Annals of Epidemiology 25 (2015) 912–917

Contents lists available at ScienceDirect

Annals of Epidemiology

journal homepage: www.annalsofepidemiology.org

Original article

Change in cardiometabolic score and incidence of cardiovascular disease: the multi-ethnic study of atherosclerosis

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ARTICLE INFO

Article history:
Received 22 May 2015
Accepted 14 September 2015
Available online 30 September 2015

Keywords:
Cardiometabolic index
Cardiovascular disease

ABSTRACT

Purpose: Examine the relationship between changes in cardiometabolic risk profiles and subsequent cardiovascular disease (CVD).
Methods: The study sample included 5557 Multi-Ethnic Study of Atherosclerosis participants, recruited in 2000 from six U.S. counties. Standardized scores were calculated for metabolic and cardiovascular components relative to accepted clinical cut points and summed to create an index of cardiometabolic risk. CVD events and/or deaths were assessed after examination 3 (years, 2004–2005) through December 2011. Cox proportional hazards models were used to examine the association between change in the cardiometabolic index (examination 3 minus examination 1) and subsequent cardiovascular outcomes adjusted for demographics, socioeconomic status, medication, and stratified by tertiles of baseline cardiometabolic risk.
Results: We found a 31% relative increase in the CVD event rate per SD change in the cardiometabolic index among those in the highest tertile of baseline cardiometabolic risk (Hazard ratio = 1.31, 95% CI = 1.14–1.50); associations were not statistically significant in the lower tertiles of baseline risk.
Conclusions: We found that larger increases in the cardiometabolic index over time were significantly associated with higher risk for subsequent CVD events among those with elevated cardiometabolic risk at baseline. These findings highlight the importance of monitoring temporal changes in risk factor profiles for predicting cardiovascular outcomes.

Introduction

Allostatic load (AL) is a multisystem, biological risk score that incorporates measures from multiple biological regulatory systems to assess overall health across these systems [1]. Each of the components usually considered in most measures of AL has been shown independently associated with cardiovascular disease (CVD), including high risk lipid levels [2], high relative weight [3], high glucose [4], high blood pressure [5], high heart rate [6], and inflammatory markers [7]. Research has suggested, however, that there is an additional predictive value for assessing these health factors in one index [1,8]. Studies have indeed shown AL to be a significant predictor of subsequent risks for overall mortality, cognitive and physical functional decline, and self-reported cardiovascular events [9,10].

We propose to extend this research by examining the association between change in AL over time and the risk for subsequent CVD events. In this study, we consider a restricted version of AL that is focused on cardiometabolic risk factors due to data availability. We recently published one of the first studies to examine changes in this cardiometabolic index over time and found a significant association between low socioeconomic status (SES) and increasing cardiometabolic index over time, among those starting out with lower levels of the cardiometabolic index at baseline (less than median) [11]. This research raised basic questions regarding the progression of cardiometabolic risk profiles over time and highlighted the overall dearth of research on changes in cardiometabolic risk, as well as the relationship between this process and subsequent “hard” outcomes, including frank CVD and CVD-related mortality.

Data from the Multi-Ethnic Study of Atherosclerosis (MESA) provide the opportunity to investigate longitudinal patterns of

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http://dx.doi.org/10.1016/j.annepidem.2015.09.006
1047-2797/

change in a multisystem index of biological risk and the relationship between such changes and subsequent CVD morbidity and mortality in a multiethnic cohort.

We propose to assess relationships between changes in cardiometabolic risk profiles during the first 4 years of follow-up (examinations 1–3) and subsequent cardiovascular events and mortality during the remaining 6–7 years of follow-up.

Material and methods

The MESA study is a prospective cohort study of the determinants of subclinical CVD with a multiethnic, population-based sample of 6814 men and women aged 45–84 years, including white, African American, Chinese, and Hispanic participants [12]. Participants were recruited from six U.S. communities: Baltimore, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; New York, New York; and St. Paul, Minnesota. The baseline examination took place July 2000 through August 2002, a second follow-up examination between September 2002 and February 2004, a third between March 2004 and September 2005, a fourth between September 2005 and May 2007, and a fifth between June 2010 and March 2012. Among those screened and eligible for the baseline examination, the participation rate was 59.8%, and the retention rates were 92.0%, 89.0%, 87.0%, and 76% of the original cohort through examinations 2–5, respectively. Details of the study design and recruitment for MESA have been published [12].

