Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Functional dependency and COVID-19 in elderly patients with mild to moderate disease. Experience of tertiary geriatric hospital

Lubart Emily a,b,*, Gal Gilad c, Mizrahi Eliyahu Haim a,b, Goltsman Galina a,d

a The Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
b Acute Geriatric Department, Shmuel Harofe Geriatric Medical Center, POB 2, Beer Yaakov, Israel
c School of Behavioral Sciences, Tel Aviv-Yaffo Academic College, Jaffa, Israel
d Internal Medicine D Department, Asaf Harofe Medical Center, Zrifin 70300, Israel

ARTICLE INFO

Section Editor: Daniela Frasca

Keywords:
Functional dependency
COVID-19 symptoms
Time to resolution of infection

ABSTRACT

Clinical course of COVID-19 may be associated with functional dependency of geriatric patients. Data from the records of patients admitted to the COVID-19 Geriatric Unit were gathered during three months, including background, clinical aspects, time to resolution of infection and functional status.

Functionally dependent patients had higher rates of diabetes \( p = 0.03 \) and stroke \( p = 0.004 \), as well as longer time to resolution of infection \( p < 0.001 \), but less respiratory COVID-19 symptoms \( p = 0.007 \), compared to independent patients. Time to resolution of infection was longer in women \( p = 0.01 \) and positively associated with WBC level \( p < 0.01 \) and age \( p < 0.001 \). An adjusted analysis which controlled these variables confirmed the significant effect of functional status on the time to resolution of infection \( p = 0.015 \).

Functionally dependent geriatric patients with mild to moderate infection had less respiratory COVID-19 symptoms but showed longer time to resolution of infection compared to independent. Assessment of functional status in the elderly population may contribute to decision making for care of geriatric inpatients with COVID-19.

1. Introduction

Older adults are particularly affected by Severe Acute Respiratory Syndrome - Coronavirus 2 (SARS-CoV-2), responsible for the Coronavirus Disease 2019 (COVID-19), which causes a broad spectrum of clinical manifestations, higher incidence of multi-organ dysfunction and mortality (Wu and Mc Googan, 2020; J. Yang et al., 2020; X. Yang et al., 2020). Eight of ten COVID-19's deaths are in patients aged \( \geq 65 \)years (Centers for Disease Control and Prevention, 2020). This is not surprising, that geriatric patients are generally frail, cognitively impaired, bed ridden, suffer from decubitus ulcers and comorbid conditions. Chronic obstructive pulmonary disease (COPD), obesity, and diabetes mellitus have been shown to be associated with higher mortality risk, especially in COVID-19 cases (American Diabetes Association, 2018; Cortopassi et al., 2017; Kalish, 2016; J. Yang et al., 2020; X. Yang et al., 2020). However, elderly patients widely differ in their functional condition, which may be associated to both COVID-19 variants of course and mortality risk. While data about the association between functional and mental condition and the clinical profile of older adults with COVID-19 is present in the literature (Aw et al., 2020; Azarpazhooh et al., 2020; Chen et al., 2020; Lian et al., 2020; Liu et al., 2020; Plotnikov et al., 2021; Wu and Mc Googan, 2020), the prognostic value of functional dependency on COVID-19 symptoms and time to resolution of infection is scarce. The aim of this study was to compare COVID-19 symptoms and time to resolution of infection between functionally dependent and independent geriatric patients.

2. Methods

This historical prospective study was performed in a 30-beds COVID-19 unit at Shmuel Harofe hospital, a geriatric medical center affiliated to Tel Aviv University Medical School (390 beds). Only mild to moderate symptomatic patients were hospitalized in our COVID-19 unit. Thus, patients with hypoxemia \(< 94\%\) on room air or needed breathing support were not admitted.

COVID-19 diagnose was performed using reverse transcriptase polymerase chain reaction (RT-PCR) tests which is detected in samples from the throat and nasal swabs.
Data was collected from the electronic medical records of the patients (N = 98) hospitalized in the COVID-19 Unit during three months; July–September 2020. The data included background, medical history, routine treatment, clinical presentation and condition, laboratory tests at the day of hospitalization, and outcomes of COVID-19 RT-PCR tests.

The functional status was evaluated at admission by the nursing team according to the Functional Independence Measure (FIM) (Granger et al., 1989). The FIM evaluation is commonly used to rate the patients' performance with 5 cognitive and 13 motor items. The total FIM scores fall in the range between 18 (indicative of a total functional dependency) through 126 (showing a total functional independency). Accordingly, functional dependency is rated dependent/non-dependent by the attribution of points for each of seven activity daily living (ADL) functions: walking, bathing, dressing, toileting, transfer, continence and feeding. Patients with and without severe functional dependency were defined according to the FIM scores; patients with cut-point score of 72 were defined as functionally dependent (FDP) if FIM < 72, and non-functionally dependent patients (NFDP) if FIM ≥72.

