

Physiological Redundancy in Older Adults in Relation to the Change with Age in the Slope of a Frailty Index

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OBJECTIVES: To test the proposition, using routinely available clinical data, that deficit accumulation results in loss of redundancy. In keeping with the reliability theory of aging, this would be quantitated by attenuation in the slope of a Frailty Index (FI) with age. The more deficits, the less steep the slope and the less redundancy.

DESIGN: Cross-sectional analysis of a prospective cohort study, with 5-year mortality data.

SETTING: The clinical sample of the second wave of the Canadian Study of Health and Aging.

PARTICIPANTS: Two thousand three hundred five people aged 70 and older at baseline.

MEASUREMENTS: A FI based on data used for a Comprehensive Geriatric Assessment (CGA), the slope of the relationship between age and the FI-CGA, the limit value of the FI-CGA, mortality.

RESULTS: An age-invariant limit to deficit accumulation was demonstrated; the observed 99% limit was 0.66. At the 25th percentile of deficit accumulation (FI-CGA \sim 0.18), the slope of the FI-CGA in relation to age was 0.044 (range 0.038–0.049). When deficits had increased to 75% of the maximum value (FI-CGA \sim 0.52), the slope fell to 0.021 (range 0.016–0.027). By the 85th percentile (FI-CGA \sim 0.6), the slope had become statistically indistinguishable from 0.

CONCLUSION: As predicted by the reliability theory of aging, the rate of deficit accumulation slows with increasing frailty. A FI derived from data routinely collected as part of a CGA can in this way quantify loss of redundancy in older adults. Quantifying loss of redundancy can aid clinical decision-making; its application to individual prognostication in clinical samples warrants further evaluation. *J Am Geriatr Soc* 58:318–323, 2010.

Key words: frailty index; deficit accumulation; comprehensive geriatric assessment; mobility; aging

Frailty is a state of vulnerability that arises with aging and undermines the ability of an organism to respond to stress.¹ It is recognized, too, as a potentially modifiable vulnerability state and therefore as a major clinical and research focus in geriatric medicine.² At this early stage in understanding, several operational definitions of frailty have emerged.^{1–5} Frailty has been defined in relation to the number of problems or impairments that people have, viewing frailty as a state that becomes more likely the greater the number of deficits that have accumulated.⁶ Deficits can be defined as symptoms, signs, diseases, disabilities, or other abnormalities. By counting the number of deficits present in an individual and dividing that count by the number of potential deficits evaluated, a “frailty index” can be calculated. For any individual, his or her frailty index value is the proportion of deficits that they have. For example, if 70 items were considered, and if an individual was found to have seven deficits, then their frailty index value would be $7/70 = 0.10$.

This approach to viewing frailty in relation to deficit accumulation has been cross-validated in several samples.^{7–14} Studying the behavior of the frailty index (e.g., its distribution or slope in relation to age) allows some insight into frailty itself. For example, just as cross-sectional studies show that the mean value of the frailty index accelerates with age, in individuals studied longitudinally, the frailty index commonly accelerates before death.¹⁴ These observations are consistent with acceleration in mortality with age and with the well-observed clinical phenomenon of a downward spiral in health in many frail older adults.

Additional evaluation of the behavior of the frailty index is needed, particularly to explore the intriguing observation that it shows a characteristic, fixed limit to deficit accumulation. This limit is manifest as an empirical maximum value to the index at approximately 0.7.¹⁵ Thus, if 70 items are considered, then the maximum number of deficits

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that people can have is not 70—a frailty index of 1.0—but closer to 50 (a frailty index value of ~ 0.7). Understanding that there is a limit to how frail an individual can be gives rise to some interest in understanding what happens as individuals approach that limit.

