Acta Clin Croat 2022; 61:11-18
doi: 10.20471/acc.2022.61.01.02

Original Scientific Paper

REVERSIBILITY OF LIPOATROPHY IN HIV-INFECTED PATIENTS TAKING ANTIRETROVIRAL THERAPY: A COHORT STUDY WITH ULTRASOUND ASSESSMENT

Ana Šoštarić Zadro[1], Klaudija Višković[1] and Josip Begovac[1,2]

[1]Dr Fran Mihaljević University Hospital for Infectious Diseases, Zagreb, Croatia;
[2]University of Zagreb, School of Medicine, Zagreb, Croatia

SUMMARY – The aim of this study was to characterize and compare changes in subcutaneous fat in the malar, brachial and crural region in a cohort of HIV-infected patients taking antiretroviral therapy. This prospective longitudinal study included 77 patients who were selected from the initial cohort evaluated in 2007 and 2008. We examined reversibility of lipoatrophy measured by ultrasound over at least five-year period and factors related to its reversibility. All 46 patients who used stavudine switched from stavudine to another combination. Of 58 patients on zidovudine, 16 (28%) were on a zidovudine based regimen at the second follow up. There was evidence for subcutaneous fat increase in the malar area ($p<0.001$) and no increase in the brachial and crural areas. Patients who were smokers and had poor adherence to the Mediterranean diet had a thinner malar area at the follow up measurement ($p=0.030$) and smaller increase in subcutaneous malar fat compared to others ($p=0.040$). Our study suggested that modest increase of subcutaneous fat in malar area coincided with stopping stavudine and fewer usage of zidovudine. Lifestyle with non-adherence to the Mediterranean diet and smoking were associated with a smaller increase in subcutaneous malar fat.

Key words**:** *Lipoatrophy; Antiretroviral therapy; Ultrasound; Mediterranean diet*

Introduction

Lipoatrophy in human immunodeficiency virus (HIV) infected patients is a medical term which is used for loss of subcutaneous body fat in the face and extremity region[1,2]. A wide range of lipoatrophy prevalence in different studies is a result of subjective criteria including personal evaluation of examinees, evaluation of physicians, and a variety of methods and measurement techniques[3]. Despite numerous studies, objective criteria for the diagnosis of lipoatrophy have not yet been established[4,5].

The pathogenesis of lipoatrophy within the HIV associated lipodystrophy seems to be multifactorial and includes antiretroviral therapy (ART) duration and drugs used, HIV infection itself, immune response of patients, hepatitis C virus coinfection, environmental factors (nutrition, physical activity level, smoking), as well as genetic and other risk factors (age, gender, ethnicity, initial total body fat content). Different clinical trials demonstrated the contribution of the choice and duration of ART to be the key risk factors in the development of body fat changes[4,6]. Nucleoside reverse transcriptase inhibitors (NRTI), especially

Correspondence to: *Ana Šostarić Zadro, MD*, Dr Fran Mihaljević University Hospital for Infectious Diseases, Mirogojska cesta 8, HR-10000 Zagreb, Croatia
E-mail: ana.sostaric4@gmail.com
Received March 18, 2019, accepted May 2, 2019

thymidine analogs (stavudine and zidovudine) and didanosine are connected with lipoatrophy[7,8].

Facial and peripheral lipoatrophy is disfiguring, has a negative impact on the patient quality of life, and may reduce adherence to ART resulting in treatment failure[9,10]. Lipoatrophy identification has great influence on HIV infection treatment and leads to reevaluation of appropriate time for therapy introduction (in particular delay of therapy), as well as various modifications in therapy, i.e., switching or discontinuing therapy[11].

Ultrasound (US) imaging has the advantage of low cost, wide availability, repeatability, safety, and has been utilized in quantitative estimation of subcutaneous fat loss with encouraging results[12]. A US investigation of lipoatrophy was performed at Dr Fran Mihaljević University Hospital for Infectious Diseases (UHID) in Zagreb in 2007 and 2008. Our findings suggested that US had a potential utility for objectively ruling out lipoatrophy in HIV-infected and ART-treated patients[2].

