovom istraživanju bio je nezadovoljavajući prema subjektivnim i objektivnim pokazateljima primjenom konzervativnih i operativnih metoda liječenja. Upotreba lijekova treba biti racionalizirana i komplementarna s fizikalnom terapijom, dok kirurške metode liječenja trebaju biti rezervirane kao metoda posljednjeg, ali pravovremenog izbora liječenja.

Ključne riječi: osteoartritis, ishod liječenja, konzervativno liječenje, operativne procedure

INTRODUCTION

Osteoarthritis (OA) is the most common chronic joint disease and is characterized by chronic pain and joint deformity, resulting in a gradual loss of joint function. The disease typically occurs in patients in their 40s and 50s and predominantly affects women. The main risk factors for the development of OA are age, genetic predisposition, female gender, previous injury or continuous load on the joint, other joint or metabolic diseases (rheumatoid arthritis, gout, diabetes), and obesity (1–6). The American College of Rheumatology (ACR) has established classification criteria for identifying patients with symptomatic OA that include clinical, physical, and radiographic findings (1, 6–9). The knees and hips are commonly affected, as these are weight-bearing joints (7, 9–12). The hand joints are also affected, especially the distal and proximal interphalangeal joints, in which larger bony growths, called Heberden's and Bouchard's nodes, can develop (8, 11, 12).

The treatment of OA is a complex process that includes non-pharmacological, pharmacological and surgical approaches, and often a combination of several forms of treatment is required for optimal results to be achieved (11). Surgical treatment is indicated for a relatively small number of patients with advanced OA. The greatest problems for patients with OA are pain and limitation of daily activities (11–13). Treatment goals for patients with OA are to reduce pain, improve mobility, and ultimately restore (or improve) functional ability (14). In general, it is recommended

UVOD

Osteoartritis (OA) je najčešća kronična bolest zglobova i karakterizirana je kroničnom boli i deformacijom zgloba, što rezultira postupnim gubitkom funkcije zgloba. Bolest se tipično javlja u četvrtom i petom desetljeću života i pretežno pogađa ženski spol. Glavni rizični čimbenici za razvoj OA jesu dob, genetska predispozicija, ženski spol, prethodna ozljeda ili kontinurano opterećenje zgloba, druge bolesti koje pogađaju zglobove ili metaboličke bolesti (reumatodini artritis, giht, šećerna bolest) i pretilost (1 – 6). Američko reumatološko društvo (ACR, prema engl. *American College of Rheumatology*) odredilo je klasifikacijske kriterije za identifikaciju pacijenata sa simptomatskim OA koji uključuju kliničke, fizikalne i radiografske nalaze (1, 6 – 9). Koljena i kukovi su uobičajeno zahvaćeni, s obzirom na to da je riječ o zglobovima koji nose težinu (7, 9 – 12). Zahvaćeni su i ručni zglobovi, osobito distalni i proksimalni interfalangealni zglobovi gdje se mogu razviti veća koštana proširenja, tzv. Heberdenovi i Bouchardovi čvorovi (8, 11, 12).

Liječenje OA je kompleksno i obuhvaća nefarmakološki, medikamentozni i kirurški pristup, a često je za optimalni rezultat potrebna kombinacija više oblika liječenja (11). Kirurško liječenje indicirano je u relativno malog broja bolesnika s uznapredovalim OA. Bolesnicima s OA najveći problem predstavljaju bol i ograničenje svakodnevnih aktivnosti (11 – 13). Ciljevi liječenja bolesnika s OA jesu smanjenje boli, poboljšanje pokretljivosti, a u konačnici restitucija (ili poboljšanje) funkcionalne sposobnosti (14). Općenito, preporučuje

that initial treatment be directed towards self-care and treatment that can be carried out by the patients themselves, while avoiding passive methods carried out by health professionals (e.g. physiotherapists) (15–19). Physical therapy exercises in patients with hip and knee OA are the main non-pharmacological measure to improve function and reduce pain (20–22). The positive effect of hydrokinesitherapy on quality of life may depend on body mass index (BMI) (4, 23). Orthoses, that is, medical support devices, can significantly relieve pressure on the joints and reduce pain in patients with hip and knee OA (24, 25). The main effect of drugs used in the treatment of OA is analgesia, and the main disadvantage of systemic drug administration is non-specificity with respect to the localization of OA (11, 12). Paracetamol can be effective as an initial oral analgesic, while non-steroidal anti-rheumatic drugs (NSAIDs) have proven to be effective and are used in practice as the first line of treatment for patients with OA. NSAIDs should be used at the lowest effective dose, for the shortest possible time. (11, 12, 26–28). Opioids are indicated in patients with OA who experience moderate to severe pain and who are refractory to other analgesic therapy or in whom other medications are contraindicated (11, 12, 29). In these patients, surgical treatment should be considered. Topical NSAIDs and capsaicin may be effective as an alternative to oral analgesics/NSAIDs in patients with knee OA and may be used as the first-line pharmacological treatment option in patients with mild to moderate disease (30–32). Intra-articular glucocorticoid injections have been proved to be beneficial in the treatment of patients with hip and knee OA (33, 34). Patients with symptomatic hip and knee OA whose disease significantly impairs their quality of life and limits their daily activities, and in whom adequate pain relief and function improvement have not been achieved with a combination of non-pharmacological and pharmacological measures, are candidates for artificial joint implants (35). Alloarthroplasty is an effective method that results in significant symptom relief and recovery of functional limitations (36). Total hip arthroplasty (THA) has been shown to have a better effect on the quality of life of patients than total knee arthroplasty (TKA) (12). Older age, higher preoperative pain, musculoskeletal comorbidities, and contralateral hip OA are predictors of poorer outcomes after hip arthroplasty (37), and higher pain, functional limitations, poor mental health, and medical comorbidities are predictors of poor outcomes after knee arthroplasty (38). Partial (unicompartmental) knee arthroplasty is used if the joint is only partially involved, while osteotomy is reserved for younger patients with hip OA, especially in cases of dysplasia (39, 40). Studies have shown that arthroscopic debridement is ineffective in unselected