How, close to its limit, the slope of the frailty index in relation to age approaches 0 has been described.^{8,15} Clinically, this would appear to mean that, when people have many deficits, they are less able to tolerate even a single new insult; the most likely explanation appears to be that additional deficit accumulation results in death. In consequence, without the opportunity to accumulate more deficits, there is no relationship between the limit and age; when people reach the limit, they have little chance of growing older, even though the maximal value of the measure (theoretically a frailty index of 1.0) has not been reached.

This tendency for the slope of the frailty index in relation to age to be 0 at its highest values can not only be understood clinically, but also appears to be in keeping with the reliability theory of aging.¹⁶ Reliability theory examines systems, which are elements that in some way operate together, as more than just a set of parts. It is concerned with when these systems fail, or become unreliable. Reliability theory aims to draw from lessons about how engineered systems fail. In engineered systems, redundancy can be built in so that, if one part of the system fails, another part can be substituted. The theory suggests that, as the redundancy of any system (in biological systems, this is commonly referred to as “loss of physiological reserve”) is exhausted, it shows a lower mortality rate. In other words, as systems fail, they become less able to accumulate deficits. The reliability theory of aging expresses this formally as the so-called “compensation law of mortality.” The compensation law (building on the seminal work of Strehler and Mildvan¹⁷ among others) states that, as a system (e.g., the population of a given country) ages, the hazard rate (e.g., the mortality rate) changes in relation to the redundancy of the system. Even in a country with a high ambient mortality rate, some few people will live to exceptional old age. So too will people in more-advanced countries, but because no one country has a monopoly on extreme longevity, the mortality rates will converge for all countries. The existence of a limit means that, in countries with fewer advantages (less developed public health, more crowding, less-developed medical care), although absolute mortality will be higher, the acceleration in mortality will be lower than it is in more-advantaged countries. In other words, a lower rate of increase in mortality with age compensates for higher absolute mortality.

By extension, it seems reasonable to propose that, as the redundancy of a system is exhausted, it will show a lower rate of accumulation of deficits. In other words, similar to the “compensation law of mortality,” there may be a “compensation law of deficit accumulation.”¹⁸ Indeed, reliability theory suggests that redundancy exhaustion—mortality at the limit of survival—reflects how systems become unreliable through the accumulation of deficits (classically called “damages” in reliability theory). In short, attenuation in the slope of deficit accumulation should happen as the redundancy of the system becomes exhausted. With mortality data, this is illustrated as a change in the mortality rate, which goes to 0 at the lowest level of redundancy.

Here, a Frailty Index (FI) that was based on the items that would be collected as part of routine Comprehensive Geriatric Assessment (CGA)¹⁹ (the FI-CGA) was employed. The objective, having confirmed an empirical limit to deficit accumulation, which was hypothesized would be approximately 0.7, was to evaluate whether the FI-CGA would manifest less redundancy as a change in the slope of deficit accumulation with age. The hypothesis was that the slope of the value of the FI-CGA in relation to age would decrease as the value of the FI-CGA increased and that it would approach 0 at the limit of deficit accumulation. It was also sought further to confirm that, with increasing values of the FI-CGA, mortality would also increase, even though the rate of deficit accumulation had slowed

METHODS

Patients, Setting, and Sample

The data came from the second clinical examination of the Canadian Study of Health and Aging (CSHA-2), a cohort study of dementia and other health problems of older adults.²⁰ The CSHA-2 clinical cohort, which was enriched to study frailty, has been described in other reports.^{21–23} Briefly, in 1990/91, 9,008 community-dwelling elderly people were screened for cognitive impairment using the modified Mini-Mental State Examination (3MS).²⁴ People who screened positive and a sample who screened negative were invited for a structured clinical examination.²⁵ In 1995/96, the CSHA-2 clinical examination cohort was expanded to include more people who had screened negative for cognitive impairment. It consists of 716 residents of long-term care institutions and 1,589 community-dwelling people, of whom 767 had no cognitive impairment, 528 were cognitively impaired but did not have dementia, and 294 had dementia as adjudicated using standard criteria.

