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Pooperacinių rizikos skaičiuoklių ir laboratorinių markerių tikslumas, nuspėjant ankstyvąsias pooperacines komplikacijas ir mirštamumą pacientams, patyrusiems artimojo šlaunikaulio galo lūžius

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Accuracy of the Surgical Risc Calculators and Laboratory Markers in Predicting Adverse Postoperative Outcomes in the Hip Fracture Patients

DOCTORAL DISSERTATION

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SANTRUMPOS

ACS NSQIP	Nacionalinė chirurginės kokybės gerinimo programa
AUC	Plotas po kreive
CAR	C reaktyvaus baltymo/albumino koncentracijos santykis
CRB	C reaktyvus baltymas
DHS	Dinaminis klubo sraigtas
DOAC	Tiesioginiai per oraliniai antikoaguliantai
HA	Dalinis klubo sąnario endoprotezavimas
HgB	Hemoglobinas
KS	Kaniuliuoti sraigtai
NHFS	Notingemo klubo lūžių įvertis
NT-proBNP	N – galinio B tipo natriuretinio propeptido koncentracija
PFN	Šlaunikaulio artimojo galo vinis
THA	Totalinis klubo sąnario endoprotezavimas
WBC	Leukocitų koncentracija
ŠAL	Šlaunikaulio artimojo galo lūžis
ŪFA	Ūminės uždegimo fazės atsakas

ĮVADAS

Problema ir literatūros apžvalga

Prognozuojama, kad iki šio amžiaus vidurio, kasmet, pasaulyje apie 6 milijonai žmonių patirs šlaunikaulio artimojo galo lūžius (ŠAL) [1]. Senstant pasaulio gyventojams, šios patologijos aktualumas toliau tik didės [2-6]. Pacientai po ŠAL susiduria 14 % ankstyvos mirštamumo ir iki 40 % pooperacinių komplikacijų rizika [1,7-11]. Blogų rezultatų priežastys — vyresnis amžius, didelis sergamumas (įskaitant hipertenziją, diabetą, nutukimą, širdies nepakankamumą, osteoporozę ir kt.), rūkymas, alkoholio vartojimas, bloga mityba. Dėl šių priežasčių ŠAL dažnai vadinami „paskutiniu gyvenimo lūžiu“ [1,12-14]. Nors kai kurie tyrimai rodo, kad ŠAL dažnis Šiaurės šalyse mažėja, o Vidurio Europoje stabilizuojasi, komplikacijų dažnis ir gydymo sąnaudos tik didėja, nes šie pacientai patiria lūžius, būdami dar sudėtingesnės somatinės būklės [15].

Atsižvelgiant į šių pacientų trapumą, tiksli prieš operacinė mirštamumo ir sergamumo rizikos įvertinimo po ŠAL reikšmė šiuolaikiniame gydyme užima kertinę vietą [10,16]. Šis įvertinimas ne tik padeda nuspręsti operacijos laiką ir suteikti tinkamą informaciją pacientui bei jo šeimai, bet ir identifikuoti pacientus, esančius didžiausioje rizikoje, kuriems reikalingos papildomos perioperacinės intervencijos [1,7-19]. Rizikos supratimas yra svarbus tiek pacientui, tiek chirurgui. Ankstyvos mirštamumo ir komplikacijų rizikos veiksnių įvertinimas gali padėti identifikuojant didžiausios rizikos asmenis, kuriems chirurginis gydymas kontraindikuotinas [1,7-19]. Taip pat šie aspektai yra ypatingai svarbūs tam, kad būtų galima kokybiškai ir aiškiai suteikti informaciją pacientui ir jo artimiesiems.

Siekiant spręsti šias problemas, buvo sukurti chirurginės rizikos skaičiuotuvai. Amerikos chirurgų koledžo Nacionalinė chirurginės kokybės gerinimo programa (ACS NSQIP) siūlo chirurginį rizikos skaičiuotuvą, skirtą prognozuoti 18 skirtingų procedūrai specifinių rezultatų, remiantis procedūrų CPT (atitikmuo Lietuvoje naudojamų ACHI kodų) kodais [8,10,19-24]. Tačiau jo veiksmingumas pacientams po ŠAL išlieka mažai ištirtas [24-27].

2007 m. buvo pristatytas Notingemo klubo lūžių įvertis (NHFS), kuris įrodė patikimumą prognozuojant 30 dienų ir 1 metų mirštamumą po ŠAL. NHFS buvo panaudotas kaip kontrolinis įrankis šiame tyrime [28-31].

Ūminės uždegimo fazės atsakas (ŪFA) yra gyvybiškai svarbi sisteminė reakcija į audinių pažeidimą, padedanti organizmui gyti po traumos per įvairius fiziologinius, biocheminius ir metabolinius pokyčius [32-34]. Literatūra rodo, kad tiek ŪFA hiperreakcija, tiek nepakankamumas gali lemti nepalankius rezultatus [33,34]. Su ŪFA susiję žymenys, pvz., C reaktyvus baltymas (CRB), yra nespecifiniai ir pasižymi dideliu kintamumu, kas apsunkina diferencinę diagnostiką [25,35-37]. Tai ypač aktualu vyresnio amžiaus pacientams, kuriems po operacijos dėl šlaunikaulio artimojo galo lūžio komplikacijos pasitaiko iki 40 % atvejų [1-4,38-42]. Šiems pacientams ŪFA reaktantų svyravimai gali atsirasti dėl daugelio veiksnių, įskaitant patį lūžį, chirurgines intervencijas, amžiaus sukeltus organų pokyčius ir galimas infekcines komplikacijas [1,26,27,41-45]. ŪFA žymenų pokyčių nustatymas pacientams po šlaunikaulio artimojo galo lūžio galėtų leisti intensyviau stebėti pacientus, laiku pradėti intervencijas ir kurti specializuotas priežiūros schemas, galiausiai gerinant rezultatus. Be to, C reaktyvaus baltymo/albumino koncentracijos santykis (CAR) anksčiau nustatytas kaip 30 dienų ir 1 metų mirštamumo bei sergamumo prognozuotojas įvairiose patologijose, tačiau jo efektyvumas prognozuotas išeitis po ŠAL chirurginio gydymo yra nežinomas.

Aktualumas

ŠAL, įskaitant šlaunikaulio kaklo, pertrochanterinius ir subtrochanterinius lūžius, yra dažniausias vyresnio amžiaus žmonių trauminis sužalojimas, o visuomenei senstant šių lūžių dažnis kasmet vis didėja. Kadangi pacientai yra vyresnio amžiaus, jie dažnai serga gretutinėmis ligomis, pavyzdžiui, kardiovaskulinėmis, neurologinėmis ir kitomis, taip pat turi kitų rizikos veiksnių, kurie didina mirties ir kitų nepageidaujamų baigčių patyrimo tikimybę po atliktos operacijos. Šiuolaikinėje medicinoje finansinis gydymo aspektas tampa vis

aktualesnis, todėl svarbu identifikuoti pacientus, turinčius tam tikrus rizikos veiksnius patirti nepageidaujamas baigtis, ir, esant galimybei, rizikos veiksnius koreguoti. Pasaulyje naudojami klausimynai, kurie padeda įvertinti perioperacinių nepageidaujamų baigčių riziką. Vienas iš tokių instrumentų yra Amerikos Chirurgų Kolegijos Nacionalinės Chirurginės Kokybės Gerinimo Programos (*American College of Surgeons National Surgical Quality Improvement Program – ACS NSQIP*) sukurta operacinės rizikos skaičiuoklė, kuri įvertina 20 pacientui specifiškų kintamųjų (pavyzdžiui, KMI, ASA klasę ir kt.) ir, atsižvelgiant į planuojamą intervenciją, apskaičiuoja 18 nepageidaujamų baigčių (pavyzdžiui, mirties, hospitalizacijos slaugos ligoninėje ir kt.) tikimybę per 30 dienų nuo operacijos. 30 dienų pooperaciniam mirštamumui po ŠAL nuspėti pasaulyje naudojamas Notingemo klubo lūžių įvertis (*Nottingham hip fracture score* – NHFS). NHFS įvertina pacientų amžių, lytį, hemoglobino koncentraciją atvykus į ligoninę, gyvenimą slaugos įstaigoje, gretutinių ligų skaičių, onkologinį susirgimą per 20 paskutinių metų, sutrumpinto protinės būklės testo rezultatą. Šių įrankių gebėjimas įvertinti perioperacinius rizikos veiksnius, įskaitant mirštamumą, lietuviškai kalbančioje populiacijoje iki šiol nebuvo patikrintas.

Tikslas

Įvertinti pooperacinių rizikos skaičiuoklių, paciento faktorių ir laboratorinių markerių tikslumą, nuspėjant pacientų, patyrusių artimojo šlaunikaulio galo lūžius, ankstyvąsias pooperacines komplikacijas ir mirštamumą, bei apibūdinti ūminės uždegimo fazės atsaką.

Uždaviniai

1. Įvertinti, ar Amerikos Chirurgų Kolegijos Nacionalinės Chirurginės Kokybės Gerinimo Programos (*American College of Surgeons National Surgical Quality Improvement Program – ACS NSQIP®*) skaičiuoklė gali tiksliai nuspėti pooperacines komplikacijas ir 30 dienų mirštamumą po šlaunikaulio artimojo galo lūžio operacinio gydymo.

2. Įvertinti, ar Notingemo klubo lūžių įvertis (*Nottingham hip fracture score*) gali tiksliai nuspėti 30 dienų mirštamumą po šlaunikaulio artimojo galo lūžio operacinio gydymo.
3. Palyginti ACS NSQIP, NHFS skaičiuoklių bei laboratorinių markerių gebėjimą nuspėti 30 dienų mirštamumą po šlaunikaulio artimojo galo lūžio operacinio gydymo.
4. Apibūdinti paciento, patyrusio artimojo šlaunikaulio galo lūžius, ankstyvos uždegimo fazės atsako profilį.
5. Įvertinti, ar laboratoriniai markeriai gali tiksliai nuspėti 30 dienų mirštamumą po šlaunikaulio artimojo galo lūžio operacinio gydymo.
6. Įvertinti rizikos faktorius ankstyvam mirštamumui ir komplikacijoms po ŠAL operacinio gydymo.
7. Įvertinti antikoaguliantų vartojimo įtaką ankstyvoms pooperacinėms komplikacijoms ir mirštamumui įvykti po ŠAL operacinio gydymo.

Naujumas

Mūsų žiniomis, Lietuvoje iki šiol neturime patvirtintų įrankių ar klausimynų, kurie būtų naudojami klinikinėje praktikoje arba akademinėje veikloje ir padėtų įvertinti nepageidaujamų baigčių tikimybę pooperaciniu laikotarpiu pacientams, operuotiems dėl ŠAL. Kadangi iki šiol neturime tokių duomenų, mes ištirsime ACS NSQIP operacinės rizikos skaičiuoklės gebėjimą įvertinti nepageidaujamų baigčių riziką ir NHFS gebėjimą įvertinti 30 dienų pooperacinį mirštamumą perioperaciniu laikotarpiu pacientams, patyrusiems proksimalinės šlaunikaulio dalies lūžius. Patvirtinti įrankiai būtų naudingi ne tik klinikinėje praktikoje, siekiant identifikuoti didžiausią riziką turinčius pacientus ir pagal tai atlikti klinikinius sprendimus, bet ir mokslinėje veikloje, siekiant ištirti, palyginti bei rasti optimalią tokių pacientų gydymo taktiką.

Ankstyvos uždegimo fazės atsakas yra normali organizmo reakcija į audinių pažeidimą, kuri reikalinga kraujavimo stabdymui, infekcijos stabdymui ir žaizdos gijimui. Yra žinoma, kad chirurginė trauma sukelia šį atsaką, o sveikiems pacientams po atliktos klubo ar kelio

endoprotezavimo operacijos ankstyvos uždegimo fazės atsakas yra nuspėjamas ir pastovus. Taip pat žinoma, kad šio fiziologinio proceso disreguliacija gali pasireikšti komplikacijomis. Šiuo metu nėra apibrėžta ŪFA ŠAL patyrusiems pacientams. Šių pacientų ŪFA įvertinimas ateityje leistų lengviau identifikuoti atvejus, kuriems reikalingos papildomos intervencijos.

TIRIAMOJI METODIKA IR TIRIAMIEJI

Tiriamųjų atranka, tiriamosios analitės ir imties dydžio nustatymas

Tyrimui atlikti gautas „Vilniaus regioninio biomedicininių tyrimų etikos komiteto“ leidimas nr.: 2022/11-1473-94. Pacientai konsultuojami skubos tvarka VŠĮ Respublikinėje Vilniaus universitetinėje ligoninėje. Remiantis anamneze (pacientas pargriuvo, negali atlikti aktyvių judesių sužeista koja, teigia, kad koja jo „neklauso“), objektyviu ištyrimu (sužeista koja sutrumpėjusi, rotuota į išorę, pasyvūs klubo judesiai labai skausmingi, deformacija klubo srityje), radiologiniu ištyrimu (stebimas šlaunikaulio kaklo, pertrochanterinis arba subtrochanterinis lūžiai) diagnozuojamas šlaunikaulio kaklo, pertrochanterinis arba subtrochanterinis lūžiai. Jeigu pacientas atitinka visus įtraukimo kriterijus ir nepritaikomas nei vienas atmetimo kriterijus, pacientui pasiūloma dalyvauti biomediciniame tyrime ir pacientas įtraukiamas į tyrimą.

- tiriamųjų įtraukimo į biomedicininį tyrimą kriterijai:
    - ≥ 65 metų pacientai.
    - Tiriamieji, operuoti dėl šlaunikaulio kaklo, pertrochanterinio arba subtrochanterinio mažos energijos traumos sukelto lūžio.
    - Laikas nuo traumos iki kreipimosi į gydymo įstaigą ne ilgesnis kaip 72 valandos.
    - Ramybės metu pacientas apibūdina traumuotos galūnės skausmą 5 ir daugiau balų pagal VAS.
    - Pasyvių judesių metu arba apkraunant traumuotą galūnę pacientas apibūdina skausmą kaip 7 balai ir daugiau pagal VAS. Aktyvūs galūnės judesiai negalimi.
    - Lūžis uždaras.
    - Lūžis be neurovaskulinio pažeidimo.
    - Mažos energijos trauma – pacientas pargriuvo.

- neįtraukimo į biomedicininį tyrimą kriterijai:
    - Tiriamieji, kurie atsisako dalyvauti tyrime.
    - Tiriamieji, patyrę politraumą arba didelės energijos traumą.

- Atviri lūžiai.
- Lūžiai kartu su neurovaskulinio pluošto sužalojimu.
- Dokumentuota priklausomybė nuo alkoholio ir kitų psichoaktyvių medžiagų.
- Tiriamieji dėl nuo jų priklausančių priežasčių negalės sugrįžti galutiniam rezultatų surinkimui arba jų duomenys nebus pasiekiami esveikata.lt platformoje.
- Tiriamasis dalyvauja kitame moksliniame tyrime, kuris gali turėti įtakos šio mokslinio tyrimo rezultatams.
- Nėščiosios.

Jeigu pacientas yra sąmoningas ir kritiškai vertinantis savo būklę, pasirašo informuoto sutikimo formą. Jeigu pacientas priklauso pažeidžiamai grupei, negali suprasti pateikiamos informacijos (yra iš slaugos namų ir/arba serga demencija), tuomet informuoto sutikimo formą pasirašo įgaliotas paciento atstovas. Tiriamasis yra įtraukiamas į tiriamųjų duomenų bazę EXCEL lentelės pavidalu. Tiriamąjį įtraukus į duomenų bazę, jam priskiriamas unikalus identifikacinis numeris. Informacija apie tiriamąjį renkama dviem būdais – tiesiogiai renkant paciento anamnezę apklausos būdu jo ligos istorijai ir renkant anamnezę iš paciento elektroninės sveikatos istorijos. Prieš numatomą operacinį gydymą (viena iš šių operacijų pasirenkama pagal ligoninėje galiojančius algoritmus – osteosintezė kaniuluotais sraigtais (KS), osteosintezė dinaminiu klubo sraigtu (DHS), osteosintezė šlaunikaulio artimojo galo rakinama vinimi (PFN), dalinė artroplastika (HA), totalinė artroplastika (THA)) tyrėjas įvertina pacientą užpildydamas ACS NSQIP ir NHFS skaičiuokles. Gautą 30 dienų pooperacinio mirštamumo, komplikacijų tikimybę ir numatomos hospitalizacijos laiką įtraukia į tiriamojo EXCEL bylą. Taip pat į paciento bylą buvo įtraukiami šie paciento duomenys: amžius, gretutinių ligų skaičius, lytis, ASA klasė, tiesioginių peroralinių antikoaguliantų (DOAC) vartojimas. Papildomai į EXCEL bylą buvo įtrautki šie laboratoriniai rodikliai: priešoperaciniai, pirmos pooperacinės dienos ir trečios - ketviros pooperacinės dienos. Surinkti šie priešoperaciniai rodikliai: hemoglobino koncentracija (HgB), bendro baltymo koncentracija, albumino koncentracija, troponino koncentracija, N – galinio B tipo natriuretinio propeptido koncetracija (NT-proBNP), vitamino D

koncentracija, fibrinogeno koncentracija, CRB koncentracija. Pirmos pooperacinė dienos rodikliai: HgB koncentracija, CRB koncentracija. Trečios - ketvirtos pooperacinės dienos rodikliai – HgB koncentracija, CRB koncentracija, NT-proBNP koncentracija. CAR indeksas buvo apskaičiuotas kaip CRB ir albumino priešoperacinių koncentracijų santykis. Paciento sekimo trukmė yra 30 dienų po operacijos, nepaisant, ar pacientas vis dar hospitalizuotas, ar gydomas ambulatoriškai. Jeigu pacientas gydomas ambulatoriškai, tuomet 30 dieną susisiekiama su juo arba jo artimaisiais (jį globojančiais asmenimis/institucija) ir apklausos būdu surenkami duomenys apie įvykusias komplikacijas ar nepalankias baigtis. Buvo fiksuotos šios sunkios komplikacijos: pneumonija, kardiologinė komplikacija, operacinė infekcija, šlapimo takų infekcija, giliųjų venų trombozė, ūminis inkstų pažeidimas, rehospitalizacija, reoperacija, mirtis, slaugos ligoninė, sepsis, delyras, funkcijos pablogėjimas, pagalbinės ėjimo priemonės, pragulos. Bet kokia komplikacija buvo fiksuojama kaip bet koks įvykis, kuris buvo įvardintas kaip nuokrypis nuo normalios gydymo eigos. Visas įtraukimo laikas į tyrimą nuo 2022 gruodžio 1 dienos iki 2023 metų gruodžio 1 dienos.

Toliau pateikiamas naudotų perioperacinės rizikos skaičiuoklių aprašymas.

ACS NSQIP chirurginės rizikos skaičiuoklė – tai perioperacinės rizikos vertinimo priemonė, sukurta Amerikos chirurgų kolegijos (American College of Surgeons, ACS). Ji leidžia individualiai įvertinti paciento 30 dienų pooperacinių komplikacijų ir kitų nepageidaujamų baigčių riziką, atsižvelgiant į paciento charakteristikas ir planuojamą chirurginę procedūrą. Vertinami tokie veiksniai kaip: amžius, lytis, KMI, funkcinė būklė, gretutinės ligos, rūkymas, ASA fizinės būklės klasė, planuojama chirurginė procedūra (CPT kodas), skubos tvarka atliekama ar planinė operacija.

