Managing frailty in people with human immunodeficiency virus

Abstract

The population of people living with human immunodeficiency virus (HIV) is ageing and has an increasing burden of non-acquired immune deficiency syndrome (AIDS)-related morbidity and mortality, including frailty. Frailty is prevalent at a younger age in this population and is associated with multimorbidity, disability and death. This article examines the key interventions to ameliorate the advancement of frailty in people living with HIV. It explores methods of successfully delivering a multidisciplinary holistic approach to this complex patient group, using three case studies. The most effective frailty intervention is exercise. Group-based physiotherapy classes protect against functional decline and frailty symptomatology. Optimisation of medical and psychiatric comorbidities, including deprescribing when appropriate, is also essential. Addressing the social determinants of frailty, such as social isolation and loneliness, are beneficial, but are dependent on local charities and resources. More research is required to assess pharmacological and nutritional interventions in frailty. This requires a greater understanding of the exact pathophysiology of frailty, which remains poorly understood.

Key words: Exercise; Frailty; Geriatrics; HIV; human immunodeficiency virus

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Introduction

Since the introduction and global scale-up of successful antiretroviral therapy, people living with human immunodeficiency virus (HIV) are living to a near-normal life expectancy (Antiretroviral Therapy Cohort Collaboration, 2017). Over 22% of people living with HIV in the UK are aged 50 years and over, with 3.5% aged 65 years and over (National AIDS Trust, 2020).

This demographic shift is associated with non-acquired immune deficiency syndrome (AIDS)-related morbidity and mortality, including the premature expression of geriatric syndromes, such as frailty. Frailty occurs in people living with HIV over a decade before their non-HIV counterparts (Onen et al, 2009). The prevalence of frailty in people living with HIV is reported to be 5–28% (Desquilbet et al, 2007; Onen et al, 2009). This parallels the trend of cardiovascular disease, diabetes and malignancy, found at an increased prevalence in people living with HIV in their middle age, which further contributes to frailty through disability, functional decline and polypharmacy (Bourgi et al, 2018; Patel et al, 2018; Franzetti et al, 2019).

Frailty, ageing and HIV infection share a common pathophysiology of inflammation, immune dysregulation and metabolic disturbance, which continue despite achieving virological suppression (Fukui et al, 2018). This is compounded by HIV-induced mitochondrial toxicity, gut bacterial translocation and telomere attrition, intertwining with ageing pathology (Piggott et al, 2016). Toxic side effects of antiretroviral therapy and social factors, such as poverty, intravenous drug use and social isolation, all contribute to the predisposition of frailty in this cohort of patients.

This article examines current evidence-based interventions for frailty and a management strategy used to implement these – a specialist geriatric HIV clinic. This includes discussion of three frail patients and their interventions and management within this setting. Interventions requiring further research are explored within the scope of this article.

Frailty

Frailty is a vulnerability to physiological stressors, distinct from but overlapping with ageing, disability and comorbidity (Fried et al, 2001). It is characterised by reduced

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physiological reserve and results in multisystem impairment in the response to both internal and external stressors. Frailty is a predictor of multiple poor outcomes, such as disability, falls, prolonged and frequent hospital admission, and death (Fried et al, 2001). Unlike other chronic conditions, frailty can be a dynamic state, especially if HIV control is not achieved. Therefore, early diagnosis is key to ameliorating and redirecting the trajectory of frailty. The most used frailty diagnostic technique is the Fried frailty phenotype, which examines five phenotypic domains that illustrate frailty – physical weakness, slow walking speed, exhaustion, unintentional weight loss and low physical activity.

Managing frailty in the UK

Frailty is multidimensional and requires a managed, integrated approach. This includes detailed examination and optimisation of physical functioning, medical complexities, and the psychosocial impacts of frailty.

Biological management

Exercise

Weakness, slow walking speed and fatigability are all components of the Fried frailty phenotype that can be directly related to muscle breakdown and reduced physical activity. Physical exercise can reduce muscle inflammation, prevent muscle breakdown, improve balance and improve cardiovascular health (Ricci and Cunha, 2020). This protects against falls and prevents functional decline, allowing extended independence (Daly, 2017). Exercise is associated with an improved quality of sleep, which may further reduce subjective exhaustion and fatigue (dos Santos et al, 2017). These benefits persist in a HIV-positive population; physical exercise can delay and reverse disability despite mitochondrial impairments and cardio-metabolic abnormalities in people living with HIV (Erlandson et al, 2018). Exercise in physiotherapist-led classes gave extremely favourable outcomes of improved physical function (including increased walking speed) and an improvement in quality of life of HIV-positive patients (Brown et al, 2016). Enrolling patients into specialised exercise programmes, which are at a suitable intensity for their comorbidity and disability, is the most effective intervention to halt and reverse frailty in this cohort (Brown et al, 2016).