se da početno liječenje bude usmjereno prema samopomoći i liječenju koje može provesti sam bolesnik uz izbjegavanje pasivnih metoda koje provode zdravstveni djelatnici (npr. fizioterapeuti) (15 – 19). Terapijske vježbe bolesnika s OA kuka i koljena predstavljaju glavnu nefarmakološku mjeru kojom se poboljšava funkcija i reducira bol (20 – 22). Pozitivni učinak hidrokineziterapije na kvalitetu života može biti ovisan o indeksu tjelesne mase (BMI) (4, 23). Ortoze, tj. pomagala za podupiranje mogu značajno rasteretiti pritisak na zglobove i smanjiti bol u bolesnika s OA kuka i koljena (24, 25). Glavni učinak lijekova koji se primjenjuju u liječenju OA jest analgezija, a glavni nedostatak sustavne primjene lijekova jest nespecifičnost s obzirom na lokalizaciju OA (11, 12). Paracetamol može biti djelotvoran kao početni oralni analgetik, dok su se nesteroidni antireumatici (NSAR) pokazali učinkovitima i u praksi su prva linija liječenja bolesnika s OA. NSAR bi se trebali primjenjivati u najnižoj učinkovitoj dozi, što je moguće kraće (11, 12, 26 – 28). Primjena opioida indicirana je u bolesnika s OA koji imaju umjerenu do jaku bol, a koji su refraktorni na drugu analgetsku terapiju ili su drugi lijekovi kontraindicirani (11, 12, 29). U tih bolesnika potrebno je razmotriti mogućnost kirurškog liječenja. Topički primijenjeni NSAR i kapsaicin mogu biti učinkoviti kao alternativa oralnim analgeticima/NSAR u bolesnika s OA koljena, a u bolesti blage do umjerene težine mogu biti prva opcija farmakološkog liječenja (30 – 32). Intraartikularne injekcije glukokortikoida pokazale su se korisnima u liječenju bolesnika s OA kuka i koljena (33, 34). Bolesnici sa simptomatskim OA kuka i koljena kojima bolest značajno narušava kvalitetu života i ograničava ih u aktivnostima svakodnevnog života, a u kojih nije postignuto odgovarajuće smanjenje boli i poboljšanje funkcije kombinacijom nefarmakoloških i farmakoloških mjera, kandidati su za implantaciju umjetnih zglobova (35). Aloartroplastika je učinkovita metoda koja rezultira značajnim smanjenjem simptoma i oporavkom funkcionalnih ograničenja (36). Pokazalo se da implantacija totalne endoproteze kuka ima bolji učinak na kvalitetu života bolesnika nego implantacija totalne endoproteze koljena (12). Visoka dob, viši stupanj predoperativne boli, mišićno-koštani komorbiditeti i OA kontralateralnog kuka prediktori su nepovoljnijeg ishoda nakon operacije ugradnje endoproteze kuka (37), a viši stupanj boli, funkcionalna ograničenja, narušeno mentalno zdravlje i medicinski komorbiditeti prediktori su takvog ishoda nakon ugradnje endoproteze koljena (38). Parcijalna endoproteza koljena primjenjuje se ako je zglob zahvaćen samo djelomično, dok je osteotomija rezervirana za mlađe bolesnike s OA kuka, osobito u slučajevima displazije (39, 40). Istraživanja su pokazala da artroskopski *debridement* nema učinka u neselekcioniranih bolesnika s OA koljena (41). U pa-

patients with knee OA (41). In patients with knee OA, arthrodesis is considered as a salvage procedure in cases where arthroplasty is not an option or has failed to yield successful results (42).

The aim of this paper is to evaluate the success of treatment in patients with OA treated with different treatment methods during an eight-year follow-up study.

PARTICIPANTS AND METHODS

The study was conducted as a prospective clinical observational cohort study conducted over a period of 8 years on 77 participants with OA from Eastern Croatia who were treated at the University Hospital Centre Osijek. All participants underwent screening, the first inclusion round (1st February 2008 – 31st January 2009), and at the final round (1st February 2016 – 31st January 2017) participants who were monitored in the study until the final round were examined.

The inclusion criteria for this study included:

1. osteoarthritis diagnosis made by a rheumatologist according to the current classification criteria for osteoarthritis of the American College of Rheumatology (ACR),
2. signed informed consent to participate in the study, which the patient must confirm by signing the informed consent form,
3. registered permanent residence / permanent residence in one of the five counties of Eastern Croatia which must be continuous during the study duration,

The exclusion criteria for this study included:

1. patients with a confirmed diagnosis of cardiovascular diseases (previous myocardial infarction, confirmed coronary artery disease through diagnostic tests, angina pectoris, ischemic cardiomyopathy, previous ischemic stroke, transient ischemic attack, confirmed aortic dissection or aneurysm, confirmed peripheral artery disease), diagnosed primary cardiomyopathy, uncorrected severe valve disease or decompensated heart failure before the first round,
2. patient's refusal to participate in further study analysis after the first round,
3. permanent cessation of residence in one of the five counties of Eastern Croatia during the study duration, with migration within the region not being an exclusion criterion,
4. patient's unavailability after the first study round.

During the follow-up, participants were instructed to inform the investigators of any changes in their health status, diagnosis of new diseases, changes in medication therapy, or surgical procedures by in-person visit, telephone/fax, e-mail, or through contact ini-

cijenata s OA koljena artrodeza dolazi u obzir kao procedura spasa u slučajevima kada artroplastika ne dolazi u obzir ili je neuspjela (42).