Skaičiuoklė pateikia individualizuotą 30 dienų po operacijos nepageidaujamų baigčių riziką. Šios komplikacijos skaičiuoklėje įvardinamos kaip sunkios: pneumonija, kardiologinė komplikacija, operacinės žaizdos infekcija, šlapimo takų infekcija, ūminis inkstų pažeidimas, giliųjų venų trombozė, pakartotinė hospitalizacija, pakartotinė operacija, išrašymas į slaugos įstaigą, delyras, pragulos,

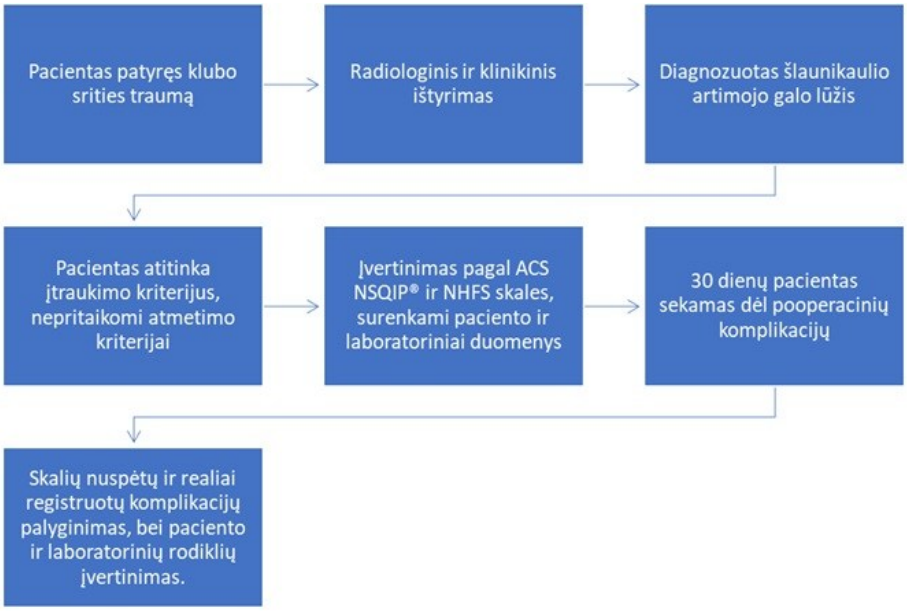
sepsis, mirtis. Tyrime sunkias komplikacijas įvardijome pagal šios skaičiuoklės siūlymą. Kardiologinę komplikaciją vertinome kaip, bet kokį kardiologinį įvykį – miokardo infarktas, ūmus širdies nepakankamumas, lėtinio širdies nepakankamumo paūmėjimas, nauja krūtinės angina.

Ši skaičiuoklė naudojama perioperacinei rizikai įvertinti, informuotam paciento sutikimui ir bendram gydytojo bei paciento sprendimų priėmimui.

Notingamo klubo lūžio įvertis – tai perioperacinės rizikos vertinimo priemonė, naudojama 30 dienų mirštamumo rizikai įvertinti vyresnio amžiaus pacientams, patyrusiems ŠAL.

Jį sudaro 7 vertinami veiksniai: amžius, lytis, hemoglobino koncentracija hospitalizavimo metu, kognityvinė būklė (sutrumpintas psichikos būklės testas, *Abbreviated Mental Test Score*), gyvenimas globos ar slaugos įstaigoje, gretutinių ligų skaičius, piktybinio naviko (onkologinės ligos) buvimas.

Balas svyruoja nuo 0 iki 10, didesnis balas rodo didesnę mirtingumo riziką. Šis balas daugiausia naudojamas rizikos stratifikacijai, perioperaciniam planavimui ir pacientų, kuriems gali būti reikalinga intensyvesnė stebėsena ar papildoma palaikomoji priežiūra, identifikavimui. Dėl patogumo, balas konvertuojamas į procentinę 30 dienų mirštamumo išraišką.



1 pav. Tyrimo eigos schema

Imties dydis apskaičiuotas naudojant *StatCalc* programą - literatūros duomenimis, mirštamumas po artimojo šlaunikaulio galo yra 13,3% per 30 dienų nuo operacijos, VŠĮ Respublikinėje Vilniaus universitetinėje ligoninėje per metus skubos tvarka hospitalizuojama iki 1000 pacientų su šia patologija. Norint nustatyti 13,3 įvykio dažnį su 95% pasikliautinuoju intervalu, reikia įtraukti 540 tiriamųjų. Numatoma, kad apie 5% pacientų atsisakys dalyvauti tyrime arba iškris iš tyrimo, todėl reikia įtraukti ne mažiau kaip 567 pacientus. Pagal metodiką buvo nuspręsta pacientų įtraukimą vykdyti per vienerius metus, o pasibaigus įtraukimo terminui, spręsti dėl jo pratęsimo pagal jau turimą įtrauktų pacientų skaučių. Galutinis įtrauktųjų skaičius buvo 583, todėl įtraukimas nebuvo pratęstas.

1 lentelė. Bendrieji rodikliai

Kintamieji	
Lytis (moteris/vyras)	452(77.5%) / 131(22.5%)
Amžius	82±8
Gretutinės ligos	6±3
Lūžio tipas:	
Kaklas	292 (50.1%)
Pertrochanterinis	259 (44.4 %)
Subtrochanterinis	32 (5.5 %)
Operacijos tipas:	
Klubo dalinis endoproteavimas	191 (32.8)
Totalinis klubo endoprotezavimas	70 (12.0%)
Artimojo šlaunikaulio galo vinis	236 (40.5%)
Dinaminis klubo sraigtas	69 (11.8%)
Kaniuliuoti sraigtai	17 (2.9%)



2 pav. Imties dydžio sudarymas

Statistinė analizė

Duomenų analizei ir statistiniams skaičiavimams buvo naudojama nuasmenintų duomenų rinkmena iš duomenų rinkimo formos, kuri

buvo eksportuojama į statistinę programą (SPSS statistinių programų paketą) tolimesniam apdorojimui. Tolydieji duomenys, pasiskirstę pagal normalųjį skirstinį, bus vertinami naudojant *Shapiro-Wilk* metodą ($p>0,05$). Normaliai pasiskirstę tolydieji kintamieji bus išreikšti vidurkiu (vidurkis ± standartinis nuokrypis), ne pagal normalųjį skirstinį pasiskirstę duomenys bus išreikšti mediana ir kvartilių skirtumu (Q3–Q1).

ACS NSQIP, NHFS skaičiuoklių generuotam 30 dienų mirštamumui ir komplikacijų dažniui bei laboratorinių tyrimų įverčiams suformuoti logistinės regresijos modeliai, kurių sutapimas su iš tikrųjų įvykusiomis komplikacijomis įvertintas kaip nepriklausomas kintamasis. C statistika bus naudojama modelių sutapimui įvertinti (pakankamas sutapimas vertinamas kuomet $C > 0.80$). ROC kreivės bus naudojamos pavaizduoti nustatytos rizikos gebėjimą nuspėti konkrečią komplikaciją.

Papildoma analizė atlikta siekiant palyginti uždegiminio atsako rodiklius tarp skirtingų lūžio ir operacijų tipų. Uždegiminio atsako dalyje iš visų įtrauktų pacientų buvo pašalinti visi pacientai, kuriems įvyko infekcinės komplikacijos. Tai buvo atlikta tam, kad pavyktų nustatyti kiekvieno lūžio natūralų ŪFA ir jam neturėtų poveikio įvykuios infekcijos. Šioje dalyje galutinis pacientų skaičius buvo 431. Normaliam pasiskirstymui turimiems duomenims palyginti buvo naudojamas ANOVA testas. Nenormaliai pasiskirsčiusiems duomenims palyginti naudotas Kruskal–Wallis testas. Jei vienoje grupėje duomenys buvo normaliai pasiskirstę, o kitoje — nenormaliai, taip pat naudotas Kruskal–Wallis testas. Be to, daugialypiams palyginimams atlikti naudotos porinės (pairwise) palyginimo procedūros. Skaitinių kintamųjų koreliacijai apskaičiuoti naudotas Pearsono koreliacijos koeficientas, pateiktas skliaustuose su *p* reikšme. Reikšmingumo lygmuo α nustatytas kaip $p < 0,05$.

REZULTATAI

Komplikacijos

Komplikacijų dažniai pateikti 2 lentelėje.

2 lentelė. Komplikacijų dažniai

Kintamieji	
Sunki komplikacija	207 (35.5%)
Bet kokia komplikacija	287 (49.2%)
Pneumonija	66 (11.3%)
Kardiologinė komplikacija	68 (11.7%)
Operacinė infekcija	20 (3.4%)
Šlapimo takų infekcija	58 (9.9%)
Giliųjų venų trombozė	7 (1.2%)
Ūminis inkstų pažeidimas	26 (4.5%)
Rehospitalizacija	62 (10.6%)
Reoperacija	11(1.9%)
Mirtis	47 (8.1%)
Slaugos ligoninė	269 (46.1%)
Sepsis	10 (1.7%)
Delyras	59 (10.1%)
Funkcijos pablogėjimas	406 (69.6%)
Pagalbinės ėjimo priemonės	556 (95.4%)
Pragulos	51(8.7%)

Bet kokios komplikacijos atsiradimas statistiškai reikšmingai padidino 30 dienų mirštamumo riziką 5,6 karto (95 % CI 1,6–19,9) (p = 0,008). Iš visų komplikacijų tik širdies įvykiai parodė statistiškai reikšmingą (p = 0,010) šansų santykį — 3,6 (95 % CI 1,3–8,5).

3 lentelė. Komplikacijų regresijos modelio rezultatai prognozuojant ankstyvą mirštamumą.

	Ankstyvas mirštamumas	
	P reikšmė	Šansų santykis (95% pasikliautinasis intervalas)
Bet kokia komplikacija	***0.008****	**5.606(1.579-19.901)**
Pneumonija	*0.563*	1.323(0.513-3.412)
Kardiologinė komplikacija	***0.010****	**3.359(1.329-8.487)**
Operacinė infekcija	*0.260*	0.240(0.020-2.866)
Šlapimo takų infekcija	*0.535*	1.387(0.493-3.899)
Ūminis inkstų pažeidimas	*0.504*	1.526(0.441-5.280)
Rehospitalizacija	*0.748*	0.836(0.280-2.494)
Reoperacija	*0.148*	5.046(0.563-45.192)
Išrašymas į slaugą	*0.561*	0.789(0.355-1.755)
Sepsis	*0.899*	0.882(0.127-6.108)
Delyras	*0.130*	2.192(0.793-6.057)
Pragulos	*0.926*	1.057(0.329-3.395)

Pooperacinės rizikos skaičiuoklės

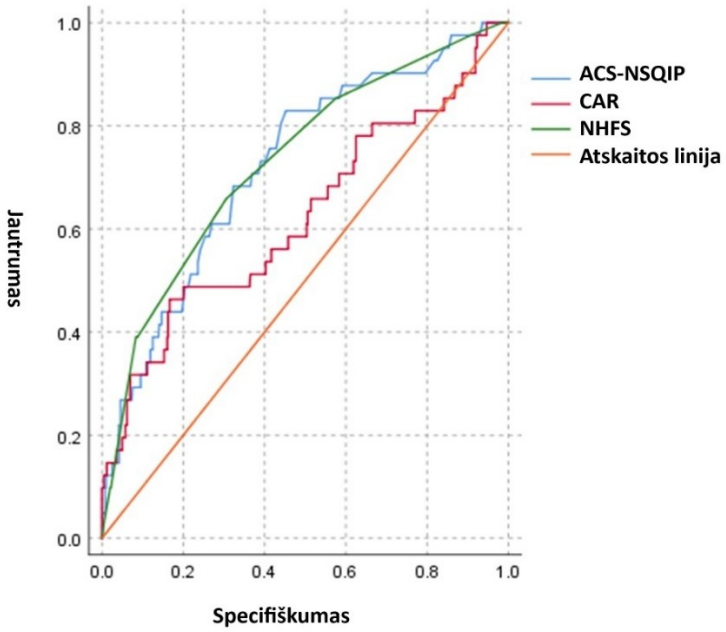
ACS NSQIP ir NHFS skalės parodė plotą po kreive (AUC) atitinkamai 0,724 ir 0,731. CAR pasirodė silpniau — AUC 0,623, kas apibrėžiama kaip prastas 30 dienų mirštamumo prognozuotojas. Be to, prognozuojant bet kokią komplikaciją, ACS NSQIP AUC buvo 0,645, NHFS — 0,611, o CAR — 0,594 — nė vienas rizikos skaičiuotuvas nerodė pakankamo prognozavimo lygio, o CAR prognozė bet kokiai komplikacijai nebuvo geresnė už atsitiktinumą. NHFS, palyginti su ACS NSQIP, pateikė žemesnį vidutinį mirštamumo rodiklį (5,4 % prieš 7,9 %), priešingai tyrimo rezultatui — 8,1 %. Jokia iš ACS NSQIP skalės prognozuojamų komplikacijų neparodė priimtino veikimo; AUC reikšmės pateiktos 4 lentelėje. Koreguojant pagal lūžio tipą, NHFS pasiekė AUC 0,858 prognozuojant 30 dienų mirštamumą pacientams, patyrusiems šlaunikaulio kaklo lūžius; CAR ir ACS NSQIP, testuoti pagal lūžio tipą, išliko tose pačiose patikimumo ribose.

4 lentelė. ACS NSQIP ir NHFS skaičiuoklių bei CAR AUC ir p reikšmės bei pasikliautinieji intervalai prognozuojant mirštamumą ir komplikacijas

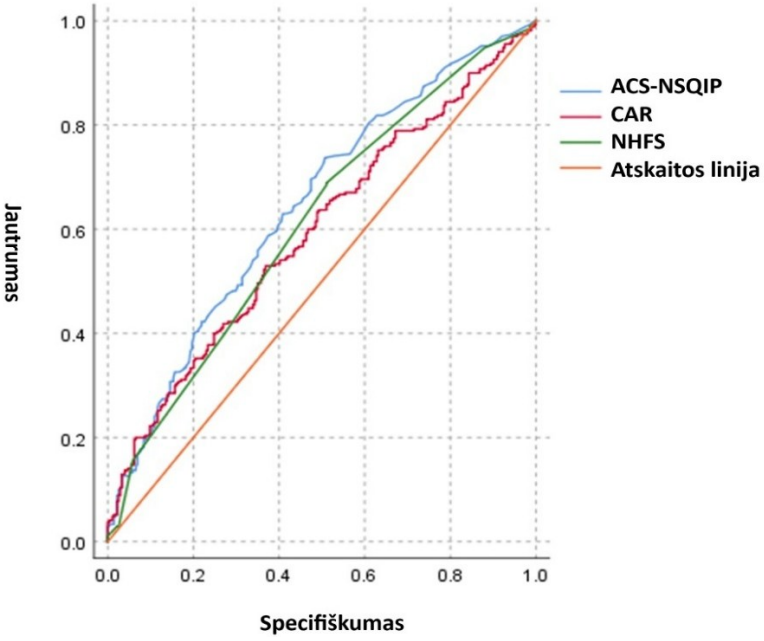
	ACS NSQIP	NHFS	CAR
Mirtis	.724 (.642-.805)	.731 (.648-.815)	.623 (.521-.725)
	p<.001	p<.001	p.=018
Bet kokia komplikacija	.645 (.599-.691)	.611 (.564-.658)	.594 (.547-.642)
	p<.001	p<.001	p.<001

5 lentelė. ACS NSQIP skaičiuoklės AUC ir p reikšmės bei pasikliautinieji intervalai prognozuojant specifines komplikacijas.

	ACS NSQIP AUC (CI) ir *p* reikšmė
Sunki komplikacija	.688 (.619-.757) p.<000
Bet kokia komplikacija	.669 (.603-.735) p.<000
Pneumonija	.628 (.482-.773) p=.087
Kardiologinė komplikacija	.571 (.487-.655) p=.097
Operacinė infekcija	.473 (.226-.720) p=.830
Šlapimo takų infekcija	.668 (.543-.794) p=.008
Giliųjų venų trombozė	.497 (.418-.575) p=933
Ūminis inkstų pažeidimas	.643 (.498-.787) p=.053
Rehospitalizacija	.467 (.420-.514) p=.172
Reoperacija	.643 (.465-.822) p=.114
Mirtis	.655 (.578-.732) p<.000
Slaugos ligoninė	.523 (.474-.571) p=.356
Sepsis	.598 (.509-.687) p=.030
Delyras	.625 (.550-.700) p=.001



3 pav. Rizikos skaičiuoklių ir CAR indekso ROC kreivės ankstyvam mirštamumui prognozuoti.



4 pav. Rizikos skaičiuoklių ir CAR indekso ROC kreivės komplikacijoms prognozuoti.

Paciento faktoriai

Pacientų duomenų regresijos modelių rezultatai, prognozuojant ankstyvą mirštamumą ir komplikacijas, pateikti 6 ir 7 lentelėse. Gretutinių ligų skaičius ir amžius statistiškai reikšmingai prognozavo ankstyvą mirštamumą (atitinkamai $p = 0,005$ ir $p = 0,015$). Daugiau nei 6 ligos padidino 30 dienų mirštamumo riziką 8,2 karto (95 % CI 1,9–35,5) ir padidino ankstyvų komplikacijų riziką 2,3 karto (95 % CI 1,9–35,5, p = 0,000). Pacientams vyresniems nei 85 metai 30 dienų mirštamumo rizika padidėjo 2,2 karto (95 % CI 1,2–4,1), o ankstyvų komplikacijų rizika — 1,7 karto (95 % CI 1,2–2,4, p = 0,005).

6 lentelė. Paciento faktorių regresijos modelio rezultatai ankstyvam mirštamumui prognozuoti.

	Ankstyvas mirštamumas	
	p reikšmė	Šansų santykis (95% pasikliautinasis intervalas)
Lytis	*0.371*	1.391(0.675-2.866)
Ligos > 6	***0.005****	**8.182(1.884-35.537)**
Amžius > 85	***0.015****	**2.196(1.168-4.130)**
ASAII	*0.686*	1.698(0.131-22.023)
ASAIII	*0.937*	1.088(0.133-8.908)
ASAIV	*0.335*	3.072(0.314-30.041)
DOAC	*0.798*	0.909(0.438-1.886)

7 lentelė. Paciento faktorių regresijos modelio rezultatai ankstyvoms sunkioms komplikacijoms prognozuoti.

	Ankstyvos sunkios komplikacijos	
	p reikšmė	Šansų santykis (95% pasikliautinasis intervalas)
Lytis	*0.692*	1.091(0.710-1.676)
Ligos > 6	***0.000****	**2.323(1.468-3.676)**
Amžius > 85	***0.005****	**1.678(1.167-2.413)**
ASAII	*0.557*	0.660(0.165-2.644)
ASAIII	*0.847*	1.116(0.366-3.400)
ASAIV	*0.211*	2.392(0.609-9.391)
DOAC	*0.667*	1.097(0.719-1.675)

Pradinių laboratorinių žymenų reikšmė ankstyvajai mirčiai ir komplikacijoms pateikta 5 lentelėje. Vitamino D koncentracija statistiškai reikšmingai (*p = 0,028*) prognozavo 2,1 didesnę (95 % CI 1,1–4,1) ankstyvajam mirštamumui. Be to, bazinis NT-proBNP statistiškai reikšmingai prognozavo ankstyvą mirštamumą ir komplikacijas (atitinkamai *p = 0,040* ir p = *0,000*). Priešoperacinė serumo koncentracija >780 ng/l prognozavo 2,3 karto padidėjusią 30 dienų mirštamumo riziką (95 % CI 1,0–4,9) ir 2,6 karto padidėjusią ankstyvų komplikacijų riziką (95 % CI 1,7–3,9). Pradinis CRB > 10 mg/l statistiškai reikšmingai (*p = 0,011*) prognozavo 1,7 karto padidėjusią 30 dienų komplikacijų riziką (95 % CI 1,1–2,6).

8 lentelė. Laboratorinių rodiklių logistinės regresijos analizė ankstyvam mirštamumui.

	Ankstyvas mirštamumas	
	p reikšmė	Šansų santykis (95% pasikliautinasis intervalas)
HgB pirminis < 100 g/l	*0.443*	0.710(0.296-1.703)
HgB 1 diena < 100 g/l	*0.476*	1.348(0.594-3.059)
HgB 3-4 diena < 100 g/l	*0.755*	1.129(0.527-2.415)
Albuminas < 35 g/l	*0.365*	0.658(0.266-1.627)
Bendras baltymas < 60 g/l	*0.422*	0.693(0.283-1.697)
Vitaminas D < 20 ng/ml	***0.028****	**2.102(1.083-4.078)**
NT-proBNP pirminis > 780 ng/l	***0.040****	**2.256(1.036-4.913)**
NT-proBNP 3-4 diena > 780 ng/l	*0.308*	0.687(0.333-1.414)
CRB pirminis > 10 mg/l	*0.335*	1.438(0.687-3.011)
CRB 1 diena > 50 g/l	*0.334*	1.386(0.715-2.685)
CRB 3-4 diena > 50 g/l	*0.130*	1.737(0.851-3.547)
Troponinas > 9 ng/l	*0.252*	1.724(0.678-4.384)
Fibrinogenas > 4 g/l	*0.154*	0.575(0.269-1.230)

10 lentelė. Laboratorinių rodiklių logistinės regresijos analizė ankstyvoms sunkioms komplikacijoms.