Measures

The CSHA-2 clinical examination protocol included physical performance measures, a Clinical Frailty Scale,²¹ and a standardized evaluation based on a CGA. As detailed elsewhere,²³ the data also allow for comparison with the five items that constitute the phenotypic operational definition of frailty.²⁶ Briefly, *weight loss* was defined as loss of 10 pounds or 5% of body weight in the past year. *Exhaustion* (poor endurance and energy) was based on self-report of feeling “tired all the time.” *Low physical activity* levels and energy expenditure were operationalized as needing assistance with walking or being unable to walk. *Slowness* was defined as a time of longer than 19 seconds on the Timed Up and Go (TUG) Test.²⁷ (The 19-second cutoff identifies the slowest quintile of noninstitutionalized individuals examined.) *Weakness* was identified as abnormal strength on physical examination. According to the phenotypic definition, a person is frail when he or she exhibits any three of those five characteristics.

In the standardized CGA, modeled in the CSHA-2 clinical examination, in addition to cognition, affect, and other aspects of the mental state, assessments are made of communication (vision, hearing, speech) mobility, balance, bowel and bladder function, activities of daily living, nutrition and social factors, medications, and active diagnoses.

In an earlier version of the FI-CGA using CSHA-2 data,²² deficits were grouped in each domain and scored according to domain as 0 (no problem in that domain), 0.5 (a minor problem), and 1 (a major problem). Here, reflecting a more-recent scoring of the CGA in a clinical patient series,²⁸ each item was assessed individually. For example, vision, hearing, and language were no longer combined in a single communication score but instead were each scored as individual deficits, using the convention that 0 indicates the absence of the deficit and 1 its presence. In consequence, the number of items now considered in the FI-CGA is 52, compared with 14 in the earlier version. The FI-CGA variables that included a single intermediate response (e.g., sometimes or maybe) are coded with the intermediate value 0.5. Frailty index variables can also accommodate ordinal and continuous variables as deficits. To do so requires grading the continuum or rank into a score between 0 (where no deficit is present) and 1 (where the given variable maximally expresses the deficit). The items are not weighted, although some items have grades (e.g., poor = 1, fair = 0.75, good = 0.25, and very good to excellent = 0). A list of the items is included in Appendix A; a separate report details a standard procedure for how to score a FI.⁸

Comorbidity was assessed using the Cumulative Illness Rating Scale (CIRS).²⁹ The CIRS assesses comorbidity in 14 domains, each of which is scored such that 0 = no impairment and 4 = life threatening impairment. Functional disability was scored using the CSHA-2 disability scale.¹⁹

Analysis

The FI-CGA was first evaluated to see whether it showed a skewed distribution and had a submaximal limit of approximately 0.7; these are usual characteristics of a frailty index.^{6,7} The chief test conducted was to evaluate the change in the slope of the FI-CGA in relation to age at varying degrees of deficit accumulation. As noted, reliability theory suggests that the curve should flatten (approach a 0 slope) with increasing frailty, estimated here as quartiles of the FI-CGA. Given that the relationship between the hazard rate and age is nonlinear (exponential), to calculate slopes, the data are presented on a semilogarithmic scale. The rate of accumulation of deficits was calculated by evaluating the slope (and 95% confidence intervals (CIs)) of a best fit line of the frailty index in relation to age. Finally, to evaluate deficit accumulation and mortality, the relationship between the FI-CGA and the risk of death was esti-

mated using bivariate Cox regression analysis, adjusting for age and sex.

Ethics

The research ethics committees of each institution approved the CSHA, and all participants (or their designates) signed informed-consent forms. Approval for secondary analyses of the CSHA came from the Research Ethics Committee of the Capital District Health Authority, Halifax.

RESULTS

As the FI-CGA value increased, so did the chance of being classified as frail, ill, or disabled (Table 1). The density distribution of the FI-CGA showed a typical asymmetrical pattern. The 99% upper limit value was 0.66.

