MedicalXpress

Regional chemotherapy technique for extremity sarcoma salvages limbs from amputation

February 15 2017

Patients with a type of advanced malignant cancer of the arms or legs have typically faced amputation of the afflicted limb as the only treatment option. However, a technique that limits the application of chemotherapy to the cancerous region can preserve limbs in a high percentage of these patients, researchers from five cancer centers in the United States and Australia report in a study published online as an "article in press" on the *Journal of the American College of Surgeons* website in advance of print publication.

The researchers used the treatment technique, known as regional chemotherapy with isolated limb perfusion (ILI), in 77 patients with treatment-resistant, locally advanced soft tissue sarcomas (STS), and were able to salvage limbs in 77.9 percent of the cases. "Isolated limb infusion is a safe and effective technique of treatment of patients with locally advanced soft tissue sarcoma who otherwise might require amputation," said lead study author John E. Mullinax, MD, from Moffitt Cancer Center, Tampa, Fla.

The study, conducted over a 22-year period from 1994-2016, is the largest one to date of limb preservation using ILI for sarcoma. "Advocates for ILI in these patients would argue that, with similar long-term survival data and meaningful overall response rates, patients would much prefer a treatment that preserves the affected extremity to one that does not," Dr. Mullinax said. ILI has historically been used primarily for

melanoma of the extremities and the use of this technique in sarcoma is a more novel approach. Sarcoma is a rare type of cancer in the extremities with several different subtypes; the study patients who underwent ILI had 17 different subtypes of sarcoma.

The rationale for amputation of soft tissue sarcoma of the arm or leg has been to prevent the cancer from spreading to, or metastasizing to, other parts of the body. Dr. Mullinax noted that one concern with the use of ILI in these cancers is that it does not address distant metastatic disease. "The reality is that those patients who develop metastatic disease after amputation or ILI likely may already have distant microscopic disease at the time of the procedure, but the radiographic staging studies are not sensitive enough to detect it," Dr. Mullinax said. "In this sense, the treatment of the extremity disease is not to the determinant of long-term survival."

In the study population, 19 patients had 21 procedures for upper-extremity disease and 58 patients had 63 infusions for lower-extremity disease. The results varied significantly for the two groups. The overall three-month response rate to ILI was 58 percent, but it was only 37 percent for those with upper-extremity disease vs. 66 percent for lower-extremity disease. Likewise, those who had upper-extremity sarcomas had a lower median overall survival than their lower-extremity counterparts, 27.9 months vs. 56.6 months. For the entire study population, the median overall survival was 44.3 months.

Entering the study, all the patients had sarcomas that could only be removed with an amputation, but afterward 30 percent had a complete response to ILI, many of these because patients were able to have a surgical procedure to remove the tumors without amputation. For those who eventually needed an amputation, the median time to do so was 4.5 months following ILI.

The ILI technique involves circulating the chemotherapy agents melphalan and actinomycin D in the blood vessels of the affected area of the arm or leg, and the use of a tourniquet to block the chemotherapy drugs from circulating through the rest of the body, thus creating a closed circuit. The drugs circulate in the target area for 30 minutes, and then are flushed out before the tourniquet is removed and full circulation is restored. ILI for soft tissue sarcoma of the extremities can be repeated, whereas another procedure to administer chemotherapy to the arms or legs, hyperthermic isolated limb perfusion, requires an incision to openly cannulate the vessels and generally cannot be repeated, Dr. Mullinax explained.

The ILI technique requires a team to help perform the procedure such as an interventional radiology team to place the catheter in the artery before the procedure, a perfusionist to oversee the circuit and an operating room staff familiar with chemotherapy precautions, Dr. Mullinax said.

"Most patients would prefer to have more time with their leg rather than face an amputation," Dr. Mullinax said. "It's known that for patients with soft-tissue sarcoma, the life-limiting disease is not in the extremity but it's actually in the metastatic disease. An inoperable sarcoma of the thigh does not affect survival to the degree that metastatic disease in the lung does."

Dr. Mullinax said one limitation of the study was that it did not randomize patients between ILI and amputation, so a head-to-head comparison of response to treatment and survival cannot be performed with this dataset. The study also did not evaluate quality of life or patient-related factors for those who had limb salvage vs. those who had amputation.

More information: Isolated Limb Infusion as a Limb Salvage Strategy for Locally Advanced Extremity Sarcoma, *Journal of the American*

College of Surgeons, 2017.