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Evidence-Based Criteria for Sarcopenia with Clinically Important Weakness

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A recent conference sponsored by the Biomarkers Consortium of the Foundation of the National Institutes of Health (FNIH) brought together representatives from academia, health professions organizations, the private sector, the National Institutes of Health (NIH), and the Food and Drug Administration (FDA) to review and discuss new preliminary evidence for the diagnosis of sarcopenia with clinically important weakness. Sarcopenia has been defined as age-related loss of muscle mass and strength. Numerous epidemiologic studies have shown that various measures of sarcopenia are important predictors of disability and mortality, although the relationship between muscle mass and outcomes is not always consistent (^{1–5}). In recent years, multiple pathways that influence muscle growth have been elucidated and have led to promising new therapeutic opportunities to prevent or treat sarcopenia (⁶). Development of these novel molecules for clinical use has been impeded by the lack of consensus about criteria for case findings, as well as appropriate outcome measures. Two working groups have previously proposed guidelines for the definition of sarcopenia based on expert opinion (^{7,8}). However, no evidence-based consensus guidelines for the diagnosis of clinically important sarcopenia have been published.

Based on this perceived need, starting in 2008, the FNIH sponsored a consortium of investigators who pooled individual subject level data from existing data resources to develop evidence-based criteria for the definition of clinically significant weakness and low muscle mass. The consortium worked from a conceptual framework assuming that one of the main causes of mobility disability is weakness and one of the causes of weakness is low lean mass. Between 2009 and 2012, the consortium analyzed data on over 31,000 older adults representing multiple cohort studies and clinical trials.

At the conference, representatives from participating organizations initially spoke about their priorities and needs regarding the development of this relatively new area of aging. Subsequently, the Project investigators presented the data sets, explained their analytical strategies, and summarized their main findings. Primary indicators, which were selected based on prior literature, models of causation, and feasibility of use in clinical practice, included objective measures of physical performance, grip strength, and body composition by dual energy radiographic absorptiometry. Using a variety of analytical techniques, with a focus on classification and regression tree analyses, the investigators developed models using thresholds for reduced mobility performance as a gold standard to derive cut points for reduced strength and then used strength to derive cut points for reduced muscle mass. These models and cut points were then subjected to numerous sensitivity analyses.

Breakout groups, panels, and surveys were used to obtain feedback from all conference attendees on the concerns of the sponsoring organizations and on the data-based processes. Overall, there was strong support for using mobility and strength testing as the primary gold standard and relevant outcome for problems of muscle weakness and low muscle mass. Most conference participants felt that low muscle mass without weakness was not clinically relevant. Although the measurement of grip strength was acknowledged to be highly feasible in clinical settings, some participants recommended that grip strength serve only as a screen for clinically important weakness, followed by more detailed testing of lower extremity strength. Many participants felt that further data for evidence-based criteria are needed from more disabled and chronically ill populations than were available for study in the Project data sets. Based on this feedback, the investigators are pursuing further analyses, exploring potential new funding, and seeking investigative partners with relevant data sets. A summary of conference recommendations will be circulated to interested professional organizations for written commentary. The conference agenda and the slides of some of the speakers can be viewed at http://biomarkersconsortium.org/sarcopenia_pdfs.html.

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APPENDIX

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