Cilj je ovog rada procijeniti uspješnost liječenja bolesnika s OA liječenih različitim metodama liječenja tijekom osmogodišnjeg praćenja.

ISPITANICI I METODE

Istraživanje je provedeno kao prospektivna klinička opservacijska kohortna studija koja se provodila u razdoblju od osam godina na 77 ispitanika oboljelih od OA s područja istočne Hrvatske liječenih u KBC-u Osijek. Svi ispitanici su prošli probir, prvu uključnu vizitu (1. veljače 2008. – 31. siječnja 2009.), a na završnoj viziti (1. veljače 2016. – 31. siječnja 2017.) pregledani su ispitanici koji su do tada bili praćeni u istraživanju.

Kriteriji za uključivanje bolesnika u istraživanje bili su:

1. dijagnosticiran osteoartritis od strane reumatologa prema važećim klasifikacijskim kriterijima *American College of Rheumatology* (ACR) za osteoartritis
2. potpisani informirani pristanak za sudjelovanje u studiji
3. prijavljeno prebivalište / trajni boravak u jednoj od pet županija istočne Hrvatske neprekidno tijekom trajanja studije.

Kriteriji za isključivanje bolesnika iz istraživanja bili su:

1. bolesnici s dijagnosticiranim kardiovaskularnim bolestima (preboljeli infarkt miokarda, dokazana koronarna bolest putem dijagnostičkih testova, angina pektoris, ishemijska kardiomiopatija, preboljeli ishemijski moždani udar, tranzitorna ishemijska ataka, dokazana disekcija ili aneurizma aorte, dokazana periferna arterijska bolest), dijagnosticirana primarna kardiomiopatija, teška nekorigirana valvularna bolest ili srčana dekopmenzacija prije prve vizite
2. odbijanje bolesnika da sudjeluje u istraživanju nakon prve vizite
3. trajni prestanak boravka na području jedne od pet županija istočne Hrvatske tijekom razdoblja istraživanja, pri čemu migracija unutar regije nije isključni kriterij
4. nedostupnost bolesnika nakon prve vizite istraživanja.

Tijekom praćenja sudionici su upućeni da ispitivače obavijeste o svakoj promjeni zdravstvenog stanja, dijagnosticiranju novih bolesti, promjeni u medikamentoznoj terapiji ili učinjenom operacijskom zahvatu putem osobnog dolaska, telefona/telefaksa, e-pošte ili su kontaktirani od strane istraživača najmanje jednom godišnje. Ispitanici su također dolazili na svoje redo-

tiated by the investigator at least once a year. The participants also attended their regular check-ups at the rheumatology clinic, where all changes in their health status were recorded, and at the final round, a thorough check of the participants' medical documentation was performed. In the study, we used data collected during the eight-year follow-up, medical histories, outpatient forms from the archives and computer database of the Division of Rheumatology, Clinical Immunology and Allergology, and the Department of Physical Medicine and Rehabilitation, and data obtained from family physicians.

Clinical and laboratory methods include a detailed analysis of the medical history, completion of a preprepared form for the first initial round, final round and annual follow-up forms, physical examination with anthropometric measurements; assessment of general health status, assessment of pain intensity, completion of the AUSCAN index form for hand osteoarthritis (43), completion of the Lequesne index form for hip osteoarthritis (44), completion of the Lequesne index form for knee osteoarthritis (44) and completion of the Croatian translation of the Health Assessment Questionnaire (HAQ) (45).

Ethical standards

This research was conducted in accordance with the Declaration of Helsinki and approved by the ethics committees of the University Hospital Centre Osijek and the School of Medicine in Osijek (no.: 602-04/21-08/07).

Written informed consent for participation was obtained from all participants.

Statistical methods

Descriptive statistics were used to describe and summarize the study data. Inferential statistics were used to test hypotheses. Independent samples t-test was used to test the significance of mean differences. Depending on the results of Levene's test, a t-test assuming equal or unequal variances was used to determine statistical significance between groups. Chi-square test of independence was used to analyse the relationship between qualitative variables. Fisher's exact test was used in cases in which the assumptions for the chi-square test were not met. The significance level was set at $p < 0.05$, while $0.05 < p < 0.10$ was considered a trend (marginally significant). The IBM SPSS Statistics version 26, New York, USA, was used for the analysis.

RESULTS

Demographic data

Out of the 77 participants who were included in the study after screening, a total of 55 OA patients com-

vite preglede u reumatološku ambulantu gdje su bilježene sve promjene zdravstvenog stanja, a na završnoj viziti izvršena je temeljita provjera medicinske dokumentacije ispitanika. U istraživanju smo koristili podatke prikupljene tijekom osmogodišnjeg praćenja, povijesti bolesti, ambulantne listove iz pismohrana i računalne baze podataka Kliničkog zavoda za kliničku imunologiju, reumatologiju i alergologiju i Odjela za fizikalnu medicinu i rehabilitaciju te podatke dobivene od liječnika obiteljske medicine.

Kliničke i laboratorijske metode uključuju detaljnu analizu povijesti bolesti, popunjavanje unaprijed pripremljenog obrasca za prvu početnu vizitu, završnu vizitu te obrasce za godišnje praćenje, fizikalni pregled uz antropometrijske mjere, procjenu općeg zdravstvenog stanja, procjenu intenziteta boli, popunjavanje ispunjavanje obrasca AUSCAN indeksa za *osteoartritis* šake (43), popunjavanje obrasca Lequesne indeksa za *osteoartritis* kuka (44), popunjavanje obrasca Lequesne indeksa za *osteoartritis* koljena (44) te popunjavanje hrvatskog prijevoda *Health Assessment Questionnaire* (HAQ) (45).

