New approach to assessing rejection in heart transplant patients far more effective

Patients may benefit by receiving less anti-rejection medication

ORLANDO, Fla. April 5, 2019 --- A new method of assessing organ rejection in heart transplant patients is more effective at estimating the probability of rejection than current practices, a finding that may improve the precision of the diagnosis and reduce over treating patients with post-transplant medications. The research was presented by Luciano Potena, MD, PhD, Bologna University Hospital, Italy, at the International Society for Heart and Lung Transplantation’s 39th annual meeting in Orlando, Fla.

Physicians routinely biopsy heart transplant patients to monitor for rejection, which in current practice is diagnosed by histology-based grading. The grading consists of descriptive categories that rely on the pathologist’s interpretation, requiring them to describe the degree of tissue damage and infiltration by inflammatory cells. The new method, based on Gene Expression Profiling (GEP) techniques, foregoes descriptive histology and, instead, allows for analysis of genes that are active in the tissue. The analysis of GEP is based on patented technology called MMDx, Molecular Microscope Diagnostic System, which was initially developed for kidney transplantation, and is now being validated in heart, lung, and liver transplantation. MMDx algorithms have been developed based on graft function and outcomes by using machine learning and reveals how cells are functioning, not how they look.

“Try to ask four poets to describe the same landscape. You’ll obtain four different descriptions of the truth, which may be artistically intriguing, but would be difficult to interpret if you need to make technical decisions based on those descriptions,” said Potena. “This new research will help us provide a more accurate diagnosis of rejection.”

Shortcomings in current system

The current ISHLT grading system, adopted in 2006, provides categories of rejection severity, both for cellular and antibody-mediated rejection. It describes the degree of tissue damage and
infiltration by inflammatory cells and relies on the concept that the larger the infiltrate, the worse the rejection. The purpose of the grading is to guide clinicians in treating rejection before symptoms onset. However, histology reading, like any diagnostic technique, is subjected to false positives and false negatives.

This study showed that about 30 percent of the biopsies showing morphologically significant rejection had a quiescent GEP, suggesting that the rejection process was not actually occurring.

“These biopsies might be ‘false positives’ of histology that are now unnecessarily treated with immunosuppression bursts,” said Potena.

In addition, the study found that about half of the biopsies graded as “mild” rejection, and thus not requiring treatment according to current ISHLT classification, did show significant molecular activity, potentially needing treatment.

Moreover, Potena said, the current grading system does not account for the coexistence of cellular- and antibody-mediated rejection features, considering them as separate entities. The study found that most of the “mild” cellular rejections showed an antibody-mediated rejection molecular profile.

“We should remember that infections and other downsides of immunosuppressive therapy are more threatening and frequent than rejection per se,” said Potena. “Improving the precision of the diagnostic information we can gain from tissue samples can direct more appropriate treatments, and ultimately improved outcomes.”

The work is part of a global, multi-center, multi-organ collaborative consortium, the INTERHEART, led by the University of Alberta, Edmonton, AB, Canada. Potena’s site in Bologna, Italy, worked from the largest set of heart biopsies.

“The goal is to begin to better understand the processes that are beyond rejection and to customize the treatment,” said Potena. “With the current system, all patients are treated the same. But we are learning that the molecules that correspond with each grade may, actually, vary a lot from patient to patient.”

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**About ISHLT**
The International Society for Heart and Lung Transplantation is a not-for-profit, multidisciplinary professional organization dedicated to improving the care of patients with advanced heart or lung disease through transplantation, mechanical support and innovative therapies. With more than 3,800 members in more than 45 countries, ISHLT is the world’s largest organization dedicated to the research, education and advocacy of end-
stage heart and lung disease. ISHLT members represent more than 15 different professional disciplines. For more information, visit www.ishlt.org.