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Conclusions

- This retrospective cohort study of adults hospitalized with COVID-19 in Japan used linked insurance and annual health check (AHC) data to assess frailty and functional changes pre- and post-infection.
- Frailty increased by 57.6% within 2-62 days post-admission (p < 0.0001).
- The average post-COVID weight loss in those patients that lost weight was 2.6 kg (s.d. 2.5), substantially greater than the expected annual decline of 0.23-0.28 kg expected in older adults.
- New cognitive symptoms (e.g., forgetfulness, disorientation) and functional impairments (e.g., slower walking, increased falls) were common.

Plain language summary

- This study looked at adults in Japan who were hospitalized with COVID-19, using their healthcare billing records and data from annual check-ups.
- After hospitalisation with COVID-19, the average frailty score increased by 57.6%.
- Even longer-term declines in health were seen in the annual health check up data. For patients who lost weight, the average weight loss was 2.6 kg - much higher than typical for older adults.
- Many reported new memory issues, confusion, slower walking, and more falls after COVID-19 hospitalisation.
- These changes may affect long-term patient independence.

Introduction

- COVID-19 has imposed a substantial burden of morbidity and mortality worldwide, including in Japan. The virus was first detected in Japan on January 16, 2020, and the country experienced multiple waves of infection throughout 2020 and beyond.
- As of September 1, 2024, Japan had reported 33,803,572 confirmed COVID-19 cases and 74,694 deaths. During 2020-2021 alone, the total Quality Adjusted Life Years (QALYs) lost due to COVID-19 in Japan was estimated at 286,782 years<sup>1</sup>.
- COVID-19 has been associated with long-term health consequences, including increased frailty. Frailty is recognized as a key risk factor for poor outcomes with COVID-19 infection<sup>2</sup>.
- Many definitions for frailty exist, the most basic of which is: low grip strength, low energy, slowed walking speed, low physical activity, delirium or confusion, and/or unintentional weight loss. In a 2017 study it was estimated that 8.1% of women and 7.4% of men in Japan are frail<sup>3</sup>.
- The association of frailty and COVID-19 infection has been studied in an Italian cohort<sup>4</sup>. It found that over one-third (34.5%) of older patients hospitalized for COVID-19 scored worse on a frailty score assessment at six months follow up compared to their original score at admission, and nearly one in eight (12.4%) patients developed new frailty<sup>4</sup>.
- Japan has an annual health check (AHC) programme which provides a comprehensive medical examination of residents through employers or through voluntary participation.
- The health check involves a physical examination which includes a wide array of tests, such as weight measurements and blood tests, along with lifestyle questionnaires.
- This study sought to assess the change in frailty scores immediately pre-and post-COVID-19 infection in adults hospitalized with COVID-19. It also aimed to understand the development longer-term frailty using AHC data.

Objectives

- To descriptively summarize frailty scores before and after COVID-19 infection in the following patient subgroups: a) Overall population, b) Older (aged 65+) patients, and c) Patients with prior immunocompromised status.
- To describe any difference in health states observed in AHC data pre- and post-COVID-19 infection.

