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Quality of Recovery after Intraoral Surgery: Total Intravenous Anaesthesia versus Sevoflurane: A Randomised Controlled Trial

Kvaliteta oporavka nakon intraoralnoga kirurškog zahvata: totalna intravenska anestezija prema anesteziji sevofluranom: randomizirano kontrolirano ispitivanje

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Abstract

Objectives: To compare the quality of recovery between total intravenous anaesthesia (TIVA) with propofol and balanced inhalational anaesthesia with sevoflurane in patients undergoing intraoral surgical procedures. **Materials and Methods:** We conducted a prospective randomised controlled clinical trial on 50 patients (25 per group) who underwent intraoral surgical procedures longer than 30 minutes. The primary outcome was the quality of recovery measured by the QoR-40 questionnaire at 1 hour, 24 hours, and 30 days after surgery. Secondary outcomes included bite force, hand grip strength, incidence of postoperative nausea and vomiting (PONV), and postoperative shivering. **Results:** QoR-40 scores did not differ between groups at any time point (differences from -0.04 to 1.2 points, all p>0.05). Bite force and hand grip strength did not differ between groups. However, TIVA eliminated PONV (0% vs 28%, p=0.010, NNT=4) and shivering (0% vs 36%, p=0.002, NNT=3). **Conclusion:** TIVA and sevoflurane result in a similar quality of recovery after intraoral procedures. However, TIVA eliminates PONV and shivering, which represents a clinically significant benefit for patients undergoing intraoral surgery.

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Introduction

Intraoral surgery encompasses a broad spectrum of procedures performed on the soft tissues of the mouth - from simple extractions to complex reconstructive procedures. Most of these procedures require general anaesthesia due to duration, invasiveness, or patient anxiety. The choice of maintenance technique, either total intravenous anaesthesia (TI-

Uvod

Intraoralna kirurgija obuhvaća širok spektar zahvata na mekim tkivima usne šupljine – od jednostavnih ekstrakcija do složenih rekonstrukcijskih zahvata. Većina tih zahvata zahtijeva opću anesteziju zbog trajanja, invazivnosti ili anksioznosti bolesnika. Izbor tehnike održavanja – totalna intravenska anestezija (TIVA) propofolom ili balansirana inha-

VA) with propofol or balanced inhalational anaesthesia with sevoflurane, remains a subject of debate in clinical practice.

Propofol and sevoflurane differ in pharmacokinetic and pharmacodynamic properties, which may affect the quality of recovery. Propofol exhibits antiemetic properties and is associated with a lower incidence of postoperative nausea and vomiting (PONV) compared to volatile anaesthetics (1,2). A meta-analysis including 67 randomised controlled trials showed that TIVA reduces the risk of PONV by 19% compared to inhalational anaesthesia (3). Sevoflurane, on the other hand, is characterised by faster emergence and shorter extubation time, thus making it a popular choice for ambulatory surgery (4, 5).

Quality of recovery after anaesthesia has become an important outcome in perioperative medicine. The Quality of Recovery-40 (QoR-40) questionnaire enables a comprehensive assessment of recovery through five domains: physical independence, patient support, physical comfort, emotions, and pain (6). Several studies have compared TIVA and volatile anaesthesia regarding quality of recovery; however, the results have been inconsistent. A study in patients undergoing gynaecological laparoscopic surgery did not show a difference in QoR-40 scores between propofol and sevoflurane (7). Research in patients undergoing endoscopic transsphenoidal pituitary surgery showed that TIVA improves the postoperative recovery quality compared with sevoflurane (8). The effects of anaesthesia clearly depend on the type of surgery.

For intraoral surgery, data are scarce. Most existing studies have focused on dental procedures in pediatric populations or on specific complications such as emergence agitation (9, 10), or on preoperative and infection control measures (11). Studies examining the quality of recovery after intraoral procedures in adult patients are rare. One study examined the effect of aromatherapy on PONV after oral surgery, but did not directly compare TIVA and volatile anaesthesia (12). A retrospective report from a Croatian centre documented indications and complications of general anaesthesia for oral surgery, including vomiting (13). Randomised controlled trials comparing TIVA and sevoflurane in the context of quality of recovery after intraoral procedures in adult patients are lacking.

In addition to the quality of recovery, functional aspects of recovery, such as bite force and hand grip strength, are important for patients undergoing intraoral surgery. These parameters may affect the ability to eat and perform daily activities. The available literature on the impact of anaesthesia on muscle strength after intraoral procedures is limited (14).

The aim of this study was to compare the quality of recovery between TIVA with propofol and balanced inhalational anaesthesia with sevoflurane in patients undergoing intraoral surgical procedures. The primary outcome was the quality of recovery measured by the QoR-40 questionnaire. Secondary outcomes included bite force, hand grip strength, incidence of PONV, and postoperative shivering. We hypothesised that TIVA with propofol would result in a better quality of recovery compared to sevoflurane, particularly in the early postoperative period, due to propofol's known antiemetic properties and its lower incidence of complications.

lacijska anestezija sevofluranom – ostaje predmet rasprave u kliničkoj praksi.

Propofol i sevofluran razlikuju se prema farmakokinetičkim i farmakodinamičkim svojstvima, što može utjecati na kvalitetu oporavka. Propofol pokazuje antiemetička svojstva i povezan je s nižom učestalošću postoperativne mučnine i povraćanja (PONV) u usporedbi s hlapljivim anesteticima (1, 2). Metaanaliza koja je obuhvaćala 67 randomiziranih kontroliranih ispitivanja pokazala je da TIVA smanjuje rizik od PONV-a za 19 % u usporedbi s inhalacijskom anestezijom (3). S druge strane, sevofluran se odlikuje bržim buđenjem i kraćim vremenom do ekstubacije, što ga čini popularnim izborom za ambulantnu kirurgiju (4, 5).

Kvaliteta oporavka poslije anestezije postala je važan ishod u perioperativnoj medicini. Upitnik QoR-40 (engl. *Quality of Recovery-40*) omogućuje sveobuhvatnu procjenu oporavka na temelju pet domena: tjelesne neovisnosti, potpore bolesniku, tjelesne udobnosti, emocija i bolova (6). U nekoliko studija uspoređivani su TIVA i hlapljiva anestezija s obzirom na kvalitetu oporavka, no rezultati nisu bili dosljedni. U studiji na bolesnicama podvrgnutima ginekološkoj laparoskopskoj kirurgiji autori nisu pokazali razliku u vrijednostima QoR-40 između propofola i sevoflurana (7). Istraživanje na bolesnicima podvrgnutima endoskopskoj transsfenoidalnoj kirurgiji hipofize pokazalo je da TIVA poboljšava kvalitetu postoperativnog oporavka u usporedbi sa sevofluranom (8). Učinci anestezije očito ovise o vrsti kirurškoga zahvata.

Za intraoralnu kirurgiju podatci su oskudni. U većini postojećih studija autori su bili usmjereni na stomatološke zahvate u pedijatrijskoj populaciji ili na specifične komplikacije poput agitacije pri buđenju (9, 10), odnosno na preoperativne mjere i mjere kontrole infekcija (11). Istaknimo da su rijetke studije u kojima se ispituje kvaliteta oporavka poslije intraoralnih zahvata, kad je riječ o odraslim bolesnicima. U jednoj je ispitivan učinak aromaterapije na PONV poslije oralnokirurškog zahvata, ali nisu izravno uspoređivane TIVA i hlapljiva anestezija (12). U retrospektivnom izvješću iz hrvatskoga centra dokumentirane su indikacije i komplikacije opće anestezije za oralnu kirurgiju, uključujući povraćanje (13). Nedostaju i randomizirana kontrolirana ispitivanja u kojima se kod odraslih bolesnika uspoređuju TIVA i sevofluran u kontekstu kvalitete oporavka poslije intraoralnih zahvata.

Uz kvalitetu oporavka, funkcionalni aspekti oporavka, poput sile zagriza i snage stiska šake, važni su za bolesnike podvrgnute intraoralnoj kirurgiji. Ti parametri mogu utjecati na sposobnost prehrane i obavljanja svakodnevnih aktivnosti. Postojeća literatura o utjecaju anestezije na mišićnu snagu poslije intraoralnih zahvata ograničena je (14).

