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Frailty and Mortality Among Chinese at Advanced Ages

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Objectives. This study investigates the factors associated with frailty and the association of frailty with mortality in a national sample of adults aged 65–109 in China.

Methods. Using the 2002 wave of the Chinese Longitudinal Healthy Longevity Survey, we construct a frailty index (FI) based on 39 measures available in the data set. We use ordinal logistic regressions to examine the factors associated with the FI and use Weibull hazard regression to examine the association between frailty and 3-year mortality from 2002 to 2005.

Results. Age, sex, ethnicity, urban–rural residence, economic condition, religious involvement, and daily exercise are significantly associated with levels of frailty. Hazard analyses further reveal that the FI is a robust predictor of mortality at advanced ages and that the relationship between frailty and mortality is independent of various covariates.

Discussion. The measurement and analysis of frailty have broad implications for public health initiatives designed to target individuals with the diminished capacity to effectively compensate for external stressors and to prevent further declines associated with aging and mortality. A key to healthy longevity is the prevention, postponement, and potential recovery from physical and cognitive deficits at advanced ages through enhanced medical interventions and treatments.

Key Words: China—Old adults—Frailty index—Mortality.

GERIATRICIANS and gerontologists generally agree that frailty is a physiological state of nonspecific vulnerability to stressors resulting from decreased physiological reserves and the deregulation of multiple physiological systems associated with advancing age (Bortz, 2002; Campbell & Buchner, 1997; Cohen, 2000; Fried, Ferrucci, Darer, Williamson, & Anderson, 2004; Kulminski et al., 2006; Kulminski, Ukraintseva et al., 2007; Markle-Reid, 2003; Morley, Perry, & Miller, 2002; Rockwood, Mogilner, & Mitnitski, 2004; Yashin et al., 2007). Conceptually, frailty is more than an association with specific diseases or disabilities, but rather a systemic manifestation of physical and cognitive deficits—including signs, symptoms, illnesses, and impairments—that accumulate over the life course (Fried et al., 2004; Kulminski et al., 2006; Kulminski, Ukraintseva et al., 2007; Markle-Reid, 2003; Morley, Perry, & Miller, 2002; Rockwood, Mogilner, & Mitnitski, 2004; Yashin et al., 2007). Empirically, a variety of methods have been used to operationalize frailty, although the most common applications are perhaps the phenotypic approach and the frailty index (FI) (Bergman et al., 2007; Kulminski et al., 2008; Levers, Estabrooks, & Ross Kerr, 2006; Rockwood, Andrew, & Mitnitski, 2007). The phenotypic approach defines frailty based on several items, such as weight loss, exhaustion, weakness, slowness, or low physical activity, and considers any three conditions as an indication of frailty (see Fried et al., 2001). Alternatively, the FI focuses less on the specific deficits of individuals and focuses instead on the cumulative number of health deficiencies (Kulminski et al., 2006; Mitnitski et al., 2005). Despite the similarities between these two approaches, the choice of measurement is often dictated by the outcome under investigation.

Accordingly, recent research shows that FI is more applicable for predicting mortality than is the phenotypic method (Kulminski et al., 2006, 2008; Rockwood et al., 2007). In practice, most studies compute FI as the proportion of cumulative health deficits to all possible deficits for a given individual (Rockwood, 2005). Thus, FI quantifies the general concept of frailty by incorporating a variety of psychological, physiological, and functional conditions and abilities that represent an individual's balance of health assets to deficits (Fisher, 2005; Rockwood, Fox, Stolee, Robertson, & Beattie, 1994). In other words, FIs characterize basic human functioning by emphasizing the aggregate (or systemic) deterioration in psychophysiological performance (Kulminski et al., 2006) rather than focusing on the substance of the specific conditions that define the index. The validity of the FI has been demonstrated in various populations as a proxy for biological age, as a robust predictor of health change, health care utilization, and death, and as an effective tool among geriatricians and others for studying the determinants of aging and its implications for public health monitoring and intervention (Goggins, Woo, Sham, & Ho, 2005; Janssen, Shepard, Katzmarzyk, & Roubenoff, 2004; Kulminski et al., 2006; Mitnitski, Graham, Mogilner, & Rockwood, 2002; Mitnitski, Mogilner, & Rockwood, 2001; Mitnitski et al., 2005; Puts, Lips, & Deeg, 2005; Song, Mitnitski, MacKnight, & Rockwood, 2004; Yashin et al.,

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2007). We argue that FIs also provide unique insight into age-related processes such as mortality because frailty is independent of chronological age and incorporates so-called "mild-effect traits" that are typically ignored due to their limited individual effects (Kulminski, Yashin, et al., 2007).

