Intermitentna klaudikacija – funkcionalna procjena u praćenju bolesnika nakon uspješne perkutane revaskularizacije

Intermittent Claudication – Functional Status Assessment in Patient Follow-up after Successful Percutaneous Revascularization

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SAŽETAK: Porast angiointervencijskih zahvata posljedica je rastuće incidencije okluzivne bolesti perifernih arterija, ali i boljih tehničkih mogućnosti perkutane revaskularizacije. Odluka o načinu liječenja temelji se na pomnoj kliničkoj procjeni bolesnika s intermitentnom klaudikacijom Fontaine II klase i odabira terapijskih mogućnosti: endovaskularne ili kirurške revaskularizacije ili pak konzervativnog medikamentnog liječenja uz intenzivan nadzirani trening hodanja. Posebno je važna racionalizacija u načinu praćenja bolesnika nakon provedenog revaskularizacijskog zahvata u eri različitih novih tehničkih mogućnosti medicinske prakse 21. stoljeća. Cilj ovoga retrospektivnog istraživanja odnosio se na skupinu bolesnika s bolešću perifernih arterija, funkcionalne klase Fontaine II u kojih smo nakon uspješne angiointervencije analizirali promjene vrijednosti ABI-ja (od engl. *ankle brachial index*) i dužine HP-a (hodna pruga) kroz vremenski slijed: prije i neposredno nakon intervencije te u kontrolnom razdoblju. Uspješna endovaskularna revaskularizacija (PTA od engl. *percutaneous transluminal angioplasty*) u usporedbi sa standardnom farmakoterapijom i nenadziranim vježbama hodanja u bolesnika funkcionalne klase Fontaine II rezultirala je produljenjem HP-a i porastom ABI-ja, a koji nisu pokazali poboljšanje nakon inicijalnog 6-mjesečnog razdoblja primijenjene optimalne farmakoterapije i nekontroliranoga tjelesnog treninga. Prisutnosti komorbiditeta nisu utjecale na rezultate ispitivanih parametara. Vrijednost je ABI-ja kontralateralnog ekstremiteta tijekom praćenja porasla i korelira s porastom ABI-ja ekstremiteta podvrgnuta angiointervenciji. Porast duljine HP-a i porast vrijednosti ABI-ja u analizi statistički vrlo značajno prati angiografski uspješnu revaskularizaciju. Rezultati ispitivanja potvrđuju važnost procjene uspjeha PTA-a primjenom ABI-ja, a posebno procjenu dužine HP-a u praćenju uspješne endovaskularne revaskularizacije koja se u svim ispitivanim podskupinama višestruko pratila i pokazala se statistički značajnim parametrom koji obilježava promjenu funkcionalnoga statusa. Smatramo da bi se naoko zanemareni podatak o dužini hodne pruge trebao repozicionirati u rutinskoj procjeni i praćenju funkcionalnog statusa nakon endovaskularne revaskularizacije u bolesnika s intermitentnom klaudikacijom.

SUMMARY: The rate of percutaneous endovascular treatment is increasing because of the high incidence of peripheral artery disease and improved endovascular techniques. Therapeutic decisions in patients with intermittent claudication are based on the patient's functional impairment, specifically in the Fontaine II class. Endovascular or surgical revascularization versus optimal medical therapy with supervised exercise training is a very frequent dilemma in clinical practice. Patient surveillance and follow up after angiointerventions requires a rational approach in the era of new technical advancements in the 21st century. The aim of this retrospective study was to analyze changes in ankle brachial index (ABI) values and walking distance changes as functional status parameters after successful angiointerventions in the observational period: before intervention, after the procedure, and in follow-up. Increased ABI values and walking distance were associated with successful revascularization in the group of patients who did not respond to the initial standard medical treatment in the 6-month period. Comorbidities had no influences on data evaluated in the study. ABI values on the contralateral leg revealed a positive correlation with the incremental ABI values in the leg where revascularization was successfully performed. Significant increase in walking distance after percutaneous revascularization and significantly greater ABI values in follow-up confirmed the importance of both parameters that reflect successful angiographic findings after percutaneous transluminal angioplasty (PTA). Both parameters were consistent with successful revascularization and improved functional status in the follow-up period. Walking distance deserves to be reevaluated in the assessment of functional status in patients after successful percutaneous angiointerventional revascularization. It should not be neglected as a valuable parameter in estimating functional status after PTA.

KLJUČNE RIJEČI: intermitentna klaudikacija, perkutana transluminalna angioplastika, pedobrahijalni indeks, dužina hodne pruge.

KEYWORDS: intermittent claudication, percutaneous transluminal angioplasty, ankle-brachial index, claudication distance.