	Ankstyva sunki komplikacija	
	p reikšmė	Šansų santykis (95% pasikliautinasis intervalas)
HgB pirminis < 100 g/l	*0.132*	0.626(0.340-1.151)
HgB 1 diena < 100 g/l	*0.435*	1.192(0.767-1.852)
HgB 3-4 diena < 100 g/l	*0.315*	0.799(0.515-1.238)
Albuminas < 35 g/l	*0.126*	1.623(0.872-3.020)
Bendras baltymas < 60 g/l	*0.326*	0.744(0.411-1.344)
Vitaminas D < 20 ng/ml	*0.881*	1.032(0.684-1.557)
NT-proBNP pirminis > 780 ng/l	***0.000****	**2.564(1.679-3.915)**
NT-proBNP 3-4 diena > 780 ng/l	*0.531*	0.877(0.583-1.321)
CRB pirminis > 10 mg/l	***0.011****	**1.739(1.137-2.659)**
CRB 1 diena > 50 g/l	*0.244*	1.252(0.858-1.829)
CRB 3-4 diena > 50 g/l	*0.625*	1.105(0.740-1.649)
Troponinas > 9 ng/l	*0.726*	0.923(0.587-1.449)
Fibrinogenas > 4 g/l	*0.230*	1.297(0.848-1.983)

Uždegiminis atsakas

Priešoperacinės CRB ir albumino koncentracijos tarp visų pacientų koreliavo statistiškai reikšmingai neigiamai *($p = 0,038$*, Pearson koeficientas = *$-0,108$*). Panašus statistiškai reikšmingas neigiamas ryšys nustatytas tarp priešoperacinio CRB ir vitamino D (*$p = 0,021$*, Pearson koeficientas = *$-0,116$*). Kintamųjų aprašomoji statistika pagal grupes pateikta 10 ir 11 lentelėse.

Lūžio tipas reikšmingai neįtakojo priešoperacinio CRB koncentracijos (*$p = 0,083$*). Pirmą pooperacinę dieną šlaunikaulio kaklo lūžiai turėjo žemesnes CRB reikšmes nei intertrochanteriniai (*$p = 0,046$*) ir subtrokanteriniai lūžiai (*$p = 0,007$*); skirtumo tarp ekstrakapsulinių lūžių nebuvo (*$p = 0,077$*). 3–4 pooperacinę dieną šlaunikaulio kaklo lūžiai ir toliau rodė žemesnes CRB (*$p < 0,001$*) reikšmes, o intertrochanteriniai lūžiai turėjo žemesnį CRB nei subtrochanteriniai (*$p = 0,034$*). Prieš operaciją intrakapsuliniai lūžiai turėjo aukštesnę fibrinogeno koncentraciją nei intertrochanteriniai (*$p = 0,025$*) ir subtrochanteriniai (*$p = 0,039$*); skirtumo tarp ekstrakapsulinių lūžių nebuvo (*$p = 0,308$*). Šlaunikaulio kaklo lūžiai taip pat rodė aukštesnę albumino koncentraciją nei intertrochanteriniai (*$p < 0,001$*) ir subtrochanteriniai lūžiai

(p = 0,020); tarp ekstrakapsulinių lūžių skirtumo nebuvo (*p = 0,729*). Vitamino D lygiai pagal lūžio tipą reikšmingai nesiskyrė (*p = 0,112*).

Pirmą pooperacinę dieną reikšmingai žemesnes CRB reikšmes rodė tik THA grupė, palyginti su PFN (*p = 0,002*) ir DHS (*p = 0,017*). Šis skirtumas padidėjo 3–4 pooperacinėmis dienomis (*p < 0,001*). 3–4 dienomis HA ir KS taip pat rodė reikšmingai žemesnes CRB reikšmes nei PFN (atitinkamai *p < 0,001 ir p = 0,018*) ir DHS (atitinkamai *p < 0,001 ir p = 0,024*). Subtrochanteriniai lūžiai turėjo reikšmingai mažesnį CAR nei intertrochanteriniai (*p = 0,017*) ir šlaunikaulio kaklo lūžiai (*p = 0,011*).

10 lentelė. Laboratorinių rodiklių aprašomoji statistika pagal lūžio tipus.

Kintamasis	Visos grupės	Lūžio tipas		
	N=431	Kaklas N=208	Pertrochanterinis N=199	Subtrochanterinis N=24
WBC (x10^12/l) pirminis	9.9 (8-12)	9.7 (7.8-11.9)	10.1 (8.1-12.2)	9.8 (8.8-13.3)
WBC (x10^12/l) 1 diena	8.9 (7.1-11.1)	10 (7.7-11.9	8.4 (6.9-10.1)	8.2 (6.7-10.5)
WBC (x10^12/l) 3-4 diena	7.1 (5.7-8.5)	7.2 (5.8-8.4)	7 (5.6-8.6)	5.7 (6.8-9.4)
CRB (mg/l) pirminis	4 (1.4-20.8)	4.3(1.6-21.7)	5(1.3-23.7)	1.7(.65-11)
CRB (mg/l) 1 diena	60.3 (36.5-63)	58.3(34.1-85.4)	69.5(41.8-101.5)	98.9±58.2
CRB (mg/l) 3-4 diena	65.9 (32.1-65.5)	45(27.9-72.9)	77(52.7-111.4)	110.8±55.1
Fibrinogenas (g/l)	3.7±0.9	3.7±0.9	3.6±0.9	3.5±8
Albuminas (g/l)	39.3±6.7	40.5±10.2	38.2±4.1	38.1±3.6
Vitaminas D (nmol/l)	48.5±33	54±35	45.3±33	58.2±41.4

11 lentelė. Laboratorinių rodiklių aprašomoji statistika pagal operacijos tipus.

Kintamasis	Operacijos tipas				
	HA N=126	THA N=61	PFN N=183	DHS N=48	KS N=13
CRB (mg/l) 1 diena	59.8(34.6-93.8)	48.4(22.7-78.2)	69.9(43-101.2)	72.2±24.9	70.8±51
CRB (mg/l) 3-4 diena	50.5(28.8-72.3)	40.7±24.2	80.4(57.6-111.9)	86.3±39.4	50.9±29.7

Statistiškai reikšmingi skirtumai nustatyti tiek gulėjimo ligoninėje dienų skaičiuje ($p < 0,05$), tiek laiko tarp hospitalizacijos ir operacijos ($p < 0,0001$), palyginus antikoaguliacinę terapiją gaunančius pacientus su tais, kurie jos negavo. Mediana nuo hospitalizacijos iki operacijos antikoaguliacijos grupėje buvo 3 dienos (Q1: 2; Q3: 4), o kontrolinėje grupėje – 2 dienos (Q1: 1; Q3: 4). Nepaisant to, antikoaguliantais gydytų pacientų vidutinė hospitalizacijos trukmė buvo ilgesnė — 9 dienos (Q1: 6; Q3: 11), o pacientų be antikoaguliacijos mediana siekė 7 dienas (Q1: 6; Q3: 10).

Antikoaguliacijos grupėje 64,04 % (n = 73) operuotų pacientų laukė daugiau nei 48 valandas. Tačiau, lyginant pooperacines komplikacijas tarp kontrolinės grupės, antikoaguliacijos grupės pacientų, kurie laukė mažiau nei 48 val., ir tų, kurie laukė ilgiau, reikšmingų skirtumų nenustatyta ($p > 0,05$). Hemoglobino koncentracijos pokyčių procentiniai dydžiai buvo panašūs visose trijose grupėse ($p > 0,05$): be antikoaguliacijos grupėje vidurkis buvo 16,7 ± 10,1 %, antikoaguliacijos grupėje, kurioms operacija atlikta per 48 val., — 16,6 ± 10,0 %, o antikoaguliacijos grupėje, kurios laukė operacijos daugiau nei 48 val., — 14,1 ± 10,3 %.

REZULTATŲ APTARIMAS

Komplikacijos

Mūsų kohortoje stebėtas komplikacijų dažnis buvo 49,2%, tai atitinka literatūroje nurodytą 12,5–75% intervalą [7]. Variacija literatūroje daugiausia kyla dėl skirtingų tyrimų metodologijų — retrospektyvūs tyrimai paprastai randa mažesnį komplikacijų dažnį nei prospektyvūs [7,46]. Be to, literatūroje skiriasi stebėjimo laikotarpiai, tai reikia turėti omenyje. Taip pat komplikacijos įvairiuose tyrimuose dokumentuojamos skirtingai. Mūsų tyrime registravome sunkias komplikacijas pagal ACS NSQIP anketą ir bet kokias kitas, kurias įvardinome kaip bet kokį nuokrypį nuo standartinio gydymo, reikalavusį papildomos intervencijos ar konsultacijos. Ši metodika, fiksuojanti visas komplikacijas, galėjo padidinti mūsų stebėtą komplikacijų dažnį. Mūsų rezultatai rodo, kad ŠAL pacientai turi labai didelę riziką patirti komplikacijas ir juos bei jų artimuosius reikia tinkamai informuoti apie šį aspektą. Bet kokios komplikacijos atsiradimas statistiškai reikšmingai 5,6 karto padidina ankstyvos mirštamumo riziką, o iš komplikacijų tik širdies įvykiai pasiekė reikšmingumą.

Pooperacinės rizikos skaičiuoklės

Chirurginės rizikos skaičiuotuvai yra labai vertingi įrankiai — jie pagerina pacientų ir jų artimųjų supratimą ir padeda priimti chirurginius sprendimus remiantis kiekybiniais duomenimis. Mūsų kohortoje nė vienas modelis nerodė puikios diskriminacijos (AUC > 0,80) prognozuojant 30 dienų mirštamumą ir sergamumą tarp ŠAL pacientų. Kadangi stebėtas AUC yra didesnis nei 0,7, tiek ACS NSQIP, tiek NHFS yra efektyvūs 30 dienų mirštamumo prognozuotojai. Tik koregavus pagal lūžio tipą, NHFS parodė puikią diskriminaciją 30 dienų mirtingumui pacientams su šlaunikaulio kaklo lūžiais. Reikėtų pažymėti, kad NHFS prognozavo žemesnį mirštamumo lygį nei stebėtas šiame tyrime.

Mūsų žiniomis, tai pirmasis tyrimas, palyginęs CAR su rizikos skaičiuotuvais toje pačioje kohortoje. CAR mūsų tyrime buvo neveiksmingas prognozuoti ankstyvą mirštamumą ir dar prastesnis prognozuojant sergamumą. Šis rezultatas prieštarauja literatūrai: *Cacciola ir kt*. rado CAR AUC = 0,816 kaip patikimą prognozuotoją, o *Balta ir kt*. pranešė AUC = 0,727 intertrochanteriniams lūžiams [27,47]. Reikia pažymėti, kad abu ankstesni tyrimai buvo retrospektyvūs, ir iki šio tyrimo neradome prospektyvių ROC analizės tyrimų apie CAR ŠAL pacientams. Be to, CRB mėginio paėmimo

laikas gali turėti didelę reikšmę CAR įverčiams — mes įtraukėme tik ūmius lūžius ir naudojome tik priešoperacinius mėginius, kuriuose CRB gali būti nespėjęs padidėti. Tačiau ši hipotezė reikalauja tolesnių tyrimų. Nors CAR buvo identifikuotas kaip naudingas prognozuotojas įvairiose patologijose, mūsų rezultatai rodo, kad jo galimybės ŠAL pacientams yra ribotos.

ACS NSQIP yra naujas įrankis, naudojantis procedūrai specifines prognozes pagal CPT („*Current procedural terminology*“) kodą (Lietuvoje atitikmuo ACHI procedūrų kodai). Šis skaičiuotuvas parodė patikimumą įvairiose planinėje ir skubios pagalbos srityse. ROC analizė rodo, kad jis yra adekvatus 30 dienų mirštamumo prognozuotojas; tačiau jo gebėjimas prognozuoti konkrečias komplikacijas yra ribotas, tai mūsų sąlygomis yra reikšmingas trūkumas. Be to, ACS NSQIP buvo sukurtas naudojant tik Jungtinių Amerikos valstijų NSQIP ligoninių duomenis, kas gali paaiškinti prastą diskriminaciją kitose šalyse [8]. Vis dėlto šis įrankis nuolat atnaujinamas ir vertas tolesnio vertinimo, nes jo principas rodo didelį potencialą.

ACS NSQIP skaičiuotuvas buvo sukurtas iš *„National Surgical Quality Improvement Program“* duomenų, siekiant gerinti chirurginės priežiūros kokybę JAV. Vėliau *Harris ir kt*. sukūrė „*Hip Fracture Surgery Risk Calculator“* naudodami tuos pačius duomenis; jis prieinamas https://s-spire-clintools.shinyapps.io/hip_deploy/.(16) Modelis prognozuoja 30 dienų mirštamumą su AUC = 0,76. Priklausomai nuo mirštamumo slenksčio, jo jautrumas ir specifiškumas kito: 15% slenkstis parodė 97% specifiškumą ir 78% jautrumą. Tai reiškia, kad nors modelis yra prognozuojantis, jis gali kai kuriems pacientams pervertinti mirštamumą, dėl to šie pacientai galimai įvertinami kaip per rizikingi ir ne oporuojami, nors potencialiai galėtų gauti naudos iš operacijos. Chirurgai turėtų tai apsvarstyti priimdami gydymo sprendimus su pacientais. Mes šio modelio neišnagrinėjome, nes jis nebuvo prieinamas tyrimo metu. Autorius taip pat siūlė analizuoti rizikos skaičiuotuvų veikimą pacientams, kuriems nebuvo atlikta operacija. Kiek žinome, tokio tyrimo literatūroje nėra, ir tai yra vienas iš mūsų tyrimo trūkumų.

Iš pradžių NHFS buvo sukurtas visų artimojo šlaunikaulio galo lūžių rizikai įvertinti. Tačiau intrakapsuliniai lūžiai parodė didesnį mirštamumą ir sergamumą nei ekstrakapsuliniai [28-30]. Tai rodo, kad NHFS gali būti naudojamas mirštamumo rizikos stratifikacijai šlaunikaulio kaklo lūžiams mūsų sąlygomis. Be to, NHFS yra patikimas prognozuotojas ir lengvai naudojamas, nes reikalauja tik priešoperacinių duomenų. Kadangi NHFS naudoja objektyvias reikšmes, jis turėtų būti mažiau paveikiamas kultūrinių ir

socialinių skirtumų tarp populiacijų. Tačiau prieš naudojimą kiekvienoje šalyje reikalinga išorinė validacija.

Kadangi NHFS reikalauja mažiau priešoperacinių verčių, jis yra paprastesnis naudoti nei ACS NSQIP. Mūsų kohortoje NHFS parodė reikšmingą gebėjimą prognozuoti 30 dienų mirštamumą intrakapsuliniams lūžiams. Remiantis šiais rezultatais, NHFS rekomenduojamas rizikos stratifikacijai šlaunikaulio kaklo lūžiams mūsų sąlygomis. Be to, rezultatai rodo, kad intrakapsuliniai ir ekstrakapsuliniai šlaunikaulio artimojo galo lūžiai, kuriems reikalingi skirtingi chirurginiai metodai, galėtų naudoti lūžiui specifinius rizikos skaičiuotuvus.

Kaip ir visi tyrimai, šis tyrimas turi apribojimų. Pirma, tai vieno centro tyrimas — negalime patvirtinti, kad tie patys rezultatai galioja visai populiacijai. Antra, mes įtraukėme tik ŠAL specifinius rizikos skaičiuotuvus ir išskyrėme kitose chirurgijos srityse populiarius įrankius (pvz., P-POSSUM, E-PASS, Clarkson komorbidumo indeksas). Šių skaičiuotuvų nenaudojome tik metodologiniais sumetimais — tyrimo išplėtimas reikalautų papildomų žmogiškųjų išteklių ir laiko. Be to, naujesni įrankiai, tokie kaip Hip Fracture Surgery Risk Calculator, nebuvo prieinami tyrimo metu, tačiau juos reikėtų apsvarstyti būsimuose palyginimuose. Galiausiai, įrankiai turėtų būti įvertinti pagal jų jautrumą ir specifiškumą.

Pacientų faktoriai

Duomenys rodo, kad amžius ir gretutinės ligos yra reikšmingi veiksniai, susiję su 30 dienų mirštamumu ir komplikacijomis pacientams po šlaunikaulio artimojo galo lūžio. Pacientams vyresniems nei 85 metai 30 dienų mirštamumo rizika padidėjo 2,2 karto, o pooperacinių komplikacijų tikimybė — 1,7 karto. Daugiau nei šešios gretutinės ligos susijusios su 8,2 karto didesne ankstyvos mirties rizika ir 2,3 karto didesne komplikacijų rizika.

Laboratoriniai markeriai

Kalbant apie laboratorinius rodiklius, vitamino D koncentracija žemiau 20 ng/ml siejama su 2,1 karto padidėjusia ankstyvos mirštamumo rizika. Padidėjęs pradinės NT-proBNP lygis atitinka 2,3 karto padidėjusią ankstyvos mirties riziką ir 2,6 karto didesnę komplikacijų riziką. Aukštesnis pradinio CRB lygis taip pat susijęs su didesne ankstyvųjų komplikacijų tikimybe. Amžius ir gretutinės ligos yra gerai žinomi ankstyvos mirštamumo rizikos veiksniai ŠAL pacientams, todėl kiekybinis jų įvertinimas mūsų tyrime yra svarbus kaip įrodantis reprezentatyvią kohortą.

NT-proBNP slenkstį 781 ng/L taikėme remdamiesi *Zhang ir kt.* rezultatais, autorius įvertino 1354 pacientus ir nustatė šią vertę kaip prognozuojančią bendrą mirštamumo riziką [1]. Nors jų vidutinis stebėjimo laikotarpis buvo 34 mėnesiai ir slenkstis daugiausia susijęs su vidutinės trukmės mirštamumu, mūsų tyrimas parodė jo taikomumą ankstyvajai mirčiai mūsų kohortoje. Tyrimų, vertinusių NT-proBNP prognozines galimybes ŠAL pacientams, yra nedaug. Nepaisant metodologinių skirtumų, vieni nustato slenkstines vertes, kiti kategorizuoja pacientus pagal kvartilius ar tertilius, konsensusas rodo, kad pro-BNP koncentracijos, viršijančios 741–842 ng/L, yra vertingi mirštamumo prognozuotojos ŠAL pacientams ir NT-proBNP koncentracijos tyrimas turėtų būti rutininis [48,49].

Mūsų tyrimo rezultatai sutampa su ankstesniais darbais — žemi vitamino D kiekiai kraujyje turi prognostinę vertę ankstyvai mirčiai po šlaunikaulio artimojo galo lūžio [23,50,51]. Vitamino D trūkumo apibrėžimai literatūroje labai skiriasi; naudotos tokios klasifikacijos: 1) sunkus (<10 ng/ml), vidutinis (10–19,9 ng/ml), nepakankamas (20–29,9 ng/ml) ir normalus (≥30 ng/ml); 2) <50 nmol/l; 3) deficitinis <12 ng/ml, nepakankamas 12–<20 ng/ml; 4) nepakankamumas 20–<30 ng/ml ir normalus ≥30 ng/ml. Mes panaudojome <20 ng/ml vien dėl metodologinių priežasčių. Tiksli patofiziologija, kaip vitamino D koncentracija veikia ankstyvą mirštamumą, nėra pilnai suprantama, tačiau galimi keli mechanizmai. Rasta, kad vitaminas D koreliuoja neigiamai su albumino lygiu; abu rodikliai gali rodyti blogą mitybą ir sarkopeniją, vedančią prie neigiamų rezultatų. Kita vertus, abu yra neigiami ūminio fazės reaktantai ir gali atspindėti ūmios uždegimo fazės disbalansą [24,37,45]. Abu mechanizmai palaikomi atradimu, kad albumino lygis veikia kaip konfounderis, vertinant vitamino D prognostinę vertę [51]. Svarbus aspektas — vitamino D koncentracija yra modifikuojamas rizikos veiksnys ir į jį reikėtų koreguoti gerokai prieš įvykstant lūžiui.