The aim of this study was to characterize and compare changes in subcutaneous fat over at least five-year follow up in the malar, brachial and crural region by US, in a cohort of HIV-infected patients taking ART, who had been evaluated at the UHID, Zagreb, in 2007 and 2008.

Material and Methods

Study design

We conducted a prospective longitudinal study to compare the reversibility of lipoatrophy measured by US over at least five-year period and examined factors related to this reversibility.

Study population

Patients were selected from the initial cohort evaluated in 2007 and 2008. The US examination took place during a routine follow up visit at the UHID, Zagreb. Out of the initial cohort of 151 individuals seen in the 2007-2008 period, 77 (51%) completed the second US examination.

The study was approved by the UHID Ethics Committee (March 22, 2013; No. 01-255-1-2013) and all patients provided written informed consent prior to enrolment.

All human research procedures were done in accordance with the World Medical Association Declaration of Helsinki 2013[13].

Measurements

We used the same US methodology that had been used in the first study of lipoatrophy at UHID in 2007-2008, according to the technique described by Martinez *et al*.[2,12]. All measurements were performed by the same experienced radiologist at the same visit. US measurements of subcutaneous fat tissue thickness were performed in three anatomic regions, i.e., malar (over the right malar bone), brachial (approximately 10 cm above the right elbow), and crural (approximately 6 cm above the right lateral malleolus) without pressing the US probe upon the underlying skin. A Siemens Sonoline G50 machine (Siemens Medical Solition, Malvern, PA, USA) in B mode was used. The measurements were done in supine position using a linear array probe (10 MHz and 42 mm) from the skin-fat (excluding skin) to fat-muscle interfaces where electronic calipers were positioned. All measurements were taken in triplicate for each anatomic site and then averaged. The values were expressed in millimeters[12].

Weight was measured with a standard physician's office scale, rounded to the nearest 0.1 kg. Height was measured with a wall-mounted stadiometer and rounded to the nearest 0.1 cm.

A 14-point food-item questionnaire developed by Babio *et al*.[14] was used to assess adherence to the traditional Mediterranean diet. A score less than 5 was considered as poor adherence to the Mediterranean diet. Additional data including medication history for each patient were extracted from medical records.

We determined plasma HIV viral load with commercially available assays (COBAS Amplicor HIV-1 Monitor Test, version 1.5 [Roche Diagnostic Systems, Basel, Switzerland], Abbott RealTime HIV-1 [Abbott Molecular, Inc., Des Plaines, IL, USA] and Roche Cobas TaqMan HIV-1 Version 2.0). We measured absolute CD4 T-cell counts (cells/mm^3) using Flow Count Fluorospheres (Beckman Coulter, Fullerton, CA, USA). Four-color flow cytometry was performed using a Cytomics FC500 flow cytometer (Beckman Coulter).

Statistical analysis

The primary outcome variables were change in the subcutaneous fat thickness in the malar, brachial and crural region. The following explanatory variables for the association of subcutaneous malar fat thickness differences between two measurements were examined:

age, sex, type of diet (better *versus* worse adherence to the Mediterranean diet), and smoking. Descriptive statistics was used for all variables analyzed. The correlation of fat tissue thickness differences between the two measurements according to sex, adherence to the Mediterranean diet and smoking was tested by Student's t-test if the condition of homogeneity of the variance was met. If this condition was not met, the nonparametric Mann Whitney test was used. The correlation of fat tissue thickness differences between the two measurements with age and age difference between the two measurements was tested by Pearson's correlation coefficient and its significance. The Wilcoxon signed-rank test was used to compare measurements at two time points. In all statistical tests, statistical significance was set at $p<0.05$.

The analysis was done using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and StatSoft, Inc. (2007) and STATISTICA (data analysis software system) version 8.0 (TIBCO Software Inc., Palo Alto, CA, USA).