Although there is a growing body of literature on frailty in developed countries, research is scarce in developing countries. Perhaps the most apparent lack of research on frailty is in mainland China (hereafter China), which has the world's largest oldest-old population. Compared with many Western nations, China has a rapidly aging population and a burgeoning health care system that has recently weakened despite the nation's economic growth (Yip & Hsiao, 2008). In the coming decades, China will face dramatic population aging; it remains unknown how China's unique social and cultural makeup will respond to the challenges of caring for frail elders and enhancing healthy longevity.

To our knowledge, the associations among frailty, its risk factors, and mortality have not been examined in China. Also unclear is how mortality risks are associated with levels of frailty across age. This study uses the 2002 and 2005 waves of the Chinese Longitudinal Healthy Longevity Survey (CLHLS) to examine the factors associated with age-related frailty and its association with prospective mortality. Unlike most studies, which lack adequate samples of older adults (for exceptions, see Kulminski et al., 2006; Yashin et al., 2007), we employ longitudinal data from a large national sample of adults aged 65 to 109 that includes more than 4,200 octogenarians, 3,700 nonagenarians, and over 3,000 centenarians. We conclude by discussing the implications of our results and what they mean for China's unique sociopolitical landscape and the promotion of exceptional aging for all populations.

Data and Measurement

Data

This study utilizes the 2002 and 2005 waves of the CLHLS. Initiated in 1998 as a multidisciplinary study, the CLHLS is the first nationwide longitudinal survey on the determinants of healthy longevity with the largest sample of oldest old from a developing country. The survey was conducted in half of the randomly selected counties/cities in 22 out of 31 provinces in China and interviewed all known centenarians in the sampled counties/cities with informed consent. For every centenarian with a predesignated random code, interviews were conducted for nearby adults with a predesignated age and sex who were randomly selected from the following age ranges: 65–79, 80–89, and 90–99. The term "nearby" refers to the same village or street or the same town, county, or city, where applicable. The sampling strategy is designed to include comparable numbers of randomly selected men and women at ages 65–99. Our analyses are restricted to the third and fourth waves of the CLHLS (2002 and 2005) because the first two waves of the CLHLS (1998 and 2000) recruited only adults ages 80 and older. Of the 15,919 participants sampled in 2002, 4,845 were ages 65–79 and 11,074 were ages 80–109, with 3,747 nonagenarians and 3,088 centenarians. Of the total participants (N = 15,919), 8,108 (50.9%) were reinterviewed in the 2005 wave, 5,753 (36.1%) died before 2005, and 2,058 (12.9%) were lost to follow-up.

Extensive data were collected on demographic characteristics, family and household characteristics, lifestyle, diet, psychological characteristics, economic resources, family support, self-reported health, self-reported life satisfaction, lower and upper extremities performance, instrumental activities of daily living (IADL), activities of daily (ADL), cognitive functioning, and chronic diseases suffered and their impacts on daily life. All information was obtained through in-home interviews. The dates of death for deceased respondents were collected from various sources including death certificates, next of kin, and neighborhood committees. All dates were validated, and the dates reported on death certificates were ultimately used when available—otherwise the next of kin's report was used, followed by neighborhood registries. Systematic assessments of the CLHLS regarding the accuracy of age reporting, the randomness of attrition, and the reliability, validity, and consistency of numerous measures show that data quality in the CLHLS is high (Gu, 2008; Gu & Dupre, 2008; Zeng & Gu, 2008).