Tiek priešoperaciniai, tiek pooperaciniai C-reaktyvaus baltymo lygiai anksčiau buvo identifikuoti kaip ankstyvos ir vienerių metų mirštamumo prognozuotojai po ŠAL operacijos [43,44]. Mūsų tyrime priešoperacinis CRB siejosi su ankstyvomis komplikacijomis; tačiau statistiškai reikšmingų rezultatų dėl jo gebėjimo prognozuoti ankstyvą mirštamumą nenustatėme. Reikia pažymėti, kad ankstesni tyrimai apie ankstyvą mirštamumą dažniau buvo retrospektyvūs ir naudojo mažesnes imtis nei šis tyrimas [44]. Be to, mūsų kohortoje buvo tik pacientai su ūmiais lūžiais (hospitalizuoti per 72 val. po traumos), tai galėjo lemti žemesnius stebėtus CRB lygius. Metodologiniai skirtumai ir skirtingi ribiniai taškai taip pat gali paaiškinti neatitikimus tarp tyrimų. Kadangi sisteminis uždegimas pripažįstamas kaip prognozinis

veiksnys ŠAL rezultatams, mūsų pastebėjimas, kad CRB neprognozuoja ankstyvos mirštamumo, turėtų būti laikomas negalutiniu.

Uždegiminis atsakas

Intrakapsulinių ir ekstrakapsulinių ŠAL pooperacinis uždegiminis atsakas yra menkai ištirtas — mūsų tyrimo metu literatūroje duomenų buvo nedaug. Mūsų tyrimo rezultatai rodo, kad gydytojai turėtų būti budrūs dėl pooperacinio uždegiminio atsako, ypač pacientams su subtrochanteriniais lūžiais. Šie lūžiai susiję su reikšmingai aukštesniais pooperacinėmis CRB koncentracijomis palyginti su šlaunikaulio kaklo ir intertrochanteriniais lūžiais — tai reikšmingas ir unikalus mūsų tyrimo stebėjimas. Subtrochanterinių lūžių chirurginis gydymas dažniausiai apima ilgus proksimalinius vinis ir atvirą repoziciją, o intertrochanteriniai lūžiai dažniau gydomi uždarai su trumpais proksimaliniais vinimis. Šie skirtingi chirurginiai metodai reikalauja „lūžio specifinio“ požiūrio ir greičiausiai veikia ŪFA po operacijos. Ši sąsaja tarp lūžio tipo ir chirurginio metodo sukuria galimą problemą: ne tik pats subtrochanterinis lūžis, bet ir jo specifinis chirurginis priėjimas keičia ŪFA, tačiau šiuo atveju lūžio ir operacijos tipai yra neatskiriami.

Intrakapsulinių lūžių (THA, HA, CS) chirurginiai būdai buvo susiję su žemesnėmis CRB koncentracijomis, palyginti su ekstrakapsulinių lūžių (PFN, DHS) metodais. Kadangi pradinis CRB tarp lūžio tipų ženkliai nesiskyrė, rezultatai rodo, kad pooperacinį ŪFA labiau lemia operacijos tipas nei pats lūžis.

Sukūrėme daugiamatės regresijos modelius, siekdami ištirti galimus konfounderius, darančius įtaką CRB reikšmėms. Modeliai, įtraukę lūžio tipą, amžių ir gretutines ligas, parodė, kad THA ir HA buvo reikšmingi pirmos pooperacinės dienos CRB prognozuotojai, tačiau šis reikšmingumas sumažėjo koreguojant pagal amžių. Šis veiksnys neišliko vertinant CRB 3–4 pooperacinėmis dienomis, o gretutinių ligų skaičius neturėjo poveikio. Lūžio tipas išliko statistiškai reikšmingas CRB prognozuotojas tiek 1-os, tiek 3–4-os pooperacinės dienos matavimuose, neįtakojamas korekcijos pagal amžių ar gretutines ligas. Mūsų duomenys rodo, kad amžius yra konfounderis tarp chirurginio metodo (THA/HA) ir ankstyvo pooperacinio CRB, tai atitinka faktą, kad THA paprastai atliekamas jaunesniems, aktyvesniems pacientams nei HA.

Nereikėtų tikėtis normalių CRB reikšmių pacientams po ŠKL. Mūsų tyrimas parodė: 1) priėmimo metu 48,3 % pacientų turėjo CRB > 5 mg/l, 35,3 % — > 10 mg/l; 2) pirmą pooperacinę dieną 83,5 % pacientų turėjo CRB > 5

mg/l, 80,5 % > 10 mg/l, o 18,8 % viršijo 100 mg/l; 3) 3.–4. pooperacinę dieną atitinkamai 82,8 % ir 81,7 % pacientų išliko virš atitinkamų ribų. Siekdami tikslesnio normalaus ŪFA įvertinimo, analizėje specialiai pašalinome visus pacientus su infekcinėmis komplikacijomis.

Apskritai stebėjome, kad ekstrakapsuliniai klubo lūžiai sukelia didesnį ŪFA nei intrakapsuliniai — tai buvo unikalus mūsų tyrimo atradimas. Tai matoma ne tik CRB, bet ir albumino (neigiamo ŪFA reaktanto) reikšmėse — intrakapsulinėse grupėse albumino koncentracija buvo reikšmingai aukštesnė nei ekstrakapsulinėse. Reikia turėti omenyje, kad hipalbuminemija yra dažna vyresnio amžiaus pacientų problema — mūsų imtyje ji siekė 14,4 % (albuminas < 35 g/l).(43,45,52) Visi pacientai buvo ≥65 metų, todėl manyta, kad šis veiksnys paveikė imtį tolygiai, o skirtumas tarp grupių atsirado dėl ŪFA.

Ankstesni tyrimai rodė, kad CAR prognozuoja 30 dienų ir 1 metų mirštamumą po klubo lūžio [26,27]. Kadangi CAR atspindi santykį tarp teigiamo ŪFA reaktanto (CRB) ir neigiamo reaktanto (albumino), logiška, kad indeksas atspindi ŪFA disreguliaciją, susijusią su blogesniais rezultatais [33,34]. Šio tyrimo tikslas nebuvo vertinti ilgalaikius rezultatus, tačiau mes pastebėjome modelį — pacientams su subtrochanteriniais lūžiais prieš operaciją buvo reikšminga hipalbuminemija ir po operacijos reikšmingai padidėję CRB lygiai palyginti su kitais lūžio tipais. Mūsų apskaičiuotas CAR sudarytas iš bazinių (priešoperacinių) verčių; statistiškai reikšmingų skirtumų neradome, tačiau priešoperacinė hipalbuminemija ir pooperacinis CRB padidėjimas gali rodyti, kad subtrochanteriniai lūžiai susiję su ŪFA disreguliacija ir prastesniais rezultatais — ši hipotezė reikalauja tolesnių tyrimų.

Mūsų rezultatai sutampa su ankstesniais tyrimais, pabrėžiančiais sąveiką tarp ŪFA reaktantų, ypač neigiamą priešoperacinio CRB ir albumino koreliaciją [24,37,45]. Tyrimas papildomai parodė reikšmingą neigiamą ryšį tarp CRB ir vitamino D, tema, kuri pastaruoju metu sulaukia didėjančio dėmesio. Anksčiau literatūra siūlė, kad vitaminas D gali elgtis kaip neigiamas ŪFA reaktantas — mūsų rezultatai tai patvirtino. Pvz., *Zhao ir kt*. pranešė apie aukštesnius vitamino D lygius pacientams su paprastesniais lūžio tipais palyginti su sudėtingesniais, kas gali sietis su traumos sunkumu[53]. Mūsų tyrime vitamino D reikšmės tarp lūžio tipų nesiskyrė ir nekoregavo su albuminu, todėl galime tik siūlyti, kad vitaminas D gali būti neigiamas ŪFA reaktantas.

Atkreiptinas dėmesys į didelį vitamino D trūkumo dažnį — 75,4 % pacientų turėjo nepakankamą lygį, kas pabrėžia vitamino D papildų vartojimo svarbą vyresnio amžiaus populiacijoje.

Reikšmingai didesnės fibrinogeno koncentracijos intrakapsuliniuose lūžiuose, stebėtos šiame tyrime, gali būti labiau susijusios su krešėjimo procesu nei su ŪFA. Pastebėjome, kad ekstrakapsulinių lūžių pacientai turėjo reikšmingai žemesnį hemoglobino kiekį nei intrakapsuliniai ($p < 0,001$), tai gali reikšti didesnį fibrinogeno sunaudojimą kraujavimui sustabdyti subtrochanterinių lūžių atvejais. Be to, fibrinogeno koncentracija paprastai maksimaliai kyla po mažiausiai dviejų dienų nuo ŪFA pradžios; kadangi mūsų tyrime pooperacinio fibrinogeno nevertinome, tai yra vienas iš darbo apribojimų.

IŠVADOS

1. Rekomenduojame naudoti Notingemo lūžių rizikos skaičiuotuvą 30 dienų mirštamumo rizikos vertinimui pacientams, kurie patyrė šlaunikaulio kaklo lūžius. ŠAL atveju – nė vienas modelis nerodė stiprios prognostinės reikšmės. Mūsų kohortoje CRB/albumino santykis parodė prastą prognostinę reikšmę tiek mirštamumo, tiek komplikacijų rizikos atžvilgiu.
2. Nors ACS NSQIP skaičiuotuvas pasirodė, kaip efektyvus ankstyvo mirštamumo prognozuotojas ŠAL pacientams, tačiau jo gebėjimas prognozuoti specifines komplikacijas buvo nepakankamas. Kadangi skaičiuotuvas yra nuosekliai atnaujinamas, jo efektyvumas turėtų būti vertinamas pakarotinai ateityje.
3. Antikoaguliacinė terapija tiesiogiai nepadidino 30 dienų pooperacinių komplikacijų ar mirštamumo, tačiau buvo susijusi su chirurginių intervencijų atidėjimais ir ilgesnėmis hospitalizacijomis.
4. Bet kokios komplikacijos atsiradimas 5,6 karto padidino 30 dienų mirštamumo riziką ŠAL pacientams. Tik kardiologinės komplikacijos buvo reikšmingos ankstyvo mirštamumo prognozuotojos. Pacientams, vyresniems nei 85 m., ankstyvo mirštamumo rizika padidėja 2,2 karto, o pooperacinių komplikacijų tikimybė – 1,7 karto. Daugiau nei šešios gretutinės ligos siejamos su 8,2 karto didesne ankstyvos mirties rizika ir 2,3 karto padidėjusia komplikacijų rizika. Rekomenduojama visiems ŠAL pacientams atlikti NT-proBNP koncentracijos tyrimą rutiniškai. Visi pacientai turėtų gauti pakaitinė vitamino D terapiją.
5. Ekstrakapsuliniai ŠAL po operacijos sukelia stipresnį ūminį fazės atsaką nei intrakapsuliniai. Lūžio morfologija daro didesnį poveikį ŪFA nei operacijos tipas. Vitaminas D nustatytas kaip neigiamas ūminės fazės reaktantas. ŠAL pacientams nereikėtų tikėtis normalių CRB ir vitamino D koncentracijų.

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SANTRAUKOS

Įžanga. Prognozuojama, kad iki šio amžiaus vidurio pasaulyje kasmet apie 6 milijonai žmonių patirs artimojo šlaunikaulio galo lūžius. Šių pacientų 30 dienų mirštamumas siekia apie 14 %, o pooperacinių komplikacijų dažnis – iki 40 %. Dėl senyvo amžiaus ir poliligotumo tikslus prieš operacinis rizikos vertinimas yra svarbus gydymo planavimui, pacientų informavimui ir didžiausios rizikos pacientų identifikavimui.

Darbo tikslas. Įvertinti pooperacinių rizikos skaičiuoklių, klinikinių veiksnių ir laboratorinių žymenų tikslumą prognozuojant ankstyvąsias komplikacijas ir 30 dienų mirštamumą pacientams po ŠAL lūžių bei apibūdinti ūminės uždegimo fazės atsaką.

Tyrimo metodai. Perspektyviniame tyrime dalyvavo 583 vyresni nei 65 metų pacientai (452 (77.5%) moterys ir 131(22.5%) vyras), operuoti dėl ŠAL lūžio. 292 (50.1%) stebėti šlaunikaulio kaklo, 259 (44.4 %) pertrochanteriniai ir 32 (5.5 %) subtrochanteriniai lūžiai. Vertintos 30 dienų pooperacinės baigtys. Ankstyvojo mirštamumo ir komplikacijų rizika apskaičiuota naudojant Notingamo lūžių įvertį (NHFS) ir ACS NSQIP chirurginės rizikos skaičiuotuvą. Analizuoti demografiniai, klinikiniai ir laboratoriniai rodikliai, įskaitant NT-proBNP, C reaktyvųjį baltymą, vitaminą D, albuminą, fibrinogeną bei CRB ir albumino santykį.

Rezultatai. Bet kokios komplikacijos padidino 30 dienų mirštamumo riziką 5,6 karto (p = 0,008), o iš atskirų komplikacijų reikšmingą ryšį parodė tik širdies įvykiai (ŠS 3,6; p = 0,010). Prognozuojant 30 dienų mirštamumą, geriausiai pasirodė NHFS (AUC 0,731) ir ACS NSQIP (AUC 0,724), o CAR prognostinė vertė buvo menka (AUC 0,623). Pacientams, patyrusiems šlaunikaulio kaklo lūžį, NHFS tikslumas padidėjo iki AUC 0,858. Daugiau nei šešios gretutinės ligos, vyresnis nei 85 metų amžius ir NT-proBNP >780 ng/l buvo nepriklausomi ankstyvojo mirštamumo ir komplikacijų rizikos veiksniai. CRB >10 mg/l prognozavo didesnę komplikacijų riziką. Prieš operacinis CRB neigiamai koreliavo su albumino ir vitamino D koncentracijomis. Antikoaguliantus vartoję pacientai ilgiau laukė operacijos ir buvo ilgiau hospitalizuoti, tačiau tai nepadidino pooperacinių komplikacijų rizikos.

Išvados. NHFS rekomenduojama naudoti vertinant 30 dienų mirštamumo riziką pacientams, patyrusiems šlaunikaulio kaklo lūžį. Didesnis gretutinių ligų skaičius, vyresnis amžius, širdies komplikacijos ir padidėjusi NT-proBNP koncentracija buvo svarbiausi ankstyvojo mirštamumo prognozuotojai. Rekomenduojama rutininiu būdu tirti NT-proBNP koncentraciją. Vitaminas

D nustatytas kaip neigiamas ūminės fazės reaktantas. Nereikėtų tikėtis normalių vitamino D ir CRB koncentracijų ŠAL pacientams. Kiekvienas pacientas turėtų gauti pakaitinę vitamino D terapiją.

Introduction. It is projected that by the middle of this century, approximately 6 million people worldwide will sustain proximal femoral fractures annually. The 30-day mortality rate among these patients is approximately 14%, while the incidence of postoperative complications is as high as 40%. Due to advanced age and multimorbidity, accurate preoperative risk assessment is important for treatment planning, patient counselling, and identification of patients at the highest risk.

Aim of the study. To evaluate the accuracy of postoperative risk calculators, clinical factors, and laboratory biomarkers in predicting early complications and 30-day mortality in patients following proximal femoral fractures, and to characterize the acute-phase inflammatory response.

Methods. This prospective study included 583 patients older than 65 years (452 [77.5%] women and 131 [22.5%] men) who underwent surgery for a proximal femoral fracture. Of these, 292 (50.1%) had femoral neck fractures, 259 (44.4%) had pertrochanteric fractures, and 32 (5.5%) had subtrochanteric fractures. Postoperative outcomes within 30 days were assessed. The risk of early mortality and complications was calculated using the Nottingham Hip Fracture Score and the ACS NSQIP Surgical Risk Calculator. Demographic, clinical, and laboratory parameters were analysed, including NT-proBNP, C-reactive protein (CRP), vitamin D, albumin, fibrinogen, and the CRP-to-albumin ratio (CAR).

Results. The occurrence of any complication increased the risk of 30-day mortality 5.6-fold ($p = 0.008$), while among individual complications, only cardiac events showed a significant association (HR 3.6; $p = 0.010$). In predicting 30-day mortality, the NHFS (AUC 0.731) and ACS NSQIP (AUC 0.724) performed best, whereas the prognostic value of CAR was limited (AUC 0.623). In patients with femoral neck fractures, the accuracy of the NHFS increased to an AUC of 0.858. More than six comorbidities, age over 85 years, and NT-proBNP >780 ng/L were independent risk factors for early mortality and complications. CRP >10 mg/L predicted a higher risk of complications. Preoperative CRP was negatively correlated with albumin and vitamin D concentrations. Patients receiving anticoagulants had a longer time to surgery and longer hospital stays; however, anticoagulant use did not increase the risk of postoperative complications.

Conclusions. The NHFS is recommended for assessing the risk of 30-day mortality in patients with femoral neck fractures. A higher number of comorbidities, advanced age, cardiac complications, and elevated NT-proBNP concentrations were the most important predictors of early mortality. Routine measurement of NT-proBNP concentrations is recommended. Vitamin D was identified as a negative acute-phase reactant. Normal vitamin D and CRP concentrations should not be expected in patients with proximal femoral fractures. Vitamin D replacement therapy should be provided to every patient.

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Ačiū savo tėvams Jonui ir Vilmai, žmonai Agnietei ir visiems žmonėms, kurie mane lydi per gyvenimą ir tik dėl kurių esu kas esu.

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Disertantas yra visų žemiau pateiktų publikacijų pirmasis autorius, sukūrė tyrimų metodologiją, rinko duomenis, juos interpretavo ir tuo remdamasis parašė išvadas, parašė atitinkamų publikacijų rankraščius, juos suredagavo pagal leidyklų reikalavimus ir atliko visus reikalingus veiksmus rankraščių publikavimui.

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3. Masionis P, Derkintyte D, Bogdzevic EF, Bobina R, Satkauskas I. Impact of anticoagulation therapy on surgical timing, hospital stay, and postoperative outcomes in proximal femur fracture patients. Acta Orthop Traumatol Turc. 2025 Sep 12;59(5):253–8. doi:10.5152/j.aott.2025.25341

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Accuracy of the ACS-NSQIP Risk Calculator, Nottingham Hip Fracture Score and CRP/Albumin Ratio in Predicting Adverse Postoperative Outcomes in the Hip Fracture Surgery: A Lithuanian Single-Centre Prospective Study

Povilas Masionis, MD[1], Rokas Bobina, MD[1], Simonas Utkus, MD[1], Raminta Martinaitytė, MD[1], Valentinas Uvarovas, PhD[1], and Igoris Šatkauskas, PhD[1]

Abstract

Objective: As the global population ages, hip fracture importance will increase. The high postoperative mortality and morbidity necessitate tools for accurate risk assessment to aid surgical decisions and inform patients and families. This study aimed to compare and validate ACS NSQIP, Nottingham hip fracture risk calculators, and C reactive protein/albumin ratio in predicting complications and 30 day mortality.

Methods: 583 patients over the 65 years old who sustained hip fracture from simple fall and underwent surgical treatment for hip fracture were included in prospective study. Each patient was evaluated by ACS NSQIP and Nottingham hip fracture risk calculators and C reactive protein/albumin ratio was calculated from preoperative values. Patients were followed up for 30 days and all the complications were recorded.

Results: ACS NSQIP and Nottingham hip fracture score showed AUC of .724 and .731 respectively. C reactive protein/albumin ratio performed less and showed AUC of .623 that is defined as poor predictor for 30 day mortality. Furthermore, in terms of predicting any complication, ACS NSQIP showed AUC of .645, Nottingham hip fracture score of .611 and C reactive protein/albumin ratio of .594. Nottingham hip fracture score than compared to ACS NSQIP yielded lower average of mortality rates (5.4% compared to 7.9%) in contrast of study findings of 8.1%. None of the ACS NSQIP scale predictive complication showed acceptable performance. When adjusted for fracture type, Nottingham hip fracture score showed .858 AUC in predicting 30 day mortality in femoral neck fractures.

Conclusions: We recommend Nottingham fracture risk calculator use for 30 day mortality risk assessment in femoral neck fractures. In hip fractures combined—none of models showed strong discrimination. In our cohort C reactive protein/albumin ratio showed poor prognostic values in terms of mortality and complications.

