

# Tobacco smoke exposure before heart transplantation may increase the risk of transplant failure

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A study conducted at the University of Maryland School of Medicine in Baltimore provides the first direct evidence that cigarette smoke exposure prior to a heart transplant in either the donor, recipient, or both, accelerates the death of a transplanted heart. The study, published this month in the journal *Circulation*, showed that tobacco smoke leads to accelerated immune system rejection of the transplanted heart, heightened vascular inflammation and increased oxidative stress, and a reduction in the transplanted organ's chance of survival by 33-57 percent.

The study, conducted in rats, involved exposure to levels of tobacco equivalent to that of a habitual, light-to-moderate-range smoker and included comparisons between smoking and non-smoking donors and recipients.

"Our research shows that if a heart donor has been a habitual smoker, and you put that heart in a non-smoking recipient, that heart won't work; it will be rejected," says the study's senior author, Mandeep R. Mehra, M.B.B.S., professor of medicine, head of the Division of Cardiology at the University of Maryland School of Medicine and chief of cardiology at the University of Maryland Medical Center. "This study shows beyond a shadow of a doubt how smoking affects transplantation."

This is the first study to look at the impact of smoking in heart donors,

according to the principal investigator, Ashwani K. Khanna, Ph.D., associate professor of medicine at the University of Maryland School of Medicine. "There are already many risk factors that physicians and surgeons must consider when they try to match a donor with a recipient. This study makes clear that smoking in both the donor and the recipient should also become a part of the risk calculus in organ donation," says Dr. Khanna.

Studies from the mid-1990s have shown a connection between cigarette smoking and cardiovascular diseases. More recent studies have found a connection between smoking and the outcome of heart and other organ transplantation in recipients who resumed smoking after their transplants.

"The effects of smoking on heart health are well known and no surprise," says E. Albert Reece, M.D., Ph.D., M.B.A., vice president for medical affairs at the University of Maryland and dean of the University of Maryland School of Medicine. "The surprise in this study is the extent of the deleterious effects of smoking on the transplanted heart. Our researchers have discovered a significant connection that may lead to new ways to help patients with heart transplants live longer," he says.

## **Study design and results**

In this study, groups of donor and recipient rats were exposed to [tobacco smoke](#) while a control group of donors and recipients did not undergo any tobacco smoke exposure. Drugs are routinely used to prevent the body's immune system from attacking a transplanted organ. To better isolate the effect of [smoking](#) exposure from such factors as immunosuppression, the recipient rats in this study were not given medications to suppress their immune systems.

Transplanted hearts not exposed to tobacco were rejected an average of

eight days after transplantation. Donor hearts exposed to [cigarette smoke](#) were rejected at five days, while recipient smoke exposure elicited rejection at four days. Hearts in which both the donor and recipient were exposed to tobacco smoke lasted just three days before the immune response began destroying the transplant.

The researchers underscore that reduced survival occurred regardless of whether the [heart](#) donor or recipient smoked. "This accelerated trajectory of organ loss is similar whether tobacco smoke exposure occurred in donors, recipients, or both before cardiac transplantation," says Dr. Mehra. Further, this reduced survival occurs in the midst of a cascade of processes that add up to a poor outcome: increased inflammation, immune system activation and the resulting destruction of the heart's muscular and vascular systems.

The researchers speculate that this cascade could be interrupted at the time of transplantation with focused drug intervention in the anti-inflammatory and antioxidant pathways. They suggest that an antioxidant such as n-acetyl cysteine or widely prescribed statins (anti-inflammatory drugs) could prove useful in inhibiting these adverse responses. Dr. Khanna says a study of these interventions is being planned.

Source: University of Maryland Medical Center

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