Original Study

Effect of Routine Surveillance Imaging on the Outcomes of Patients With Classical Hodgkin Lymphoma After Autologous Hematopoietic Cell Transplantation

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Abstract

Surveillance imaging is often used following autologous hematopoietic cell transplantation (auto-HCT) to assess for relapse. We evaluated classical Hodgkin lymphoma (cHL) patients who received auto-HCT, achieved complete remission, and underwent surveillance imaging. Relapse was detected clinically or by surveillance imaging. Outcomes were similar between the two groups. There appears to be limited utility for surveillance imaging in cHL after auto-HCT.

Background: Patients with relapsed and refractory classical Hodgkin lymphoma (cHL) are often treated with autologous hematopoietic cell transplantation (auto-HCT). After auto-HCT, most transplant centers implement routine surveillance imaging to monitor for disease relapse; however, there is limited evidence to support this practice. **Patients and Methods:** In this multicenter, retrospective study, we identified cHL patients (n = 128) who received auto-HCT, achieved complete remission (CR) after transplantation, and then were followed with routine surveillance imaging. Of these, 29 (23%) relapsed after day 100 after auto-HCT. Relapse was detected clinically in 14 patients and with routine surveillance imaging in 15 patients. **Results:** When clinically detected relapse was compared with to radiographically detected relapse respectively, the median overall survival (2084 days [range, 225-4161] vs. 2737 days [range, 172-2750]; $P = .51$), the median time to relapse (247 days [range, 141-3974] vs. 814 days [range, 96-1682]; $P = .30$) and the median postrelapse survival (674 days [range, 13-1883] vs. 1146 days [range, 4-2548]; $P = .52$) were not statistically different. In patients who never relapsed after auto-HCT, a median of 4 (range, 1-25) surveillance imaging studies were performed over a median follow-up period of 3.5 years. **Conclusion:** A minority of patients with cHL who achieve CR after auto-HCT will ultimately relapse. Surveillance imaging detected approximately half of relapses; however, outcomes were similar for those whose relapse was detected using routine surveillance imaging versus detected clinically in between surveillance imaging studies. There appears to be limited utility for routine surveillance imaging in cHL patients who achieve CR after auto-HCT.

Clinical Lymphoma, Myeloma & Leukemia, Vol. 17, No. 7, 408-14
Keywords: Auto-HCT, Classical Hodgkin lymphoma, Lymphoma, Relapse, Surveillance imaging

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Submitted: Dec 23, 2016; Revised: Mar 14, 2017; Accepted: May 4, 2017; Epub: May 12, 2017

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2152-2650/$ - see frontmatter
http://dx.doi.org/10.1016/j.clml.2017.05.005

Introduction

In the United States, approximately 8500 new cases of classical Hodgkin lymphoma (cHL) are expected to be diagnosed in 2016.[1] According the National Cancer Institute's Surveillance, Epidemiology, and End Results database, the 5-year overall survival for patients with cHL is approximately 86.2%, and in patients with localized disease, the 5-year overall survival is estimated at 91.5%.[1] For patients who achieve remission, there is currently a lack of consensus regarding the optimal method and frequency of surveillance imaging.[2-7] According to the National Comprehensive Cancer Network guidelines, it is acceptable to obtain a computed tomography (CT) scan at 6, 12, and 24 months after completion of initial therapy or as clinically indicated. However, surveillance positron emission tomography (PET) imaging is not recommended because of the risk of false positive results.[8] Conversely, according to the Lugano Classification, routine surveillance scans are discouraged, with follow-up imaging only recommended as prompted by clinical indications.[9] Similarly, the European Society of Medical Oncology recommends imaging to confirm remission status, but advises against surveillance imaging thereafter unless clinical symptoms occur.[10]

Although the primary goal of surveillance imaging is to improve postrelapse survival, it comes with various potential risks. First, exposure to ionizing radiation from CT scans has been associated with an increased risk for developing secondary malignancies.[11-13] In addition, routine imaging can lead to false positive results, unnecessary follow-up procedures, and anxiety for patients.[14,15] There is also a significant financial cost associated with routine surveillance imaging. According to a study by Dann et al, the cost of detecting a single relapse was approximately 10 times more for patients who undergo routine surveillance imaging for cHL compared with those followed clinically.[16] In another study by Pingali et al, an additional estimated charge of $625,615 was incurred per relapse detected using routine surveillance imaging compared with those detected using clinical means alone.[6] Despite the increased cost, neither study showed a significant survival benefit to routine surveillance imaging.[6,16] Ultimately, the risks of routine imaging are important considerations when evaluating the utility of surveillance.

