The smoothness index: an ‘all purposes’ approach to the assessment of the homogeneity of 24-h blood pressure control?

Damiano Rizzoni\textsuperscript{a,b}, Anna Paini\textsuperscript{a}, Carolina De Ciuceis\textsuperscript{a}, Claudia Agabiti-Rosei\textsuperscript{a}, and Massimo Salvetti\textsuperscript{a}

Although an ideal antihypertensive medication providing a homogeneous blood pressure-lowering effect throughout the dosing interval may have a T/P ratio equal to 1, medications with a T/P ratio greater than 0.5 were commonly approved by the US Food and Drug Administration\cite{1,2}. However, T/P ratio takes into account only on two short time intervals (or just two single blood pressure measurements), thus potentially missing important information relative to the remaining part of the 24-h period, and is affected by variations occurring either spontaneously or as a result of patients’ posture and behaviors\cite{3}, which make the T/P ratio a somewhat imprecise indicator of the overall extent and homogeneity of the blood pressure-lowering effect\cite{1}.

In order to overcome the previously mentioned limitations of the T/P ratio in assessing the distribution of the antihypertensive effect of a given drug, a different index, the smoothness index was proposed in 1997\cite{5}, and then applied in more than 80 pharmacological studies, with the intent of assessing the homogeneity of blood pressure control through the 24 h.

The smoothness index estimates mean 24 hourly changes in blood pressure from duplicated 24-h ABPM recordings (performed before and during pharmacologic treatment). The average of these 24 hourly changes, along with its standard deviation, is then assessed. The smoothness index is calculated as the ratio between the average of the 24 hourly blood pressure changes induced by a given medication and the standard deviation of hourly reductions\cite{1,5,6}. Thus, the smoothness index not only incorporates information on the average degree of blood pressure reduction by a given drug but also on the distribution of these reductions throughout the 24 h\cite{1}.

In 1998, the smoothness index was directly compared with T/P ratio in the population of antihypertensive patients enrolled in the Study on Ambulatory Monitoring of Pressure and Lisinopril Evaluation (SAMPLE study)\cite{6} from ABPM data. The smoothness index correctly identified the occurrence of a balanced 24-h blood pressure reduction with treatment and was significantly correlated with the favorable effects of treatment on left ventricular hypertrophy...
better than the T/P ratio [6]. Even reproducibility was far greater for the smoothness index than for the T/P ratio [6,7].

The clinical usefulness of the smoothness index was then confirmed in other studies; in fact the smoothness index, but not the T/P ratio predicted changes in carotid artery wall thickness during antihypertensive treatment [8]. Campo et al. [9] observed that treatment-induced changes in left ventricular mass index induced by lercanidipine in hypertensive patients were not correlated with changes in office or 24-h blood pressure, or with the T/P ratio; on the contrary, a significant correlation was found between left ventricular mass index changes and the smoothness index at 6 months.

Therefore, a greater reduction in mean blood pressure levels and in blood pressure variability throughout the 24 h is associated with a higher smoothness index (usually >1) and with a greater cardiovascular protection [1,6,8,9].

The differential effects of antihypertensive medications on the smoothness index were assessed in a large meta-analysis including randomized, controlled studies in hypertension. The smoothness index was influenced by age, race, sex, behavioural and haemodynamic factors [10]. It was also able to differentiate the 24-h blood pressure effects of antihypertensive drugs, with telmisartan and amlodipine achieving the highest values compared with other angiotensin II receptor blockers or with ramipril, possibly because of their long plasma half-lives [10]. All combination therapies had a higher smoothness index than monotherapies [10].

The advantage of combination treatments over monotherapies was also confirmed by Omboni et al. [11]. The smoothness index was significantly higher in hypertensive patients treated with olmesartan with a thiazide diuretic or a calcium-channel blocker (dual treatment), as well as in those treated with olmesartan with a thiazide diuretic and a calcium-channel blocker (triple treatment), than in those treated with monotherapies alone [11]. High doses of the different drugs had a smoother effect than low doses [11]. The olmesartan/amlodipine combination, in particular, compared with amlodipine, was associated to a better homogeneity of blood pressure reduction (higher smoothness index) [12] which was, again, dose-related. Similar results were obtained comparing telmisartan/amlodipine combination versus monotherapies [13,14].

The smoothness index was high in responders to felodipine treatment and low in nonresponders [15] during the first 2-week treatment period. It increased in nonresponders after an additional 2 weeks of treatment with extended-release felodipine 10 mg/day [15]. The smoothness index of SBP and DBP was comparably high for nifedipine and

FIGURE 1 Calculation of the trough/peak (T/P) ratio and the smoothness index from hourly blood pressure values obtained before and during treatment by 24 h ambulatory blood pressure recordings. \( \Delta H \), average of treatment-induced blood pressure reductions for each hour over 24 h; SD, standard deviation of the average hourly blood pressure reductions. Data from ref. [6].
The smoothness index, but not the trough-to-peak ratio between mean 24-h blood pressure reduction and the reduction over 24 h and with a more favorable balance treatment was associated with a smoother blood pressure profile (as suggested by the higher smoothness index) as well as the achievement of significantly lower and smoother blood pressure levels over 24 h; in fact the smoothness index provides a superior measure of the homogeneity of blood pressure control compared with the T/P ratio [1]. However, further studies are still needed to confirm that, in humans, interventions that are associated with higher smoothness index and with a reduced blood pressure variability can also decrease the rate of cardiovascular events [21–24].

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Conflicts of interest

There are no conflicts of interest.

REFERENCES


