type 2 diabetic patients are under the treatment of metformin too. Similar results were also found in the study of Bruckbauer and colleagues to evaluate the synergistic effects of metformin, resveratrol and hydroxymethylbutyrate on insulin sensitivity.[14] They suggested that resveratrol-hydroxymethylbutyrate combined with metformin might act synergistically on adenosine monophosphate-activated protein kinase-dependent pathways, leading to increased insulin sensitivity, which might reduce the therapeutic doses of metformin necessary in the treatment of diabetes. Thus, according to the renoprotective efficacy of silymarin in our study and hypoglycemic effect of this medicinal plants in the study conducted by Sheela and colleagues, it is possible that the combination of metformin and silymarin may have additive renoptective efficacy beyond better controlling the diabetes.[13-16] In this regard, to better understand the renoprotective properties of silymarin, especially in combination with metformin, more experimental rat models and clinical studies are suggested.

**Hamid Nasri**

Division of Nephropathology, Department of Nephrology, Isfahan University of Medical Sciences, Isfahan, Iran
E-mail: hamidnasri@med.mui.ac.ir

## REFERENCES

1. Sheela N, Jose MA, Sathyamurthy D, Kumar BN. Effect of silymarin on streptozotocin-nicotinamide-induced type 2 diabetic nephropathy in rats. Iran J Kidney Dis. 2013;7:117-23.
2. Nematbakhsh M, Pezeshki Z, Moaeidi B, et al. Protective role of silymarin and deferoxamine against iron dextran-induced renal iron deposition in male rats. Int J Prevent Med. 2013;4:286-91.
3. Tolouian R, Hernandez GT. Prediction of Diabetic Nephropathy: The need for a sweet biomarker. J Nephropathol. 2013;2:4-5.
4. Rahimi Z.ACE insertion/deletion (I/D) polymorphism and diabetic nephropathy. J Nephropathol.2012;1:143-51.
5. Rouhi H, Ganji F. Effect of N-acetyl cysteine on serum Lipoprotein (a) and proteinuria in type 2 diabetic patients. J Nephropathol. 2013;1:61-66.
6. Baradaran A. Lipoprotein(a), type 2 diabetes and nephropathy; the mystery continues. J Nephropathol. 2012;1:126-29.
7. Hundal RS, Krssak M, Dufour S, et al. Mechanism by which metformin reduces glucose production in type 2 diabetes. Diabetes. 2000;49:2063-9.
8. Tavafi M. Diabetic nephropathy and antioxidants. J Nephropathol. 2013;2:20-7.
9. Morales AI, Detaille D, Prieto M, et al. Metformin prevents experimental gentamicin-induced nephropathy by a mitochondria-dependent pathway. Kidney Int. 2010;77:861-9.
10. Sahni N, Gupta KL. Dietary antioxidents and oxidative stress in predialysis chronic kidney patients. J Nephropathol. 2012;1:134-42.
11. Amini FG, Rafieian-Kopaei M, Nematbakhsh M, Baradaran A, Nasri H. Ameliorative effects of metformin on renal histologic and biochemical alterations of gentamicin-induced renal toxicity in Wistar rats. J Res Med Sci. 2012;17:621-5.
12. Rafieian-Kopaei M, BaradaranA, Merrikhi A, Nematbakhsh M, Madihi Y, Nasri H. Efficacy of Co-administration of Garlic Extract and Metformin for Prevention of Gentamicin–Renal Toxicity in Wistar Rats: A biochemical study. Int J Prevent Med. 2013;4:258-64.
13. Nasri H, Nematbakhsh M, Rafieian-kopaei M. Ethanolic garlic extract attenuates gentamicin-induced nephrotoxicity in Wistar rats. Iran J Kidney Dis. 2013. In press.
14. Bruckbauer A, Zemel MB. Synergistic effects of metformin, resveratrol, and hydroxymethylbutyrate on insulin sensitivity. Diabetes Metab Syndr Obes. 2013;6:93-102.
15. Rafieian-Kopaei M, Nasri H, Nematbakhsh M, et al. Erythropoietin ameliorates gentamicin-induced renal toxicity: A biochemical and histopathological study. J Nephropathol. 2012;1:109-16.
16. Nasri H. Hypertension and renal failure with right arm pulse weakness in a 65 years old man. J Nephropathol. 2012;1:130-3.