Frailty Index and Covariates

To capture the cumulative health deficits of an individual (Cohen, 2000; Markle-Reid, 2003; Mitnitski et al., 2005), most studies calculate FI using multiple variables that encompass various dimensions of health and limitations (Kulminski, Ukraintseva et al., 2007; Kulminski et al., 2008; Mitnitski et al., 2005). Although studies using this approach often do not include the same number or type of indicators to estimate frailty (Rockwood et al., 2007, p. 742), it is shown that a random selection of variables yields comparable results (Rockwood, Mitnitski, Song, Steen, & Skoog, 2006); however, it is necessary to include the same indicators over time to evaluate individual change (Mitnitski et al., 2005; Rockwood et al., 2007).

Following established research (Kulminski, Yashin, et al., 2007; Mitnitski et al., 2001), we defined FI as an unweighted count of the number of deficits divided by the total number of possible deficits for a given person. We used 39 indicators of various dimensions of self-reported health status, cognitive functioning, disability, auditory and visual ability, depression, heart rhythm, and numerous chronic diseases that were collected in the 2002 CLHLS (see Appendix for all items). The items comprising our FI are similar to those used in studies from Canada (Mitnitski et al., 2005), the United States (Kulminski et al., 2006), and Hong Kong (Goggins et al., 2005). Individual items were dichotomized and coded 1 when a deficit is present. Consistent with prior research (Goggins et al., 2005), we assigned a score of 2 if the respondent had a

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Table 1. Relative Frequency Distributions of the 2002 Chinese Longitudinal Healthy Longevity Survey Variables

	Age			
	65–79	80–89	90–99	100+
Men				
Total % (*N*)	100% (2,438)	100% (2,128)	100% (1,584)	100% (655)
FI (mean)	0.10	0.19	0.26	0.32
% Non-Han ethnicity	5.3	4.8	5.1	4.4
% Urban residence	44.5	49.6	46.0	44.6
% 1+ years education	72.8	68.0	59.2	45.0
% White collar occupation	21.0	15.8	11.1	8.7
% Economic independence	61.6	38.5	28.0	19.5
% Good family economic standing	18.3	19.2	18.5	18.9
% Currently married	72.9	43.9	24.4	12.2
% High proximity to children	81.9	78.7	79.7	79.5
% Religious involvement	13.7	11.7	10.8	9.8
% Regularly exercise	44.9	43.9	35.7	30.2
% Smoked in the past 5 years	51.9	43.5	34.3	26.1
Women				
Total % (*N*)	100% (2,407)	100% (2,111)	100% (2,163)	100% (2,433)
FI (mean)	0.12	0.23	0.32	0.38
% Non-Han ethnicity	6.0	6.4	6.3	5.2
% Urban residence	43.8	52.1	43.1	44.9
% 1+ years education	30.0	18.0	13.7	9.0
% White collar occupation	5.5	3.5	2.5	1.1
% Economic independence	33.0	12.7	5.7	2.6
% Good family economic standing	15.6	15.5	17.4	16.4
% Currently married	46.7	14.5	3.2	0.7
% High proximity to children	86.8	80.7	82.5	82.2
% Religious involvement	30.4	26.1	18.2	12.1
% Regularly exercise	35.6	29.1	20.5	13.4
% Smoked in the past 5 years	11.6	10.7	9.9	7.7

serious illness that caused him/her to be hospitalized or bedridden two or more times. The FI was then computed by summing all deficits and then dividing by the total number of possible deficits (range = 0–1). To assess the validity and sensitivity of our FI, we also analyzed FIs based on different combinations of the individual indicators. We found that the results are consistent as long as the major domains of health are included in the index (i.e., ADLs, IADLs, chronic diseases, and cognitive functioning). For analytical purposes, the FI is categorized into quartiles to minimize skewness.

