CARDIOVASCULAR RISK FACTORS EXHIBIT DIFFERENTIAL EFFECTS IN PATIENTS WITH MYELODYSPLASTIC NEOPLASMS THAN NON-CANCER CONTROLS

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Introduction

Clonal hematopoiesis emerging as a cardiovascular disease (CVD) risk factor has drawn attention to cardiovascular outcomes in myelodysplastic neoplasms (MDS).

CVD is the most common non-cancer cause of mortality (~25% of deaths) in MDS.

Objective

To better understand cardiovascular risk in MDS, we investigated if traditional risk factors are differentially associated with CVD in MDS and non-cancer controls.

Methods

Retrospective matched case-cohort study.

MDS patients ≥66 years were identified in SEER-Medicare between 2007-2017 and Medicare non-cancer controls, assigned a pseudodiagnosis date based on MDS distribution, were matched 1:4 based on age, sex, race, year, and region.

Baseline cardiovascular risk factors and incident CVD events were identified using ICD-9/10 codes.

Cause-specific regression estimated the risk of CVD with death as competing risk. Effect modification by MDS status was calculated with cross-product interaction terms.

Results

We included 15,227 MDS and 60,908 controls.

Table 1. Risk of Ischemic Heart Disease in MDS and controls

	Hazard Ratio (95% Confidence Interval)		
	Non-Cancer	MDS	p-interaction
Hypertension	1.13 (1.09, 1.17)	0.98 (0.91, 1.05)	<0.001
Diabetes	1.29 (1.23, 1.36)	1.26 (1.15, 1.38)	0.627
Hyperlipidemia	1.06 (1.02, 1.10)	1.22 (1.12, 1.33)	0.003
Chronic Kidney Disease	1.33 (1.24, 1.42)	1.04 (0.94, 1.14)	<0.001
Obesity	1.42 (1.25, 1.62)	1.38 (1.09, 1.74)	0.821
Tobacco	1.71 (1.48, 1.97)	0.96 (0.74, 1.24)	<0.001
Chronic lung disease	1.46 (1.37, 1.56)	1.08 (0.95, 1.21)	<0.001
Chronic liver disease	1.59 (1.40, 1.79)	0.74 (0.55, 0.98)	<0.001
Atrial fibrillation	1.50 (1.39, 1.62)	1.14 (0.98, 1.32)	0.001
Heart failure	1.87 (1.73, 2.02)	1.33 (1.19, 1.49)	<0.001
Previous stroke	1.36 (1.22, 1.51)	0.90 (0.67, 1.22)	0.013
Autoimmune Disease	1.16 (1.05, 1.27)	0.99 (0.90, 1.09)	0.021
Anemia	1.24 (1.17, 1.32)	0.88 (0.82, 0.94)	<0.001

Adjusted for age, sex, race, region, year of diagnosis

Objective

Diabetes and obesity had similar association to ischemic heart disease (IHD) in MDS and non-cancer-cases, but there was significant effect modification by MDS status in the risk of IHD associated with other risk factors.

The risk was lower in MDS for hypertension, tobacco, chronic kidney disease (CKD), atrial fibrillation, and heart failure. However, the risk of IHD associated with hyperlipidemia was higher in MDS patients than non-cancer-cases (HR=1.22 vs 1.06, p<0.001).

Table 2. Risk of Myocardial Infarction in MDS and controls

	Hazard Ratio (95% Confidence Interval)		
	Non-Cancer	MDS	p-interaction
Hypertension	1.31 (1.22, 1.40)	1.24 (1.10, 1.40)	0.468
Diabetes	1.53 (1.41, 1.67)	1.58 (1.38, 1.81)	0.699
Hyperlipidemia	1.19 (1.11, 1.28)	1.54 (1.36, 1.75)	<0.001
Chronic Kidney Disease	1.74 (1.56, 1.94)	1.21 (1.05, 1.40)	<0.001
Obesity	1.36 (1.08, 1.71)	1.47 (1.06, 2.03)	0.698
Tobacco	1.41 (1.05, 1.88)	1.24 (0.84, 1.83)	0.606
Chronic lung disease	1.59 (1.43, 1.78)	1.10 (0.92, 1.32)	<0.001
Chronic liver disease	1.13 (0.88, 1.46)	0.99 (0.65, 1.49)	0.584
Atrial fibrillation	1.14 (0.99, 1.30)	0.69 (0.52, 0.91)	0.001
Heart failure	1.78 (1.59, 1.99)	1.16 (0.99, 1.35)	<0.001
Ischemic heart disease	1.73 (1.60, 1.87)	1.55 (1.37, 1.75)	0.140
Previous stroke	1.32 (1.11, 1.58)	1.36 (0.91, 2.04)	0.893

Adjusted for age, sex, race, region, year of diagnosis

Similarly, MDS status did not influence the risk of acute myocardial infarction (AMI) associated with diabetes and obesity, but there was significant effect modification by MDS status for other factors.

The risk of AMI was lower in MDS for hypertension, CKD, atrial fibrillation, and heart failure. However, the risk of AMI associated with hyperlipidemia was higher in MDS than non-cancer-cases (HR=1.54 vs 1.19, p<0.001).

Discussion

The risk of CVD associated with traditional risk factors is modified by MDS status, explaining the poor performance of standard CVD risk prediction models in MDS.

Most risk factors have a lower association with CVD in MDS than non-cancer-cases, but the risk associated with hyperlipidemia is higher in MDS.

This should raise awareness of the impact of hyperlipidemia on cardiovascular health of MDS patients, especially since statin use is associated with improved survival.

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