Cilj ove studije bio je usporediti kvalitetu oporavka između TIVA-e propofolom i balansirane inhalacijske anestezije sevofluranom bolesnika podvrgnutih intraoralnim kirurškim zahvatima. Primarni ishod bila je kvaliteta oporavka mjerena upitnikom QoR-40. Sekundarni ishodi uključivali su silu zagriza, snagu stiska šake, učestalost PONV-a i postoperativno drhtanje. Pretpostavili smo da će TIVA propofolom rezultirati boljom kvalitetom oporavka u usporedbi sa sevofluranom, osobito u ranom postoperativnom razdoblju zbog poznatih antiemetičkih svojstava propofola i niže učestalosti komplikacija.

Materials and Methods

We conducted a prospective randomised controlled clinical trial at University Hospital Centre Zagreb, at the Department of Otorhinolaryngology and Head and Neck Surgery and the Department of Anaesthesiology, Reanimatology and Intensive Care Medicine. The study was approved by both ethics committees: the Ethics Committee of University Hospital Centre Zagreb (272nd session, February 29, 2024) and the Ethics Committee of School of Dental Medicine, University of Zagreb (XXVI session, March 20, 2024). The study was registered in the international clinical trials database (ClinicalTrials.gov: NCT06275087).

All participants signed written informed consent before inclusion in the study. Documents of ethics committee approvals and written consents of participants are kept by the authors and are available upon request. The study protocol and statistical analysis plan are available upon request from the corresponding author. De-identified individual participant data, statistical code, and materials will be available upon reasonable request to the corresponding author after publication.

Patients were randomly assigned to two groups according to a pre-prepared computer-generated randomisation table: TIVA (total intravenous anaesthesia with propofol) and OETA (general balanced inhalational anaesthesia with sevoflurane). Randomisation was performed after patient inclusion using sealed opaque envelopes to ensure allocation concealment. Both participants and the researcher measuring outcomes were blinded; they did not know who was in which group. The assessor did not participate in the administration of anaesthesia.

All patients received standard anaesthetic monitoring: electrocardiogram, non-invasive blood pressure measurement, pulse oximetry, capnography, temperature probe, and SedLine (PSI, DSA; Masimo, USA) electroencephalogram for monitoring depth of anaesthesia. We also monitored the depth of neuromuscular blockade using kinemyography with recording of train-of-four (TOF) responses (M-NMT, Drägerwerk AG & Co. KGaA).

Anaesthesia induction was identical in both groups. We used sufentanil 0.3 mcg/kg, propofol 2 mg/kg, and cisatracurium 0.1 mg/kg. After achieving appropriate depth of anaesthesia and muscle relaxation (TOF = 0), the patients were intubated with an endotracheal tube and mechanically ventilated with a mixture of oxygen and air (inspired oxygen fraction 40%) at a flow rate of 3 L/min.

In the OETA group, we maintained anaesthesia with inhalational sevoflurane and additional doses of cisatracurium. Cisatracurium was administered when the TOF ratio exceeded 5%, at a dose of 0.01 mg/kg. The depth of anaesthesia was controlled using BIS, maintaining values between 25 and 50. Dosing of sevoflurane and additional doses of cisatracurium were guided by TOF and BIS values.

In the TIVA group, anaesthesia was maintained with a continuous propofol infusion (5-10 mg/kg/h) and additional cisatracurium doses according to the same protocol. The depth of anaesthesia was also controlled using BIS with the

Materijali i metode

Proveli smo prospektivno randomizirano kontrolirano kliničko ispitivanje u Kliničkome bolničkom centru Zagreb, u Klinici za otorinolaringologiju i kirurgiju glave i vrata te Klinici za anesteziologiju, reanimatologiju i intenzivno liječenje. Studiju su odobrila oba etička povjerenstva: Etičko povjerenstvo Kliničkoga bolničkog centra Zagreb (272. sjednica, 29. veljače 2024.) i Etičko povjerenstvo Stomatološkoga fakulteta Sveučilišta u Zagrebu (XXVI. sjednica, 20. ožujka 2024.). Studija je registrirana u međunarodnoj bazi kliničkih ispitivanja (ClinicalTrials.gov: NCT06275087).

Svi sudionici potpisali su informirani pristanak prije uključivanja u studiju. Odobrenja etičkih povjerenstava i pristanci sudionika pohranjeni su kod autora i dostupni su na zahtjev. Protokol studije i plan statističke analize dostupni su na zahtjev od autora zaduženog za dopisivanje. Deidentificirani individualni podatci sudionika, statistički kôd i materijali bit će dostupni na temelju opravdanog zahtjeva autoru zaduženom za dopisivanje nakon objave.

Bolesnici su nasumično raspoređeni u dvije skupine prema unaprijed pripremljenoj računalno generiranoj tablici randomizacije: TIVA (totalna intravenska anestezija propofolom) i OETA (opća endotrahealna anestezija — balansirana inhalacijska anestezija sevofluranom). Randomizacija je provedena nakon uključivanja bolesnika uporabom zapečaćenih neprozirnih omotnica kako bi se osiguralo prikrivanje raspodjele. I sudionici i istraživač koji je mjerio ishode bili su zaslijepljeni i nisu znali tko je u kojoj skupini. Procjenitelj nije sudjelovao u provođenju anestezije.

Svi su bolesnici primili standardni anesteziološki nadzor: elektrokardiogram, neinvazivno mjerenje krvnoga tlaka, pulsnu oksimetriju, kapnografiju, temperaturnu sondu i SedLine (PSI (engl. *Patient State Index*, hrv. *indeks stanja bolesnika*), DSA (engl. *Density Spectral Array*, hrv. *spektralni niz gustoće*); Masimo, (SAD) elektroencefalogram za praćenje dubine anestezije. Također smo pratili dubinu neuromuskularnog bloka kinemografijom s bilježenjem odgovora na vlak četiriju podražaja (engl. *train-of-four* – TOF) (M-NMT, Drägerwerk AG & Co. KGaA).

Uvod u anesteziju bio je identičan u objema skupinama. Primijenili smo sufentanil 0,3 mcg/kg, propofol 2 mg/kg i cisatrakurij 0,1 mg/kg. Nakon što je postignuta odgovarajuća dubina anestezije i mišićne relaksacije (TOF = 0) bolesnici su intubirani endotrahealnim tubusom i mehanički ventilirani mješavinom kisika i zraka (inspiracijski udio kisika 40 %) pri protoku od 3 L/min.

U skupini OETA anestezija je održavana inhalacijskim sevofluranom i dodatnim dozama cisatrakurija. Cisatrakurij je primjenjivan kada je omjer TOF-a premašio 5 %, u dozi od 0,01 mg/kg. Dubina anestezije kontrolirana je s pomoću BIS-a (engl. *Bispectral Index*, hrv. bispektralni indeks), uz održavanje vrijednosti između 25 i 50. Doziranje sevoflurana i dodatnih doza cisatrakurija vođeno je vrijednostima TOF-a i BIS-a.

U skupini TIVA anestezija je održavana kontinuiranom infuzijom propofola (5 – 10 mg/kg/h) i dodatnim dozama cisatrakurija prema istom protokolu. Dubina anestezije tako-

same target values (25-50). Dosing of propofol and cisatracurium was guided by TOF and BIS values.

At the end of surgery, we antagonised muscle blockade with neostigmine (0.05 mg/kg) and atropine (0.01 mg/kg) when the patient began spontaneous breathing. Extubation was performed when the TOF index was>90%.

In the perioperative period, all patients in the perioperative period were placed on the same ward, where all of them received equal postoperative care.

We included adult patients with ASA status 1 and 2 who were indicated for intraoral surgical procedures lasting more than 30 minutes on soft tissues of the mouth. We excluded patients with an ASA status higher than 2, those requiring postoperative care in the intensive care unit, and those whose surgery was expected to last longer than 2 hours. We also excluded procedures involving muscle attachments, muscles, or bones, as these could independently affect bite force (a prespecified secondary outcome) and confound the comparison between anaesthetic techniques. Patients with known allergies to any of the study medications or those who declined participation were also excluded.

Primary outcome

The primary outcome was the quality of recovery measured by the Croatian version of the Quality of Recovery-40 (QoR-40) questionnaire (6,15). Permission to use the questionnaire was obtained from the author, professor P.S. Myles, PhD, and the Croatian translation from M. Miklić Bublić, MD who translated and validated the questionnaire (15).

