

**MEDICINSKI
FAKULTET**

Adresa: Kruševac bb
81000 PODGORICA
CRNA GORA
Tel: +382 20 246 651
Fax: +382 20 243 842
url: www.ucg.ac.me/medf
E-mail: infomedf@ac.me



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Address: Krusevac bb
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MONTENEGRO
Phone: +382 20 246 651
Fax: +382 20 243 842
url: www.ucg.ac.me/medf
E-mail: infomedf@ac.me

Broj: 1958/5-1
Podgorica, 22.11.2021. godine

**Univerzitet Crne Gore
Odbor za doktorske studije**

Poštovani,

U skladu sa članom 33 Pravila doktorskih studija i tačkom 3.7. Vodiča za doktorske studije, dostavljamo Odluku Vijeća Medicinskog fakulteta i Drugi Izvještaj mentora prof. dr Nataše Popović i komentora prof. dr Milice Martinović, o radu doktoranda dr med Isidore Rovčanin Dragović, na službenom jeziku i na engleskom jeziku.

S poštovanjem.


MEDICINSKI FAKULTET
DEKAN
Prof. dr Miodrag Radunović

UNIVERZITET CRNE GORE
MEDICINSKI FAKULTET
Broj: 1958/5
Podgorica, 22.11.2021. godine

Na osnovu člana 64 Statuta Univerziteta Crne Gore (Bilten UCG br:337/15 i 447/18) člana 33 stav 2 Pravila doktorskih studija broj: 08-583 od 26.02.2015. godine, a u vezi sa godišnjim izvještajem mentora i komentora o napredovanju doktoranda broj: 1811 od 28.10.2021. godine i Izvještaja komisije za doktorske studije broj: 1811/1 od 29.10.2021. godine, Vijeće Medicinskog fakulteta na elektronskoj sjednici održanoj 19-22.11.2021. godine, donijelo je

ODLUKU

1. Usvaja se Drugi godišnji izvještaj mentora, prof. dr Nataše Popović i komentora prof. dr Milice Martinović o radu doktoranda dr med Isidore Rovčanin Dragović, na sprovedenom istraživanju i postignutim rezultatima, na izradi doktorske disertacije, sa objavljenim rezultatima rada na izradi doktorske disertacije.
2. Drugi godišnji izvještaj mentora o napredovanju doktoranda broj: 1811 od 28.10.2021. godine, na službenom jeziku i engleskom jeziku, čini sastavni dio ove odluke.
3. Izvještaji iz tačke 2 ove Odluke, dostavljaju se Centru za doktorske studije – Odboru na saglasnost.

VIJEĆE MEDICINSKOG FAKULTETA
PREDSJEDAVAJUĆI,

Prof. dr Miodrag Radunović, dekan



GODIŠNJI IZVJEŠTAJ MENTORA O NAPREDOVANJU DOKTORANDA

Akademska godina za koju se podnosi izvještaj		2020/21				
OPŠTI PODACI O DOKTORANDU						
Titula, ime, ime roditelja, prezime		Dr med. Isidora, Rade, Rovčanin Dragović				
Fakultet		Medicinski fakultet Univerziteta Crne Gore				
Studijski program		Medicina				
Broj indeksa		2013/01				
MENTOR/MENTORI						
Prvi mentor		Prof. dr Nataša Popović	Medicinski fakultet Univerziteta Crne Gore, Crna Gora	Fiziologija		
Drugi mentor		Prof. dr Milica Martinović	Medicinski fakultet Univerziteta Crne Gore, Crna Gora	Patofiziologija		
EVALUACIJA DOKTORANDA*						
Koliko ste zadovoljni kvalitetom održanih susreta sa doktorandom?		1	2	3	4	5 <input checked="" type="checkbox"/>
(Ako je prethodni odgovor „1“ ili „2“ dati obrazloženje i prijedloge za poboljšanje)						
Da li je definisan plan rada sa doktorandom?			<input checked="" type="checkbox"/> DA		NE	
Da li je doktorand ostvario napredak prema predviđenom planu rada?			<input checked="" type="checkbox"/> DA		NE	
(Ako je prethodni odgovor „ne“ dati obrazloženje i prijedloge za poboljšanje)						
Kvalitet napretka doktorandovog istraživačkog rada u periodu između dva izvještaja je:		1	2	3	4	5 <input checked="" type="checkbox"/>
(Ako je prethodni odgovor „1“ ili „2“ dati obrazloženje i prijedloge za poboljšanje)						
Dati ocjenu doktorandove spremnosti za konsultacije.		1	2	3	4	5 <input checked="" type="checkbox"/>
Dati ocjenu planiranja i izvršavanja		1	2	3	4	5 <input checked="" type="checkbox"/>

