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Editorial

Resilience And Successful Aging

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Introduction

Resilience as one of the pillars of successful aging has received increasing attention from the scientific community in recent years and has become even more important post-Covid-19 pandemic where countries worldwide are trying to build individual, community and system resilience (1, 2). Successful aging was first introduced by Rowe and Kahn emphasizing on illness avoidance, high physical and mental functioning, and active life engagement (3); and subsequently expanded to include multidimensional factors such as social functioning, psychological factors and resilience (4). The fastest growing segment worldwide is above 80 years old where the numbers are expected to triple between 2020 and 2050 to 426 million (5). Age is a risk factor for chronic disease, cancer, frailty, dementia and associated with declining resilience (6). With advances in public health and medical treatment, there is widening gap between lifespan and healthspan. Health systems across the world are challenged to find effective means of reducing prevalence of disability and promote solutions to successful aging. Most of the scientific literature in the past decade has been on prevention of chronic disease, frailty, and dementia.

The term "resilience" is not new and defined as the ability to bounce back after a stressful encounter or adversity in life (6). Older adults are a heterogenous group and demonstrate variable response to stressors despite similar clinical status or chronological age possibly explained by differences at the molecular, cellular and system level. Medium and high-level resilience is prevalent in 73% of the population and identifying resilience is of utmost importance (7). The challenge lies in its measurement as while there are many resilience measurement tools (Table 1), they rely on the concept that measurements can be generalised across the population, but studies have shown that adaptations to adversity is influenced by gender, ethnicity, generation differences, cultural variation, type and intensity of stressor and outcome (8-10). Decline in resistance with aging is possibly explained by decline in homeostasis and elevated stress response, and there is no mechanism in place to predict dose-response and tipping point for adverse outcomes. In addition, a single stressor can result in multiple adverse outcomes, e.g., bedrest causing muscle wasting, delirium or multiple stressors in combination, e.g., osteoarthritis, sedatives and antihypertensives causing falls and fracture.

There is emerging evidence on the role of genetics, dysregulated immune system, insulin resistance and alterations in metabolic pathways on resilience (Figure 1) (11-13). Eissmann et al. has recently shown that 30% of older adults are cognitively intact despite meeting Alzheimer's disease (AD) pathological criteria at autopsy (14). They demonstrated sex differences in clinical manifestation despite similar neuropathological AD burden and identified female-specific resilience locus, and numerous sex specific metabolic pathways (14). Resilience is a multifaceted and difficult construct to measure with two main categories, physical resilience and psychological (mental and / or cognitive) resilience (15, 16). Physical resilience has become a topic of interest in recent years and defined as "the ability to recover or optimize function in the face of age-related losses or disease" (17).

Resilience is a dynamic construct with multiple risk and protective factors described with mnemonic "PURPOSE OF LIFE" listed in Figure 1. Protective factors include having a purpose in life, a better perceived health, optimism, locus of control, social connectivity, spirituality, functioning independently, exercise practice, type of environment, male sex, and age < 80 years old (18). Risk factors include difficulty managing stress, depression, mobility limitation, physical illness such as diabetes and personality disorders (7). Increasing resilience has been associated with positive mental health, quality of life, increased physical activity, improved pain threshold, better physical and rehabilitative outcomes (7).

Physical Resilience in Acute Care

Aging is a complex process with multiple interacting factors. Clinicians and surgeons dealing with older patients are often faced with difficulties in predicting adverse outcomes in older adults. Most of the work in the acute care setting has been based on frailty and not resilience. Frailty is the underlying physiologic state while resilience is the speed and process of recovery after a stress event which can have an impact on overall length of stay, healthcare resource utilisation and institutionalisation (19). Static tests of physiological reserve have been shown to be better predictors of clinical recovery compared with multidimensional (physical, psychological,

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Table 1. Resilience Scale

Resilience Scale	Description
Ego Resiliency Scale (44, 45)	The ego resiliency scale was developed initially for young adults and subsequently applied to older adults.
The 25- and 14-item Resilience Scale (46)	Developed as a measure of resilience for adults across the life span.
Hardy-Gill Resilience Scale (47)	Nine questions based on most stressful life event they experienced in the past five years.
Dispositional Resilience Scale (48)	The DRS is a 45-item questionnaire that includes 15 commitment, 15 control, and 15 challenge items. The original DRS was modified to be appropriate for older adults
Connor–Davidson Resilience Scale (49)	This measure consists of 25 items, each of which is rated on a 5-point scale.
Brief Resilient Coping Scale (50)	Short unidimensional scale that aims to assess ability to cope with stress adaptively
Making it CLEAR (MiC) (51)	34 items questionnaire which assess the "individual determinants of resilience" (IDoR) and the "environmental determinants of resilience" (EDoR). Validated in older patients discharged from hospital.
Multidimensional Individual and Interpersonal Resilience Measure (MIIRM) (52)	Eight-factor structure that appeared clinically relevant for measuring the multidimensional nature of resilience.
Resilience Scale for Adults (RSA) (53)	Self-report scale targeting adults with five scoring items that examine both the intrapersonal and interpersonal protective factors that promote adaptation to adversity.

social) assessments (20). Comprehensive geriatric assessment has proven to be useful in predicting outcomes in frail older adults, but it requires special skill and is resource intensive (21). Automated frailty assessment tools such as Hospital Frailty Risk Score and Rapid Geriatric Assessment with assisted management pathway requires further validation in predicting recovery in hospitalised patients exposed to different stressors (22-24). In a group of patients with hip fracture, a panel of biomarkers explained 27% of the differences in physical resilience or expected differential recovery (25). Future studies are needed to validate the correlation of various pre-stress provocative tests (physical function, cognition, psychological) (Figure 1) and biomarkers with recovery post-surgery and / or other medical illness such as infections and stroke (26).

