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Aging and long COVID-19 syndrome: what's new in 2023?

Abstract

Since 2019 that saw the onset of the COVID-19 pandemic, its ongoing impact on many older adults remains a persistent public health concern, especially among those who report suffering from long or post-acute COVID-19 disease health challenges. This report presents data published largely since January 1 2023 on this topic and concerning: Long COVID or COVID-19, Older Adults, Post-Acute COVID-19 Outcomes, and Prevention. Data show that even though long COVID-19 was discussed in 2021 at some length, it still remains a relatively unchartered poorly understood topic in which a sizeable percentage of older adult COVID-19 survivors may experience delayed features of breathing, movement, cognitive and mental health challenges. What causes the observed and perceived problems, what may help to identify who is at risk, and what will reduce these remains unknown, but may benefit from insightful research and extended observations and possible multi pronged efforts that target those symptoms of most concern

Keywords: long covid-19 syndrome, older adults, pathology, prevention, post-acute covid-19 complications, treatment

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Background

As of mid-February 2023, and despite enormous efforts since 2020 as far as mitigating COVID-19 infections, and improving treatments for those who acquire the disease, the inability to completely eradicate the effects of the virus and its variants along with the unanticipated emergence of a what appears to be a somewhat diffuse set of distressful health symptoms especially among older adults remains a pressing public health concern in all parts of the world.[1,2]

This emergent set of distressful symptoms now termed long COVID syndrome[3] is especially challenging to avert, since these symptoms may not be evidenced until three months after recovery from an acute bout of COVID-19 and may persist for up to one year, and possibly beyond this period. Commonly found to impact the symptomatic individual's physical as well as their mental health status and life quality in multiple ways and in parallel in many instances, it appears older adults may be particularly vulnerable to this disabling condition[3] that may vary with the variant of infection and/or vaccination type or status, plus health status.[4–6]

However, how to predict who is at risk and what the precise source of long-COVID is has not been clear to date in any respect.[3] This article thus attempted to update what we know in this regard, including possible determinants that have only recently been discussed such as the role of a possible dysregulated immune system,[7] and inflammation linked pathologies within the nervous system, the cardiovascular, and the gastrointestinal or metabolic systems in vulnerable post-acute COVID-19 survivors.[6]

This report also focuses on what researchers currently conclude about long COVID-19 health attributes, and in particular any age associated insights and possible remediation factors, as reported in the PUBMED database and others in early 2023. The aim was to identify current understandings and what if anything can be recommended for addressing this health concern based on these findings.

Methodology

Using the electronic data sources PUBMED, PubMed Central, and Google Scholar articles published in the past year [January 1, 2022-February 14 2023] were sought using the key words, Long COVID, older adults, and post-acute COVID-19 syndrome. All forms of study or analysis were deemed acceptable, including any salient reports listed on the preprint website and commentary papers. However, because this is an emerging topic, with few clinically sound prospective analyses, and most reports were review articles, rather than clinical trials, a narrative summary of all available data including all forms of research design, and topics such as what long COVID-19 syndrome is, why does it occur, and what can be done to abate it was implemented. Selected material had to focus on facts relevant to long COVID-19 complications, and if possible among the older adult, rather than children or adolescents. No drug or basic laboratory studies were included. Excluded too were articles that did not focus specifically on this set of issues, proposals for future study, and non English based articles.

Results

Although several articles among the 191 key articles currently categorized as being reflective of long COVID issues as of 2023, as in 2021-2022, the PUBMED data base and others employed yielded a high number of reports that did not actually discuss long-COVID-19 issues in any way. As well, most reports that do broach this topic are aggregate reviews of various observational studies describing symptoms and signs of reports subjectively derived in survey or medical record formats of limited samples and most of these were conducted in 2021 or early 2022. Regardless of study origin though, most concur that long-COVID is a complicated syndrome that does not affect all COVID-19 survivors, but that it appears to emerge and persist to varying degrees for up to one year or beyond[8] following an acute COVID-19 bout of infection, especially in older people. However, no report was found that exclusively examined adults older than 65 years of age as a subgroup. The data that have been largely collected through survey research methods are largely unsupported by any clinical test, even when conducted. As such, whether all data are statistically reliable or generalizable, or those minor health issues not persistently reported or followed up would yield a different clinical picture, or a more detailed account of the full spectrum of these complications remains to be uncovered. At the same time, not all populations have been included in current studies, for example, those who were not hospitalized, or those living in areas with limited health access, or access, but no research orientation. Nonetheless, there is

concordance in that most the presence of one or more long COVID-19 symptoms is a widespread and recognizable clinical syndrome, regardless of what the mix of symptoms may be,[9] and regardless of its probable underlying pathology.

