THE BERMUDA TRIANGLE: AGING, MULTIMORBIDITY, AND AUTOIMMUNE RHEUMATIC DISEASES

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Received: October 8, 2022
Accepted: November 22, 2022

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Abstract
Rapid aging of population in recent years has been accompanied by accumulation of multimorbid conditions. Chronic diseases often share common risk factors. As an example, autoimmune rheumatic diseases often evolve in combination with other autoimmune conditions. High rates of inflammatory disorders and rheumatic diseases are common multimorbidities in the elderly. A lack of practice guidelines for the management of multimorbidities, particularly in the elderly population and those with rare rheumatic diseases, has led to the inadequate treatment and added burden on the healthcare system. This opinion piece aims to draw attention on rising multimorbidity in the aging population prone to autoimmune rheumatic diseases and justify further research in this field.

Keywords: aging; multimorbidity; rheumatic diseases; inflammaging.


Advancing longevity has led to a rising proportion of elderly among the world’s population. Estimates suggest that the elderly will double to 2.1 billion by 2050 [1]. Unfortunately, the aging population has also been accompanied by a rise in the burden of disease. As an example, the rising prevalence of osteoarthritis has manifested as an epidemic of frailty compounded by other issues like osteoporosis, poor mobility, and rising DALY [2]. Frailty is also often seen in those with diagnosed autoimmune rheumatic diseases, a potential reflection of adverse outcomes in the event of geriatric multimorbidity [3]. Accelerated aging due to inflammatory disorders is yet another relatively unexplored facet of immune-mediated conditions.

Oftentimes, multiple chronic diseases (multimorbidity) impact the health of the aging population in a dynamic interaction of different pathologies and drug pharmacokinetics in a frail individual. Notably, the occurrence of multimorbidity in those aged 75 and above has increased in 2010-2014 compared to 2005-2009 [4]. Many diseases co-occurring in multimorbidities have a high prevalence in the elderly population, causing them to manifest simultaneously. However, they may also have shared risk factors; for example, rheumatoid arthritis is associated with a 60% increase in the risk of cardiovascular death [5]. In some cases, one disease may cause another co-occurring illness, for example, osteoarthritis leading to reduced physical activity that may lead to an increased risk of ischemic heart disease [6].
A major challenge in treating multimorbidity in an aging population is a lack of practice guidelines for physicians to make informed choices with their patients when encountering dynamic interactions of multiple diseases. A recent study involving several focus group interviews from primary care clinicians identified major problems in dealing with such patients: lack of adequate data and evidence-based approaches, lack of collaboration with specialists, and conflicts with patients’ preferences regarding their treatment [7].

With no specific guidelines in place, treatment of multimorbidity often leads to polypharmacy [8], where several medications may counter each other’s effects or, even worse, put the patients at heightened risks of dynamic interactions. Failing organs in the elderly are another impediment to following routine prescribing practice, and multiple intersecting decisions can be challenging in limited clinic times in the post-COVID healthcare systems. Besides, inter-clinician variation in the management may be accentuated in such settings, leading to a lack of unanimity in healthcare provision. This situation is further aggravated by the lack of agreement on multimorbidity definitions, variably referring to two, three, or even more comorbidities as multimorbid conditions [9,10].

Most research studies on complex chronic conditions focus on only one condition at a time, excluding the population suffering from multimorbidities. This is especially true for the older population since they are faced with more severe health concerns than the younger population, which interferes with their participation in research, such as incomplete data collection and loss of follow-up [11]. This leads to an underrepresentation of this patient population in most research and to a lack of proper practice guidelines to treat these patients. Multimorbidity has also been traditionally excluded from clinical trials, resulting in a lack of evidence-based approaches.

Multimorbidity in conjunction with rare rheumatic diseases like idiopathic inflammatory myopathies (IIM) is a relatively under-researched topic due to the lower prevalence of these diseases in the world. This makes it more challenging to plan a treatment regimen for these patients, where clinicians are forced to resort to the general guidelines and practices used to treat most patients with common rheumatic diseases and multimorbidities without taking into account any separate needs of these patients.

Inflammaging, which is defined as chronic, sterile, low-grade inflammation contributes to the pathogenesis of age-related diseases such as Alzheimer’s disease, Parkinson’s disease, multiple sclerosis, atherosclerosis, heart disease, type 2 diabetes, osteoporosis, and insulin resistance, cancer, and other diseases leading to an increased risk of morbidity and mortality [12-15]. The proposed pathogenesis includes chronic stress response, oxidative stress impairing homeostatic mechanisms, presence of elevated levels of proinflammatory cytokines like IL-1, IL-6, TNF-alpha, DNA damage response, autophagy, and stem cell aging in senescent cells [16].

Autoimmune rheumatic diseases can lead to persistent inflammation, further enhancing the risk of other aging disease. For example, atherosclerosis, whose pathogenesis also involves inflammation, has been observed in young individuals with rheumatoid arthritis. This, if left untreated, can lead to an increased risk of ischemic heart disease, arterial hypertension, and myocardial infarction [17]. Similarly, rheumatic diseases targeting the muscles (IIM) may lead to accelerated and early senescence in muscles. For example, elevated myostatin levels, which are reflective of muscle aging, have been noted in active myositis, and higher levels have been reported in active versus inactive myositis [18].

Autoimmune rheumatic diseases often enhance the risk of other autoimmune conditions, particularly in women. Autoimmune multimorbidity may bring risks specific to a heightened autoimmune axis and its interaction with environmental triggers, another area that merits further exploration.

To sum up, future research on managing multimorbidities in the older population may be facilitated by agenda setting and study designs suitable for the elderly, with the involvement of multiple stakeholders and patient research partners with experience with specific rare disorders. Big datasets facilitated by global collaboration would be well-placed to foster an understanding of the true prevalence, profile and risk factors and develop guidance on adequate management of senile multimorbidity.

CONFLICTS OF INTEREST
None declared

AUTHOR CONTRIBUTIONS
Both authors have substantially contributed to the writing and take full responsibility for all aspects of the accuracy and integrity of the work.

DISCLOSURE
No part of this opinion piece is copied or published elsewhere in whole or in part.
REFERENCES


