

Temporal Decline in Early Mortality in Acute Myeloid Leukemia Across Chemotherapy, Hypomethylating Agent, and Venetoclax-Based Therapeutic Eras: A Four-Decade Population-Based Analysis



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INTRODUCTION:

Early mortality remains a critical barrier in acute myeloid leukemia (AML), particularly among older patients. While therapeutic strategies have evolved from intensive chemotherapy to hypomethylating agents (HMAs) and venetoclax-based regimens, the extent to which these advances have translated into reductions in early mortality at a population level remains unclear.

METHOD:

We conducted a retrospective cohort study using the SEER-8 database (1975–2022) including adults with non-M3 AML. Early mortality was defined as death within 1 month (EM1; 0–30 days) and within 2 months (EM2; 0–60 days) of diagnosis. Patients were stratified into chemotherapy (1975–2005), HMA (2006–2017), and venetoclax (2018–2022) eras. Multivariable logistic regression was performed to evaluate associations between diagnostic era and early mortality. All tests were two-sided, with statistical significance defined as $p < 0.05$.

CONCLUSION:

Despite progressive reductions across therapeutic eras, early mortality in AML remains high, underscoring the need for optimized early intervention and risk-adapted strategies.

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RESULTS

In era-stratified multivariable analyses, receipt of chemotherapy was consistently associated with reduced early mortality, with progressively lower odds across eras (EM1 OR 0.26 [0.23–0.28], 0.16 [0.15–0.18], and 0.14 [0.12–0.16], respectively). Age remained a dominant predictor in all eras, with patients >75 years demonstrating significantly higher odds of early mortality (OR ~3.5–4.2; all $p < 0.001$). Overall, the greatest reduction in early mortality occurred between the chemotherapy and HMA eras, with more modest improvements observed in the venetoclax era.