The questionnaire contains 40 questions divided into five domains: physical independence (12 questions), patient support (7 questions), physical comfort (12 questions), emotions (9 questions), and pain (7 questions). The total score ranges from 40 to 200 points; a higher score indicates better recovery. Patients completed the questionnaire four times: before anaesthesia (baseline measurement), 1 hour after awakening in the recovery room, and at 24 hours and 30 days after surgery.

Secondary outcomes

Secondary outcomes included:

Bite force measured with a gnathodynamometer (Bite force sensor, Monad electronics, India); Hand grip strength measured with a hand dynamometer (GIMA, Italy); Frequency of postoperative nausea and vomiting (PONV); Frequency of postoperative shivering.

Bite force and hand grip strength were measured four times: before anaesthesia (baseline measurement), after awakening in the operating room, one hour later in the recovery room, and 24 hours after surgery.

PONV and shivering were recorded throughout the entire postoperative period.

Statistical methods

The analysis plan was defined in advance. For sample size calculation, we used G*Power software (version 3.1.9.6)) (16). For a power of 80% and a significance level α=0.05, we needed 42 participants (21 per group). We finally included

đer je kontrolirana s pomoću BIS-a s jednakim ciljnim vrijednostima (25 – 50). Doziranje propofola i cisatrakurija vođeno je vrijednostima TOF-a i BIS-a.

Na kraju zahvata antagonizirali smo mišićni blok neostigminom (0,05 mg/kg) i atropinom (0,01 mg/kg) kada je bolesnik počeo spontano disati. Ekstubacija je provedena kada je TOF indeks bio > 90 %.

Svi su bolesnici u perioperativnom razdoblju bili smješteni na isti odjel, gdje su svi primili jednaku postoperativnu skrb.

Uključili smo odrasle bolesnike s ASA statusom (engl. *American Society of Anesthesiologists*) 1 i 2 koji su bili indicirani za intraoralne kirurške zahvate dulje od 30 minuta na mekim tkivima usne šupljine. Isključili smo bolesnike s ASA statusom višim od 2, one koji su zahtijevali postoperativnu skrb u jedinici intenzivnog liječenja te one za koje se pretpostavljalo da će zahvat trajati dulje od 2 sata. Također smo isključili zahvate koji uključuju mišićna hvatišta, mišiće ili kosti, jer bi oni mogli neovisno utjecati na silu zagriza (unaprijed definirani sekundarni ishod) i narušiti usporedbu između anesteziooloških tehnika. Bolesnici s poznatim alergijama na bilo koji od lijekova korištenih u studiji ili oni koji su odbili sudjelovanje također su isključeni.

Primarni ishod

Primarni ishod bila je kvaliteta oporavka mjerena hrvatskom verzijom upitnika QoR-40 (engl. *Quality of Recovery-40*) (6, 15). Dopuštenje za uporabu dobiveno je od autora, prof. P. S. Mylesa, a za hrvatski prijevod od dr. M. Miklić Bublić koja je prevela i validirala upitnik (15).

Upitnik sadržava 40 pitanja podijeljenih u pet domena: tjelesna neovisnost (12 pitanja), potpora bolesniku (7 pitanja), tjelesna udobnost (12 pitanja), emocije (9 pitanja) i bol (7 pitanja). Ukupni rezultat kreće se od 40 do 200 bodova; viši rezultat upućuje na bolji oporavak. Bolesnici su upitnik ispunili četiri puta: prije anestezije (početno mjerenje), 1 sat nakon buđenja u sobi za oporavak te 24 sata i 30 dana poslije zahvata.

Sekundarni ishodi

Sekundarni ishodi uključivali su silu zagriza mjerenu gnatodinamometrom (Bite force sensor, Monad electronics, Indija), snagu stiska šake mjerenu ručnim dinamometrom (GIMA, Italija), učestalost postoperativne mučnine i povraćanja (PONV) i učestalost postoperativnog drhtanja.

Sila zagriza i snaga stiska šake mjerene su četiri puta: prije anestezije (početno mjerenje), nakon buđenja u operacijskoj dvorani, jedan sat poslije u sobi za oporavak te 24 sata nakon zahvata.

PONV i drhtanje bilježeni su tijekom cijeloga postoperativnog razdoblja.

Statističke metode

Plan analize definiran je unaprijed. Za izračun veličine uzorka koristili smo se programskom podrškom G*Power (inačica 3.1.9.6) (16). Za snagu od 80 % i razinu značajnosti α = 0,05 trebali smo 42 sudionika (21 po skupini). Konačno

ed 50 participants (25 per group) to ensure additional statistical power.

Continuous variables were presented as mean ± standard deviation or median [interquartile range], depending on distribution. Categorical variables were presented as frequencies and percentages.

Normality of distribution was tested using the Shapiro-Wilk test. Variables with $p<0.05$ were considered non-normally distributed.

Baseline demographic and clinical characteristics were compared between groups to assess the success of randomisation. Continuous variables (age, body weight, height, BMI) were compared using Student's t-test. Charlson Comorbidity Index (CCI) was compared using the Mann-Whitney U test due to non-normal distribution. Categorical variables were compared using the χ^2 test or Fisher's exact test when the number of expected frequencies was less than 5.

The primary outcome was analysed by comparing change from baseline at each time point (Student's t-test or Mann-Whitney U test, depending on distribution) and by longitudinal analysis using mixed-effects models (lme4 package). We fitted unadjusted and adjusted models (including age, BMI, sex, and CCI).

Secondary outcomes were analysed by comparing changes from baseline (continuous outcomes) or using χ^2 or Fisher's exact tests (binary outcomes). We calculated risk ratios, risk differences, NNT, and Cohen's d.

For the analysis of QoR-40 subscales (5 subscales × 3 time points = 15 comparisons), we used Holm-Bonferroni correction for multiple comparisons to control the family-wise error rate type I while preserving statistical power. For secondary outcomes (hand grip strength and bite force, each with 3 time points), we applied Holm-Bonferroni correction within each outcome.

All analyses were performed using R version 4.5.1 (R Foundation for Statistical Computing, Vienna, Austria) and IBM SPSS Statistics v27. For all analyses, we used a two-sided significance level of $\alpha=0.05$ and reported exact p-values, with Holm-Bonferroni correction where applicable. Two-sided tests were chosen as they represent the standard approach for clinical trials and do not assume a direction of effect a priori. Missing data: No missing data were encountered for any of the primary or secondary outcomes. All 50 randomised participants completed all follow-up assessments at all time points.

Results

A total of 50 patients were randomised into two groups of 25 each (Figure 1). There were no exclusions after randomisation. Groups were well balanced - they did not differ in any baseline demographic or clinical characteristic (Table 1).

Mean age of participants was 54.7 ± 14.4 years (52.7 ± 15.5 in the OETA group, 56.7 ± 13.2 in the TIVA group,

smo uključili 50 sudionika (25 po skupini) kako bismo osigurali dodatnu statističku snagu.

Kontinuirane varijable prikazane su kao srednja vrijednost ± standardna devijacija ili medijan (interkvartilni raspon), ovisno o raspodjeli. Kategorijske varijable prikazane su kao frekvencije i postotci.

Normalnost raspodjele ispitana je Shapiro-Wilkovim testom. Varijable s $p < 0,05$ smatrane su nenormalno raspodjeljenima.

Početne demografske i kliničke značajke uspoređene su između skupina radi procjene uspješnosti randomizacije. Kontinuirane varijable (dob, tjelesna masa, visina, BMI (engl. *body mass index*, hrv. indeks tjelesne mase)) uspoređene su Studentovim t-testom. Charlsonov indeks komorbiditeta (engl. *Charlson Comorbidity Index* – CCI) uspoređen je Mann-Whitneyjevim U testom zbog nenormalne raspodjele. Kategorijske varijable uspoređene su χ^2 testom ili Fisherovim egzaktnim testom kada je broj očekivanih frekvencija bio manji od 5.

Primarni ishod analiziran je usporedbom promjena od početne vrijednosti u svakoj vremenskoj točki (Studentov t-test ili Mann-Whitneyjev U test, ovisno o raspodjeli) te longitudinalnom analizom s pomoću modela s mješovitim učincima (paket lme4). Prilagodili smo nekorigirane i korigirane modele (uključujući dob, BMI, spol i CCI).

Sekundarni ishodi analizirani su usporedbom promjena od početne vrijednosti (kontinuirani ishodi) ili uporabom χ^2 ili Fisherova egzaktnoga testa (binarni ishodi). Izračunali smo omjere rizika, razlike u riziku, NNT (engl. *number needed to treat*, hrv. broj potrebnih liječenja) i Cohenov d.