Nutrition

In the Fried frailty phenotype, unintentional weight loss and exhaustion can be diagnostic for frailty. There is a paucity of data that examines nutritional supplementation among older people with HIV. Theoretically, supplementation of protein and vitamins such as vitamin D may help to combat muscle loss and thus functional decline. The literature describes a benefit when used in conjunction with exercise, although there is limited evidence for its benefit as a lone intervention (Bolzetta et al, 2018; Liao et al, 2018). Although it is unclear to what extent nutritional optimisation can alleviate frailty, it is important to recognise that food insecurity is highly prevalent in people living with HIV (Hessol et al, 2017). Further research needs to be conducted in this area of frailty intervention, as vulnerable frail adults can face food insecurity even in resource-rich settings and this needs to be addressed.

Comorbidity management

A main contributor to frailty is complex medical comorbidity. HIV infection increases the risk of cardiovascular disease, diabetes, osteoporosis, malignancy, renal disease and liver disease (Patel et al, 2018). Lifestyle factors more common in people with HIV, such as smoking and substance abuse, increase the risk of lung disease (Thornton et al, 2017; Bigna et al, 2018). These factors contribute to frailty beyond medical comorbidity (Willig et al, 2016). In addition, sequelae of previous AIDS-related diseases further contribute to the increased burden of disease that older people living with HIV face. These, in combination with polypharmacy, lead to disability and frailty. An important part of managing frailty as a clinician is acting as a care coordinator, ensuring that the intricacies of an individual's medical care are appropriately managed with specialist input. HIV characteristics, such as CD4 count (including nadir CD4 and CD4:CD8 ratio), AIDS diagnosis and length of HIV diagnosis, all impact upon the progression of frailty (Brothers et al, 2017; Guaraldi

et al, 2019). Therefore achieving virological control, early diagnosis of HIV and patient-centred HIV care remain paramount. An important part of this care includes implementing screening, such as bone density scans for osteoporosis and regular eye screening for HIV-associated ophthalmological disorders.

Polypharmacy

Polypharmacy, typically described as the use of five or more concurrent medications, goes hand in hand with the management of complex chronic conditions. Polypharmacy places patients at an increased risk of adverse outcomes, including frailty (which persists when matching for comorbidity), falls, hospitalisation, cognitive impairment, exhaustion and death (Davies et al, 2020). Research estimates the prevalence of polypharmacy to be 15–39% in people living with HIV (Edelman et al, 2020). Older patients are at high risk of drug-related harm as a result of altered metabolism, greater patient intravariability and poor representation in clinical trials (Davies et al, 2020). This effect is exaggerated in the HIV population, as there is an increased prevalence of liver and renal disease, impacting on drug pharmacokinetics and the expression of drug-related toxicity. Antiretroviral therapy regimens can cause numerous harmful drug–drug interactions. Regimens can be tailored for a frail older population to minimise these interactions, as well as lowering the risk of side effects from antiretroviral therapy, such as weight gain, cardiovascular disease, renal disease, dyslipidaemia and decreased bone mineral density. Simple choices may include switching away from HIV boosters (pharmacokinetic enhancers) if these are not required virologically, and reviewing the use of older reverse transcriptase inhibitors such as abacavir, tenofovir disoproxil fumarate or efavirenz.

Polypharmacy can further exacerbate poor adherence to antiretroviral therapy and thus poor virological control (Edelman et al, 2020). Central to reducing unnecessary pill burden and adverse reactions is consideration of deprescribing. Deprescribing requires a health professional to thoroughly examine the balance of benefits vs harms of a patient's medications, to streamline and reduce unnecessary drug use (Blanco et al, 2020). Deprescribing with a specialist HIV pharmacist can help to reduce and hospital admission, improving the quality of life in the older population of people living with HIV.

