Co-occurrence of cardiometabolic diseases and frailty in older Chinese adults in the Beijing Longitudinal Study of Ageing

ZHÉ TANG¹, CHUNXIU WANG¹, XIAOWEI SONG², JING SHI³, ARNOLD MITNITSKI², XIANGHUA FANG¹, PULIN YU³, KENNETH ROCKWOOD¹

¹Department of Evidence-based Medicine, Xuanwu Hospital, Beijing, China
²Department of Medicine, Dalhousie University, Suite 1421-5955 Veterans’ Memorial Lane, Halifax, Nova Scotia, Canada B3H 2E1
³Beijing Institute of Geriatrics, Beijing Hospital, Beijing, China

Address correspondence to: K. Rockwood, 1421, Veterans’ Memorial Building, 5955 Veterans’ Memorial Lane, Halifax, NS. Tel: (902) 473-8687; Fax: (902) 473-1050. Email: kenneth.rockwood@dal.ca

Abstract

Background: All cardiometabolic disorders become more common with age. Frailty and increased vulnerability to adverse outcomes are also common with aging. Even so, how commonly elderly people who are affected by cardiometabolic disorders are also frail remains unclear.

Objectives: (i) To evaluate the prevalence of cardiometabolic disorders in relation to frailty. (ii) To estimate to which extent cardiometabolic diseases, when compared with frailty, affects mortality.

Methods: This is a secondary analysis of the Beijing Longitudinal Study of Ageing, a population-based representative cohort study (n = 3,257) assembled in 1992 and followed to 2007. The baseline frailty index (FI) considered 35 potential health deficits. People with an FI >0.22 were considered frail. The relationships between frailty and cardiometabolic disorders and mortality outcomes were evaluated using the Cox proportional hazard model, adjusted for baseline age, sex and education.

Results: The mean FI was 0.11 in men (SD = 0.10) and 0.14 (SD = 0.11) in women. On average, the FI increased with each cardiometabolic disorder (e.g. in men, mean ± SD = 0.16 ± 0.11 with hypertension, 0.23 ± 0.14 with stroke). As the number of disorders increased, so did the mean FI, and the proportion with the FI >0.22. For each condition, people with the FI >0.22 had a higher mortality, even after adjusting for sex, age and education.

Conclusion: Cardiometabolic disorders do not occur in isolation and commonly increase not just together, but in the presence of other health deficits. Healthcare providers who work with older adults with such problems need to develop methods to adapt their treatments to the needs of frail older adults.

Keywords: ageing, cardiometabolic disorders, frailty, frailty index, mortality, older people

Introduction

Older adult populations are typically characterised by a high prevalence of chronic diseases; this is particularly true for cardiometabolic disorders. Many of these disorders occur in older adults who are frail [1]. In previous reports, we have assessed frailty using the frailty index (FI), which is based on the accumulation of deficits and expressed as a ratio of the number of problems present in an individual to the total number of problems considered [2, 3]. For physicians who care for older adults with cardiometabolic disorders this is important. This is because frailty is likely to influence the outcomes of each such disorder; even so, how it should be incorporated in risk assessment remains largely unexplored. In addition, the effect of a comprehensive geriatric assessment in elderly adults who have been referred to cardiology service needs to be evaluated. Although frailty commonly influences the outcomes of cardiometabolic disorders [4–7], there are few systematic studies on how often the diseases occur together, or of the association between cardiometabolic disorders and frailty [5–12].
This issue is of particular concern in developing countries such as China, which has a rapidly growing elderly population. Its healthcare systems were designed chiefly for managing people with single acute illness, rather than multiple complex illnesses. China has the world’s largest population of older adults, so that this is an increasing problem; even so, it has been little studied. To explore how frailty is associated with the occurrence of cardiometabolic diseases, we used prospectively collected data from the Beijing Longitudinal Study of Ageing (BLSA). The aim of this study was to assess the prevalence of cardiometabolic disorders in a cohort of older adults and to evaluate the relation between cardiometabolic diseases and, compared with frailty, affect on mortality.