Resilience, Frailty, and Intrinsic Capacity

Frailty, intrinsic capacity (IC) and physical resilience should be regarded as separate, but highly intertwined entities. IC and physical resilience are positive attributes while frailty is a negative attribute. IC and resilience can be applied to all stages of life course, and frailty to later stages of life (27). Frailty expresses deficit whereas resilience is the coping and / or recovery aspect (27). Frailty is a state of declining physiological reserve which increases vulnerability to adverse outcomes (19). Physical resilience can be described as ability to mobilise the reserve and can co-exist with frailty in the same older adult but to date, there are limited studies on physical resilience trajectory in frail older adult (16, 27). IC framework was first proposed by the World Health Organization (WHO) and includes cognition, vitality, mobility, psychological and sensory functions (5). IC domains have shown to predict functional recovery after exposure to adversity (28). Woo initially described IC as a determinant of physical resilience through the physiologic reserve concept and later supported by Chhetri et al. (27, 29). Although IC is only one of the determinants of physical resilience besides genetic, environment and other factors shown in Figure 1, it may be reversible with interventions (30). We need more studies to measure longitudinal impact of interventions to reverse frailty and managing declines in IC on improving physical resilience (25).

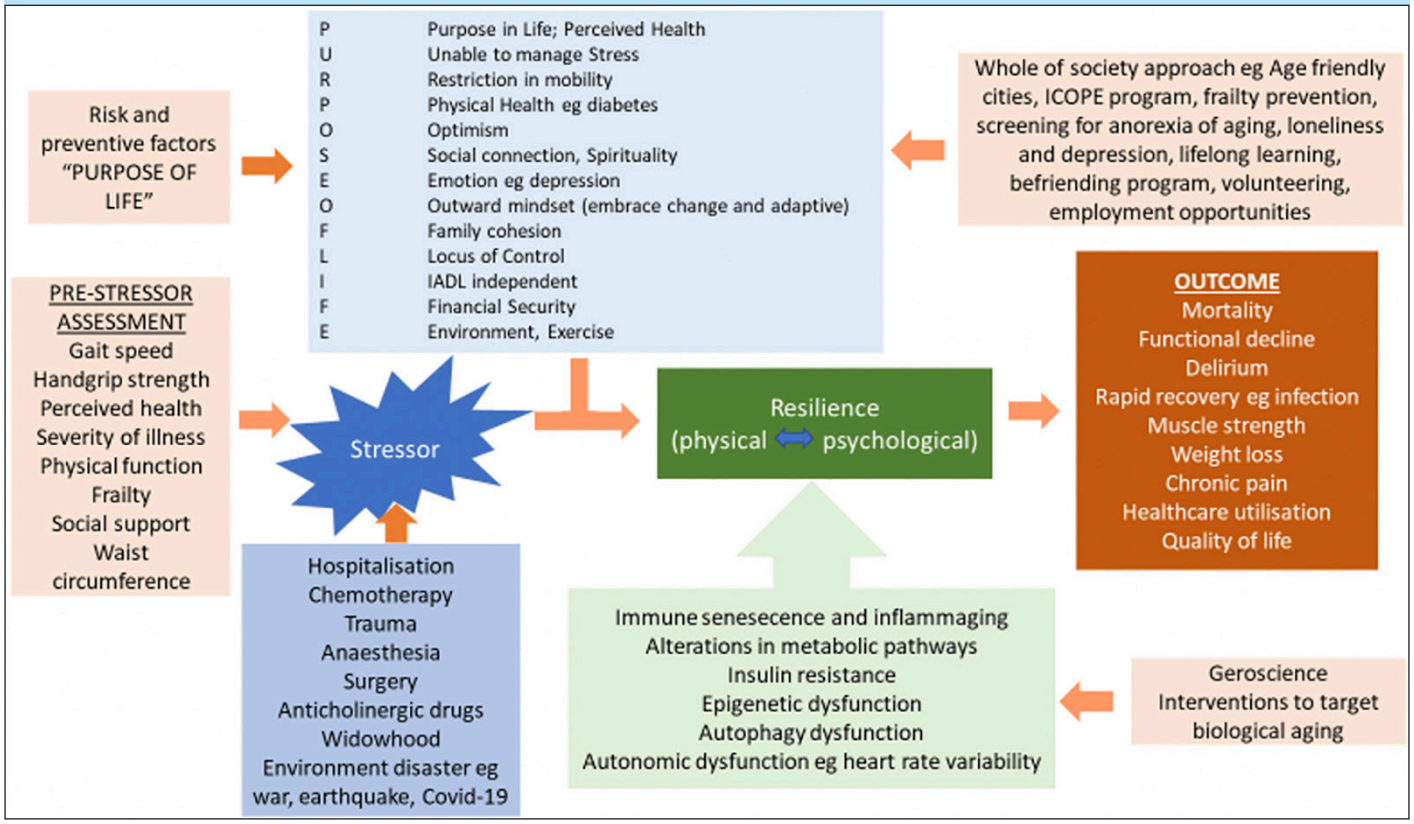
Geroscience and Resilience

The geroscience approach assumes all diseases affecting older adults are major cause of function and resilience decline possibly mediated through proinflammatory cytokines, persistent inflammation, and immune senescence (11). An intact and responsive immune system is a pre-requisite for resilience and dysregulation of the immune system is thought to mediate the adverse outcomes in older adults from acute illness, chemotherapy, post-surgery, trauma, etc (12). Aging and resilience trajectories are also determined by multiple interacting factors such as genetic, environment, exposure to microorganisms and toxins across lifespan, comorbidities, polypharmacy, and lifestyle factors such as exercise, obesity, nutrition, smoking, and stress, which also contributes to immune senescence and overall decline in immunologic capability (12). Other risk factors for aging and disease, which can have an impact on resilience, include impaired autophagy and endoplasmic reticulum stress, insulin resistance, epigenetic, autonomic, and vascular dysfunction (Figure 1), which are all interrelated, and possibly mediated through dysregulated immune system and cytokine production (11, 31). Future studies need to focus on understanding the relationship between resilience, chronic diseases at molecular level and biological aging.

Interventions

Interventions to build and / or maintain resilience needs to include whole of societal approach, multisectoral collaborations and "ensure that communities foster the abilities of older people" as described in the WHO Decade of Healthy Aging report (32). IC is one of the determinant of physical resilience, and the WHO released the "Integrated care for older people:

Figure 1. Resilience: Risk and Protective Factors, Pre-stressor Assessment, Outcomes and Possible Interventions



ICOPE: Integrated Care for Older People

Table 2. Country specific programs which may help in resilience building