Table 1 lists the covariates and their frequency distributions. Based on the well-established literature on the health and mortality of older adults, we include covariates for basic demographic factors (ethnicity and urbanicity), socioeconomic status (SES) (education, primary lifetime occupation, economic independence, and family economic condition), family/social support (marital status, proximity to children, and religious participation), and health practices (regular exercise and smoking in the past five years) (see Ferrucci et al., 2003; Liang, Bennett, Sugisawa, Kobayashi, & Fukaya, 2003; Strawbridge, Shema, Cohen, & Kaplan, 2001; Stuck et al., 1999). All covariates are coded dichotomously and include non-Han ethnicity (vs. Han), urban residence (vs. rural), one or more years of education (vs. no schooling), white-collar occupation (vs. all other occupations), economic independence (coded 1 if the primary financial source for daily expenses, excluding medical costs, comes from the respondent's own work income or pension, as opposed to children, government subsidies, or other sources), good family economic standing (coded 1 if the familial economic status is reported to be "rich" or "very rich" compared with others in their community), currently married (vs. no), high proximity to children (coded 1 if coresiding or in the same neighborhood, town, or village), religious involvement (vs. no), regularly exercise (vs. no), and whether the respondent smoked in the past five years (vs. no). Although associations between these covariates and health are well established in the literature, there is the possibility of endogeneity between some covariates and the FI. For example, frailty can lead to reduced economic independence, exercise, and religious participation; therefore, interpretations of these associations should be cautious.

All measures come from the 2002 interview, and less than 2% of data are missing for all variables. Following recommendations by Landerman, Land, & Pieper (1997), we use modal and mean values to impute missing data for the categorical and continuous variables, respectively. Further details of the variable coding are available upon request.

Methods

The analyses involve two sets and are stratified by age and sex due to the well-documented sex differences in disability and mortality (e.g., Crimmins, Hayward, & Saito, 1996; Lamb, 1997) and recent evidence of sex differences

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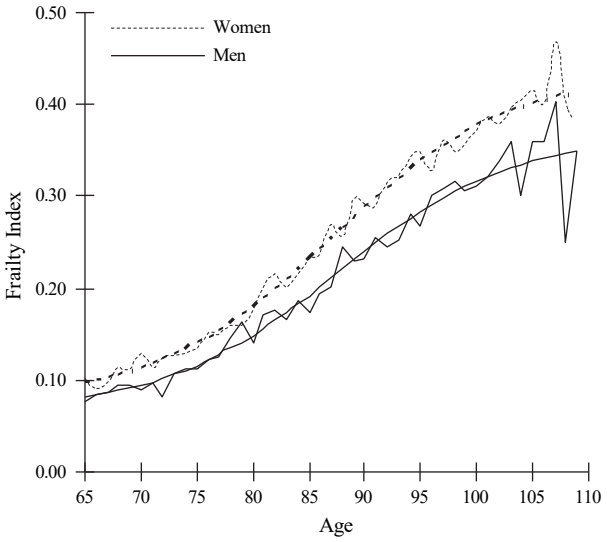


Figure 1. Observed and fitted mean frailty levels by age and sex.

in frailty (Yashin et al., 2007). First, we estimate ordinal logistic models to examine the factors associated with frailty. A test of the proportional odds assumption—that the odds ratios are proportional across the FI quartiles—indicated a violation for age and exercise variables. Although these two variables had small p values in the sensitivity testing, there was evidence to suggest that the proportional odds assumption was not necessarily invalid (Contractor & Kundu, 1998; Peterson & Harrell, 1990). In practice, the assumption is frequently violated, and alternative models often induce more stringent assumptions (Long & Freese, 2006). To be sure, we used quintile regression methods (Buchinsky, 1998) to compare estimates from various quintile intervals, and we found similar results; we also found consistent results from binary logistic models (see Bender & Grouven, 1998).

In the second set of analyses, we use hazard regression models to examine the relationship between frailty and mortality. A Weibull model is selected for the hazard analyses based on model fit and because the estimates are consistent with other full- and semiparametric hazard functions (e.g., Gompertz and Cox). To account for nonlinearity between the FI and mortality (Yashin et al., 2007), we again use FI quartiles and include two groups of covariate adjustments. Because all analyses are stratified by age group and sex, the first group of purely demographic controls includes single year of age and ethnicity (Model I); the second group further adds the remaining covariates described above (Model II). Survival time in the regression analyses is measured in days from the 2002 interview until death or the time of the 2005 interview. Additional sensitivity analyses using other percentile cut-points of the FI were conducted and the results were essentially identical. Those who were lost to follow-up in the 2005 survey were dropped from the hazard analyses because their survival status (dead or alive) was not known. Although persons lost to follow-up are more likely to be women, urban residents, have higher SES, live alone, and be in poor health (Gu, 2007), the inclusion of these individuals' estimated survival status using multiple imputation—based on their characteristics—yielded minor differences and suggested that the exclusion of those lost to follow-up introduced little bias in the estimates. Therefore, the analytic sample consists of 13,861 respondents (7,929 women and 5,932 men) with 8,108 survivors and 5,753 decedents.

