the individual patient, possibly by using a quantitative variable of arterial extent, as was described in another recent study [4].

The authors could serially assess evolution of angiographic extent in the North American cohort, but not in the Indian cohort [1]. Overall, the patients in the Indian cohort had a shorter disease duration (median 1–1.5 years) than their North American counterparts (median 4–6.2 years). Therefore, while angiographic changes did not differ to an extent necessitating change in cluster assignment in the latter group for most patients, this might not be the case for the Indian cohort. An earlier Indian study serially reported angiographic changes at 1-year interval in patients with TAK, with a mean disease duration of 12 months. Over this duration, out of 54 stenotic vascular segments, regression was noted in 17 segments, and improvement in 8 segments [5]. Similar progression of angiography has also been noted in other Indian studies involving patients with longer disease duration [6, 7]. Therefore, the potential for angiographic changes could possibly be greater in Indian patients with TA later in the course of their disease. Whether cluster assignment changes in such patients over time remains to be explored.

The heterogeneity of disease assessment and angiographic techniques used to detect angiographic changes in these patients might be another point of importance [1], particularly since magnetic resonance angiography might overestimate the degree of vascular involvement [8]. However, the present study involved patients in real-life clinical settings; therefore, achieving uniformity of imaging techniques and disease assessment instruments for this rare disease was not practical. Overall, the present study is a welcome step towards understanding a rare disease. The therapeutic and prognostic implications of the cluster assignment based on angiography will require further exploration, and validation across different ethnic groups.

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Comment on: Derivation of an angiographically based classification system in Takayasu's arteritis: reply

SIR, We thank Misra and colleagues for their interest and insightful comments on our work [1, 2]. We agree that our classification scheme needs to be tested further to determine its ultimate value in guiding medical management and facilitating scientific discovery.

Takayasu's arteritis (TAK) is a clinically heterogeneous and rare disease. Most physicians do not manage enough patients with TAK to recognize and appreciate the full clinical spectrum of the disease. The new angiographic

classification system we proposed provides a simple framework to conceptualize different subsets of patients. By defining three major patterns of angiographic disease (predominant abdominal artery involvement, symmetric arch disease and asymmetric focal disease), clinicians can easily recognize subsets of patients with TAK. Because these subsets differ in terms of clinical symptoms and outcomes, this classification system may lead to the development of more individualized and directed approaches to the management of TAK. For example, understanding that patients with symmetric arch disease are at highest risk for stroke and are less likely to achieve clinical remission may help guide approaches to clinical assessments and treatment in these patients that may differ from such decisions in patients with TAK who have disease exclusively in the abdominal arteries.

Patterns of arterial disease have long been recognized in TAK. Prior angiographic classification schemes were developed based on physician observation, which is limited with respect to recognizing complex patterns of association [3–5]. By using computer-driven approaches, the new classification system we propose avoids the limitations of physician-based observation. For this reason, as Misra and colleagues note, the resultant three subsets are not defined exclusively by specific arterial territories but rather by complex multi-dimensional interactions. Fortunately, a simple decision tree based on assessment of key arterial territories approximates computer-derived cluster assignment with 87–92% accuracy. While such an approach may result in misclassification for a minority of patients, a problem with almost all such classification systems in medicine, this limitation is balanced by the simplicity and feasibility of cluster assignment using a decision tree.

TAK may be a conglomeration of different diseases driven by different causal factors that ultimately converge in resultant damage to large arteries. The new angiographic classification system should enable researchers to study more homogeneous subsets of patients and eventually identify causal drivers of disease, including genetic, immunologic and environmental factors. Classifying patients with TAK based on consequences of inflammation (e.g. angiographic patterns of disease) are not likely to be as reproducible or clinically relevant as classification schemes based on causal disease factors. The search for causality remains the central objective in understanding clinical heterogeneity in TAK.

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Comment on: Subclassifying ANCA-associated vasculitis: a unifying view of disease spectrum

DEAR EDITOR, In their editorial on the subclassification of ANCA-associated vasculitis (AAV), Mahr *et al.* [1] suggest dissecting AAV into non-severe AAV, severe PR3-AAV and severe MPO-AAV. The proposed subgrouping is based on genetic, immunological and clinical considerations and thus, addresses fundamental aspects of AAV pathophysiology and clinical presentation [1]. Subclassifying AAV along its major phenotypes implies, as the authors state, abandonment of present-day AAV-classification with granulomatosis with polyangiitis (GPA) representing one entity and microscopic polyangiitis (MPA) another [1, 2]. Although not explicitly addressed by the authors, subclassification of AAV according to