Etički standardi

Ovo istraživanje je provedeno u skladu s Helsinškom deklaracijom, a odobreno od strane etičkih povjerenstava KBC-a Osijek i Medicinskog fakulteta Osijek (br. 602-04/21-08/07).

Pisani informirani pristanak za sudjelovanje dobiven je od svih sudionika.

Statističke metode

Deskriptivna statistika korištena je za opisivanje i sažimanje podataka studije. Za testiranje hipoteza primijenjena je diferencijalna statistika. Za provjeru značajnosti srednjih razlika korišten je t-test neovisnih uzoraka. Ovisno o rezultatima Leveneovog testa, t-test koji pretpostavlja jednaku ili nejednaku varijancu korišten je za određivanje statističke značajnosti između skupina. Za analizu odnosa između kvalitativnih varijabli primijenjen je hi-kvadrat test neovisnosti. Fisherov egzaktni test korišten je kada pretpostavke za hi-kvadrat test nisu bile ispunjene. Razina značajnosti postavljena je na $p < 0,05$, dok se $0,05 < p < 0,10$ smatra trendom (marginalno značajno). Za analizu je upotrijebljen računalni program SPSS verzija 26, IBM, New York, SAD.

REZULTATI

Demografski podatci

Od 77 ispitanika koji su uključeni u istraživanje nakon probira, istraživanje je završilo ukupno 55 oboljelih od OA. Preminuli ispitanici i oni koji su tijekom istraživanja odbili daljnje sudjelovanje, ukupno 22 ispi-

Table 1. Demographic data and parameters monitored during the course of the study
Tablica 1. Demografski podatci i parametri praćeni tijekom istraživanja

	Initial round / Početna vizita	Final round / Završna vizita
Number of participants / Broj ispitanika (N)	77	55
Male / Muški spol (N)	11	10
Female / Ženski spol (N)	66	45
Average age (years) / Prosječna životna dob (godine)	63.23 (27-80)	71.2 (26-89)
Average disease duration (years) / Prosječno trajanje bolesti (godine)	5.64 (0.1-31)	
OA hand involvement (N) / Zahvaćenost OA šake (broj ispitanika)	2 (3.64%)	
OA knee involvement (N) / Zahvaćenost OA koljena (broj ispitanika)	2 (3.64%)	
OA hip involvement (N) / Zahvaćenost OA kukovi (broj ispitanika)	5 (9.90%)	
OA hand and knee involvement (N) / Zahvaćenost OA šake i koljena (broj ispitanika)	15 (27.27%)	
OA hand and hip involvement (N) / Zahvaćenost OA šake i kukovi (broj ispitanika)	4 (7.27%)	
OA knee and hip involvement (N) / Zahvaćenost OA koljena i kukovi (broj ispitanika)	15 (27.27%)	
OA hand, knee and hip involvement (N) / Zahvaćenost OA šake, koljena i kukovi (broj ispitanika)	12 (21.81)	
Average BMI / Prosječni BMI	29.45 (19.5 – 45.5)	29.28 (19.8 – 48.1)
Average waist/hip ratio / Prosječni omjer struk/bokovi	0.89 (0.7-1.09)	0.92 (0.72-1.15)
Average HAQ score / Prosječni HAQ skor	1.37 (0-2.25)	1.53 (0-2.28)
Average HAQ score > 1 (N) / Prosječni HAQ skor > 1 (broj ispitanika)	39 (70.9%)	39 (70.9%)
Average chronic pain score / Prosječni skor kronične boli (VAS)	55.55 (0-100)	50.18 (0-100)
Average overall health assessment / Prosječna ukupna procjena zdravstvenog stanja	43.45 (0-100)	40.38 (0-90)
Operativni zahvati na zglobovima, zahvati tijekom istraživanja: šake / Joint surgeries during the course of the study – hand		0
Operativni zahvati na zglobovima, zahvati tijekom istraživanja: kukovi / Joint surgeries during the course of the study – hip		9 (16.36%) (TEP)
Operativni zahvati na zglobovima, zahvati tijekom istraživanja: koljena / Joint surgeries during the course of the study – knee		15 (27.27) (TEP)

Legend / Tumač: OA – osteoarthritis / osteoartritis, BMI – body mass index / indeks tjelesne mase, HAQ – Health Assessment Questionnaire, VAS – visual analogue scale/mm / vizualno-analogna skala/mm, TEP – total endoprosthesis (arthroplasty) / totalna endoproteza
** Proportion of patients / Proporcija bolesnika*
*** Data in parentheses represent the interval between the measured minimum and maximum values. / Podatci u zagradama su interval između izmjerene minimalne i maksimalne vrijednosti.*

pleted the study. Participants who died and those who refused further participation during the course of the study (22 participants in total; 17 died and 5 refused further participation) were excluded from the analysis. The average age of the deceased patients was 76.94, and the leading causes of death were cardiovascular diseases. There were 25.45% of former smokers, and 10.9% of active smokers. The average duration of follow-up was 8 years and 4 months. The subjective assessment of the state of the disease (OA) in relation to the beginning of the study was: extremely worsened 10.9%, significantly worsened 36.36%, slightly worsened 25.45%, equal 10.9%, slightly improved 7.27%, significantly improved 9.09%. Table 1 shows the demographic data and parameters monitored during the course of the study at the initial and final round.