However, among these varied consistently reported symptoms, it is especially noteworthy that no unique symptom or body of symptoms has yet been observed, and the link of any COVID 19 syndrome to any pre existing health indicator is generally not evident.[10] As well, age alone cannot be a factor because the condition appears to randomly affect older as well as younger COVID survivors, regardless of vaccination or health status. Key findings echoed in most publications as of February 2023 are: perceptions of persistent fatigue and/or cognitive impairments and sleep challenges that may prove to be of a highly debilitating interactive nature.[11,12] In addition to a host of related functional challenges, long COVID-19 complications may also involve multiple organs and body systems such as the respiratory, cardiovascular, neurological, gastrointestinal, and musculoskeletal systems in diverse ways,[12] as well as diverse psychological correlates[9] that render its prevention and treatment highly challenging at best.

Zeng et al.,[3] who examined 36,625 records embedded in 151 studies involving 1,285,407 participants from 32 countries identified at least one post acute COVID finding including lung tissue abnormalities, as well as generalized symptoms, such as those of fatigue, psychiatric and neurological symptoms. Subgroup analysis showed participants with a higher risk of long-term COVID complications were older, and mostly male, living in a high-income country and who had more severe initial acute COVID status, but the samples studied may have been limited to certain health centers, and/or to those cases with care access or mild rather than severe symptoms.

In aggregating data from convenience samples and by employing very simple survey procedures, individuals with severe infection and who may suffer more from post traumatic stress syndrome, sleep disturbances, cognitive deficits, concentration impairments, and gustatory dysfunction may not be readily detected unless concerted efforts are made to follow up all COVID survivors for at least one year post infection. Survivors with mild infection who may have a high burden of anxiety and memory impairment after recovery may also be challenged to undertake follow up appointments if they live alone or are now too ill to venture out. The role of vaccination status, type, lifestyle, the application of medications or nutrients to reduce long COVID-19 syndrome prior to a diagnosis, and body mass index believed to heighten COVID-19 infection risk, is also relatively unaccounted for in the majority of current reports that employ questionnaires and only detail certain persistent symptoms and not others, and often only via remote media rather than face to face discussions.[13]

Nonetheless, despite these potential limitations in acquiring a comprehensive and complete COVID-19 syndrome body of knowledge, the aggregate findings as published to date in most leading peer reviewed papers consistently show that even after an apparent recovery from an acute COVID-19 bout, a sizeable number of survivors may experience late onset physical and/or mental challenges or both for up to one year, and intuitively if this is not recognized especially in older people, may lead to more rather than less health challenges over time.

Moreover, this clinical condition now termed long COVID-19 syndrome, which is placing an increasing burden on individuals and society, may worsen in multiple ways if it remains unaddressed and obscured by its diffuse nature and by the variously defined symptoms that may accompany this, but can possibly not be differentiated by any standard diagnostic tool. Consequently, conditions such as diabetes and metabolic syndrome that raise the risk for COVID-19 infections may hence be worsened or newly diagnosed in the case of an untreated or poorly treated long COVID syndrome survivor.[14] In this sense, a Physiological Society virtual meeting in February 2022 brought clinicians and researchers together to discuss the current understanding of long COVID mechanisms, risk factors and recovery, as well as exploring its links with other post-viral illnesses such as myalgic encephalomyelitis/chronic fatigue syndrome, and neurovascular injury.[15] It was concluded that long COVID research is highly warranted to better support those suffering from all post-viral syndromes and especially COVID-19 and its variants. As opposed to the idea of a role for performance monitoring in active populations, along with cardiopulmonary exercise training, the translation of such recommendations to an older adult who may already be in poor health cannot be assumed. In particular since little is known about long COVID mechanisms that may impair oxygen delivery, and bone health, as well as balance, more careful consideration of what treatment strategies will be safe to deliver and recommend to the older adult COVID-19 survivor, where sustained attention and processing speed, physical problems and mood issues may well prevail. As well, there may be serious safety issues,[16] especially among those with signs of a reduced limb muscle mass.[17]

As per Malik et al.,[18] who conducted a systematic review of 12 of 4828 cases up to March 2021 detailing post-acute COVID complaints, mobility was noted among at least a third even though what specifically accounted for this was not apparent. However, a role for fatigue, or joint pain, leading long COVID syndrome complaints along with others may have been partly responsible. However, as with that group, the researchers were unable to uncover any directional associations between any of the observed health challenges, thus had no apparent management recommendations.