All analyses are performed using Stata version 10.1 (StataCorp, 2007). The sampling weight in the publicly released CLHLS data set is calculated based on the age–sex–urban/rural residence-specific distribution of the population and does not capture other important compositional variables (e.g., marital status, economic status); therefore, we do not use weights in our multivariate analysis. Previous research shows that results from unweighted regression models produce unbiased coefficients when including variables related to sample selection (i.e., age, sex, and urbanicity) (Winship & Radbill, 1994) and that weighted regressions will unnecessarily increase standard errors (see http://www.sociology.ohio-state.edu/people/ptv/faq/weights.htm). Preliminary analyses confirmed that the overall patterns and conclusions were similar between the weighted and unweighted data.

Results

Table 1 presents sample distributions by age and sex. Several distinguishing features are evident; for instance, frailty increases with age for both women and men, and women are frailer than men at all ages. Men tend to have higher SES than women, and with the exception of family economic condition, SES declines steadily with age. As expected, the proportion of respondents who are currently married is higher for men than women but decreases dramatically with age for both sexes. The proportion of respondents with a high proximity to children is relatively stable across age, and the difference between older men and women is marginal. More women are involved in religious activities than men, although religious activity and the sex difference decrease with age. Not surprisingly, the prevalence of regular exercise and smoking in the past five years is much higher among men than women and declines steadily with age.

Figure 1 presents the observed and fitted logistic curves of the mean FI by age from 65 to 109 for men and women in 2002. Analyses (not shown) indicated that a logistic distribution describes the data better than exponential, linear, or quadratic specifications. The calculated R^2s for the fitted and observed FIs in Figure 1 are 0.95 for men and 0.98 for women, which are comparable to results among older Americans (Kulminski et al., 2006) and from grouped data from Australia, Canada, Sweden, and the United States (Mitnitski et al., 2005, p. 2187). The mean FI value for

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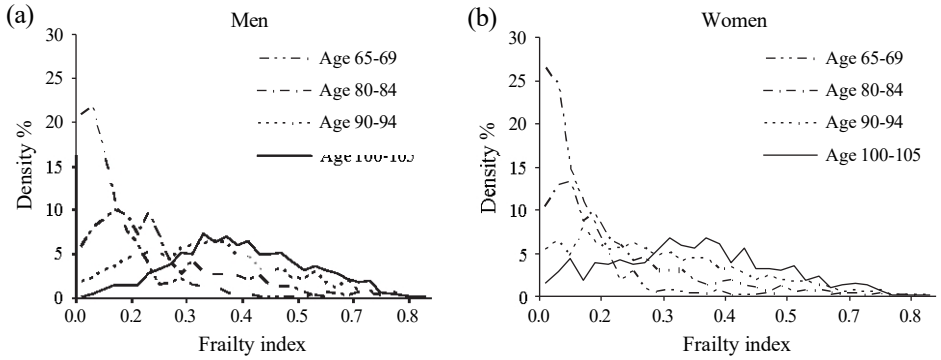


Figure 2. Observed density distributions of frailty by selected ages and sex.

women is approximately 0.10 at age 65, 0.15 at age 80, and about 0.40 by ages 100 and older. Men have lower overall levels of frailty compared with women, although they exhibit a similar pattern across age. Figure 2 illus- trates the density distributions of the FI by sex and shows that frailty levels become less skewed across age. This suggests that the absolute heterogeneity in frailty (i.e., standard deviation of the FI) increases with age, and the relative heterogeneity in frailty (i.e., the inversion of the square root of the shape parameter of the curve) decreases with age. This age pattern is not unexpected given that younger elders on average are healthier than their older counterparts—a pattern similar to that observed in the U.S. and Canada (Kulminski, Ukraintseva et al., 2007; Rockwood, Mogilner, & Mitnitski, 2004).

