## Association of gene polymorphism methylenetetrahydrofolate reductase cytosine-to-thymidine substitution at nucleotide 677 with cardiovascular and metabolic risk in morbidly obese patients

- Rea Levicki¹\*,
- DJuraj Jug²,
- ©lnes Vinković²,
- ©Filip Mustač²,
- Martina Matovinović³,
- DLada Bradić³,
- Jadranka Sertić<sup>3</sup>,
- ©Martina Lovrić Benčić<sup>3</sup>

<sup>1</sup>Požega General County Hospital, Požega, Croatia <sup>2</sup>University of Zagreb School of Medicine, Zagreb, Croatia <sup>3</sup>University of Zagreb School of Medicine, University Hospital Centre Zagreb, Zagreb, Croatia **KEYWORDS:** methylenetetrahydrofolate reductase, hypertension, diabetes.

CITATION: Cardiol Croat. 2019;14(9-10):235. | https://doi.org/10.15836/ccar2019.235

\*ADDRESS FOR CORRESPONDENCE: Rea Levicki, Opća županijska bolnica Požega, A. Starčevića 4, HR-35000 Slavonski Brod, Croatia. / Phone: +385-98-550-309 / E-mail: rlevicki@gmail.com

ORCID: Rea Levicki, https://orcid.org/0000-0003-3687-1310 • Juraj Jug, https://orcid.org/0000-0002-3189-1518
Ines Vinković, https://orcid.org/0000-0003-1705-8295 • Filip Mustač, https://orcid.org/0000-0003-2851-6183
Martina Matovinović, https://orcid.org/0000-0002-6325-7394 • Lada Bradić, https://orcid.org/0000-0001-8296-699X
Martina Lovrić Benčić, https://orcid.org/0000-0001-8446-6120

## 

**Introduction**: Region near the gene encoding methylenetetrahydrofolate reductase (MTHFR) is among eight loci associated with blood pressure. <sup>1-3</sup> The aim of this study is to show connection between polymorphism of MTHFR C667T and hypertension, diabetes, prediabetes and obstructive sleep apnea in obese Croatian patients.

Patients and Methods: We included 88 patients from a multidisciplinary weight management program in which genetic analysis on MTHFR gene polymorphism was tested. Patients were divided in 3 groups: 36 patients with MTHFR C677T healthy genotype CC (27 women, 9 men; age 46.4±10.1 year; BMI 44.9±8.8 kg/m²), 38 patients with MTHFR C677T heterozygous mutation CT (27 women, 11 men; age 46.9±11.4 year; BMI 44.6±8.6 kg/m²), 14 patients with MTHFR C677T homozygous mutation TT (12 women, 2 men; age 50.1±15.5 year; BMI 40.2±6.9 kg/m²). In each group the incidence of hypertension, prediabetes, diabetes and obstructive sleep apnea (OSA) was determined.

Results: Patients with genetic mutation MTHFR C677T:CT (Figure 1) had the highest incidence of arterial hypertension (65.8%), diabetes (18.4%), prediabetes (18.4%) and OSA (31.6%) with the highest average apnea hypopnea index (AHI) of 17.3±24.7, even 13.2% of patients used continuous positive airway pressure (CPAP). Patients with healthy genotype MTHFR C677T:CC had lower incidence of arterial hypertension (44.4%), prediabetes (11.1%), diabetes (13.9%), OSA (25%), average AHI 11.3±15.9 and only 8% of patients used CPAP. Patients with MTHFR C677T:TT polymorphism had the lowest arterial hypertension incidence (42.9%), the highest prediabetes incidence (42.9%), middle OSA prevalence (28.6%), AHI 7.7±7.6.

**Conclusion**: MTHFR C677T:CT polymorphism is the most common gene polymorphism in our group of morbidly obese patients. MTHFR C677T:CT polymorphism compared to MTHFR

TO%

HYPERTENSION

PREDIABETES

OBSTRUCTIVE SLEEP APNEA

OS

MITHER

M

FIGURE 1. The graph shows hypertension, prediabetes and obstructive sleep apnea distribution in the group of patients with methylenetetrahydrofolate reductase cytosine-to-thymidine substitution at nucleotide 677 healthy genotype CC, heterozygous mutation CT and homozygous mutation TT.

MTHFR C677T:CC - methylenetetrahydrofolate reductase cytosine-to-thymidine substitution at nucleotide 677 healthy genotype CC; MTHFR C677T:CT - methylenetetrahydrofolate reductase cytosine-to-thymidine substitution at nucleotide 677 heterozygous mutation CT; MTHFR C677T:TT - methylenetetrahydrofolate reductase cytosine-to-thymidine substitution at nucleotide 677 homozygous mutation TT.

RECEIVED: August 5, 2019 ACCEPTED: September 16, 2019



C677T:CC and MTHFR C677T:TT polymorphisms carries the highest risk for arterial hypertension, metabolic disorders (diabetes) and obstructive sleep apnea. Homozygotes MTHFR C677T:TT carries the highest risk for prediabetes. Further investigation is needed to explore this correlation.

## 

- McNulty H, Strain JJ, Hughes CF, Ward M. Riboflavin, MTHFR genotype and blood pressure: A personalized approach to prevention and treatment of hypertension. Mol Aspects Med. 2017 Feb;53:2-9. https://doi.org/10.1016/j.mam.2016.10.002
- Wu YL, Hu CY, Lu SS, Gong FF, Feng F, Qian ZZ, et al. Association between methylenetetrahydrofolate reductase (MTHFR) C677T/A1298C polymorphisms and essential hypertension: a systematic review and meta-analysis. Metabolism. 2014 Dec;63(12):1503-11. https://doi.org/10.1016/j.metabol.2014.10.001
- Yigit S, Karakus N, Inanir A. Association of MTHFR gene C677T mutation with diabetic peripheral neuropathy and diabetic retinopathy. Mol Vis. 2013 Jul 25;19:1626-30. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23901246