Original Article

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Need for revision of the ACMG/AMP guidelines for interpretation of X-linked variants

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SUMMARY The guidelines provided by American College of Medical Genetics and Genomics (ACMG) and the Association of Molecular Pathology (AMP) (ACMG/AMP guidelines) suggest a framework for the classification of clinical variants. However, the interpretations can be inconsistent, with each definition sometimes proving to be ambiguous. In particular, there can be difficulty with interpretation of variants related to the X-linked recessive trait. To confirm whether there are biases in the interpretation of inherited traits, we reanalyzed variants reported prior to the release of the ACMG/AMP guidelines. As expected, the interpretation ratio as pathogenic or likely pathogenic was significantly lower for variants related to the X-linked recessive trait. Evaluation of variants related to the X-linked recessive trait, hence, need to consider whether the variant is identified only in males in accordance with the X-linked recessive trait. The ACMG/AMP guidelines should be revised to eliminate the bias revealed in this study.

Keywords ACMG/AMP guidelines, X-linked recessive, interpretation, sequence variant, diagnostic odyssey

1. Introduction

When medical diagnoses are difficult to achieve based on just the clinical information, patients and their families often experience a "diagnostic odyssey" that requires unnecessary medical evaluations (*1*). The longer the diagnostic odyssey, the greater the disadvantage to the patients and their families. Patients subjected to a diagnostic odyssey may have rare and undiagnosed genomic disorders that can only be identified using genomic analyses. Rare diseases only occur in a fraction of the general population. However, collectively, they comprise approximately 7,000 different disorders, the majority of which have a genetic origin (*2*). Thus, systematic and comprehensive genomic analyses to identify the causative genetic variants of rare and undiagnosed diseases would assist patients and their families (*3*).

Massive parallel sequencing analyses using next generation sequencing to detect causative variants of Mendelian disorders in undiagnosed patients have led to the identification of unprecedented numbers of genomic variants. Almost all variants have been unrelated to the disease diagnosis. Thus, for Mendelian disorders, the identification of one or two disease-causing sequence variants typically represents a bottleneck in the filtering of many sequence variants (*4*). This filtering step generally uses population data, computational predictive data, variant types, gene-specific information, variant segregation, and functional data (*5*). After narrowing down the potential candidate variants, it needs to be determined whether these variants are indeed causative. This requires a process of systematic interpretation. In 2008, the American College of Medical Genetics and Genomics (ACMG) issued recommendations for interpretative categories of sequence variants (*6*). In 2015, a workgroup of the ACMG and the Association of Molecular Pathology (AMP) provided defined terms and detailed variant classification guidance as updated standards and guidelines for the interpretation of sequence variants (*7*).

The ACMG/AMP guidelines are recommended for the interpretation of sequence variants in Mendelian disorders. Using the guidelines, variants are classified into five categories: pathogenic, likely pathogenic, uncertain significance (VUS), likely benign, and benign (*8*). However, the interpretations can be inconsistent, with each definition sometimes proving to be ambiguous, and molecular geneticists can have a bias favoring overestimation of pathogenicity (*9*). Therefore,

it is necessary to share the nuances that enable more accurate variant interpretations to be obtained among molecular geneticists through professional training (*10*). The guidelines in fact mention that it is necessary to develop more focused guidance regarding the classification of variants in specific genes (*7*). Indeed, hearing loss-specific guidelines have been established, and these have resolved discrepancies in variation classification, leading to more consistent results for patients in need of an accurate diagnosis (*11*).

In the past decade, we have participated in research to identify the genomic background of patients with undiagnosed neurodevelopmental disorders (*12*). In this research project, we experienced difficulties in determining disease-causing variants related to X-linked genes, and we considered whether the ACMG/AMP guidelines may exhibit biases in the scoring system depending on the mode of inheritance. Here, we evaluated the scoring system of the ACMG/AMP guidelines for inheritance patterns, and we considered whether there is a better way to interpret such sequence variants.