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Uvod

Prevalencija aterosklerotske bolesti perifernih arterija je u porastu. Incidencija u populaciji starijih od 60 godina iznosi oko 20 %[1]. U visokorizičnih bolesnika oboljelih od šećerne bolesti, arterijske hipertenzije, koronarne i cerebrovaskularne bolesti incidencija je i do 30 %. Periferna aterosklerotska bolest (PAB) prati i rastuću životnu dob pa je incidencija u starijih od 85 godina čak i 50 %[2]. Mnogobrojni komorbiditeti, posebno u starijoj životnoj dobi, osim toga što modificiraju tipičnu kliničku sliku, pokatkad utječu i na ishod liječenja povećavajući u ovoj populaciji vrlo visok kardiovaskularni rizik. S obzirom na vulnerabilnost populacije zbog kardiovaskularnog rizika i čestih komorbiditeta važno je slijediti smjernice u dijagnostici i liječenju oboljelih od PAB-a, a personaliziranim se pristupom u izboru najpogodnijega terapijskog rješenja nastoji postići maksimalan učinak uz najmanje nuspojava[3]. Dijagnostika i praćenje kliničkog toka oboljelih od PAB-a temelji se na procjeni funkcionalnog statusa, anamneze, kliničkog statusa, pletizmografije i ABI-ja (od engl. *ankle brachial index*, pedobrahijalni indeks). Ultrazvučnim se pregledom u dijagnostici PAB-a objektivizira anatomska i hemodinamska značajnost aterosklerotskoga procesa. Slikovne metode (MSCT ili MR angiografija) neizostavni su dio dijagnostičkog algoritma kada je anatomski prikaz nužan radi planiranja i donošenja odluke o najpogodnijim mogućnostima revaskularizacije. Specifičnost je ABI-ja oko 95 % ako je njegova vrijednost manja od 0,9, a osjetljivost oko 79 – 95 % u usporedbi s angiografijom kao metodom u otkrivanju okluzivne bolesti arterija[4]. Vrijednosti ABI-ja i simptomi bolesti često ne koreliraju pa je stoga pokatkad potrebno provesti test opterećenja i odrediti ABI nakon završetka testa. Funkcionalna dijagnostika i anamneza često su zanemarene u procjeni težine kliničke slike, nerijetko zbog neracionalne primjene tehnički sofisticiranih dijagnostičkih metoda poput MR-a i MSCT-a koje nedvojbeno imaju svoje mjesto u dijagnostici, ali i pojedina ograničenja[4-6]. Klasifikacija PAB-a po Fontaineu i Rutherfordu temelji se na procjeni statusa i funkcionalne sposobnosti bolesnika. Klasu I po Fontaineu čine oboljeli od PAB-a koji nemaju ograničavajućih simptoma i bolova u hodu. Klasa II uključuje bolesnike koji imaju simptome intermitentne klaudikacije. Podskupina II A ima hodnu prugu (HP) dužu od 200 metara, a oboljeli iz podskupine II B pri prijeđenom putu kraćem od 200 metara osjećaju bol u ekstremitetu. Klasa III obuhvaća bolesnike koji imaju bolove u mirovanju, a klasu IV čine bolesnici s ulceracijama ili gangrenom. Klasi III i IV nedvojbeno pripadaju bolesnici u kojih je revaskularizacija apsolutno indicirana zbog ugroženosti ekstremiteta. Bolesnici klase I zahtijevaju praćenje uz modifikaciju stila života i korekciju i liječenje čimbenika rizika, dok izbor optimalnog liječenja bolesnika sa stabilnom klaudikacijom (Fontaine II) zahtijeva pomnu kliničku procjenu uz primjenu medikamentnog liječenja te provođenje strukturiranih vježbi hodanja uz nadzor. Zbog izostanka sredstava iz zdravstvenih fondova za provođenje strukturiranih nadziranih vježbi hodanja, bolesnici treninge najčešće provode proizvoljno, što je često nedovoljno učinkovito[4]. Odluka o revaskularizaciji temelji se na kliničkoj procjeni, tijeku bolesti, prisutnim komorbiditetima, dobi bolesnika i kliničkom tijeku bolesti, napose kad učinak fizikalnih i farmakoloških metoda liječenja nije učinkovit. U liječenju stabilnog tijeka intermitentne klaudikacije uz korekciju čimbenika rizika, apstinencije od nikotina, regulacije tjelesne težine,