Change in the Slope of the FI-CGA

In general, the mean value of the FI-CGA increases at 0.026 per year on a log scale, (95% CI = 0.022–0.029) in relation to age (Figure 1A), but at the 95% and 99% values of the FI-CGA, the slopes are statistically indistinguishable from 0 (0.0003 and 0.0001, respectively). This transition from a slope of 0.026 to a slope of 0 occurs over the entire observed course of deficit accumulation (Figure 1B). For the people with the lowest 25% of deficits, the slope of the line relating the FI-CGA to age is 0.044 (range 0.038–0.049). At the 75% value, the corresponding slope is 0.021 (range 0.016–0.027).

The change in the slope to being indistinguishable from 0 (the point of redundancy exhaustion) occurs by an FI-CGA value of approximately 0.55. The age at which, on average, redundancy exhaustion would occur is approximately 115 years.

Change in the Slope in Relation to Mortality

Although the rate of deficit accumulation declines with age, increasing values of the FI-CGA were associated with increasing mortality risk (Figure 2). Overall, the mortality risk increased from 22.4% for the one-third of people with FI-CGA values less than 0.15 to 59.9% for the one-third with FI-CGA values greater than 0.30. At the limit of the FI-CGA, 5-year mortality was 100%.

Table 1. Clinical Characteristics of People with Increasing Values of Frailty Index-Comprehensive Geriatric Assessment (FI-CGA) Score

Frailty Index Value FI-CGA Tertiles	Age, Mean ± SD	Female, %	Cumulative Illness Rating Scale Score, Mean ± SD	%			
				Frail (Phenotype) (>2 Items)	Frail (Clinical Frailty Scale) >4	Disabled ≥1 Disability	5-Year Survival
<0.15 Mean = 0.09	81.7 ± 6.2	52.6	2.8 ± 2.6	3.2	3.3	8.3	77.6
0.15–0.30 Mean = 0.21	85.1 ± 6.9	64.1	4.9 ± 3.2	30.0	38.0	47.1	52.0
>0.30 Mean = 0.41	87.8 ± 6.7	69.2	6.6 ± 3.8	74.1	87.7	74.3	40.1

SD = standard deviation.

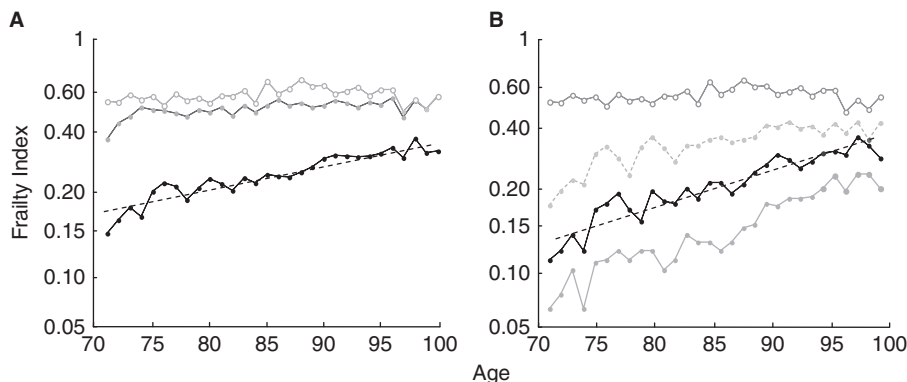


Figure 1. Loss of redundancy in relation to deficit accumulation in a Frailty Index based on Comprehensive Geriatric Assessment (FI-CGA). (A) Mean value of the FI-CGA in relation to age (lowest line). The slope of the best fit line for mean change is 0.026. The two upper lines show the 95th and 99th percentiles of the FI-CGA. (B) Mean values of the four quartiles of the FI-CGA in relation to age; as the mean value of the FI-CGA increases, the slope of the line in relation to age becomes smaller and ultimately is indistinguishable from 0.

