

Exceeding Expectations

CPRA policy leads to gains in placement efficiency, transplants of highly sensitized candidates

In October 2009, an OPTN/UNOS policy was implemented that has significantly changed kidney and pancreas allocation for candidates with immune sensitivity to potential donor antigens.

Until then, candidates' overall immune sensitivity was measured by lab tests that generated a panel reactive antibody (PRA) score. The tests were run against panels of cells or, more recently, against panels of purified HLA antigens. There was a great deal of variation in PRA values, depending on the type of assay and the panels used.

To address those problems, the OPTN/UNOS histocompatibility committee proposed a new method for a consistent definition of antibody sensitization to HLA antigens, the major transplantation antigens. The method, the calculated panel reactive antibody (CPRA), is not determined directly from the lab tests used to define antibodies against HLA antigens.

It is, instead, a calculation of how many potential donors would be considered incompatible for a given candidate based on that patient's known HLA specific antibodies.

If a candidate has antibodies to one or more HLA antigens, he or she is more likely to reject an organ from a donor who has those antigens. If the risk with the antibodies is judged to be high, those antigens can be listed as "unacceptable."

The CPRA is then based on how many unacceptable antigens are listed and their corresponding frequency among donors.

The CPRA policy also requires that antibody testing has to be performed using one of the newer, more sensitive assays. That requirement increases both the accuracy and consistency of antibody testing among transplant centers.

The goals of the CPRA policy were to provide a more consistent and accurate definition of sensitization and to improve

the efficiency of organ allocation by reducing the number of positive crossmatches (a confirmatory blood test that indicates the candidate would encounter immune system rejection if he or she received the organ being offered).

ADDITIONAL BENEFITS

Based on postimplementation data analyzed by the histocompatibility committee, the policy has been effective—and has yielded additional benefits.

Committee chair Nancy Reinsmoen, Ph.D., presented data at the November OPTN/UNOS board of directors meeting showing the difference in organ refusals based on positive crossmatches for deceased donor kidney offers for six-month periods before and after implementation of the CPRA policy. After implementation, the number of such refusals declined by more than 80 percent (see graph below).

"That decline also represents a huge cost savings," she noted. Fewer serum tests

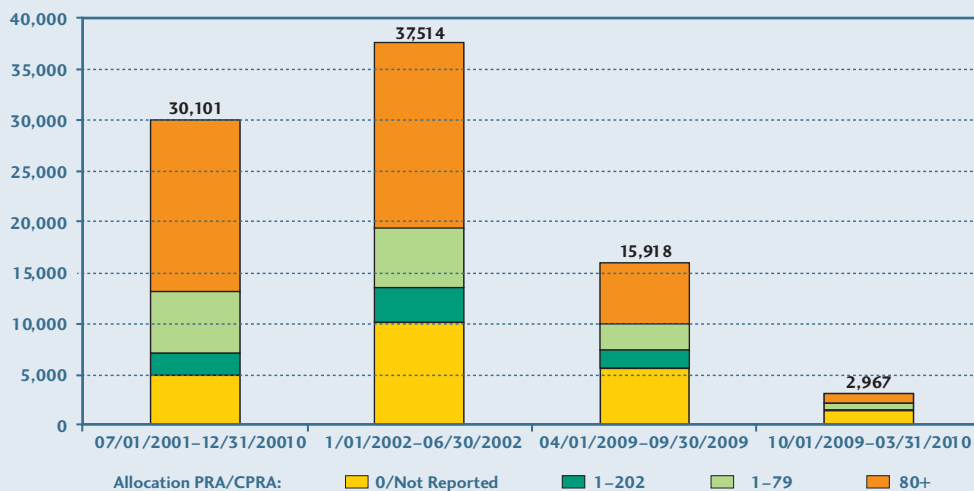
can be performed, and duplicate samples are required to be banked less often.

Since Dr. Reinsmoen's presentation, additional data have revealed that the transplant rate for highly sensitized kidney transplant candidates (those with a CPRA of 80 percent or higher) has increased significantly. That result is particularly gratifying to M. Sue Leffell, Ph.D., who chaired the histocompatibility committee when the CPRA initiative began.

"We expected a reduction in the refusals due to positive crossmatches," she said. "That we have seen both a dramatic decrease in the number of positive crossmatches and a significant increase in the number of highly sensitized recipients being transplanted is very rewarding."

Under the policy, each transplant program may define the criteria for listing unacceptable antigens it considers as contraindications for transplantation. Transplant teams may opt to enter all the specific antigens that could possibly

Positive Crossmatches Reported as a Reason for Deceased-Donor Organ Refusals



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Far-left column shows refusals before introduction in 2002 of solid-phase antibody assays. Three columns to the right show refusals after use of solid-phase antibody assays; after the requirement to enter at least one unacceptable antigen for a candidate to receive four points; and, on far-right column, after full implementation of CPRA.

cause a positive crossmatch or fewer values. Dr. Reinsmoen noted that the benefit of allowing teams the option is that they can apply their own medical judgment.

“Centers can look at their own data and know what their goals are for their candidate and can enter unacceptable antigens accordingly,” she said.

STUDYING FURTHER REFINEMENTS

While the policy has performed well, the committee continues to study refinements to address questions and concerns.

One key issue is whether more moderately sensitized patients (those with CPRA scores from 50 to 80) could benefit from additional allocation points, rather than having only four extra points reserved for those with scores of 80 or higher. The committee is studying possible approaches, such as establishing a ratio or sliding scale of sensitization points, so that moderately sensitized candidates might receive some proportionate level of priority.

Another issue that will continue to affect histocompatibility is the increasingly standardized usage of molecular typing.

“As HLA typing improves, the accuracy of our calculations also will improve,” Dr. Leffell said. “We anticipate ongoing review and will add to the calculations additional HLA loci or possibly other alleles as they are better defined.”

Dr. Leffell views the success of the CPRA policy as a “culmination of the years of development that has gone into histocompatibility testing. Labs are no longer viewed as obstacles to the matching process; instead,” she said, “we’re now facilitating transplantation in an important manner.”

Dr. Reinsmoen agrees and also notes that the ultimate benefit is new opportunities and benefits to highly sensitized candidates.

“The more accurate interpretation of immune sensitivity has greatly increased the efficiency of matching,” she said, “and it positively impacts their chance of getting a donor organ.” [U](#)



UNOS e-Newsletter Turns 1

A timely, efficient way to access key information

In the not-too-distant past, OPTN/UNOS members would receive multiple e-mails from UNOS, sometimes several in one day, to inform them of policy changes, upcoming events and miscellaneous transplant-related information.

But last January members began receiving one consolidated e-mail a month from UNOS. The new e-newsletter format presents standing categories (policy, patient safety, etc.), under which headlines and concise plain-language descriptions appear. Clicking on a headline links the user to the complete article, which is permanently housed at UNOS’ communications archive, <http://communication.unos.org>.

The e-newsletter is distributed once a month, but members can visit the archive anytime. Bookmarking the site and adding it to your “favorites” list provides instant access to policy notices distributed after board meetings, online registration links to training and conferences, updates to the OPTN Evaluation Plan, newsletters for patient safety and disease transmission, and much more.

It’s also easy to subscribe to an RSS feed, which alerts subscribers every time an article is added to the archive.

Popularity of the archive is growing. In its inaugural year 8,116 individuals visited the archive 17,388 times to view pages a total of 43,736 times. Visitors also read an average of 2.5 articles.

To receive the e-newsletter, send an e-mail to unoscommunication@unos.org. [U](#)



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