Introduction

The prevalence of atherosclerotic peripheral artery disease is increasing. Incidence in the population over 60 years of age is about 20%[1]. In high-risk patients suffering from diabetes, arterial hypertension, and coronary and cerebrovascular disease, the incidence can be up to 30%. Peripheral artery disease (PAD) also increases with age, so the incidence in those over 85 years of age is as high as 50%[2]. Numerous comorbidities, especially at an advanced age, not only modify the typical clinical presentation but also occasionally influence the treatment outcomes, increasing the already very high cardiovascular risk in this population. Given the vulnerability of this population due to cardiovascular risk and very common comorbidities, it is important to follow the guidelines for the diagnosis and treatment of PAD, and a personalized approach should be used in choosing the optimal treatment with the goal of achieving the maximum effect with minimal side-effects[3]. Diagnostics and monitoring the clinical course in patients with PAD is based on assessing functional status, anamnesis, clinical status, plethysmography, and ankle brachial index (ABI). Ultrasound examination in PAD diagnosis can objectivize the anatomic and hemodynamic significance of the atherosclerotic process. Imaging methods (MSCT or MR angiography) are an integral part of the diagnostic algorithm when anatomic imaging is necessary for planning and decision-making regarding the optimal method of revascularization. The specificity of ABI is approximately 95% if its value is below 0.9, and the sensitivity is 79-95% in comparison with angiography as a method of discovering occlusive arterial disease[4]. ABI values and disease symptoms are often uncorrelated, so it is sometimes necessary to perform an exertion test and measure ABI after the test. Functional diagnostics and anamnesis are often neglected in assessing the severity of the clinical presentation, often due to over-implementation of technically sophisticated diagnostic methods such as MR and MSCT, which undoubtably have a role in diagnostics but are not without certain limitations[4-6]. Classification of PAB according to Fontaine and Rutherford is based on assessing the status and functional capacity of the patient. Fontaine stage I comprises patients with PAD who do not have limiting symptoms and pain while walking. Stage II comprises patients who have intermittent claudication symptoms. The II A subgroup has a walking distance (WD) over 200 m, whereas patients in subgroup II B report pain in the extremities at walking distances below 200 m. Stage III comprises patients who report rest pain, and stage IV comprises patients with ulcerations or gangrene. Stage III and IV undoubtably represent patients in whom revascularization is absolutely indicated due to danger to the extremities. Stage I requires monitoring and lifestyle modification with correction and treatment of risk factors, whereas the optimal treatment choice for patients with stable claudication (Fontaine II) requires a detailed clinical assessment with the application of medication treatment and structured walking exercises with supervision. Due to lack of financial support from healthcare funds for the implementation of structured supervised walking exercises, patients usually conduct trainings arbitrarily, which is often not sufficiently effective[4]. The decision on implementing revascularization is based on clinical assessment, disease progression, comorbidities, patient age, and the clinical course of the disease, especially when physiotherapy and pharmacological treatments are not effective. In addition to risk factor correction, nicotine abstinence, and regulation of body weight, blood sugar levels, blood pressure, LDL cho-

glikemije, arterijskog tlaka, LDL kolesterola i triglicerida potrebno je intenzivirati svakodnevno hodanje i tjelovježbu uz nadzor. Neizostavna je primjena antiagregacijskih lijekova u simptomatskoj bolesti, statina i ACE inhibitora[4,7]. Svakako se preporučuje tjelesna aktivnost, odnosno trening hodanja pod nadzorom jer je učinkovitost usporediva i s endovaskularnim metodama revaskularizacije ako se trening ispravno provodi. Upravo zbog tog razloga postoje i kliničke dvojbe oko donošenja odluke o odabiru liječenja; optimalno medikamentno liječenje i vježbe hodanja, endovaskularna ili kirurška revaskularizacija[8-10]. Revaskularizacija u klasi Fontaine II indicirana je ako klaudikacija ograničava kvalitetu života unatoč primijenjenoj optimalnoj farmakoterapiji i modifikaciji čimbenika rizika[11]. Posljednje je desetljeće obilježeno trostrukim porastom endovaskularnih revaskularizacija zbog povećane prevalencije bolesti, bolje dijagnostike, ali i boljih tehničkih mogućnosti endovaskularne terapije pa se kompleksnije lezije sve više liječe endovaskularnim, a manje kirurškim metodama[12,13]. Svrha je ovoga retrospektivnog istraživanja analiza vrijednosti ABI indeksa i dužine hodne pruge, parametara koji bi se trebali rutinski primjenjivati u funkcionalnoj procjeni neposrednih i kasnih učinaka endovaskularne revaskularizacije. Analiza je provedena u grupi bolesnika u kojih je učinjena perkutana endovaskularna revaskularizacija imala dobar angiografski učinak sa svrhom praćenja dinamike promjene vrijednosti parametara ABI-ja i HP-a u razdoblju prije angiointervencije, nakon nje i tijekom praćenja.

Ispitanici i metode

Za istraživanje su iskorišteni podatci iz medicinske dokumentacije bolesnika liječenih u Klinici za bolesti srca i krvnih žila i u Kliničkom zavodu za dijagnostičku i intervencijsku radiologiju KBC-a Zagreb. Od ukupno 135 bolesnika liječenih endovaskularnim metodama revaskularizacije tijekom 2018. godine, samo je 67 bolesnika ispunjavalo zadane uvjete ovoga retrospektivnog ispitivanja, a to su: klinička slika intermitentne klaudikacije funkcionalne klase Fontaine II, izostanak terapijskog učinka konzervativnog liječenja tijekom početnog razdoblja od 6 mjeseci, učinjena perkutana endovaskularna revaskularizacija s dobrim angiografskim rezultatom, postojanje podataka o praćenju postproceduralno i 3 do 6 mjeseci u kontrolnom intervalu. Svi su bolesnici prije revaskularizacije u šestomjesečnom intervalu liječeni statinima, ACE inhibitorima i acetilsalicilatnom kiselinom (ASK), apstinirali su od nikotina i imali su motivacijski razgovor o potrebi svakodnevnog hodanja u trajanju od najmanje 30 minuta, tempom kojim je trebalo provocirati bol u ekstremitetu. Bolesnici su s prirodom bolesti, načinom liječenja i potrebom svakodnevnog hodanja upoznati s pomoću pisanog teksta namijenjena bolesnicima koji boluju od PAB-a. Oboljeli su reevaluirani 6 mjeseci nakon postavljanja dijagnoze. Zbog izostanka učinka ili čak pogoršanja funkcionalnoga statusa, HP-a ili i ABI-ja nakon šestomjesečnog liječenja, provedena je MSCT angiografija na temelju koje je vaskularni tim procijenio koji su bolesnici pogodni za angiointervencijsko liječenje. Iako su svi bolesnici imali bilateralne aterosklerotske promjene arterija donjih ekstremiteta, revaskularizacija je izvedena na simptomatskom ekstremitetu. Svim je bolesnicima unutar 48 sati nakon uspješno obavljene intervencije izmjeren ABI te u kontroli, od 3 do 6 mjeseci postproceduralno, kada je evidentirana dužina HP-a na temelju bolesnikove procjene. U malog

