Cardiovascular Disease and Diabetes Mellitus Impact Outcomes of Patients With Acute Myeloid Leukemia (AML-382)

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INTRODUCTION

The incidence of both cardiovascular disease (CVD) and acute myeloid leukemia (AML) increases with age, and patients with AML more frequently have preexisting diabetes mellitus (DM), congestive heart failure, and myocardial infarction than non-cancer patients.

We examined the influence of preexisting CVD and cardiovascular risk factors on the clinical outcomes of patients with AML.

DESIGN AND METHODS

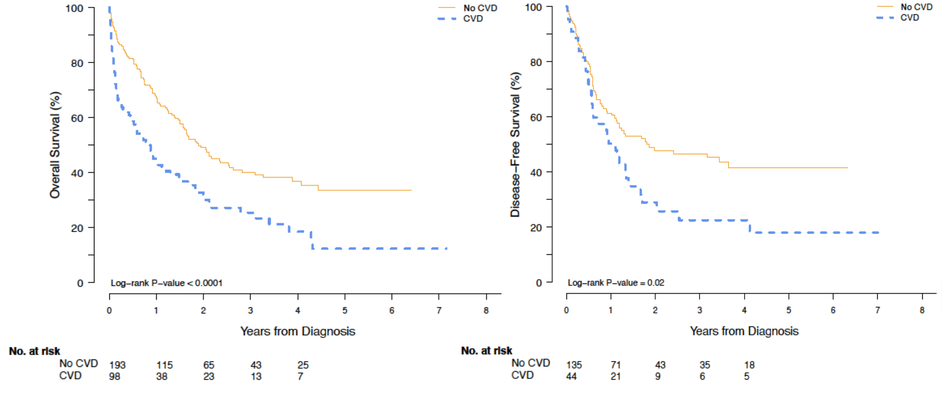
- 291 adult patients with AML with available smoking history treated at the UMMC from 2014–2020 were reviewed retrospectively.
- Comorbidities identified through chart review were analyzed individually.
- Fisher's exact and t-tests were used to compare on-study characteristics and the outcomes of patients with and without CVD.
- Response rate (CR, CRi), overall survival (OS), and cumulative incidence of relapse were evaluated.
- OS was estimated by the Kaplan–Meier method.
- The multivariable logistic regression model was used to estimate the probability of achieving the best response.

RESULTS

Table 1. Baseline characteristics (n = 291)

	All patients N = 291 (%) [range]	CVD N = 98 (%) [range]	No-CVD N = 193 (%) [range]	p-value
Age at diagnosis, yrs	64 [53 – 73]	69 [62 – 76]	61 [49 – 71]	0.0001
Gender				
• Male	172 (59)	65 (66)	107 (55)	0.07
Race				
• White	194 (67)	76 (78)	118 (61)	0.005
ECOG				
• 0 - 1	218 (84)	66 (75)	152 (88)	0.009
HEMATOLOGIC DATA				
de novo AML	192 (66)	56 (57)	136 (70)	0.02
Blood counts				
• ANC, K/mcL	1.09 [0.34 – 3.28]	1.05 [0.39 – 2.88]	1.09 [0.25 – 3.36]	0.6
• Hgb, g/dL	8.35 [7.3 – 9.6]	8.3 [7.4 – 9.4]	8.6 [7.2 – 9.7]	0.6
• Platelets, 10^9/L	49 [26 – 83]	49 [24 – 79]	49 [27 – 85]	0.9
• Peripheral blasts, %	25 [7 – 60]	20 [4 – 52]	30 [8 – 67]	0.3
Classification				
• Favorable	152 (57)	46 (54)	106 (59)	0.6
• Intermediate	45 (17)	15 (17)	30 (17)	
• Unfavorable	68 (26)	25 (29)	43 (24)	
Karyotype				
• No complex	204 (71)	69 (71)	135 (71)	0.9
Mutations				
• ASXL1	24 (13)	11 (16)	13 (10)	0.3
• FLT3-ITD	41 (15)	10 (11)	31 (18)	0.2
• FLT3-TKD	25 (11)	9 (11)	16 (11)	0.9
• IDH1	18 (9)	4 (6)	14 (11)	0.2
• IDH2	24 (12)	11 (15)	13 (10)	0.2
• JAK2	7 (4)	3 (4)	4 (3)	0.7
• RUNX1	29 (15)	8 (12)	21 (17)	0.3
• TET2	34 (18)	17 (25)	17 (14)	0.1
• TP53	43 (23)	17 (25)	26 (21)	0.5
CARDIOVASCULAR DATA				
CVD risk factors				
• Hypertension	166 (57)	78 (80)	88 (46)	<0.0001
• Hyperlipidemia	117 (40)	62 (63)	55 (28)	<0.0001
• Obesity	152 (52)	58 (59)	94 (49)	0.09
• Diabetes	71 (24)	35 (36)	36 (19)	0.001
Smoking history				
• Ever smoker	151 (52)	49 (50)	102 (53)	0.7
• Pack-years	0 [0 – 20]	0.13 [0 – 20]	0 [0 – 16]	0.4
Others				
• BMI, kg/m^2	28 [24 – 33]	30 [24 – 34]	27 [24 – 32]	0.04
• Total cholesterol, mg/dL	147 [112 – 180]	135 [107 – 164]	151 [121 – 184]	0.05
• LDL cholesterol, md/dL	79 [57 – 104]	67 [53 – 96]	85 [61 – 108]	0.08
• Hemoglobin A1c	6.6 [5.8 – 7.4]	7 [6.3 – 7.9]	6.1 [5.3 – 6.9]	0.02
• # cardiac meds	1 [0 – 3]	3 [1 – 4]	0 [0 – 2]	0.0001
• # diabetes meds	0 [0 – 0]	0 [0 – 1]	0 [0 – 0]	0.01
• Use of insulin	28 (10)	12 (12)	16 (8)	0.3

Fig 1: Overall survival and disease-free survival of AML patients (n=291)



Treatment received:

- 26% of CVD patients received anthracyclines vs 60% in the no-CVD group.

Hematologic outcomes:

- CVD was associated with a lower probability of achieving CR or CRi (0.45 vs. 0.71, p<0.001).
- DM was independently associated with a worse response to treatment (OR=0.24, 95% CI:0.08–0.80, p=0.01).
- CVD patients had worse OS than non-CVD patients (HR=1.5, 95% CI: 1.1-2.2, *P*=0.002), but no difference in cumulative incidence of relapse.
- Patients with CVD that underwent allogeneic stem cell transplant (27%) had a worse OS (HR=2, 95% CI: 1- 3.9).

Cardiovascular outcomes:

- Early cardiac events were more frequent in the CVD (48%) vs no-CVD group (2%):
  - Heart failure exacerbation: 26% vs 6% (p<0.0001).
  - Atrial fibrillation or flutter: 15% vs 5% (p=0.003).
  - Acute coronary syndrome or demand ischemia: 13% vs 2% (p=0.0003).

SUMMARY

Our study demonstrated that in one third of patients with AML, CVD is a common comorbidity, which is associated with a lower survival rate, sub-optimal treatment response, as well as an increased risk for cardiac events.

Larger randomized studies are needed to evaluate the overall impact of CVD and myeloid mutations on survival and response to treatment in AML patients.

CONCLUSION

AML patients with CVD and those with DM have worse treatment outcomes and survival. Further clinical studies are required to understand the impact of CVD on the outcomes of AML patients.

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