*Ocjene su: 1 - nedovoljan, 2 - dovoljan, 3 - dobar, 4 - vrlo dobar, 5 - odličan

ObrazacIM:Godišnji izvještaj mentora o napredovanju doktoranda

godišnjih istraživačkih aktivnosti i stručnog usavršavanja doktoranda.					
Dati ocjenu napretka u savladavanju metodologije naučno-istraživačkog rada.	1	2	3	4	<input checked="" type="checkbox"/> 5
Dati ocjenu o aktivnostima sprovedenim na pisanju i objavljivanju naučnih radova	1	2	3	<input checked="" type="checkbox"/> 4	5
Dati ocjenu doktorandovog generalnog odnosa prema studijama.	1	2	3	4	<input checked="" type="checkbox"/> 5
Dati ocjenu ukupnog kvaliteta doktorandovog rada.	1	2	3	4	<input checked="" type="checkbox"/> 5
(Ako je prethodni odgovor „1“ ili „2“ dati obrazloženje i prijedloge za poboljšanje)					
SAGLASNOST ZA NASTAVAK STUDIJA					
Može li doktorand nastaviti studije?	<input checked="" type="checkbox"/> Da <input type="checkbox"/> Da, uz određene uslove <input type="checkbox"/> Ne				
(Ako je prethodno dat odgovor pod „Da, uz određene uslove“ ili „Ne“ dati obrazloženje i prijedloge za poboljšanje)					
Napomene					
<p>Kandidatkinja, dr med. Isidora Rovčanin Dragović, položila je sve ispite predviđene planom Doktorskih studija u roku, sa prosječnom ocjenom 10.</p> <p>Dr Rovčanin Dragović je, potom, prijavila temu Doktorske disertacije, pod nazivom: „Nova metoda za stratifikovanje rizika za obolijevanje od Alchajmerove bolesti kod pacijenata u Crnoj Gori“ i sa odličnom ocjenom je dana 12.11.2020. godine odbranila polazna istraživanja doktorske disertacije. Odbrana je bila pred prisutnom komisijom, u sastavu: Dr Miodrag Radunović, redovni profesor Medicinskog fakulteta Univerziteta Crne Gore, (predsjednik Komisije), dr Nataša Popović, vanredni profesor Medicinskog fakulteta Univerziteta Crne Gore (mentor), dr Milica Martinović, redovni profesor Medicinskog fakulteta Univerziteta Crne Gore (komentor), dr Elka Stefanova, redovni profesor na Katedri za neurologiju Medicinskog fakulteta Univerziteta u Beogradu i dr Apollonia Tullo, istraživač u oblasti biomedicinskih nauka na Institutu za biomembrane, bienergetiku i biotehnologiju u Bariju, Italija (članovi Komisije).</p> <p>Odlukom Senata Univerziteta Crne Gore, broj 03-6711, od 21.01.2021. godine, izvještaj Komisije za ocjenu podobnosti Doktorske disertacije je usvojen, a predložena Doktorska teza i kandidatkinja prihvaćeni kao podobni, te dr Rovčanin Dragović nastavlja realizaciju plana disertacije. Naime, kako se istraživanje sprovodi u okviru naučnoistraživačkog projekta Medicinskog fakulteta koje je finansirano od strane Ministarstva nauke Crne Gore, pod nazivom: “Nove metode za stratifikaciju rizika za progresiju kancera i Alchajmerove bolesti kod pacijenata u Crnoj Gori”, njegova realizacija je započeta u aprilu 2019. godine, a završena</p>					

septembra 2021. godine. Istraživanje je sprovedeno u Kliničkom centru Crne Gore i Centru za naučno-istraživački rad Medicinskog fakulteta, a u saradnji sa Institutom za biomembrane i bioenergetiku iz Barija.

Planirano istraživanje u okviru Doktorske disertacije dr Rovčanin Dragović, bilo je prospektivnog i multidisciplinarnog karaktera i obuhvatalo je:

- 1) regrutaciju pacijenata,
- 2) kliničko istraživanje,
- 3) molekularno biološko istraživanje

Kandidatkinja je, najprije, aktivno učestvovala u kreiranju kriterijuma za regrutaciju kao i u samom procesu regrutacije pacijenata. Budući da je ljekar na specijalizaciji iz Neurologije, a takođe sertifikovana za neuropsihološku procjenu pacijenata, kandidatkinja je sprovodila predviđeno kliničko istraživanje, kroz neurološki pregled i procjenu kognitivnog funkcionisanja ispitanika. Na kraju, po prikupljanju predviđenog broja bioloških uzoraka, u laboratoriji Centra za naučno-istraživački rad, dr Rovčanin Dragović je bila zadužena i za molekularno biološko istraživanje. U tom procesu rada, savladala je nove i usavršila ranije usvojene molekularno biološke tehnike. Naime, nakon inicijalne obrade uzoraka pune periferne krvi pacijenata, odvajanjem ćelijskih elemenata i plazme, sproveden je protokol izolacije ukupne cirkulišuće mikroRNK (miRNK) iz odvojene plazme. Ta metoda je prvi put primijenjena u Crnoj Gori, a time je, osim pripreme uzoraka za konkretno istraživanje, otpočeto kreiranje banke miRNK za potencijalno buduće istraživanje kompletnog profila ekspresije. Na kraju je, qRT-PCR metodom utvrđen nivo ekspresije specifičnih miRNK. Naime, odabrane su one miRNK, čija deregulisana ekspresija je utvrđena i kod Alchajmerove bolesti i kod kolorektalnog karcinoma:

- miR-29a/b
- miR-101
- miR-125b
- miR-146a
- miR-155

Trenutno kandidatkinja radi na predstavljanju rezultata molekularno biološkog istraživanja, čije se publikovanje planira do kraja 2021. godine. Kandidatkinja je, zajedno sa mentorima, identifikovala prvi izbor časopisa gdje će rad biti poslat na recenziju - Journal of Alzheimer's disease (Impakt faktor za 2020. godinu 4.472). U toku je statistička obrada podataka i sistematizacija rezultata u skladu sa zahtjevima formata za publikaciju u ovom časopisu.