Za analizu podljestvica QoR-40 (5 podljestvica × 3 vremenske točke = 15 usporedbi) upotrijebili smo Holm-Bonferronijevu korekciju za višestruke usporedbe radi kontrole pogreške tipa I na razini obitelji testova uz očuvanje statističke snage. Za sekundarne ishode (snaga stiska šake i sila zagriza, svaki s 3 vremenske točke) primijenili smo Holm-Bonferronijevu korekciju unutar svakoga ishoda.

Sve su analize obavljene u programu R inačice 4.5.1 (R Foundation for Statistical Computing, Beč, Austrija) i IBM SPSS Statistics v27. Za sve analize upotrijebili smo dvostranu razinu značajnosti $\alpha = 0,05$ i naveli točne p-vrijednosti, s Holm-Bonferronijevom korekcijom gdje je bilo primjenjivo. Dvostrani testovi odabrani jer su standardni pristup u kliničkim ispitivanjima i ne pretpostavljaju smjer učinka *a priori*. Nedostajući podatci: nije bilo nedostajućih podataka ni za jedan primarni ni sekundarni ishod. Svih 50 randomiziranih sudionika završilo je sve kontrolne procjene u svim vremenskim točkama.

Rezultati

Ukupno je 50 bolesnika randomizirano u dvije skupine od po 25 sudionika (slika 1.). Nije bilo isključivanja nakon randomizacije. Skupine su bile dobro uravnotežene – nisu se razlikovale ni u jednoj početnoj demografskoj ili kliničkoj značajki (tablica 1.).

Srednja dob sudionika bila je 54,7 ± 14,4 godine (52,7 ± 15,5 u skupini OETA, 56,7 ± 13,2 u skupini TIVA, p >

Table 1 Baseline characteristics
Tablica 1. Početne značajke

Characteristic • Značajka	Overall • Ukupno	OETA	TIVA
Sample size, n • Veličina uzorka, n	50	25	25
Age, years • Dob, godine	54.70 (14.40)	52.68 (15.53)	56.72 (13.18)
Male • Muškarci	24 (48%)	13 (52%)	11 (44%)
Female • Žene	26 (52%)	12 (48%)	14 (56%)
Weight, kg • Tjelesna masa, kg	79.56 (15.71)	81.08 (12.29)	78.04 (18.65)
Height, cm • Visina, cm	172.30 (11.34)	172.88 (11.17)	171.72 (11.71)
BMI, kg/m²	26.69 (3.81)	27.12 (3.31)	26.26 (4.29)
ASA status	2 [2, 2]	2 [2, 2]	2 [2, 2]
Charlson Comorbidity Index • Charlsonov indeks komorbiditeta	4.10 (2.44)	4.04 (2.54)	4.16 (2.39)

Table 2 QoR-40 total score changes from baseline
Tablica 2. Promjene ukupnoga rezultata QoR-40 od početne vrijednosti

Timepoint • Vremenska točka	OETA mean • srednja vrijednost (SD)	TIVA mean • srednja vrijednost (SD)	Difference • Razlika (95% CI)	p-value • p-vrijednost	Cohen's d • Cohenov d
1 hour • 1 sat	-21.72 (13.89)	-20.56 (14.84)	1.16 (-7.02 to 9.34)	.683	0.08
24 hours • 24 sata	-9.84 (6.85)	-9.88 (4.51)	-0.04 (-3.35 to 3.27)	.629	-0.01
30 days • 30 dana	-0.96 (2.68)	-0.12 (3.09)	0.84 (-0.81 to 2.49)	.527	0.29

Table 3 Mixed-effects model for QoR-40 total score
Tablica 3. Model s mješovitim učincima za ukupni rezultat QoR-40

Term • Pojam	Estimate • Procjena (95% CI)	p value • p-vrijednost
Group (TIVA vs OETA) • Skupina (TIVA naspram OETA)	3.84 (-2.66 to 10.35)	.245
Time • Vrijeme	0.90 (-1.30 to 3.10)	.420
Age • Dob	-0.06 (-0.30 to 0.18)	.601
BMI	0.22 (-0.38 to 0.83)	.463
Sex (Male vs Female) • Spol (muški naprama ženski)	4.43 (-0.26 to 9.11)	.063
Charlson Comorbidity Index • Charlsonov indeks komorbiditeta	0.43 (-0.99 to 1.86)	.545
Group × Time • Skupina × Vrijeme	0.13 (-2.98 to 3.25)	.933

p>0.05). Sex distribution was balanced - 48% males overall (52% in OETA, 44% in TIVA, p>0.05). Mean BMI was 26.7 ± 3.8 kg/m² (27.1 ± 3.3 in OETA, 26.3 ± 4.3 in TIVA, p>0.05). Median ASA status was 2 [2, 2] in both groups. Charlson Comorbidity Index was 4.1 ± 2.4 overall, with no difference between compared groups (4.0 ± 2.5 in OETA, 4.2 ± 2.4 in TIVA, p>0.05).

Primary outcome: QoR-40 total score

QoR-40 scores did not differ between groups at any time point (Table 2). The differences in changes from baseline were minimal. At 1 hour, the difference was 1.2 points (95% CI: -7.0 to 9.3, p=0.683). At 24 hours, the difference was -0.04 points (95% CI: -3.4 to 3.3, p=0.629), and at 30 days, 0.8 points (95% CI: -0.8 to 2.5, p=0.527). Effect sizes were small, with Cohen's d ranging from -0.007 to 0.29.

Longitudinal analysis using mixed-effects models confirmed that recovery progressed similarly in both groups over time. There was no significant group effect (β=3.84, 95% CI: -2.66 to 10.35, p=0.245) or group × time interaction (β=0.13, 95% CI: -2.98 to 3.25, p=0.933) (Table 3, Figure 2).

Analysis of QoR-40 subscales showed mostly minor differences without clinical or statistical significance (Table 4,

0,05). Raspodjela prema spolu bila je uravnotežena – 48 % muškaraca ukupno (52 % u OETA-i, 44 % u TIVA-i, p > 0,05). Srednji BMI iznosio je 26,7 ± 3,8 kg/m² (27,1 ± 3,3 u OETA-i, 26,3 ± 4,3 u TIVA-i, p > 0,05). Medijan ASA statusa bio je 2 (2, 2) u objema skupinama. Charlsonov indeks komorbiditeta iznosio je 4,1 ± 2,4 ukupno, bez razlike između skupina (4,0 ± 2,5 u OETAI, 4,2 ± 2,4 u TIVA-i, p > 0,05).

Primarni ishod: ukupni rezultat QoR-40

Vrijednosti QoR-40 nisu se razlikovale između skupina ni u jednoj vremenskoj točki (tablica 2.). Razlike u promjenama od početne vrijednosti bile su minimalne. U 1. satu razlika je iznosila 1,2 boda (95 % CI (engl. *confidence interval*, hrv. interval pouzdanosti): -,0 do 9,3, p = 0,683). U 24. satu razlika je iznosila -0,04 boda (95 % CI: -3,4 do 3,3, p = 0,629), a u 30. danu 0,8 bodova (95 % CI: -0,8 do 2,5, p = 0,527). Veličine učinka bile su male, s Cohenovim d u rasponu od -0,007 do 0,29.

Longitudinalna analiza s pomoću modela s mješovitim učincima potvrdila je da je oporavak napredovao slično u objema skupinama tijekom vremena. Nije bilo značajnoga skupinskog učinka (β = 3,84, 95 % CI: -2,66 do 10,35, p = 0,245) ni interakcije skupina × vrijeme (β = 0,13, 95 % CI: -2,98 do 3,25, p = 0,933) (tablica 3., slika 2.).

1.

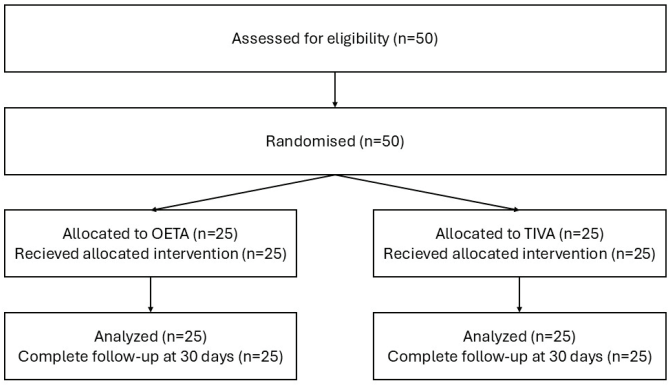


Figure 1 Participant flow diagram through the study (CONSORT flow diagram)
Slika 1. Dijagram toka sudionika kroz studiju (dijagram toka CONSORT)

2.