Keywords

hip fracture, hemiarthroplasty, total hip arthroplasty, osteosynthesis, mortality

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Introduction

It is predicted that by the middle of the century, approximately 6 million people worldwide will sustain hip fractures (HF) annually.[1] As the global population ages, the significance of this condition will continue to grow. HF patients are known to experience up to 14% early mortality and up to 40% post-operative complications.[1-6] These poor outcomes are attributed to factors such as age, high morbidity (including hypertension, diabetes, obesity, heart failure, osteoporosis, etc.), smoking, alcohol abuse, malnutrition. Due to these reasons, HP is often regarded as "the last fracture of whole life".[1,7-9] Despite some studies showing a decreasing incidence in Northern countries and stabilisation in Central Europe, the rate of complications and treatment costs are expected to rise.[10]

Given the fragility of these patients, accurate preoperative assessment of mortality and morbidity risk following HF is essential to modern treatment.[5,11] This assessment not only aids in determining the timing of surgery and providing appropriate information to the patient and their family but also identifies patients at the highest risk who require perioperative interventions.[1-14] Understanding the risk of surgery is crucial for both the patient and the surgeon.

To address these concerns, risk calculators has been introduced. The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) surgical risk calculator is a unique tool designed to predict 18 different procedure-specific outcomes based on The Current Procedural Terminology (CPT) codes.[3,5,14-18] However, its performance in HF patients is understudied. Additionally, C reactive protein/albumin ration (CAR) has previously been found to predict 30 day and 1 year mortality and morbidity in various pathologies, but its effectiveness compared to risk calculators in HF patients is unknow.[19-22]

In 2007, Nottingham hip fracture score (NHFS) was introduced and has shown reliability in predicting 30 day and 1 year mortality in HF. The NHFS was used as a control measure in the present study.[23-25]

The objective of this study was to assess and validate the ACS NSQIP, NHFS surgical risk calculators and CAR index in predicting complications and 30 day mortality among HF patients.[26]

Table 1. General information on patients.

Variables	
Gender (female/male)	452 (77.5%)/131 (22.5%)
Age	82 ± 8
Number of comorbidities	6 ± 3
Fracture type	
Neck	292 (50.1%)
Pertrochanteric	259 (44.4%)
Subtrochanteric	32 (5.5%)
Surgery type	
Hip hemiarthroplasty	191 (32.8)
Total hip arthroplasty	70 (12.0%)
Proximal femoral nail	236 (40.5%)
Dynamic hip screw	69 (11.8%)
Cannulated screws	17 (2.9%)

Methods

The manuscript was written according to STROBE guidelines. The prospective study was conducted in a tertiary orthopaedic trauma centre from December 1, 2022, to December 31, 2023. All patients or their proxies provided informed consent to participate in the study, which was approved by the Institutional Review Board of our hospital and the regional bioethics committee. The inclusion criteria were as follows: ≥65 years patients; intertrochanteric fracture; subtrochanteric fracture; femoral neck fracture; patients who underwent surgical treatment; low energy trauma (simple fall); closed fractures; isolated trauma; acute trauma. All surgical interventions were performed or supervised by a consultant orthopaedic surgeon. After surgery, patients were followed-up for 30 days. At the 30th day, patient or his proxy was contacted by the investigator for interview. Additionally, patient's electronic medical history was examined. The following serious complications were registered: pneumonia, cardiac complications, surgical site infection, urinary tract infection, deep venous thrombosis, acute renal failure, readmission, reoperation, death, sepsis, delirium, and pressure sores. For any complication, we recorded any additional intervention or consultation that deviated from the normal treatment pathway. Furthermore, time from trauma to hospitalization, time from hospitalization to surgery, in-hospital stay, functional decline, new mobility aid, and discharge to a nursing home were recorded. General information on patients is presented in Table 1. Final sample size of 583 patients is presented in flow chart Figure 1. Upon admission, ACS NSQIP and NHFS scores were calculated. For CAR, pre-operative values of C reactive protein (CRP) and albumin were used. In our cohort we used NHFS to validate it and furthermore, as a control for ACS NSQIP and CAR performance.

All analyses were conducted using IBM SPSS version 26.0 software (SPSS Inc, Chicago, IL) for Windows. Normally distributed data are presented as mean (±standard deviation). Non normally distributed data are presented as median (25-75th IQR). Shapiro-Wilk test was used to assess the normality of data distribution. Discrimination in this study was evaluated using the area under the receiver operating characteristic (ROC) curve, also known as the AUC or c-statistic. The AUC ranges from 1.0 (perfectly discriminating model) to 0.5 (no better than chance). An AUC of 0.6-0.69 indicates poor discrimination, 0.7-0.79 indicates adequate discrimination, 0.8-0.89 indicates strong discrimination, and 0.9-1.0 indicates excellent discrimination.

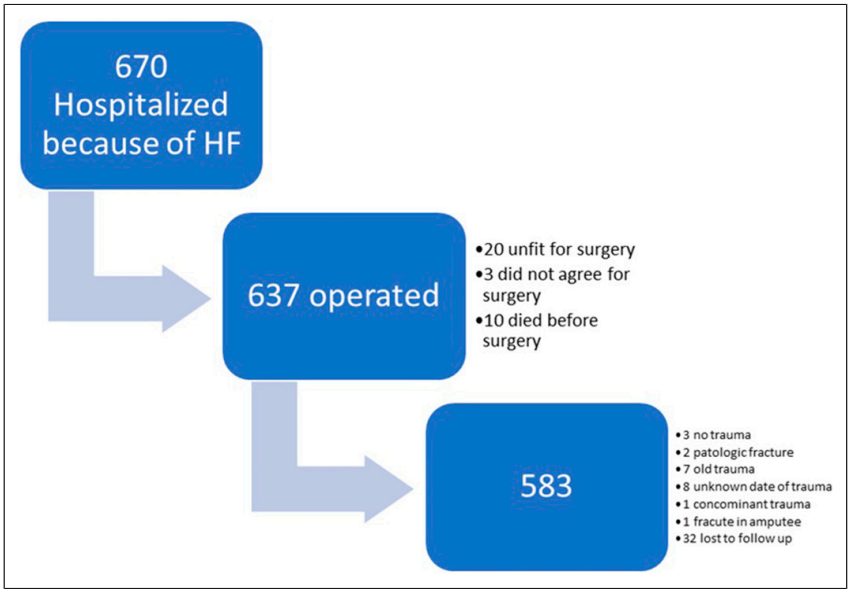

Figure 1. Final Sample Size of Included Patients

Results

Frequencies of complications are presented in Table 2. ACS NSQIP and NHFS showed AUC of .724 and .731 respectively (Figure 2). To continue, CAR performed less and showed AUC of .623 that is defined as poor predictor for 30 day mortality (Table 3.). Furthermore, in terms of predicting any complication, ACS NSQIP showed AUC of .645, NHFS of .611 and CAR of .594—none of risk calculators showed adequate predicting power and CAR prediction of any complication was not better than chance (Figure 3). NHFS than compared to ACS NSQIP yielded lower average of mortality rates (5.4% compared to 7.9%) in contrast of study findings of 8.1%. None of the ACS NSQIP scale predictive complication showed acceptable performance, AUC values are presented in Table 4. When adjusted for fracture type, NHFS reached AUC of .858 in predicting 30 day mortality, CAR and ACS NSQIP tested for fracture type remained in the same reliability margins.

Table 2. Frequencies of complications.

Variables	
Serious complication	207 (35.5%)
Any complication	287 (49.2%)
Pneumonia	66 (11.3%)
Cardiac complication	68 (11.7%)
Surgical site infection	20 (3.4%)
Urinary tract infection	58 (9.9%)
Deep venous thrombosis	7 (1.2%)
Acute renal failure	26 (4.5%)
Readmission	62 (10.6%)
Reoperation	11 (1.9%)
Death	47 (8.1%)
Discharge to nursery	269 (46.1%)
Sepsis	10 (1.7%)
Delirium	59 (10.1%)
Functional decline	406 (69.6%)
New mobility aid	556 (95.4%)
Pressure sores	51 (8.7%)

Discussion

Surgical risk calculators are highly valuable tools that enhance the understanding of patients and their families, as well as assist in making surgical decisions based on numerical data. In our cohort, none of the models demonstrated excellent discrimination results (AUC >.80) in predicting 30 day mortality and morbidity among HP patients. Since the AUC is greater than 0.7, both the ACS NSQIP and NHFS are effective predictors of 30 day mortality. Only after adjusting for fracture type, did the NHFS show excellent discrimination for 30 day mortality in patients with femoral neck fractures. It should also be noted that the NHFS predicted a lower mortality rate than what was observed in the current study.

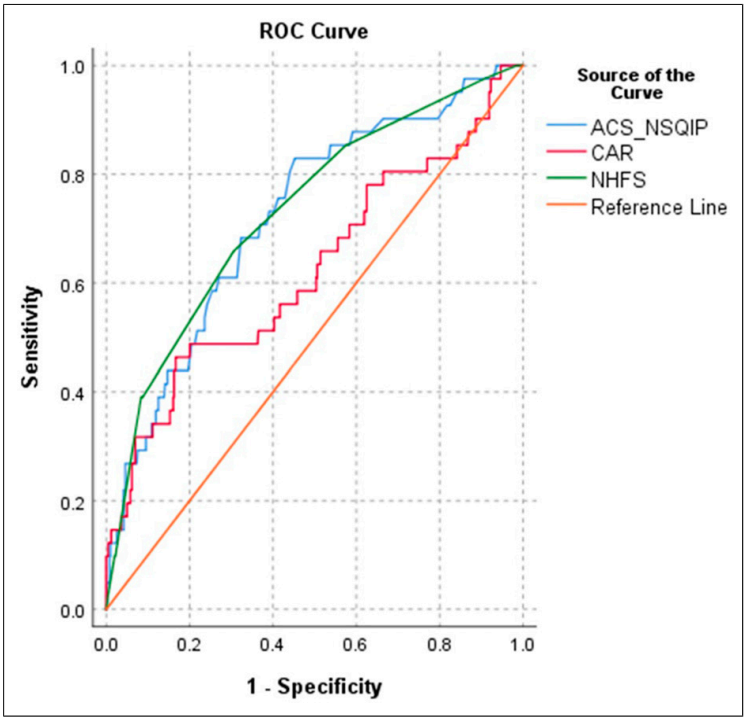

Figure 2. Receiver Operating Characteristics (ROC) of the The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) Surgical Risk Calculator, Nottingham Hip Fracture Score (NHFS) and C Reactive Protein/ Albumin Ration (CAR) for Prediction of 30 day Mortality

To our knowledge, this is the first study to compare CAR to risk calculators in the same cohort. CAR was ineffective in predicting early mortality and even worse in predicting morbidity in our study. This result contrasts with findings in the literature: Cacciola et al found CAR .816 as a reliable predictor, and Balta et al reported an AUC of .727 for intertrochanteric fractures.[22,27] It is important to note that both previous studies were retrospective, and at the time of writing, we did not identify any prospective study ROC analysis of CAR in HF patients. Additionally, the timing of CRP sample collection might be crucial—we only included acute fractures, and in this scenario, CRP may not be elevated. However, this hypothesis needs further investigation. Although CAR has been identified as a valuable predictor in various pathologies, our results indicate that its capabilities are understudied in HF patients.

ACS NSQIP is a recent tool that utilizes procedure-specific prediction based on CPT code. The calculator has been shown to be a reliable predictor in various fields of elective and emergency settings. ROC analysis indicates it is adequate predictor of 30 day mortality; however, its ability to predict specific complications is limited, which is a notable drawback in our settings. Additionally, ACS NSQIP was developed using patient data exclusively from United States NSQIP hospitals, which may contribute to its poor discrimination in other countries.[3] Nonetheless, this tool is continuously updated and should be evaluated over time as its design shows significant potential.

The ACS NSQIP calculator was developed from the National Surgical Quality Improvement Program (NSQIP) data to enhance surgical care quality in the USA. Harris et al[11] later created the Hip Fracture Surgery Risk Calculator using the same data, available at https://s-spire-clintools.shinyapps.io/hip_deploy/. The model predicts 30-day mortality with an AUC of .76. Depending on the mortality risk threshold, its sensitivity and specificity vary: a 15% threshold shows 97% specificity and 78% sensitivity. These results suggest that while the model is predictive, it may overestimate mortality for some patients who could benefit from surgery. Surgeons should consider this when making treatment decisions with patients. We did not analyse this model as it was unavailable during development of our study. The author also suggested analysing the performance of risk calculators on patients who were not operated, which

Table 3. AUC and p values of risk calculators performances in prediction of death and any complication.

	ACS NSQIP	NHFS	CAR
Death	.724 (.642-.805) *P* < .001	.731 (.648-.815) *P* < .001	.623 (.521-.725) *P* = 018
Any complication	.645 (.599-.691) *P* < .001	.611 (.564-.658) *P* < .001	.594 (.547-.642) *P* <001

has not been done to our knowledge in literature and is 1 of the limitations of our study.

Originally, NHFS was developed to assess the risk for all types of proximal femur fractures. However, intracapsular fractures have been found to have higher mortality and morbidity than compared to extracapsular ones.[23-25] This suggests that NHFS could be used for mortality risk stratification for femoral neck fractures in our settings. Moreover, NHFS is a reliable predictor and easy to use, as it only requires preoperative data. To continue, as NHFS inputs objective values, it should be less vulnerable to cultural and social differences among different populations. However, external validation in each country should be conducted before its use.

The observed complication rate in our cohort was 49.2%, which aligns with the 12.5–75% range reported in the literature.[2] The variation in complication rates found in the literature is largely due to differences in study methodologies—retrospective studies typically report lower complication rates compared to prospective studies.[2,28] Additionally, follow-up times vary across the literature and should be considered. Furthermore, complications are documented differently across studies. In our study, we registered serious complications according to the ACS NSQIP questionnaire, and for any complication, we recorded every event requiring additional intervention or consultation that deviated from the normal treatment pathway. This methodology for documenting

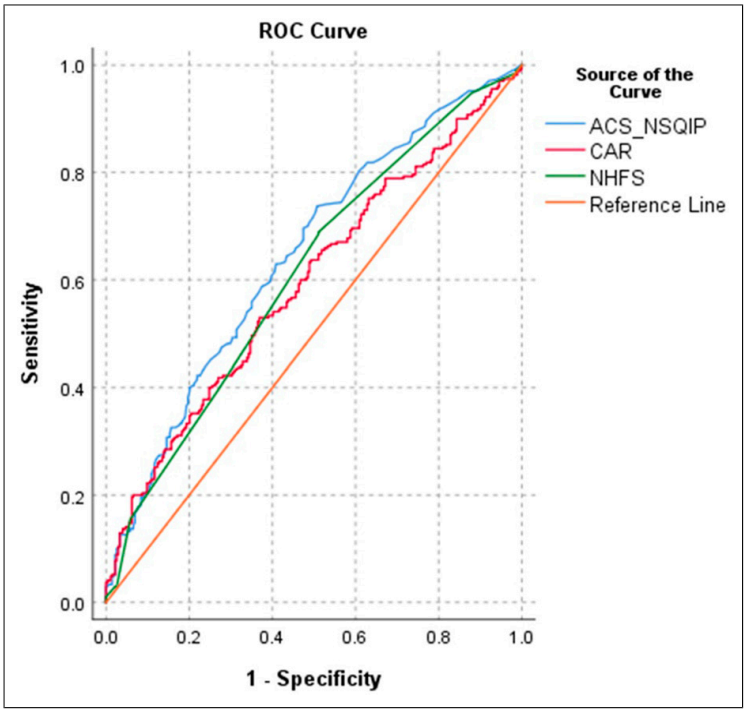

Figure 3. Receiver Operating Characteristics (ROC) of the The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) Surgical Risk Calculator, Nottingham Hip Fracture Score (NHFS) and C Reactive Protein/Albumin Ration (CAR) for Prediction Of Any Complication

Table 4. AUC and p values of ACS NSQIP risk calculator performance in predicting complications.

	ACS NSQIP AUC (CI) and *P* value
Pneumonia	.688 (.619-.757) *P* < 000
Cardiac complications	.669 (.603-.735) *P* < 000
Surgical site infection	.628 (.482-.773) *P* = .087
Urinary tract infection	.571 (.487-.655) *P* = .097
Deep venous thrombosis	.473 (.226-.720) *P* = .830
Acute renal failure	.668 (.543-.794) *P* = .008
Readmission	.497 (.418-.575) *P* = 933
Reoperation	.643 (.498-.787) *P* = .053
Discharge to nursery hospital	.467 (.420-.514) *P* = .172
Sepsis	.643 (.465-.822) *P* = .114
Delirium	.655 (.578-.732) *P* < .000
Pressure sores	.523 (.474-.571) *P* = .356
New mobility aid	.598 (.509-.687) *P* = .030
Functional decline	.625 (.550-.700) *P* = .001

all complications may have increased our reported complication rate. Generally, HF patients should be expected to experience complications, and they and their relatives must be properly informed about this possibility. Considering that NHFS uses fewer preoperative values, it is easier to use compared to ACS NSQIP. In our cohort, NHFS demonstrated strong discrimination in predicting 30 day mortality in intracapsular fractures. Based on these findings, NHFS is recommended for risk stratification in femoral neck fractures within our settings. Additionally, the results indicate that intracapsular and extracapsular proximal femur fractures, which require different surgical approaches, might benefit from fracture-specific risk calculators.

As with all studies, this study has limitations. Firstly, it is a single-centre study of 1 hospital cohort, we cannot confirm that the same results would apply to the entire population. Secondly, we only included risk calculators specific to hip fractures and excluded tools popular in other surgical fields (eg, P-POSSUM, E-PASS, Clarkson comorbidity index). These calculators were excluded purely for methodological reasons—expanding study requires additional human resources and working time. Additionally, recent tools such as the Hip Fracture Surgery Risk Calculator were not available at the time of the study but should be considered for comparison in future research.[2] Lastly, the tools should be evaluated for their sensitivity and specificity.

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Ethical Approval

The study was approved by the Institutional Review Board of Republic Vilnius University Hospital and Vilnius Regional Biomedical Research Ethics committee.

Patient Consent

All patients or their proxy gave their informed consent to participate in the study.

Author Contributions

PM conceptualized the present study, collected, analyzed and interpreted the data, performed statistical analysis, interpreted the results and drafted manuscript; RB, SU, RM, VU and IŠ collected, analyzed and interpreted the data, interpreted the results. The manuscript was reviewed by all authors. Finally, all authors read and approved the final manuscript for publication.

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Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Original Article

Characterizing the Acute Phase Response in Hip Fracture Patients

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SUMMARY

Background: The acute phase response (APR) is systemic body reaction to tissue injury, and its dysregulation leads to poor outcomes. Acute phase reactants exhibit a lot of variation, which makes differential diagnosis difficult – especially in fragile patients. The aim of the present study is to describe the perioperative acute phase response kinematics in hip fracture patients.
Materials and methods: 431 hip fracture patients over 65 years old who underwent surgical treatment were included in a prospective study. Pre-operative C reactive protein, albumin, vitamin D, and fibrinogen concentrations and C reactive protein of the 3–4th day post-operatively were obtained. Patients were followed up for 30 days and all infectious complications were removed.
Results: The admission C-reactive protein (CRP) levels exhibited a statistically significant negative correlation with both albumin ($p = .038$) and vitamin D ($p = .021$). On the first post-operative day, patients with femoral neck fractures showed statistically significantly lower CRP levels compared to those with intertrochanteric ($p = .046$) and subtrochanteric ($p = .007$). This pattern persisted on the 3rd–4th post-operative days ($p < .001$). Hemiarthroplasty, total hip arthroplasty, and cannulated screws groups demonstrated statistically lower post-operative CRP values compared to the dynamic hip screw ($p < .001$, $p < .001$, $p = .024$) and proximal femoral nail groups ($p < .001$, $p < .001$, $p = .024$).
Conclusions: Surgeries for extracapsular hip fractures are associated with a greater acute phase response compared to surgeries for intracapsular fractures. Vitamin D was found as possible negative acute phase reactant.

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1. Background

The acute phase response (APR) is a vital systemic reaction to tissue injury, playing a crucial role in the organism ability to heal after trauma through various physiological, biochemical, and nutritional changes.[1–3] Literature indicates that both hyperactivity and hypoactivity of the APR can lead to adverse outcomes.[1,2] Biomarkers associated with the APR, such as C-reactive protein (CRP), are non-specific and exhibit significant variability, complicating differential diagnosis.[4–7] This issue is particularly important in geriatric patients with hip fractures (HF), who face complications in up to 40% of cases following surgery.[8–16] In these patients, fluctuations in APR reactants can occur due to multiple factors, including the fracture itself, surgical interventions, age related organ changes, and potential infectious complications.[4,15–21] While some studies have suggested a decrease in incidence of HP in Northern countries and a stabilization in Central Europe, the prevalence and significance of hip fractures are expected to rise as the population ages and individuals become more polymorbid. This demographic shift is likely to lead to higher complication and mortality rates among these patients.[8,10,11,22,23] Identifying alterations in APR biomarkers in hip fracture patients could facilitate more intensive monitoring, prompt early interventions, and the establishment of specialized care pathways, ultimately improving patient outcomes.