Dio rezultata dobijenih kliničkim istraživanjem, dr Rovčanin Dragović je na svjetskoj neurološkoj konferenciji „14th World Congress on Controversies in Neurology (CONy)“ kao prvi autor prezentovala poster, pod nazivom: „Improving the Diagnosis of Cognitive Impairment in Montenegro - on the

Path of Learning.”

Takođe, dr Rovčanin Dragović je, podstaknuta rezultatima kliničkog istraživanja koje je prezentovala na CONy konferenciji, osmislila dodatnu studiju na temu stigmatičnih uvjerenja u vezi sa Alchajmerovom bolešću u Crnoj Gori. Kandidatkinja je, u saradnji sa mentorkom, već jasno definisala karakteristike ciljane populacije koja će biti obuhvaćena ovom studijom, identifikovala je i adekvatne standardizovane upitnike i metode pomoću kojih mogu da se sakupe relevantne informacije. Kandidatkinja planira da uporedo sa istraživanjem za Doktorsku disertaciju odradi i ovo istraživanje. Rezultati ovog dodatnog istraživanja će biti komplementarni sa rezultatima Doktorske disertacije u smislu da će ukazati na značaj podizanja svijesti o Alchajmerovoj demenciji među stanovništvom u našem regionu i naglasiće značaj rezultata same Doktorske disertacije na kojoj kandidatkinja intenzivno radi. U vezi sa izloženim, planiramo objavljivanje još jednog originalnog naučnog rada, potencijalno u časopisu BMC Geriatrics (impakt faktor za 2019-20 godinu je 3.516), na kom će kandidatkinja takođe biti prvi autor.

Kandidatkinja, dr Isidora Rovčanin Dragović je u dosadašnjem radu pokazala maksimalnu angažovanost i motivaciju, kao i posebnu širinu u svom pristupu naučnom istraživanju. Svoje obaveze je uspješno izvršavala na vrijeme, zahvaljujući čemu svoj naučnoistraživački rad, sakupljanje i obradu podataka privodi kraju. Važno je naglasiti da je, zahvaljujući izuzetnoj predanosti u toku svog istraživanja, kandidatkinja uspjela da prebrodi i brojne neplanirane izazove koji su bili direktno uzrokovani COVID-19 pandemijom - od pravovremene nabavke instrumenata i potrošnog materijala, preko regrutacije starijih pacijenata koji predstavljaju najvulnerabilniji dio populacije, do učešća na konferencijama i prezentovanja rezultata pred internacionalnom naučnom zajednicom u uslovima kada su u cijelom svijetu granice zatvorene.

Na osnovu svega izloženog, smatram da kandidatkinja dr Isidora Rovčanin Dragović uspješno napreduje ka odbrani svoje doktorske disertacije i predlažem da joj se omogući nastavak rada u cilju završetka doktorskih studija.

IZJAVA MENTORA

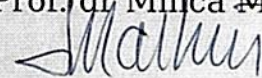
Izjava mentora o vremenskom periodu i realizaciji polaznih istraživanja
(popunjava se samo za prvi izvještaj mentora)

U Podgorici,
19.10.2021.

Ime i prezime prvog mentora
Prof. dr Nataša Popović



Ime i prezime drugog mentora
Prof. dr Milica Martinović



MP

Prilog dokumenta sadrži:

- Objavljeni rezultati rada na izradi doktorske disertacije (za drugi izvještaj mentora):

Poster prezentacija: Improving the Diagnosis of Cognitive Impairment in Montenegro- on the Path of Learning. Isidora Rovčanin Dragović, Ljiljana Radulović, Jevto Eraković, Miodrag Radunović, Goran Popivoda, Tijana Vuković, i Nataša Popović, November 2020, 14th World Congress on Controversies in Neurology - CONy 2020, <https://simul-europe.com/2020/cony/Files/220953.pdf>

SAŽETAK: Improving the diagnosis of cognitive impairment in patients in Montenegro - on the path of learning


Isidora Rovčanin Dragović, Ljiljana Radulović, Jevto Eraković, Miodrag Radunović, Goran Popivoda, Tijana Vuković and Nataša Popović

The estimated prevalence of dementia in Montenegro was lower compared to most of the European countries in 2019 (1.06%). There is a concern that with currently used diagnostic approach, dementia in Montenegro is underdiagnosed.

To assess currently used neuropsychologic screening tests, 15 patients with clinical signs of cognitive impairment (CI) were recruited at the Clinical Center of Montenegro in 2019. Following the clinical assessment, patients were divided in 2 groups: mild cognitive impairment (MCI) and dementia. They were subsequently subjected to Mini-Mental State Examination (MMSE), routinely used in primary health care; and to Montreal Cognitive Assessment (MoCA), designed for improved detection of MCI.