lesterol, and triglycerides, treating stable course intermittent claudication also requires daily walking and supervised physical exercises. It is also necessary to include the application of antiaggregant medication as well as statins and ACE inhibitors in symptomatic phases of the disease[4,7]. Physical activity consisting of walking training with supervision is certainly recommended, since its effectiveness is comparable to endovascular revascularization methods if the training is properly conducted. This is the reason for clinical dilemmas in deciding on treatment choice; optimal medication treatment and walking exercises, endovascular or surgical revascularization[8-10]. Revascularization in Fontaine stage II is indicated if claudication reduces quality of life despite the application of optimal medication treatment and risk factor modification[11]. The past decade was marked by a tripling of endovascular revascularizations due to increased disease prevalence, improved diagnostics, but also due to improved technical options for endovascular treatment, resulting in increased application of endovascular instead of surgical methods for more complex lesions[12,13]. The goal of this retrospective study was to analyze ABI and walking distance values, parameters which should be routinely used in the functional assessment of the immediate and delayed effects of endovascular revascularization. The analysis was conducted in a group of patients who had undergone percutaneous endovascular revascularization leading to a good angiographic effect, with the goal of studying the dynamics of changes in ABI and WD parameters in the periods before and after angiointervention and during follow-up.

Patients and Methods

We used data from medical documentation of patients treated at the Clinic for Cardiovascular Diseases and the Clinical Institute for Diagnostic and Interventional Radiology at the University Hospital Centre Zagreb. Out of a total of 135 patients treated with endovascular revascularization methods in 2018, only 67 fulfilled the inclusion criteria for this retrospective study, which were: a clinical picture with Fontaine stage II intermittent claudication, lack of response to conservative treatment in the initial 6-month period, application of percutaneous endovascular revascularization with good angiographic results, availability of postprocedural follow-up data in 3- to 6-month intervals. Before revascularization, all patients underwent a 6-month interval of treatment that involved statins, ACE inhibitors, and aspirin, nicotine abstinence, and a motivational conversation on the need for daily walks lasting at least 30 minutes at a pace that provoked pain in the extremities. The patients were also informed of the nature of their disease, the treatment method, and the need for daily walks via a leaflet designed for patients suffering from PAD. Patients were re-evaluated 6 months after the establishment of the diagnosis. Due to lack of treatment response or even deterioration of functional status, walking distance, and ABI after 6 months of treatment, MSCT angiography was used to allow the vascular team to asses suitability for angiointerventional treatment. Although all patients had bilateral atherosclerotic changes in arteries of the lower extremities, revascularization was performed only on the symptomatic leg. The ABI of all patients was measured within 48 h of successful completion of the procedure, followed by postprocedural ABI measurements at 3- to 6-month follow-up when the walking distance was noted based on the patient's self-assessment.

je broja bolesnika učinjena i bilateralna revaskularizacija pa ti bolesnici nisu bili uključeni u ispitivanje, kao ni bolesnici Fontaine klase III ili IV s vitalno ugrožavajućom kritičnom ishemijom te oni u kojih angiointervencija tehnički nije bila uspješna. Svi su bolesnici u razdoblju od minimalno mjesec dana nakon izvedene intervencije liječeni dvojnom antiagregacijskom terapijom primjenom ASK-a 100 mg i klopidogrela 75 mg jednom na dan, a potom dugotrajno ASK-om te trajno visokim dozama statina i prilagođenim dozama ACE inhibitora kao standarda u liječenju PAB-a. Vježbe hodanja i dalje su bile dio uobičajenih standardnih preporuka. Svim je bolesnicima izmjeren ABI 24 do 48 h postproceduralno i u kontrolnom razdoblju od 3 do 6 mjeseci.

Mjerenje je provedeno uporabom *Vaso Guard Viasys* aparata za standardnu procjenu protoka na temelju pletizmografije i mjerenja segmentalnih tlakova i određivanjem ABI-ja. Pretraga je učinjena nakon odmora od 10 minuta u prostoriji sobne temperature.

