Frailty is a relatively young area of investigation in cardiovascular research. The first wave of published research, circa 2001 to 2006, uncovered the epidemiological and pathophysiological links between frailty and cardiovascular disease (CVD). Compared to those without CVD, older adults with CVD were reported to have an odds ratio of 2.7 to 4.1 for prevalent frailty in cross-sectional studies and an odds ratio of 1.5 to 1.7 for incident frailty in the Women’s Health Initiative Observational Study (WHI-OS). The connection between frailty and CVD was reinforced by a seminal mechanistic study from Walston et al, in which the clinical phenotype of frailty was found to be independently associated with biomarkers of inflammation, coagulation, and glucose metabolism. The second wave, circa 2006 to 2016, has highlighted the prognostic value of frailty in older adults with various forms of CVD. Frailty was consistently found to be a potent risk factor (often trumping traditional risk factors in multivariable models) for mortality and major morbidity after cardiac surgery, transcatheter aortic valve replacement, myocardial infarction, percutaneous coronary intervention, and stable or unstable angina (CVD). Compared to those without CVD, older adults had worse FI scores than younger adults at baseline and more deficits seen with biological aging. The main findings can be summarized as follows: women had worse FI scores than men at baseline but similar FI progression over time and older adults had worse FI scores than younger adults at baseline and worse FI progression over time—particularly those aged ≥75 undergoing surgical revascularization therapy who accrued an average of 3 new deficits (in contrast to the predicted population average of 1 new deficit). In most other subgroups, FI scores tended to transiently improve at the 6-month assessment and then either plateau or slowly worsen at the 12-month and 30-month assessments. Greater baseline FI did not seem to be associated with worse FI progression over time although...
This was only partially addressed; it would have been informative to know whether there was an interaction between baseline FI and therapy, with the natural hypothesis being that frail patients would fare worse than their nonfrail counterparts after invasive therapeutic procedures (such as surgical revascularization). The finding that patients with greater baseline FI were more dynamic in improving or worsening may simply reflect an epiphenomenon because these patients had a greater number of deficits to potentially improve, and moreover, they may have had a higher acuity of illness to inflate their FI relative to their steady-state values.

The authors should be applauded for having had the foresight to collect these data longitudinally, a feat that was surely facilitated by leveraging the infrastructure of the ENRICA and 3C parent studies, in which repeated measures of frailty were efficiently embedded. This approach—embedding frailty measures as key covariates within larger studies—is sorely needed in contemporary cardiovascular research, where the comparative effectiveness of our proven cardiovascular therapies has yet to be elucidated in the infamous subgroup of frail older adults. The Hypertension in the Very Elderly Trial (HYVET)9 is one example where an FI was assessed at baseline and used to demonstrate that there was no interaction between frailty and hypertension treatment; in other words, frail and nonfrail patients equally benefited from the treatment. Of course, an implicit prerequisite for this type of analysis is inclusion and adequate representation of frail elders in clinical trials.

Fourth, frailty was ascertained after a relatively short period of 2.5 to 3.5 years; more frequent short-term follow-up assessments in the study by Freiheit et al8 would have been of interest to pinpoint the timing and magnitude of the nadir of postprocedural frailty, and more long-term follow-up assessments (>5 years) in the study by Graciani et al would have better captured the insidious manifestations of age-related muscle wasting and weakness. Fifth, given the small absolute changes in frailty measures observed over time, the effect size is difficult to gauge in practical terms; the so-called clinically meaningful change conferring an important increase in mortality and disability has not been explicitly defined for Fried’s scale or Rockwood’s FI (knowledge gap). Finally, an analytic concern—the core variables in both studies were analyzed in transformed categorical format using (at times arbitrary) cutoffs instead of preserving their original continuous or pseudo-continuous format; beyond the loss of statistical power (risk of type II error),10 it is not known whether the reported associations would have been as significant if different categorization schemes were used for the FI or for the number of ideal health metrics (risk of type I error).

Ultimately, one may ask, what overarching message can be drawn from these 2 studies and how can this new knowledge advance our ability to care for vulnerable older adults with CVD? A compelling lesson is that frailty is not a predetermined trait but rather a dynamic state influenced by everyday choices. Individuals may choose to forgo physical activity just as their treating physicians may choose to forgo or gloss over nonpharmacological noninterventional therapies. The downstream effect of these choices, as we have learned from the eloquent work of Graciani et al and Freiheit et al, is accelerated biological aging and frailty. Sedentary older adults with or without comorbid obesity and (pre)diabetes mellitus are at higher risk of developing frailty, and in parallel, are known to be at higher risk of presenting with coronary events and undergoing revascularization procedures.11 Once this stage is reached, frailty confers a heightened risk of having postprocedural mortality, morbidity, and deconditioning, thus perpetuating the cycle of sedentary behaviors and progressive frailty (Figure). Just as the patient and physician played a role leading up to this predicament, the former by making poor lifestyle choices and the latter by prioritizing pharmacotherapy and procedures, so too do they have an opportunity to play a joint role in the solution. According to our systematic review of randomized trials,12 prescribed physical activity is the single most robust intervention to mitigate frailty and prevent its undesirable consequences. There are many ways to engage older adults in physical activity; depending on local accessibility and patient capability, a Cochrane review concluded that both...
center-based cardiac rehabilitation programs and home-based programs were effective options. Many home-based programs have been adapted to older adults, notably, the National Institute on Aging’s Go4Life program (https://go4life.nia.nih.gov/), and simpler yet, the American Heart Association’s recommendation to perform 150 minutes per week of moderate-intensity aerobic activity, such as brisk walking, and 2 sessions per week of muscle strengthening activity. By emphasizing these healthy lifestyle behaviors, physicians can empower their patients to curb the concerning tendencies for frailty development and progression observed in the aforementioned studies.

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References


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The Road to Frailty Is Paved With Good Intentions
Jonathan Afilalo

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