

ASSESSING CARDIOMETABOLIC HEALTH RISK AMONG U.S. CHILDREN WHO LIVE IN GRANDPARENT-HEADED HOUSEHOLDS

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Many interventions have been designed to leverage parent-caregivers as change agents for improving children's cardiometabolic health (CMH), however very few have been designed to leverage grandparent-caregivers for that purpose. This is surprising since there has been a steady increase in children living in grandparent-headed households. As a first step in assessing the potential impact of interventions with grandparent-caregivers, we used data from the National Survey of Children's Health (2018) to compare CMH measures in children living in grandparent-headed households with CMH measures in children living in parent-headed households. Our hypothesis was that CMH risk might be higher in grandparent households – given that research shows that grandparents taking over caregiving from parents is associated with worse overall health outcomes for both grandparents and their grandchildren. Additionally, since research indicates that children who experience ≥ 4 adverse childhood experiences (ACEs) have significantly worse health outcomes, we assessed levels of ACEs. Our analytic sample included children aged 10-17 years ($n=14,941$). Adjusting for age, sex, race/ethnicity, and health insurance coverage status, children living in grandparent households were more likely to be obese (Adjusted Odds Ratio [95% confidence interval]= 2.04 [1.02, 4.09]), exposed to secondhand smoke (2.32 [1.49, 3.59]), and less likely to meet recommended age-appropriate standards for sleep (0.42 [0.27, 0.67]). The children living in grandparent households were more likely to experience ≥ 4 ACEs (8.59 [5.42, 13.62]). Our results provide indirect evidence that interventions with grandparent-caregivers may be particularly critical for improving CMH risk in families.

ASSESSMENT OF APPROPRIATENESS OF CARDIOVASCULAR PREVENTIVE MEDICATION IN ADULTS ≥ 75 YEARS

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Physicians are confronted with dilemma's on cardiovascular preventive medication for older people with complex health problems. With accumulation of diseases, limitations and shortening life expectancy, questions arise for whom cardiovascular preventive treatment is still appropriate (the expected benefits of treatment exceeds the negative consequences by a sufficiently wide margin resulting that treatment is worth doing). There is a need for more guidance in clinical situations. With the RAND/UCLA appropriateness method (RUAM), we investigated the appropriateness of cardiovascular preventive medication in adults ≥ 75 years. The RUAM

is a systematic, formalized method, to combine available scientific evidence with the collective judgment of experts. Fourteen interdisciplinary panelists (9 physicians representing 6 medical disciplines, 1 medical ethics expert, 1 pharmacist and 3 older adults [lay man]), discussed and rated the appropriateness of starting and stopping of three medication groups (cholesterol lowering, blood pressure lowering and thrombocyte aggregation inhibitors) for different clinical scenarios (combinations of cardiovascular history, systolic blood pressure, complexity of health problems, age, life-expectancy, side-effects). Depending on the medication group, different patterns of appropriateness judgments across the clinical scenarios were found. In general, absence of cardiovascular disease, presence of complex health problems, a short life-expectancy or hindering side-effects were important factors to judge cardiovascular preventive medication as inappropriate. Results were summarized into colored reading maps. These findings can offer more guidance in clinical decision making about cardiovascular preventive treatment for adults ≥ 75 years.

REDUCTION OF ELEVATED PROTON LEAK REJUVENATES MITOCHONDRIA IN THE AGED CARDIOMYOCYTE

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Rational: Aging-associated diseases, including cardiac dysfunction, are increasingly common in the population. However, the mechanisms of physiologic aging in general, and cardiac aging in particular, remain poorly understood. While effective medical interventions are available for some kinds of heart failure, one age-related impairment, diastolic dysfunction in Heart Failure with Preserved Ejection Fraction (HFpEF) is lacking a clinically effective treatment. Methods and Results: Using the pH indicator cpYFP in the model of naturally aging mice and rats, we show direct evidence of increased mitochondrial proton leak in aged heart mitochondria following a pH gradient stress. Furthermore, we identified Adenine Nucleotide Translocator 1 (ANT1) as mediating the increased proton permeability of old cardiomyocytes. Most importantly, acute (2 hours) in vitro treatment with the tetrapeptide drug SS-31 (elamipretide) reverses age-related excess proton entry, decreases the mitochondrial flash activity and mitochondrial permeability transition pore (mPTP) opening and rejuvenates mitochondrial function. Moreover, we show that SS-31 benefits the old mitochondria by direct association with ANT1 and stabilization of the mitochondrial ATP synthasome, leading to substantial reversal of diastolic dysfunction. Conclusion: Our results uncover excessive mitochondrial proton leak as a novel mechanism of age-related cardiac dysfunction and elucidate how SS-31 is able to reverse this clinically important complication of cardiac aging.