Results

Main characteristics of study patients

A total of 77 subjects completed the study. There were 51 (79%) men and 16 (21%) women. The main characteristics of study patients are presented in Table 1. The majority of subjects were men (79%). Median age at the time of HIV diagnosis confirmation was 38.1 years and median duration of HIV infection at the first visit was approximately 5 years. The patient median age at the first visit was 43.4 years and at the second visit 50.4 years, with median time between the first and second visit of almost 7 years. The most frequent way of HIV infection transmission was unprotected sex between men (51%), followed by heterosexual sex (43%), and a small proportion of transmission by drug injection (3%) or an unknown way (4%).

Subcutaneous fat tissue changes

Comparison of subcutaneous fat tissue thickness in the malar, brachial and crural region measured by US at two time points is displayed in Figure 1.

There was a statistically significant increase in the median value of malar subcutaneous fat in the patients measured at the follow up visit ($p<0.001$), while the increase was not statistically significant in the brachial region ($p=0.498$). In the crural region, subcutaneous fat was thinner at the follow up visit, however, the difference was not statistically significant ($p=0.068$).

Antiretroviral therapy history

Out of 77 patients, stavudine was ever used in 46 (60%), zidovudine in 58 (75%), efavirenz in 50 (65%) and protease inhibitor in 55 (71%) patients. Stavudine was used for more than 12 months in 29 (38%), zidovudine in 50 (65%), efavirenz in 42 (55%) and protease inhibitor (lopinavir) in 31 (40%) patients. All 46 patients having used stavudine switched from stavudine to another combination. The initial switch was to an abacavir regimen (n=21), zidovudine-based regimen (n=20) and other, or a regimen without any nucleoside analogs (n=5). The median time of taking stavudine at the second visit was 3564 days (Q1 to Q3 = 2881 to 3913).

Of 58 patients on zidovudine, 16 (28%) were on a zidovudine-based regimen at the second follow up. Twenty-five (60%) patients were switched to an abacavir-containing regimen, 8 were switched to a stavudine-based regimen, 7 to a tenofovir-based regimen, and two to other regimens. All patients switched to stavudine were later switched to another regimen. In 42 patients not on zidovudine on the second assessment, the median time of the drug use was 1964 days (Q1 to Q3 = 1041 to 3258).

Only 8 patients did not have a history of switching antiretrovirals. Those 8 patients had a zidovudine-based regimen. Twenty-five patients had only a switch from stavudine, whereas 21 had both a zidovudine and stavudine switch. Twenty-one patients had a zidovudine switch without a stavudine switch, and 2 patients had another type of switch (neither stavudine- nor zidovudine-based).

Subcutaneous fat tissue changes according to explanatory variables

There was no correlation between age (r=-0.01-0.02) or age differences (r=-0.02-0.1) and subcutaneous fat thickness differences between two measurements in the malar, brachial and crural region. Also, gender had no significant impact on subcutaneous fat thickness differences between two measurements in the malar ($p=0.093$), brachial ($p=0.356$) and crural ($p=0.221$) region (Table 2). There was no correlation between the subcutaneous fat thickness at follow up measurement or subcutaneous fat thickness increase

Table 1. Main characteristics of 77 study patients

Characteristic	Median and Q1 to Q3 or frequency with percentages	n
Age at HIV diagnosis (years)	38.1 (30.8 to 45.9)	77
Age at first visit (years)	43.4 (37.3 to 50.9)	77
Age at follow up visit (years)	50.4 (44.0 to 57.8)	77
Time between first and follow up measurement (days)	2554 (2484 to 2656)	77
Nadir CD4 cell count *per* mm^3	85 (29 to 172)	77
Male gender	61 (79)	77
BMI (kg/m^2)	24.2 (22.3 do 26.0)	77
Known duration of HIV infection at first visit (days)	1846 (1051 to 2971)	77
Had clinical AIDS	34 (44)	77
Transmission risk: Men who have sex with men Heterosexual People who inject drugs Unknown	 39 (51) 33 (43) 2 (3) 3 (4)	77
CD4 cell count at first visit *per* mm^3	459 (348 to 579)	77
CD4 cell count at follow up visit *per* mm^3	637 (464 to 869)	43
<50 copies of HIV-1 RNA *per* mL at first visit	73 (95)	77
<200 copies of HIV-1 RNA *per* mL at first visit	76 (99)	77
<50 copies of HIV-1 RNA *per* mL at follow up visit	71 (92)	77
<200 copies of HIV-1 RNA *per* mL at follow up visit	74 (96)	77