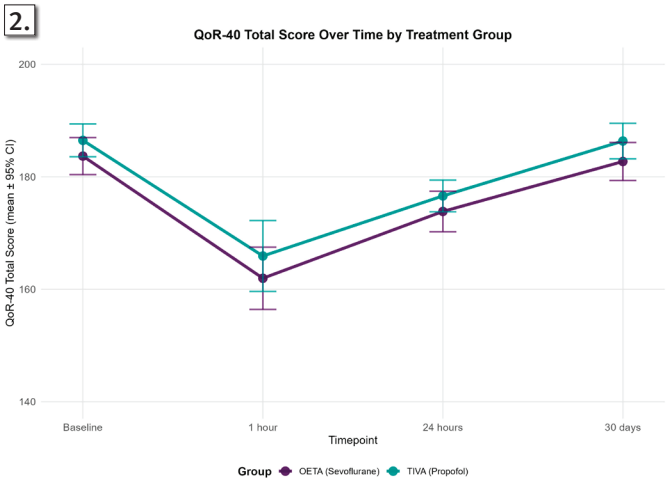


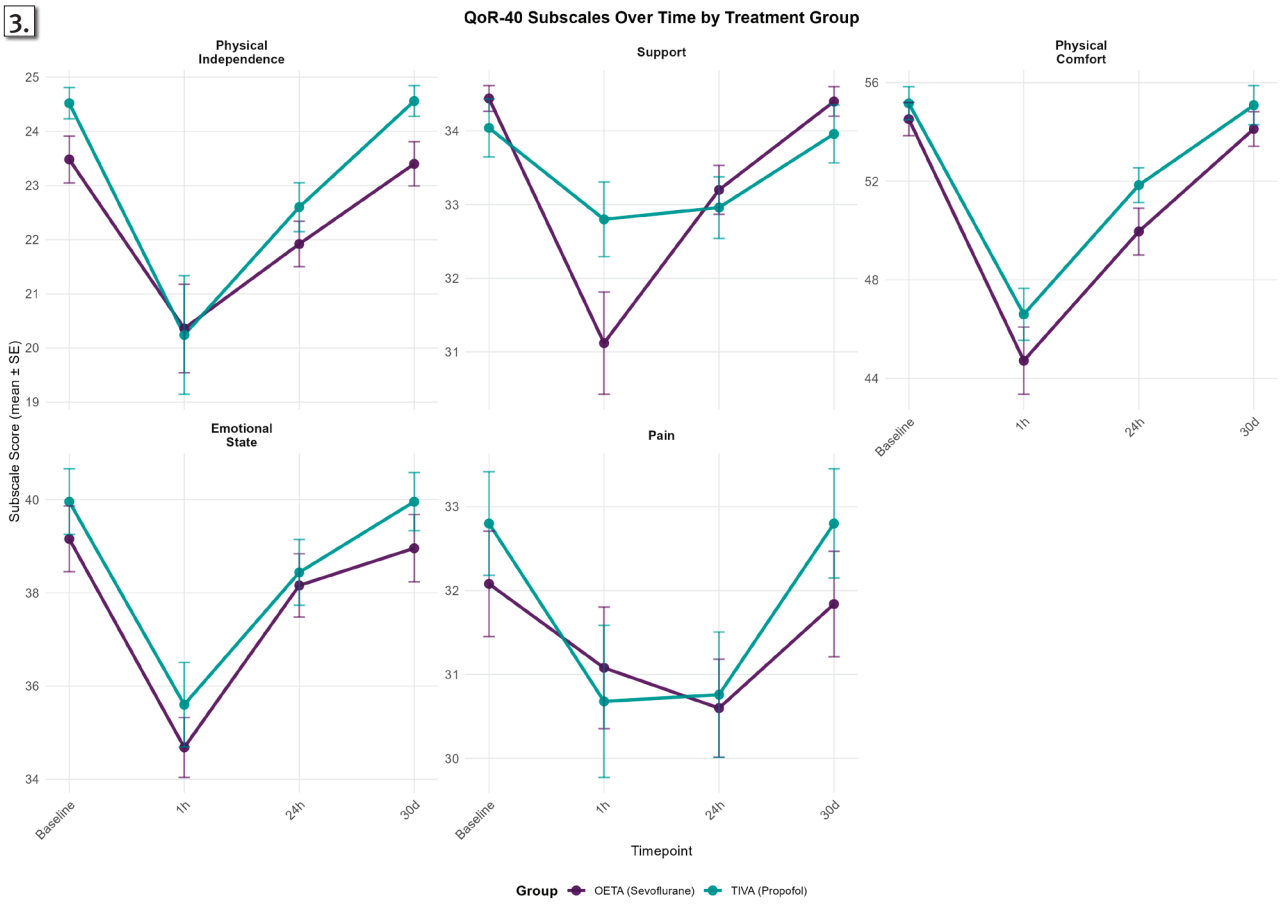
Figure 2 Longitudinal analyses of QoR-40 total score - recovery trajectories by groups
Slika 2. Longitudinalna analiza ukupnoga rezultata QoR-40 – putanje oporavka po skupinama

Table 4 QoR-40 subscales changes from baseline
Tablica 4. Promjene podljestvica QoR-40 od početnog mjerenja

Subscale • Podljestvica	Timepoint • Vremenska točka	OETA mean • srednja vrijednost (SD)	TIVA mean • srednja vrijednost (SD)	Difference • Razlika (95% CI)	p-value • p-vrijednost	Cohen's d • Cohenov d
Emotional State • Emocionalno stanje	1 hour • 1 sat	-4.48 (3.63)	-4.36 (4.79)	0.12 (-2.3 to 2.54)	.349	0.03
Emotional State • Emocionalno stanje	24 hours • 24 sata	-1 (2.35)	-1.52 (2.68)	-0.52 (-1.95 to 0.91)	.469	-0.21
Emotional State • Emocionalno stanje	30 days • 30 dana	-0.2 (1.53)	0 (1.29)	0.2 (-0.6 to 1)	.772	0.14
Pain • Bol	1 hour • 1 sat	-1 (4.14)	-2.12 (3.59)	-1.12 (-3.32 to 1.08)	.350	-0.29
Pain • Bol	24 hours • 24 sata	-1.48 (1.87)	-2.04 (2.85)	-0.56 (-1.94 to 0.82)	.704	-0.23
Pain • Bol	30 days • 30 dana	-0.24 (0.44)	0 (0.29)	0.24 (0.03 to 0.45)	.029	0.65
Physical Comfort • Tjelesna udobnost	1 hour • 1 sat	-9.8 (5.99)	-8.56 (4.64)	1.24 (-1.81 to 4.29)	.465	0.23
Physical Comfort • Tjelesna udobnost	24 hours • 24 sata	-4.56 (3.51)	-3.32 (2.98)	1.24 (-0.61 to 3.09)	.541	0.38
Physical Comfort • Tjelesna udobnost	30 days • 30 dana	-0.4 (1.71)	-0.08 (2.53)	0.32 (-0.91 to 1.55)	.894	0.15
Physical Independence • Tjelesna neovisnost	1 hour • 1 sat	-3.12 (4.11)	-4.28 (5.76)	-1.16 (-4.01 to 1.69)	.654	-0.23
Physical Independence • Tjelesna neovisnost	24 hours • 24 sata	-1.56 (1.23)	-1.92 (1.63)	-0.36 (-1.18 to 0.46)	.813	-0.25
Physical Independence • Tjelesna neovisnost	30 days • 30 dana	-0.08 (0.4)	0.04 (0.35)	0.12 (-0.09 to 0.33)	.267	0.32
Support • Podrška	1 hour • 1 sat	-3.32 (3.52)	-1.24 (2.83)	2.08 (0.26 to 3.9)	.058	0.65
Support • Podrška	24 hours • 24 sata	-1.24 (1.56)	-1.08 (1.38)	0.16 (-0.68 to 1)	.555	0.11
Support • Podrška	30 days • 30 dana	-0.04 (0.35)	-0.08 (0.28)	-0.04 (-0.22 to 0.14)	.682	-0.13

Note: p-values corrected using Holm-Bonferroni method.
Napomena: p-vrijednosti korigirane Holm-Bonferronijevom metodom

3.