2. Materials and Methods

Variants reported as disease-related prior to the establishment of the ACMG/AMP guidelines were reanalyzed to assess whether there were any discrepancies in the scoring using the ACMG/AMP guidelines depending on the differences in the inheritance traits, including autosomal dominant, autosomal recessive, and X-linked. The variants reported prior to the establishment of the ACMG/AMP guidelines are not considered to be affected by the ACMG/AMP guidelines. Variants were selected from reports published in international journals with an impact factor greater than 4 at the time of analyses. In the variant interpretation step, InterVar, a bioinformatics software tool for clinical interpretation of genetic variants by the ACMG/AMP guidelines (*https://wintervar.wglab.org/*), was used as the reference (*13*). Web-based tools, including wANNOVAR (*https://wannovar.wglab.org/*) (*14,15*), gnomAD (*https://gnomad.broadinstitute.org/*), and ClinVar (*https://www.ncbi.nlm.nih.gov/clinvar/*), were also used. Finally, two or more curators confirmed the scoring based on the ACMG/AMP guidelines.

According to the obtained results of the variants previously reported as disease-causing prior to 2015, the proportion of the variants classified as pathogenic or likely pathogenic was aggregated according to the inheritance manner and statistically analyzed by Fisher's Exact Test and Yate's chi-squared test.

If the proportion of X-linked variants determined to be pathogenic or likely pathogenic was significantly lower, we hypothesized that an additional score specific for X-linked variants might eliminate the difference from other inheritance mechanisms and added a new score for Pathogenicity of Strong Evidence (PS score) or Pathogenicity of Moderate Evidence (PM score) in cases where the target patient was a male and females carrying the same variant did not exhibit any clinical symptoms except for in specific cases. We further examined whether the above difference could be eliminated by the addition of new scores when the target patient was a male, and females carrying the same variant did not exhibit any clinical symptoms except for in specific cases.

3. Results

We selected the reports published prior to 2015. For variants associated with the autosomal dominant trait, 158 variants of 13 genes were selected from 7 reports (*16-22*). All scores in accordance with the ACMG/AMP guidelines are summarized in Supplemental Table S1 (*http://www.irdrjournal.com/action/getSupplementalData.php?ID=113*). Among the evaluated variants, 143 (90.5%) were interpreted as pathogenic or likely pathogenic (Table 1). For the autosomal recessive trait, 109 variants of 17 genes were selected from 11 reports (*23-33*). All scores are presented in Supplemental Table S2 (*http://www.irdrjournal.com/action/getSupplementalData.php?ID=113*). Among these, 93 variants (85.3%) were interpreted as pathogenic or likely pathogenic (Table 1). For the X-linked recessive trait, 105 variants of 35 genes were selected from 9 reports (*34-42*). All scores are presented in Supplemental Table S3 (*http://www.irdrjournal.com/action/getSupplementalData.php?ID=113*). Among these, 42 variants (40.0%) were interpreted as pathogenic or likely pathogenic (Table 1). There were significant differences between autosomal dominant versus X-linked, and autosomal recessive versus X-linked. However, there was no significant difference between the autosomal dominant and autosomal recessive traits.

As the ratio of the variants interpreted as pathogenic or likely pathogenic was significantly low in case of the X-linked recessive trait, we examined whether those difference can be compensated after additions of a new PS score (PSX) or PM score (PMX) as described above. By these modifications, the ratio of the variants interpreted as pathogenic or likely pathogenic changed (Supplemental Tables S4 & S5, *http://www.irdrjournal.com/action/getSupplementalData.php?ID=113*). However, the statistical analysis still revealed a significant difference between X-linked and others (Table 1).

These results are demonstrated as a bar graph for better understanding (Figure 1).

4. Discussion

The ACMG/AMP guidelines for interpretation of nucleotide variants were published in 2015 (*7*).

