

Survival Deficit for HIV-Infected Lymphoma Patients in the National Cancer Database

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In this issue, Han and colleagues report that HIV-infected lymphoma patients experience a survival disadvantage compared with HIV-uninfected lymphoma patients during the era of highly active anti-retroviral therapy (HAART; ref. 1). Despite reductions in the incidence of AIDS-defining malignancies such as non-Hodgkin lymphoma (NHL) with the advent of HAART, the rate of lymphoma among HIV-infected individuals remains high compared with the general population (2–4). Whether HIV-infected patients additionally have worse survival after a lymphoma diagnosis is unclear. As referenced by the authors, clinical trials data suggest that overall mortality for lymphoma patients may be comparable by HIV status. However, population-based data from observational cohort, registry linkage, and health care system studies indicate that HIV-related immunosuppression remains an important predictor of mortality after a lymphoma diagnosis (5–7).

Here, the authors compare overall mortality between HIV-infected and HIV-uninfected lymphoma patients using the National Cancer Database, a nationwide hospital-based registry jointly sponsored by the American Cancer Society and the American College of Surgeons. This nationally representative study included 179,520 lymphoma patients diagnosed from 2004 to 2011. The large sample size afforded a rare opportunity to measure survival by histologic subtype: Hodgkin lymphoma, Burkitt lymphoma, diffuse large B-cell lymphoma, and peripheral T-cell lymphoma. Follicular lymphoma was included as a "control," a common NHL with no strong HIV association. Approximately 79% of patients had ≥ 3 years of complete follow-up. Furthermore, the authors used propensity score matching to efficiently adjust for critical covariates including health insurance status, presence of B-symptoms, comorbidities, tumor stage, and cancer treatment. In short, this study had a number of strengths, with a very large sample size relative to previous studies.

The authors report that HIV-infected lymphoma patients experienced poorer survival than HIV-uninfected lymphoma patients. Notably, this survival deficit was observed for all histologic subtypes assessed, with HRs indicating an increased risk of overall mortality in HIV-infected lymphoma patients ranging from 1.43 to 1.95. Higher mortality was also observed after attempts to control for confounding by factors such as tumor stage and health insurance status and remained after restriction to lymphoma patients who received chemotherapy (HR range: 1.31–1.86).

However, survival in follicular lymphoma cases was no longer significantly associated with HIV status among those who received chemotherapy—consistent with the use of follicular lymphoma as a control tumor.

Despite its strengths, this study also had limitations. Chief among these was the exclusive use of overall rather than cancer-specific mortality, especially given concerns regarding competing risks in HIV-infected patients (e.g., death due to other causes) (8), which were compounded in the current investigation by lack of patient-level CD4⁺ T-cell data. There was also limited information regarding important prognostic factors such as number of nodal sites affected or extent of abdominal involvement, and future work should include more detailed cancer treatment data (e.g., specific chemotherapy regimens). The authors do note these limitations and correctly conclude, based upon this report and previous population-based studies, that HIV plays a role in determining a patient's outcome after their lymphoma diagnosis.

When considered alongside previous reports of HIV-associated survival deficits for other common tumors (e.g., lung cancer) and randomized trial data demonstrating improved cancer patient survival after the administration of immune-based therapies (9–14), the evidence suggests that immunosuppression plays a fundamental role in cancer progression. Mechanisms underlying the HIV-associated survival deficit reported here likely include both uncontrolled immune activation/inflammation and the depletion of functional T cells to impede tumor growth. Future studies that could shed light on this association include the correlation of detailed immunologic metrics (e.g., CD4/8 T-cell counts) with specific clinical outcomes (e.g., response to chemotherapy). Although such research is often hampered by the lack of longitudinal CD4/8 T-cell measures in a large sample of either HIV-infected or HIV-uninfected cancer patients, longer term follow-up of clinical cohorts could provide the data to evaluate the degree to which immunosuppression is important for cancer patient outcomes.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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