Anamnestički podatak o dužini HP-a smatrao se relevantnim i uvršten je u analizu. Dužina prijeđenog puta bez bolova u hodu izražena je u metrima, a analiziran je bio podatak prije angiointervencije i 3 do 6 mjeseci nakon zahvata.

Za statističku analizu primijenjen je statistički program SPSS 20.0 i Python verzija 3.7.1., Friedmanov test i Wilcoxonov test za signifikantnost parametara kontinuiranih varijabli, Spearmanov test regresijske analize te x^2 test za usporedbu kategorijskih varijabli. Razina signifikantnosti smatrana je uz vrijednost $p < 0,05$.

Rezultati

U analizu su uvršteni podatci 67 bolesnika sa simptomatskom bolešću Fontaine II i unilateralnom endovaskularnom intervencijom koja je postigla angiografski dobar rezultat. Bolesnici su imali bilateralnu bolest, a intervencija je provedena samo na ekstremitetu koji je bio simptomatičan i limitirajući čimbenik kvalitete života bolesnika. Rezultati su analizirani u vremenskom slijedu: prije, neposredno nakon i u 3 do 6-mjesečnom razdoblja praćenja (kontrola) nakon PTA-a (engl. *percutaneous transluminal angioplasty*). Komplikacije vezane uz proceduru bile su prisutne u 5 (7,4 %) bolesnika, i to jedno retroperitonealno krvarenje, 3 hematoma punkcijskog mjesta koja nisu zahtijevala transfuzijsko liječenje i 1 arteriovenska fistula. Karakteristike bolesnika prikazane su u **tablici 1**.

Bilateral revascularization was performed in a small number of patients, so these patients were not included in the study, and neither were patients at Fontaine stage III or IV with life-endangering critical ischemia and those in whom the angiointervention was not technically successful. All patients were treated with aspirin 100 mg and clopidogrel 75 mg daily for a minimum of one month after intervention, followed by long-term treatment with aspirin and high doses of statins as well as adjusted doses of ACE inhibitors as the treatment standard for PAD. Walking exercises were still part of the usual standard recommendations. All patients underwent ABI measurement 24 to 48 h after the procedure and at 3- to -6-month follow-up.

Measurements were performed using the *Vaso Guard Viasys* device for standard flow assessment based on plethysmography, segmental pressure measurement, and determining ABI. The test was performed after the patient had a 10-minute rest in a space at room temperature.

Anamnesis regarding walking distance was considered relevant and was included in the analysis. Pain-free walking distance was expressed in meters and data before the intervention and 3 to 6 months after the procedure were analysed.

SPSS 20.0 and Python version 3.7.1 were used for statistical analysis. The Friedman and Wilcoxon tests were used for determining significance for parameters with continuous variables. The Spearman regression analysis test and the Chi-squared test were used to compare categorical variables. The level of significance was set at $p<0.05$.

Results

Data from 67 patients with symptomatic Fontaine stage II disease and unilateral endovascular intervention with good angiographic results were included in the analysis. The disease was bilateral in all the patients, and the intervention was performed only on the leg that was symptomatic and therefore a limiting factor for patient quality of life. The results were analysed chronologically: before intervention, immediately after intervention, and at 3- to 6-month follow-up after percutaneous transluminal angioplasty (PTA). Complications associated with the procedure were present in 5 (7.4%) of patients and included one retroperitoneal haemorrhage, 3 puncture site hematomas that did not require transfusion treatment, and 1 arteriovenous fistula. Patient characteristics are shown in **Table 1**.

TABLE 1. Patient clinical characteristics.

Number of patients (mean age+standard deviation)	67 (66.58±9.17)
Men	35 (65.71±6.5)
Women	32 (67.53±11.5)
Comorbidity	**N (%)**
Arterial hypertension	61 (91%)
Diabetes	31 (46%)
Chronic renal disease	6 (9%)
Ischemic heart disease	12 (18%)
Cerebrovascular disease	6 (9%)

Vrijednosti ABI-ja izmjerene neposredno nakon intervencije, tj. unutar 48 sati, bile su signifikantno više u usporedbi s vrijednostima prije zahvata (0,65 ± 0,19 prije, 0,84 ± 0,18 poslije p <0,05). Značajna se razlika održala konstantnom i na kontrolnom pregledu 3 do 6 mjeseci poslije. Pozitivan učinak revaskularizacije u postproceduralnom razdoblju praćenja od 3 do 6 mjeseci uočen je na obama ekstremitetima: na ekstremitetu na kojemu je učinjena revaskularizacija, ali i na kontralateralnoj strani (**tablice 2, 3** i **4**). Promjena vrijednosti ABI-ja ekstremiteta podvrgnuta revaskularizaciji u postintervencijskom razdoblju praćenja pozitivno korelira i s vrijednostima ABI-ja suprotne noge u kontrolnom intervalu (Spearmanov koeficijent korelacije = 0,45, p <0,01).

