New method identifies which asthma patients respond to systemic corticosteroids

February 20 2019

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Physicians will be able to predict which of their patients with severe asthma are likely to benefit from treatment with systemic corticosteroids—and which might only suffer their side effects—with

help from a dozen clinical variables researchers have identified using machine learning techniques.

Physicians already have some clues about which patients are most helped by corticosteroid injections or pills. But the newly identified set of variables—when processed by computer software—will yield more precise predictions of a patient's response, said Wei Wu, a faculty member in Carnegie Mellon University's Computational Biology Department.

"Systemic corticosteroids are the most effective therapy we have for asthma, but not all patients respond in the same way," Wu said. "Unfortunately, when clinicians don't see a big improvement after initial treatment, they might give patients even higher doses. If a patient is one of those who can't be helped by corticosteroids, the higher dose just means worse side effects."

The study, led by Wu and Dr. Sally E. Wenzel, director of the University of Pittsburgh Asthma Institute at UPMC, was recently published online by the *American Journal of Respiratory and Critical Care Medicine*.

Asthma affects about one in every 12 Americans and the rate continues to rise. The lifelong disease causes wheezing, breathlessness, chest tightness and coughing. Predicting how people will respond to corticosteroid therapy could significantly reduce the suffering of many patients, Wenzel said.

"I see so many patients in my clinic who have been ravaged by the side effects of corticosteroids," said Wenzel, also chair of the Department of Environmental and Occupational Health at Pitt's Graduate School of Public Health. Weight gain, extreme emotions, inability to sleep, glaucoma and thinning of the skin are among the possible side effects of corticosteroid pills and injections, so physicians would like to prescribe

them only to patients they know will benefit from them, she added.

She emphasized that the study addresses corticosteroid pills and injections, not the widely used corticosteroid inhalers, although there is likely to be some overlap in patient response to the medications in either form.

To better understand how different subgroups of patients respond to systemic corticosteroid therapy, the researchers used a machine learning algorithm to sift through 100 variables for each of 346 adult patients in the federally funded Severe Asthma Research Program (SARP).

The algorithm, developed by Wu and Seojin Bang, a Ph.D. student in CMU's Computational Biology Department, recognizes patterns in massive volumes of complex clinical data. It clustered patients into four subgroups, including two for severe asthmatics—one that responded to systemic corticosteroids and one that didn't.

Of the original 100 variables, they identified 12—including age of onset, weight, race and scores on a quality-of-life questionnaire—that could correctly categorize patients with high confidence if processed by a computer app. To test this process, they used the 12 variables (or their equivalents) to categorize a group of 182 SARP participants not included in the original analysis. The variables proved effective in successfully categorizing these additional patients.

The benefits of systemic corticosteroids can be substantial, so physicians likely will continue to try them initially in the treatment of severe asthma , Wenzel said. But once software becomes available for practitioners to predict patient response, she said they will likely switch to alternative therapies, rather than increase corticosteroid dosages, if patients haven't responded and fall into the subgroup of patients that don't usually benefit from the drugs.

"We believe we've made progress toward making precision medicine a reality," Wei said. "Five years ago, we were only able to categorize patients clinically. Now, using incredibly complex data, we're able to predict how these subgroups will respond to a critical drug treatment."

More information: Wei Wu et al, Multiview Cluster Analysis Identifies Variable Corticosteroid Response Phenotypes in Severe Asthma, *American Journal of Respiratory and Critical Care Medicine* (2019). DOI: 10.1164/rccm.201808-1543OC

Provided by Carnegie Mellon University