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Researchers develop more accurate tool to predict whether liver cancer will recur in transplant patients

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UCLA transplant researchers have developed a novel method to more accurately calculate the risk of disease recurring in people with liver cancer who have undergone a liver transplant. The approach gives physicians a new tool to help make treatment and surveillance decisions.

The study, led by Dr. Ronald Busuttil, the William P. Longmire, Jr. Chair in Surgery and director of the Pfleger Liver Institute and Dumont–UCLA Transplant and Liver Cancer Centers, was published by the peer-reviewed *Journal of the American College of Surgeons*.

The research team developed a predictive calculator called a nomogram after analyzing 30 years' worth of data from liver transplants for people with liver cancer. The study drew from records of 865 patients at UCLA between 1984 and 2013, said Dr. Vatche Agopian, an assistant professor of surgery in UCLA's division of liver transplantation and the study's first author.

Prior to 1996, there were no criteria to guide which liver cancer patients might be good candidates for transplants. Patients with tumors of all sizes and numbers underwent transplants, and many of them suffered early recurrence of the disease. In 1996, guidelines known as the "Milan criteria" were introduced, recommending that transplants be limited to patients who had a single tumor measuring 5 centimeters or less and those who had up to three tumors, as long as no single tumor was larger

than 3 centimeters.

Agopian said one shortcoming of the Milan criteria was that they didn't take into account the aggressiveness of the tumor or other blood biomarkers that can help predict recurrence. UCLA's nomogram uses three groups of factors to predict recurrence more accurately than the Milan criteria and the existing American Joint Committee on Cancer pathologic TNM staging system, giving transplant physicians and oncologists more information to help decide how often to monitor patients for recurrence and whether or not adjuvant treatment is necessary.

"This novel nomogram includes three important groups of information that proved to be very accurate in predicting recurrence in liver cancer patients—better than any other system out there," Agopian said. "Physicians can use our nomogram and have a meaningful discussion with transplant recipients regarding their post-transplant risk of cancer recurrence. It can help them decide how closely to follow their patient—a patient with a low risk of recurrence may not need screening as often—or whether a patient with a high risk of recurrence might need treatment following the transplant."

The three groups of factors that comprise the UCLA nomogram are:

- Pre-transplant radiologic information, or the number and size of tumors on MRI and CT scans
- Three pre-transplant blood biomarkers thought to be predictive for cancer recurrence
- Pathological characteristics of the explanted liver. (The diseased liver is studied to determine the aggressiveness of the tumor and whether the cancer has invaded the liver's blood vessels, factors that can't be determined before transplant.)

Under the Milan criteria, for example, a patient with a 5 centimeter tumor might have qualified for a liver transplant, but the UCLA-developed criteria might discover that the tumor was very aggressive and likely to recur after transplant. The nomogram also might find that a patient with a larger tumor might have a very low grade cancer and have a lower risk for recurrence. Using specific details about each patient provides an individualized profile of predicted risks for cancer recurrence, Agopian said.

"The Milan criteria presented a major step in improving the outcomes of liver cancer patients undergoing transplant," Agopian said. "However, there is now a growing consensus and body of evidence that these criteria are too conservative, and that incorporation of other factors may improve the ability to select for patients with favorable tumor biology, regardless of size, who stand to benefit from liver transplantation."

About 32,000 Americans will be diagnosed with liver cancer this year. Of those, 23,000 will die of their disease. Liver cancer is the sixth most common cause of cancer worldwide, and the third most common cause of cancer-related death. In the U.S., the incidence of liver cancer has nearly doubled over the past two decades. For most patients who are diagnosed with liver cancer, the disease generally is too advanced to treat with surgery. For patients with underlying liver dysfunction who are unable to undergo surgery to remove the tumor, a liver transplant is the best way to treat the patient.

"In the largest single-institution experience with liver transplant for liver cancer, excellent long-term survival was achieved," the study reports. "Incorporation of routine pre-transplant biomarkers to existing radiographic size criteria significantly improves the ability to predict post-transplant recurrence, and should be considered in recipient selection. A novel clinicopathologic prognostic nomogram accurately predicts liver cancer recurrence after liver transplant and may guide

frequency of post-transplant surveillance and adjuvant therapy."

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