The aim of the present study was to describe perioperative APR kinematics in HF patients, considering fracture types (femoral neck, intertrochanteric, and subtrochanteric) and surgery types (hemiarthroplasty (HA), total hip arthroplasty (THA), osteosynthesis by proximal femoral nail (PFN), dynamic hip screw (DHS), and cannulated screws (CS)) during in-hospital stay. The authors propose that the APR of HF patients may differ based on the type of fracture and the specific surgical procedure performed.

2. Materials and methods

The prospective study was conducted at a tertiary orthopaedic trauma centre from December 1, 2022, to December 31, 2023. All patients or their proxies provided informed consent to participate, and the study received approval from both the Institutional Review Board of our hospital and "Vilnius Regional Biomedical Research Ethics Committee" (2022/11-1473-941). Following were the inclusion criteria: ≥ 65 years patients; intertrochanteric fracture; subtrochanteric fracture; femoral neck fracture; patients who underwent surgical treatment; low energy trauma (simple fall); closed fractures; isolated trauma; acute trauma (no more than 72 hours). Exclusion criteria were patients who had infectious complications

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(urinary infection, pneumonia, superficial or deep surgical site infection), pathological fractures, fractures without trauma, old trauma, trauma with neurovascular damage, concomitant trauma, unknown time of trauma. All patients were followed up for 30 days post-surgery. On the 30th day, the patient or their proxy was contacted to collect information regarding their condition. The final sample size consisted of 431 patients, as depicted in the flow chart (Figure 1). All surgical interventions were either performed or supervised by a consultant orthopaedic surgeon.

We routinely evaluated pre-operative white blood cell count (WBC), CRP, fibrinogen, albumin, vitamin D (25(OH)D), and fibrinogen on the day of hospitalization. Furthermore, all patients were obtained and checked on the first and 3-4th post-operative days for CRP levels. Following laboratory markers were used to evaluate the APR: CRP, fibrinogen, albumin, vitamin D. The first two are positive reactants (increases with the APR) and the last two are negative (decreases when APR is increasing). Furthermore, CRP/albumin ratio (CAR) was calculated from the pre-operative values. Previous studies have identified the CAR as a predictor of adverse outcomes across various pathologies.[20,21] Given that CAR is a ratio of positive and negative acute phase reactants, it may offer greater sensitivity within patient groups than measuring these reactants independently. To further investigate this, we included CAR in the present study. The patients were categorized based on the type of hip fracture – femoral neck (intracapsular), intertrochanteric (extracapsular), and subtrochanteric (extracapsular) – as well as the type of surgical intervention performed. Surgical interventions included hemiarthroplasty, total hip arthroplasty, osteosynthesis via proximal femoral nail, osteosynthesis via dynamic hip screw, and osteosynthesis via cannulated screws.

Pre-operative values for C-reactive protein (CRP), fibrinogen, vitamin D, and albumin were not stratified according to the type of surgery, as these biochemical markers are not influenced by the surgical procedure itself.

All analyses were performed by IBM SPSS version 26.0 software (SPSS Inc., Chicago, IL) for Windows. Normally distributed data is presented as mean (± standard deviation). Non-normally distributed data is presented as median (25–75th interquartile range (IQR)). For comparison of normally distributed data ANOVA test was used. Shapiro-Wilk test was used to evaluate the normality of data distribution. To compare non-normally distributed variables, Kruskal-Wallis test was used. In case of normally distributed data in one group and non-normally distributed data in the other, Kruskal-Wallis test was used. Furthermore, we used pairwise comparison to compare multiple groups. Pearson correlation coefficient was used to correlate scale variables and is presented in brackets with p value. Level of significance α was set as $p < 0.05$.

3. Results

General information on patients is presented in Table 1.

Table 1
Descriptive statistics of the general information on the patients and the groups.

Variables	
Gender (female/male)	333 (77.3%)/98 (22.7%)
Age	82 ± 8
Number of comorbidities	6 ± 3
Fracture type	
Femoral neck	208 (48.3%)
Pertrochanteric	199 (46.2 %)
Subtrochanteric	24 (5.6 %)
Surgery type	
Hip hemiarthroplasty (HA)	126 (29.2%)
Total hip arthroplasty (THA)	61 (14.2%)
Dynamic hip screw (DHS)	48 (11.1%)
Proximal femoral nail (PFN)	183 (42.5%)
Cannulated screws (CS)	13 (3.0%)

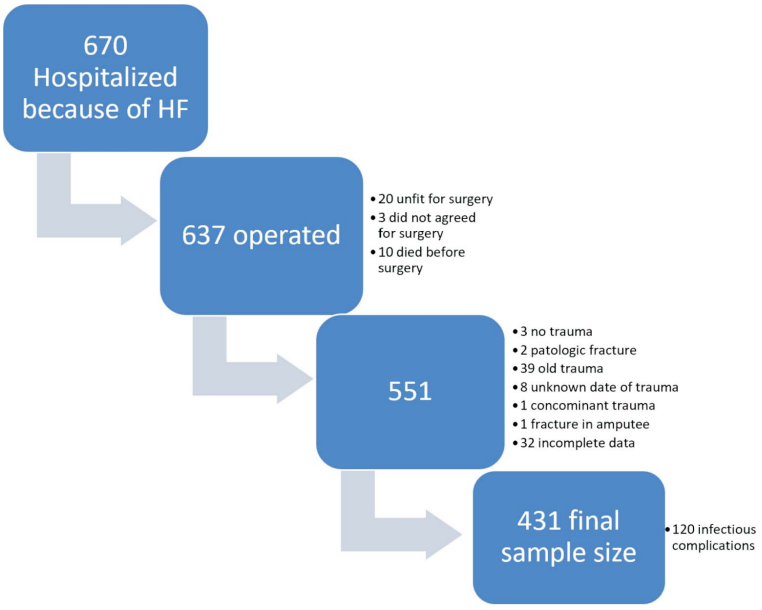

Figure 1. Flow chart of the final sample size.

Among all the patients, on admission, CRP and albumin concentration had statistically significant negative correlation (p = 0.038, Pearson coefficient = -0.108). The same statistically significant negative correlation was observed between pre-op CRP and vitamin D (p = 0.021, Pearson coefficient = -0.116). Descriptive statistics of the variables within the groups are presented in Table 2 and Table 3.

On admission, fracture type did not significantly affect CRP levels (p = 0.083). By the first post-operative day, femoral neck fractures had lower CRP than intertrochanteric (p = 0.046) and subtrochanteric fractures (p = 0.007); there was no significant difference among extracapsular fractures (p = 0.077). On days 3–4 post-op, femoral neck fractures continued to show lower CRP (p < 0.001), and intertrochanteric fractures had lower CRP than subtrochanteric fractures (p = 0.034). Intracapsular fractures had higher pre-operative fibrinogen than intertrochanteric (p = 0.025) and subtrochanteric fractures (p = 0.039), with no difference between extracapsular fractures (p = 0.308). Femoral neck fractures also showed higher albumin than intertrochanteric (p < 0.001) and subtrochanteric fractures (p = 0.020); no difference was found among extracapsular fractures (p = 0.729). Vitamin D levels did not differ significantly by fracture type (p = 0.112).

On the first post-operative day, only the THA group had significantly lower CRP levels compared to PFN (p = 0.002) and DHS (p = 0.017). This difference increased by days 3–4 (p < 0.001). At days 3–4, HA and CS also showed significantly lower CRP values than PFN (p < 0.001 and p = 0.018) and DHS (p < 0.001 and p = 0.024). Subtrochanteric fractures had significantly lower CAR than intertrochanteric (p = 0.017) and femoral neck fractures (p = 0.011).

4. Discussion

In HF patients, APR is understudied and at the time of writing, literature was spare on data. The findings of this study indicate the need for physicians to maintain a high level of awareness regarding the postoperative inflammatory response, particularly in patients with subtrochanteric fractures. These fractures are associated with significantly elevated postoperative CRP levels compared to femoral neck and intertrochanteric fractures, which is a notable and unique observation of this research. The surgical management of subtrochanteric fractures typically involves long proximal nails and open reduction, while intertrochanteric fractures are generally treated with closed reduction and short proximal nails. This difference in surgical technique necessitates a "fracture-specific" approach, which likely impacts the APR following surgery. This inherent link between fracture type and surgical approach introduces a potential bias in the study: not only subtrochanteric fracture itself, but its specific surgical approach alters APR, but in this case fracture and surgery type are inseparable. Surgical approaches for intracapsular fractures (THA, HA, CS) were associated with lower CRP values compared to those for extracapsular fractures (PFN, DHS). As there was no significant difference in baseline CRP between fracture patterns, these results suggest that the type of surgery has a greater influence on postoperative APR than the type of fracture.

We developed multivariable regression models to examine potential confounding factors influencing CRP values. Models incorporating fracture type, age, and comorbidities indicated that THA and HA were significant predictors of CRP on the first post-operative day, but this significance was reduced after adjusting for age. This trend did not persist for CRP measured on days 3–4, and number of comorbidities had no impact. Fracture type remained a statistically significant predictor of CRP on both the first and 3rd–4th postoperative days, unaffected by adjustment for age or comorbidities. Our findings suggest that age confounds the relationship between surgical procedure (THA/HA) and early post-operative CRP, which aligns with the fact that THA is typically performed on younger, more active patients than HA.

Clinically, it is important to recognize that normal CRP values should not be anticipated in patients with HF, as demonstrated by our study findings: 1. Upon admission, 48.3% of patients exhibited CRP levels exceeding 5 mg/l, with 35.3% surpassing 10 mg/l; 2. On the first postoperative day, 83.5% of patients had CRP levels above 5 mg/l, 80.5% above 10 mg/l, and 18.8% exceeded 100 mg/l. 3. By the 3rd to 4th postoperative day, 82.8% of patients still had CRP levels above 5 mg/l, while 81.7% remained above 10 mg/l. To ensure a more accurate assessment of the normal APR in HF patients, we specifically excluded all individuals with infectious complications from our analysis.

In general, we have observed that extracapsular hip fractures

Table 2
Descriptive statistics of the variables within the fracture types.

Variable	All groups (N = 431)	Fracture type		
		Femoral neck (N = 208)	Pertrochanteric (N = 199)	Subtrochanteric (N = 24)
WBC ($\times 10^{12}$/l) pre-op	9.9 (8–12)	9.7 (7.8–11.9)	10.1 (8.1–12.2)	9.8 (8.8–13.3)
WBC ($\times 10^{12}$/l) first day after surgery	8.9 (7.1–11.1)	10 (7.7–11.9)	8.4 (6.9–10.1)	8.2 (6.7–10.5)
WBC ($\times 10^{12}$/l) 3rd–4th day after surgery	7.1 (5.7–8.5)	7.2 (5.8–8.4)	7 (5.6–8.6)	5.7 (6.8–9.4)
CRP (mg/l) pre-op	4 (1.4–20.8)	4.3 (1.6–21.7)	5 (1.3–23.7)	1.7 (.65–11)
CRP (mg/l) first day after surgery	60.3 (36.5–63)	58.3 (34.1–85.4)	69.5 (41.8–101.5)	98.9 ± 58.2
CRP (mg/l) 3rd–4th day after surgery	65.9 (32.1–65.5)	45 (27.9–72.9)	77 (52.7–111.4)	110.8 ± 55.1
Fibrinogen (g/l) pre-op	3.7 ± 0.9	3.7 ± 0.9	3.6 ± 0.9	3.5 ± 8
Albumin (g/l) pre-op	39.3 ± 6.7	40.5 ± 10.2	38.2 ± 4.1	38.1 ± 3.6
Vitamin D (nmol/l) pre-op	48.5 ± 33	54 ± 35	45.3 ± 33	58.2 ± 41.4
CRP/albumin ratio	.1 (.03–.5)	.1 (.04–.6)	.1 (.03–.6)	.03 (.02–.2)

CRP, C reactive protein; WBC, white blood cell count.

Table 3
Descriptive statistics of the variables within the fracture types.

Variable	Surgery type				
	HA (N = 126)	THA (N = 61)	PFN (N = 183)	DHS (N = 48)	CS (N = 13)
CRP (mg/l) first day after	59.8 (34.6–93.8)	48.4 (22.7–78.2)	69.9 (43–101.2)	72.2 ± 24.9	70.8 ± 51
CRP (mg/l) 3rd–4th day after surgery	50.5 (28.8–72.3)	40.7 ± 24.2	80.4 (57.6–111.9)	86.3 ± 39.4	50.9 ± 29.7

CRP, C reactive protein; CS, cannulated screws; DHS, dynamic hip screw; HA, hemiarthroplasty; PFN, proximal femoral nail; THA, total hip arthroplasty.

yield higher APR than compared to intracapsular, which was unique at the time of writing. It is observed not only in CRP values, but in negative APR reactant albumin values too – intracapsular fractures had significantly higher concentration than compared to extracapsular fractures. However, it should be taken in mind that hypoalbuminemia is common in the elderly.[4,19,24] We found it to be 14.4% (albumin lower than 35 g/l). In our case all our patients were 65 and older, we assumed that our sample was affected by this matter equally and difference between groups is present because of the APR. At the time of the writing, the CAR was previously found to predict 30 day and 1 year mortality after hip fracture surgery.[20,21] As CAR represents the ratio between positive APR reactant (CRP) and negative reactant (albumin) it is logical, that the index represents the dysregulation of APR which was found previously to represent poor patient outcomes.[1,2] The aim of this study was not to evaluate the outcomes of hip fracture patients, but we observed a pattern those patients with subtrochanteric fractures had the significant hypoalbuminemia pre-operatively and significantly higher CRP values post-operatively compared with other fracture types. Our calculated CAR was combined from admission values, and we did not find statistically significant differences, but pre-operative hypoalbuminemia and post-operative CRP elevation might show that patients with subtrochanteric fractures are prone to APR dysregulation and poor outcomes. However, this hypothesis needs to be proven in further studies.

The findings of our study align with previous research that highlights the interplay between various APR reactants, particularly the negative correlation between pre-operative CRP and albumin concentrations.[7,17–19] Our investigation extends this understanding by demonstrating a significant negative correlation between CRP and vitamin D levels, a relationship that has garnered increasing attention in recent studies. Previous literature has posited that vitamin D may function as a negative APR reactant, and our results lend support to this hypothesis.[3] For instance, Zhao et al. reported higher vitamin D levels in patients with simple fracture patterns compared to those with more complex fractures, suggesting a potential link between vitamin D status and injury severity.[25] In our study, vitamin D levels did not differ significantly between fracture groups, nor did they correlate with albumin concentration. Thus, while there are limitations, we can only suggest that vitamin D may be a negative APR reactant. Notably, we identified a concerning prevalence of vitamin D deficiency, with 75.4% of patients exhibiting insufficient levels. This finding underscores the importance of vitamin D supplementation in the elderly population.

The observed significantly higher fibrinogen concentrations in intracapsular fractures compared to extracapsular fractures in this study may not be primarily linked to the APR. A more plausible explanation lies in the role of fibrinogen in the coagulation process. Notably, we found that patients with extracapsular fractures exhibited significantly lower haemoglobin levels compared to those with intracapsular fractures ($p < 0.001$). This suggests a potential higher use of fibrinogen for coagulation process in subtrochanteric fractures. Moreover, it is important to consider that fibrinogen levels typically peak at least two days following the initiation of the APR. Since our study did not assess postoperative fibrinogen levels, it becomes one of the limitations of present study.

As with all studies, ours has certain limitations. First, it is a single centre study, which means that the findings may not be generalizable to other hospitals or settings. The patient population examined is limited to those admitted to our institution, potentially affecting the external validity of the results. Moreover, we did not analyse complications, as this was beyond the scope of our study. This omission is a notable shortcoming, as understanding complications could provide valuable insights into patient outcomes. We excluded all patients with infectious complications to minimize their impact on the APR. However, it would be beneficial to assess the comorbidities of the patients using a standardized tool, such as the Charlson Comorbidity Index, to ensure comparability and to better understand the influence of underlying conditions on APR.

5. Conclusions

Extracapsular hip fractures trigger a higher acute phase response than intracapsular one's post-surgery. Fracture morphology impacts APR more than surgery type. Vitamin D was found as a negative acute phase reactant. Normal CRP and vitamin D levels should not be expected in HF patients.

Conflicts of interest

The authors declare no conflicts of interest.

Author contributions

PM conceptualized the present study, collected, analysed and interpreted the data, performed statistical analysis, interpreted the results and drafted manuscript; RB, SU, RM, VU and IŠ collected, analysed and interpreted the data, interpreted the results. The manuscript was reviewed by all authors. Finally, all authors read and approved the final manuscript for publication.

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Research Article

Impact of anticoagulation therapy on surgical timing, hospital stay, and postoperative outcomes in proximal femur fracture patients

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ABSTRACT

Objective: This study aimed to evaluate the association between preoperative anticoagulant use and time to surgery, hospital length of stay, and 30-day postoperative complications in elderly patients with proximal femur fractures.

Methods: This study included 572 patients with low-energy proximal femur fractures who required surgical treatment. Patients were categorized into two groups based on anticoagulation therapy use. The following data was collected and compered between the groups: time from hospitalization to surgery, hospital length of stay, percent changes in hemoglobin and other post-operative complications: death, cardiac complications, sepsis, deep venous thrombosis, pneumonia, urinary tract infection, surgical site infection, pressure ulcers, acute kidney injury and delirium. Multivariate regression analysis was performed to analyze possible confounders.

Results: The median age of study participants was 83 years. 78.2% being female. Anticoagulation therapy was used by 19.9% of patients, predominantly non-vitamin K oral anticoagulants. Patients receiving anticoagulants experienced significantly longer hospital stays (median 9 vs. 7 days; $P < .05$) and surgical delays (median 3 vs. 2 days; $P < .0001$) compared to those without anticoagulation. Complication rates and hemoglobin level changes did not differ significantly among the groups ($P > .05$). Multivariate analysis identified age, time to surgery, and hospital length of stay as independent predictors of 30-day postoperative complications, with age and hospital stay also significantly associated with 30-day mortality.

Conclusion: Anticoagulation therapy did not directly increase 30-day postoperative complications or mortality but was associated with surgical delays and prolonged hospital stays, which negatively impacted outcomes. Delayed surgery and extended hospitalization emerged as key risk factors. These findings underscore the clinical importance of minimizing surgical delays in anticoagulated patients to improve postoperative outcomes.

Level of Evidence: Level II, Prognostic study.

Introduction

Hip fractures remain the leading cause of morbidity and mortality in the elderly trauma population, and the notable prevalence of anticoagulant usage among these geriatric patients, often due to underlying cardiovascular comorbidities, further complicates their clinical management and outcomes.[1,2] The arrival of novel oral anticoagulants (NOACs), including dabigatran, rivaroxaban, and apixaban, has almost doubled global anticoagulant utilization.[3] Consequently, the management of hip fractures in NOAC-receiving patients still poses a challenge. These individuals frequently encounter surgical delays and prolonged hospitalization periods relative to non-anticoagulated patients.[4]

While perioperative management of anticoagulant therapy in surgery necessitates a delicate balance between bleeding and thrombotic risks, a 2021 survey revealed that 73.6% of surgeons believe adequate clinical guidelines for anticoagulated patients with hip fractures are lacking.[5] A new retrospective study by Fenwick et al[6] demonstrated that a structured surgical timing protocol based on renal function and pharmacokinetics of the direct oral anticoagulants (DOACs) enables safe operative management of hip fractures within a 48-hour window. Patients with adequate renal function underwent surgery within 24 hours, while those with impaired clearance or on dabigatran were delayed to 24-72 hours based on drug-specific half-lives. Despite longer surgical delays in the anticoagulated cohort, mortality did not increase when surgery occurred within 48 hours; however, delays beyond 48 hours were associated with significantly higher mortality (9.8%; $P < .001$).[6] Current American College of Chest Physicians (ACCP) guidelines recommend withholding DOACs for 24-48 hours prior to elective surgery, with extended interruption—up to 96 hours—for dabigatran in patients with reduced renal function. Postoperative resumption is advised within 24-72 hours once adequate hemostasis is achieved. For patients treated with vitamin K antagonists such as warfarin, the ACCP recommends discontinuation at least 5 days before surgery, with a target international normalized ratio (INR) of ≤1.5 prior to intervention.[7]

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This evidence supports individualized but timely surgery in DOAC-treated patients, minimizing bleeding risk while preserving the benefits of early intervention.

