Effects of Chemotherapy Dose Reductions in Overweight and Obese Patients with Acute Myeloid Leukemia – A Danish Nationwide Cohort Study

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P546 EFFECTS OF CHEMOTHERAPY DOSE REDUCTIONS IN OVERWEIGHT AND OBESE PATIENTS WITH ACUTE MYELOID LEUKEMIA – A DANISH NATIONWIDE COHORT STUDY

Topic: 04. Acute myeloid leukemia - Clinical

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Background: The majority of chemotherapeutic agents are dosed according to a body weight derived variable. Studies in solid cancers have shown that overweight patients frequently receive dose reduction (DR) of chemotherapy, despite no evidence corroborates increased toxicity of full dosing. Rather, DR to ≤95% of actual weight-based dose, has been shown to result in shortened overall survival (OS). Consequently, the American Society of Clinical Oncology does not recommend up-front dose reduction based on body mass index (BMI) or body surface area (BSA) in overweight patients. Current evidence regarding DR and outcome among overweight patients with acute myeloid leukemia (AML) receiving induction chemotherapy (IC) is limited.

Aims: The purpose of this study was to investigate the association between DR and outcome in overweight patients with AML.

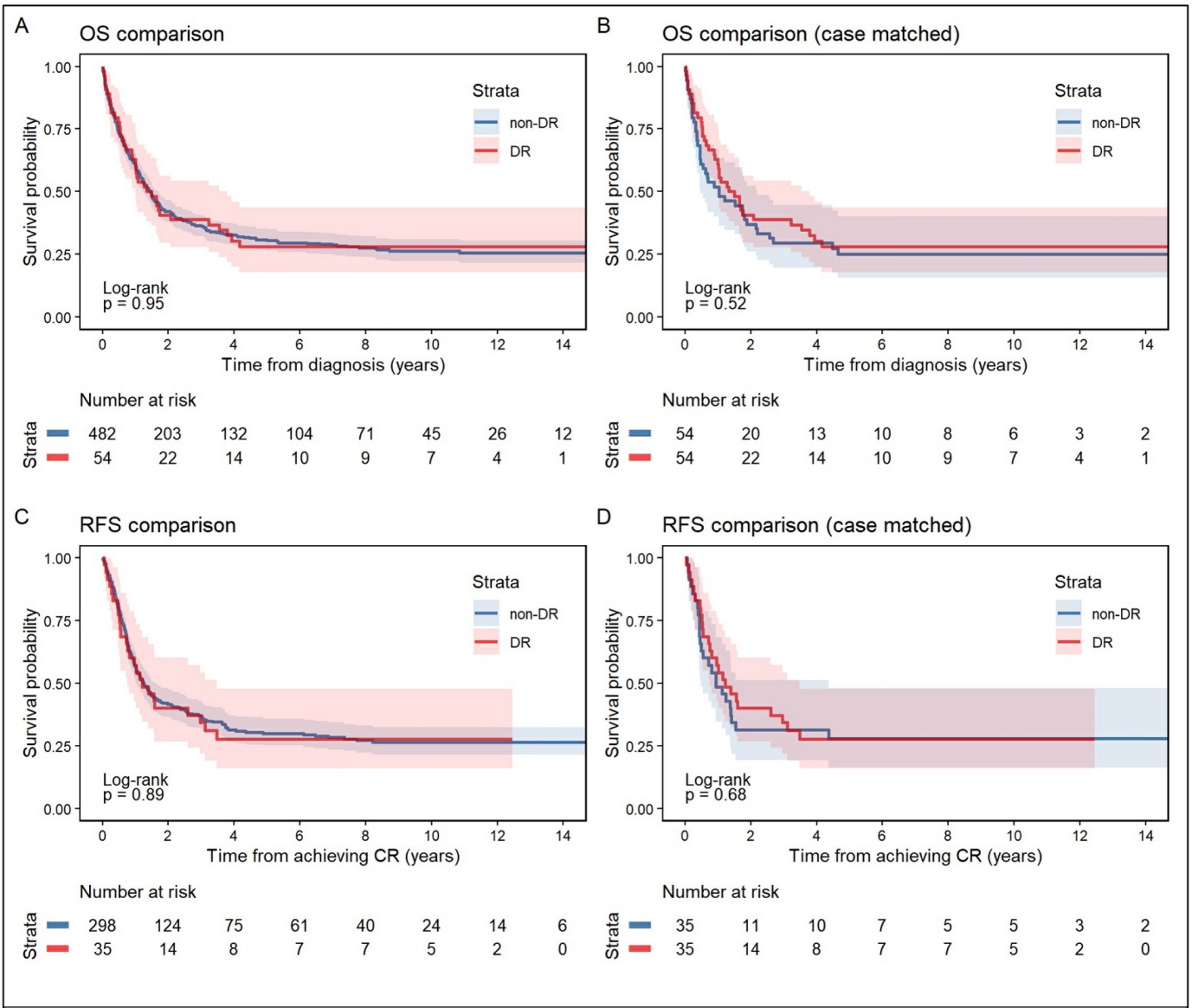
Methods:

