Dear Sir,

We read with great interest the article by Crescente et al. on the variability of platelet responses to aspirin, assessed using the PFA-100® device and collagen-epinephrin cartridges (CEPI), as well as the potential determinants of this variability and its association with vascular events (1). The authors conducted an exhaustive review of all relevant studies and defined “responders” and “non-responders” based on closure time (CT) cut-off values, which vary across studies. The authors provide a wealth of information on a large number of studies, meticulously analyze the data, and provide insights into factors potentially associated with the prevalence of aspirin non-responsiveness. Crescente et al. have to be commended for this work. Some results are intriguing, however. First, the higher frequency of non-responders among patients taking the highest aspirin doses is unexpected, as is the trend towards a higher frequency of non-responders in studies with the lowest PFA-100 CT_{CEPI} cut-off values. These observations conflict with common sense, as acknowledged by the authors themselves, and also challenge previous data based on various laboratory definitions of aspirin resistance (2). The variable contribution of results obtained in healthy subjects, patients with acute events, and patients with acute and chronic diseases may partly explain these discrepancies. Multivariate analysis and a search for interactions between explanatory variables might have helped. Second, the reported median prevalence would be better replaced by a weighted mean prevalence rate, as done elsewhere (2); this might be a better indicator, given the wide range of study sizes. Third, the analysis of the association between aspirin non-responder status and the occurrence of vascular events should have been restricted to prospective studies, in order to better assess the potential predictive value of aspirin non-responder status. Fourth, we feel that studies of patients treated with clopidogrel plus aspirin should have been included, as clopidogrel has no major effect on PFA-100 CT_{CEPI} values, and aspirin-clopidogrel treatment does not seem to have a major effect on the magnitude of the association between aspirin non-responder status and clinical events (3). Finally, it would be more relevant to report the results with odds ratios instead of relative risks, to provide the Cochran Q statistic with its associated p-value for heterogeneity, and to use a random effects model if heterogeneity is present in a fixed effects model. This methodology and choice of data expression would probably not affect Crescente’s overall results but would provide the reader with critical information (4).

The main issue raised by this meta-analysis is obviously the need for a consensus definition of aspirin resistance. An important step forward has been made with the meta-analyses of studies involving a single biological assay (PFA-100 CT_{CEPI}) (1, 5). The results of these meta-analyses need to be confirmed in stable ischemic patients, and the clinically relevant PFA-100 CT_{CEPI} cut-off needs to be refined in a large prospective study of aspirin-treated stable cardiovascular patients.
References


