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Physical capability predicts mortality in late mid-life as well as in old age: Findings from a large British cohort study

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ABSTRACT

Introduction: Low physical capability predicts mortality, perhaps by association with co-morbidity. However, few studies include participants < 70 years old with lower co-morbidity burdens compared to older adults. We examined relationships between usual walking speed (UWS), timed chair stands speed, grip strength, standing balance and all-cause mortality in 8477 participants aged 48–92 years enrolled in the European Prospective Investigation of Cancer-Norfolk study.

Methods: Participants (55.1% female) were followed up for 6.0 years (inter-quartile range 4.6, 7.5). Associations were examined using Cox proportional hazards regression by age-group (< 70 years versus ≥70 years) and then in the whole cohort adjusted for age, sex, anthropometry, history of diabetes/stroke/myocardial infarction/cancer, smoking, alcohol intake, socioeconomic status, television viewing time and physical activity.

Results: Age and sex adjusted associations were similar in younger and older participants ($P_{interaction}$ all > 0.05) and those with lower physical capability had higher mortality risk. For example, in those < 70 years old hazard ratios (95% confidence interval) for mortality in the third, second and lowest sex-specific quartiles of UWS compared to the highest were 1.21 (0.75, 1.96), 2.11 (1.35, 3.28) and 2.91 (1.84, 4.62) and in participants ≥70 years old were 1.19 (0.73, 1.95), 2.09 (1.35, 3.24) and 2.64 (1.73, 4.02) respectively. In the whole cohort, strong associations between all physical capability tests and mortality persisted after multivariable adjustment and after excluding participants with co-morbidity.

Conclusions: Physical capability was independently predictive of future mortality risk with similar associations in late mid-life, when co-morbidity burden is lower, as at older age.

1. Introduction

Physical capability, the ability to carry out everyday activities, can be objectively measured using simple tests such as grip strength (GS), timed chair stands speed (TCSS), usual walking speed (UWS) and standing balance (SB). Low performance on these tests has been associated with higher future mortality in both community-based cohorts and patient populations (Wang et al., 2005). In particular, the association between low physical capability and higher mortality has been well described in adults over 70 years old (Cooper, Kuh, & Hardy, 2010; Studenski et al., 2011) with results of a meta-analysis suggesting a linear dose-response relationship (Cooper et al., 2010). This has led to measures such as UWS being termed the sixth 'vital sign' of health (Fritz & Lusardi, 2009) and there is growing interest in their use as markers of clinical geriatric syndromes, such as sarcopenia and frailty (Keevil & Romero-Ortuno, 2015).

However, the association between low physical capability and mortality has been less well characterised in adults < 70 years old and only a limited number of new reports have been published (Cooper, Strand, Hardy, Patel, & Kuh, 2014; Elbaz et al., 2012; Leong et al., 2015; Ortega & Silventoinen, 2012; Rantanen et al., 2012) since a meta-analysis identified this evidence gap (Cooper et al., 2010). These studies, similar to those included in the previous meta-analysis (Cooper et al., 2010), under-represent women (Elbaz et al., 2012; Ortega & Silventoinen, 2012; Rantanen et al., 2012) and often only evaluate associations between mortality and grip strength rather than

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exploring a range of physical capability measures (Leong et al., 2015; Ortega & Silventoinen, 2012; Rantanen et al., 2012). Emerging evidence from these studies suggests that the association is weaker in younger adults (Cooper et al., 2010) and that there may be a threshold effect, with only the very lowest performers experiencing increased risk of mortality (Cooper et al., 2014; Elbaz et al., 2012; Katzmarzyk & Craig, 2002; Ortega & Silventoinen, 2012), rather than the linear dose-response relationship described in older adults. A recent meta-analysis of the short physical performance battery (SPPB), which combines performance on UWS, TCS and SB tests, aimed to address part of this evidence gap and did demonstrate a linear relationship between the SPPB score and mortality in a range of community and patient populations in different geographical areas (Pavasini et al., 2016). However, none of the studies included were from the United Kingdom and only 2 included adults with a mean age of < 70 years.

If measures of physical capability are to be used in clinical practice it is important to know whether they predict mortality similarly in populations of different ages. Additionally, younger population groups are likely to have lower levels of co-morbidity than older cohorts, an important potential confounding factor in physical capability-mortality associations. Therefore, establishing whether associations differ depending on the age of participants could help us understand why low physical capability predicts mortality. Does physical capability simply reflect the underlying cumulative disease burden of older adults or is there another explanation for its association with mortality?

We used the infrastructure of the European Prospective Investigation of Cancer (EPIC)-Norfolk study to evaluate associations between a range of physical capability measures and mortality in men and women spanning a wide age range (48–92 years old). We hypothesised that if underlying co-morbidity explained the relationship, the association between low physical capability and higher mortality would be weaker in younger compared to older cohort members and a threshold effect may be evident in younger participants.