Diskusija

Angiointervencijsko liječenje s angiografski uspješnim rezultatom dovelo je do signifikantnog porasta vrijednosti ABI-ja i HP-a u bolesnika u kojih u razdoblju od šest mjeseci prije intervencije konzervativno liječenje nije imalo učinka. Promjena ABI-ja neposredno nakon uspješne PTA uz stabilno nepromijenjenu vrijednost tijekom praćenja te statistički značajno produljenje hodne pruge u razdoblju praćenja dokaz su stabilnosti uspješnoga angiointervencijskog zahvata u ukupnoj populaciji bolesnika.

Rezultati dosadašnjih istraživanja[8,14,15] i sada prikazani rezultati potvrđuju da se od treninga hodanja i farmakoterapije može očekivati kliničko i funkcionalno poboljšanje u PAB-u jer je u ovom ispitivanju zabilježen porast vrijednosti ABI-ja na ekstremitetu koji nije bio podvrgnut revaskularizaciji. Po-

ABI values measured immediately after intervention, i.e. within 48 h, were statistically significantly higher in comparison with values before the procedure (0.65±0.19 before, 0.84±0.18 after; p<0.05). The statistically significant difference remained constant during the follow-up examination 3 to 6 months later. A positive effect of revascularization in the postprocedural 3- to 6-month follow-up period was observed on both legs; both the leg on which the procedure was performed and on the contralateral side (**Table 2**, **Table 3**, and **Table 4**). Change in postinterventional follow-up ABI values in the leg on which revascularization was performed also had a positive correlation with ABI values in the other leg in the follow-up period (Spearman correlation coefficient=0.45; p<0.01).

Discussion

Angiointerventional treatment with angiographically successful results lead to a significant increase in ABI and walking distance values in patients who showed lack of response to conservative treatment in a 6-month period before the intervention. ABI changes immediately after successful PTA with stable, unchanged values during follow-up and statistically significant increase in walking distance during follow-up represent evidence for the stability of successful angiointerventional procedures in the general patient population.

The results of previous studies[8,14,15] as well as those from the present study confirm that walking training and pharmacotherapy can be expected to lead to clinical and functional improvement of PAD given that this study has found an increase in ABI values on the leg that did not undergo revascularization.

TABLE 2. Ankle brachial index values and walking distance before endovascular interventions and in follow-up.

ABI value/number of pts	Before PTA	Follow up	P value
Right (N=27)	0.66±0.21	0.84±0.15	**0.012**
Left (N=40)	0.65±0.13	0.91±0.18	**0.002**
Walking distance (meters)			
Right side intervention	191.8±267.7	846.1±269.6	**0.004**
Left side intervention	194.9±285.5	867.8±311.1	**0.003**

ABI = ankle brachial index; PTA = percutaneous transluminal angioplasty

TABLE 3. Ankle brachial index values before and after interventions and in follow-up on the contralateral leg.

	Before PTA	After PTA	Follow up	P value
ABI left **Right leg PTA** (N=27)	0.86±0.21	0.81±0.26	0.89± 0.16	0.10
ABI right **Left leg PTA** (N=40)	0.81±0.20	0.87±0.15	0.91±0.15	**0.05**

ABI = ankle brachial index; PTA = percutaneous transluminal angioplasty

TABLE 4. Ankle brachial index values and claudication distance before percutaneous transluminal angioplasty and in follow-up.

	ABI before	ABI follow up	P value	CD before	CD in follow up	P value
Age years **<65 N=26**	0.77±0.17	0.89±0.16	0.07	161±239	824±347	**0.001**
Age years **> 65 N=41**	0.58±0.15	0.87±0.18	**0.006**	217±299	883±247	**0.001**
Diabetes YES (46%)	0.65±0.22	0.85±0.15	**0.049**	267±343	757±322	**0.02**
NO (54%)	0.66±0.15	0.91±0.18	**0.03**	143±207	942±237	**0.001**
Hypertension YES (91%)	0.67±0.18	0.87±0.18	**0.01**	183±255	869±285	**0.001**
NO (9%)	0.60±0.22	0.93±0.05	0.09	300±468	700±424	0.32
Target lesion CIA, EIA, SFA, PA (94%)	0.65±0.19	0.88±0.17	**0.001**	203±284	854±293	**0.001**
Below the knee (6%)	0.70±0.15	0.84±0.15	0.223	85±85*	1000*	*

ABI = ankle brachial index; PTA = percutaneous transluminal angioplasty; CD = claudication distance; CIA = common iliac artery; EIA = external iliac artery; SFA = superficial femoral artery; PA = popliteal artery