Methods

Study setting and participants

This is a secondary analysis of the BLSA, a representative cohort study with a 15-year follow-up. Community-dwelling people aged 55+ years at baseline were followed from 1992 to 2007 [n = 3,257; age (mean ± SD) = 70.1 ± 9.0; 51.1% women], during which time 51% died. A self-reported questionnaire recorded information on demographic and socio-economic characteristics, function, lifestyle, health service use, psychological and physical health and body mass index (BMI). Information regarding mortality was checked and completed by medical records.

Construction of the frailty index

As described elsewhere [13, 14], the FI was constructed following a standard procedure [15], by which the deficits included in the FI consist of any variables that contain <5% missing data, are biologically meaningful, accumulate with age, and do not saturate too early (i.e. do not always become a deficit by some relatively young age) and are present in at least 1% of the sample. This yielded 35 variables that measured health or disability [13, 14]. Deficits were either binary or 3-scale variables. For the 35 variables, 15 variables were binary; the other 20 had three levels each. For each binary variable, the presence of a deficit was coded as ‘1’ and its absence was coded as ‘0’. For each three-level variable, 0.5 represented the intermediate response level, e.g. ‘don’t hear clearly when I am spoken to’, ‘yes’ was coded as 1, ‘sometimes’ as 0.5 and ‘no’ as 0. The MMSE was coded as 0 (MMSE > 23), 0.5 (MMSE = 14–23) and 1 (MMSE ≤ 14). The CES-D was coded as 0 (CES-D < 16) and 1 (CES-D ≥ 16). For missing data, the FI was calculated based on the items which were present, i.e. the missing variable was excluded from both the numerator and the denominator. No individual had >5% missing deficit items. People with eight or more deficits (FI >0.22) were considered to be frail. The choice of cut points followed previous reports from population-based studies [3, 16–18].

Cardiometabolic diseases

Participants with hypertension, heart disease, diabetes or history of stroke/transient ischaemic attack (TIA) were identified based on self-reports of a physician’s diagnosis. The presence of one or more was considered as having ‘cardiometabolic disease’ [1].

Analysis

Results are presented as mean and standard deviations for continuous variables and percentages for discrete variables. The Cox proportional hazards model was applied to evaluate the independent association between frailty, the presence of major cardiometabolic disorders and outcomes at 180 months, adjusted for sex, age and education level. The Cox proportional survival probability curves were assessed separately for FI value-based on non-frail and frail, and for people with different cardiometabolic disorders, differences in survival between groups adjusted for sex, age and education level. Data analysis was performed using SPSS version 17.0 and Matlab version 7.1.

Results

The mean FI for the 3,257 participants in a baseline cohort was 0.11 ± 0.10 in men and 0.14 ± 0.11 in women. The mean FI was higher in people with cardiometabolic disorders and increased as the number of such disorders increased (Table 1). With any three or more cardiometabolic disorders, 28.9% of the men and 30.8% of the women were frail (i.e. had FI >0.22).

In a multivariable Cox regression analysis (Table 2), FI and cardiometabolic disorders (e.g. diabetes, heart disease and stroke) generally affected the survival after adjusting for age, sex and education. Compared with people without any such disorders, the risk in those who had just one disorder was 1.12-fold (95% CI: 1.01–1.25), and people with any three or more disorders had a 2.15-fold increase in risk (95% CI: 1.38–3.51).

For example, the probability of death after 15 years of an 80-year-old male university graduate was 36.7 (95% CI: 33.2–42.1) if he had an FI of 0.08 without any cardiometabolic disorders. The probability of death increased to 46.8 (95% CI: 40.9–51.1), if he had hypertension and heart disease. If the FI of this person was 0.38, the probability of death increased to 78.6 (95% CI: 70.9–81.3) without any cardiometabolic disorders, and the probability of death was 84.8 (95% CI: 79.3–96.9) if he also had hypertension and heart disease.

A progressively decreased survival probability was observed as the number of cardiometabolic disorders increased in both men and women (Supplementary data are available in Age and Ageing online). The 180-month survival curve showed people that had more cardiometabolic disorders generally had a higher mortality rate. Nevertheless, for each condition (e.g. 0, 1, 2, 3 and more cardiometabolic...
disorders), people with an FI >0.22 had an even higher rate of mortality (Figure 1, A–D), although this difference appeared to be less profound when ≥3 cardiometabolic disorders compared with ≤2 such disorders.

