Biomarkers of Aging: A Biological and Social Assessment | Meaghan Bailey

The growing proportion of individuals over the age of sixty-five will have noticeable social and economic effects, especially as they relate to health and health care. Since incidences of chronic disease and disability increase in individuals over sixty-five years of age,[1] it will become increasingly costly to run government supported social and economic programs as the total number of older individuals increases in the population without a corresponding increase in working individuals to support these programs. Managing these exponential costs will only be truly effective by improving our ability to prevent or cure age-dependent diseases and disorders.[2] Our ability to cope with the health needs of an older population is intricately linked to understanding the mechanisms that cause us to age in the first place, and the relationship between aging and disease.

However, the inability to quantify aging in individuals has limited the study of the biology of aging. Currently, aging is indirectly measured as a function of the increasing rate of mortality within populations. While aging contributes to the progressive increase in mortality, it is only indirectly related to life span.[3] Life span and chronological age give little indication of the dynamic changes that occur within an individual and the functional capabilities of that individual. There currently is no way to relate the population-level phenomenon of increasing mortality to the age-related biological declines within individuals. As well, the field of aging is left without a standardized measure for measuring aging in studies or monitoring potential interventions in the aging process.

The proposed solution to this problem is to find a set of biomarkers to act as a meter of the aging process. A biomarker would be a physiological or genetic parameter that changes with age, and it would predict mortality and morbidity better than chronological age.[3] It should be able to predict mortality while the majority of the population was still alive, and it would be able to predict the outcome of other age-sensitive tests.[4] A set of biomarkers would allow researchers to assess an individual's biological age, and their expected individual life span, as opposed to their chronological age.

It is difficult to quantify aging within and between individuals for two major reasons, which is primarily why biomarker research has thus far yielded no positive results. First, genotype alone does not explain the rate of aging. In human twins, as well as genetically identical organisms raised in the lab life span varies substantially. A second major problem in quantifying aging is variation within individuals. Different organ systems age at various rates within the body, so the existence of a single indicator of the rate of aging seems unlikely. Traits that most directly relate to the aging process would make the best biomarkers; that is, their effect would not be included by other variables. However, without an established theory of aging it is difficult to determine which traits or systems best reflect aging.

The main goal of this thesis is to determine whether the use of multiple biomarkers can predict mortality more accurately than chronological age. Grip strength and four biochemical

markers of kidney function were assessed as potential biomarkers of aging. These measurements and mortality data came from a data set of 432 twins from the Longitudinal Study of Aging Danish Twins. In previous studies, grip strength scores have been shown to correlate with physical functioning, and to predict all causes of mortality over a thirty-year period of time.[5] The four biochemical kidney measures—urea, urate, creatinine, and sodium—reflect kidney functioning and also have been associated with increased risk for cardiovascular disease and other causes of mortality.[6] The thesis aims to determine whether grip strength and kidney function will separately account for mortality better than age; second, it predicts that combining kidney function with grip strength will improve model's ability to account for risk of morbidity. A Cox proportional hazards regression was used to determine the influence of the covariates on survival time. Age and sex were included in the statistical analysis in order to account for their contribution to risk of mortality and to compare to the physiological variables of interest.

The results of the study show that age and sex have a fairly significant influence on mortality, but that grip strength measures and creatinine have a more substantial contribution to the risk of mortality over a seven-year period of time. In the Cox regression model of kidney variables alone, high creatinine levels had the most significant risk of mortality, followed by age and sex. In the second model, grip strength scores have a statistically significant influence on survival time, along with age and sex. When creatinine and grip strength scores were entered into the model together, they were more statistically significant in predicting morality than age and sex; as well, this model was the most statistically significant of the three models.

Although these conclusions confirmed the hypotheses of the thesis, it cannot be concluded that these two measures are biomarkers of aging. First, the number of abnormal creatinine scores was very small (N=14); second, a substantial number of individual grip strength scores over time tended to show unsteady fluctuations. Lastly, the statistical significance of the variables is affected by the number and strength of other variables entered into the model. Thus, without a strong justification based on theories of aging for the total number of variables entered, the results of the regression may be inaccurately influenced. Nonetheless, the results of this study support for the case for continuing biomarker research. Further research should look at the relationship between kidney function and grip strength to other age-related declines; it should also look at the ability of these variables to predict the outcome of age-sensitive tests.

Although biomarker research faces many biological and technical obstacles, the social impact that the discovery of valid biomarkers could have should not be disregarded. The ability to measure biological age could be an important clinical tool in assessing risk for medical procedures, or the likelihood of developing an early onset of age-related diseases. However, the results of testing biomarkers of aging could also be of great interest to insurance companies and employers who would like this information for setting premiums and retirement age, respectively. Second, the discovery of biomarkers could accelerate the development of anti-aging interventions in humans. Although interventions could compress mortality and reduce the severity of age-related declines, they also could lead to an increase in life span. Thus, ethical

issues related to enhancement and justice need to be considered as well. Despite some scientific pessimism, biomarker research should remain a fundamental part of biogerontology in order to better study aging and hopefully improve the health of an aging population.

References

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