USA	Age-Friendly Health System with screening for geriatric syndromes and intervention utilizing the 4M's ("what Matters"; "Medication"; "Mentation"; and "Mobility") (38)
Europe	INSPIRE ICOPE-CARE program in the Occitania region (40)
Hong Kong	The Integrated Health and Social Care Model with Personalised Care Plan (41)
Japan	"Work For Purpose" and "Second Life Platform Project" in Kashiwa City which links older adult with volunteer activities, life-long learning, hobbies, and health promotion activities (54)
Taiwan	Taiwan Integrated Geriatric Care (TIGER) Multidomain Intervention (55)
South Korea	Integrated Care of Older Patients with Frailty in Primary Care (ICOOP_Frail) (56)
Singapore	Peer-led Healthy Aging Promotion Program for You (39); Health District @ Queenstown (36)

guidelines on community-level interventions to manage declines in intrinsic capacity" in 2017 (33) and the "Handbook: Guidance on person-centred assessment and pathways in primary care" in 2019 with digital app for community level screening and intervention (34) .

The WHO Global Age-Friendly Cities Project also aims to promote active aging by optimizing environment (transportation, housing, outdoor spaces and buildings), social (participation, respect and inclusion), employment, community support and health services (35). Many countries are implementing various programs at individual, community, and city level to prevent or delay decline in physiological reserve which may possibly improve resilience in longer term (36-41) (Table 2). There is currently limited literature on geroscience interventions in improving resilience outcomes.

Gaps and Future Opportunities

To date, most publications on resilience are on broad concept and epidemiology without targeting specific stressors, organ systems, biological aging, and outcomes. Resilience scales need to be validated in different regions, ethnic groups, gender, specific stress, and outcome measures. There is lack of data on the role of genetic predisposition and biomarkers on resilience to specific stressors although GDF-15 shows some promising results (13, 42). We need future prospective studies on the role of geroscience interventions targeting specific biological pathways personalised to stressors and impact on desired resilience outcome. While decline or tipping point in resilience is often attributed to aging, disease and stressors such as hospitalisation, we need more data on the role of P4 medicine (prevention, predictive, personalised and

participatory) in building lifelong resilience and impact of psychosocial, physical and cognitive reserve on modifying the tipping point (43). Effect of immune modulation through diet e.g. Mediterranean diet, exercise types and intensity, social interventions and pharmacologic interventions on effect of resilience requires further evaluation (12).

Conclusion

Resilience is increasingly being considered as a pillar of successful aging. Due to its contextual nature, measuring resilience has become a challenge with downstream impact on providing appropriate interventions to promote resilience. There are still significant gaps in research from a geroscience perspective and future studies need to focus on understanding the relationship between resilience, chronic diseases at molecular level, functional reserve, and biological aging.

Conflicts of interest: The authors declare no conflicts of interest for this work.

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