Pharmacological

Frailty interventions are currently centred on lifestyle modification, with concurrent optimisation of disease states, environment and drug regimens. However, research is underway examining the use of pharmacological management to help prevent and treat the root pathology of frailty. Rapamycin (a protein kinase inhibitor that reduces pro-inflammatory cytokine production) has shown positive results in mice modelling (Erlandson and Piggott, 2021). The metabolic changes and anti-inflammatory effects seen with use of metformin have been shown to have use in frailty and ageing, preventing the damaging effects of insulin resistance on muscle mass (Espinoza et al, 2019). Other drugs, such as testosterone and resveratrol (an antioxidant), are also undergoing investigation (Erlandson and Piggott, 2021).

Psychological interventions

Psychiatric mood disorders, such as depression, are interrelated with the Fried frailty phenotype, as exhaustion and reduced physical activity categorise both depressive symptomatology and frailty, leading to overlapping but distinct syndromes (Erlandson and Piggott, 2021). However, there is a relationship between frailty and depression, despite the clinical ambiguity. The prevalence of depressive symptoms in patients seen in a frailty clinic was 51% (Jones et al, 2022). Therefore, prompt diagnosis and treatment of mood disorders may help to reduce frailty, or at the very least reduce the physical symptoms of exhaustion and fatigue.

Social interventions

Social isolation

Social isolation and loneliness greatly impact and can lead to frailty in people living with HIV. Loneliness affects over a quarter of older adults in the UK (Age UK, 2018). This is

often the result of the bereavement of loved ones, physical illness and a societal shift away from intergenerational living towards family dispersal and less cohesive communities. People living with HIV are at greater risk of social isolation because of the stigmatisation of their disease, bereavement of partners and friends from AIDS-related mortality before the initiation of antiretroviral therapy, and a higher prevalence of mood disorders (Chapman Lambert et al, 2020).

Loneliness and social isolation negatively impact psychological and psychiatric health, increasing anxiety and depression, and adversely impacting on cognition, sleep and general wellbeing. The correlation of functional decline and frailty with loneliness is less well understood. It is thought that social isolation and frailty may share a pro-inflammatory state, working synergistically with one another (Ellis et al, 2021). Loneliness and social isolation have been exacerbated throughout the COVID-19 global pandemic. Many of these vulnerable patients will have been shielding, reducing their already limited social interaction. The effect of this on this population is yet to be quantified, but it is likely to be substantial.

Interventions to alleviate social isolation and combat frailty, such as befriending and social facilitation, can be difficult to access for patients, often because of a lack of awareness. These services are available through national charities such as Age UK and smaller local charities, thus signposting patients towards these services as a care coordinator is an important part of holistic care for older frail people living with HIV. A UK study found that people living with HIV desired social support from other HIV-positive individuals, which often does not exist within the heterosexual community (Rosenfeld and Anderson, 2020). This reinforces the emphasis of HIV-specific support and social groups.

Environment

Environmental modification of the home through occupational health assessment can help to reduce falls risk and ensure achievement of maximal functional independence. Further to this, recognition of the appropriate time to move into supported living or residential care is essential, which can also help to alleviate social isolation. As with HIV, the health inequalities that exist in the UK are reflected in frailty. Those facing socioeconomic deprivation, poverty and economic stress bear the heaviest burden of frailty and disability (Erlandson and Piggott, 2021). A national survey conducted in 2017 found that 53% of participants with HIV did not always have enough money to meet their basic needs and 28% were received welfare benefits (Kall et al, 2020). Alleviating poverty and the disadvantaged social status of frail people living with HIV on a broader, national scale is imperative. Tackling food insecurity, improving access to health and social care, quality of education, quality of housing and addressing the social gradient of health through a change in government policy are essential in managing frailty in people living with HIV.

Multidisciplinary care

Multidisciplinary collaborative clinics are fundamental to coordinating these interventions and the complex management of people living with HIV affected by frailty. These clinics, focused on geriatric care and frailty in a HIV population, can help to give a holistic overview and thorough assessment of the breadth of frailty determinants and elderly care needs. Many good examples exist within the UK, including the Silver clinic in Brighton and the Sage clinic at the Royal Free Hospital in London, in which geriatricians, specialist HIV consultants, pharmacists, occupational therapists and physiotherapists collaborate. These clinics provide extended initial consultations and further follow-up appointments. Patient feedback from the Sage clinic displays high levels of patient satisfaction with the service, especially the holistic and personalised nature of the clinic (TJ Barber, unpublished observations, 2021). A popular aspect of the Sage clinic was the ability to discuss multiple medical issues, psychological challenges and difficulties faced at home in the same appointment. Three anonymised case studies of frail HIV-positive patients from the Sage clinic are presented (**Case studies 1–3**). These demonstrate and aid understanding of the benefits and delivery of frailty interventions and management by this method.