Table 1. Summary of the interpretation of the variants and the results of statiscial analyses

Items	Total number of the variants	Number of the variants interpreted as		Fisher's Exact Test *p* values		Chi-squared values Yates' correction	
		Pathogenic/ Likely pathogenic	Others	versus AD	versus AR	versus AD	versus AR
Autosomal dominant trait (AD)	158	143 (90.5%)	15 (9.5%)	NA	0.27	NA	1.2
Autosomal recessive trait (AR)	109	93 (85.3%)	16 (14.7%)	0.27	NA	1.2	NA
X-linked recessive trait (XLR)	105	42 (40.0%)	63 (60.0%)	$2.2 \times 10^{16*}$	$3.7 \times 10^{12*}$	74.7^{***}	45.2^{***}
X-linked recessive trait (plus PS score)	105	72 (68.6%)	33 (31.4%)	$1.4 \times 10^{5*}$	0.00534^{*}	18.9^{***}	7.6^{**}
X-linked recessive trait (plus PM score)	105	62 (59.0%)	43 (41.0%)	$2.6 \times 10^{9*}$	$1.7 \times 10^{5*}$	34.5^{***}	17.2^{***}

$^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$, NA, not applicable.

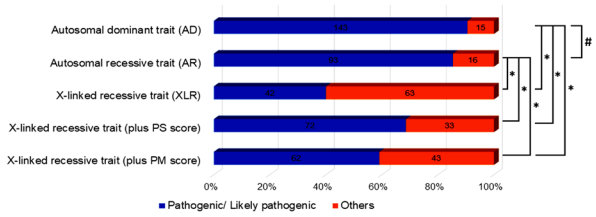

Figure 1. Distribution of the interpretation of the variants for each inheritance trait represented by a 100% stacked chart. The numbers in the boxes indicate the corresponding numbers of the variants. *, Statistically significant ($p < 0.05$); #, no significant difference.

These guidelines define the basic method for variant interpretation. The interpretations provided by these guidelines are crude, and the interpretation of each score is somewhat ambiguous. Establishment of an individual interpretation method corresponding to each disease or gene is, therefore, recommended (*5*).

The ACMG/AMP guidelines provide a framework for clinical variant classification (*7*). However, in the process of applying the ACMG/AMG guidelines to the classification of thousands of variants, many groups have identified several areas in which the guidelines lack specificity or are subject to ambiguous or contradictory interpretation (*43*). Najafi *et al.* analyzed the variants related to fibrillinopathies, and they noted that it is necessary to pay attention to the possibility that disease-related variants are included in population-based information (*4*). Furthermore, disease-specific guidelines have been published, specifically for MYH-associated inherited cardiomyopathy (*44*), RASopathy (*45*), hearing loss (*11*), and Alport syndrome (*46*). Nonetheless, best practice guidelines specific for X-linked recessive rare disorders have not yet been reported.

In this study, we evaluated variants reported before the publication of the ACMG/AMP guidelines. As a result, the interpretation ratio as pathogenic or likely pathogenic was significantly lower in variants related to the X-linked recessive trait. This indicates the existence of a bias between inheritance traits. Most of the variants related to the rare disorders in the autosomal dominant trait were occurred as the consequence of de novo. The de novo variants correspond to "PS2", indicating strong evidence of pathogenicity. Therefore, variants associated with autosomal dominant inheritance are more likely to be interpreted as pathogenic/likely pathogenic. For variants related to autosomal recessive inheritance, "PM3" can be assigned if another pathogenic variant was present in the trans-related allele. Therefore, many variants related to the autosomal recessive trait have been interpreted as either pathogenic or likely pathogenic.

In comparison, it is difficult to interpret variants related to the X-linked recessive trait as pathogenic or likely pathogenic because there are no specific scores for variants involved in the X-linked recessive inheritance. De Luca *et al.* suggested that assessing pathogenicity is more challenging in X-linked cases (*47*). For X-linked variants, segregation analysis has been recommended as a powerful tool to further confirm pathogenicity for early-onset and high-penetrance disorders. The identification of the variant in several affected male family members together with their healthy or mildly affected carrier mothers is in strong support for pathogenicity. Thus, we considered a specific score for variants that may be related to the X-linked recessive inheritance.

When variants associated with the X-linked recessive trait were identified only in male patients and the carrier females did not exhibit any related symptoms, we temporarily assigned a PS or a PM score, and the

ratio of interpretation as pathogenic/likely pathogenic increased. However, the significant difference was not eliminated (Figure 1). Considering the situation of each variant, some variants were inappropriately interpreted as pathogenic after the addition of a PS score, even for variants that should be interpreted as benign. Therefore, assignment of a PS score may be excessive, and assigning a PM score may be more appropriate.

