Review suggests many men with early prostate cancer may not need lymph node removal

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For years, the treatment of early-stage prostate cancers that haven't spread beyond the organ has often included the removal of nearby lymph nodes in the pelvis. It's done as a precaution and as a means of "staging"
Now, a major expert review on the topic suggests that, in many cases, men in this situation may be better off keeping their lymph nodes. Doing so may help them avoid harmful side effects, such as disabling lymphedema.

But even more importantly, leaving the pelvic nodes intact might also boost the success of newer immune-based cancer drugs, the experts suspect.

The bottom line: "It is perhaps time to rethink whether lymph nodes are truly foes or friends in the oncologic management of prostate cancer," said senior study author Dr. Ash Tewari, chair of urology at Icahn Mount Sinai in New York City.

He and the review's co-authors believe that a closer look at the issue is overdue.

"An in-depth assessment of indiscriminate lymph node removal during surgery, which has not been definitively shown to have therapeutic benefits, is prudent," he said. "Our paper opens the door to potentially new strategies in the treatment of prostate cancer, focusing on harnessing the power of the immune system rather than removing lymph nodes indiscriminately."

Their review was published recently in the journal Nature Reviews Urology.

As Tewari's team explained, early-stage localized prostate cancers are often treated with surgical removal of the prostate, as well as an average of six of the nearby lymph nodes.
One study found that, between 2004 and 2013, surgeons removed pelvic lymph nodes in 63.5% of such cases.

Of course, doctors are often concerned that even a localized prostate cancer has spread to lymph nodes, where it can become systemic. So lymph node removal is often used to help determine what stage of prostate cancer a man has.

However, according to one major study, only a small minority of these excised lymph nodes—just 3.7%—ended up containing any cancerous cells.

Removal of lymph nodes for early-stage tumors also has dubious value as a treatment, Tewari's group said.

In studies where patients either did or did not have their nodes removed (along with their prostates), "no statistically significant differences" in terms of tumor recurrence, tumor spread or overall survival were found, the experts noted.

Then there's the potential help that intact lymph nodes might provide to men treated with newer, immune-focused cancer therapies called immune checkpoint inhibitors.

According to the National Cancer Institute, these cutting-edge drugs work by disabling a mechanism that cancer cells rely on to evade the immune system. When that mechanism is set to "off" mode, the patient's immune system T-cells are able to spot and destroy malignant cells.

Immune checkpoint inhibitors include Keytruda, Opdivo, Yervoy and Tecentriq.

As Tewari and his colleagues explained, there's a growing body of
evidence that pelvic lymph nodes near the prostate tumor (so-called "tumor-draining lymph nodes") contain cells that help immune checkpoint inhibitors do their work.

"Identifying the importance of tumor-draining lymph nodes [TDLN] and other lymph nodes in the anti-cancer immune response has gained increased attention," the review authors noted.

In one study in mice injected with colon cancer cells, "activation of adaptive immune cells" occurred within TDLN soon after the animals received an immune-focused anti-cancer drug, the experts said.

And in the same mouse study, rodents who had their TDLN removed before they received an immunotherapy drug had a "substantially diminished therapeutic effect" measured by tumor size, compared to mice whose nodes had been left intact.

Of course, studies in animals don't always pan out in people, which is why Tewari and his colleagues are urging further studies in humans.

"Longitudinal studies to assess the long-term effects of partial lymph node dissection [removal] on anti-tumor autoimmunity in patients are necessary," they contend.

From early studies, however, "it seems that lymph nodes have a vital role in the mobilization" of immune cells that have been targeted to fight tumors, the team said.

In any case, "Whether lymph nodes are truly 'foes' or whether they are actually 'friends' in oncological care is an important idea to discuss," Tewari and colleagues said.

**More information:** Raghav Gupta et al, From foes to friends:
rethinking the role of lymph nodes in prostate cancer, *Nature Reviews Urology* (2024). [DOI: 10.1038/s41585-024-00912-9](https://doi.org/10.1038/s41585-024-00912-9)

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