

Who Benefits From Surveillance Imaging?

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Routine imaging in remission is performed for patients with many types of cancer in an attempt to detect early, asymptomatic relapse. In patients with lymphoma in the United States, imaging is often performed as routine practice, frequently required in clinical trials, and recommended in treatment guidelines. This is all in the absence of proof that these images improve overall survival or provide other benefits. In *Journal of Clinical Oncology (JCO)*, Voss et al¹ report a trial that included routine surveillance imaging for children and adolescents with Hodgkin's lymphoma in remission. Most relapses were detected by changes in symptoms, physical findings, or laboratory results; there was no evidence that detection of relapse by routine imaging changed survival.

This report by Voss et al¹ addresses an issue that is equally pertinent to adult patients with lymphoma. Because many patients with lymphoma relapsing after complete remission have a chance for a durable second remission with salvage therapy (ie, usually autologous hematopoietic stem-cell transplantation), it is reasonable to consider the possibility that early detection of relapse in asymptomatic patients might increase the chance for cure. To achieve this goal, screening for early relapse with surveillance imaging would need to be accurate and not associated with excessive toxicity or cost.

Although the sensitivity and specificity of the imaging technique affect its accuracy, the largest impact is related to the prevalence of the condition in the population being screened. There are many reports of the sensitivity and specificity of computed tomography (CT) scanning in detecting lymphoma. Although these range from well less than 50% to 100%, a reasonable average would be a sensitivity of approximately 60% to 65% and specificity of approximately 90% to 95%. It is more difficult to be certain of the sensitivity and specificity for positron emission tomography (PET)/CT scanning, although it seems that the sensitivity is higher, and the specificity is lower. The most important variable is the prevalence of lymphoma in the population being screened. A study by Radford et al² in patients with Hodgkin's lymphoma in remission found that relapse was detected during one in 68 follow-up visits to an oncologist. In our clinic, the frequency of detecting relapse for patients with diffuse large B-cell lymphoma in remission is between one in 40 to 50 visits. Thus, applying the data from the Radford et al² study, the chance that an abnormality on a routine surveillance CT scan would represent lymphoma would be approximately 10%, and applying the data from Nebraska for diffuse large B-cell lymphoma, the chance would be approximately 20%. Of course, these calculations almost certainly overestimate the utility of these images, because in most patients, relapse is detected by obvious

changes in clinical status—often in patients returning to clinic between planned visits.

The potential value of routine surveillance CT scanning in aggressive non-Hodgkin's lymphoma, indolent non-Hodgkin's lymphoma, and Hodgkin's lymphoma has been evaluated in numerous reports.³ A report by Liedtke et al⁴ found that patients with relapsed diffuse large B-cell lymphoma detected by surveillance CT scan were likely to have low-volume disease, and the lymphoma was likely to be chemosensitive. However, they found only a nonsignificant trend toward better survival. Studies of Hodgkin's lymphoma, including that reported by Voss et al,¹ have not shown improved treatment outcome with routine imaging using CT scans. There are fewer reports on using surveillance CT scans for follicular lymphoma in remission. This lymphoma typically grows slowly, and asymptomatic relapse might be present for an extended time. Gerlinger et al⁵ described 71 patients who achieved complete remission from relapsed follicular lymphoma through autotransplantation and were observed with annual surveillance imaging. Surveillance imaging detected relapse in 16 patients, and routine clinical evaluation found relapse in 18 patients. The relapses detected by surveillance imaging did not require therapy for a longer time compared with the clinical relapses, but overall survival was not affected.

The impact of surveillance PET/CT scans on identifying early relapse in patients with lymphoma has also been studied.³ In general, surveillance PET/CT scanning to detect relapse has a higher false-positive rate than CT scans and has not had an impact on survival. A report from Denmark described 53 patients with Hodgkin's lymphoma who underwent 127 surveillance PET/CT scans.⁶ The positive predictive value was 19%, and the negative predictive value was 100%. Lambert et al⁷ reported using PET/CT scans to screen for early relapse in patients after allogeneic transplantation and found that PET/CT scans in this setting detected relapse earlier than CT scans and allowed for early administration of donor lymphocyte infusions.

There are several potential risks of routine surveillance imaging in patients with lymphoma. These include the possibility of inducing a second cancer because of the radiation dose, the risk of biopsies necessary to document relapse after a positive image, and potential anxiety and fear associated with these images, which could lower quality of life. The risk of causing cancer through medical imaging has recently been highlighted^{8,9}; reports suggested that medical imaging might be a significant cause of cancer in the United States. This seems to be a particular concern in young patients. Shenoy et al¹⁰ tried to calculate the risk of subsequent cancers after surveillance images in patients of different ages and sexes. The anticipated incidence of second cancers

was higher in younger patients than in older patients and higher in women than in men—largely because of the risk of inducing breast cancer in young women. It is difficult to quantitate the risk of injury after biopsies performed to document recurrence in patients with abnormal images. Given the low positive predictive value of surveillance images, treatment should never be instituted in this setting without documentation of relapse by biopsy. Some of these biopsies will be associated with serious or even fatal complications. Thompson et al¹¹ attempted to measure the psychologic impact of surveillance imaging in patients with lymphoma. They found that patients reported that recurrent cancer was one of their major concerns, and the authors found an increase in anxiety associated with surveillance imaging.