4.

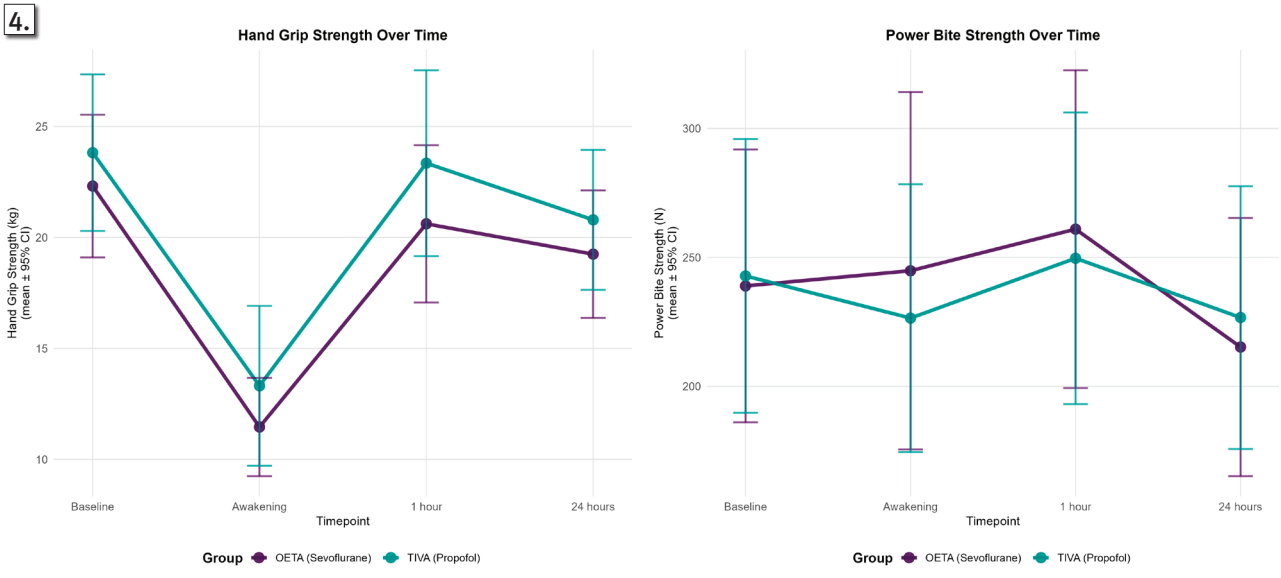


Figure 3 QoR-40 subscales - changes from baseline measurement by groups
Slika 3. Podljestvice QoR-40 – promjene od početnoga mjerenja po skupinama
Figure 4 Hand grip strength and bite force - changes from baseline measurement by groups
Slika 4. Snaga stiska šake i sila zagriza — promjene od početnoga mjerenja po skupinama

Figure 3). The only difference that reached statistical significance without correction was on the "Pain" subscale at 30 days (difference: 0.2 points, p=0.029), but after Holm-Bonferroni correction for multiple comparisons (15 comparisons), this difference was no longer statistically significant (p=0.438). The clinical importance of this slight difference is questionable.

Secondary outcomes

Hand grip strength and bite force did not differ significantly between groups at any time point (Table 5, Figure 4). All p-values were >0.05, and effect sizes were small (Cohen's d <0.5).

PONV occurred in 7 of 25 patients (28%) in the OETA group, and in none of the patients (0%) in the TIVA group (p=0.010). NNT was 3.6 (95% CI: 2.2 to 10.0).

Shivering occurred in 9 of 25 patients (36%) in the OETA group, and in none of the patients (0%) in the TIVA group (p=0.002). NNT for prevention of shivering was 2.8 (95% CI: 1.8 to 5.9) (Table 6).

Analiza podljestvica QoR-40 pokazala je uglavnom male razlike bez kliničke ili statističke značajnosti (tablica 4., slika 3.). Jedina razlika koja je dosegnula statističku značajnost bez korekcije bila je na podljestvici *Bol* u 30. danu (razlika: 0,2 boda, p = 0,029), ali nakon Holm-Bonferronijeve korekcije za višestruke usporedbe (15 usporedbi) ta razlika više nije bila statistički značajna (p = 0,438). Klinička je važnost te neznatne razlike upitna.

Sekundarni ishodi

Snaga stiska šake i sila zagriza nisu se značajno razlikovale između skupina ni u jednoj vremenskoj točki (tablica 5., slika 4.). Sve su p-vrijednosti bile >0,05, a veličine učinka male (Cohenov d < 0,5).

PONV se pojavio kod 7 od 25 bolesnika (28 %) u skupini OETA te ni kod jednog bolesnika (0 %) u skupini TIVA (p = 0,010). NNT je iznosio 3,6 (95 % CI: 2,2 do 10,0).

Drhtanje se pojavilo kod 9 od 25 bolesnika (36 %) u skupini OETA te ni kod jednoga (0 %) u skupini TIVA (p = 0,002). NNT za prevenciju drhtanja iznosio je 2,8 (95 % CI: 1,8 do 5,9) (tablica 6.).

Table 5 Hand grip strength and bite force changes from baseline
Tablica 5. Promjene snage stiska šake i sile zagriza od početne vrijednosti

Outcome • Ishod	Timepoint • Vremenska točka	OETA mean • srednja vrijednost (SD)	TIVA mean • srednja vrijednost (SD)	Difference • Razlika (95% CI)	p-value • p-vrijednost
Hand grip strength • Snaga stiska šake	After awakening • Nakon buđenja	-10.86 (6.8)	-10.5 (7.26)	0.35 (-3.65 to 4.35)	.860
Hand grip strength • Snaga stiska šake	1 hour • 1 sat	-1.7 (3.7)	-0.47 (4.2)	1.23 (-1.02 to 3.48)	.278
Hand grip strength • Snaga stiska šake	24 hours • 24 sata	-3.07 (1.11)	-3.02 (1.31)	0.04 (-0.65 to 0.73)	.900
Power bite strength • Sila zagriza	After awakening • Nakon buđenja	5.9 (61.97)	-16.35 (36.51)	-22.25 (-51.35 to 6.85)	.140
Power bite strength • Sila zagriza	1 hour • 1 sat	22.01 (44.03)	6.84 (28.95)	-15.17 (-36.45 to 6.11)	.157
Power bite strength • Sila zagriza	24 hours • 24 sata	-23.68 (23.23)	-16.14 (15.15)	7.54 (-3.66 to 18.74)	.180

Note: p-values corrected using Holm-Bonferroni method.
Napomena: p-vrijednosti korigirane Holm-Bonferronijevom metodom

Table 6 Postoperative nausea and vomiting (PONV) and shivering
Tablica 6. Postoperativna mučnina i povraćanje (PONV) te drhtanje

Outcome • Ishod	OETA Events Total • OETA događaji ukupno	TIVA Events Total • TIVA događaji ukupno	p-value • p-vrijednost
Postoperative nausea and vomiting (PONV) • Postoperativna mučnina i povraćanje (PONV)	7/25 (28%)	0/25 (0%)	.010
Shivering • Drhtanje	9/25 (36%)	0/25 (0%)	.002

Discussion

Our study showed that TIVA with propofol and balanced inhalational anaesthesia with sevoflurane result in similar quality of recovery, as measured by the QoR-40 questionnaire, in patients undergoing intraoral surgical procedures. The differences in the primary outcome were minimal and statistically nonsignificant at all follow-up time points. However, TIVA eliminated postoperative nausea and vomiting and shivering, which represents a clinically significant benefit.

Rasprava

Naša studija pokazala je da TIVA propofolom i balansirana inhalacijska anestezija sevofluranom rezultiraju sličnom kvalitetom oporavka, mjerenom upitnikom QoR-40, bolesnika podvrgnutih intraoralnim kirurškim zahvatima. Razlike u primarnom ishodu bile su minimalne i statistički neznačajne u svim vremenskim točkama praćenja. Međutim, TIVA je eliminirala postoperativnu mučninu i povraćanje te drhtanje, što je klinički značajna korist.