Methods

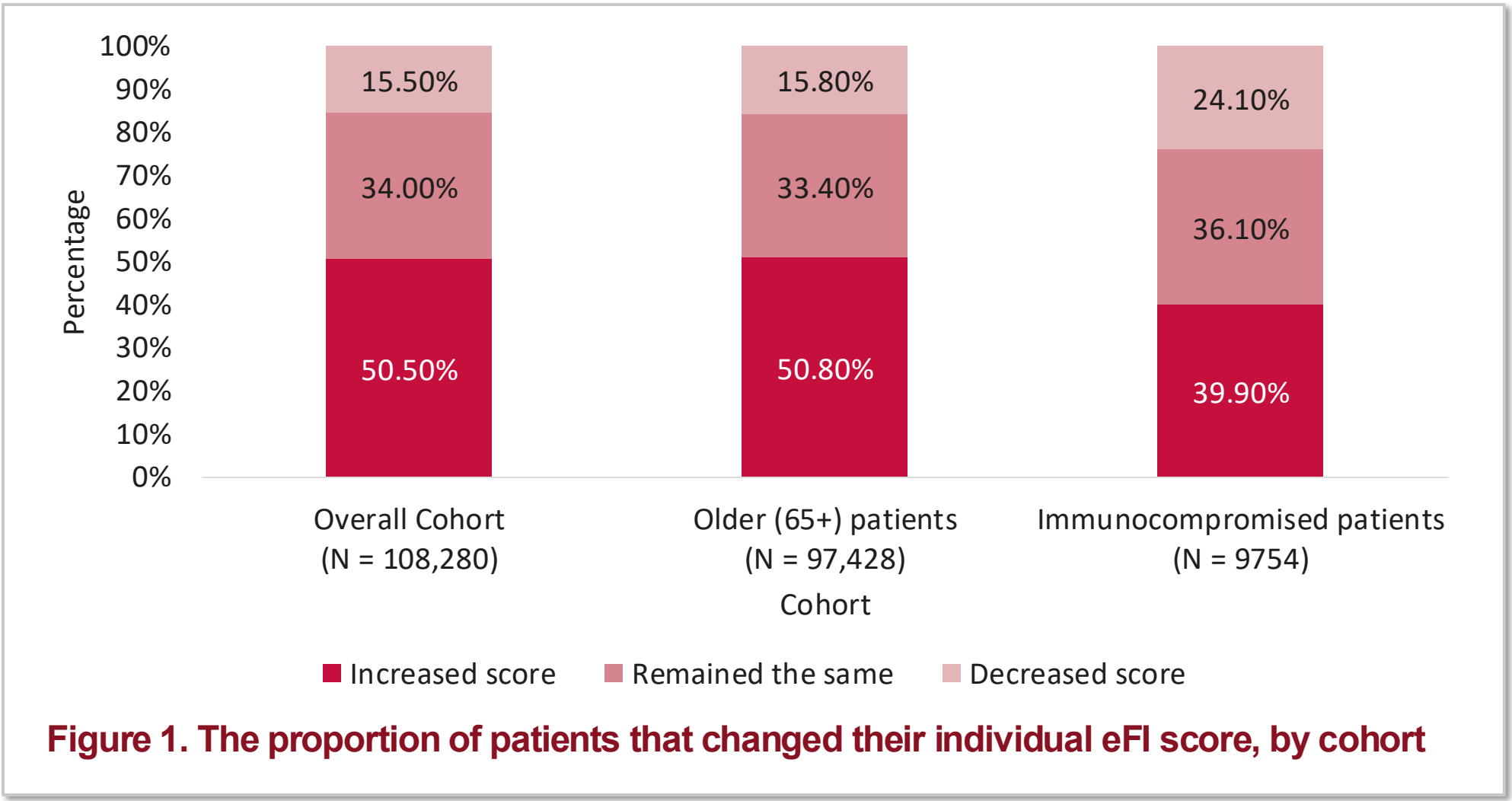
- This retrospective cohort study used linked health insurance claims and AHC data from DeSC healthcare Japan<sup>5</sup>. The study period was from January 1, 2020, to August 31, 2023.
- Adults hospitalised with diagnosed COVID-19 infection were included in the analysis. Patients were excluded if they were pregnant, under 18, died within 62 days of admission, or were enrolled in clinical studies at hospital admission.
- Prior immunocompromised status was assessed at -183 to -1 days prior to admission date.

Methods

- Frailty was assessed using a validated claims-based electronic frailty index (eFI). The eFI uses ICD-10 codes to reflect 36 deficits representing frailty<sup>6</sup>. The eFI is numerical score, where a larger score represents the frailer state of the individual<sup>6</sup>.
- The eFI was calculated for each patient using claims data from -61 to -1 days prior to admission and 2 to 62 days post-admission.
- AHC data were analysed in a subset of patients with two AHCs available spaced 250 to <480 days apart, and with variable information available from both visits.
- Paired comparisons were used to evaluate temporal changes in frailty and AHC measures.

Results

- A total of 119,976 patients met the inclusion criteria. The average age of the cohort was 80.0 (s.d. 13.5) years. Just over half of the cohort (51.3%) were female. Most patients possessed insurance through the latter-stage elderly healthcare system (82.5%), while 15.4% had national health insurance, and 2.1% had employee health insurance.
- Paired pre-post COVID-19 eFI scores were evaluable in 108,452 patients. The mean eFI score increased from 0.033 to 0.052. This represents a 57.6% increase in frailty score post-COVID-19 (p < 0.0001). At the individual level, 50.5% of patients experienced an increase in eFI. In contrast, only 15.5% of patients showed a decrease in eFI (figure 1), with the rest maintaining their eFI score.