Although a growing body of literature seems to discourage the use of routine surveillance imaging for cHL in first remission, there are limited data on the potential benefit of routine imaging for relapsed and refractory cHL in complete remission (CR) after autologous hematopoietic cell transplantation (auto-HCT). Although the risk of relapse for patients in first CR is relatively low at 10% to 15%, the relapse risk for patients in CR after auto-HCT is estimated to be 40% to 50%.[4,17,18] With an increased relapse rate in the post-transplant setting, surveillance imaging could be more likely to detect relapses earlier, which in turn could allow for earlier initiation of therapy and potentially result in improved clinical outcomes. As a result, most transplant centers currently implement some form of routine surveillance imaging in the post-transplant setting. However, there is limited evidence to support this practice. Routine surveillance imaging has not been associated with improved survival, and the practice comes along with various risks.

We conducted a multicenter retrospective study of cHL patients who achieved CR after auto-HCT and subsequently underwent routine surveillance imaging. We determined the number of surveillance imaging studies obtained, and we compared the number of relapses detected using routine surveillance imaging with those detected clinically as directed by patient symptoms, physical exam findings, and laboratory data. We also sought to determine whether relapse detection occurred earlier, and whether survival improved when relapse was detected with routine surveillance imaging compared with when relapse was detected clinically.

Patients and Methods

Adult patients who underwent auto-HCT between January 2000 and December 2013 at 3 academic tertiary care medical centers (Medical College of Wisconsin [Milwaukee, WI], Rush Medical Center [Chicago, IL] and Houston Methodist Hospital [Houston, TX]) were identified. The Medical College of Wisconsin was the coordinating center. Institutional review boards at all 3 sites approved this study.

Because the question of long-term surveillance is only relevant for patients in CR after transplantation, to be eligible for the study, the patients must have achieved CR (confirmed using CT and/or PET scan) on their first post-transplant evaluation, typically conducted between days 30 and 100 after auto-HCT. Patients were selected after screening for eligibility criteria. After retrospective chart review, the patients were classified into 2 groups: those who never relapsed and those who relapsed. The latter group was further categorized as "clinical relapse" and "radiographic relapse" on the basis of the method for relapse detection.

A total of 148 relapsed or refractory cHL patients who underwent auto-HCT were identified. Patients who achieved CR after first-line therapy and then underwent upfront auto-HCT without any evidence of relapsed or refractory disease were not eligible. Twenty patients were excluded because of disease progression or relapse before the day 100 evaluation leaving 128 patients who met the inclusion criteria. Of these, 31 patients (24%) relapsed after day 100 after auto-HCT; however, there was insufficient information on 2 of these patients leaving a total of 29 patients (23%) for further evaluation.

At all 3 participating academic centers, the mode of surveillance was history, physical examination, laboratory testing, and either CT or PET/CT imaging every 3 to 12 months during the first 3 years after auto-HCT. All 29 patients were followed with routine radiographic surveillance. Relapse was either detected in the asymptomatic patient with routine surveillance imaging, or it was detected clinically on the basis of patient symptoms, physical exam findings, or laboratory data. In general, if relapse was suspected clinically, imaging was obtained to confirm clinical suspicion for relapsed disease. In some cases, this confirmatory imaging happened to fall around the time of a previously scheduled surveillance interval. However, more commonly, this confirmatory imaging was obtained in between previously scheduled surveillance intervals. In our patient population, relapse was detected clinically in 14 patients (48%), whereas the remaining 15 patients (52%) had relapse detected using routine surveillance imaging alone (Figure 1).

Study Objectives

The primary objective of our study was to compare overall survival for cHL patients who relapse after day 100 after auto-HCT and either have relapse detected clinically or have relapse detected