The frequency of pain medication use at the beginning of the study was 90.9% and at the end of the study

Table 2. Medications used to treat OA during the course of the study
Tablica 2. Lijekovi primijenjeni za liječenja OA tijekom istraživanja

	Upotreba tijekom istraživanja (%) Usage during the course of the study (%)
Non-steroidal anti-inflammatory drugs / Nesteroidni antireumatik	61.81
Opioids / Opioidi	12.72
Combination of analgesics and opioids / Kombinacija analgetika i opioida	49.09
Other medications / Ostali lijekovi	3.64

tanika (17 ih je preminulo i pet ih je odbilo sudjelovanje) isključeno je iz analize. Prosječna dob preminulih bila je 76,94 godine, a vodeći uzroci smrti bile su kardi-

Table 3. Comparison of parameters for participants that underwent surgery and participants that did not undergo surgery during the course of the study

Tablica 3. Uspoređeni parametri za operirane i neoperirane ispitanike tijekom istraživanja

	Underwent surgery / Operirani	Did not undergo surgery / Neoperirani	P
Number of participants / Broj ispitanika	23	32	
Average age (years, final round) / Prosječna životna dob (godine, završna vizita)	73.3 (57 – 89)	69.75 (36 – 88)	0.244
Average duration of disease (years, initial round) / Prosječno trajanje bolesti (godine, početna vizita)	5.57 (0.1 – 37)	5.03 (0.1 – 20)	0.742
Average BMI at beginning of the study / Prosječni BMI na početku istraživanja	30.59 (19.5 – 45.5)	28.64 (20.12 – 38)	0.151
Average BMI at the end of the study /Prosječni BMI na završetku istraživanja	30.2 (19.8 – 48.1)	28.6 (20.6 – 38)	0.268
Average waist/hip ratio at the beginning of the study / Prosječni omjer struk/bokovi na početku istraživanja	0.88 (0.7 – 1.09)	0.9 (0.74 – 1.05)	0.430
Average waist/hip ratio at the end of the study / Prosječni omjer struk/bokovi na završetku istraživanja	0.9 (0.72 – 1.06)	0.94 (0.78 – 1.15)	0.172
Average HAQ score at the beginning of the study / Prosječni HAQ skor na početku istraživanja	1.45 (0.375 – 2.25)	1.31 (0 – 2.125)	0.375
Average HAQ score at the end of the study / Prosječni HAQ skor na završetku istraživanja	1.65 (0.88 – 2.13)	1.45 (0 – 2.75)	0.341
Average chronic pain score (VAS) at the beginning of the study / Prosječni skor kronične boli (VAS) na početku istraživanja	56.74 (10 – 90)	54.69 (0 – 100)	0.750
Average chronic pain score (VAS) at the end of the study / Prosječni skor kronične boli (VAS) na završetku istraživanja	55.25 (10 – 100)	49.06 (10 – 80)	0.700
Average overall health assessment at the beginning of the study / Prosječna ukupna procjena zdravstvenog stanja na početku istraživanja	51.74 (0 – 100)	40.47 (10 – 80)	0.144
Average overall health assessment at the end of the study / Prosječna ukupna procjena zdravstvenog stanja na završetku istraživanja	35.96 (0 – 85)	43.96 (3 – 90)	0.260
HAQ > 1 at the final round / HAQ > 1 na završnoj viziti	18	21	0.361

** Data in parentheses represent the interval between the measured minimum and maximum values. / Podatci u zagradama su interval između izmjerene minimalne i maksimalne vrijednosti.*

it was 89.1%. Table 2 shows the types of medications used for the treatment and control of OA symptoms during the course of the study.

All participants underwent physical therapy measures prescribed by a physiatrist under the supervision of a physiotherapist at least two times during the course of the study.

Comparison of participants who underwent surgery and those who did not

Out of a total of 55 participants included in the outcome analysis, 23 (41.81%) participants underwent orthopaedic surgery (9 participants underwent total knee arthroplasty (TKA) and 15 participants underwent total hip arthroplasty (THA).

The subjective assessment of the state of the disease in relation to the beginning of the study in participants who did not undergo surgery was: extremely worsened

ovaskularne bolesti. Bivših pušača bilo je 25,45%, a sadašnjih pušača 10,9%. Prosječno trajanje praćenja bilo je osam godina i četiri mjeseca. Subjektivna ocjena stanja bolesti (OA) u odnosu na početak istraživanja bila je: izuzetno pogoršano 10,9%, značajno pogoršano 36,36%, blago pogoršano 25,45%, jednako 10,9%, blago poboljšano 7,27%, značajno poboljšano 9,09%. U tablici 1 prikazani su demografski podatci i parametri praćeni tijekom istraživanja na početnoj i završnoj viziti.

Učestalost upotrebe lijekova protiv bolova na početku istraživanja bila je 90,9%, dok je na završetku istraživanja bila 89,1%. Tablica 2 prikazuje vrste lijekova primijenjenih u liječenju i kontroli simptoma OA tijekom istraživanja.

Svi ispitanici provodili su mjere fizikalne terapije propisane od liječnika specijalista fizijatara pod nadzorom fizioterapeuta najmanje dva puta tijekom istraživanja.

9.36%, significantly worsened 40.63%, slightly worsened 21.86%, equal 11.5%, slightly improved 3.13%, significantly improved 12.5%.

The subjective assessment of the state of the disease in relation to the beginning of the study in patients who underwent surgery was: extremely worsened 13.4%, significantly worsened 30.43%, slightly worsened 30.43%, equal 8.7%, slightly improved 13.04%, significantly improved 4.35%. Table 3 shows the compared parameters for participants who underwent surgery and those who did not at the beginning and the end of the study.

Knees

The knee area affected by osteoarthritis was present in 44 out of 55 participants (80%), and 9 participants (41.67%) underwent orthopaedic surgery for total knee arthroplasty (TKA). The average duration of OA in the group of patients who did not undergo surgery was 5.41 years, while in the group of patients who underwent surgery it was 7.51 years, which is not a statistically significant difference (t=1.045, p=0.30). The average severity of OA measured by the Lequesne index was 13.83 (4–22) in the group of patients who did not undergo surgery and 11.78 (4–19) in the group of patients who underwent surgery, which is not a statistically significant difference (t=-0.82, p=0.42).