COVID-19 diagnosis was based on the Xpert Xpress test on Gene Xpert Dx Instrument Systems, Cepheid. This molecular in vitro diagnostic test aids in the diagnosis and detection of RT-PCR COVID-19 in separate throat and nasal swab specimens. The samples were collected and placed into a transport tube, mixed and transferred to the sample chamber of the Xpert Xpress RT-PCR COVID-19 cartridge for automated sample processing and detection of viral RNA.

In the study period of COVID-19 outbreak in Israel throat and nasal swabs for RT-PCR COVID-19 were collected one week after the initial positive test. In case of a negative outcome, an additional swab was taken 72 hours thereafter and in case of a positive outcome the next swab was taken after 7 days. Time to resolution of infection was defined as the number of days from the date of the first positive test to the date of the second consecutive negative PCR results (i.e., effective negative). Later, from November 2020, the discharge criteria were changed and based on ten days from the beginning of COVID-19 infection and symptoms only, while the PCR test was no longer applied.

2.1. Statistical analysis

Bivariate associations were tested using Pearson correlations, chi-square, and t-tests. An adjusted analysis of the time to resolution of infection performed using an analysis of covariance (ANCOVA). Possible confounders were added to the analysis according to their associations with both the dependent variable and the main factor (functional status). The threshold significance of confounders’ associations was set on a significance of p < 0.1. Statistical significance was defined according to α = 0.05, two-tailed. Analysis performed using SPSS 25 software (IBM Inc.).

3. Results

The patients were mostly women 54 (65%), average age was 84.5 ± 7.1 years (mean ± SD). According to functional status, measures 54 patients (55%) were FDP and 44 (45%) NFDP. FDP were older (88.2 ± 3.9) compared to NFDP (80.0 ± 7.6) (t = 6.9, df = 96, p < 0.001). A higher rate of women (67.2%) compared to men (32.8%) (72, and non-functionally dependent patients. The second main finding was that FDP had longer time to resolution of respiratory COVID-19 symptoms, such as cough and dyspnea compared to NFDP. The main finding was that FDP had longer time to resolution of infection compared to NFDP.

It is well known that age can make the diagnosis more complex, as older adults with infections frequently have atypical manifestations (Gómez-Belda et al., 2020; Limpawattana et al., 2016), that make common infections, such as pneumonia less likely to present with classicpipe (e.g., cough and sputum production), and they more commonly present with a change in cognitive (e.g., confusion) or physical function (e.g., inability to perform ADL or falls) (Berman et al., 1986; Deandrea et al., 2010).

The high rate of atypical presentations for a general medical patient cohort, aged more than 80 years presenting to an emergency

### Table 1

| Disease                      | FDP¹ n (%) | NFDP² n (%) | χ², p |
|------------------------------|------------|-------------|------|
| Hypertension                 | 35 (64.8)  | 27 (61.4)   | 0.12, 0.7 |
| Diabetes mellitus            | 29 (53.7)  | 14 (31.8)   | 4.7, 0.03 |
| Dementia                     | 23 (42.6)  | 15 (34.1)   | 0.7, 0.39 |
| Hypercholesterolemia         | 19 (35.2)  | 15 (34.1)   | 0.01, 0.9 |
| Osteoporosis                 | 14 (25.9)  | 11 (25.0)   | 0.01, 0.9 |
| Cerebro-vascular accident    | 18 (33.3)  | 4 (9.1)     | 8.1, 0.004 |

¹ FDP - functionally dependent patients.
² NFDP – non-functionally dependent patients.

| Symptoms         | FDP¹ n (%) | NFDP² n (%) | χ², p |
|------------------|------------|-------------|------|
| Cough            | 10 (18.5)  | 20 (45.5)   | 8.3, 0.004 |
| Headache         | 6 (11)     | 3 (6.8)     | 0.5, 0.46 |
| Taste and smell loss | 5 (9.3) | 3 (6.8)     | 0.2, 0.66 |
| Weakness         | 14 (26)    | 13 (26.8)   | 0.4, 0.5 |
| Breathlessness   | 5 (9.3)    | 12 (27.3)   | 5.5, 0.02 |
| Fever            | 23 (42.6)  | 12 (27.3)   | 0.5, 0.46 |

¹ FDP - functionally dependent patients.
² NFDP – non-functionally dependent patients.

This study compared COVID-19 symptoms and time to resolution of infection according to the functional status of geriatric patients. The main finding was that FDP with mild to moderate infection had less respiratory COVID-19 symptoms, such as cough and dyspnea compared to NFDP. The second main finding was that FDP had longer time to resolution of infection compared to NFDP.

