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Does the regional use of intensive chemotherapy impact the outcome of adults with AML?

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Prolonged survival, including cure in some patients, may be achieved in adult patients receiving intensive chemotherapy (ICT) for acute myeloid leukaemia (AML).[1 2] Although not all patients are fit to receive ICT, disparities exist.[3] Especially, large epidemiological studies have shown differences in patient survival according to geographical regions, independently of education, insurance or income, suggesting that local healthcare infrastructure might affect outcome.[4] Specifically, it is observed that patients treated in an academic centre have lower early and late mortality rates while underlying reasons for these observed survival differences are not fully understood.[5 6]

Some have speculated that regional disparities in patient outcome might be related to the use of ICT in older patients.[3 7] Kaplan *et al*, therefore, sought to validate this hypothesis in a nationwide epidemiological study.[8] They explored practice variation in nine regional networks in the Netherlands by analysing data from 4060 adults, with a median age of 70 years, diagnosed with AML between 2014 and 2018. The use of ICT varied greatly between regions from 36% to 57% of patients. Non-intensively treated patients mostly received hypomethylating agents (34%), followed by hydroxyurea (11%) and low-dose cytarabine (3%) while 52% received best supportive care only. Due to the study period, none received intermediate-intensity regimens such as combination therapies with venetoclax. With a mixed-effect logistic regression model, they showed significant between-region differences regarding the use of ICT. In some instances, a patient with similar baseline characteristics would have up to a 36% higher chance of receiving ICT if treated in another region. This rate increased to 43% in patients older than 60 years. While median overall survival ranged from 4.9 to 8.4 months with between-region differences of 11%, variations in the use of ICT only partially accounted for these survival differences.

Although many healthcare systems aim at providing its citizens with equal access to care, especially for those affected by cancer, important disparities are frequently observed. Understanding the underlying reasons for these differences may help improve equal access for patients. In this study, the authors focused on AML that has a specific treatment strategy that relies on ICT for fit patients. They show that patients were not as likely to receive ICT according to the region they live in and that may partially impact their survival. It is the first study to quantify variations in the use of ICT and brings novel hypothesis regarding survival differences. While it shows that some survival gain may be obtained by a wider use of ICT, reasons for between-region disparities in mortality are not fully elucidated. Other uncontrolled factors inherent to regional management of AML patients may also explain these disparities, including the management of early AML-related complications (eg, leucocytosis and infectious complications), admission strategies to intensive care units or the enrolment of patients in clinical trials. Nevertheless, this study encourages us to improve our evaluation of patients for ICT, especially in older patients.

The main strength of this study is that it analysed almost all adults diagnosed with AML in a single country during a specific time-period (2014–2018). It has a few limitations due to the registry-based design that frequently lacks individual patient data. This included performance status, comorbidities and molecular data that could help in understanding survival differences in otherwise seemingly alike patients. Also, due to the inclusion period, outcome of patients receiving more recent 'intermediate dose' regimens with azacitidine and venetoclax combinations could not be assessed. As the

authors state, standardisation of treatment might be even more important now that many treatment options exist (ICT, azacitidine-venetoclax combination, azacitidine monotherapy, etc). Finally, the role of allogeneic haematopoietic cell transplantation was not assessed and one may speculate that there may also exist some regional disparities in its use while some studies suggest that it may be associated with improved survival, including in older patients.[9]

This study calls for additional investigations, with epidemiological studies that include data regarding patient and disease characteristics and treatment strategies, to further understand regional differences in the use of ICT in AML patients. Additional data are required to confirm that uniform care delivery, with increased use of ICT, may improve patient outcome. Developing standardised ICT eligibility criteria, by identifying which patients are suitable for ICT, may help in this endeavour. Although currently available tools are limited in predicting survival,[10] ongoing efforts can lead to individual decision-making in the era of personalised medicine. Then, prospective controlled studies will have to demonstrate that patients evaluated as unsuitable for ICT would have better outcome if treated less intensively.

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