Hips

The hip area affected by osteoarthritis was present in 36 out of 55 participants (65.45%), and 15 participants (20.45%) underwent orthopaedic surgery for total hip arthroplasty (THA) (1 participant underwent bilateral and 14 participants unilateral total hip arthroplasty). The average duration of OA in patients who did not undergo surgery was 6.56 years and in patients who underwent surgery it was 4.26 years, which does not represent a statistically significant difference (t=-1.08, p=0.29). The average severity of OA measured by the Lequesne index in was 11.9 (5–19) in patients who did not undergo surgery and 12.93 (2–20) in patients who underwent surgery, which does not represent a statistically significant difference (t=0.62, p=0.54).

DISCUSSION

In this study, two or more joint areas were affected in the majority of participants, which is consistent with the results of previous studies (1, 11, 46). During the eight-year follow-up period, over two-thirds of participants described their subjective assessment of OA status as worsening compared to the state of the disease at beginning of the study. The overall disability assessment measured by the HAQ score did not show a significant difference at the beginning and the end of the study, nor did it show a difference in the assessment of

Usporedba operiranih i neoperiranih ispitanika

Od ukupno 55 ispitanika uključenih u analizu ishoda, ortopedskom zahvatu bilo je podvrgnuto 23 (41,81%) ispitanika (9 TEP koljena i 15 TEP kukova).

Subjektivna ocjena stanja bolesti u odnosu na početak istraživanja kod neoperiranih bila je: izuzetno pogoršano 9,36%, značajno pogoršano 40,63%, blago pogoršano 21,86%, jednako 11,5%, blago poboljšano 3,13%, značajno poboljšano 12,5%.

Subjektivna ocjena stanja bolesti u odnosu na početak istraživanja kod operiranih bila je: izuzetno pogoršano 13,4%, značajno pogoršano 30,43%, blago pogoršano 30,43%, jednako 8,7%, blago poboljšano 13,04%, značajno poboljšano 4,35%. Tablica 3 prikazuje uspoređivane parametre za operirane i neoperirane ispitanike na početku i kraju istraživanja.

Koljena

Područje koljena zahvaćeno osteoartritisom imalo je 44 od 55 ispitanika (80%), a ortopedskom zahvatu ugradnje totalne endoproteze bilo je podvrgnuto devet ispitanika (41,67%). Prosječno trajanje OA kod neoperiranih bilo je 5,41 godina, dok je kod operiranih 7,51 godina, što ne predstavlja statistički značajnu razliku (t = 1,045, p = 0,30). Prosječna težina OA mjerena Lequesne indeksom kod neoperiranih iznosila je 13,83 (4 – 22) a kod operiranih 11,78 (4 – 19), što ne predstavlja statistički značajnu razliku (t = -0,82, p = 0,42).

Kukovi

Područje kukova zahvaćeno osteoartritisom imalo je 36 od 55 ispitanika (65,45%), a ortopedskom zahvatu ugradnje totalne endoproteze bilo je podvrgnuto 15 ispitanika (20,45%) (jedan bilateralnoj i 14 unilateralnoj ugradnji endoproteze). Prosječno trajanje OA kod neoperiranih bilo je 6,56 godina, a kod operiranih 4,26 godina, što ne predstavlja statistički značajnu razliku (t = -1,08, p = 0,29). Prosječna težina OA mjerena Lequesne indeksom kod neoperiranih iznosila je 11,9 (5 – 19), a kod operiranih 12,93 (2 – 20), što ne predstavlja statistički značajnu razliku (t = 0,62, p = 0,54).

RASPRAVA

U ovom istraživanju većina ispitanika imala je zahvaćena dva ili više zglobnih područja bolešću, što je u skladu s ranijim studijama (1, 11, 46). Tijekom osmogodišnjeg praćenja kod više od dvije trećine ispitanika subjektivna ocjena stanja OA bilo je pogoršanje u odnosu na početak istraživanja. Ukupna procjena onesposobljenosti mjerena pomoću HAQ nije pokazala značajnu razliku na početku i kraju istraživanja, kao niti razliku u ocjeni značajne onesposobljenosti (HAQ

significant disability (HAQ > 1). The assessment of chronic pain on VAS was moderately high throughout the course of the study, while the overall health assessment was unsatisfactory. These parameters indicate a generally unsatisfactory success in the treatment and control of OA symptoms during the course of the study.

During the course of the study, the participants occasionally underwent inpatient physical therapy, which is an important step in the treatment of OA (1, 2). Passive physical therapy methods are most valuable in the form of preparing the joints for therapeutic exercises and during the exacerbation phase of the disease (47). Physical therapy with controlled exercise in OA of the hip and knee significantly reduces pain and improves joint function and the quality of life, especially in younger patients with moderate OA. However, the effect of physical therapy may decrease as the disease progresses (48). Thermal modalities of physical therapy and transcutaneous electrical nerve stimulation (TENS) also help in short-term pain control in patients with hip and knee OA, and the effect can last from 2 to 4 weeks (11, 12). The participants were on average obese, which contributes to the severity of the disease and reduced adherence to physical therapy exercises. A smaller number of participants were smokers, while the number of former smokers was significantly higher, which is an indicator of the relative success of (secondary) prevention and education in this area. According to a recent meta-analysis conducted by V. Silverwood et al., smoking has a neutral effect on the risk of developing OA and successful treatment of this disease (49).