DISCUSSION

Data were used that would be collected as part of a routine CGA to score a FI (the FI-CGA). The FI-CGA had several characteristics of other FI measures^{6,7} (including ones developed from the same database^{22,23}) with a skewed distribution and a submaximal limit (99% value 0.66). The slope of the FI-CGA in relation to age attenuated as deficits accumulated. The slope became indistinguishable from 0 at a FI-CGA value of approximately 0.55, which is approximately 85% of the observed limit to deficit accumulation.

These data must be interpreted with caution. The CSHA-2 clinical sample, although population based, is not representative. Even so, it includes many people who would be fitter than those seen in clinical practice. Also, this is a new version of the FI-CGA, which in its earlier versions, considered fewer deficits.

These data represent a test of the reliability theory of aging using an actual measure that corresponds to loss of redundancy and not a theoretical one. As such, analyses using the frailty index approach are able to draw on the considerable predictive power of that theory and apply it to human data. Briefly, the theory proposes that, as the redundancy of a system is exhausted, it tends to show less deficit accumulation, because it is less able to accumulate deficits. When the system is at the edge of failure, even a

single additional deficit can cause it to fail. So although more-reliable (robust) systems have lower absolute deficit counts, they accumulate them at a greater rate—in this sense, they age faster, even though at any given time, a person with fewer deficits is not as old—has a lower risk of death than does someone with more deficits. This is in accord with the so-called “compensation law of mortality,” in which a lower rate of accumulation “compensates for” the higher number of deficits, but the compensation comes at a price. At the limit, a system cannot age any more; if it accumulates even a single deficit, it fails. In this way, although the faster rate of aging is at odds with clinical intuition, the idea that a very frail person cannot withstand even a single more thing wrong is clinically sensible.

The limit is a matter of some interest to clinicians, and it is not an artifact. From a cross-sectional perspective, attenuation in the slopes occurs because a limit exists as a point to which all lines must converge.

Given that the individual data points that make up the FI-CGA are readily collected within specialized geriatric medicine practice, they provide some basis to conduct further clinical studies that might help quantify the concept of loss of physiological reserve. Such a quantification can help bring some precision to bear to aid in sometimes difficult clinical decisions about whether a given patient has the

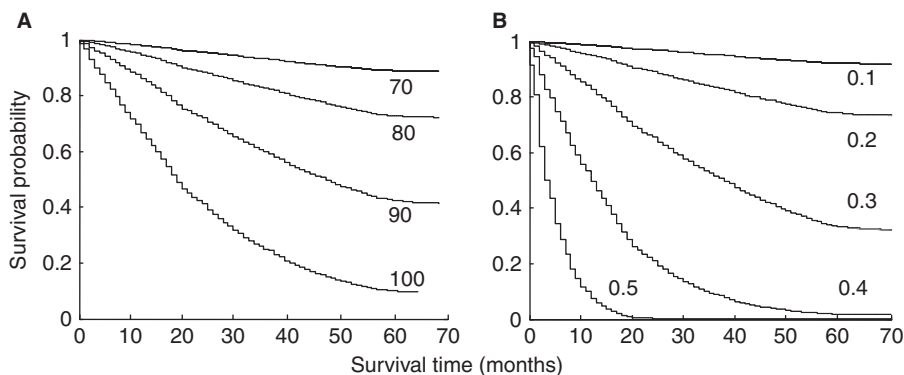


Figure 2. Survival in relation to age and frailty. (A) With increasing age strata, survival declined. (B) With increasing values of the Frailty Index based on a Comprehensive Geriatric Assessment, survival declined.

reserve to withstand a given procedure, especially those with nontrivial risk, such as many invasive interventions or others with high toxicity. This intriguing possibility is motivating additional inquiries.

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Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper.