The average time from the first disease manifestation until the diagnosis was 13.4 months. The higher the level of education was, the longer was the time to diagnosis ($r=0.545$, $p<0.05$). Nevertheless, more patients with longer education were among those with MCI ($p<0.05$), without significant difference in age between the groups. The MMSE and MoCA results showed strong correlation ($r=0.974$; $p<0.01$). However, while the MoCA scores aligned with clinical assessment, MMSE identified 46.7% patients as normocognitive.

Better cognitive reserve in more educated people might explain delayed onset of CI. However, it does not explain longer time to diagnosis, since once diagnosed with CI, patients with better cognitive reserve have faster cognitive decline. Thus, stigma associated with CI might be the cause. Our results suggest that elimination of negative behavioral model in patients and use of adequate screening tools by physicians could greatly improve timely diagnosis of CI in Montenegro.




IMPROVING THE DIAGNOSIS OF COGNITIVE IMPAIRMENT IN MONTENEGRO – ON THE PATH OF LEARNING

Isidora Rovčanin Dragović¹, Ljiljana Radulović², Jevto Eraković², Miodrag Radunović³, Goran Popivoda³, Tijana Vuković² and Nataša Popović¹

¹Faculty of Medicine, University of Montenegro
²Department of Neurology, Clinical Center of Montenegro
³Faculty of Natural Sciences and Mathematics, University of Montenegro

The research is financial support by the scientific research project DEMONSTRIC, through the grant awarded by the Ministry of Science of Montenegro, Grant Agreement No. 01-23/22



Abstract

The estimated prevalence of dementia in Montenegro was lower compared to most of the European countries in 2019 (1.06%). There is a concern that with currently used diagnostic approach, dementia in Montenegro is underdiagnosed.

To assess currently used neuropsychological screening tests, 15 patients with clinical signs of cognitive impairment (CI) were recruited at the Clinical Center of Montenegro in 2019. Following the clinical assessment, patients were divided in 2 groups: mild cognitive impairment (MCI) and dementia. They were subsequently subjected to Mini-Mental State Examination (MMSE), routinely used in primary health care, and to Montreal Cognitive Assessment (MoCA), designed for improved detection of MCI.

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Better cognitive reserve in more educated people might explain delayed onset of CI. However, it does not explain longer time to diagnosis, since once diagnosed with CI patients with better cognitive reserve have faster cognitive decline. Thus, stigma associated with CI might be the cause. Our results suggest that elimination of negative behavioral model in patients and use of adequate screening tools by physicians could greatly improve timely diagnosis of CI in Montenegro.

Introduction

The estimated prevalence of dementia in Montenegro was 1.06% in 2019, which is lower compared to most of the European countries (1). There is a serious concern that with the currently used diagnostic approach, dementia in Montenegro is underdiagnosed, and that the number of people with dementia requiring care might be much higher.

Is cognitive impairment a sufficiently recognized problem in Montenegro?



Methods and Materials

In the prospective study conducted in 2019, patients with clinical signs of cognitive impairment were recruited at the Clinical Center of Montenegro. To assess currently used neuropsychological screening tests, they were subjected to the Mini-Mental State Examination (MMSE), routinely used in primary health care, and to the Montreal Cognitive Assessment (MoCA), designed for improved detection of MCI. Further clinical evaluation followed for the 15 patients scored with <24 in any of the tests, which is accepted cutoff score for cognitive impairment (2). In order to set definite diagnosis and evaluate potentially excluding criteria, patients filled out a questionnaire, neurological examination was conducted, so as laboratory and radiological assessment. Finally, using Petersen criteria for MCI (3) and American Academy of Neurology's Dementia Guidelines (4), patients were divided in two groups: MCI and dementia. The excluding criteria were alcohol or drug consumption, other neurological and psychiatric diseases.

The data was processed using the following statistical tests: the statistical program R - Chi square test of homogeneity, Fisher's exact test, Wilcoxon rank sum test and Pearson's correlation test.

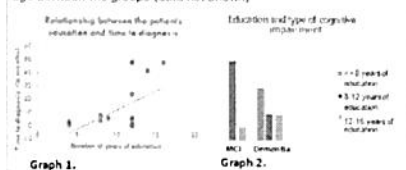
Characteristic	Mild cognitive impairment	Dementia
Age 10		
41-51	0	5.6%
51-61	0	5.6%
61-71	14.6%	5.6%
71-81	20%	26.6%
81-91	0	5.6%
Sex		
Men	26.7%	25%
Women	20%	33.3%
Educational		
0-9 years of education	0	25.7%
10-12 years of education	40%	33.3%
13-16 years of education	6.7%	33.3%
Hypertension	33.3%	33.3%
Hyperlipidemia	20%	33.3%
Diabetes mellitus	26.7%	20%
Previous cerebrovascular disease	0	0
Smoking		
Current smoking	0	6.7%
History of smoking	33.3%	33.3%
Alcohol consumption		
Current alcohol consumption	0	0
History of alcohol consumption	0	16.7%
Physical activity (≥30 min/day)	33.3%	33.3%

Table 1. Patient socio-demographic profile and clinical features

Results

The patients were on average 70 years old, with almost equal sex representation and 10.5 years of education (Table 1). An average time from the first disease manifestation until the diagnosis was 13.4 months and this was in strong correlation with the educational status of patients. Interestingly, the higher the level of the patient's education, the longer it took to diagnosis ($r=0.545$, $p<0.05$), Graph 1.