In conclusion, we confirmed the bias of the ACMG/AMP guidelines regarding inheritance traits. Evaluation of variants related to the X-linked recessive trait should consider whether the variant was identified only in males in accordance with the X-linked recessive trait. The bias revealed in this study should be eliminated by future revision of the ACMG/AMP guidelines.

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References

1. Wu AC, McMahon P, Lu C. Ending the diagnostic odyssey-Is whole-genome sequencing the answer? JAMA Pediatr. 2020; 174:821-822.
2. Umlai UI, Bangarusamy DK, Estivill X, Jithesh PV. Genome sequencing data analysis for rare disease gene discovery. Brief Bioinform. 2022; 23:bbab363.
3. Takahashi Y, Date H, Oi H, Adachi T, Imanishi N, Kimura E, Takizawa H, Kosugi S, Matsumoto N, Kosaki K, Matsubara Y; IRUD Consortium, Mizusawa H. Six years' accomplishment of the Initiative on Rare and Undiagnosed Diseases: nationwide project in Japan to discover causes, mechanisms, and cures. J Hum Genet. 2022. doi: 10.1038/s10038-022-01025-0.
4. Najafi A, Caspar SM, Meienberg J, Rohrbach M, Steinmann B, Matyas G. Variant filtering, digenic variants, and other challenges in clinical sequencing: a lesson from fibrillinopathies. Clin Genet. 2020; 97:235-245.
5. Kim YE, Ki CS, Jang MA. Challenges and considerations in sequence variant interpretation for mendelian disorders. Ann Lab Med. 2019; 39:421-429.
6. Richards CS, Bale S, Bellissimo DB, Das S, Grody WW, Hegde MR, Lyon E, Ward BE; Molecular Subcommittee of the ACMG Laboratory Quality Assurance Committee. ACMG recommendations for standards for interpretation and reporting of sequence variations: Revisions 2007. Genet Med. 2008; 10:294-300.
7. Richards S, Aziz N, Bale S, Bick D, Das S, Gastier-Foster J, Grody WW, Hegde M, Lyon E, Spector E, Voelkerding K, Rehm HL; ACMG Laboratory Quality Assurance Committee. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015; 17:405-424.
8. Bahcall OG. Genetic testing. ACMG guides on the interpretation of sequence variants. Nat Rev Genet. 2015; 16:256-257.
9. Amendola LM, Muenzen K, Biesecker LG, *et al.* Variant classification concordance using the ACMG-AMP Variant Interpretation Guidelines across nine genomic implementation research studies. Am J Hum Genet. 2020; 107:932-941.
10. Strande NT, Brnich SE, Roman TS, Berg JS. Navigating the nuances of clinical sequence variant interpretation in Mendelian disease. Genet Med. 2018; 20:918-926.
11. Patel MJ, DiStefano MT, Oza AM, *et al.* Disease-specific ACMG/AMP guidelines improve sequence variant interpretation for hearing loss. Genet Med. 2021; 23:2208-2212.