We utilized the Danish National Acute Leukemia Registry to conduct a retrospective cohort study. Overweight (BMI≥25) AML patients aged 18-75 years and treated with IC between 2000-2012 were included. We defined DR as ≤95% of actual BSA-based chemotherapy dose. Relative risks (RR) for DR, complete remission (CR) rates, and 30- and 90-day mortality were modeled, and OS and relapse-free-survival (RFS) were calculated and compared using the 5-year restricted mean survival time difference (Δ5y-RMST).

Results:

The study population included 536 overweight AML-patients of whom 54 patients (10.1%) were categorized as DR (mean reduction 11.2%). Risk factors for DR in univariate analysis were increasing BMI (30-34.9: RR, 2.52 [95% CI, 1.32-4.71]; ≥35: RR, 4.66 [95% CI, 2.37-8.91]), increasing BSA (2.0-2.2: RR 4.61 [95% CI, 1.96-12.6]; ≥2.2: RR 15.21 [95% CI, 6.75-40.67]), therapy-related AML (RR 2.85 [95% CI, 1.12-7.24]) and favorable risk cytogenetics (RR 2.20 [95% CI, 1.02-4.33]). No significant differences were observed for rates of CR, 30- and 90-day mortality between patients receiving DR and non-DR IC. Dose reduction did not affect median RFS (DR, 14.5 [95% CI, 9.0 to 41.7] months; non-DR, 15.0 [12.3 to 19.3]) with an adjusted Δ5y-RMST of 0.2 (-8.4 to 8.8) months nor median OS (DR, 17.0 [11.9-45.5] months; non-DR, 17.5 [14.8-20.5]) with an adjusted Δ5y-RMST of 0.8 (-5.7 to 7.3) months (figure panel A+C). We constructed a case-matched cohort matched on age, sex, AML subtype and BMI (figure panel B+D) and performed a sensitivity analysis using ≤90% cut-off to define DR which led to the same conclusions.

Image:



Crude overall survival (OS), relapse-free survival (RFS), and 95% CI for patients with acute myeloid leukemia (AML) by dose reduction status, a) OS for the total cohort (n = 536), b) OS for the case matched cohort (n = 108), c) RFS for the total cohort (n = 333), and d) RFS for the case matched cohort (n = 70). Survival time is displayed as time after diagnosis (OS) or time after achieving CR (RFS). P-value from log rank test.

Summary/Conclusion: This study demonstrates that ~10% of Danish overweight AML-patients treated with IC are dose reduced ≥5% compared to full BSA-based doses. Risk factors were increasing BMI and BSA in addition

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to therapy-related AML and favorable cytogenetic risk. Importantly, our results suggest that IC dose reduction does not adversely impact AML outcomes including 30- and 90-day mortality, rates of CR, RFS and OS. However, we encourage future prospective clinical studies to address this question with specific and uniform standards or protocol specifications for dose reduction or dose capping in overweight and obese patients with AML.