However, there were more patients with longer education among those with MCI ($p<0.05$), Graph 2, without a significant difference in age between the groups (data not shown).



The two neuropsychological tests also strongly correlated with one another ($r=0.974$, $p<0.01$) (Graph 3). However, while MoCA scores aligned with the clinical assessment, MMSE identified 46.7% patients as normocognitive (Table 2).



Table 2. Clinical vs. MMSE vs. MoCA results

Discussion

Our results suggest that a better cognitive reserve (CR) in more educated people, delays the onset of cognitive impairment, as other studies have shown (5,6). This means that at the same age, the more educated people are more likely to develop MCI, while those less educated will develop dementia. However, according to the literature, better CR could not explain the longer time to diagnosis, since once diagnosed with CI, these patients sometimes demonstrate a faster cognitive decline (6,7). Therefore, it is probable that more educated people are aware of the potential diagnosis, develop fear from stigmatization and delay medical consultation. The growing body of evidence show, that experience of stigma is significant among people with dementia (8), and that they are stigmatized across a range of layman and professional populations (9).

Although MMSE and MoCA scores strongly correlated with one another, MMSE classified even 46.7% of patients as normocognitive if the MoCA test was not conducted, which would not be subjected to further clinical assessment, which confirmed cognitive deficit in all patients. Unlike the even distribution of MoCA scores on the graph 3, which confirms the presence of cognitive deficit in all patients, the MMSE scores are distributed in a higher range, between 24 and 30 for almost the half of the patients, indicating normal cognitive function. So, this study once more confirmed higher sensitivity of the MoCA test for mild cognitive impairment, compared to MMSE, and suggest its use as a preferred test at primary health care level.

Conclusions

Although limited by small sample, study shows that both patients and health care professionals need educational support. In order to eliminate the negative behavioral model in patients and decrease stigmatic beliefs among the general public, it is necessary to improve patients information and raise awareness about dementia. Also, there is a need for continuous education at the primary health care level and use of adequate screening tools by physicians. According to our study results, these activities could significantly improve the timely diagnosis of cognitive impairment in patients in Montenegro.

Health care professionals and patients are together on the path of learning!

References

1. Alzheimer's Association. *Demographics in Europe*. [https://www.alzheimers-disease/prevalence-and-risk-factors/dementia-in-europe](https://www.alz.org/alzheimers-disease/prevalence-and-risk-factors/dementia-in-europe). 2019. Accessed 2023 Aug 20.
2. Petersen TR, Prince ML, McHugh PR, et al. *International criteria for diagnosis and classification of dementia*. *Alzheimer Dis Assoc*. 2011;25(12):1275-1284.
3. Petersen TR, Prince ML, McHugh PR, et al. *International criteria for diagnosis and classification of dementia*. *Alzheimer Dis Assoc*. 2011;25(12):1275-1284.



Primjere	18.10.2021		
Org. jed.	Broj	Prilog	Vrijednost
med	1811		

UNIVERSITY OF MONTENEGRO

Form IM: Annual report of the mentor on the progress of the doctoral student

ANNUAL REPORT OF THE MENTOR ON THE PROGRESS OF THE DOCTORAL STUDENT

Academic year for which the Report is submitted	2020/21				
GENERAL DATA ABOUT THE DOCTORAL STUDENT					
Title, name, name of the parent, surname	Dr. Isidora, Rade, Rovčanin Dragović				
Faculty	Faculty of Medicine, University of Montenegro				
Study program	Medicine				
Index number	2013/01				
MENTOR/MENTORS					
First mentor	Prof. Dr. Nataša Popović	Faculty of Medicine, University of Montenegro, Montenegro	Physiology		
Second mentor	Prof. Dr. Milica Martinović	Faculty of Medicine University of Montenegro, Montenegro	Pathophysiology		
EVALUATION OF THE DOCTORAL STUDENT*					
The quality of the meetings with the doctoral student.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input checked="" type="checkbox"/> 5
(If the previous answer is „1“ or „2“ give the rationale and suggestions for the improvement)					

*Grades are: 1 - insufficient, 2 - sufficient, 3 - good, 4 - very good, 5 - excellent

Form IM: Annual report of the mentor on the progress of the doctoral student

Is the work plan with the doctoral student defined?	<input checked="" type="checkbox"/> YES	<input type="checkbox"/> NO			
Has the student made the progress according to the scheduled work plan?	<input checked="" type="checkbox"/> YES	<input type="checkbox"/> NO			
(If the previous answer is „no“ give the rationale and suggestions for the improvement)					
Quality of the progress of the doctoral student on the research, between the two reports is:	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input checked="" type="checkbox"/> 5
(If the previous answer is „1“ or „2“ give the rationale and suggestions for the improvement)					
Evaluate readiness of the doctoral student for consultations.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input checked="" type="checkbox"/> 5
Evaluate planning and performing of annual research activities and professional training of the doctoral student.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input checked="" type="checkbox"/> 5
Evaluate progress in mastering of methodology of the scientific-research work.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input checked="" type="checkbox"/> 5
Evaluate activities conducted on writing and publishing of scientific papers.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input checked="" type="checkbox"/> 4	<input type="checkbox"/> 5
Evaluate doctoral students' general attitude towards studies.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input checked="" type="checkbox"/> 5
Evaluate overall quality of work of the doctoral student.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input checked="" type="checkbox"/> 5
(If the previous answer is „1“ or „2“ give the rationale and suggestions for the improvement)					