Case study 1

A 63-year-old man who was diagnosed with HIV in 1985 was referred to the Sage clinic, meeting all five criteria of the Fried frailty phenotype. He had a background of HIV-associated dementia and had a once-daily package of care. He was experiencing daily falls and multiple hospital admissions, partly as a result of previously diagnosed postural hypotension. He was also experiencing anhedonia. At the Sage clinic he was seen by the psychologist, enrolled into a balance exercise programme with the physiotherapy team and referred to a specialist neuro-vestibular outpatient service. The occupational health team assessed him and made home alterations to aid mobility. His medication was reviewed: his antiretroviral therapy regimen was altered to include a nucleoside reverse transcriptase inhibitor that would be bone protective and his dose of fludrocortisone was increased. He commented that his falls had reduced in frequency and he had fewer admissions to hospital (two admissions in the 18 months after his Sage appointment compared to three in the 18 months before). Following psychological input with balance training, he felt increasingly confident to mobilise, allowing him to sit out in his garden.

Case study 2

A 59-year-old woman who had lived with HIV for 20 years was referred to the Sage clinic with weakness, reduced energy and fatigue. She had multiple medical comorbidities including peripheral neuropathy and a previous stroke. She reported short-term memory problems, which had caused her to forget her medication. She had fallen twice recently and was worried about her balance. She was taking seven medications, including a high dose of zopiclone. On patient health questionnaire 9 depression screening it was clear that she was experiencing low mood with a very negative self-image. Therefore, she was referred to a psychology service for cognitive-behavioural therapy and prescribed an antidepressant. She was enrolled into a community physiotherapy balance programme, given a dosette box and started on a weaning dose of zopiclone. Her mood had improved at her next clinic appointment 6 months later, which in turn had benefited her memory and sleep, improving antiretroviral therapy compliance. She had experienced one fall at her yearly review.

Case study 3

A 67-year-old man diagnosed with HIV in 1995 was seen in the Sage clinic. He had multiple comorbidities, including type 2 diabetes, hypothyroidism, and alcoholic liver cirrhosis with oesophageal varices. He complained of fatigue with dizziness and change of bowel habit. At the clinic he was found to be pancytopaenic. He was referred for a colonoscopy and to the haematology team. His home was assessed by the occupational health team and was provided with mobility aids to help conserve energy, including a stair lift. He was diagnosed with a terminal malignancy and with palliative care input died peacefully.

Conclusions

As people living with HIV age, the management of geriatric syndromes such as frailty is becoming an integral part of HIV care. Evidence for active interventions to change the trajectory of frailty in people living with HIV is limited. Exercise, an evidence-based frailty intervention in people living with HIV, can improve physical function, reduces disability and prevents falls. Beyond this, there is limited evidence for other focused interventions, such as nutritional and pharmacological treatment. As a result, current key management of frailty needs to address the factors that predispose to frailty, such as optimisation of the management of medical comorbidities, reduction of unnecessary polypharmacy by deprescribing, and tackling social isolation and loneliness. Specialist HIV geriatric clinics are a beneficial method of coordinating complex HIV care in a holistic manner. In combination with further research into active interventions to ameliorate frailty in people living with HIV, it is important to collate data from specialised services and examine outcomes to look at the best method of delivering services to meet the needs of ageing people with HIV.

Key points

- People living with HIV experience frailty at a younger age than their non-HIV counterparts.
- Frailty in this population is associated with HIV disease control and medical comorbidity, polypharmacy and psychosocial factors.
- Exercise, such as group exercise classes and physiotherapy-led sessions, is an evidence-based intervention for frailty.
- Specialist HIV frailty geriatric clinics are useful to coordinate the complex care required for frail patients.
- Health inequalities, poverty and food insecurity need to be addressed on a national scale to further combat frailty.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

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