This study aims to evaluate the association between preoperative anticoagulant use and time to surgery, hospital length of stay, postoperative complications, and patient mortality, with the specific objective of determining whether current perioperative management strategies influence these outcomes and highlight the need for more standardized, evidence-based protocols.

Material and methods

Study design

This prospective, single-center, observational study included 572 patients with proximal (pertrochanteric, subtrochanteric, femoral neck) femur fractures who received surgical treatment between December 2022 and November 2023 at a tertiary trauma center. For each patient, the following information was recorded: age, sex, dates of admission and surgery, hospitalization period, time to surgery, ASA score, type of hip fracture, surgical method, type of anesthesia, hemoglobin pre and post-surgery, anticoagulant drug usage, 30-day postoperative complications, and mortality.

Patients were categorized into 2 groups based on anticoagulation status, which was ascertained from their chronic medication lists at the time of admission: no anticoagulant use (control group) and patients receiving anticoagulation therapy (including non-vitamin k antagonist oral anticoagulants (dabigatran, rivaroxaban, apixaban, and edoxaban) and warfarin). While data on the precise timing of the last medication dose were not available for all patients, it was assumed that patients were managed according to established medication cessation protocols, and the time of the last medication was set as the time of hospitalization. To evaluate the impact of both the time from hospitalization to surgery and anticoagulation treatment on postoperative complications, the anticoagulation therapy cohort was divided into 2 subgroups: patients who underwent surgery within 48 hours and those who waited longer.

Although direct measurement of blood loss was not possible, the percentage change in hemoglobin levels was calculated using a formula proposed by Schermann et al.[8] This formula determines hemoglobin change by the difference between pre- and post-operative hemoglobin levels divided by preoperative hemoglobin level and multiplied by 100.[8] In this patient cohort, blood transfusion therapy was administered when the hemoglobin level was below 80 g/L or in cases of acute ongoing bleeding with a significant decline in hemoglobin. To ensure accurate statistical evaluation of the percentage change in hemoglobin levels, outliers were identified and removed.

Surgical techniques

Perioperative anticoagulation management followed standardized institutional protocols. Patients receiving warfarin were administered vitamin K, with INR levels monitored to guide the timing of surgery. For individuals on apixaban or rivaroxaban, plasma drug concentrations were measured, and surgery was performed once levels declined below 30 ng/mL. In patients treated with dabigatran or edoxaban, surgical intervention was postponed for 48 hours to allow for adequate drug clearance. Anticoagulation therapy was resumed on the first postoperative day.

Anesthetic management for all patients consisted of either general or neuraxial anesthesia, selected at the discretion of the attending anesthesiologist. Regional anesthesia was performed on 90.53% of the patients, while general anesthesia was administered to 9.47%. The majority of patients (88.21%) had an ASA grade 3, while an additional substantial proportion (4.46%) were classified as ASA grade 4, indicating a generally high preoperative risk profile within the study cohort. Tranexamic acid was administered preoperatively in all surgical cases.

The largest group consisted of patients who had sustained femoral head or neck (intracapsular) fractures (49.65%). A significant portion also suffered from pertrochanteric femoral fractures (44.93%), while a smaller proportion experienced subtrochanteric fractures (5.42%). Details regarding the surgical techniques employed for each fracture type are provided in Table 1. All procedures were either performed or directly supervised by a consultant orthopedic surgeon.

Follow-up and outcomes

After surgery, patients were followed up for 30 days. On the 30th day, the patient or his surrogate was contacted for an interview. Furthermore, the patient's electronic medical history was analyzed during the interview. The following complications were recorded: pneumonia, cardiac complications, surgical site infection, urinary tract infection, deep venous thrombosis, acute renal failure, readmission, reoperation, death, sepsis, delirium, and pressure sores.

Inclusion and exclusion criteria

This study included patients aged 65 years or older who experienced low-energy (simple fall) proximal femur fracture (pertrochanteric, subtrochanteric, femoral neck) and required surgical treatment. However, individuals with open fractures, fractures involving neurovascular bundle injuries, polytrauma or high-energy trauma, documented alcohol or psychoactive substance dependence, pregnancy, or insufficient data were excluded from the study.

HIGHLIGHTS

- This study demonstrates that preoperative anticoagulant therapy in elderly patients with proximal femur fractures does not significantly increase the incidence of postoperative complications when compared to patients without anticoagulation.
- While anticoagulant use correlates with a statistically significant prolongation of time to surgical intervention and increased hospital length of stay, this delay did not translate to a higher rate of adverse outcomes.
- Analysis revealed no statistically significant differences in perioperative hemoglobin level changes between patients receiving anticoagulation and those who did not, suggesting that anticoagulation does not substantially elevate the risk of significant blood loss in this patient population.
- Age and prolonged hospital stay were significant risk factors for both 30-day mortality and postoperative complications, while delayed surgery independently predicted 30-day postoperative complications.

Table 1. Distribution of surgical procedures by fracture type

	Femoral head or neck (intracapsular) fractures n = 284	Petrochanteric fractures n = 257	Subrochanteric fractures n = 31
Surgical method	n (%)	n (%)	n (%)
HA	184 (64.79)	4 (1.56)	0 (0)
THA	63 (22.18)	3 (1.17)	0 (0)
PFN	4 (1.41)	199 (77.43)	31 (100)
DHS	16 (5.63)	51 (19.84)	0 (0)
CS	17 (5.99)	0 (0)	0 (0)

CS, cannulated screws; DHS, dynamic hip screw; HA, hip hemiarthroplasty; PFN, proximal femoral nailing; THA, total hip arthroplasty.

Statistical methods

The data was registered in Microsoft Excel and analyzed using IBM SPSS Statistics v. 30.0 (IBM SPSS Corp.; Armonk, NY, USA) / R Commander version: 2.9-5 (John Fox et al., Department of Sociology, McMaster University; Hamilton, Ontario, Canada). To test the normality of the data, the Kolmogorov–Smirnov test was chosen, which is recommended for large sample sizes ($n \geq 50$).[9] Data were presented as numbers (percentages) for categorical variables and median (Q1; Q3) or mean (SD) for continuous variables. Statistical differences for variables with a normal distribution were evaluated with Student's t-test, while the Wilcoxon test was used for non-normally distributed data. The chi-square test of independence and Fisher's exact test were applied to determine statistical differences between nominal variables. A sample size of 572 participants was calculated to achieve 81.4% statistical power (post hoc analysis) to detect a medium effect size ($r=0.306$) for the primary outcome, ensuring adequate power to reliably detect meaningful differences. Differences were considered statistically significant if $P < .05$. A one-way ANOVA was used to analyze statistical differences and compare means between more than 2 groups. Multivariate logistic regression analyses were performed to determine independent predictors of 30-day postoperative complications and mortality.

This study was approved by the Lithuanian Bioethics Research Ethics Committee, Issue No. 2022/11-1473-941, Date: 22.11.2022.

Written informed consent was obtained from all individual participants included in the study.

Results

The median age of study participants was 83 years (Q1: 77, Q3: 88), and the majority were women (78.15%). A total of 19.93% (n=114) of patients with a proximal femur fracture who presented for surgical management were undergoing anticoagulation therapy. The majority were treated with non-vitamin k antagonist oral anticoagulants (rivaroxaban, apixaban, endoxaban, and dabigatran), though some patients received warfarin (Figure 1).

Statistically significant differences were found in both the number of days spent in the hospital ($P < .05$; 95% CI: −0.26 to −0.03) and the time between hospitalization and surgery ($P < .0001$; 95% CI: −0.37 to −0.17) when comparing patients receiving anticoagulation therapy and those who were not. The median time from hospitalization to surgery was 3 days (Q1: 2; Q3: 4) in the anticoagulation therapy group and 2 days (Q1: 1; Q3: 4) in the control group (Figure 2). In addition, patients receiving warfarin experienced a longer median surgical delay compared to those on NOAC therapy: 5 days (Q1: 2.5, Q3: 5.5) and 3 days (Q1: 2, Q3: 4), respectively ($P < .05$). Despite this, patients receiving anticoagulation therapy spent more time in the hospital, with a median duration of 9 days (Q1: 6, Q3: 11), while patients without anticoagulation therapy had a significantly shorter stay, with a median of 7 days (Q1: 6, Q3: 10).

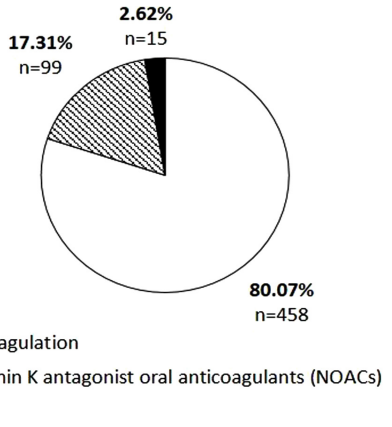

Figure 1. Incidence rates of anticoagulation therapy use among patients with proximal femur fractures requiring surgical treatment.

In the anticoagulation therapy group, 64.04% (n=73) of patients undergoing surgery waited more than 48 hours. To assess the potential influence of anticoagulant therapy and surgical delay on 30-day postoperative complications, the study cohort was divided into 3 groups: a control group with no anticoagulation (n=458), an anticoagulation group with surgery performed within 48 hours (n=41),

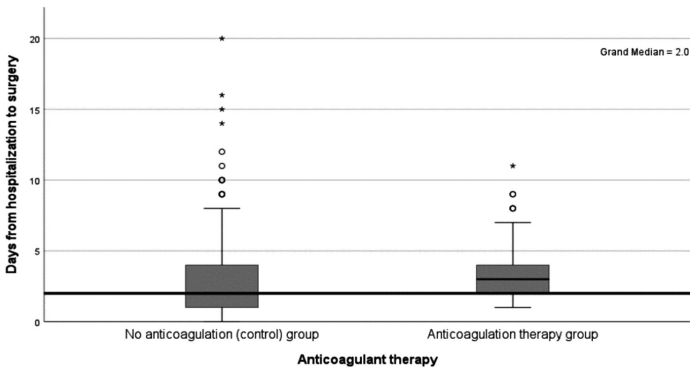

Figure 2. Median time from hospitalization to surgery. The Y-axis represents the number of days waited from hospitalization to surgery, while the X-axis categorizes patients into 2 study groups: no anticoagulation (control) and anticoagulation therapy. The grand median (long black line) is 2.0 days, aligning with the no anticoagulation group's median, while the median for the anticoagulation therapy group is shown as a short black line. Outliers, represented by small circles and asterisks, indicate patients who experienced significantly longer surgical delays.

Table 2. Incidence rates of postoperative complications and statistical differences among 3 study groups: a control group with no anticoagulation, a group receiving anticoagulation therapy who underwent surgical treatment within 48 hours, and a group receiving anticoagulation therapy who waited more than 48 hours before surgery

	No anticoagulation (control) group n = 458	Anticoagulation therapy group (surgery < 48 hours) n = 41	Anticoagulation therapy group (surgery > 48 hours) n = 73	*P*
Postoperative complications	n (%)	n (%)	n (%)	
Deaths	36 (7.86)	2 (4.88)	8 (10.96)	.493
Cardiac complications	48 (10.48)	7 (17.07)	12 (16.44)	.184
Sepsis	7 (1.53)	0 (0)	3 (4.11)	.199
Deep venous thrombosis	5 (1.09)	1 (2.44)	1 (1.37)	.748
Pneumonia	54 (11.79)	4 (9.76)	6 (8.22)	.638
Urinary tract infection	45 (9.83)	2 (4.88)	10 (13.70)	.312
Surgical site infection	11 (2.40)	1 (2.44)	5 (6.85)	.113
Pressure ulcers	40 (8.73)	2 (4.88)	9 (12.33)	.389
Acute kidney injury	20 (4.37)	0 (0)	6 (8.22)	.119
Delirium	49 (10.70)	4 (9.76)	5 (6.85)	.597

and an anticoagulation group with surgery delayed beyond 48 hours (n = 73). Cardiac complications were more common in both anticoagulation therapy groups (surgery <48 h-17.07%; surgery >48 h-16.44%) compared to the control group (10.48%). However, these differences were not statistically significant (P = .184). Similarly, no statistically significant differences were observed in other postoperative complications among the 3 groups (P > .05). Detailed information about complication rates and statistical comparisons is summarized in Table 2. Percent changes in hemoglobin were similar across all 3 groups (P > .05), with mean values (± SD) of 16.7 ± 10.1% (95% confidence interval [CI]: 15.8-17.7) in the no anticoagulation group, 16.6 ± 10.0% (95% CI: 13.3-19.8) in the anticoagulation therapy group that underwent surgery within 48 hours, and 14.1 ± 10.3% (95% CI: 11.7-16.6) in the anticoagulation therapy group that waited more than 48 hours for surgery.

Multivariate logistic regression analyses were performed to determine whether age, sex, anticoagulation therapy, time to surgery, and length of hospital stay (LOS) are independent predictors of 30-day postoperative complications and mortality. Age and LOS were significantly associated with increased mortality risk (P < .05), with odds ratios of 1.10 (95% CI: 1.04-1.15) and 1.09 (95% CI: 1.01-1.18), respectively. Anticoagulant therapy, sex, and time to surgery did not demonstrate significant associations with mortality (Table 3). Regarding 30-day postoperative complications, age (odds ratio [OR] = 1.06, 95% CI: 1.04-1.09), time to surgery (OR = 1.60, 95% CI: 1.03-1.31), and length of stay (OR = 1.15, 95% CI: 1.07-1.24) were identified as independent risk factors (P < .05). Anticoagulant therapy and sex were not significantly associated with complication rates (Table 4).

Discussion

This study demonstrated that patients receiving anticoagulation therapy experienced significantly longer times to surgical intervention and prolonged hospital stays compared to controls. Specifically, 64.04% (n = 73) of patients on anticoagulation experienced a delay of more than 48 hours before undergoing surgery, with a median time to surgery of 3 days, compared to 2 days in the control group. These findings are clinically meaningful given current international guidelines, including those from the Fragility Fracture Network, which advocate for surgical intervention within 48 hours—preferably within 36 hours in some regions—to minimize morbidity and mortality.[10] The study confirms that both age and LOS are significant risk factors for mortality and the occurrence of 30-day postoperative complications. Moreover, time to surgery was identified as an independent risk factor for 30-day postoperative complications, highlighting the clinical importance of minimizing surgical delays. Although anticoagulation therapy was not an independent risk factor for 30-day postoperative complications or mortality, it was significantly associated with longer hospital stays and delayed surgery, which may indirectly contribute to poorer outcomes.

Table 3. Multivariate logistic regression analysis identifying predictors of 30-day mortality

Independent variables	Coefficient B	Standard error	*Z*	*P*	Odds ratio	95% confidence interval
Age	0.09	0.02	3.7	<.001**	1.1	1.04-1.15
Sex	0.37	0.38	0.98	.329	1.45	0.69-3.05
Anticoagulative therapy	−0.04	0.39	0.12	.908	0.96	0.45-2.04
Time to surgery	0.04	0.07	0.55	.579	1.04	0.91-1.19
Length of stay	0.09	0.04	2.26	.024*	1.09	1.01-1.18

R squared for model = 0.11, P < .001.
*Indicates P < .05.
**Indicates P < .01.

Table 4. Multivariate logistic regression analysis identifying predictors of 30-day postoperative complications

Independent variables	Coefficient B	Standard error	*Z*	*P*	Odds ratio	95% confidence interval
Age	0.06	0.01	4.28	<.001**	1.06	1.04-1.09
Sex	0.04	0.24	0.15	.879	1.04	0.65-1.65
Anticoagulative therapy	0.06	0.23	0.27	.79	1.06	0.68-1.67
Time to surgery	0.15	0.06	2.38	0.017*	1.6	1.03-1.31
Length of stay	0.14	0.04	3.7	<.001**	1.15	1.07-1.24

R squared for model = 0.2, P < .001.
*Indicates P < .05.
**Indicates P < .01.

These results are consistent with existing literature. A recent systematic review reported that anticoagulated patients undergoing hip fracture surgery experienced a mean surgical delay of 13.7 hours and had approximately a 3-fold higher likelihood of surgical delay beyond 48 hours compared to non-anticoagulated individuals.[11] Importantly, the current findings reinforce these observations, with over 60% of patients on anticoagulation exceeding this threshold.

The current study also contributes to the growing evidence base assessing whether DOAC-related surgical delays translate into increased perioperative risk. While a delay beyond 48 hours has previously been linked to higher mortality and complication rates, the current data did not reveal statistically significant differences in 30-day mortality or major complications between anticoagulated and non-anticoagulated patients.[8,12] These findings align with prior retrospective studies indicating no significant differences in hemoglobin drop, transfusion requirement, reoperation, or 30-day mortality among patients undergoing early hip fracture surgery while on DOAC therapy.[13,14] This study demonstrated similar hemoglobin changes between the anticoagulation and control groups, suggesting that anticoagulation status did not significantly influence perioperative blood loss.

The findings of this study are partially consistent with those reported by Kavak et al,[15] who evaluated 596 geriatric hip fracture patients and identified a mean surgical delay of 3.21 days (range: 1-9 days) as a significant predictor of 30-day mortality ($P < .001$, OR: 2.006). Their study found that patients who died within 30 days postoperatively had a median surgical delay of 5 days, compared to 3 days among survivors. Similarly, in the anticoagulated cohort, the median surgical delay was 3 days, a duration in line with the threshold described by Kavak et al[15] as potentially acceptable for medical optimization without excessive risk. However, the absence of a significant difference in 30-day mortality in the population suggests that in carefully selected patients—particularly those with well-controlled comorbidities—a 3-day delay may not independently increase early mortality risk. Notably, both studies underscore that delays beyond 3 days should prompt clinical reassessment, particularly in the presence of additional risk factors such as a high ASA score or significant perioperative complications.[15]

Notably, both this study and others underscore that delays should prompt reassessment, particularly in the presence of additional risk factors. For instance, Bombacı et al[16] found that a high ASA score (ASA 4), abnormal preoperative creatinine levels, and the presence of cognitive dysfunction such as dementia were all significant preoperative indicators of postoperative mortality. That study also highlighted that the majority of deaths (57.14%) occurred within the first 3 months, emphasizing the vulnerability of this early recovery period.[16] Similarly, Zehir et al[17] identified delayed surgical intervention as a critical factor influencing 30-day mortality in patients receiving clopidogrel therapy. Their findings indicate that patients who underwent surgery more than 48 hours after clopidogrel administration experienced significantly prolonged hospitalizations ($P < .01$) and a higher incidence of postoperative complications.[17]

In terms of LOS, patients receiving anticoagulant therapy had a significantly longer LOS (median: 9 days) compared to controls (median: 7 days). Despite the increased LOS, no statistically significant differences were observed between groups regarding rates of mortality, cardiac events, infections, sepsis, deep vein thrombosis, or other postoperative complications ($P > .05$). This aligns with findings from studies on preoperative cardiac evaluations, where extensive testing was shown to significantly delay surgery and prolong hospital stays, also without a corresponding reduction in perioperative mortality.[18] This phenomenon is consistent with previous analyses demonstrating a weak correlation between complication rates and extended LOS (Spearman's rho = 0.56, $P < .01$), suggesting that other factors—including preoperative delay, social discharge barriers, or institutional practices—contribute to prolonged hospitalization.[19] In contrast, other studies have identified medical complications such as urinary tract infections (15.4%), pneumonia (9.0%), and constipation (6.8%) as primary drivers of extended LOS.[20] The discrepancy between findings reinforces the multifactorial nature of hospital stay duration in this patient population, in which age, frailty, comorbid burden, and postoperative recovery dynamics interplay.

Finally, these findings reaffirm that current surgical timing guidelines should not be rigidly deferred based solely on anticoagulation status, particularly with DOACs. As emerging evidence shows limited association between DOAC use and increased perioperative bleeding risk, the rationale for delayed surgical intervention must be patient-specific and guided by renal function, drug pharmacokinetics, and overall clinical stability. Blanket delays may unnecessarily expose patients to complications associated with prolonged immobility and hospitalization.