rast vrijednosti ABI-ja u kontralateralnom ekstremitetu statistički je značajan, iako se razlika u porastu vrijednosti ABI-ja ne može smatrati funkcionalno relevantnom jer je porast ABI-ja lijevo iznosio prosječno 0,1. Sobieszczyk *i sur.*[16] smatraju da je porast vrijednosti ABI-ja od 0,15 klinički značajna promjena vrijednosti, kao odraz boljega arterijskog protoka. O promjenama ABI-ja u slučaju konzervativnog, neintervencijskog liječenja koje bi činile diskriminirajuću razliku poboljšanja nema dovoljno podataka. Porast vrijednosti ABI-ja rezultat je porasta tlaka zbog restitucije protoka magistralnom arterijom. Promjene ABI-ja uz poboljšanje ukupne perfuzije formiranjem novonastalih kolaterala, što je uglavnom rezultat koji se očekuje primjenom konzervativnih mjera liječenja, nisu dokazane[15,16]. Pitanje izostanka učinka konzervativnih mjera liječenja prije učinjene PTA vezano je za selekciju bolesnika kakvu često susrećemo u kliničkoj praksi, iako su bolesnici liječeni u skladu sa smjernicama za liječenje PAB-a[4]. Porast vrijednosti ABI-ja na ekstremitetu koji nije bio podvrgnut endovaskularnoj revaskularizaciji vjerojatno je posljedica bolje suradljivosti bolesnika i udruženog učinka primijenjene farmakoterapije, primjene dvojne antiagregacijske terapije, ali i kvalitetnijega tjelesnog treninga koji je sada bio ustrajniji, i to zbog produljenja hodne pruge nakon provedene PTA simptomatskog ekstremiteta. Ovi su rezultati sukladni s ESC-ovim smjernicama za liječenje PAB-a[4].

Increase in ABI values on the contralateral leg was statistically significant although the difference in ABI value increase cannot be considered functionally relevant, because the ABI increase in the left leg was 0.1 on average. Sobieszczyk *et al.*[16] believed that an ABI increase of 0.15 represents a clinically significant change that reflects improved arterial flow. There is insufficient data on ABI changes that would represent a discriminating difference in improvement for conservative, non-interventional treatment. Increase in ABI values is the result of increased blood pressure due to restitution of flow in the main artery. There is insufficient evidence for ABI changes with improvement of total perfusion through the formation of new collaterals, which is usually the expected result of applying conservative treatment measures[15,16]. The issue of lack of effect from conservative treatment measures prior to PTA is associated with patient selection common in clinical practice, despite the patients having been treated according to guidelines for PAD[4]. Increase in ABI values in the leg where the endovascular revascularization was not performed is likely the consequence of improved patient compliance and the compounded effect of pharmacotherapy application, application of dual antiplatelet therapy, but also of higher-quality physical training that is being more rigorously applied due to increased walking distance after PTA on the symptomatic leg. These results are in line with ESC guidelines for PAD treatment[4].

Ispitivana je populacija bila izložena multiplim komorbiditetima, i to najčešće arterijskoj hipertenziji. Prisutnost različitih komorbiditeta nije utjecala na rezultate intervencije i ispitivane parametre, vrijednost HP-a i ABI-ja. Arterijska hipertenzija bila je odsutna u samo 9 % ispitanika, što čvrsto povezuje okluzivnu bolest arterija i povišeni arterijski tlak[17,18].

U ispitivanoj podskupini dijabetičara visoke su vrijednosti ABI-ja prije intervencije očekivane jer mediosklerozom zahvaćene arterije u dijabetičara postaju nestlačive, što dovodi do visokih vrijednosti ABI-ja. Ipak i u ovoj je grupi angiointervencija dovela do porasta ABI-ja i znatnog produljenja HP-a, sukladno rezultatima drugih autora[19].

Dobar je učinak angiointervencijske revaskularizacije, s obzirom na promjenu duljine HP-a i porast vrijednosti ABI-ja, ostvaren samo u ispitanika starijih od 65 godina. Ovakva različitost može biti posljedica manjeg uzorka bolesnika mlađih od 65 godina (37 %), ali i inicijalno boljih vrijednosti ABI-ja prije intervencije, što nije dovelo do značajne razlike u zabilježenim vrijednostima. U istoj je skupini produljenje HP-a bilo statistički značajno ($p < 0,001$). Dužina HP-a je parametar koji je, iako nije verificiran metodama mjerenja u kontroliranim uvjetima, nego je dobiven iskazom bolesnika o njegovoj dužini, u svim ispitivanim kategorijama pokazao znatan porast vrijednosti uz promjenu funkcionalnog statusa u bolesnika nakon PTA-a. Porast dužine HP-a postignut je u svim dobnim skupinama i neovisno o prisutnosti komorbiditeta, s visokom razinom i kliničke i statističke značajnosti. Porast ABI-ja nakon angiointervencije u ukupnoj je populaciji bio statistički značajan ($p < 0,05$), a ipak u pojedinim ispitivanim kategorijama i karakteristikama skupine nije pratio statistički značajan porast HP-a. Nepodudarnost je, iako je bila riječ o proporcionalno malim brojevima, uočena s obzirom na varijable: životna dob, u bolesnika koji nisu imali arterijsku hipertenziju i u grupi u kojoj je učinjena PTA potkoljeničnih arterija. Varijabilnosti vrijednosti ABI-ja zamijećene su u mnogim ispitivanjima. Rezultati Registra *PORTRAIT PAD* pokazuju da upravo maksimalna dužina HP-a i prijeđena udaljenost bez klaudikacije reproducibilno označuje i procjenjuje funkcionalni status bolesnika u svakodnevnom životu i kliničkoj praksi, dok su vrijednosti ABI-ja upitne u funkcionalnoj procjeni, ali ne i u procesu probira i rane detekcije PAB-a, kada je značenje ABI-ja neupitno[4,20].