Results expressed as frequencies with proportions or median with first or third quartile (Q1, Q3); BMI = body mass index; HIV = human immunodeficiency virus; AIDS = acquired immunodeficiency syndrome

Table 2. Effect of gender, smoking and adherence to the Mediterranean diet on the gain/loss of subcutaneous fat (all patients stopped stavudine therapy)

Variable	Difference, malar (mm) Median (Q1 to Q3)	p-value***	Difference, brachial (mm) Median (Q1 to Q3)	p-value****	Difference, crural (mm) Median (Q1 to Q3)	p-value****	n
Gender:							
Male	2.5 (0.6-4.8)	0.093	0.1 (-1.7-1.3)	0.356	-0.5 (-1.5-0.6)	0.221	61
Female	4.1 (3.6-6.8)		-0.55 (-3.4-1.6)		0.3 (-1.05-1.7)		16
Adherence to Mediterranean diet and smoking							
Current smoking and low adherence*	1.5 (0.1-3.3)	0.040	0.9 (-0.55-2.1)	0.200	0 (-0.8-0.65)	0.463	12
Other**	3.7 (1.9-6.5)		0 (-2.5-1.3)		-0.40 (-2.0-0.9)		47

*Low adherence to the Mediterranean diet, score less than 5; **included non-smokers with any adherence to the Mediterranean diet and smokers with good adherence to the Mediterranean diet; ***Student's t-test; ****Mann Whitney test