### Table 2

| Symptoms       | FDP¹ n (%) | NFDP² n (%) | χ², p |
|----------------|------------|-------------|------|
| Cough          | 10 (18.5)  | 20 (45.5)   | 8.3, 0.004 |
| Headache       | 6 (11)     | 3 (6.8)     | 0.5, 0.46 |
| Taste and smell loss | 5 (9.3) | 3 (6.8)     | 0.2, 0.66 |
| Weakness       | 14 (26)    | 13 (26.8)   | 0.4, 0.5 |
| Breathlessness | 5 (9.3)    | 12 (27.3)   | 5.5, 0.02 |
| Fever          | 23 (42.6)  | 12 (27.3)   | 0.5, 0.46 |

¹ FDP - functionally dependent patients.
² NFDP – non-functionally dependent patients.

This study compared COVID-19 signs and symptoms of functionally dependent and non-functionally dependent patients.
department, observed by Hofman et al. (2017). Ming Gan et al. (1971) concerning presentations of COVID-19 old age patients, described similar findings. The most common atypical presentation reported was weakness, demonstrated in our study too, but there was no difference in both groups. Those finding suggests, that the physiological response of older adults towards COVID-19 may be parallel to that seen in other disease processes.

Resembling to our study Ming Gan et al. (1971) showed the increased numbers of patients with underlying dementia and high pre-morbid clinical frailty scores seen in atypical presentation group.

This is well known that aging COVID-19 patients with multiple comorbidities had a more prolonged recovery time (Atkins et al., 2020; Hewitt et al., 2020; Tenforde et al., 2020; Wang et al., 2020; Wei et al., 2020). In our study we shown that in addition to comorbidity and age, functional status has an additional role in duration of time to resolution of infection even in mild-to-moderate patients. Furthermore, despite the fact that there were a significantly higher number of diabetes and stroke patients in FDP group, the functional status was statistically significant independent predictor for recovery.

Additional interesting finding of this our study was a clear association with age and prolongation of time to resolution of infection within FDP group, this is opposite to our previous study (Lubart et al., 2021), where the age was not associated with the time to resolution of infection. Plotnikov et al. (2021) study showing, that chronological age should not be used as a sole prognostic factor for elderly patients with COVID-19.

Reports of long-lasting COVID-19, the so-called 'long COVID', are rising but little known about prevalence, risk factors or whether it is possible to predict a protracted course early in the disease (Anthony et al., 2021; Sudre et al., 2021). Long COVID characterized by symptoms of fatigue, headache, dyspnea and anosmia and was more likely with increasing age and female sex. We found in our study that functionally dependency was a predictor of long-lasting time to resolution of infection.

5. Conclusion

While FDP with mild to moderate infection had less respiratory COVID-19 symptoms compared to NFDP, they had longer time to resolution of infection. Among patients with COVID-19, severe functional dependency was found to be a better predictor of the time to resolution of infection than COVID-19 symptoms. Assessment of functional status may contribute to decision making for care of older inpatients with COVID-19.

5.1. Limitation

The present study had several limitations. First, it was a historical prospective study with its inherent difficulty in limiting the exposure to bias, and missing data may have affected the results. Second, the data is from a single center, and its findings could be different in other settings. Third, the study included a relatively small cohort of patients. Last, we cannot provide data on COVID-19 treatment because the patients were in mild or moderate condition and did not get any special anti-COVID-19 treatment.

The study and the manuscript were prepared in compliance with ethical standards. The study has ethical approval.

It was prospective historical study and there was not needed informed consent of participants.

Funding

No funding in this study.

Fig. 1. Mean days to resolution of infection among NFDP and FDP patients.

NFDP – non-functionally dependent patients.

FDP - functionally dependent patients.

* NFDP – Non-functionally dependent patients
Declaration of competing interest

No conflict of interest.

References

American Diabetes Association, 2018. Economic costs of diabetes in the US in 2017. Diabetes Care 41 (5), 917–928.

Anthony, L., Kmarriff, M.D., reviewing Sudre, C.H., 2021. Predictors of ‘Long COVID-19’ NEJM journal watch. Nat. Med.

Atkins, J.L., Masoli, J.A., Delgado, J., et al., 2020. Preexisting comorbidities predicting severe Covid-19 in older adults in the UK Biobank Community Cohort. medRxiv 75, 2224–2230.

Aw, D., Woodrow, L., Ogliari, G., Harwood, R., 2020. Association of frailty with mortality in older inpatients with Covid-19: a cohort study. Age Aging 49 (6), 915–922.

Azarpazhooh, M.R., Amiri, A., Morovatdar, N., et al., 2020. Correlations between COVID-19 and burden of dementia: an ecological study and review of literature. J. Neurol. Sci. 416, 117013.