The use of medication therapy was very high. Topical or systemic NSAIDs and paracetamol/opioid combinations were most commonly used medications. In numerous studies, NSAIDs have proven to be effective and in practice they represent the first line of treatment for patients, which is in line with the results of our study (27, 28, 30, 32). Gastrointestinal side effects of NSAIDs are most often more pronounced in the elderly or in combination with certain medications, e.g. glucocorticoids, and therefore they should be used in the lowest effective dose, for the shortest possible amount of time (11, 12). Weak opioids are used in patients with hip and knee OA (for moderate to severe pain) in whom other therapy methods have proven to be ineffective or contraindicated, with relatively common side effects (nausea, constipation, dizziness) (29). According to the results of a meta-analysis of 18 placebo-controlled randomized studies, the effect of opioids on pain in OA can be assessed as moderate to severe, and in terms of their effect on physical function, it can be assessed as mild to moderate (29, 50). Nowadays, a fixed-dose combination of weak opioids and pure analgesics is widely used, which is in accordance with the

> 1). Procjena kronične boli putem VAS-a bila je umjereno visoka tijekom cijelog istraživanja, dok je ukupna procjena zdravstvenog stanja bila nezadovoljavajuća. Navedeni parametri pokazuju općenito na nezadovoljavajući uspjeh liječenja i kontrole simptoma OA tijekom istraživanja.

Ispitanici su tijekom istraživanja provodili povremeno stacionarnu fizikalnu terapiju, što predstavlja važan korak u liječenju OA (1, 2). Metode pasivne fizikalne terapije najvrjednije su kao priprema zglobova za terapijske vježbe te u fazi pogoršanja bolesti (47). Fizikalna terapija kontroliranim vježbanjem kod OA kuka i koljena značajno smanjuje bolnost, poboljšava funkciju zgloba i utječe na poboljšanje kvalitete života, osobito kod mlađih pacijenata s umjerenim OA, no učinak se može smanjiti napredovanjem bolesti (48). Termički modaliteti fizikalne terapije i transkutana električna živčana stimulacija (TENS) također pomažu u kratkotrajnoj kontroli boli u bolesnika s OA kuka i koljena, a učinak može trajati dva do četiri tjedna (11, 12). Ispitanici su prosječno bili pretili, što doprinosi težini bolesti i smanjenoj adherenciji za provođenje vježbi fizikalne terapije. Manji broj ispitanika bili su pušači, dok je značajan broj bivših pušača, što je pokazatelj razmjernog uspjeha (sekundarne) prevencije i edukacije u ovom području. Prema novijoj metaanalizi Silverwooda i suradnika pušenje ima neutralan efekt na rizik za razvoj i uspješnost liječenja OA (49).

Upotreba medikamentozne terapije bila je vrlo visoka. Najviše su primjenjivani topički ili sistemski NSAR i kombinacije paracetamola/opioida. U brojnim studijama NSAR su se pokazali učinkovitima i u praksi predstavljaju prvu linija liječenja bolesnika, što je sukladno našim rezultatima (27, 28, 30, 32). Najčešće su gastrointestinalne nuspojave NSAR, izraženije kod starijih ili u kombinaciji s nekim lijekovima, npr. glukokortikoidima; stoga bi se trebali primjenjivati u najnižoj učinkovitoj dozi što je moguće kraće (11, 12). Slabi opioidi se primjenjuju u bolesnika s OA kuka i koljena za umjerenu do jaku bol, a kod kojih se druga terapija pokazala neučinkovitom ili kontraindiciranom, uz relativno česte nuspojave (mučnina, konstipacija, vrtoglavica) (29). Prema rezultatima metaanalize 18 placebom kontroliranih randomiziranih studija, učinak opioida na bol u OA može se ocijeniti kao umjeren do jak, a za funkciju blag do umjeren (29, 50). Danas se široko upotrebljava fiksna kombinacija slabih opioida i čistih analgetika, što je sukladno s podatcima našeg istraživanja (29, 50). Tramadol se često primjenjuje u fiksnoj kombinaciji s paracetamolom s ciljem postizanja sinergističkog učinka i manjeg rizika od nuspojava. Kako bi se smanjio rizik od nuspojava i za slabe i za jake opioide liječenje se započinje nižom dozom lijeka, a potom se po potrebi doza povisuje (51).

data stated in our study (29, 50). Tramadol is often used in a fixed-dose combination with paracetamol, with the aim of achieving a synergistic effect and a lower risk of side effects. In order to reduce the risk of side effects, in the case of weak and strong opioid use, the treatment is started with a lower dose of the medication, and then the dose is increased if necessary (51).

Through a comparison of subjective and objective indicators in this study, no difference was found in the success of symptom control and preservation of joint function with the use of surgical treatment methods. A meta-regression analysis of disability in patients with knee OA with a body weight reduction of more than 5% showed a significant improvement (52). A study conducted by Skou et al. described a significant reduction in pain intensity, improvement in function, and overall quality of life in patients who underwent total knee arthroplasty (TKA) and 12 weeks of nonsurgical treatment, compared to a group that underwent 12 weeks of nonsurgical treatment alone, but surgical treatment had a significantly higher rate of complications (deep vein thrombosis, infections) (53). There are no criteria according to which the use of surgical methods is the best choice for a patient. Total hip or knee arthroplasty was proved to be the best choice (54–56). Recent studies show good results in pain control and improvement of functional status with the use of minimally invasive surgical procedures in the treatment of OA, especially of the hip and knee, but such procedures were not performed or available to the participants of this study (57). Lower body mass index (BMI) is associated with better dynamic balance, which indicates the importance of optimizing body mass index, especially in combination with therapeutic exercises (56, 57, 58). Reducing the body mass index is also important at the molecular level due to the reduction of pro-inflammatory cytokines (e.g. resistin, adiponectin, leptin) and their role in the pathogenesis of OA (59). The results of our study do not show a significant difference in the improvement of quality of life and control of OA symptoms between participants who underwent total hip (THA) or knee arthroplasty (TKA) and those who did not undergo surgery, which is different from the results of treatment outcomes in some recent studies (56, 60). Considering the generally poor outcomes of OA treatment in this study, possible explanations are poor adherence to home exercises, i.e. sedentary lifestyle, tendency to obesity due to dietary patterns specific to this area, presence of comorbidities, reliance on widespread use of analgesics and antirheumatic drugs for symptom control, late decision-making for orthopaedic procedures, application of new surgical techniques that were not available at the time of this study, and generally unhealthy lifestyle choices and lack of motivation to change them.