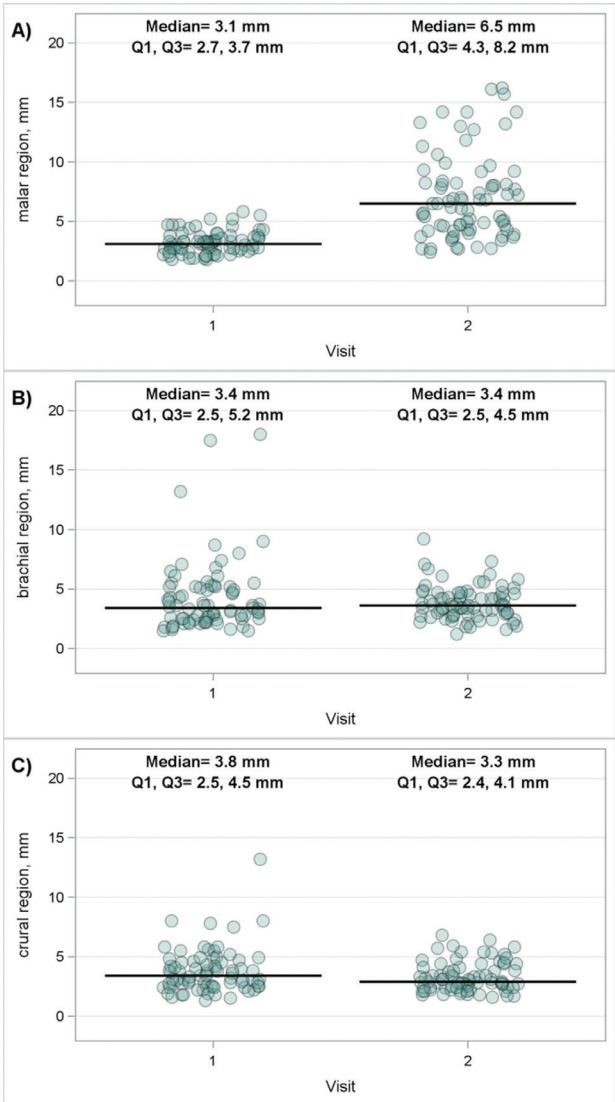

Fig. 1. Subcutaneous fat tissue thickness in malar (A), brachial (B) and crural (C) region at the first and follow up visit measured by ultrasound. Horizontal line represents the median. There was a statistically significant difference between the two visits in the malar (p<0.001) but not in the brachial (p=0.498) and crural (p=0.068) region.

Q1 = first quartile; Q3 = third quartile; Wilcoxon signed-rank test

between two measurements and Mediterranean diet score. However, patients who were smokers and had poor adherence to the Mediterranean diet had a statistically significantly thinner subcutaneous fat in malar region at the follow up measurement (median 4.3 mm *versus* 6.8 mm; p=0.030, Mann Whitney test). Patients who were smokers and had poor adherence to the Mediterranean diet had a statistically significantly smaller increase in subcutaneous malar fat thickness compared to others (p= 0.040) (Table 2).

Discussion

We performed US measurements of the malar, brachial and crural area at two time points, i.e., at average (median) 7-year follow up interval. There was evidence for increase in the subcutaneous malar and no increase in the brachial and crural area. This increase coincided with discontinuing stavudine and fewer patients receiving zidovudine. However, the increase in the malar area was modest, 3.8 mm on average over the 7-year period. Antiretroviral drug modifications were frequent in Croatia. One of the reasons were high toxicity rates, which also included lipoatrophy[15]. Several studies showed that switching of stavudine and zidovudine led to recovery of lipoatrophy. Results of the Trial to Assess the Regression of Hyperlactatemia and to Evaluate the Regression of Established Lipodystrophy-GlaxoSmithKline protocol ESS40010 (TARHEEL) showed that replacing stavudine with abacavir or zidovudine resulted in improvement in stavudine-induced lipoatrophy[16]. Results of a 'body image' questionnaire showed that a substantial percentage of patients reported some or a lot of fat gain in the arms, legs, buttocks and face[16]. The Mitochondrial Toxicity (MITOX) Study Group found that switching from stavudine or zidovudine to abacavir for 24 weeks led to significant, albeit modest, objectively measured (by computer tomography) increases in limb fat. They also found that deficit in limb fat declined over time[17]. The Research in Computational Molecular Biology (RECOMB) study showed that switching from a zidovudine/lamivudine to a tenofovir/emtricitabine-based regimen led to a statistically significant improvement in limb fat, in contrast to the progressive loss of limb fat in subjects continuing zidovudine/lamivudine assessed by dual energy x-ray absorptiometry (DEXA) over a 72-week period[18]. Martinez *et al.* found that switching from zidovudine/lamivudine to emtricitabine/tenofovir led to improvement in the fat-mass ratio (FMR), compared with progressive worsening of FMR in subjects receiving zidovudine/lamivudine. FMR was assessed by DEXA for a period of 72 weeks[19]. Unlike these studies, we did not find a significant increase of subcutaneous fat in the arms and legs but only in the

face. However, our study had a much longer follow up than randomized trials.

In our study, lifestyle with non-adherence to the Mediterranean diet and smoking were associated with a smaller increase in subcutaneous malar fat. There was no correlation between the thickness or differences in thickness and Mediterranean diet score by itself. This is in concordance with the results of the cross-sectional study conducted at UHID in Zagreb in 2004 and 2005, which showed that the risk of lipoatrophy was lowest in patients who did not smoke and were at least moderately adherent to Mediterranean diet. In that study, there was no correlation between lipoatrophy and Mediterranean diet score by itself either[20]. There are not many studies that investigated the relationship of lipoatrophy with dietary intake and smoking in HIV-infected patients. An Australian cross-sectional study did not show relationship between lipodystrophy and saturated fat or total fat intake in patients on ART. In that study, body composition was measured by DEXA[21]. Hadigan *et al*. found that HIV-infected men had similar dietary habits and did not differ from one another in total energy intake or macronutrient composition regardless of the presence of fat redistribution[22]. Forrester and Gorbach report that Hispanic HIV-infected men who smoke had less total fat, less trunk fat, and more appendicular fat than nonsmokers, as measured by DEXA[23].