- A total of 97,428 patients were aged ≥ 65 years. The average age of the cohort was 83.4 (s.d. 7.3) years, and 52.8% were female. The mean eFI in this group increased by 58.5% (p <0.0001, 0.034 to 0.054). At the individual level, 50.8% of patients experienced an increase in frailty score. In contrast, only 15.8% of patients showed a decrease in eFI score (figure 1).
- A total of 9,754 patients had prior immunocompromised status. The average age of the cohort was 79.1 (s.d. 10.7) years, and 27.7% were female. The mean eFI in this group increased by 19.6% (p < 0.0001, 0.044 to 0.053). At the individual level, 39.9% of patients experienced an increase in frailty score. In comparison, only 24.1% of patients showed a decrease in eFI score (figure 1).

Results

- A total of 3,799 patients in the main patient cohort had two AHCs 251- 479 days apart. The average age of the cohort was 68.0 (s.d. 16.4) years, with 42.8% female.
- Weight changes from first to second AHC were assessed. The majority (61.6%) of patients lost weight following their COVID-19 hospitalisation (table 1). The average weight loss for those that lost weight was 2.6 (s.d. 2.5) kg. This weight loss greatly exceeds the average expected annual weight decline of 0.23-0.28kg in older adults<sup>7</sup>.

Table 1. Weight changes observed\*

| Value change     | N     | %    |
|------------------|-------|------|
| Value increased  | 1,311 | 34.6 |
| Value decreased  | 2,341 | 61.7 |
| Value maintained | 142   | 3.7  |

\*where weight information available, n=3,794

- AHC questionnaire data was also assessed where available, with 19.1% of patients newly reporting losing 2-3 kg in the past few months.
- The AHC questionnaires were assessed for change in functional and cognitive attributes (Table 2). Functional deficits increased, with 15.3% newly reported walking slower than before. A further 17.4% newly reported falling down in the past year. Increases in cognitive deficits were also reported, with 10.5% newly reporting forgetfulness and 11.2% newly reported difficulty knowing what day it is.

Table 2. The percentage of patients with continued and newly developed of functional and cognitive deficits\*

| Question  | Total percentage of patients post COVID-19 infection | Percentage that were new onset after COVID-19 |
|---|--|---|
| Do you think that you are walking slower than before?   | 71.7% (1,153/1,609)                                  | 15.3%   |
| Have you fallen down in the past year?  | 29.0% (467/1,609)                                    | 17.4%   |
| Do people around you tell you that you forget things, such as "always asking the same thing"? | 28.3% (455/1,608)                                    | 10.5%   |
| Do you sometimes have trouble telling what day it is?   | 33.9% (544/1,603)                                    | 11.2%   |
| Do you have difficulty eating hard foods compared to six months ago?                          | 33.5% (540/1,610)                                    | 13.0%   |
| Do you sometimes choke on tea, soup, etc.?  | 30.3% (448/1,611)                                    | 10.9%   |
| Have you lost 2 to 3 kg or more in 6 months?  | 24.4% (392/1,609)                                    | 19.1%   |

\*where questionnaire information available pre- and post-COVID-19

Discussion and Limitations

- This study found that frailty increased substantially following COVID-19 infection, with most (50.5%) patients increasing their eFI score.
- Longer-term negative outcomes were also observed, such as rapid weight loss (in an older population) and the emergence of new cognitive and functional impairments.
- The subset of patients with AHC data were younger and may represent a more health-conscious population and may not be representative of the broader COVID-19 hospitalised population.
- COVID-19 was not required to be the primary reason for hospital admission, and therefore the cohort may include individuals with incidental infection.
- Future research should investigate whether early intervention strategies, such as antiviral treatment, could mitigate post-infection frailty progression and support functional recovery in vulnerable populations.

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**Disclosures:** This work was fully funded by Gilead Sciences, Inc. **HD, PM, MY, YP, MB and AC** are employees of Gilead Sciences, Inc., and may own stock in Gilead Sciences, Inc.

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