

Smoking in combination with immunosuppression poses greater risk for transplant-related carcinoma

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Spanish researchers have found that liver transplant recipients who quit smoking have a lower incidence of smoking-related malignancies (SRM) than patients who keep smoking. In fact, SRMs were identified in 13.5% of deceased patients and smoking was associated with a higher risk of malignancy in this study. Full findings are published in the April issue of *Liver Transplantation*, a journal of the American Association for the Study of Liver Diseases.

While smoking is a well-known malignancy risk factor both in the general population and in liver transplant recipients, smoking in combination with immunosuppression is presumed to be the main risk factor for transplant-related carcinomas. Several authors have suggested that a longer duration of immunosuppressive treatment or a stronger immunosuppression could be related to a higher risk of malignancy. However, the Spanish researchers failed to find such an association. Rather, they suggest that smoking after transplant which increases the risk, and smoking cessation following transplant surgery which decreases the risk, are more significant indicators.

"Smoking is related to some of the most frequent causes of posttransplant malignancy," says study leader Dr. J. Ignacio Herrero of the Clínica Universidad de Navarra in Pamplona, Spain. "We investigated whether the risks of developing malignancies was different in patients who ceased smoking than in patients who maintained smoking after



transplantation." Risk factors of lung, head and neck, esophagus, kidney and urinary tract (other than prostate) cancers after liver transplantation were examined in the present study.

The research team introduced a screening protocol, according to the risk of neoplasia, related to smoking for every patient in the study. The patient population consisted of 339 liver transplant recipients receiving their first liver transplantation between April of 1990 and December of 2009 who had a post-transplant survival greater than three months. Participants received cyclosporine- or tacrolimus-based immunosuppression. Risk factors for the development of smoking-related neoplasia were also studied in 135 patients who had a history of smoking, in order to explore if smoking withdrawal was associated with a lower risk of malignancy.

SRM risk factors examined were age, sex, alcohol abuse before liver transplantation, hepatitis C virus infection, hepatocellular carcinoma at transplantation, primary immunosuppression (cyclosporine or tacrolimus), history of rejection requiring high doses of steroids or antilymphocytic globulins in the first 3 months, number of immunosuppressive drugs at 3 months, and smoking history. A second analysis of risk factors for the development of SRM was performed only in smokers, focusing on active versus prior smoking history.

After a mean follow-up of 7.5 years, 26 patients were diagnosed with 29 smoking-related malignancies. Five and ten-year actuarial rates were 5% and 13%, respectively. In multivariate analysis, smoking and a higher age were independently associated to a higher risk of malignancy. In the subgroup of smokers, the variables related to a higher risk of malignancy were active smoking and a higher age.

"Smoking withdrawal after <u>liver transplantation</u> may have a protective effect against the development of neoplasia," concluded Dr. Herrero.



"As smoking is an important risk factor of <u>malignancy</u>, intervention programs, together with screening programs may help to reduce the rate of cancer-related mortality in liver transplant recipients."

More information: "Risk Factors of Lung, Head and Neck, Esophagus Kidney, and Urinary Tract Carcinomas after Liver Transplantation. The Effect of Smoking Withdrawal." J. Ignacio Herrero, Fernando Pardo, Delia D'Avola, Félix Alegre, Fernando Rotellar, Mercedes Iñarrairaegui, Pablo Martí, Bruno Sangro, Jorge Quiroga. Liver Transplantation; Published Online: March 28, 2011 (DOI:10.1002/lt.22247) Print Issue Date: April 2011.

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