



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,²⁻³ 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.

Table 1
Time Points

Time Points	Time Frame for Lymphocyte Counts
24, 12 and 6 months before and after starting radiotherapy	Closest sample to time point, collected within ±21 days
1 month before and after starting radiotherapy	Closest sample to time point, collected within ±14 days
0 = Baseline	Closest sample to radiotherapy start, collected within the previous 14 days

Figure 1
Selection of Patients

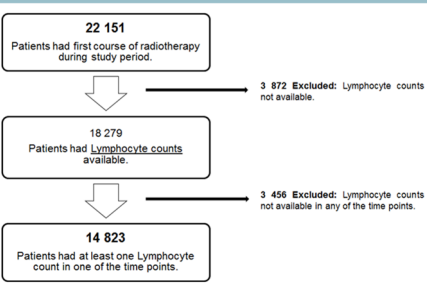


Table 2
Patient Characteristics

Characteristics	Total N = 14,823
Age, median (range)	61.1 (53.3-70.5)
Gender, males (%)	7,650 (51.6)
Cancer Type	
Hematologic Malignancies	1,902 (12.8)
Non-Hematologic Malignancies	12,919 (87.2)
Additional Chemotherapy*	4,536/12,919 (35.1)
Duration of Radiotherapy, days median (range)	28 (12-39)
Died (%)	8,411 (56.7)

*Data available from patients with non-hematologic malignancies.
*Patients may have received chemotherapy between 30 days before radiotherapy start and up to 30 days after last day of radiotherapy.

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).
- Lymphopenia before radiotherapy; and 6, 12 and 24 months after radiotherapy start was associated with increased risk of subsequent hospital admission with a diagnosis of infection (Table 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 is associated with increased risk of subsequent hospital admission with an infection.

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.

- Orth M, Lauber K, Niyazi M, Friedl AA, Li M, Maihofer C, et al. Current concepts in clinical radiation oncology. Radiation and environmental biophysics. 2014;53(1):1-29.
- Ray-Coquard I, Cropet C, Van Glabbeke M, Sebban C, Le Cesne A, et al. Lymphopenia as a prognostic factor for overall survival in advanced carcinomas, sarcomas, and lymphomas. Cancer Res. 2009; 69(13): 5383-91.
- Mellman I, Coukos G, Dranoff G. Cancer immunotherapy comes of age. Nature. 2011;480(7378):480-9.

Figure 2
Lymphocyte Count (x10³ cells/μL) Before and After Radiotherapy Start

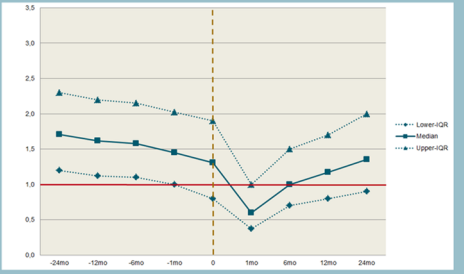


Figure 3
Type of Infection

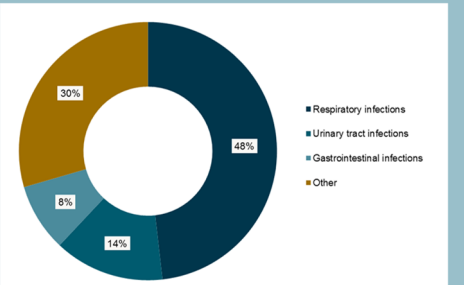


Table 3
Lymphopenia and Risk of Infection

Time since radiotherapy start (Months)	Available Lymphocyte Count n (%)	Lymphocyte Count <1.0 x 10 ³ cells/ μ L n (%)	IRR of Infection per 1,000 PY (95% CI)		IRR (95% CI) Lymphopenia vs No Lymphopenia
			Lymphocyte Count		
			<1.0 x 10 ³ cells/ μ L	$\geq 1.0 \times 10^3$ cells/ μ L	
0	6,202 (41.8)	1,986 (32.2)	158.8 (147.0-171.6)	98.4 (92.4-104.8)	1.8 (1.7-2.0)
1	6,145 (41.5)	4,496 (73.2)	108.0 (101.9-114.5)	127.8 (116.1-140.7)	1.0 (0.9-1.1)
6	3,811 (25.7)	1,733 (45.6)	112.6 (100.6-125.9)	95.6 (86.8-105.2)	1.2 (1.1-1.4)
12	2,551 (17.2)	976 (38.3)	116.4 (100.0-135.4)	85.4 (76.3-95.7)	1.3 (1.1-1.6)
24	1,637 (11.0)	468 (28.6)	176.3 (144.0-215.8)	68.5 (58.8-79.8)	2.4 (1.8-3.1)

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