Berman, P., Hogan, D.B., Fox, R.A., 1986. The atypical presentation of infection in old age. Age Aging 15, 230–234.

Chen, T., Dai, Z., Mo, P., et al., 2020. Clinical characteristics and outcomes of older patients with coronavirus disease 2019 (COVID-19) in Wuhan, China (2019): a single-centered, retrospective study. J. Gerontol. A Biol. Sci. Med. Sci. 75, 1788-1795. https://doi.org/10.1093/gerona/glz089.

Centers for Disease Control and Prevention, 2020. Coronavirus Disease 2019. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/older-adults.html.

Cortopassi, F., Gurung, P., Pinto-Plata, V., 2017. Chronic obstructive pulmonary disease in elderly patients. Clin. Geriatr. Med. 33 (4), 539–552.

Deandrea, S., Lucenteforte, E., Bravi, F., et al., 2010. Risk factors for falls in community-dwelling older people: a systematic review and meta-analysis. Epidemiology 21 (5), 658–668.

Gómez-Belda, A.R., Fernández-Garcés, M., Mateo-Sanchis, E., et al., 2020. COVID-19 in older adults: What are the differences with younger patients? Geriatr Gerontol Int. 21 (1), 60–65. https://doi.org/10.1111/ggi.14102.

Granger, C., Hamilton, B.B., Kayton, R., 1989. Guide for the Use of the Functional Independence Measure (Wee FIM) of the Uniform Data Set for Medical Rehabilitation. Research Foundation of the State University of NY, Buffalo, NY.

Hewitt, J., Carter, B., Vilches-Moraga, A., Quinn, T.J., Braude, P., Verduni, A., et al., 2020. COPE Study Collaborators. The effect of frailty on survival in patients with COVID-19 (COPE): a multicentre, European, observational cohort study. Lancet Public Health 5 (8), e444–e451.

Hofman, M.B., van den Hasenberg, J., Siersevelt, I.N., Tulner, C.B., 2017. Elderly patients with an atypical presentation of illness in the emergency department. Neth. J. Med. 75 (6), 241–246.

Kalish, V.B., 2016. Obesity in older adults. Prim. Care 43 (1), 137–144.

Lan, J., Jin, X., Hao, S., et al., 2020. Analysis of epidemiological and clinical features in older patients with Corona virus disease 2019 (COVID-19) out of Wuhan. Clin. Infect. Dis. 71, 740–747. https://doi.org/10.1093/cid/ciaa242.

Limpatwattana, F., Phungoen, P., Mitsungnern, T., Laosuangkoon, W., Tananawong, N., 2016. Atypical presentations of older adults at the emergency department and associated factors. Arch. Gerontol. Geriatr. 62, 97–102.

Liu, K., Chen, Y., Lin, R., Han, K., 2020. Clinical feature of COVID-19 in elderly patients: a comparison with young and middle-aged patients. J. Infect. 80, e14–e18.

Lubart, E., Gal, G., Mizrahi, E.H., 2021. Jpn. J. Infect. Dis. https://doi.org/10.7883/jjnd.2021.215.

Ming Gan, J., Kho, J., Akhunbay-Fudge, M., et al., 1971. Atypical presentation of COVID-19 in hospitalized older adults. Ir. J. Med. Sci. 190, 469–474 (2021).

Potnickov, G., Waizman, E., Tzur, I., et al., 2021. The prognostic role of functional dependency in older inpatients with COVID-19. BMC Geriatr. 21, 219. https://doi.org/10.1186/s12877-021-02158-1.

Sudre, C.H., Murray, B., Vaznavdy, T., et al., 2021. Attributes and predictors of long COVID. Nat. Med. https://doi.org/10.1038/s41591-021-01292-y.

Tenforde, M.W., Kim, S.S., Lindsell, C.J., et al., 2020. IVY network investigators, CDC COVID-19 response team, IVY network investigators. MMWR Morb Mortal Wkly Rep. 69 (30), 993. Epub 2020 Jul 31.

Wang, L., He, W., Yu, X., et al., 2020. Coronavirus disease 2019 in elderly patients: characteristics and prognostic factors based on 4-week follow-up. J. Infect. 80, 639–645.

Wei, C., Liu, Y., Liu, Y., et al., 2020. Clinical characteristics and manifestations in older patients with COVID-19. BMC Geriatr. 20, 395. https://doi.org/10.1186/s12877-021-02158-1.

Wu, Z., Mc Googan, J.M., 2020. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA 323, 1239–1242.

Yang, J., Zheng, Y., Gou, X., et al., 2020. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. Int. J. Infect. Dis. 1239–1242.

Yong, X., Yu, Y., Xu, J., et al., 2020. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir. Med. 8, 475–481.