

An Algorithm for Predicting AMD

Researchers have developed a formula that calculates how likely individuals with certain genetic profiles and lifestyles are to develop geographic atrophy and neovascular AMD.

BY JENNIFER KREATSOULAS, PhD, NEWS & CONTRIBUTING EDITOR

Multiple genetic, ocular, and environmental factors contribute to the prevalence and incidence of advanced age-related macular degeneration (AMD), according to a study published in *Investigative Ophthalmology & Visual Science*. Johanna M. Seddon, MD, ScM, Professor of Ophthalmology at Tufts University School of Medicine and Director of the Ophthalmic Epidemiology and Genetics Service at Tufts Medical Center in Boston, and colleagues developed an algorithm to predict which individuals are most likely to progress from the early or intermediate stages of AMD to geographic atrophy or neovascular disease. The variables assessed included six genetic variants and age, sex, education, baseline AMD grade, smoking, body mass index (BMI), and nutritional supplement use.

KEY FINDINGS

Over 1,400 individuals in the Age-Related Eye Disease Study (AREDS) with an average follow-up time of 6.3 years were evaluated. Patients' genetic specimens were genotyped in Boston, and the algorithm incorporated six genetic variants as well as lifestyle risk factor data. Over the course of the prospective, multicenter study, 279 participants progressed to geographic atrophy or neovascular disease. For prevalent AMD, 509 advanced cases were compared with 222 controls.

Dr. Seddon and colleagues found all tested variables to be independently associated with AMD. "Based on our results, the predictive power of this composite of risk factors for progression to advanced AMD is 83%, which is quite high and comparable to risk functions for cardiovascular disease," Dr. Seddon said in an interview with *Retina Today*.

The strongest predictors of progression to advanced AMD included smoking, BMI, and baseline AMD grade. Current smoking is more predictive than past smoking, Dr. Seddon stated. "Smoking increased the risk of AMD for

all genotypes. Among individuals who were homozygous for the C3 risk allele, the likelihood of progression to the advanced form of AMD increased from about threefold for nonsmokers to nearly tenfold for smokers, which suggests that healthy behaviors can affect one's genetic susceptibility," she said. Additionally, an antioxidant/zinc combination supplement reduced risk. Some gene variants were protective, whereas others carried a risk, Dr. Seddon explained.

FUTURE IMPACT

Dr. Seddon said she believes that it is only a matter of time before the AMD model is more frequently used and accepted in a variety of medical and clinical settings. "There is great potential for this algorithm to be used for prediction and personalized medicine. Our algorithm could one day enable doctors to choose the most efficacious treatment for individual patients," Dr. Seddon said. "Rather than put millions of patients on a drug, we could determine which percentage of patients would truly benefit."

The algorithm could also help companies and individual investigators with the selection of study participants for treatment trials. Because researchers would know which individuals would be at higher risk of progression and at what rate, they would be able to more effectively monitor and track the effectiveness of a drug or combination therapy. This would reduce the number of participants needed in a trial and ultimately lower costs.

On the patient level, however, Dr. Seddon hopes that the algorithm can serve as a source of motivation to practice a healthier lifestyle. "If a patient learns that he or she is at higher risk for advanced AMD due to behaviors, lifestyle, and genotypes, hopefully that individual will begin to adhere to healthier habits, avoid risk factors such as smoking and excessive weight, and have an even stronger reason to do so," she said. ■