12. Yamamoto T, Imaizumi T, Yamamoto-Shimojima K, *et al.* Genomic backgrounds of Japanese patients with undiagnosed neurodevelopmental disorders. Brain Dev. 2019; 41:776-782.
13. Li Q, Wang K. InterVar: Clinical Interpretation of Genetic Variants by the 2015 ACMG-AMP Guidelines. Am J Hum Genet. 2017; 100:267-280.
14. Chang X, Wang K. wANNOVAR: annotating genetic variants for personal genomes via the web. J Med Genet. 2012; 49:433-436.
15. Yang H, Wang K. Genomic variant annotation and prioritization with ANNOVAR and wANNOVAR. Nat Protoc. 2015; 10:1556-1566.
16. Alvarez-Dominguez JR, Amosova O, Fresco JR. Self-catalytic DNA depurination underlies human β-globin gene mutations at codon 6 that cause anemias and thalassemias. J Biol Chem. 2013; 288:11581-11589.
17. Bombelli F, Stojkovic T, Dubourg O, Echaniz-Laguna A, Tardieu S, Larcher K, Amati-Bonneau P, Latour P, Vignal O, Cazeneuve C, Brice A, Leguern E. Charcot-Marie-Tooth disease type 2A: from typical to rare phenotypic and genotypic features. JAMA Neurol. 2014; 71:1036-1042.
18. Di Gregorio E, Borroni B, Giorgio E, *et al.* ELOVL5 mutations cause spinocerebellar ataxia 38. Am J Hum Genet. 2014; 95:209-217.
19. Lalani SR, Safiullah AM, Fernbach SD, *et al.* Spectrum of CHD7 mutations in 110 individuals with CHARGE syndrome and genotype-phenotype correlation. Am J Hum Genet. 2006; 78:303-314.
20. O'Roak BJ, Vives L, Fu W, *et al.* Multiplex targeted sequencing identifies recurrently mutated genes in autism spectrum disorders. Science. 2012; 338:1619-1622.
21. Roberts ME, Riegert-Johnson DL, Thomas BC, Rumilla KM, Thomas CS, Heckman MG, Purcell JU, Hanson NB, Leppig KA, Lim J, Cappel MA. A clinical scoring system to identify patients with sebaceous neoplasms at risk for the Muir-Torre variant of Lynch syndrome. Genet Med. 2014; 16:711-716.
22. Türkmen S, Gillessen-Kaesbach G, Meinecke P, *et al.* Mutations in NSD1 are responsible for Sotos syndrome, but are not a frequent finding in other overgrowth phenotypes. Eur J Hum Genet. 2003; 11:858-865.
23. Cottenie E, Kochanski A, Jordanova A, *et al.* Truncating and missense mutations in IGHMBP2 cause Charcot-Marie Tooth disease type 2. Am J Hum Genet. 2014; 95:590-601.
24. Ehmke N, Caliebe A, Koenig R, *et al.* Homozygous and compound-heterozygous mutations in TGDS cause Catel-Manzke syndrome. Am J Hum Genet. 2014; 95:763-770.
25. Gersting SW, Kemter KF, Staudigl M, Messing DD, Danecka MK, Lagler FB, Sommerhoff CP, Roscher AA, Muntau AC. Loss of function in phenylketonuria is caused by impaired molecular motions and conformational instability. Am J Hum Genet. 2008; 83:5-17.