**Discussion**

We observed that older adults became more frail as the number of cardiometabolic disorders increased. The finding that women appeared to have higher FI scores than men at any given age was consistent with reports from many other datasets [19, 20]. The risk of death from cardiometabolic disorders in people significantly increased in relation to frailty, even after adjusting for age, sex and education.

Our results are consistent with studies from Western countries which have shown that cardiovascular disease (CVD) is associated with frailty [5–9]. These few studies have revealed worse outcomes in people with CVD who were frail. Identification of the combined impact of co-existing chronic diseases may help provide evidence about physiological processes that might trigger a frail state [21–24]. In our study, increased frailty was associated with one or more comorbid cardiometabolic diseases and elevated risk of adverse outcomes. This finding may gain support from research showing that abnormalities of metabolic syndrome (e.g. insulin resistance, hypertension and inflammation) was associated with frailty [10, 25–27]. This may be because frail older people display evidence of increased inflammation, with higher levels of C-reactive protein and interleukin-6 (IL-6) [28]. Other studies have previously hypothesised that inflammation plays a vital role in many chronic diseases, including CVD, anaemia, diabetes mellitus and chronic kidney disease [29–31]. In our study, the co-occurrence of inflammatory chronic diseases may play a pathophysiological role in the development of frailty. This study demonstrated that frailty affected survival in the population with cardiometabolic diseases over a

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### Table 1. Co-occurrence of frailty in relation to common cardiometabolic disorders (n = 3,257)

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>% frail (SD)</td>
</tr>
<tr>
<td>Total</td>
<td>1,593</td>
<td>12.3 (196)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>61</td>
<td>9.8 (6)</td>
</tr>
<tr>
<td>Heart disease</td>
<td>234</td>
<td>15.8 (37)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>301</td>
<td>20.9 (63)</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>142</td>
<td>44.4 (63)</td>
</tr>
<tr>
<td>BMI ≥25 kg/m²</td>
<td>350</td>
<td>13.2 (46)</td>
</tr>
<tr>
<td>0 of cardiometabolic disorders</td>
<td>890</td>
<td>10.3 (92)</td>
</tr>
<tr>
<td>1 of cardiometabolic disorders</td>
<td>419</td>
<td>11.2 (47)</td>
</tr>
<tr>
<td>2 of cardiometabolic disorders</td>
<td>201</td>
<td>16.4 (33)</td>
</tr>
<tr>
<td>3 or more of cardiometabolic disorders</td>
<td>83</td>
<td>28.9 (24)</td>
</tr>
</tbody>
</table>

TIA, transient ischaemic attack; BMI, body mass index; SD, standard deviation.

Cardiometabolic disorders denote diabetes, hypertension, heart disease, stroke/TIA and BMI ≥25 kg/m².

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### Table 2. Cox proportion hazard analysis for the FI and cardiometabolic disorders, adjusted for age, sex and education (n = 3,257)

<table>
<thead>
<tr>
<th></th>
<th>Present n (%)</th>
<th>B</th>
<th>SE</th>
<th>Hazard ratio (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (female = 1)</td>
<td>1,664 (51.1)</td>
<td>−0.189</td>
<td>0.065</td>
<td>0.83 (0.73–0.94)**</td>
</tr>
<tr>
<td>Age</td>
<td>708 (21.7)</td>
<td>0.090</td>
<td>0.004</td>
<td>1.10 (1.09–1.10)**</td>
</tr>
<tr>
<td>Education (&gt;9 years)</td>
<td>505 (15.5)</td>
<td>0.515</td>
<td>0.099</td>
<td>0.60 (0.49–0.73)**</td>
</tr>
<tr>
<td>Frailty index (FI &gt;0.22)</td>
<td>140</td>
<td>0.404</td>
<td>0.044</td>
<td>1.49 (1.12–1.98)**</td>
</tr>
<tr>
<td>Diabetes</td>
<td>658 (20.2)</td>
<td>0.125</td>
<td>0.088</td>
<td>1.13 (0.95–1.35)</td>
</tr>
<tr>
<td>Heart disease</td>
<td>140 (4.3)</td>
<td>0.242</td>
<td>0.094</td>
<td>1.27 (1.06–1.53)*</td>
</tr>
<tr>
<td>Hypertension</td>
<td>350 (13.2)</td>
<td>0.170</td>
<td>0.156</td>
<td>1.77 (1.31–2.41)**</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>840 (25.8)</td>
<td>0.074</td>
<td>0.073</td>
<td>1.07 (0.93–1.24)</td>
</tr>
<tr>
<td>BMI ≥25 kg/m²</td>
<td>904 (27.8)</td>
<td>0.074</td>
<td>0.073</td>
<td>1.12 (1.01–1.25)*</td>
</tr>
<tr>
<td>1 of cardiometabolic disorders</td>
<td>429</td>
<td>0.221</td>
<td>0.082</td>
<td>1.25 (1.06–1.47)**</td>
</tr>
<tr>
<td>2 of cardiometabolic disorders</td>
<td>190</td>
<td>0.684</td>
<td>0.192</td>
<td>2.15 (1.38–3.51)**</td>
</tr>
</tbody>
</table>