Our results show that QoR-40 scores did not differ between groups at any time point. Differences were minimal, from -0.04 to 1.2 points, which is far below the minimal clinically significant difference of 6.3 points. Longitudinal analysis using mixed-effects models confirmed that recovery progressed similarly in both groups over time, without significant group × time interaction.

These findings are consistent with some, but not all, studies in the literature. A study in patients undergoing gynaecological laparoscopic surgery also did not show a difference in QoR-40 scores between propofol and sevoflurane (7). Similarly, research in patients undergoing laparoscopic cholecystectomy showed that desflurane and propofol result in similar quality of recovery (4). However, a study in patients undergoing endoscopic transsphenoidal pituitary surgery showed that TIVA improves the quality of recovery compared to sevoflurane (8). These differences suggest that the effects of anaesthesia may vary depending on the type of surgery, duration of the procedure, or other patient characteristics.

For intraoral surgery, data are scarce. Most existing studies have focused on dental procedures in pediatric populations or on specific complications such as emergence agitation (9,10). Our study is the first to directly compare TIVA and sevoflurane regarding the quality of recovery after intraoral procedures in adult patients. Our results suggest that, for this specific type of surgery, the choice of maintenance technique does not significantly affect the subjective quality of recovery.

Hand grip strength and bite force did not differ significantly between groups at any time point. This is an important finding because functional aspects of recovery may affect patients' ability to eat and perform daily activities after intraoral surgery. The existing literature on the impact of anaesthesia on muscle strength after intraoral procedures is limited, making our results relevant for clinical practice.

The most significant finding of our study is a complete elimination of PONV in the TIVA group. None of the 25 patients in the TIVA group had PONV, while seven patients (28%) in the OETA group vomited. An NNT of 3.6 means that we need to treat four patients with TIVA, instead of OETA, to prevent one case of nausea and vomiting.

These results are consistent with the existing literature, which shows that propofol has antiemetic properties. A meta-analysis including 67 randomised controlled trials showed that TIVA reduces the risk of PONV by 19% compared to inhalational anaesthesia (3). A study in patients undergoing laparoscopic cholecystectomy showed that TIVA results in a lower incidence of PONV compared to sevoflurane (5). Similarly, research in bariatric patients showed that TIVA reduces the incidence of PONV compared to sevoflurane (17).

Propofol has known antiemetic properties, while sevoflurane is a pro-emetic agent and may increase the risk of PONV.

For intraoral surgery, PONV is particularly problematic because it can lead to aspiration, damage to the surgical field, or prolonged hospital stay. Our results show that TIVA may be particularly useful for patients undergoing intraoral procedures who are at high risk for PONV.

Naši rezultati pokazuju da se vrijednosti QoR-40 nisu razlikovale između skupina ni u jednoj vremenskoj točki. Razlike su bile neznatne, od -0,04 do 1,2 boda, što je daleko ispod minimalne klinički značajne razlike od 6,3 boda. Longitudinalna analiza s pomoću modela s mješovitim učincima potvrdila je da je oporavak napredovao slično u objema skupinama tijekom vremena, bez značajne interakcije skupina × vrijeme.

Ti su nalazi u skladu s nekim rezultatima studija, ali ne sa svima. U studiji s bolesnicama podvrgnutim ginekološkoj laparoskopskoj kirurgiji također se nije pokazala razlika u vrijednostima QoR-40 između propofola i sevoflurana (7). Slično tomu, istraživanje na bolesnicima podvrgnutim laparoskopskoj kolecistektomiji pokazalo je da desfluran i propofol rezultiraju sličnom kvalitetom oporavka (4). Međutim, u studiji sa bolesnicima podvrgnutima endoskopskoj transsfenoidalnoj kirurgiji hipofize pokazala je da TIVA poboljšava kvalitetu oporavka u usporedbi sa sevofluranom (8). Te razlike upućuju na to da učinci anestezije mogu varirati ovisno o vrsti kirurškoga zahvata, trajanju postupka ili drugim značajkama bolesnika.

Za intraoralnu kirurgiju podatci su oskudni. U većini postojećih studija autori su bili usmjereni na stomatološke zahvate u pedijatrijskoj populaciji ili na specifične komplikacije poput agitacije pri buđenju (9, 10). U našoj se studiji prvi put izravno uspoređuju TIVA i sevofluran s obzirom na kvalitetu oporavka nakon intraoralnih zahvata kod odraslih bolesnika. Naši rezultati upućuju na to da za tu specifičnu vrstu kirurgije izbor tehnike održavanja ne utječe značajno na subjektivnu kvalitetu oporavka.

Snaga stiska šake i sila zagriza nisu se značajno razlikovale između skupina ni u jednoj vremenskoj točki. To je važan nalaz jer funkcionalni aspekti oporavka mogu utjecati na sposobnost bolesnika da se hrane i obavljaju svakodnevne aktivnosti nakon intraoralnog zahvata. Postojeća literatura o utjecaju anestezije na mišićnu snagu nakon intraoralnih zahvata ograničena je, što naše rezultate čini relevantnima za kliničku praksu.

Najznačajniji nalaz naše studije jest potpuna eliminacija PONV-a u skupini TIVA. Nijedan od 25 bolesnika u skupini TIVA nije imao PONV, dok je sedam bolesnika (28 %) u skupini OETA povraćalo. NNT od 3,6 znači da je potrebno liječiti četiri bolesnika TIVA-om umjesto OETA-om kako bi se spriječio jedan slučaj mučnine i povraćanja.

Ti su rezultati u skladu s postojećom literaturom koja pokazuje da propofol ima antiemetička svojstva. Metaanaliza koja je uključivala 67 randomiziranih kontroliranih ispitivanja pokazala je da TIVA smanjuje rizik od PONV-a za 19 % u usporedbi s inhalacijskom anestezijom (3). Studija na bolesnicima podvrgnutima laparoskopskoj kolecistektomiji pokazala je da TIVA rezultira nižom učestalošću PONV-a u usporedbi sa sevofluranom (5). Slično tomu, istraživanje na barijatrijski operiranim bolesnicima pokazalo je da TIVA smanjuje učestalost PONV-a u usporedbi sa sevofluranom (17).

Propofol ima poznata antiemetička svojstva, a sevofluran ih nema te može povećati rizik od PONV-a.

Za intraoralnu kirurgiju PONV je osobito problematičan jer može dovesti do aspiracije, oštećenja operacijskoga polja

TIVA also completely eliminated postoperative shivering. None of the 25 patients in the TIVA group had shivering, while nine patients (36%) in the OETA group had shivering. An NNT of 2.8 means that we need to treat three patients with TIVA to prevent one case of shivering.

Sevoflurane is known to increase the risk of shivering (18-20), while propofol shows protective effects against shivering.

For intraoral surgery, shivering can be particularly problematic because it can lead to damage to the surgical field, increased metabolic demands, and patient discomfort. Our results show that TIVA may be particularly useful for preventing this complication.

TIVA does not show an advantage in overall quality of recovery, because the QoR-40 measures a wide range of aspects that are more influenced by the type of surgery and postoperative analgesia than by the type of anaesthesia itself (21). In contrast, PONV and shivering are complications directly related to the pharmacology of anaesthetics, which explains the complete elimination in the TIVA group. Also, intraoral procedures are shorter and less invasive, hence the differences between anaesthetic techniques are less pronounced than in larger surgeries.

Our study has several strengths. First, we used a randomised controlled design with blinding of participants and the researcher measuring outcomes, which minimises the risk of bias. Second, we used a validated QoR-40 questionnaire that has been translated and validated in Croatian (15). Third, we performed a longitudinal analysis using mixed-effects models that adequately account for correlation between repeated measurements. Fourth, we performed additional analyses, including MCID, Bayesian, and responder analyses, that provide further perspectives on the results. Fifth, we measured functional recovery outcomes, such as bite force and hand grip strength, which are rare in the literature for intraoral surgery.

Our study also has several limitations. First, the sample size of 50 patients (25 per group) may not be sufficient to detect small differences in quality of recovery. However, it is adequate to detect differences in binary outcomes such as PONV and shivering. Second, the study was conducted in a single centre, which may limit the generalizability of results. Third, we did not measure some potentially important outcomes, such as postoperative cognitive function or long-term functional outcomes. Fourth, all patients were placed on the same ward where they received equal postoperative care, which is suitable for control but may not reflect all clinical situations.