THE ASSOCIATION BETWEEN MYOCARDIAL STRAIN AND FRAILTY IN THE CARDIOVASCULAR HEALTH STUDY

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Myocardial strain, measured by speckle tracking echocardiography (STE), is a novel measure of subclinical cardiovascular disease and may reflect myocardial aging. We aimed to explore the association between myocardial strain and frailty, a clinical syndrome of impaired resilience and lack of physiologic reserve. Frailty was defined in 4,042 participants of the Cardiovascular Health Study (CHS) as having 3 or more of the following clinical criteria: weakness, slowness, shrinking, exhaustion, and inactivity. We examined the cross-sectional and longitudinal associations of left ventricular (LV) longitudinal strain, LV early diastolic strain rate and left atrial reservoir strain with frailty in participants with no history of cardiovascular disease or heart failure at the time of echocardiography. In cross-sectional analyses, LV longitudinal strain, LV early diastolic strain, left atrial reservoir strain and LV ejection fraction (measured by conventional echocardiography) levels were lower (worse) among frail participants than among those who were not frail and pre-frail ($p < 0.01$). This association of LV longitudinal strain and frailty was robust to adjustment by LV ejection fraction (adjusted OR: 1.34, 95% CI: 1.20, 2.09). Conversely, LV ejection fraction was not associated with frailty after adjustment for LV longitudinal strain. In longitudinal analyses, LV longitudinal strain and LV early diastolic strain were associated with incident frailty (adjusted OR: 1.49, 95% CI: 1.07, 2.08) and 1.65, 95% CI: 1.15, 2.25, respectively). In community-dwelling older adults without prevalent cardiovascular disease, worse LV longitudinal strain, reflective of subclinical myocardial dysfunction, was associated with frailty independent of LV ejection fraction and other risk factors.

SESSION 3024 (PAPER)

EPIDEMIOLOGY (PAPER)

ACCELERATING TRANSLATION OF INTERVENTIONS: DOES IT NEED TO TAKE 17 YEARS FOR OLDER ADULTS TO BENEFIT FROM SCIENCE?

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Translation of evidence refers to widespread dissemination, adoption and implementation of interventions that can have a significant effect on population health. However, effective translation has been slow; significant lags and inconsistent uptake impede intended benefits for older adults. In response, interest and investments in implementation science as the study of methods to promote the adoption and integration of evidence into real-world settings have rapidly increased. By definition, the methodology applies to evidence-based practices, interventions, and policies. But

the process of evidence generation can still be prolonged. This paper introduces a framework being tested at the Duke Roybal Center that integrates a model for behavioral intervention development and testing with principles of implementation science in order to accelerate translation across all phases of behavioral research. Attendees will first learn about the NIH Stage Model supported by NIA that guides researchers to identify, define, and clarify an array of activities across six stages of behavioral intervention development. These stages define components of intervention generation, pilot and then efficacy testing, effectiveness research and ultimately implementation of potent theory-driven interventions that improve health and well-being. With this foundation, the Duke framework will be presented to illustrate how concepts of several common implementation science frameworks and models can be integrated within the different stages. Interactive case studies will be used to illustrate application of this new integrated framework for evidence generation, accelerated implementation and scale-up, and pathways for translation. Integrating the Stage Model with principles from implementation science can accelerate translation.

ALLOSTATIC LOAD AND BIOLOGICAL AGING INDICATORS IN THE MIDUS NATIONAL SURVEY

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Indices quantifying allostatic load (AL) and biological aging (BA) have received widespread use in epidemiological and health science literature. However, little attention has been paid to the conceptual and quantitative overlap between these indicators. By reviewing literature utilizing measures of AL and BA, we highlight differences with respect to biological markers employed and approach toward scale construction. Further, we outline opportunities where AL indices might be improved by adopting analytical features of BA measures. We demonstrate the utility of this approach using data from The MIDUS National Survey, constructing three indices of allostatic load: one standard approach modeled after Gruenewald et al, 2012, and two alternative formulations informed by BA procedures. The performance of AL indices are juxtaposed against two commonly employed indices of biological aging: Klemera-Doubal Method Biological Age and Homeostatic Dysregulation. All measures were significantly associated with chronological age. Alternative AL formulations were more strongly associated with biological aging measures than with the standard approach. MIDUS participants with increased allostatic load and older biological ages performed worse on tests of physical, cognitive, perceptual, and subjective functioning. Further, MIDUS participants with history of childhood-trauma and mental-health problems were measured as having increased AL and BA. Alternative AL formulations tended to have effect-sizes equivalent to or larger than those observed for BA measures. In conclusion, indices of allostatic load and biological age approximate similar processes when constructed with comparable biomarkers and rigor, in line with their conceptual overlap as proxies of cumulative wear and tear.