CONSENT TO CONTINUE STUDIES	
Can the doctoral student continue their studies?	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> Yes, with the special conditions <input type="checkbox"/> No
(If you have previously answered with the „Yes, with the special conditions“ or „No“ give the rationale and suggestions for the improvement)	
Notes	
<p>The candidate, Dr. Isidora Rovčanin Dragović, has completed all the exams planned by the Doctoral studies curriculum, in accordance with required deadlines with an average grade 10.</p> <p>Subsequently, Dr. Rovčanin Dragović submitted the Doctoral Thesis topic, titled: „A new method for stratification of the risk for Alzheimer's disease in patients in Montenegro“ and defended the Preliminary research of the Doctoral thesis with an excellent grade, on the November 12th 2020. The defense was in front of the following Committee: Dr. Miodrag Radunović, a full professor at the Faculty of Medicine, University of Montenegro, as the president of the Committee; Dr. Nataša Popović, an associate professor at the Faculty of Medicine, University of Montenegro, as the mentor; Dr. Milica Martinović, a full professor at the Faculty of Medicine, University of Montenegro, as the comentor; Dr. Elka Stefanova, a full professor at the Neurology Department at the Faculty of Medicine, University of Belgrade, and Dr. Apollonia Tullo, a researcher in the field of Biomedicine at the Institute for the Biomembranes, Bioenergetics and Molecular Biotechnologies in Bari, Italy, as members of the Committee.</p> <p>By decision of the Senate, number 03-6711, on the January 21st 2021, Committees' assessment report on eligibility of Doctoral dissertation has been accepted, and the proposed Doctoral thesis and the candidate, have been confirmed as eligible, thus, Dr. Rovčanin Dragović continued working according to the proposed plan of her doctoral thesis. Namely, since the research is conducted within the scientific research project of the Faculty of Medicine, financed by the Ministry of Science of Montenegro, titled: "New methods for risk stratification for the progression of cancer and Alzheimer's disease in patients in Montenegro - DEMONSTRATE", its realization started in April of 2019, and finished in September 2021. The research was</p>	

conducted at the Clinical Center of Montenegro and the Center for the Scientific Research of the Faculty of Medicine, in cooperation with the Institute for Biomembranes, Bioenergetics and Molecular Biotechnologies from Bari.

Doctoral Thesis of Dr. Rovčanin Dragović plans for the prospective multidisciplinary research that includes:

- 1) patient recruitment,
- 2) clinical research,
- 3) molecular biological research

First, the candidate actively participated in the creation of the recruitment criteria, and in the recruitment process itself. Being the physician specializing in Neurology who is also certified in the neuropsychological assessment of the patients, the candidate conducted planned clinical research through neurological examination and neuropsychological evaluation of cognitive functioning of the patients. At the end, after the collection of the predicted number of the biological samples, Dr. Rovčanin Dragović was in charge of the molecular biological research at the Center for Molecular Biological Research at the Faculty of Medicine. During that process, she learned new and perfected previously adopted molecular biological techniques. Namely, after the initial processing of the samples from the full peripheral blood and separating the cells and the plasma, a new protocol of the isolation of the total circulating microRNA (miRNA) from the plasma was conducted. This was the first time that this method was applied in Montenegro. This new method not only prepared the samples for the subsequent experiments, but it allowed the creation of the miRNA bank, for potential future research of the complete miRNA expression profile. Finally, the level of the expression of the specific miRNAs was determined by qRT-PCR. Those miRNAs whose expression level is known to be deregulated in both, Alzheimer's disease and colorectal cancer have been in the focus of the study:

- miR-29a/b
- miR-101
- miR-125b
- miR-146a
- miR-155

The candidate is currently working on data processing, and submission of finalized research to the scientific journal, which is expected to occur by the end of the 2021. Dr. Rovčanin Dragović, together with her mentors, identified Journal of Alzheimer's disease (Impact factor of 4.472 in 2020) as

the first choice journal for the submission of her work. Data processing and systematization of the results in accordance with the requirements of the publication format in this journal are in progress.

Part of the results from the clinical research, Dr. Rovčanin Dragović presented at the 14th World Congress on Controversies in Neurology (CONy), as the first author of the poster presentation: „Improving the Diagnosis of Cognitive Impairment in Montenegro - on the Path of Learning.“

Inspired by the results of clinical research presented at the CONy conference, Dr. Rovčanin Dragović designed an additional study on stigmatic beliefs related to Alzheimer's disease in Montenegro. The candidate, in cooperation with the mentor, has already clearly defined characteristics of the target population which will be included in the study, identified appropriate standardized questionnaires and methods that are necessary to collect relevant information. The candidate plans to finalize this additional research by the time the work on the Thesis is completed. Results of this additional research will be complementary to the results of the doctoral dissertation. Namely, they will underline the importance of raising awareness on Alzheimer's dementia among the population in our region, and it will emphasize significance of the doctoral thesis itself, which is in the main focus of the candidates' intense work. Related to this, we plan to publish one more original scientific paper, potentially in the journal BMC Geriatrics (impact factor of 3.516 in 2019-20), in which the candidate will be the first author.

