Authors' Reply

Letter to editor, in response to letter entitled: Could monitoring normotensives delay progression to hypertension?

Dear Editor,

We must thank the authors for his scientific interest toward our study. It must be pointed out that this investigation has been suggested by the researches of Cugini et al¹⁻⁴, in office normotensives (ON), showing initial minimal signs of the cardiovascular target organ damage (TOD). Suspecting the occurrence of an undiagnosed hypertension, Cugini et al applied the Ambulatory (A) Blood (B) Pressure (P) Monitoring (M) to these ON. Interestingly, the ABPM revealed that the within-day systolic (S) and diastolic (D) BP values of these subjects were all below the pertaining day/night upper reference limits. Thus, the possibility of a true monitoring hypertension (TMH) was definitively discarded. Subsequently Cugini verified the hypothesis that these subjects should not be regarded as true monitoring normotensives (TMN) comparing their Daily Mean Level (DML) of SBP and DBP with the same estimate provided by ABPM of the TMN. Surprisingly, the statistical comparison revealed that the DML(SBP:DBP) of ON with cardiovascular TOD was significantly higher than expected, being biometrically located in between the DML(SBP:DBP) of TMN and TMH. This intermediate 24 hours BP regimen was first termed "ABPM-diagnosable prehypertension" ("Monitoring prehypertension"), suggesting that the binomial association "Initial cardiovascular TOD/monitoring prehypertension" could be regarded as a clinical syndrome, namely "Cugini's syndrome" 1-4.

This syndrome was not included in 2002, by Pickering et al⁵, in the four-items classification for the concordance/discordance between office sphygmomanometry and ABPM, i.e., (1) office normotension/monitoring normotension, alias true normotension; (2) office hypertension/monitoring hypertension, alias true hypertension; (3) office hypertension/monitoring normotension alias white coat hypertension; (4) office normotensives/monitoring hypertension, alias masked hypertension. In addition in 2003 the term "Prehypertension" was adopted by the Seventh Report (JNC-7) of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure⁶ in a tripartite classification of BP regimen, via the conventional Riva-Rocci spygmomanometry, to indicate an office prehypertension in between office normotension and office hypertension, without mention of the subset of patients, to be considered as affected by "Cugini's syndrome".

Due to the lack of sufficient literature verifying the real existence of this syndromic association, we decided to perform an investigation, via ABPM, in order to decipher whether or not an initial sign of increased carotid Intima-Media Thickness (cIMT) in ON could be associated to a monitoring prehypertension as per "Cugini's syndrome".

Interestingly, the results of our study, if further confirmed, would seem to confirm this hypothesis. In fact we agree with the authors that cIMT is strongly related to hypertension, and , as in our study, prehypertensive status at ABPM⁷.

On the other hand, we agree with the authors that results from our study have to be verified in future prospective studies, including also the evaluation of other TODs, as reported by Cugini et al. In fact the findings from the present report arise from a retrospective experimental setup, thus, limiting the prognostic value of this investigation.

Finally, we agree that there is no enough proof to recommend carotid ultrasonography monitoring and antihypertensive therapy yet in this group of patients. However, we aim to verify our preliminary findings with a prospectic follow-up of this patients' subset in order to verify also the impact of minimal TOD on their CV risk.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

- 1) CUGINI P, PETRANGELI CM, CAPODAGLIO FP, CHIERA, A, CRUCIANI, F, TURRI, M, GHERARDI, F, SANTINO, G. "Retinopatia tensiva a lesioni minime" e pre-ipertensione arteriosa: evidenze dal monitoraggio della pressione arteriosa in soggetti reputati normotesi a "rischio zero". Rec Progr Med 1997; 88: 11-16.
- 2) Cugini P, Cruciani F, Turri M, Regine F, Gherardi F, Petrangeli CM, Gabrieli CB. "Minimal-change hypertensive retinopathy" and "arterial pre-hypertension", illustrated via ambulatory blood-pressure monitoring in putatively normotensive subjects. Int Ophthalmol 1998-99; 22: 145-149.
- 3) CUGINI P, BALDONI F, DE ROSA R, PANDOLFI C, COLOTTO M, LEONE G, ZAMPARELLI C, BERTI D, PASSINI B, RONCORONI V, SABINO D, CAPRIA A. The ambulatory monitoring documents a more elevated blood pressure regimen (pre-hypertension) in normotensives with endothelial dysfunction. Clin Ter 2002:153: 167-175.
- CORNELISSEN G, HALBERG F, BEATY L, KUMAGAI Y, HALBEG E, HALBERG J, LEE J, SCHWARTZKOPFF O. Cugini's syndrome in status nascendi. Clin Ter 2009; 160: e13-e24.
- 5) PICKERING TG, DAVIDSON K, GERIN W, SCHWARTZ JE. Masked hypertension. Hypertension 2002; 40: 795-796.
- 6) The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7). Hypertension 2003; 42: 1206-1252.
- 7) AYDIN M, BULUR S, ALEMDAR R, YALÇIN S, TÜRKER Y, BASAR C, ASLANTAS Y, YAZGAN Ö, ALBAYRAK S, ÖZHAN H; MELEN INVESTIGATORS. The impact of metabolic syndrome on carotid intima media thickness. Eur Rev Med Pharmacol Sci 2013; 17: 2295-2301.

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