presence of CAD was 3.0 (95% confidence interval, 1.3 to 7.2; $p < 0.02$) for the resistin level of >6.0 ng/ml.

In 2004, Burnett et al. (9) reported 74 patients with CAD to have higher plasma resistin levels than 74 with normal coronary arteries. Reilly et al. (10) also showed resistin levels to be associated with coronary calcification by computed tomography in 879 asymptomatic subjects. We demonstrated resistin levels to be higher in patients with CAD than in those without CAD and to be an independent factor for CAD. Moreover, we showed resistin levels to be associated with the severity of CAD. Our results suggest that serum resistin levels in patients with CAD reflect the severity of coronary atherosclerosis and that resistin may play a role in the development of CAD.

Serum resistin levels were reported to be elevated in obese (3) and diabetic patients (4,5). Resistin levels were also reported to correlate with BMI (3,5). However, other studies (4,6) and ours found no such correlation. Silha et al. (6) demonstrated resistin levels to correlate with fasting insulin levels and HOMA-IR in obese subjects. Although other studies failed to show such correlations (3,4), we showed significant correlations between resistin levels and both fasting insulin levels and HOMA-IR in patients with and without CAD, suggesting a potential link between resistin and insulin resistance. Interestingly, resistin has structural similarities to proteins involved in inflammatory processes, especially FIZZ3, and may be involved in inflammatory processes associated with obesity (11). Resistin levels were reported to be associated with plasma CRP and interleukin-6 levels (10,12). We also showed resistin levels to correlate with hsCRP levels, suggesting a potential link between resistin and inflammation. Because insulin resistance became recognized to be associated with atherosclerotic disease and because atherosclerosis is recognized as a chronic inflammatory disease, resistin may play some role in linking insulin resistance and inflammation to CAD.

Our study cannot determine the main source of serum resistin in patients with CAD and cannot establish causality, because it only showed some associations. In Figure 1, there was some overlapping in resistin levels between patients with and without CAD. Serum resistin levels in patients with CAD may reflect not only coronary atherosclerosis but also the degree of atherosclerosis in other vascular beds.

Thus, serum resistin levels were associated with the presence and severity of CAD, suggesting that resistin may play a role in the development of CAD. Resistin levels also correlated with hsCRP levels and insulin resistance. Resistin may, therefore, play a role in linking inflammation and insulin resistance to CAD.

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Letters to the Editor

Standard Mutation Nomenclature in Hypertrophic Cardiomyopathy: An Urgent Need

The report by Van Driest et al. (1) is the biggest population study published searching for mutations associated with hypertrophic cardiomyopathy (389 patients). This type of study is essential to uncover the genetic basis and molecular spectrum of such a complex disease.

However, we would like to call attention to two aspects that are usually forgotten in such studies and that might create confusion. First, Van Driest et al. (1) report 46 mutations in the MyBPC3 gene, including 33 claimed as "novel." But at least one of them, the K811del mutation, has been previously reported by Jaaskelainen et al. (2); thus, it is not correct to call it "novel." Moreover, the mutation W890X was reported in 2004 (3).

Second, it is mandatory to use an unequivocal and unified nomenclature system to identify the mutations. Nowadays there is a standard nomenclature system (4,5) that includes the mention of the reference sequence employed to numerate the residues, the position of the mutated nucleotide, and the affected amino acid within the protein.

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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