Gender had no significant impact on subcutaneous fat thickness differences between two measurements in our study. Neither Grenha *et al*. found an association of gender, age and BMI with lipodystrophy[24]. We also found no correlation between age or age differences and subcutaneous fat thickness between two measurements.

Since all patients included in our study had discontinued treatment with stavudine, we can conclude that the benefits of this stopping were greater in patients who did not smoke and had any or good adherence to the Mediterranean diet because they had greater subcutaneous fat thickness increase in the malar region.

The main limitation of our study was the number of patients who presented for follow up measurement. Out of the initial cohort of 151 individuals seen on first examination, only 77 completed the second US examination. We investigated the effect of stavudine and zidovudine switching on subcutaneous fat tissue thickness differences, but it was not done in a real-world situation. So, in some patients stavudine was switched to zidovudine and *vice versa* (patients switched to stavudine were later switched to another regimen). Hence, the exact contribution of many different drugs and drug combinations could not be assessed in a relatively small sample. Additionally, adherence to the Mediterranean diet and smoking were evaluated only at the follow up visit. Nevertheless, our study determined differences in the distribution of subcutaneous fat tissue in the same subjects over a long follow up time (at least five years) in a real-life situation and assessed these differences with certain risk factors.

Conclusion

In a population of HIV-infected patients highly treated with stavudine and zidovudine and followed up for at least five years by US, there was an increase of fat tissue in the malar area, but not in the brachial and crural area. These changes coincided with stopping stavudine use and fewer zidovudine usages. A lifestyle with non-adherence to the Mediterranean diet and smoking were associated with a smaller increase in subcutaneous malar fat. There was no increase in subcutaneous fat in the crural and brachial area. Our study highlighted the very slow or no reversibility of established lipoatrophy and underlined the possible contribution of smoking and non-adherence to the Mediterranean diet to the lack of subcutaneous fat gain.

Acknowledgments

The study was supported in part by grants from the Croatian Ministry of Science and Education to Professor Josip Begovac (grant no. 108-1080116-0098) and an investigator-initiated project grant by ViiV to Dr Fran Mihaljević University Hospital for Infectious Diseases, Zagreb, Croatia (study no. 204875). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

References

1. Singhania R, Kotler D. Lipodystrophy in HIV patients: its challenges and management approaches. HIV/AIDS (Auckl). 2011;3:135-43. doi: 10.2147/HIV.S14562.
2. Viskovic K, Richman I, Klasnic K, Hernandez A, Krolo I, Rutherford GVV, *et al*. Assessment of ultrasound for use

in detecting lipoatrophy in HIV-infected patients taking combination antiretroviral therapy. AIDS Patient Care STDS. 2009;23(2):79-84. doi: 10.1089/apc.2008.0118.

