Good stress response enhances recovery from surgery, study shows

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The right kind of stress response in the operating room could lead to quicker recovery for patients after knee surgery, according to a new study led by Stanford University School of Medicine researchers. The results could be used to develop methods for predicting how well patients will fare after they leave the hospital.

The study, conducted with colleagues at Yale University and to be published Dec. 1 in the Journal of Bone and Joint Surgery, found that patients whose immune systems responded to the stress of surgery by mobilizing large numbers of pathogen-fighting cells and redistributing them to skin and other tissues recovered more quickly and completely than those patients whose immune system showed little or no reaction. The researchers also found that men were more likely than women to mount the beneficial stress response and recover more fully.

The results suggest that simple, inexpensive blood tests performed while patients are on the operating table could predict how well patients will have recovered months after they leave the hospital. Eventually, doctors might also be able to develop medical interventions to improve that recovery.

"One of the beauties of the tests is that it's so easy," said Esther Sternberg, MD, chief of the section on neuroendocrine immunology and behavior at the National Institute of Mental Health, who was not involved in the research. "The information is completely available to any physician pre- and post-surgery."

Old models of stress and the immune system predicted that stressful situations would suppress immune activity. But Firdaus Dhabhar, PhD, Stanford associate professor of psychiatry and behavioral sciences and senior author of the paper, said those models didn't differentiate between unhealthy chronic stress, which can negatively affect the immune system, and healthier short-term stress. Short-term stress, Dhabhar said, launches the "fight-or flight" response, which he described as "one of nature's fundamental protective survival mechanisms."

"In an evolutionary sense, why would a gazelle's immune system be suppressed when a lion is chasing it? This is a time when the gazelle would need a robust immune response to protect it from wounding or infection," said Dhabhar, who is also a member of the Stanford Institute for Immunity, Transplantation and Infection. "In nature, wounds and infections often occur during stressful situations, or cause stress soon after they occur. Therefore, we reasoned that the short-term stress response would prepare organisms for immune challenges, just as it prepares them for fight-or-flight."

In previous studies, Dhabhar found that when mice are put in stressful circumstances for just minutes to hours, their immune cells flood out of the spleen and bone marrow and into the bloodstream, causing a noticeable increase in their numbers within five to 10 minutes. Over the next few hours, the number of immune cells in the bloodstream decreases as the cells enter skin and other tissues, where they guard against infectious intruders. Instead of suppressing immunity, short-term stress acts like a "call to arms," Dhabhar said, sending immune cells to at-risk tissues and preparing the body to defend itself.

But could that mustering of the troops be clinically beneficial in humans? To find out, Dhabhar picked a stressful situation that would require physical healing and recovery afterward: knee surgery.

Dhabhar and his colleagues recruited 57 patients who were scheduled for surgery to repair damaged cartilage in their knee joints. To ensure that the surgical procedure would be as consistent as possible, all of the surgeries were performed by Peter Jokl, MD, professor and vice chair of orthopedics and rehabilitation at Yale University.

Three to 10 days before the surgery, patients gave blood samples to establish a baseline count of immune cells in their blood. Then, on the morning of surgery, the researchers took another blood sample just before administration of anesthesia, looking for an increase in immune cells in the bloodstream. The idea, Dhabhar said, was that patients would be somewhat anxious about the impending surgery, triggering the short-term immune response. About a half-hour after surgery, the patients gave a final sample while in the recovery room. At that point, the researchers reasoned, many blood-borne immune cells should have exited the circulation and entered tissues, including the site of surgery.

Using the data, the team calculated total "redistribution" numbers for three major types of immune cells — lymphocytes, monocytes and neutrophils. These numbers quantified the initial increase and subsequent decline in immune cells in the blood. The researchers then determined the median redistribution number for the group. Those with redistribution numbers higher than the median were categorized as "high responders." Those whose immune-cell redistribution numbers were smaller than the median or unchanged were grouped as "low responders." Researchers then followed up with patients for one year, checking knee inflammation and using the Lysholm scale, a well-respected questionnaire, to rank knee function, pain and mobility on a scale of 1 to 100, with scores above 90 representing maximal recovery.

Patients who showed the positive stress response during surgery showed increased recovery as early as one week post-surgery compared to low responders, an effect that carried all the way through the study period.

One year later, high immune responders had average Lysholm scores of more than 90. Low responders had scores around 80 and never recovered as fully as their stress-adaptive counterparts.

The researchers also uncovered a gender disparity: Women were less likely to show an adaptive response than men. On average, their lymphocyte redistribution numbers were nearly four times lower than that of their male counterparts. They also achieved lower overall knee recovery than men. However, when women did show adaptive immune cell redistribution, their recovery matched that of men with the same adaptive response.

"It was slightly surprising to see how much in tandem the immune cell redistribution appeared to be with the overall gender recovery difference," said Dhabhar. However, he said, the fact that patients' immune cells showed varying degrees of redistribution during a stressful situation is evidence that the link between stress and the immune system is complex and requires more investigation.

The next step, Dhabhar said, is to investigate the biological links between the stress-induced immune activation and recovery, and to test the immune measurements in other types of surgery. Researchers can't yet be sure how many people exhibit strong stress-induced immune cell activation and how many don't. But once the mechanisms of response are better understood, doctors could monitor immune cell movements during and after surgery to predict patients' recovery — and design treatments to bring low responders up to speed.

Source: Stanford University Medical Center (news : web)