Rezultati Amighi *i sur.* pokazali su da je kontroliranim programima tjelovježbe te metodama konzervativnog liječenja moguće postići smanjenje simptoma uz poboljšanje kvalitete života te porast maksimalne duljine hodne pruge s početnih 100 metara na duljinu od 650 metara tijekom razdoblja unutar godine dana, ali bez znatnih promjena vrijednosti ABI indeksa[7]. Osjetljivost ABI-ja u praćenju prohodnosti nakon revaskularizacije može se postići i primjenom ABI stres testa, što bi, zasigurno, bio vrijedan i reproducibilan podatak[21].

Zaključci

Uspješna endovaskularna revaskularizacija (PTA) u usporedbi sa standarnom farmakoterapijom i nenadziranim vježbama hodanja u bolesnika funkcionalne klase Fontaine II rezultirala je produljenjem vrijednosti HP-a i porastom ABI-ja. Prisutnosti komorbiditeta nisu utjecale na rezultate ispitivanih parametara. Promjena ABI indeksa na ekstremitetu na kojemu je provedena intervencija u razdoblju praćenja bila je značajna i očekivana. Uspješnost i „stabilnost" uspješne re-

The population in the present study was exposed to multiple comorbidities, most commonly arterial hypertension. The presence of different comorbidities did not affect the results of the intervention or the study parameters, namely walking distance and ABI. Normal blood pressure was present in only 9% of participants, which points to a strong association between occlusive arterial disease and elevated arterial pressure[17,18].

In the subgroup of participants with diabetes, high ABI values prior to intervention were expected because the arteries affected by medial sclerosis in diabetics become incompressible, leading to high ABI values. However, angiointervention led to ABI increase even in this subgroup, as well as to increased walking distance, which is in agreement with results reported by other authors[19].

Good effects from angiointerventional revascularization on walking distance and ABI increase were achieved only in participants above 65 years of age. The explanation for this difference could be the smaller sample of patients younger than 65 years of age (37%), but also their initially better ABI values before intervention, which led to there being no significant difference in postinterventional values. Increase in walking distance in the same group was statistically significant ($p < 0.001$). Despite the fact that walking distance is a parameter that was not verified with measurements in controlled conditions but was obtained through self-reporting, there was a statistically significant increase in walking distance with change in functional status after PTA in all patient categories. Increase in walking distance was achieved in all age groups and regardless of the presence of comorbidities, with a high level of both clinical and statistical significance. Increase in ABI after angiointervention was statistically significant in the total population ($p<0.05$), but did not parallel the statistically significant increase in walking distance for certain study categories and group characteristics. There was a lack of correspondence, albeit proportionally small, for the following variables: age, patients who did not have arterial hypertension, and in the group in which PTA was performed on the lower leg. Variable ABI values were observed in many studies. Results from the PORTRAIT PAD registry indicated that maximum walking distance and claudication-free walking distance represent a reproducible marker of functional status in patients both in their everyday life and in clinical practice, whereas ABI values were of questionable value in functional assessment, but not in the screening and early detection for PAD, where the importance of ABI is beyond question[4,20].

Results reported by Amighi *et al.* showed that controlled exercise programs and conservative treatment methods can achieve a reduction in symptoms with an improvement in quality of life, as well as increased walking distance from an initial 100 m to 650 m within a year, but with no significant change in ABI values[7]. The sensitivity of ABI for measuring flow after revascularization can also be achieved through the application of an ABI stress test, which would certainly represent valuable and reproducible data[21].

Conclusions

Successful endovascular revascularization (PTA) in comparison with standard pharmacotherapy and unsupervised walking exercises in patients with Fontaine stage II resulted in increased walking distance and ABI. Presence of comor-

vaskularizacije procijenjene vrijednostima ABI-ja i dužinom HP-a bila je prisutna i tijekom praćenja. Vrijednost ABI-ja kontralateralnog ekstremiteta u razdoblju praćenja je porasla i korelira s porastom ABI-ja ekstremiteta podvrgnuta angiointervenciji. Na temelju prikazanih rezultata analize može se repozicionirati značenje procjene dužine HP-a kao često zanemarenog podatka koji bi trebao biti neizostavan parametar u praćenju uspjeha revaskularizacije i funkcionalnoga statusa bolesnika s PAB-om.

bidities did not affect the results of the study parameters. Changes in ABI during the follow-up period in the leg where the revascularization was performed were significant and expected. The successfulness and "stability" of successful revascularization assessed through ABI values and walking distance was also observed during follow-up. ABI values in the contralateral leg were increased in the follow-up period and correlated with ABI increase in the leg on which angiointervention was performed. Based on these results, walking distance assessment represents a commonly neglected factor that should be reevaluated and considered as an important parameter in monitoring revascularization successfulness and functional status of patients with PAD.

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