Limitations of this prospective study using secondary data include the inability to directly quantify blood loss, necessitating the use of indirect estimates based on pre- and postoperative hemoglobin levels. Complete data regarding the timing of the last DOAC dose administration were not available for all patients, precluding a comprehensive analysis of the time from the last anticoagulant dose to surgical intervention. Information regarding the use and timing of platelet aggregation inhibitor administration was not recorded, limiting the ability to assess the impact of ongoing antiplatelet therapy on perioperative bleeding risk. In addition, this study did not include possible predictors of mortality and complications: patients' pre-fracture activity levels, ambulatory status, c-reactive protein-to-albumin ratio, and the modified 5-item frailty index. Finally, the single-center design may limit the extent to which these findings are applicable to other institutions or patient populations.

This study concludes that the administration of anticoagulation therapy was not associated with an elevated incidence of postoperative complications compared to the control group, and no statistically significant difference in percent change of hemoglobin levels was observed between the 2 groups. Age and LOS were found to be significant risk factors for 30-day postoperative complications and mortality. Time to surgery also emerged as an independent predictor of 30-day complications. While anticoagulation therapy itself was not an independent risk factor for 30-day postoperative complications or mortality, it was significantly associated with both extended hospital length of stay and a prolonged time to surgical intervention, which can indirectly increase the risk of poor outcomes.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethical committee approval was received from the Lithuanian Bioethics Research Ethics Committee (Approval No.: 2022/11-1473-941; Date: Date: 22.11.2022).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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Risk Factors Associated with Complications and Early Mortality of Hip Fracture Surgery in Elderly Patients

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Abstract

Background and Objectives: High rates of mortality and morbidity among elderly hip fracture patients are a recognized global issue. This study aimed to evaluate risk factors for early complications and 30-day mortality in hip fracture patients. *Materials and Methods*: The prospective study included 583 patients over 65 years old who sustained hip fractures from fall and underwent surgery. Each patient was followed up for 30 days and complications were recorded. Regression models were used to assess the influence of patient characteristics and laboratory markers on 30-day mortality and complications. *Results*: Any complication increased the risk of mortality by 5.6 times (95% CI 1.6–19.9, $p = 0.008$). Having > 6 comorbidities increased the risk of mortality by 8.2 (95% CI 1.9–35.5, $p = 0.005$) and the risk of complications by 2.3 (95% CI 1.9–35.5, $p = 0.000$). Patients > 85 years old had increased risk of mortality by 2.2 times (95% CI 1.2–4.1, $p = 0.015$) and a 1.7-fold increase in risk of complications (95% CI 1.2–2.4, $p = 0.005$). Vitamin D significantly predicted mortality with odds ratio of 2.1 (95% CI 1.1–4.1, $p = 0.028$). Serum N-terminal pro-brain natriuretic peptide levels > 780 ng/L predicted 2.3-fold increase in mortality (95% CI 1.0–4.9, $p = 0.040$) and a 2.6-fold risk of complications (95% CI 1.7–3.9, $p = 0.000$). *Conclusions*: Occurrence of complication increases the risk of mortality. Age and comorbidities are significant factors associated with 30-day mortality and complications. Vitamin D levels are associated with higher risk of mortality. N-terminal pro-brain natriuretic peptide levels correspond to higher risks of death and complications.

Keywords: hip fracture; hemiarthroplasty; total hip arthroplasty; osteosynthesis; mortality

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1. Introduction

Due to the ageing global population, it is estimated that 6 million people worldwide will experience hip fractures (HF) annually by the end of the century [1]. These patients often present with multiple comorbidities, such as hypertension, diabetes, obesity, heart failure, osteoporosis, alcohol addiction, and sarcopenia, and most cases require surgical intervention [1–5]. Early mortality rates among HF patients can reach up to 14%, and post-operative complication rates can reach up to 48% [6–10]. Given the fragility of these patients, identifying those at highest risk for adverse outcomes is important for determining the need for additional perioperative interventions [11]. Assessing factors associated with increased early mortality and morbidity may enhance post-operative outcomes through

earlier identification and intervention for high-risk individuals [6,7,12–15]. This approach also clarifies surgical risks for both clinicians and patients and supports communication with patients' relatives.

The aim of this study was to evaluate risk factors for early complications and 30-day mortality in elderly patients with hip fractures.

2. Materials and Methods

A prospective study was carried out at a tertiary orthopedic trauma centre from 1 December 2022 to 31 December 2023. All participants or their proxies signed informed consent, and the study received approval from the Institutional Review Board and the regional bioethics committee. Inclusion criteria included patients aged 65 years or older; diagnosis of intertrochanteric, subtrochanteric, or femoral neck fracture; surgical treatment; low-energy trauma (simple fall); closed fractures; isolated trauma; and acute trauma (within 72 h). All surgeries were performed or supervised by a consultant orthopedic surgeon. Postoperative follow-up was conducted for 30 days. On day 30, investigators contacted the patient or proxy for an interview, and electronic medical records were reviewed. The following complications were documented: pneumonia, cardiac complications, surgical site infection, urinary tract infection, deep venous thrombosis, acute renal failure, readmission, reoperation, death, sepsis, delirium, and pressure sores. Additional data collected included age, gender, ASA classification, and use of direct oral anticoagulants (DOAC). Blood samples were obtained prior to surgery, as well as on the first and third or fourth postoperative days. Preoperative tests included hemoglobin (Hgb), C-reactive protein (CRP), troponin, N-terminal pro-brain natriuretic peptide (NT-proBNP), fibrinogen, total protein, albumin, and vitamin D. Hgb and CRP levels were measured again on the first and third or fourth postoperative days, and NT-proBNP was repeated on the third or fourth postoperative day. General patient data are summarized in Table 1. The final sample size of 583 patients is shown in Figure 1.

Table 1. General patient data.

Variables	
Gender (female/male)	452 (77.5%)/131 (22.5%)
Age	82 ± 8
Number of comorbidities	6 ± 3
Fracture type:	
Neck	292 (50.1%)
Pertrochanteric	259 (44.4%)
Subtrochanteric	32 (5.5%)
Surgery type:	
Hip hemiarthroplasty	191 (32.8)
Total hip arthroplasty	70 (12.0%)
Proximal femoral nail	236 (40.5%)
Dynamic hip screw	69 (11.8%)
Cannulated screws	17 (2.9%)
ASA class:	
ASA II	41 (7.0%)
ASA III	516 (88.5%)
ASA IV	26 (4.5%)
DOAS use:	124 (21.3%)

All analyses were performed using IBM SPSS version 26.0 software (SPSS Inc., Chicago, IL, USA) for Windows. Data that were normally distributed are reported as mean (±standard deviation). The Shapiro–Wilk test was utilized to assess the normality of

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data distribution. Multinomial regression models were constructed to evaluate the influence of patient characteristics (age, gender, fracture type, number of comorbidities, use of DOACs, and ASA class) and laboratory markers (preoperative Hgb, CRP, NT-proBNP, troponin, vitamin D, fibrinogen, albumin, and total protein concentrations; postoperative Hgb, CRP, and NT-proBNP concentrations on days 1 and 3–4) on early 30-day mortality and complications. An additional model was developed to assess the impact of each complication on early mortality. Individual models were generated for the evaluation of complications, patient factors and laboratory markers. Early death was set as a dependent variable in all models. Complications were set as dependent variables in models for patient factors and laboratory markers, but each specific complication was tested as an independent variable in the model for mortality prediction. Patient factors and laboratory markers were set as independent factors and converted to dummy variables. Specific ranges of dummy variables for continuous data are presented in the tables in the results section. The level of significance α was set at $p < 0.05$. Following initial modelling, deep venous thrombosis and fracture type were excluded from the models due to insufficient sample size—variables became redundant and had to be removed from analysis. Furthermore, the fracture type variable was eliminated because analysis without subtrochanteric fractures would be illogical.

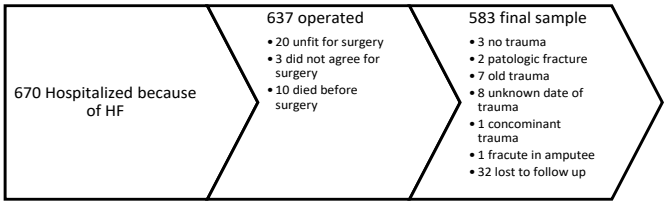

Figure 1. Flow chart of the final sample size.

3. Results

Incidence of complications is presented in Table 2.

Table 2. Incidence of complications.

Variables	
All complications	207 (35.5%)
Pneumonia	66 (11.3%)
Cardiac complication	68 (11.7%)
Surgical site infection	20 (3.4%)
Urinary tract infection	58 (9.9%)
Deep venous thrombosis	7 (1.2%)
Acute renal failure	26 (4.5%)
Readmission	62 (10.6%)
Reoperation	11 (1.9%)
Death	47 (8.1%)
Discharge to nursery	269 (46.1%)
Sepsis	10 (1.7%)
Delirium	59 (10.1%)
Functional decline	406 (69.6%)
New mobility aid	556 (95.4%)
Pressure sores	51 (8.7%)

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Results regarding the complications' influence on early mortality after HP surgery are presented in Table 3. The occurrence of any complication statistically significantly, by 5.6 times (95% CI 1.6–19.9), increased the risk of 30-day mortality of HF patients ($p = 0.008$). Of all the complications, only cardiac events showed a statistically significant ($p = 0.010$) odds ratio of 3.6 (95% CI 1.3–8.5).

Table 3. Results regarding the complications' influence on early mortality. * indicates significant result.

	Early Mortality	
Early Mortality	***p* Value**	**Odds Ratio (95% Confidence Interval)**
Any complication	***0.008* ***	**5.6 (1.6–19.9)**
Pneumonia	*0.563*	1.3 (0.5–3.4)
Cardiac complication	***0.010* ***	**3.4 (1.3–8.5)**
Surgical site infection	*0.260*	0.2 (0.1–2.9)
Urinary infection	*0.535*	1.4 (0.5–3.9)
Renal failure	*0.504*	1.5 (0.4–5.1)
Readmission	*0.748*	0.8 (0.3–2.5)
Reoperation	*0.148*	5 (0.6–45)
Discharge to nursery	*0.561*	0.8 (0.4–1.8)
Sepsis	*0.899*	0.9 (0.1–6.1)
Delyrium	*0.130*	2.2 (0.8–6.1)
Pressure sores	*0.926*	1.1 (0.3–3.4)

Regression model results for patient data predicting early mortality and complications are presented in Table 4. The number of comorbidities and age showed a statistically significant effect on early mortality ($p = 0.005$ and $p = 0.015$ respectively). More than six diseases increased risk of 30-day mortality by 8.2 times (95% CI 1.9–35.5) and the risk of early complications was increased by 2.3 times (95% CI 1.5–3.7, $p = 0.000$). Patients older than 85 years had an increased risk of 30-day mortality by 2.2 times (95% CI 1.2–4.1) and the risk of early serious complications increased by 1.7 times (95% CI 1.2–2.4, $p = 0.005$).

Table 4. Regression model results for patient data predicting early mortality and complications. * indicates significant result.

	Early Mortality		Early Complications	
	***p* Value**	**Odds Ratio (95% Confidence Interval)**	***p* Value**	**Odds Ratio (95% Confidence Interval)**
Gender	*0.371*	1.4 (0.7–2.9)	*0.692*	1.1 (0.7–1.7)
Comorbidities > 4	*0.277*	1.2 (0.6–2.9)	*0.752*	0.9 (0.3–2.1)
Comorbidities > 5	*0.209*	1.4 (0.7–3)	*0.395*	0.6 (0.2–2)
Comorbidities > 6	***0.005****	**8.2 (1.9–35.5)**	***0.000* ***	**2.3 (1.5–3.7)**
Age > 85	***0.015* ***	**2.2 (1.2–4.1)**	***0.005* ***	**1.7 (1.2–2.4)**
ASAII	*0.686*	1.7 (0.1–22)	*0.557*	0.7 (0.2–2.6)
ASAIII	*0.937*	1.1 (0.1–8.9)	*0.847*	1.1 (0.4–3.4)
ASAIV	*0.335*	3.1 (0.3–30)	*0.211*	2.4 (0.6–9.4)
DOAC	*0.798*	0.9 (0.4–1.9)	*0.667*	1.1 (0.7–1.7)

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Laboratory markers' performance regarding early mortality and complications is presented in Table 5. Vitamin D concentration showed a statistically significant ($p = 0.028$) prediction, with a 2.1 odds ratio (95% CI 1.1–4.1), of early mortality. Furthermore, admission NT-proBNP showed a statistically significant prediction of early mortality and complication ($p = 0.040$ and $p = 0.000$ respectively). Before surgery, > 780 ng/L serum levels predicted a 2.3 times increase (95% CI 1.0–4.9) in 30-day mortality and 2.6 times increase (95% CI 1.7–3.9) in the risk of early complications. Baseline CRP > 10 mg/L showed a statistically significant ($p = 0.011$) predicted 1.7 increase in the risk of 30-day complications (95% CI 1.1–2.6).

Table 5. Laboratory marker models' results in the prediction of early mortality and complications. * indicates significant result.

	Early Mortality		Early Complications	
	***p* Value**	**Odds Ratio (95% Confidence Interval)**	***p* Value**	**Odds Ratio (95% Confidence Interval)**
HgB baseline < 100 g/L	*0.443*	0.7 (0.3–1.7)	*0.132*	0.6 (0.3–1.2)
HgB 1st day < 100 g/L	*0.476*	1.3 (0.6–3.1)	*0.435*	1.2 (0.8–1.9)
HgB 3–4th day < 100 g/L	*0.755*	1.1 (0.5–2.4)	*0.315*	0.8 (0.5–1.2)
Albumin < 35 g/L	*0.365*	0.7 (0.3–1.6)	*0.126*	1.6 (0.9–3)
Total protein < 60 g/L	*0.422*	0.7 (0.3–1.7)	*0.326*	0.7 (0.4–1.3)
Vitamin D < 20 ng/mL	***0.028* ***	**2.1 (1.1–4.1)**	*0.881*	1 (0.7–1.6)
NT-proBNP baseline > 780 ng/L	***0.040* ***	**2.3 (1–4.9)**	***0.000* ***	**2.6 (1.7–3.9)**
NT-proBNP 3–4th day > 780 ng/L	*0.308*	0.7 (0.3–1.4)	*0.531*	0.9 (0.6–1)
CRP baseline > 10 mg/L	*0.335*	1.4 (0.7–3)	***0.011* ***	**1.7 (1.1–2.7)**
CRP 1st day > 50 g/L	*0.334*	1.3 (0.7–2.7)	*0.244*	1.3 (0.9–1.8)
CRP 3–4th day > 50 g/L	*0.130*	1.7 (0.9–3.5)	*0.625*	1.1 (0.7–1.6)
Troponin > 9 ng/L	*0.252*	1.7 (0.7–4.4)	*0.726*	0.9 (0.6–1.4)
Fibrinogen > 4 g/L	*0.154*	0.6 (0.3–1.2)	*0.230*	1.3 (0.8–2)

4. Discussion

The data indicate that age and comorbidities are significant factors associated with 30-day mortality and complications in HP patients. The occurrence of any complication statistically significantly, by 5.6 times, increases the risk of early mortality and the risk of only cardiac complications also reached the level of significance. Patients aged over 85 present a 2.2-fold increased risk of early mortality and a 1.7-fold higher likelihood of postoperative complications. Having more than six comorbidities is linked to an 8.2-fold greater risk of early death and a 2.3-fold higher risk of complications. Regarding laboratory markers, vitamin D levels below 20 ng/mL are associated with a 2.1-fold increase in early mortality risk. Elevated baseline NT-proBNP corresponds with a 2.3-fold rise in early death risk and a 2.6-fold increase in the risk of complications. Higher baseline CRP levels are also associated with an increased likelihood of early complications. Age and comorbidities are established risk factors for early mortality in HF patients, highlighting the relevance of a quantitative evaluation in our HP cohort [1,6,16].

We applied a threshold of 781 ng/L for NT-proBNP based on the findings of Zhang et al., who followed 1354 patients and identified this value as predictive of all-cause mortality [1]. Although their mean follow-up was 34 months and the threshold was primarily associated with mid-term mortality, our study demonstrated applicability to early mortality within our cohort. Furthermore, there are limited studies evaluating the prognostic

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capabilities of NT-proBNP in HP patients. Despite methodological differences—some investigations identify threshold values while others categorize patients by quartiles or tertiles of NT-proBNP levels—the consensus is that pro-BNP concentrations exceeding 741–842 ng/L serve as valuable predictors of mortality in HP patients and should be routinely assessed [17,18].

Our study agrees with the results of previous research—low vitamin D levels in the blood have predictive value in showing early mortality in hip fracture patients [9,19,20]. The definition of vitamin D deficiency highly varies across the literature. In this study, the following classification ranges were used: (1) severe (<10 ng/mL), moderate (10–19.9 ng/mL), insufficient (20–29.9 ng/mL), and normal (≥30 ng/mL); (2) less than 50 nmol/L; (3) deficient <12 ng/mL, inadequate 12–<20 ng/mL; (4) insufficiency 20–<30 ng/mL and normal ≥30 ng/mL. We used < 20 ng/mL purely for methodological reasons. Furthermore, the exact mechanism of how vitamin D concentrations impact early mortality is not understood, but there are a few possible mechanisms. It was found that vitamin D has a negative correlation with albumin blood levels and they both might present with malnutrition and sarcopenia, which leads to adverse results; one the other hand, they are both negative acute phase reactants and may lead to dysregulation of the inflammation process [21–23]. Both mechanisms support the use of albumin levels as a confounder rather than evaluating vitamin D's predictive value [19]. One of the most important factors is that vitamin D concentration is modifiable risk factor and requires intervention way before incidence of fracture.

Both preoperative and postoperative C-reactive protein levels have previously been identified as predictors of early and one-year mortality following HP surgery [24,25]. In our study, preoperative CRP was associated with early complications; however, we did not observe statistically significant results regarding its ability to predict early mortality. Notably, earlier studies on early mortality were retrospective in nature and utilized smaller sample sizes compared to the present analysis [24]. Additionally, our cohort included only patients with acute fractures (hospitalized within 72 h of trauma), which may have contributed to the lower observed CRP values. Methodological differences and varying cut-off points may also account for discrepancies between studies. As systemic inflammation is recognized as a predictor of hip fracture outcomes, our finding that CRP does not predict early mortality should be considered inconclusive.

Like other studies, this research has certain limitations. First, as a single-centre study conducted with one hospital cohort, the results may not be generalizable to the broader population. Second, fracture type and deep venous thrombosis could not be assessed in our models. In the case of subtrochanteric fractures, there were too few death events and too small a sample size for analysis; therefore, this variable became redundant. Subsequentially, all fracture types had to be removed because the analysis without one type is incorrect. We encountered the same problem with deep venous thrombosis—only seven cases were registered and the variable had to be removed from the model. These two maters potentially indicate that the sample size of 583 patients was not large enough. Furthermore, we had 32 cases of patients lost to follow-up, which might have an impact on the results. In all cases we could not contact the patient or his proxy and access the patient's electronical health data—there is a good possibility that lost patients experienced complications or even death, but we were not able to confirm this. Furthermore, our multinomial regression model has a few potential flaws: (1) death is often the final outcome of complications, and it might be arguable that complications are an independent variable; (2) we did not match the recommended ratio of cases-to-variables, which indicates the low sample size. However, we found age and number of comorbidities to be significant predictors, which, in our opinion, shows that the models were capable.

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5. Conclusions

The occurrence of any complication increased the risk of 30-day mortality in HF patient by 5.6 times. Only cardiac complications were significant predictors of early mortality. Patients aged over 85 present a 2.2-fold increased risk of early mortality and a 1.7-fold higher likelihood of postoperative complications. Having more than six comorbidities is linked to an 8.2-fold greater risk of early death and a 2.3-fold higher risk of complications. Vitamin D levels below 20 ng/mL are associated with a 2.1-fold increase in early mortality risk. Elevated baseline NT-proBNP corresponds with a 2.3-fold rise in early death risk and a 2.6-fold increase in the risk of complications. Higher baseline CRP levels are also associated with an increased likelihood of early complications.

Author Contributions: P.M. conceptualized the present study, collected, analyzed and interpreted the data, performed a statistical analysis, interpreted the results and drafted the manuscript; G.V., A.M., V.U. and I.Š. collected, analyzed and interpreted the data, interpreted the results and drafted the manuscript. The manuscript was reviewed by all authors. Finally, All authors have read and agreed to the published version of the manuscript.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Data available on request due to ethical restrictions.

Conflicts of Interest: The authors declare no conflicts of interest.

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