The financial cost of surveillance imaging is considerable. At the University of Nebraska Medical Center, the current charge for a CT scan of the chest, abdomen, and pelvis is \$6,931, and the charge for a PET/CT scan is \$7271. Thus, total charges for patients receiving five to 10 surveillance images via one of these techniques would range from \$34,655 to \$72,710. Multiplied by all the patients who achieve remission from lymphoma in the United States, this is not an insignificant contribution to health care costs, particularly in light of the lack of proof of benefit. The increasing number of oncologists who own CT and PET/CT scanners raises the issue of conflicts of interest in performing these studies.

So, what is the answer to the question, “Who benefits from surveillance imaging?” The report by Voss et al¹ in *JCO* suggests that the answer is not children with Hodgkin’s lymphoma who achieve remission. However, it is still possible that in high-risk patients (ie, where the higher chance of relapse would increase the positive predictive value of an abnormal image) for whom potentially curative salvage therapy is available, these images might improve survival.^{12,13} One subgroup where this could be possible is younger adults with high-risk diffuse large B-cell lymphoma. A clinical trial in this group of patients comparing routine follow-up using history, physical examination, and laboratory studies with the same evaluation plus surveillance imaging could have an important impact on practice—either to make surveillance routine or to decrease its use. Until such a trial is completed, surveillance imaging for patients with lymphoma in remission should not be routinely performed.

AUTHOR’S DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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REFERENCES

1. Voss SD, Chen L, Constine LS, et al: Surveillance computed tomography imaging and detection of relapse in intermediate- and advanced-stage pediatric Hodgkin’s lymphoma: A report from the Children’s Oncology Group. *J Clin Oncol* 30:2635-2640, 2012
2. Radford JA, Eardley A, Woodman C, et al: Follow up policy after treatment for Hodgkin’s disease: Too many clinic visits and routine tests? A review of hospital records. *BMJ* 314:343-346, 1997
3. Wagner-Johnston ND, Bartlett NL: Role of routine imaging in lymphoma. *J Natl Compr Canc Netw* 9:575-584, 2011; quiz 585
4. Liedtke M, Hamlin PA, Moskowitz CH, et al: Surveillance imaging during remission identifies a group of patients with more favorable aggressive NHL at time of relapse: A retrospective analysis of a uniformly-treated patient population. *Ann Oncol* 17:909-913, 2006
5. Gerlinger M, Rohatiner AZ, Matthews J, et al: Surveillance investigations after high-dose therapy with stem cell rescue for recurrent follicular lymphoma have no impact on management. *Haematologica* 95:1130-1135, 2010
6. El-Galaly TC, Hutchings M, Bukh A, et al: PET/CT surveillance in patients with Hodgkin lymphoma in first remission. *Ann Oncol* 22:160, 2011 (suppl 4; abstr 228)
7. Lambert JR, Bomanji JB, Peggs KS, et al: Prognostic role of PET scanning before and after reduced-intensity allogeneic stem cell transplantation for lymphoma. *Blood* 115:2763-2768, 2010
8. Berrington de González A, Mahesh M, Kim KP, et al: Projected cancer risks from computed tomographic scans performed in the United States in 2007. *Arch Intern Med* 169:2071-2077, 2009
9. Smith-Bindman R, Lipson J, Marcus R, et al: Radiation dose associated with common computed tomography examinations and the associated lifetime attributable risk of cancer. *Arch Intern Med* 169:2078-2086, 2009
10. Shenoy P, Sinha R, Tumej JW, et al: Surveillance computed tomography scans for patients with lymphoma: Is the risk worth the benefits? *Clin Lymphoma Myeloma Leuk* 10:270-277, 2010
11. Thompson CA, Charlson ME, Schenkein E, et al: Surveillance CT scans are a source of anxiety and fear of recurrence in long-term lymphoma survivors. *Ann Oncol* 21:2262-2266, 2010
12. Petrusch U, Samaras P, Haile SR, et al: Risk-adapted FDG-PET/CT-based follow-up in patients with diffuse large B-cell lymphoma after first-line therapy. *Ann Oncol* 21:1694-1698, 2010
13. Petrusch U, Samaras P, Veit-Haibach P, et al: Hodgkin’s lymphoma in remission after first-line therapy: Which patients need FDG-PET/CT for follow-up? *Ann Oncol* 21:1053-1057, 2010

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