TIA, transient ischaemic attack; BMI, body mass index. β, correlation coefficient. SE, standard error.

Hazard ratio represents the risk of 15-year mortality.

Cardiometabolic disorders denote diabetes, hypertension, heart disease, stroke/TIA and BMI ≥25 kg/m².

*P < 0.05.

**P < 0.01.
long-term follow-up period. The clinical importance of this study would encourage physicians who deal in ‘chronic disease management’ to do case-finding for frailty (something they may not know a lot about) as they encounter people with many co-morbid cardiometabolic disorders (something they probably do know a lot about). These patients often have intricate situations including advanced age, falls, multifactorial health conditions and high death rates. Their management will need to look more like comprehensive geriatric assessments the frailer their patients are. Optimising therapies need to be considered in potentially delaying or reversing frailty, and preventing adverse outcomes in patients with cardiometabolic disorders.

The need for healthcare professionals to competently deal with challenges posed by frailty in patients with cardiometabolic disease is of growing importance, even if recognition of this need still lags. For example, it appears still to be necessary to make the case for geriatric medicine as the complex care of frail older adults, whose multiple, interacting medical and social problems challenge routine health care, and require comprehensive approaches to treatment [32]. The need to defend the practice of geriatric medicine, to make the case that special skills are required [33], and that the issue extends beyond being a service that feeds patients to more lucrative, procedure-driven, specialties that focus on narrowly defined problems for people who can afford such undertakings [34]. This issue also extends beyond so-called ‘multi-morbidity’, itself a narrower concept than frailty, but one that is enjoying rapid growth [35]. The growth of this idea perhaps reflects the not uncommon tendency to view frailty itself in narrow terms, as more a specific, physical syndrome than an at risk state. By drawing attention to how often patients with a set of disorders that are common in older adults are also frail, we hope to show that their needs legitimately extend beyond management of cardiometabolic disorders, into the type of complex management that is at the heart of geriatric medicine.
Our data have limitations. First, the BLSA relied on self-reported information and it is arguable such data may not be as accurate as clinical examinations. Some variables like disease diagnosis may be biased, depending on local norms. Secondly, many older participants might not possess medical records stating diseases due to the inability to access medical diagnostic services in the past in China. On the other hand, because most cardiometabolic disorders are chronic diseases, the follow-up period was only 15 years in our study and the association between the co-occurrence of cardiometabolic disorders with frailty in the elderly may need to be examined for a longer follow-up period.

In conclusion, we found the chance of frailty (and likely frailty severity) increases with more cardiometabolic diseases. Frailty was strongly and independently associated with mortality in elderly adults with cardiometabolic disorders, which do not occur in isolation and commonly increase, not just together, but in the presence of other health deficits (which were summarised as frailty). Healthcare providers who work with older adults with such problems need to develop methods to adapt their therapy to the needs of frail older adults.

Key points

- Cardiometabolic disorders do not occur in isolation and commonly increase, not just together, but in the presence of other health deficits.
- Elderly adults became more frail when the number of cardiometabolic disorders increased.
- People who had more cardiometabolic disorders generally had a higher mortality rate.
- Frailty strongly predicted the survival of the population with cardiometabolic diseases over time.

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Conflicts of interest

None declared.

Ethical approval

Approval for these secondary analyses was granted by the Research Ethics Committee of the Capital District Health Authority, Halifax, Nova Scotia, Canada.

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Supplementary data

Supplementary data mentioned in the text is available to subscribers in Age and Ageing online.

References

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