Dr. Isidora Rovčanin Dragović showed outstanding engagement and motivation in her work so far, as well as unique versatility in her approach to the scientific research. She performed her responsibilities successfully and on time, and managed to near her Thesis research close to the end. It is important to emphasize that due to her exceptional dedication to the work, the candidate managed to overcome numerous unexpected challenges directly caused by the COVID-19 pandemic - from the timely purchase of instruments and consumable materials, over the recruitment of the elderly patients who represent the most vulnerable part of the population, to the participation at the conferences in order to present her results in front of the international scientific community, during the time when borders all over the world were closed.

Based on the stated, I consider that Dr. Isidora Rovčanin Dragović has made significant progress towards the defense of her doctoral dissertation and I propose for this candidate to be allowed to continue her work in order to complete her doctoral studies.

STATEMENT OF THE MENTOR

Statement of the mentor about the timeline and the realization of the initial research.

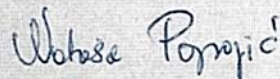
(Fill out only for the first report of the mentor)

In Podgorica,

10.18.2021.

Name and surname of the first mentor

Prof. Dr. Nataša Popović



Name and surname of the second mentor

Prof. Dr. Milica Martinović

MP



Document attachment contains:

- Published results of the work on the Doctoral dissertation (for the second mentor's report):

Poster presentation: Improving the Diagnosis of Cognitive Impairment in Montenegro- on the Path of Learning. Isidora Rovčanin Dragović, Ljiljana Radulović, Jevto Eraković, Miodrag Radunović, Goran Popivoda, Tijana Vuković, i Nataša Popović, November 2020, 14th World Congress on Controversies in Neurology - CONy 2020, <https://simul-europe.com/2020/cony/Files/220953.pdf>

ABSTRACT: Improving the diagnosis of cognitive impairment in patients in Montenegro - on the path of learning

Isidora Rovčanin Dragović, Ljiljana Radulović, Jevto Eraković, Miodrag Radunović, Goran Popivoda, Tijana Vuković and Nataša Popović


The estimated prevalence of dementia in Montenegro was lower compared to most of the European countries in 2019 (1.06%). There is a concern that with currently used diagnostic approach, dementia in Montenegro is underdiagnosed.

To assess currently used neuropsychologic screening tests, 15 patients with clinical signs of cognitive impairment (CI) were recruited at the Clinical Center of Montenegro in 2019. Following the clinical assessment, patients were divided in 2 groups: mild cognitive impairment (MCI) and dementia. They were subsequently subjected to Mini-Mental State Examination (MMSE), routinely used in primary health care; and to

Montreal Cognitive Assessment (MoCA), designed for improved detection of MCI.

The average time from the first disease manifestation until the diagnosis was 13.4 months. The higher the level of education was, the longer was the time to diagnosis ($r=0.545$, $p<0.05$). Nevertheless, more patients with longer education were among those with MCI ($p<0.05$), without significant difference in age between the groups. The MMSE and MoCA results showed strong correlation ($r=0.974$; $p<0.01$). However, while the MoCA scores aligned with clinical assessment, MMSE identified 46.7% patients as normocognitive.

Better cognitive reserve in more educated people might explain delayed onset of CI. However, it does not explain longer time to diagnosis, since once diagnosed with CI, patients with better cognitive reserve have faster cognitive decline. Thus, stigma associated with CI might be the cause. Our results suggest that elimination of negative behavioral model in patients and use of adequate screening tools by physicians could greatly improve timely diagnosis of CI in Montenegro.




IMPROVING THE DIAGNOSIS OF COGNITIVE IMPAIRMENT IN MONTENEGRO – ON THE PATH OF LEARNING

Isidora Rovčanin Dragović¹, Ljiljana Radulović², Jevto Eraković³, Miodrag Radunović¹, Goran Popivoda³, Tijana Vuković² and Nataša Popović¹

¹Faculty of Medicine, University of Montenegro
²Department of Neurology, Clinical Center of Montenegro
³Faculty of Natural Sciences and Mathematics, University of Montenegro

The research is funded in part by the scientific research project DEMENTIAS, through the grant awarded by the Ministry of Science of Montenegro, Grant Agreement No. 01-781/2



Abstract

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Introduction

The estimated prevalence of dementia in Montenegro was 1.06% in 2019, which is lower compared to most of the European countries (1). There is a serious concern that with the currently used diagnostic approach, dementia in Montenegro is underdiagnosed, and that the number of people with dementia requiring care might be much higher.

Is cognitive impairment a sufficiently recognized problem in Montenegro?