Study sample

Our study sample included MESA participants who had no CVD events before MESA examination 3 (when follow-up for incidence of CVD begins in this analysis), attended MESA examinations 1 and 3, had available data for measuring cardiometabolic risk factors at examinations 1 and 3, and had no missing follow-up data for CVD after examination 3. Of the original 6814 participants, 89 were excluded because of experiencing a CVD event before examination 3 and missing examination 3, and an additional 119 were excluded because of non–CVD-related death before examination 3. Another 142 participants were excluded because of experiencing a CVD event before examination 3 (although they attended that MESA examination). An additional 659 were excluded because of missing examination 3, and 248 participants were excluded because of missing follow-up surveillance for cardiovascular events after examination 3 ($n = 35$), missing cardiometabolic risk factor data at examination 1 or 3 ($n = 33$), missing education, home ownership or medication use ($n = 36$), or missing car/land ownership or investment data ($n = 144$). Our final study sample was $n = 5557$. As described in Table 1, those excluded from the analyses were significantly older, had higher cardiometabolic risk at each examination, included more African American, Hispanic and immigrant participants, had lower levels of SES, and higher levels of medication use at baseline.

Table 1
Frequency distributions for select characteristics

Characteristics	Study sample ($n = 5557$)	Excluded MESA sample ($n = 1257$)*
	Percentage or mean, median, SD	
Age (range, 44–84)†	61.50, 61.0, 10.04	65.03, 66.0, 10.57
Male	46.73	49.01
Race/ethnicity†		
African American	26.63	32.70
Chinese	12.02	10.82
Hispanic	21.07	25.86
White	40.27	30.63
Born outsid e the United States†	30.72	35.06
Income†		
≤$19,999	20.41	33.89
$20–39,999	25.72	25.46
$40–74,999	26.97	20.29
≥$75,000	23.97	11.61
Missing	2.93	8.75
Education†		
≤high school	33.63	47.97
some college	28.79	27.31
≥college	37.57	24.72
Wealth		
Home ownership (yes vs. no)†	69.01	58.66
Land/property ownership (yes vs. no)	30.45	27.40
Car ownership (yes vs. no)†	83.10	79.94
Investments/stocks/bonds (yes vs. no)†	64.12	50.63
Medication use at baseline		
Hypertensive medication†	35.61	44.42
Statins	14.61	15.94
Insulin†	1.39	3.62
Any new medication use at visit 2 or 3†	23.39	16.87
Cardiometabolic index at baseline (continuous)†	−7.87, −7.89, 3.83	−6.46, −6.60, 4.01
Difference in cardiometabolic index (examination 3 − examination 1)†	0.06, 0.18, 2.64	−0.61, −0.36, 3.09
Incidence of any CVD event after examination 3†	6.57	7.07
Follow-up time‡ (y; range, 0.01–7.8)†	6.68, 7.15, 1.52	6.29, 6.89, 1.83

* Sample sizes were reduced when data missing: nativity status ($n = 1235$), education ($n = 1234$), home ownership ($n = 1224$), land ($n = 635$), car ($n = 648$), investment ($n = 634$), hypertension medication ($n = 1254$), statin/insulin ($n = 1242$), cardiometabolic index ($n = 1209$), difference in index ($n = 354$), study follow-up time ($n = 213$) and incidence of CVD event ($n = 608$ including those who attended visit 3 and those who did not and still have passive MESA surveillance).

† Difference between included and excluded sample is statistically significant, $P < .05$.

‡ Follow-up time included time between examination 3 (approximately 3 years after baseline MESA examination) and end of surveillance period at year 11 of the MESA study.

Outcome

Cardiovascular disease and mortality events were ascertained based on MESA participant surveillance after examination 3 (calendar period, March 2004–September 2005) through December 31, 2011. Participants were contacted by telephone every 9–12 months and asked about hospital admission, CVD outpatient diagnoses, procedures, and deaths. Occasional medical visits were ascertained through regular MESA study examinations, participant call-ins, medical record abstractions, or obituaries. Self-reported diagnoses were all verified with copies of hospital and/or physician medical records or death certificates, and next-of-kin interviews were obtained for out of hospital CVD deaths. Two physicians independently reviewed and classified all CVD events and assigned incidence dates. In this study, we considered all CVD events according to the MESA definition, including myocardial infarction, resuscitated cardiac arrest, definite and/or probable angina, stroke, or deaths related to stroke, coronary heart disease, or other CVD.

Exposure

We use a restricted measure of AL based on the metabolic and cardiovascular markers measured in MESA [11]. We refer to this restricted measure as a cardiometabolic index to distinguish it from other more broadly based measures of AL that reflect a wider array of biological systems, including inflammatory markers and stress hormones (that were not available longitudinally in MESA) [11]. Metabolic indicators included waist-to-hip ratio, triglycerides, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein