

Introduction

The COVID-19 pandemic has hit older people particularly hard. In the Netherlands, of all COVID-19 mortality, 91% takes place in people of 70 years or older (source: RIVM). Furthermore, during the pandemic, older people both with and without COVID-19 suffer more from social isolation, functional decline as a result of inactivity and delirium in case of COVID-19, which decrease quality of life. During the course of the disease, many older patients are transferred to the hospital, where they benefit from various treatments. There are however still high rates of adverse outcomes, such as delirium (1), functional decline and mortality and the conditions in the hospital in times of COVID-19 are poor with respect to palliative care (limited number of visitors) and prevention of delirium and functional decline (restricted mobility and orientation).

Older patients living with frailty have particularly poor outcomes. During the first wave of the pandemic various international studies have reported mortality rates up to 60% in older patients admitted to the hospital with frailty (2). Given these poor outcomes, it is questionable whether hospital admission is the optimal treatment for these patients. The Clinical Frailty Scale has been implemented in several guidelines (Leidraad Triage, Draaiboek Pandemie, inclusief Triage Code Zwart). In a multi-center study in the Netherlands, the COVID-OLD study, performed in 15 hospitals in the Netherlands, risk of mortality of hospitalized older patients was 38% and increased with increasing levels of frailty, as measured using the Clinical Frailty Scale (3). Interestingly, older patients with frailty presented to the hospital earlier in the disease course and with milder COVID-19 symptoms.

However, as this study only included patients referred to the hospital, it remains unclear what the value of the CFS is in referring patients to the hospitals as studies in GP practice using the CFS are scarce. Furthermore, it is unclear what the exact determinants of outcomes are that relate to the presence of frailty and the biological changes that occur with ageing and which may change disease prognosis and pharmacology treatment effect. For instance, ageing of the immune system (“immunosenescence”) and disturbed metabolic homeostasis (metabolomics) may be present in different stages in older people and may predict the course of the disease and effectiveness of pharmacological treatment. It is however unknown how these phenomena relate to clinical frailty and with outcomes in COVID-19.

Based on these knowledge gaps, two research questions were added to the FMS research agenda (see box). The work in the present project will be based largely on studies that have already been performed in large consortia, among older COVID-19 patients, among which further analyses of the COVID-OLD study and other cohort and intervention studies.

Box: Research questions related to older people in the FMS research agenda

“What is the association of frailty and biological ageing processes with disease course, mortality and functional outcomes in prevention and treatment of COVID-19 in older people” (question #4)

“Is the Clinical Frailty Scale also predictive outcomes in community-dwelling (“thuiswonende”) older people with a COVID-19 infection?” (question #4)

With the answers to these research questions, we aim to improve the treatment of older people with COVID-19 in the Netherlands on the short term:

- Further underpinning of the use and meaning of the Clinical Frailty Scale to triage for hospital referral and in-hospital treatment decisions (Leidraad, Draaiboek, guidelines)

- More effective targeting of prevention (vaccination) and treatment (both pharmacological and non-pharmacological) of older patients with COVID-19 in the hospital

Furthermore, results may impact treatment of older patients of SARS-COV-2, which is expected to become endemic and future pandemics ('pandemic preparedness'). Studying changes in treatment strategies and outcomes during the course of the pandemic (now already 12 months) may yield interesting insights for the future.

References

1. Martín-Sánchez, F.J., Del Toro, E., Cardassay, E., Valls Carbó, A., Cuesta, F., Vígara, M., Gil, P., López Picado, A.L., Martínez Valero, C., Miranda, J.D. *et al.* (2020) Clinical presentation and outcome across age categories among patients with COVID-19 admitted to a Spanish Emergency Department. *Eur Geriatr Med*, 1-13.
2. Hewitt, J., Carter, B., Vilches-Moraga, A., Quinn, T.J., Braude, P., Verduri, A., Pearce, L., Stechman, M., Short, R., Price, A. *et al.* (2020) The effect of frailty on survival in patients with COVID-19 (COPE): a multicentre, European, observational cohort study. *Lancet Public Health*, 5, e444-e451.
3. Blomaard, L.C., van der Linden, C.M.J., van der Bol, J.M., Jansen, S.W.M., Polinder-Bos, H.A., Willems, H.C., Festen, J., Barten, D.G., Borgers, A.J., Bos, J.C. *et al.* (2021) Frailty is associated with in-hospital mortality in older hospitalised COVID-19 patients in the Netherlands: the COVID-OLD study. *Age and Ageing*.