Lymphopenia After Radiotherapy and Risk of Infection

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BACKGROUND

- At least 60% of cancer patients receive radiotherapy as part of their treatment.¹
- Radiation may cause immune dysfunction when compromising tissue or circulating immune cells, such as lymphocytes.
- Lymphocytes are essential cells in the immune response to cancer;²³ and certain infections.
- The extent of lymphocyte depletion after radiation as well as the duration and possible associated excess risk of infection from lymphopenia are unknown.

Aim of the Study

- To examine the kinetics of lymphocyte counts before and after radiotherapy; and its association with the long term risk of infection.

METHODS

- The cohort constitutes patients who received a first course of radiotherapy in the period 2005-2016 at Copenhagen University Hospital.
- Lymphocyte counts were identified at pre-defined time points according to radiotherapy start (Table 1).
- Patients contributing with a lymphocyte count in at least one of the pre-defined time points were included in the analysis (Figure 1).
- Lymphopenia was defined as a lymphocyte count < 1.0 x 10³ cells/µL.
- Risk of infection was defined as the time to first hospital admission with a diagnosis of infection, according to ICD-10 codes.

Statistical Analysis

- Association between lymphopenia at pre-defined time points and incidence of first hospital admission with an infection was assessed by Poisson regression analysis, adjusted for age, sex and calendar year.
- Follow-up started at each time-point and it was censored when either outcome, death or 1 January 2017 was reached.

RESULTS

- General characteristics for 14,823 patients included in the study are described in Table 2.
- Lymphocyte counts declined in the first month after initiation of radiotherapy, median 0.60 (0.37-1.00) cells/µL, then increased gradually during follow-up.
- At month 24, 28.6% of cohort under follow-up had lymphopenia (Figure 2).
- During 39,620 person-years of follow-up, 3,644 (24.6%) patients had at least one hospital admission with a diagnosis of infection.
- Respiratory tract infections accounted for almost 50% of the infectious diagnoses (Figure 3).

CONCLUSIONS

- The majority of cancer patients appear to develop lymphopenia shortly after radiotherapy has been initiated; and for some, this persist for at least 24 months thereafter.
- Lymphopenia just prior to and after radiotherapy start was associated with increased risk of subsequent hospital admission with a diagnosis of infection (Table 3).

PERSPECTIVES

- These findings are preliminary, and should be confirmed in cohorts with more complete assessment of lymphocyte counts during follow-up.
- The functional immunological correlates of lymphopenia should be examined with the aim to understand the extent of immune impairment caused by radiotherapy.
- Finally, the factors explaining the variation in degree and duration of lymphopenia need to be explored.

REFERENCES


Table 1

<table>
<thead>
<tr>
<th>Time Points</th>
<th>Time Frame for Lymphocyte Counts</th>
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</thead>
<tbody>
<tr>
<td>0 = Baseline</td>
<td>Closest sample to time point, collected within within 21 days</td>
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<tr>
<td>1 month before</td>
<td>Closest sample to time point, collected within 14 days</td>
</tr>
<tr>
<td>1 month after starting radiotherapy</td>
<td>Closest sample to time point, collected within 21 days</td>
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Table 2

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No. (%)</th>
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<tbody>
<tr>
<td>Gender, males (%)</td>
<td>8,583 (58.7)</td>
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<tr>
<td>Ethnic Group</td>
<td>7,893 (53.6)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>1,902 (12.8)</td>
</tr>
<tr>
<td>Non-Hematologic Malignancies</td>
<td>12,919 (87.2)</td>
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<tr>
<td>Hematologic Malignancies</td>
<td>4,536/12,919 (35.1)</td>
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<tr>
<td>Additional Chemotherapy</td>
<td>4,496 (73.2)</td>
</tr>
<tr>
<td>Duration of Radiotherapy, days</td>
<td>28 (12-39)</td>
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<td>Died (%)</td>
<td>8,411 (56.7)</td>
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<td>Data available from patients with non-hematologic malignancies.</td>
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Figure 1

Selection of Patients

Figure 2

Lymphocyte Count (x10³ cells/µL) Before and After Radiotherapy Start

Figure 3

Type of Infection