3. Signorini DJ, Oliveira Netto AM, Monteiro MC, Signorini DH, Torres Codeço C, Bastos FI, *et al*. Differences in body fat distribution assessed by ultrasonography in patients receiving antiretroviral drugs. Rev Assoc Med Bras. 2012;58:197-203. doi: 10.1016/S2255-4823(12)70180-7.
4. Milinković A. HIV-associated lipodystrophy syndrome. Coll Antropol. 2006 Dec;30 Suppl 2:59-62.
5. Beraldo RA, Santos APD, Guimarães MP, Vassimon HS, Paula FJA, Machado DRL, *et al*. Body fat redistribution and changes in lipid and glucose metabolism in people living with HIV/AIDS. Rev Bras Epidemiol. 2017;20(3):526-36. doi: 10.1590/1980-5497201700030014.
6. Freitas P, Carvalho D, Souto S, Santos AC, Xerinda S, Marques R, *et al*. Impact of lipodystrophy on the prevalence and components of metabolic syndrome in HIV-infected patients. BMC Infect Dis. 2011;11(1):246. doi: 10.1186/1471-2334-11-246.
7. Rakotoambinina B, Médioni J, RabianC, Jubault V, Jais JP, Viard JP. Lipodystrophic syndrome and hyperlipidemia in a cohort of HIV-1-infected patients receiving triple combination antiretroviral therapy with a protease inhibitor. J Acquir Immune Defic Syndr, 2001;27(5):443-9.
8. Fiorenza CG, Chou SH, Mantzoros CS. Lipodystrophy: pathophysiology and advances in treatment. Nat Rev Endocrinol. 2011;7(3):137-50. doi: 10.1038/nrendo.2010.199.
9. Ammassari A, Antinori A, Cozzi-Lepri A, Trotta MP, Nasti G, Ridolfo AL, *et al*. AdICoNA Study Group. LipoICoNA Study Group. Relationship between HAART adherence and adipose tissue alterations. J Acquir Immune Defic Syndr. 2002;31 Suppl 3:S140-4.
10. Leclercq P, Goujard C, Duracinsky M, Allaert F, L'henaff M, Hellet M, *et al*. High prevalence and impact on the quality of life of facial lipoatrophy and other abnormalities in fat tissue distribution in HIV-infected patients treated with antiretroviral therapy. AIDS Res Hum Retroviruses. 2013;29(5):761-8. doi: 10.1089/AID.2012.0214.
11. Freitas P, Santos AC, Carvalho D, Pereira J, Marques R, Martinez E, *et al*. Fat mass ratio: an objective tool to define lipodystrophy in HIV-infected patients under antiretroviral therapy. J Clin Densitom. 2010;13(2):197-203. doi: 10.1016/j.jocd.2010.01.005.
12. Martinez E,Bianchi L, Garcia-Viejo MA, Bru C, Gatell JM. Sonographic assessment of regional fat in HIV-1 infected people. Lancet. 2000;356:1412-3.
13. World Medical Association. World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191.
14. Babio N, Bullo M, Salas-Salvado J. Mediterranean diet and metabolic syndrome: the evidence. Public Health Nutr. 2009;12:1607-17. doi: 10.1017/S1368980009990449
15. Perović Mihanović M, Haque NS, Rutherford GW, Zekan Š, Begovac J. Toxicity-related antiretroviral drug treatment modifications in individuals starting therapy: a cohort analysis of time patterns, sex, and other risk factors. Med Sci Monit. 2013;19:483-92. doi: 10.12659/MSM.889283.
16. McComsey GA, Ward DJ, Hessenthaler SM, Sension MG, Shalit P, Lonergan JT, *et al*. Trial to assess the regression of hyperlactatemia and to evaluate the regression of established lipodystrophy in HIV-1-positive subjects (TARHEEL; ESS40010) Study Team. Improvement in lipoatrophy associated with highly active antiretroviral therapy in human immunodeficiency virus-infected patients switched from stavudine to abacavir or zidovudine: the results of the TARHEEL study. Clin Infect Dis. 2004;38:263-70. doi: 10.1086/380790.
17. Carr A, Workman C, Smith DE, Hoy J, Hudson J, Doong N, *et al*. Mitochondrial Toxicity (MITOX) Study Group. Abacavir substitution for nucleoside analogs in patients with HIV lipoatrophy: a randomized trial. JAMA. 2002;288:207-15.
18. Ribera E, Larrousse M, Curran A, Negredo E, Clotet B, Estrada V, *et al*. Impact of switching from zidovudine/lamivudine to tenofovir/emtricitabine on lipoatrophy: the RECOMB study. HIV Med. 2013;14(6):327-36. doi: 10.1111/hiv.12011.
19. Martínez E, Ribera E, Clotet B, Estrada V, Sanz J, Berenguer J, *et al.* Switching from zidovudine/lamivudine to tenofovir/emtricitabine improves fat distribution as measured by fat mass ratio. HIV Med. 2015;16(6):370-4. doi: 10.1111/hiv.12210.
20. Turcinov D, Stanley C, Rutherford GW, Novotny TE, Begovac J. Adherence to the Mediterranean diet is associated with a lower risk of body-shape changes in Croatian patients treated with combination antiretroviral therapy. Eur J Epidemiol. 2009;24(5):267-74. doi: 10.1007/s10654-009-9330-2.
21. Batterham MJ, Garsia R, Greenop PA. Dietary intake, serum lipids, insulin resistance and body composition in the era of highly active antiretroviral therapy 'Diet FRS Study'. AIDS. 2000;14(12):1839-43.
22. Hadigan C, Jeste S, Anderson EJ, Tsay R, Cyr H, Grinspoon S. Modifiable dietary habits and their relation to metabolic abnormalities in men and women with human immunodeficiency virus infection and fat redistribution. Clin Infect Dis. 2001;33(5):710-7. doi: 0.1086/322680.
23. Forrester JE, Gorbach SL. Fat distribution in relation to drug use, human immunodeficiency virus (HIV) status, and the use of antiretroviral therapies in Hispanic patients with HIV infection. Clin Infect Dis. 2003;37:S62-8. doi: 10.1086/375883.
24. Grenha I, Oliveira J, Lau E, Santos AC, Sarmento A, Pereira J, *et al*. HIV-infected patients with and without lipodystrophy under combined antiretroviral therapy: evaluation of body composition. J Clin Densitom. 2018;21(1):75-82. doi: 10.1016/j.jocd.2016.07.010.