Usporedbom subjektivnih i objektivnih pokazatelja u ovom istraživanju nije bilo razlike u uspješnosti kontrole simptoma i očuvanju funkcije zgloba primjenom operativnih načina liječenja. Metaregresijska analiza o onesposobljenosti bolesnika s OA koljena uz smanjenje tjelesne težine za više od 5% pokazala je značajno poboljšanje (52). U studiji Skou i suradnika opisano je značajno smanjenje intenziteta boli, poboljšanje funkcije te ukupne kvalitete života u bolesnika koji su podvrgnuti ugradnji totalne endoproteze koljena te potom dvanaestotjednom nekirurškom liječenju, u usporedbi sa skupinom koja je bila podvrgnuta isključivo dvanaestotjednom nekirurškom liječenju, no kirurško liječenje je imalo značajno veći postotak komplikacija (duboka venska tromboza, infekcije) (53). Ne postoje kriteriji prema kojima je primjena kirurških metoda najbolji izbor za bolesnika. Kao najbolji izbor pokazala se ugradnja TEP-a kuka ili koljena (54 – 56). Novija istraživanja pokazuju dobre rezultate u kontroli boli i poboljšanju funkcionalnog statusa kod primjene minimalno invazivnih kirurških procedura u liječenju OA, osobito kuka i koljena, no ovakvi zahvati nisu se provodili niti su bili dostupni za ispitanike ovog istraživanja (57). Niži indeks tjelesne mase (BMI, prema engl. *body mass index*) povezan je s boljim dinamičkim balansom, što ukazuje na važnost optimiziranja BMI osobito u kombinaciji s terapijskim vježbama (56, 57, 58). Smanjenje BMI-a važno je također na molekularnoj razini zbog smanjenja lučenja proupalnih citokina (npr. resistin, adiponektin, leptin) i njihove uloge u patogenezi OA (59). Naši rezultati ne pokazuju značajnu razliku u poboljšanju kvalitete života i kontroli simptoma OA između ispitanika koji su bili podvrgnuti TEP-u kuka ili koljena i neoperiranih, što se razlikuje u usporedbi s rezultatima ishoda liječenja nekih novijih istraživanja (56, 60). Uzevši u obzir općenito loše ishode liječenja OA u ovom istraživanju, moguća objašnjenja su loša adherencija u provođenju vježbi kod kuće, tj. sedentarni način života, sklonost pretilosti zbog načina prehrane specifičnog za ovo područje, prisutnosti komorbiditeta, oslanjanje na široko rasprostranjenu upotrebu analgetika i antireumatika za kontrolu simptoma, kasno odlučivanje za ortopedske zahvate, primjena novih operativnih tehnika koje nisu bile dostupne u vremenu provođenja istraživanja i općenito lošije životne navike i nemotiviranost za njihove promjene.

Provedeno istraživanje je ograničeno relativno malim uzorkom s obzirom na ukupnu prevalenciju osteoartritisa. Zbog toga je moguće da su bolesnici uključeni u provedeno istraživanje imali težu bolest ili su pak bili više motivirani za redovito praćenje. Ipak, smatramo da su saznanja dobivena provedenim istraživanjem mogući putokaz za provođenje većih istraživanja problema osteoartritisa u našoj zemlji.

The conducted study is limited by a relatively small sample size considering the overall prevalence of osteoarthritis. Therefore, it is possible that the patients included in the conducted study were suffering from a more severe form of this disease and were more motivated for a regular follow-up. Nevertheless, we believe that the findings obtained from the conducted study can serve as a possible guide for conducting larger studies of osteoarthritis in our country.

CONCLUSION

The effect of OA treatment in this study was unsatisfactory, regardless of the use of conservative or surgical treatment methods. It is necessary to educate the patients in a better way, especially in the persistence of applying physical therapy (self-help) at home, changing a sedentary lifestyle, and implementing methods for a better control and reduction of body weight, as shown by numerous studies. The use of medications should be rationalized and complementary to physical therapy, while surgical treatment methods should be reserved as a method of last but timely treatment choice. The approach to osteoarthritis as the main representative of non-inflammatory rheumatic diseases remains very complex and demanding, primarily due to its high prevalence, and the inability of current therapeutic measures to achieve control of the course of the disease, which has been achieved in recent decades in the example of inflammatory rheumatic diseases.

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ZAKLJUČCI

Učinak liječenja OA u ovom je istraživanju nezadovoljavajući, bez obzira je li riječ o konzervativnim ili pak operativnim metodama liječenja. Potrebno je bolje educirati pacijente, posebno u ustrajnosti primjene fizikalne terapije (samopomoći) kod kuće i promjeni sedentarnog životnog stila te osobito boljoj kontroli i smanjenju tjelesne mase, što pokazuju brojna istraživanja. Upotreba lijekova treba biti racionalizirana i komplementarna s fizikalnom terapijom, dok kirurške metode liječenja trebaju biti rezervirane kao metoda zadnjeg, ali pravovremenog izbora liječenja. Pristup osteoartritisu kao glavnom predstavniku neupalnih reumatskih bolesti i dalje ostaje vrlo složen i zahtjevan, ponajprije zbog visoke prevalencije i potom zbog nemogućnosti aktualnih terapijskih mjera u postizanju kontrole tijeka bolesti, što je zadnjih desetljeća postignuto na primjeru upalnih reumatskih bolesti.

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