Table 2 presents the results from the ordinal logistic models. Consistent with Table 1, age is strongly related with increased levels of frailty for both men and women. Non-Han ethnic minorities have less frailty than the Han majority, and this finding is more pronounced among women

Table 2. Odds Ratios of the Factors Associated With Frailty by Age and Sex: Chinese Longitudinal Healthy Longevity Survey, 2002

	Age groups			
	65–79	80–89	90–99	100+
Men				
Age	1.08 (0.01)***	1.12 (0.02)***	1.12 (0.02)***	1.10 (0.06)
Non-Han (ref.: Han)	0.53 (0.10)**	0.73 (0.14)	0.45 (0.10)***	0.60 (0.27)
Urban (ref.: rural)	1.04 (0.10)	1.17 (0.12)	1.42 (0.17)**	0.82 (0.15)
1+ years education (ref.: 0)	0.68 (0.07)***	0.92 (0.09)	0.94 (0.10)	1.02 (0.18)
White collar occupation (ref.: others)	1.24 (0.15)†	1.36 (0.18)*	1.19 (0.24)	1.71 (0.75)
Economic independence (ref.: dependence)	0.99 (0.10)	0.80 (0.08)*	0.86 (0.13)	1.32 (0.35)
Good family economic standing (ref.: no)	0.89 (0.10)	0.76 (0.08)**	0.65 (0.09)**	0.80 (0.18)
Currently married (ref.: no)	0.90 (0.09)	1.04 (0.09)	0.81 (0.10)*	0.69 (0.19)
High proximity to children (ref.: no)	0.87 (0.10)	0.94 (0.10)	0.95 (0.13)	1.13 (0.27)
Religious involvement (ref.: no)	0.79 (0.10)†	0.66 (0.09)**	0.56 (0.09)***	0.39 (0.10)***
Regularly exercise (ref.: no)	0.70 (0.06)***	0.37 (0.03)***	0.25 (0.03)***	0.23 (0.04)***
Smoked in the past 5 years (ref.: no)	0.87 (0.07)	1.00 (0.09)	0.84 (0.09)	0.69 (0.13)†
N	2,438	2,128	1,584	655
-Log pseudo-likelihood	2416.8	2437.4	1603.1	563.8
Women				
Age	1.10 (0.01)***	1.12 (0.02)***	1.06 (0.02)***	1.08 (0.03)**
Non-Han (ref.: Han)	0.51 (0.10)**	0.68 (0.13)*	0.50 (0.08)***	0.45 (0.10)***
Urban (ref.: rural)	1.11 (0.11)	1.31 (0.12)*	1.23 (0.11)*	1.21 (0.11)*
1+ years education (ref.: 0)	0.98 (0.11)	1.03 (0.13)	0.98 (0.13)	1.22 (0.21)
White collar occupation (ref.: others)	1.11 (0.26)	1.09 (0.27)	1.51 (0.39)	3.41 (1.85)*
Economic independence (ref.: dependence)	0.77 (0.08)*	0.69 (0.11)*	0.76 (0.18)	0.42 (0.13)**
Good family economic standing (ref.: no)	0.52 (0.07)***	0.66 (0.08)**	0.59 (0.07)***	0.65 (0.08)***
Currently married (ref.: no)	0.87 (0.08)	0.78 (0.10)†	0.68 (0.16)	0.35 (0.14)*
High proximity to children (ref.: no)	1.05 (0.16)	1.07 (0.12)	0.84 (0.10)	0.80 (0.09)*
Religious involvement (ref.: no)	0.80 (0.08)*	0.63 (0.06)***	0.54 (0.06)***	0.52 (0.07)***
Regularly exercise (ref.: no)	0.66 (0.07)***	0.36 (0.04)***	0.28 (0.03)***	0.28 (0.03)***
Smoked in the past 5 years (ref.: no)	1.10 (0.16)	0.99 (0.14)	1.03 (0.14)	0.92 (0.15)
N	2,407	2,111	2,163	2,433
-Log pseudo-likelihood	1906.7	2395.9	2331.7	2185.0

Notes: Odds ratios are from ordinal regression models predicting frailty quartiles. Numbers in the parentheses are standard errors.
†$p < 0.1$; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

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