# Re: Correlation Between Ankle-Brachial Index and Microalbuminuria in Type 2 Diabetes Mellitus

Dear Editor,

We read the article ''Correlation Between Ankle-Brachial Index and Microalbuminuria in Type 2 Diabetes Mellitus" by Makhdoomi and colleagues with interest.[1] They investigated the value of ankle-brachial ındex (ABI) for prediction of microalbuminuria in type 2 diabetic patients. They demonstrated significant relationship was found

between an ABI less than 0.9 and cardiovascular events; there was a strong correlation even after omitting the bias-inducing variants.

Peripheral arterial disease (PAD) is very common in male population aged greater than 50 years and affects approximately many millions people in the worldwide. The ABI is known to be unreliable in patients with vascular stiffness and fails to detect the early phase of arteriosclerotic development. ABI is a valuable diagnostic tool for PAD. PAD was considered present if the ABI was less than 0.9 or greater than 1.4 in at least 1 leg.[2] The early diagnosis of PAD and the initiation of conservative measures is related not only with a reduction in disease progression but also with numerous additional beneficial actions. For example, PAD is associated with the metabolic syndrome which requires treatment in its own right.Furthermore, some medications such as antihypertensive treatment, aspirin and statins may influence ABI paremeters. A low ABI has been demonstrated as a marker of decreased renal function over time in a general population patients and the presence of concomitant renal dysfunction in PAD patients is associated with higher morbidity and mortality rates, as well as the occurrence of cardiovascular events.[3] It would be useful, if the authors provide data about these risk factors and their possible relationship with the ABI.

Finally, measurement of ABI manually by Doppler ultrasonography is a well-known method to diagnose PAD. Also, ABI is the easiest, low-cost, reliable, noninvasive and most widely available parameter among the tested tools and could help detect the presence of PAD. However, in a previous study,[4] measuring the photoplethysmography and continuous-wave Doppler ultrasonography in addition to ABI measurement in subjects with a probable PAD was suggested in suspected patients as the ABI has a sensitivity of 69.3% and a specificity of 99.6% and in this regard it may miss a real diagnosis of PAD. But in real life, a measurement of ABI and the practice of these additional tools may consume more time and lead to higher costs. Additionally, because many factors can affect ABI measurement, all risk factors and confounders should be discussed in patients with microalbuminuria.[5] These may decrease the effectiveness of these methods in clinical practice.[6] Further studies will be needed to reveal the clinical relevance of these additional investigations. We believe that these findings will provide useful information about the measurements of ABI and PAD management.

Sevket Balta,[1]* Ugur Kucuk,[1] Mustafa Cakar,[1] Sait Demirkol,[2] Murat Unlu,[1] Zekeriya Arslan[1]

[1]Department of Internal Medicine, Gulhane Medical Academy, Ankara, Turkey

[2]Department of Cardiology, Gulhane Medical Academy, Ankara, Turkey

*E-mail: drsevketb@gmail.com

## REFERENCES

1. Makhdoomi K, Mohammadi A, Yekta Z, Aghasi MR, Zamani N, Vossughian S. Kidney diseases Correlation Between Ankle-Brachial Index and Microalbuminuria in Type 2 Diabetes Mellitus. Iran J Kidney Dis. 2013;7:204-9.
2. Balta S, Balta I, Demirkol S, Cakar M, Sarlak H, Kurt O. Subclinical peripheral arterial disease and ankle-brachial index. Angiology. 2013;64:395-6.
3. Paraskevas KI, Giannoukas AD, Mikhailidis DP. Renal function impairment in peripheral arterial disease: an important parameter that should not be neglected. Ann Vasc Surg. 2009;23:690-9.
4. Ro DH, Moon HJ, Kim JH, Lee KM, Kim SJ, Lee DY. Photoplethysmography and continuous-wave Doppler ultrasound as a complementary test to ankle-brachial index in detection of stenotic peripheral arterial disease. Angiology. 2013;64(:314-20.
5. Balta S, Cakar M, Demirkol S. All Risk Factors and Confounders Should Be Discussed in Order To Precisely Describe the Ankle-Brachial Index and Albuminuria. J Atheroscler Thromb. 2013;20:601.
6. Sarlak H, Cakar M, Balta S, Arslan E, Demirkol S, Akhan M. Peripheral arterial disease assessment with photoplethysmography and continuous-wave Doppler ultrasound in addition to ankle-brachial index may loss time and funds. Angiology. 2013;64:321.