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Review

The association between telomere length and frailty: A systematic review and meta-analysis

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ABSTRACT

Background: Several studies have examined the association between telomere length and frailty, but results from these studies are contradictory. Therefore, we conducted a systematic review and meta-analysis to examine the association between telomere length and frailty.

Methods: We searched the literature in Ovid (MEDLINE), Embase, PubMed, Web of Knowledge and Cochrane databases in July 2017 for studies evaluating the association of telomere length and the risk of frailty.

Results: A total of 5 studies (3268 participants) were eligible in our study. The prevalence of frailty ranged from 5.4% to 51.1%. The pooled mean difference of telomere length for the non-frail versus frail was 0.06 (95% CI: −0.01, 0.13), suggesting that no significant association was found between telomere length and frailty. In addition, the subgroup analysis indicated that telomere length was not significantly associated with the risk of frailty in all gender groups. Similar results were also found when frailty was defined by the Fried criteria (mean difference = 0.07, 95% CI: −0.03, 0.16) and frailty index (mean difference = −0.02, 95% CI: −0.05, 0.01), but not by the frailty scale (mean difference = 0.18, 95% CI: 0.04, 0.32).

Conclusion: Telomere length is not associated with the risk of frailty. Well-designed prospective studies are needed to evaluate further whether telomere length is a meaningful biological marker for frailty.

1. Introduction

Human telomeres are composed of TTAGGG tandem repeats and telomere associated proteins, which are required for regulating the cell-cycle and maintaining chromosomal integrity and stability (Blackburn, 2001; Yao and Dai, 2014). Telomere shortening has been regarded as a biomarker of aging (Mather et al., 2011) because telomere loss induces irreversible cell-cycle arrest, thus leading to cellular senescence and apoptosis (Balk et al., 2013). There is much evidence to show that shorter telomeres are closely associated with various age-related diseases such as hypertension, chronic obstructive pulmonary disease, type 2 diabetes mellitus and dementia (Albrecht et al., 2014; Forero et al., 2016; Tellechea and Pirola, 2016; Zhao et al., 2013). Shortened telomeres have also been proved to be associated with some geriatric syndromes such as depression, disability and sarcopenia (Darrow et al., 2016; Marzetti et al., 2014; Risques et al., 2010; Schutte and Malouff, 2015).

Frailty is one of the most common geriatric syndromes (Morley, 2015). It is regarded as a clinical marker of biological aging (Zhao et al., 2013) and characterised by weakness and decreased physiologic reserve, which contributes to increased risk for multiple adverse outcomes such as institutionalisation, disability and even mortality (Clegg et al., 2013). Woo et al. first reported that there was no association between telomere shortening and frailty (Woo et al., 2008). After the initial association discovery, several subsequent replicative studies have been conducted in different population cohorts, including Europeans, Asians and Africans (Collerton et al., 2012; Marzetti et al., 2014; Pathai et al., 2013; Yu et al., 2015). However, results from

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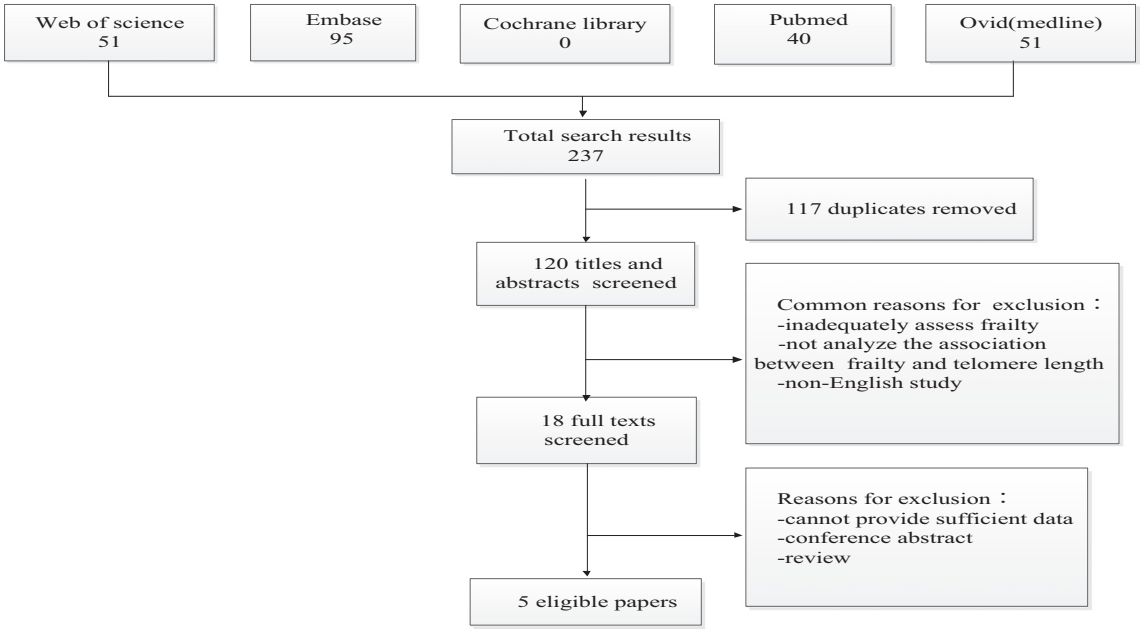