Methods and Materials

In the prospective study conducted in 2019, patients with clinical signs of cognitive impairment were recruited at the Clinical Center of Montenegro. To assess currently used neuropsychologic screening tests, they were subjected to the Mini-Mental State Examination (MMSE), routinely used in primary health care, and to the Montreal Cognitive Assessment (MoCA), designed for improved detection of MCI. Further clinical evaluation followed for the 15 patients scored with <24 in any of the tests, which is accepted cutoff score for cognitive impairment (2). In order to set definite diagnosis and evaluate potentially excluding criteria, patients filled out a questionnaire, neurological examination was conducted, so as laboratory and radiological assessment. Finally, using Petersen criteria for MCI (3) and American Academy of Neurology's Dementia Guidelines (4), patients were divided in two groups: MCI and dementia. The excluding criteria were alcohol or drug consumption, other neurological and psychiatric diseases.

The data was processed using the following statistical tests of the statistical program R: Chi-square test of homogeneity, Fisher's exact test, Wilcoxon rank sum test and Pearson's correlation test.

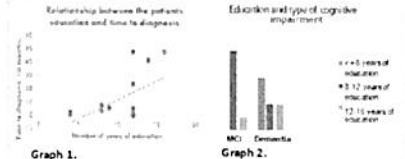
Characteristic	MCI (n=10)	Dementia (n=5)
Age (M)		
43-51	0	5.00%
52-60	0	5.00%
61-70	26.64%	5.00%
71-80	20%	26.64%
81-90	0	5.00%
Sex		
Men	26.7%	20%
Women	20%	33.33%
Education (M)		
0-8 years of education	0	26.7%
9-12 years of education	45%	13.33%
13-16 years of education	9.7%	13.33%
Hypertension	15.51%	33.33%
Hyperlipidemia	20%	33.33%
Diabetes mellitus	26.7%	20%
Previous cerebrovascular disease	0	0
Smoking		
Current smoking	0	5.7%
History of smoking	13.33%	13.33%
Alcohol consumption		
Current alcohol consumption	0	0
History of alcohol consumption	0	16.7%
Physically fit (2-30 min daily)	22.22%	13.33%

Table 1. Patient socio-demographic profile and clinical features

Results

The patients were on average 70 years old, with almost equal sex representation and 10.5 years of education (Table 1). An average time from the first disease manifestation until the diagnosis was 13.4 months and this was in strong correlation with the educational status of patients. Interestingly, the higher the level of the patient's education, the longer it took to diagnose ($r=0.545$, $p<0.05$), Graph 1.

However, there were more patients with longer education among those with MCI ($p<0.05$), Graph 2, without a significant difference in age between the groups (data not shown).



The two neuropsychological tests also strongly correlated with one another ($r=0.974$, $p<0.01$) (Graph 3). However, while MoCA scores aligned with the clinical assessment, MMSE identified 46.7% patients as normocognitive (Table 2).

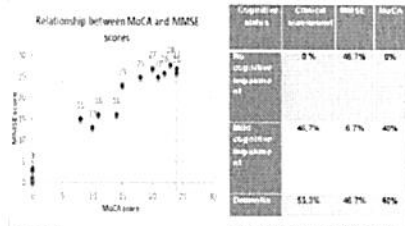


Table 2. Clinical vs. MMSE vs. MoCA results

Discussion


Our results suggest that a better cognitive reserve (CR) in more educated people, delays the onset of cognitive impairment, as other studies have shown (5,6). This means that at the same age, the more educated people are more likely to develop MCI, while those less educated will develop dementia. However, according to the literature, better CR could not explain the longer time to diagnosis, since once diagnosed with CI, these patients sometimes demonstrate a faster cognitive decline (6,7). Therefore, it is probable that more educated people are aware of the potential diagnosis, develop fear from stigmatization and delay medical consultation. The growing body of evidence show, that experience of stigma is significant among people with dementia (8), and that they are stigmatized across a range of layman and professional populations (9).

Although MMSE and MoCA scores strongly correlated with one another, MMSE classified even 46.7% of patients as normocognitive if the MoCA test was not conducted, they would not be subjected to further clinical assessment, which confirmed cognitive deficit in all patients. Unlike the even distribution of MoCA scores on the graph 3, which confirms the presence of cognitive deficit in all patients, the MMSE scores are distributed in a higher range, between 24 and 30 for almost the half of the patients, indicating normal cognitive function. So, this study once more confirmed higher sensitivity of the MoCA test for mild cognitive impairment, compared to MMSE, and suggest its use as a preferred test at primary health care level.

Conclusions

Although limited by small sample, study shows that both, patients and health care professionals need educational support. In order to eliminate the negative behavioral model in patients and decrease stigmatic beliefs among the general public, it is necessary to improve patients' information and raise awareness about dementia. Also, there is a need for continuous education at the primary health care level and use of adequate screening tools by physicians. According to our study results, these activities could significantly improve the timely diagnosis of cognitive impairment in patients in Montenegro.

Health care professionals and patients are together on the path of learning!



References
 1. Alzheimer Europe. Dementia in Europe: Facts and Figures 2019. Retrieved from the website of Alzheimer Europe. <https://www.alzheimer-europe.org/Publications/Dementia-in-Europe-Facts-and-Figures-2019>