Pancreatic cancer study finds most early staging is inaccurate

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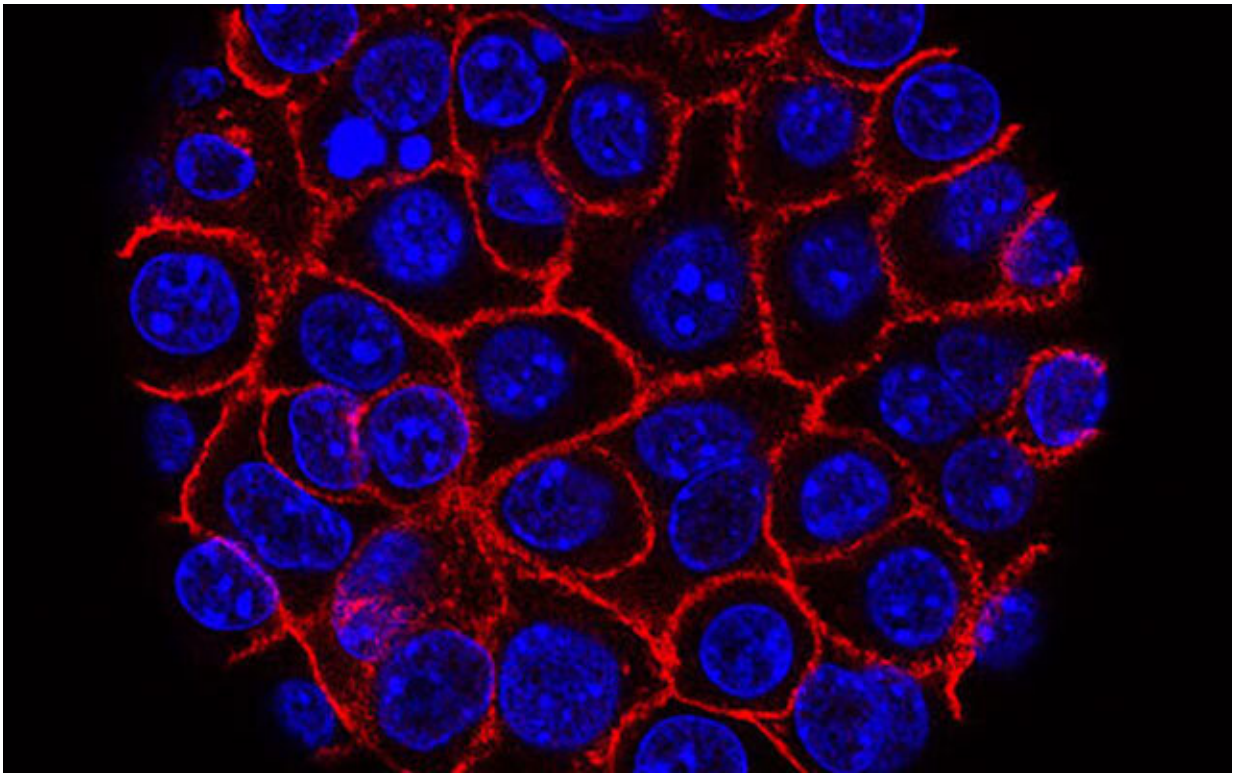

Pancreatic cancer cells (blue) growing as a sphere encased in membranes (red). Credit: National Cancer Institute

Staging of patients with early pancreatic cancer is inaccurate as much as 80% of the time, according to a new Cedars-Sinai Cancer study published in *JAMA*. The finding underscores the urgent need for

advancements in diagnostic technology and staging, which could significantly alter early pancreatic cancer treatment and research.

In this study, investigators looked at data from more than 48,000 patients in the National Cancer Database. Based on preoperative imaging, all of the patients in the study had either stage 1 or stage 2 pancreatic cancer.

Following surgery to remove their tumors, more than 78% of stage 1 patients and more than 29% of stage 2 patients were upstaged—generally to a stage that includes lymph node involvement.

"Our research reveals that staging—essential for making treatment decisions and determining research eligibility—is often inaccurate in early-stage pancreatic cancer," said Srinivas Gaddam, MD, associate director of Pancreatic Biliary Research at Cedars-Sinai and senior author of the study. "As the field is racing toward earlier diagnosis, early staging will become increasingly important."

Diagnosis and staging of pancreatic cancer are difficult for the same reason. The pancreas, a digestive organ, is located deep in the body and current imaging technology isn't always able to detect smaller tumors or lymph node involvement, said Gaddam, who is also an associate professor of Medicine and runs the Pancreatic Cancer Screening and Early Detection Program at Cedars-Sinai.

Lymph nodes, clusters of small immune structures, are an important factor in cancer staging and a key difference between early-stage and later-stage pancreatic cancer.

"Patients who have lymph node involvement have a worse survival rate than those without lymph node involvement," Gaddam said. "When imaging is unable to detect lymph node involvement, staging may not reflect the true extent of the disease. Our findings suggest that lymph

node involvement is being missed in four out of every five patients during the staging process."

The five-year survival rate for stage 1 pancreatic cancer is more than 83%, but that drops to just 3% for patients with stage 4 disease—which is when most patients are currently diagnosed.

"Pancreatic cancer is a difficult diagnosis and there is a tremendous need to improve outcomes for patients," said Dan Theodorescu, MD, Ph.D., director of Cedars-Sinai Cancer and the PHASE ONE Foundation Distinguished Chair.

"Through leading-edge tools, such as our Molecular Twin Precision Oncology Platform, we are developing tests that will guide precision treatment of pancreatic and other cancers. We first demonstrated the utility of Molecular Twin by identifying new biomarkers for pancreatic cancer; these biomarkers assist in the diagnosis, which must be coupled with accurate cancer staging to appropriately guide therapeutics."

Gaddam's take-home message for clinicians staging pancreatic cancer is to recognize the limitations of current imaging technology and actively assess and report lymph node involvement. And for those at the forefront of innovation, he stresses the urgent need to improve screening and diagnostic technologies.

Pancreatic cancer screening employs MRI and endoscopic ultrasound. Screening is recommended for people with a family history of pancreatic cancer and those who carry variants in certain genes associated with the disease.

"We know that our current screening and staging tools aren't great," Gaddam said. "My hope is that within the next 10 years, we will develop advanced tools for screening and staging pancreatic cancer, allowing us

to diagnose most patients at stage 1 and stage 2 rather than stage 4. With these advancements, we can catch this disease much earlier, improving outcomes for many more patients."

More information: Gerardo Perrotta et al, Accuracy of Clinical Staging in Early-Stage Pancreatic Ductal Adenocarcinoma, *JAMA* (2024). DOI: 10.1001/jama.2024.16332. jamanetwork.com/journals/jama/ … cle-abstract/2823280

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