None of the mutations reported by Van Driest et al. (1) follow the admitted nomenclature system, and because of this, in some cases it is not possible to identify the exact place where the mutation occurs. For example (Table 1, p. 1906 in their study), the SNPs 2, 23, 30, 34, and 35 cannot be positioned in the reference sequence (it seems to be the GI:2920822, even though it is not mentioned in the report) because the investigators only give the amino acid number, and never the nucleotide. The description of the nucleotide change in essential because the genetic code is degenerated.

Also, with the use of an equivocal nomenclature system, the same mutation may be reported in two or more different ways. We believe that Van Driest et al. consider as novel—because of a nomenclature error—mutations that have been previously described. For example, they refer the SNP 43 as “ins aa G1041fs”; in this case, it is impossible to determine where the mutation occurs, because the number of the nucleotide where aa is inserted is not given, but we believe it could correspond to g.20025_20026insAA T1042fs described by Niimura et al. (6). The same occurs with the SNPs 8 described by Erdmann et al. (7).

Finally, we have detected similar pitfalls in other published studies on cardiomyopathies. Because of this, we would like to see an increase in the quality of the genetic information published on cardiomyopathies by employing the standard mutations’ nomenclature.

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REPLY

In their letter to the editor, Hermida and colleagues illuminate an issue of ever-increasing importance not only to pathogenetic studies involving hypertrophic cardiomyopathy (HCM), but for genomics research as a whole. Their letter calls for standardization of the format for mutation nomenclature to previously published recommendations (1,2). Indeed, our laboratory has conformed to alternate published recommendations (3), and a perusal of the HCM mutation literature quickly reveals that each laboratory has developed its own style for mutation reporting.

The pitfalls associated with mutation-formatting inconsistencies are illustrated in our own study (4), where owing to inconsistencies in published mutation nomenclature, three previously reported mutations in MYBPC3 were mistakenly reported as novel. The K811del in exon 25 was previously annotated as “exon 25 deletion 3 bp codon 811–815” (5). Exon 13, del c, D389 fs/15 was previously reported as “exon 14 del of c at nt 1200” (6). Finally, exon 29, ins aa, G1041 fs/5 was previously reported as “Ins AA1042” (7), and “exon 30, ins of AA at nt 3156” (6). Certainly, standardization of format as well as nucleotide and exon numbering in future publication will enhance data accuracy. However, several obstacles exist to the implementation of such standardization. Nomenclature schemes must be acceptable and, ideally, required uniformly by all publications. More importantly, any recognized scheme must be useful for colleagues with diverse research objectives including linkage analysis, candidate gene screening, functional characterization, and genetic counseling.

Furthermore, to enable the amalgamation of past mutation data with current and future discoveries including alternatively spliced transcripts, large-scale sequence variants, and changing “wild-type” genetic sequences, a dynamic compendium of sequence data is required. Indeed, this has been attempted at the genome level with the National Center for Biotechnology Information database (8), and tailored specifically for HCM by the Familial HCM DNA Mutation Database (9). Continued submission to, and support of, these resources will enable correlation of the vast data forthcoming with the foundational groundwork provided by published works. The request for standardization is much appreciated and has our complete endorsement.

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Effect of Two Different Neuroprotection Systems on Microembolization During Carotid Artery Stenting

After reading the study titled "Effect of Two Different Neuroprotection Systems on Microembolization During Carotid Artery Stenting" by Schmidt et al. (1) in the Journal and after having an extensive experience with a system that holds several similarities with the MO.MA device (Invatec s.r.l., Roncadelle, Italy), I can make the following comments.

The investigators stated that 71% of their patients had microembolic signals (MESs) after balloon dilation of the stent; MESs during stent placement and balloon dilation were more than six times higher than during wire passage. This latter observation suggests that antegrade flow was still present using the MO.MA device.

The utilization of balloon occlusion of the common carotid artery (CCA) and external carotid artery (ECA) and the description of continuous MESs during carotid artery stenting (CAS) using a filter device was reported earlier by us (2). The researchers did not reference this original study.

Using occlusion of the CCA and ECA, we experienced, as did Schmidt et al. (1), that MESs were still present; we attributed them to antegrade flow through branches not occluded by the balloon. The other potential explanation is a Venturi effect of the circle of Willis suctioning from the column of stagnant flow in the internal carotid artery after balloon occlusion.

Finally, owing to the above-mentioned findings, we added flow reversed to the occlusion of the CCA and ECA.

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REPLY

Dr. Parodi mentions his experience with a similar protection device, the PAES (Parodi antiembolism system) (1). Because of the requirement of brevity of our study (2), the comparative technical discussion of both systems (MO.MA vs. PAES) was not possible. An advantage of the PAES over the MO.MA system could be the potential continuous retrograde flow through the target lesion during the intervention. Establishment of a continuous retrograde flow in the internal carotid artery using this concept has been demonstrated in an animal model (3). However, there are no scientific data demonstrating and quantifying that, during the critical phases of stent placement, delivery and postdilation of the PAES permits an effective retrograde flow in humans. Dr. Parodi mentioned in his study (1) the use of this protection device in nine patients. Transcranial Doppler monitoring revealed no microembolic signals (MESs) during clamping of the common carotid artery in these patients. In our study, using the MO.MA system there was also a considerable number of subjects (48% of 21 patients) showing no MESs during stent deployment and during balloon dilation (29% of 21 patients). It is regrettable that a controlled multicenter registry, showing the safety and feasibility of the PAES, as it has been conducted recently using the MO.MA system (4), is not yet available. A randomized comparison between the PAES and MO.MA device using transcranial Doppler with detection of MESs would be of interest.

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