LONG-TERM TRENDS IN THE LOSS OF LIFE EXPECTANCY AFTER A DIAGNOSIS OF CHRONIC LYMPHOCYTIC LEUKEMIA: A POPULATION-BASED STUDY IN THE NETHERLANDS, 1989-2018

Topic: Chronic lymphocytic leukemia and related disorders - Clinical

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Background:
The introduction of chemoimmunotherapy heralded a new era for chronic lymphocytic leukemia (CLL) management. More recently, the chemoimmunotherapy paradigm has shifted towards more novel targeted agents that can further improve progression-free survival and overall survival. Population-based studies have shown that the five-year relative survival in CLL increased markedly since the introduction of chemoimmunotherapy, approximating 90% for patients up to age 70. Seeing the comparatively favorable prognosis of CLL patients in modern times, other survival estimates may be more informative because relative survival does not inform on patient survival across the entire remaining life span.

Aims:
Studies estimating the life expectancy of CLL patients are hitherto lacking. Therefore, we assessed trends in the life expectancy of CLL patients from a historical and contemporary perspective.

Methods:
We selected all CLL patients diagnosed in the Netherlands between 1989 and 2018—with follow-up for survival up to December 31, 2020—from the Netherlands Cancer Registry. We estimated the loss in expectation of life (LEL)—quantifying the difference between the life expectancy of CLL patients and the general population, the latter being matched to patients by age, sex, and calendar year—using flexible parametric relative survival models. The LEL is interpreted as the average number of life years lost due to a CLL diagnosis. The LEL can vary markedly across ages because life expectancy is age-dependent. Therefore, the proportional LEL (PLEL) was estimated (calculated as the LEL divided by the population life expectancy). These survival measures were presented by year of diagnosis for four age categories at diagnosis (i.e., 50, 60, 70, and 80 years), stratified by sex.

Results:
Our cohort included 23,692 CLL patients (median age, 69 years, interquartile range 61-77 years; 61% males) diagnosed in the Netherlands between 1989-2018. The life expectancy of CLL patients increased gradually across all ages between 1989-2018, with a most pronounced increase in patients aged 50 and 60 years at diagnosis (Fig 1A). CLL patients diagnosed in 1990 and 2018 lost 3.1-19.0 and 1.7-8.2 life-years depending on age and sex, respectively (Fig 1A). The increase in the life expectancy of CLL patients was greater than in the general population. Consequently, the LEL (Fig 1B) and PLEL (Fig 1C) of CLL patients across all four age categories decreased over time. Despite the decrease in LEL over time, all studied age groups diagnosed in 2018 had excess mortality, reflected in a LEL ranging from 1.7 to 8.2 life-years, depending on age and sex (Fig 1B). The PLEL estimates showed that the age differential in survival became less pronounced over time and eventually disappeared for female patients, of which the former indicates that older patients (i.e. 70 and 80 years), who generally have fewer life-years left, experience the same improvement in life expectancy as younger patients.

Summary/Conclusion:

The life expectancy of CLL patients diagnosed in the Netherlands between 1989-2018 has steadily increased over time. This increase is likely attributed to the broader application of more efficacious therapies over time. Notwithstanding, continuous population-based surveillance is essential to assess the impact of the rapidly evolving management of CLL on survival since excess mortality is still a threat in contemporary diagnosed and managed patients.