What we do know as of early 2023 is that as far as older adults are concerned, a fair proportion are likely to suffer from persistently distressful post-COVID symptoms, that reduce their life quality and should be studied further as discussed by Patel et al.[19] Moreover, this idea is not just theoretical, or an aging indicator that is inevitable, since younger adults have expressed similar challenges in attaining their pre-illness physical abilities, such as their ability to walk any distance. There is thus a high probability that long COVID complaints of poor functional capacity have some physical rather than only a cognitive basis, including possible very serious postural balance impacts[20] that lead to overall deficits in physical functioning and participation.[21] In addition, observed structural abnormalities in muscle that have been identified[22] surely imply the feeling of physical distress including muscle pain commonly expressed by some long COVID sufferers do have some organic basis.[23] Evidence further shows signs of skeletal muscle weakness, wasting, and exercise intolerance,[22] rather than the sole presence of low grade inflammation,[24] along with poor neuro-immunity and oxidative processes.[25]

While the world awaits more data and a possible model for reducing or preventing long COVID complications, a role for antioxidants such as melatonin,[24,26] plus supplements[27] such as Co enzyme Q delivery and/or spa therapy has been put forth.[28,29] However, clearly extensive individualized assessments and an ensuing array of treatment options based on the patient's personal profile appears imperative to avert what has been termed a pervasive and possible future case of widespread 'medical devastation'.[30,31] Specific attention to the possible important role of blood clotting pathologies, oxidative stress, endothelial damage,[27] persistent autoimmune symptoms and indications,[32] and possible nutrient deficiencies[33–36] and weighting their importance is

key to mitigating one or more of these possible determinants that may be fostering some degree of post acute COVID-19 fatigue, shortness of breath, and muscle weakness, as well as persistent inflammation.[37,38] The role of organ damage, post-critical care practices and methods, post COVID viral infections and other explanations may also direct clinicians more ably as to what must remedies are indicated in the individual case to assure optimal outcomes.[39,40]

In sum, there is no doubt that many older adults, and possible those who were healthy in 2019, but who sustained a COVID-19 infection and survived, have not uniformly recovered. A very understudied group as a whole, it is possible the extent of the suffering that has been uncovered is only the tip of the iceberg.

Areas of promise include, but are not limited to, examining the role of:

1) Impaired folate metabolism.[41]
2) Vitamin B12 deficiency.[42]
3) One carbon metabolism.[43]
4) Food supplements.[44]
5) Social determinants, marginalization, and deficient mast cell behavior.[45]
6) Endocannabinoid-like mediators.[46]

Discussion

After its unexpected emergence in Wuhan, China, in December 2019, and in spite of multiple global efforts to mitigate COVID-19 and its variants, an additional unanticipated challenge has been increasing evidence that recovery from acute COVID-19 disease is often attenuated and associated with multiple symptoms of ill health that may preside for up to one year or longer after the initial infection. In addition, second or third COVID infections, the exacerbation of chronic health conditions, or their novel emergence may ensue. At the same time, what long COVID syndrome constitutes, varies across and within a limited number of case control and cross sectional studies, and its pathology remains unclear, along with what approaches should be advanced in ameliorating one or more signs of the many long COVID-19 perceptions of distress, such as 'brain fog' joint pain and breathing challenges.

As was implied in the aforementioned section, there may yet be additional emergent health challenges that unfold over time and become evident especially among older adults in the higher age ranges who are very often not included or separated out in the prevailing survey reports that are published to date. There may also be a host of observable health features that tend to cluster or manifest readily, but these are not reported, or acknowledged as being unique to the older adult. They are also vague, and non measureable as a rule, hence may be overlooked. Inaccuracies in data collection procedures and results of the various retrospective studies based on electronic records in specific high profile health and well funded and organized venues may not represent the big picture at all successfully,[47] given the manifestations of COVID syndrome are inconsistent and diffuse at best and may not have yet emerged in controls when studied.[48]

Moreover, the role of rehabilitation in long COVID remains unclear even though as a general principle rehabilitation in its widest sense appears most strongly indicated to safely offset long COVID symptoms.[49] But what is needed here specifically requires careful assessment that takes into account 'brain fog' issues-that may have an organic basis[46] and its possible implications for excess fatigue, dizziness, muscle pain, memory impairment; and reduced grip strength and gait speed, and cognitive response times and their functional consequences in the older adult. Moreover, while the variously described long COVID health complications remain similar no matter what study is reviewed what the role of measurement approaches selected and what aspect is measured and how and when in this regard-is generally not discussed at any length-despite its strong bearing on elucidating the magnitude and extent of the long COVID-19 syndrome.

As well, how one can work towards preventing long COVID is hardly mentioned in any report, even though this may prove to have most cost benefit outcomes. In addition, the role of gender, COVID-pathology, vaccine status and type, plus nature of health access, and the impact of possible organ or systems damage and their long COVID syndrome association remains poorly studied. Thus, whether long COVID has any link to any pre-existing health condition[s] and their collective or independent influence on one or more aging processes and health outcomes is unknown.