2. Materials and methods

2.1. Study population and data collection

At baseline (1993–1997) the EPIC-Norfolk study enrolled over 25 000 community-dwelling men and women (40–70 years old) who were registered with participating GP surgeries in and around the city of Norwich (Norfolk, United Kingdom). This study utilises data from 8477 men and women, now aged 48–92 years old, who underwent tests of physical capability (GS, TCSS, UWS and SB) at the study's third health examination (3HC, 2006–2011) and had complete follow-up in terms of vital status until January 31st 2015. Full details of the study design have been reported elsewhere (Hayat et al., 2014) and ethical approval was received from the Norfolk Local Research Ethics Committee and the East Norfolk and Waveney NHS Research Governance Committee.

The 3HC was held at a central research clinic. Maximum grip strength was ascertained using a hand-held Smedley Dynamometer (Scandidact, Kvistgaard, Denmark). Participants performed the test standing with their forearms bent at 90 ° and the strongest force (kilograms, kg) generated after two trials in each hand was used. UWS was measured as participants walked a 4 m course at a comfortable pace, using aids if necessary. UWS was calculated by dividing the distance walked by the average time taken out of two attempts (cm/s). TCSS was measured by asking participants to rise from a chair five times as quickly as possible with their arms folded across their chest and their feet flat on the floor. TCSS was calculated by dividing five by the time taken (stands/minute: 60*[5/time, s]). Standing balance was ascertained by asking participants to stand for 10 s with their feet apart in parallel, semi-tandem and then tandem positions. Reasons for non-participation were recorded, identifying those unable to attempt the tests for health reasons.

During the clinic appointment, weight and height were measured using digital scales (to the nearest 0.1 kg, Tanita) and a stadiometer (to the nearest 0.1 cm, Chasmores, UK). Waist circumference (WC) was also measured using a D-loop non-stretch fibreglass tape (to the nearest 0.1 cm) placed around the narrowest point between the ribs and iliac crest (or the level of the umbilicus). The average of two measurements was used.

Additionally, each participant self-reported their smoking status (current, ex-smoker, never smoker), alcohol intake (units/week), current wealth (more than enough, just enough or not enough money), television (TV) viewing (hours/day) and physical activity (active, moderately active, moderately inactive, inactive) by returning a health and lifestyle questionnaire mailed to them with their 3HC clinic appointment. In particular, physical activity was measured using a four point index derived from activity at work, at home and during leisure time, validated against daily energy expenditure (Wareham et al., 2003). Occupational social class had been ascertained at baseline using a similar questionnaire.

A history of heart attack, stroke, cancer (all cancers except non-melanoma skin cancers) and/or diabetes was established by combining self-report of these conditions at baseline (and during the 2HC, 1998-2000) with incident data captured over the follow-up period via record linkage with hospital episode statistics (International Classification of Disease [ICD] codes: non-fatal MI- ICD9 code 410 and ICD10 codes I21-I22; non-fatal stroke- ICD9 codes 430–438 and ICD10 codes I60-I69; non-fatal cancers- ICD9 codes 140–208 and ICD10 codes C00-C97; diabetes- ICD9 code 250 and ICD10 codes E10-E14). Each co-morbid condition was entered as a separate binary variable in analyses (yes/no).

Participants were followed up from the date of their 3HC clinic appointment until the date of their death or 31st January 2015. The entire cohort has been linked to the NHS Central Register for death and the Office of National Statistics (UK) for death certification since the study's inception ensuring that no participants were lost to follow-up.

2.2. Statistical analyses

Participant characteristics were described using means, medians and proportions by vital status. Relationships between physical capability and all-cause mortality were explored using Kaplan-Meier curves and Cox proportional hazard regression. For these analyses, sex-specific quartiles (Q) of maximum GS and UWS were generated, with the small number of participants who had been unable to undertake the tests for health reasons added to the lowest performance quartile (GS n = 95; UWS n = 45). TCSS 'quartiles' were also generated. However, those unable to do the TCS test for health reasons (n = 939) were categorised as the lowest performance 'quartile' (Q1) and sex-specific tertiles of TCSS became the upper three 'quartiles'. The range of each sex-specific category of physical capability are described in Table S1 (Supplementary data). SB was dichotomised into those able versus unable to hold a tandem stand for 10s. Although the standing balance test is usually scored from 0 to 4 depending on ability to stand with feet in a side-by-side and semi-tandem, as well as tandem position (Guralnik et al., 1994), very few members of our cohort were unable to complete the side-by-side and semi-tandem stands. For all physical capability measures the best performance category was chosen as the reference category, so that hazard ratios (HR) represented the risk of mortality associated with lower physical capability.

No interactions between sex and physical capability were identified (GS: p = 0.71; UWS: p = 0.47; TCSS: p = 0.53; SB: p = 0.10) so both sexes were combined in analyses. To check for violations of the proportional hazards (PH) assumption, Kaplan-Meier plots were inspected for each physical capability measure. Additionally, plots of Schoenfeld's residuals against time were inspected (Schoenfeld, 1982). No violations were identified.

To investigate the possibility of different associations with mortality in younger versus older participants, age and sex adjusted hazard ratios