Sažetak

REVERZIBILNOST LIPOATROFIJE U HIV-om ZARAŽENIH BOLESNIKA NA ANTIRETROVIRUSNOJ TERAPIJI: KOHORTNA STUDIJA S ULTRAZVUČNIM PRAĆENJEM

A. Šoštarić Zadro, K. Višković i *J. Begovac*

Cilj ovog istraživanja bio je okarakterizirati i usporediti promjene potkožnog masnog tkiva na licu, nadlaktici i potkoljenici u skupini HIV-om zaraženih bolesnika koji uzimaju antiretrovirusne lijekove. Radi se o prospektivnoj longitudinalnoj studiji u koju je bilo uključeno 77 bolesnika koji su odabrani iz početne kohorte koja je evaluirana 2007. i 2008. godine. Istraživali smo reverzibilnost lipoatrofije mjerene ultrazvukom u razdoblju od najmanje pet godina i čimbenike povezane s tom reverzibilnošću. Kod svih 46 bolesnika koji su uzimali stavudin on je zamijenjen nekom drugom kombinacijom lijekova. Od 58 bolesnika koji su uzimali zidovudin 16 (28%) ih je uzimalo kombinacije temeljene na zidovudinu kod kontrolnog mjerenja. Dokazan je porast potkožne masti na licu ($p<0,001$), dok na nadlaktici i potkoljenici nije bilo porasta. Bolesnici koji su bili pušači i slabo su se pridržavali mediteranske dijete imali su tanje potkožno masno tkivo na licu kod kontrolnog mjerenja ($p=0,030$), kao i manji porast potkožne masti na licu u usporedbi s ostalima ($p=0,040$). Naše istraživanje upućuje na to da se blaži porast potkožne masti na licu podudara s prestankom uzimanja stavudina i manjim uzimanjem zidovudina. Način života uz nepridržavanje mediteranske dijete i pušenje bio je povezan s manjim porastom potkožne masti na licu.

Ključne riječi: *Lipoatrofija; Antiretrovirusni lijekovi; Ultrazvuk; Mediteranska dijeta*