26. Hussain MS, Battaglia A, Szczepanski S, *et al.* Mutations in CKAP2L, the human homolog of the mouse Radmis gene, cause Filippi syndrome. Am J Hum Genet. 2014; 95:622-632.
27. Kopajtich R, Nicholls TJ, Rorbach J, *et al.* Mutations in GTPBP3 cause a mitochondrial translation defect associated with hypertrophic cardiomyopathy, lactic acidosis, and encephalopathy. Am J Hum Genet. 2014; 95:708-720.
28. Law R, Dixon-Salazar T, Jerber J, *et al.* Biallelic truncating mutations in FMN2, encoding the actin-regulatory protein Formin 2, cause nonsyndromic autosomal-recessive intellectual disability. Am J Hum Genet. 2014; 95:721-728.
29. Malik S, Percin FE, Bornholdt D, Albrecht B, Percesepe A, Koch MC, Landi A, Fritz B, Khan R, Mumtaz S, Akarsu NA, Grzeschik KH. Mutations affecting the BHLHA9 DNA-binding domain cause MSSD, mesoaxial synostotic syndactyly with phalangeal reduction, Malik-Percin type. Am J Hum Genet. 2014; 95:649-659.
30. Ohlenbusch A, Henneke M, Brockmann K, Goerg M, Hanefeld F, Kohlschütter A, Gärtner J. Identification of ten novel mutations in patients with eIF2B-related disorders. Hum Mutat. 2005; 25:411.
31. Sosnay PR, Siklosi KR, Van Goor F, *et al.* Defining the disease liability of variants in the cystic fibrosis transmembrane conductance regulator gene. Nat Genet. 2013; 45:1160-1167.
32. Thomas AC, Williams H, Setó-Salvia N, *et al.* Mutations in SNX14 cause a distinctive autosomal-recessive cerebellar ataxia and intellectual disability syndrome. Am J Hum Genet. 2014; 95:611-621.
33. Zhang K, Jordan MB, Marsh RA, Johnson JA, Kissell D, Meller J, Villanueva J, Risma KA, Wei Q, Klein PS, Filipovich AH. Hypomorphic mutations in PRF1, MUNC13-4, and STXBP2 are associated with adult-onset familial HLH. Blood. 2011; 118:5794-5798.
34. Hirata H, Nanda I, van Riesen A, *et al.* ZC4H2 mutations are associated with arthrogryposis multiplex congenita and intellectual disability through impairment of central and peripheral synaptic plasticity. Am J Hum Genet. 2013; 92:681-695.
35. Homan CC, Kumar R, Nguyen LS, Haan E, Raymond FL, Abidi F, Raynaud M, Schwartz CE, Wood SA, Gecz J, Jolly LA. Mutations in USP9X are associated with X-linked intellectual disability and disrupt neuronal cell migration and growth. Am J Hum Genet. 2014; 94:470-478.
36. Kato M, Das S, Petras K, *et al.* Mutations of ARX are associated with striking pleiotropy and consistent genotype-phenotype correlation. Hum Mutat. 2004; 23:147-159.
37. Martínez-Montero P, Muñoz-Calero M, Vallespín E, Campistol J, Martorell L, Ruiz-Falcó MJ, Santana A, Pons R, Dinopoulos A, Sierra C, Nevado J, Molano J. PLP1 gene analysis in 88 patients with leukodystrophy. Clin Genet. 2013; 84:566-571.
38. Piton A, Redin C, Mandel JL. XLID-causing mutations and associated genes challenged in light of data from large-scale human exome sequencing. Am J Hum Genet. 2013; 93:368-383.
39. Ramser J, Ahearn ME, Lenski C, Yariz KO, Hellebrand H, von Rhein M, Clark RD, Schmutzler RK, Lichtner P, Hoffman EP, Meindl A, Baumbach-Reardon L. Rare missense and synonymous variants in UBE1 are associated with X-linked infantile spinal muscular atrophy. Am J Hum Genet. 2008; 82:188-193.
40. Rosenberg EH, Almeida LS, Kleefstra T, deGrauw RS, Yntema HG, Bahi N, Moraine C, Ropers HH, Fryns JP, deGrauw TJ, Jakobs C, Salomons GS. High prevalence of SLC6A8 deficiency in X-linked mental retardation. Am J Hum Genet. 2004; 75:97-105.
41. Royer G, Hanein S, Raclin V, Gigarel N, Rozet JM, Munnich A, Steffann J, Dufier JL, Kaplan J, Bonnefont JP. NDP gene mutations in 14 French families with Norrie disease. Hum Mutat. 2003; 22:499.
42. Vulto-van Silfhout AT, de Vries BB, van Bon BW, *et al.* Mutations in MED12 cause X-linked Ohdo syndrome. Am J Hum Genet. 2013; 92:401-406.
43. Nykamp K, Anderson M, Powers M, Garcia J, Herrera B, Ho YY, Kobayashi Y, Patil N, Thusberg J, Westbrook M, Topper S. Sherloc: a comprehensive refinement of the ACMG-AMP variant classification criteria. Genet Med. 2017; 19:1105-1117.
44. Kelly MA, Caleshu C, Morales A, *et al.* Adaptation and validation of the ACMG/AMP variant classification framework for MYH7-associated inherited cardiomyopathies: recommendations by ClinGen's Inherited Cardiomyopathy Expert Panel. Genet Med. 2018; 20:351-359.
45. Gelb BD, Cavé H, Dillon MW, Gripp KW, Lee JA, Mason-Suares H, Rauen KA, Williams B, Zenker M, Vincent LM. ClinGen's RASopathy Expert Panel consensus methods for variant interpretation. Genet Med. 2018; 20:1334-1345.
46. Savige J, Storey H, Watson E, *et al.* Consensus statement on standards and guidelines for the molecular diagnostics of Alport syndrome: refining the ACMG criteria. Eur J Hum Genet. 2021; 29:1186-1197.
47. De Luca C, Race V, Keldermans L, Bauters M, Van Esch H. Challenges in molecular diagnosis of X-linked Intellectual disability. Br Med Bull. 2020; 133:36-48.

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