Fig. 1. Search results and study selection.

published studies on the association of telomere length with frailty were contradictory (Brault et al., 2014; Collerton et al., 2012; Marzetti et al., 2014; Pathai et al., 2013; Yu et al., 2015). No meta-analyses have specifically examined the relationship between telomere length and frailty. Therefore, the present study aimed to conduct a systematic review and meta-analysis to give a more precise estimate of the relationship between frailty and telomere length.

2. Methods

2.1. Search strategy and selection criteria

A systematic literature search was conducted in MEDLINE (Ovid SP), Embase, PubMed, Cochrane databases and Google Scholar in July 2017. The search strategy was tailored to each database and used a combination of text words such as frailty (frail elderly), telomere (telomere shortening, telomere homeostasis, telomere binding protein, telomerase inhibitor), as well as explosion MeSH terms. Truncation symbol and subject terms were also used in our search strategy. We identified potential grey studies by searching references of relevant reviews and original papers and Google Scholar.

2.2. Study selection

Literature screening was performed independently by two blinded investigators. In case of disagreement about whether a study would be included, the issue was discussed until consensus was reached by the investigators.

2.3. Inclusion and exclusion criteria

The inclusion criteria comprised the following: (i) cross-sectional, case-control or cohort studies, (ii) studies investigating the association between telomere length and frailty status, (iii) studies reporting a clear definition of frailty. Exclusion criteria comprised the following: (i) insufficient data, (ii) review or conference abstracts, (iii) language of studies in languages other than English.

2.4. Data extraction

Data were collected by two independent reviewers. The data were extracted from the included studies, including year of publication, country, study design, number of subjects, measuring methods of frailty and telomere length. Telomere length was represented as mean ± SD. The investigators cross-checked all extracted data. Disagreement was resolved when consensus was reached.

2.5. Assessment of risk of bias

Assessment of risk of bias was performed by two independent reviewers according to the Newcastle Ottawa Scale (NOS). All studies were scored in three categories, including selection, comparability and exposure/outcome. The maximum score was 9. Higher scores indicated a better literature quality.

2.6. Statistical analysis

Data were used for analysis in statistical software (RevMan, version 5.3, 2016, the Nordic Cochrane Centre, the Cochrane Collaboration, Copenhagen, Denmark). The resulting equation for conversion from base pairs to the telomere/single-copy (T/S) gene ratio is: base pairs = 3274 + 2413*(T/S). For continuous data, mean difference (MD) and corresponding 95% confidence interval (CI) were calculated. The chi-square test for Cochrane's Q statistic and I-squared were used to test heterogeneity, with thresholds of ≧25%,≧50% and≧75%, indicating low, moderate and high heterogeneity, respectively. A fixed-effects model with the mean difference (95% CIs) was undertaken by using the inverse variance method. If heterogeneity existed, the random effects model was used. Subgroup analyses were planned by age, gender, sample size, region, study quality and study design.

3. Results

3.1. Search results

The search yielded 237 relevant articles (Fig. 1). After removal of duplicates, 120 articles were screened for potential eligibility. After title and abstract screening, irrelevant articles were removed, resulting in 18