Our results have important clinical implications. Although TIVA does not show advantages in subjective quality of recovery measured by the QoR-40 questionnaire, it offers complete elimination of two of the most common postoperative complications - nausea with vomiting and shivering. NNT values of 4 for PONV and 3 for shivering are clinically very relevant and suggest that TIVA might be preferred for patients undergoing intraoral surgical procedures, especially for those at high risk for PONV or shivering.

ili produljenog bolničkog boravka. Naši rezultati pokazuju da TIVA može biti osobito može koristiti bolesnicima podvrgnutima intraoralnim zahvatima koji su pod visokim rizikom od PONV-a.

TIVA je također u cijelosti eliminirala postoperativno drhtanje. Nijedan od 25 bolesnika u skupini TIVA nije drhtao, a devet bolesnika (36 %) u skupini OETA jest. NNT od 2,8 znači da je potrebno liječiti tri bolesnika TIVA-om kako bi se spriječio jedan slučaj drhtanja.

Sevofluran je poznat po tome da povećava rizik od drhtanja (18 – 20), a propofol pokazuje zaštitne učinke protiv drhtanja.

Za intraoralnu kirurgiju drhtanje može biti osobito problematično jer može oštetiti operacijsko polje, povećati metaboličke zahtjeve i neugode za bolesnika. Naši rezultati pokazuju da TIVA može biti osobito korisna za prevenciju te komplikacije.

TIVA ne pokazuje prednost u ukupnoj kvaliteti oporavka jer QoR-40 mjeri širok raspon aspekata na koje više utječu vrsta kirurškog zahvata i postoperativna analgezija nego vrsta same anestezije (21). Nasuprot tomu, PONV i drhtanje komplikacije su izravno povezane s farmakologijom anestetika, što objašnjava potpunu eliminaciju u skupini TIVA. Također, intraoralni su zahvati kraći i manje invazivni, pa su razlike između anesteziooloških tehnika manje izražene nego kod većih kirurških zahvata.

Naša studija ima nekoliko prednosti. Kao prvo, upotrijebili smo randomizirani kontrolirani dizajn sa zaslijepljivanjem sudionika i istraživača koji je mjerio ishode, čime se smanjuje rizik od pristranosti. Kao drugo, upotrijebili smo validirani upitnik QoR-40 koji je preveden na hrvatski jezik i validiran (15). Kao treće, proveli smo longitudinalnu analizu s pomoću modela s mješovitim učincima koji adekvatno uzimaju u obzir korelaciju između ponovljenih mjerenja. Kao četvrto, obavili smo dodatne analize, uključujući analizu MCID-a (engl. *minimal clinically important difference*, hrv. minimalna klinički važna razlika), Bayesovu analizu i analizu odgovarača koje pružaju dodatne perspektive na rezultate. Kao peto, mjerili smo funkcionalne ishode oporavka, poput sile zagriza i snage stiska šake, koji su rijetki u literaturi za intraoralnu kirurgiju.

Naša studija ima i nekoliko ograničenja. Kao prvo, veličina uzorka od 50 bolesnika (25 po skupini) možda nije dostatna za otkrivanje malih razlika u kvaliteti oporavka. No dostatna je za otkrivanje razlika u binarnim ishodima poput PONV-a i drhtanja. Kao drugo, studija je provedena u jednom centru, što može ograničiti poopćavanje rezultata. Kao treće, nismo mjerili neke potencijalno važne ishode, poput postoperativne kognitivne funkcije ili dugoročnih funkcionalnih ishoda. Kao četvrto, svi su bolesnici bili smješteni na istom odjelu gdje su primili jednaku postoperativnu skrb, što je prikladnije za kontrolu, ali ne mora obuhvaćati sve kliničke situacije.

Naši rezultati imaju važne kliničke implikacije. Premda TIVA ne pokazuje prednosti u subjektivnoj kvaliteti oporavka mjerenoj upitnikom QoR-40, ona nudi potpunu eliminaciju dviju najčešćih postoperativnih komplikacija – mučnine s povraćanjem i drhtanja. Vrijednosti NNT-a od 4 za PONV i 3 za drhtanje klinički su vrlo relevantne i upućuju na to da bi TIVA mogla biti poželjan izbor za bolesnike podvrgnute intraoralnim kirurškim zahvatima, osobito za one s visokim rizikom od PONV-a ili drhtanja.

Conclusions

Our study showed that TIVA with propofol and balanced inhalational anaesthesia with sevoflurane result in similar quality of recovery, as measured by the QoR-40 questionnaire, in patients undergoing intraoral surgical procedures. Differences in the primary outcome were minimal and statistically nonsignificant at all follow-up time points. Functional aspects of recovery - bite force and hand grip strength - also did not differ between groups.

However, TIVA eliminated postoperative nausea and vomiting and shivering. None of the 25 patients in the TIVA group had PONV, while seven patients (28%) in the OETA group vomited. Shivering occurred in 9 patients (36%) in the OETA group, and in none in the TIVA group. The number needed to treat was 4 for PONV and 3 for shivering, which represents a clinically very relevant finding.

For clinical practice, our results suggest that the choice between TIVA and sevoflurane for intraoral surgery may be guided by anaesthetist preferences and equipment availability, as the quality of recovery is not significantly different. However, for patients at high risk for PONV or shivering, TIVA might be the preferred option due to its protective effects on these complications.

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Zaključak

Naša je studija pokazala da TIVA propofolom i balansirana inhalacijska anestezija sevofluranom rezultiraju sličnom kvalitetom oporavka, mjerenom upitnikom QoR-40, kod bolesnika podvrgnutih intraoralnim kirurškim zahvatima. Razlike u primarnom ishodu bile su minimalne i statistički neznačajne u svim vremenskim točkama praćenja. Funkcionalni aspekti oporavka – sila zagriza i snaga stiska šake – također se nisu razlikovali između skupina.

Međutim, TIVA je eliminirala postoperativnu mučninu i povraćanje te drhtanje. Nijedan od 25 bolesnika u skupini TIVA nije imao PONV, a sedam bolesnika (28 %) u skupini OETA je povraćalo. Drhtanje se pojavilo kod 9 bolesnika (36 %) u skupini OETA te ni kod jednoga u skupini TIVA. Broj potrebnih liječenja iznosio je 4 za PONV i 3 za drhtanje, što je klinički vrlo relevantan nalaz.

Za kliničku praksu naši rezultati upućuju na to da se izbor između TIVA-e i sevoflurana za intraoralnu kirurgiju može voditi preferencijama anesteziologa i dostupnošću opreme, s obzirom na to da se kvaliteta oporavka značajno ne razlikuje. No za bolesnike s visokim rizikom od PONV-a ili drhtanja, TIVA bi mogla biti poželjan izbor zbog svojih zaštitnih učinaka na te komplikacije.

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Sažetak

Cilj: Usporediti kvalitetu oporavka između totalne intravenske anestezije (engl. *total intravenous anaesthesia* – TIVA) propofolom i balansirane inhalacijske anestezije sevofluranom bolesnika podvrgnutih intraoralnim kirurškim zahvatima. **Materijali i metode:** Proveli smo prospektivno randomizirano kontrolirano kliničko ispitivanje na 50 bolesnika (25 po skupini) koji su bili podvrgnuti intraoralnim kirurškim zahvatima duljima od 30 minuta. Primarni ishod bila je kvaliteta oporavka mjerena upitnikom QoR-40 (engl. *Quality of Recovery-40*) 1 sat, 24 sata i 30 dana poslije zahvata. Sekundarni ishodi uključivali su silu zagriza, snagu stiska šake, učestalost postoperativne mučnine i povraćanja (engl. *postoperative nausea and vomiting* – PONV) te postoperativno drhtanje. **Rezultati:** Vrijednosti QoR-40 nisu se razlikovale između skupina ni u jednoj vremenskoj točki (razlike od -0,04 do 1,2 boda, sve $p > 0,05$). Sila zagriza i snaga stiska šake također se nisu razlikovale između skupina. Međutim, TIVA je potpuno eliminirala PONV (0 % prema 28 %, $p = 0,010$), NNT (engl. *number needed to treat*, hrv. broj potrebnih liječenja) = 4) i drhtanje (0 % prema 36 %, $p = 0,002$, NNT = 3). **Zaključak:** TIVA-om i sevofluranom postiže se slična kvaliteta oporavka poslije intraoralnih zahvata. Međutim, TIVA eliminira PONV i drhtanje, što je klinički značajna korist za bolesnike podvrgnute intraoralnoj kirurgiji.

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