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Appendix A. Health Variables Included in the Frailty Index-Comprehensive Geriatric Assessment

Deficit Count	List of Variables Included in the FI-CGA	Cut Point
1.	Help bathing	Yes = 1, No = 0
2.	Help dressing	Yes = 1, No = 0
3.	Help getting in/out of chair	Yes = 1, No = 0
4.	Help walking around house	Yes = 1, No = 0
5.	Help with mobility outside house	Yes = 1, No = 0
6.	Help eating	Yes = 1, No = 0
7.	Help grooming	Yes = 1, No = 0
8.	Help using toilet	Yes = 1, No = 0
9.	Help up/down stairs	Yes = 1, No = 0
10.	Help lifting 10 lbs	Yes = 1, No = 0
11.	Help shopping	Yes = 1, No = 0
12.	Help with housework	Yes = 1, No = 0
13.	Help with meal preparations	Yes = 1, No = 0
14.	Help taking medication	Yes = 1, No = 0
15.	Help with finances	Yes = 1, No = 0

(Continued)

Appendix A. (Contd.)

Deficit Count	List of Variables Included in the FI-CGA	Cut Point
16.	Urinary incontinence	Yes = 1, No = 0, catheter = 1
17.	Bowel incontinence	Yes = 1, No = 0
18.	Lost more than 10 lbs in last year	Yes = 1, No = 0
19.	Self-rating of health	Poor = 1, Fair = 0.75, Good = 0.25, Very Good to Excellent = 0
20.	History of falls	Yes = 1, No = 0
21.	Impaired vision	Yes = 1, No = 0
22.	Impaired hearing	Yes = 1, No = 0
23.	Difficulty speaking	Yes = 1, No = 0
24.	Sleep disturbance	Yes = 1, No = 0
25.	High blood pressure	Yes = 1, Suspect = 0.5, No = 0
26.	Heart rhythm disorder	Yes = 1, Suspect = 0.5, No = 0
27.	Heart attack	Yes = 1, Suspect = 0.5, No = 0
28.	Congestive heart failure	Yes = 1, Suspect = 0.5, No = 0
29.	Peripheral vascular disease	Yes = 1, Suspect = 0.5, No = 0
30.	Stroke	Yes = 1, Suspect = 0.5, No = 0
31.	Cancer	Yes = 1, Suspect = 0.5, No = 0
32.	Diabetes mellitus	Yes = 1, Suspect = 0.5, No = 0
33.	Arthritis	Yes = 1, Suspect = 0.5, No = 0
34.	Chronic lung disease	Yes = 1, Suspect = 0.5, No = 0
35.	Kidney disease	Yes = 1, Suspect = 0.5, No = 0
36.	Constipation	Yes = 1, No = 0
37.	Other medical problems	None = 0; Maximum = 2
38.	Depression	Yes = 1, Suspect = 0.5, No = 0
39.	Anxiety	Yes = 1, Suspect = 0.5, No = 0
40.	Alcohol use	Yes = 1, Suspect = 0.5, No = 0
41.	Other psychiatric illness	Yes = 1, Suspect = 0.5, No = 0
42.	Timed Up and Go	> 14 = 1, 10–14 = 0.5, < 10 = 0
43.	Functional Reach	≤ 15 = 1, 15–25 = 0.5, ≥ 25 = 0
44.	Mini-Mental State Examination	< 10 = 1, 11–17 = 0.75, 18–20 = 0.5, 20–24 = 0.25, > 24 = 0
45.	Measured systolic hypertension	> 160 = 1, > 141–160 = 0.5
46.	Measured diastolic hypertension	> 100 = 1, > 90–100 = 0.5
47.	Measured orthostatic hypotension	> 20 = 1, 14–19 = 0.5
48–52.	Medications	> 5 medications = 1, > 10 = 2, > 15 = 3, > 20 = 4,

The list of health deficit variables included in the FI and how they were coded as deficits. Cut points for performance tests were as previously standardized.⁷