What is confusing is that it appears the severity of the COVID-19 illness, which is as independent predictor of breathlessness, anxiety and fatigue, poor sleep in those with no prior illness history, and who are not older adults may foster a post COVID impact of possible secondary COVID-19 infection risk as well as adverse cardiovascular events, but who is at risk cannot truly be accurately determined. Moreover, the impact of poor or no high level rehabilitation access and provision, or a program where there is an emphasis on one symptom and not any other may fail to offer adequate pain relief, reduce fear and depression, or enhance stress control or sleep quality, among other distressful symptoms. At the same time, in cases where long COVID patient is encouraged to exercise without supervision, those older adults who acquire or already have signs of marked muscle mass and bone attrition may find this to be more harmful than not, even in the event the older individual tests negative for COVID-19.

Hence, while the present 2023 data echo the 2021-2022 data, and show that the risk of prolonged ill health that can follow COVID-illness and its many challenges remains,[49] more comprehensive attention to resolving this health complication is urgently needed. Moreover, while it is assumed that the condition is self limiting, this should be explored more intently over longer time periods to verify this. More mechanistic studies are especially indicated to advance understandings of who is likely to sustain severe long term immune system dysfunction, 'brain fog', excess muscle and joint pain, adiposity, or frailty or all these adverse health challenges. Even if there is no current 'cure' for COVID-19, for those older adults who survive an acute COVID-19 episode, but who may develop long COVID complications, it appears geriatric providers and others are strongly encouraged to apply every effort to combat exposure to COVID-19 and its variants in all populations and to foster positive health behaviors and optimal care access to all at possible risk.

Duly supporting all aspects of a healthy lifestyle, regardless of whether their clients have had COVID disease or not, making sure they have exposure to fresh air and some form of vitamin D, plus anti inflammatory and muscle, possible respiratory muscle training, along with bone building foods, social support, and counseling are likely to prove especially helpful and should be further investigated.[50] Researchers too can greatly help by conducting more well delineated case control and prospective studies, as well as expanding their assessment procedures in efforts to accurately identify future health care needs using sound research design approaches, careful sub group

analyses, and high technology for diagnosing or uncovering any preventable health determinants or correlates. Efforts too to develop more standardized assessment and evaluation procedures are strongly indicated.[51,52]

In the interim it can be assumed that a substantive proportion of older COVID-19 survivors may continue to incur post-COVID related albeit delayed and persistent adverse physical, mental and medical symptoms that reduce, rather than foster, longevity and life quality.[1–30] These complaints are not merely signs of aging or emotional distress alone, and many older adults who already have multiple needs and who cannot take on a highly proactive approach to their recovery must hence warrant special attention. This is because they may not only fail to recover, but may be at high risk for future infections, as well as falls and bone fractures, plus multiple adverse albeit preventable health outcomes.[30] In this sense, while some progress has been made,[53–56] more carefully construed diagnostic and intervention studies are needed to develop more disease specific treatments, plus evidence based intervention approaches that are able to impact the wellbeing of the older adult with long COVID to recover more ably, and to thereby possibly mitigate its adverse repercussions that threaten life quality as well as the limits of social resources that are paramount for securing optimal health care practices and resources. As of 2023, however, even though it appears that, 10-35% of COVID survivors develop long COVID, with common symptoms including fatigue, breathlessness, chest pain, cough, depression, anxiety, features of post-traumatic stress disorder, memory loss, and difficulty concentrating, what percentage are over 65 years of age, and what their specific issues are is not documented. As per Hueme et al.,[57] and Sherestha et al.,[58] delineating these and other mechanistic issues, such as endothelial damage and immunological associated factors[59,60] using more universal definitions and focused research approaches should help to better inform and support any potentially beneficial post-pandemic health policy and public health protection efforts against long COVID-19 syndrome, and its apparent persistently adverse health impacts and immense social costs among both the older population and others.[61,62]

Conclusion

This overview of the current evidence base, albeit one with both multiple intrinsic as well as extrinsic limitations, appears to show that:

1) Many older adults, even if vaccinated or previously healthy, may experience one or more long COVID-19 complications that can predictably jeopardize their ability to function physically and cognitively, and/or magnify or induce multiple chronic health concerns

2) Despite no agreed upon its origins or its remedies in this regard, the condition termed long COVID syndrome demands early, ongoing, insightful personalized multi dimensional assessments and interventions of the older COVID-19 survivor to avert possible excess personal and social costs

3) Respiratory, nutritional, psychotherapy, immunotherapy, and physical therapy approaches, plus supplements, stress and weight control, and very carefully construed and non fatiguing exercises appear possible promising approaches

4) More population wide COVID preventive efforts and protection measures against COVID-19 and its variants, plus carefully construed clinical research that embraces the social ecology and its influences on COVID-19 vulnerability including its long term impacts are parallel highly warranted mitigation approaches.

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Conflicts of interest

The author declares that they have no direct or indirect conflicts.

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