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Epidemiology of frailty in old age

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Frailty is a state of greater vulnerability to adverse health outcomes due to diminishing physiological reserves. Aging research of the last decade found evidence that frailty is associated with increased risk for falls, disability, long-term care and death. Recent studies reported 3 to 7% prevalence in people aged 65 years and older, and more than 20% in people who are greater or equal to 80 years old. Several operational definitions of frailty have been suggested over the last years. One wide-spread approach defines frailty as a clinical syndrome based on five physical indicators. Another well-known approach is based on the proposition that frailty is a nonspecific multifactorial state which is characterized by the number of health disorders accumulated by an individual. Both definitions have been validated in several studies and have shown to be frailty related, yet there is still no consensus of a generally accepted definition of frailty. Even though frailty has become a major interest of aging research, detailed epidemiological data in this field are still scarce. Current research mostly focusses on genetic and biological factors as well as behavioural and socio-demographic factors to gain better understanding of the underlying mechanisms of frailty and to identify potential preventive factors. Most recent studies come from North America and Europe. Epidemiological data for Germany have been particularly limited.

In this thesis frailty prevalence was determined by the two best established instruments to measure frailty in the elderly in a large population of of older adults from Germany. In baseline analyses of the ESTHER study including 9886 subjects aged 50-75 years, the Frailty Index (FI) was used to assess prevalence of frailty. Baseline prevalence was 9.2% and 10.5% in women and men, respectively. Age-specific prevalence of frailty ranged from 4.6% in 50-54 year old participants to 17.0% in 70-75 year old participants. The follow-up analysis after

8 years included 3112 participants, a subsample of the whole ESTHER cohort that underwent comprehensive geriatric assessments in a home visit. In this analysis, higher prevalence of frailty among women (11.4%) than among men (6.1%) and a strong rise of frailty prevalence with age was observed. Of the same subsample of 3112 participants, 2034 also participated in the 11-year follow-up home visit, underwent another comprehensive geriatric assessment and were not already frail at the 8-year examination. Of those, overall 9.2% became frail after 3 years of follow-up. Incident frailty was more often observed in women (10.8%) than in men (7.5%). The 3-year incidence rate increased with increasing age from 5.8% in the age group ≤69 years to 29.1% in the age group ≥80 years.

By using baseline data of the ESTHER study, the predictive value of frailty on mortality was also assessed. A strong association of the FI with mortality was observed which was independent of age and smoking, even for age group 50-64. Participants with high FI values had 2-3 times higher mortality than those with low FI values. There was also a strong dose-response relationship between the FI and total mortality among both men and women and among both younger (<65 years) and older subjects.

Even though both telomere length and frailty have been shown to be associated with age and age-related diseases, the results of the association analysis between telomere length and frailty showed no statistically significant relationship. However, in the analysis of oxidative stress and inflammatory biomarkers, significant associations with frailty were observed for d-ROM, where an increase of 50 units was associated with a 1.29 (95% CI: 1.17–1.43) fold increase of being frail compared to being non-frail. CRP was positively associated with frailty. An inverse significant association was observed for TTL with frailty (OR: 0.73, 0.66–0.80). Lower BAP levels were inversely associated with frailty (OR: 0.51, 95% CI: 0.32-0.79). The observed strong associations with OS biomarkers and CRP support a major role of OS and inflammation in the development of frailty and should be further investigated.