Resilience and Frailty in People Living With HIV During the COVID Era: Two Complementary Constructs Associated With Health-Related Quality of Life

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Background: Resilience is defined as an individual's positive adaptation to stressors. The COVID-19 pandemic represents a generalized stressor which may affect differently people living with HIV (PLWH). The objective of this study was to characterize resilience in PLWH with particular regarding the identification of frailty-resilience phenotypes, which may differently affect health-related quality of life (HR-QoL).

Methods: This was an observational study of PLWH attending Modena HIV Metabolic Clinic. Frailty was assessed in 2019, before the onset of the COVID-19 pandemic by using 37-Item frailty index ranging from 0 to 1. The frailty index score was categorized as fit (<0.25) or frail (>0.25). In January 2021, PLWH were offered to complete a set of electronic questionnaires including the CD-RISC-25 for resilience and EQ-5D5L and SF-36 for HR-QoL. Resilience was defined as CD-RISC-25 score >75.7 (ranging from 0 to 100).

Results: Of 800 PLWH reached by mail, 575 (72%) completed the questionnaires. The median age and HIV duration were 54.5 and 24.3 years, respectively. Impaired resilience was associated with loneliness [odds ratio (OR = 2.39; 1.20 to 4.76, $P < 0.001$)]. Predictors for EQ-5D5L <89.7% were the phenotypes "frail/nonresilient" [OR = 5.21, 95% confidence interval (CI): 2.62 to 10.33] and "fit/nonresilient" (OR = 5.48, 95% CI: 2.8 to 10.74). Predictors for SF-36 <64.40 were the phenotypes "frail/nonresilient" (OR = 7.43, 95% CI: 2.57 to 21.22) and "fit/nonresilient" (OR = 6.27, 95% CI: 2.17 to 18.16). Both models were corrected for age, sex, HIV duration, and nadir CD4.

Conclusions: Resilience characterizes the well-being of PLWH during the COVID-19 crisis. This construct is complementary to frailty in the identification of clinical phenotypes with different impacts on HR-QoL.

Key Words: HIV, AIDS, aging

BACKGROUND

The COVID-19 pandemic represents the biggest health crisis of modern time. Almost not a single individual in resource limited or wealthy countries have been unaffected by the social, economic, and political consequence of the COVID-19 pandemic. It therefore represents a unique model of generalized stress which, nevertheless, may affect differently vulnerable people.

In particular, people living with HIV (PLWH) may be at a heightened risk for severe physical and psychological condition compared with the general population.[1] This risk derives from potential interactions between COVID-19, HIV, and other risk factors for COVID-19 complications such as comorbidities and frailty that are common in PLWH.[2–4] Concerns also refer to high rates of psychosocial burdens in the form of violence, stigma, discrimination, isolation, and hate experienced by PLWH.[5] As such, a syndemic framework provides a meaningful and robust paradigm to understand the impact of COVID crisis in PLWH and to develop health services in the era of the COVID-19 pandemic. Moreover, it represents a unique research setting where to study drivers and protective factors affecting health trajectories in the reach or maintenance of satisfactory health-related quality of life (HR-QoL). Since introducing the global agenda of HIV cascade of care through the well-known 90-90-90 goals, contemporary health care and research has progressively shifted to patient-reported outcomes (PROs) and quality of life (HR-QoL), often referred as the fourth 90 goal in PLWH.[6–8]

Frailty is a well-known negative driver affecting health trajectories being described as a condition of reduced strength, endurance, and physiologic function resulting in

an increased risk of developing disability or other unfavorable health outcomes.[9] Most of the currently proposed criteria are based on measures of accumulation of damage.[10] The condition of "frailty" in older persons is also often defined as a "reduction of physiological compensation".[11]

Complementary to the construct of "frailty" is the construct of "resilience" which also affects health trajectories and indicates the ability to recover function after stressful events.[12]

The construct of resilience has been conceptualized as a dynamic trajectory over time in which functions after a stressor leads to recovery or decline into a new equilibrium.[13] More recently, Ferrucci et al underlined the need to describe resilience as complementary to frailty in aging trajectories. Resilience at a young age is capable to compensate damage. During life course, damage accumulates and resiliency is overwhelmed. Unopposed damage accumulation leads to frailty and eventually to death.[11]

Assessment of resilience is not yet standardized. Measurement of resilience requires that the type and magnitude of stress is taken into account. Moreover, different questionnaires used in clinical practice are often unbalanced in the description of physical or rather psychological resilience. Thus, it is unlikely that a single test can be sufficient to measure resilience complementary to frailty, and resilience should be assessed jointly with frailty.

Damage emerges clinically when compensatory mechanisms are exhausted. Physical decline and cognitive decline may therefore result from 2 inter-related mechanisms, one inducing and the other preventing damage, which may act separately or jointly. The interaction between damage and repair could explain why some individuals are aging "faster" and studying them jointly may point to the mechanisms of accelerated aging.[11]

Finally, COVID crisis, independently from COVID-19 disease, and more specifically the burden of lockdown and its socioeconomic impact, can be used as a generalized stressor that challenged resilience. In this setting, we can test the effect of resilience, jointly with frailty, as an add-on clinical judgment about future health trajectory of PLWH.

The objective of this study was to characterize resilience in PLWH with particular regards to the identification of frailty–resilience phenotypes, which may differently affect HR-QoL.

METHODS

Study Design

This was a cross-sectional observational study of PLWH attending Modena HIV Metabolic Clinic (MHMC), Italy. MHMC is a tertiary-level referral center established in 2004, where PLWH are screened for comorbidities, frailty, and PROs. MHMC interrupted services from February to September 2020, and since then, it has reduced its activities from 5 to 2 days a week because of deployment of ID physicians to COVID-19 wards. In January 2021, PLWH who visited MHMC at least once from 2019 were offered to participate in this study assessing PROs, by completing a set of electronic questionnaires.

Inclusion and Exclusion Criteria

We included all antiretroviral therapy (ART)-experienced PLWH who completed the electronic questionnaires. PLWH without frailty evaluation in 2019 and who did not finalize the questionnaires were excluded from the study.

Covariates

Demographic, anthropometric, HIV-related variables, and comorbidities were evaluated at the last visit at MHMC in 2019. Multimorbidity was defined as the presence of ≥ comorbidities. Polypharmacy was defined as the use of more than 5 comedications other than antiretroviral therapy. Electronic questionnaires included resilience score (CD-RISC-25); Insomnia Severity Index (ISI); Depression, Anxiety, and Stress Scale (DASS-21); SUNFRAIL screening questionnaire, as outcomes, Symptoms Short Form health survey (SF-36), and HR-QoL (EQ-5D-5L).

SUNFRAIL screening questionnaire included 9 questions with simple "yes/no" answers.[14] In this study, a particular attention was given to the following questions: "Have you fallen one or more times during last year?," "Do you feel lonely most of the time?," and "In case of need, can you count on someone close to you?"

DASS-21 questionnaire comprised 21 questions with possible scores and answers: "0—did not apply to me at all," "1—applied to me to some degree or some of the time," "2—applied to me to a considerable degree or a good part of time," and "3—applied to me very much or most of the time." Each domain (ie, depression, anxiety, and stress) is covered by 7 questions. The score of each question is multiplied by 2, and the final score is categorized according to severity as normal, mild, moderate, severe, and extremely severe.[15]

The ISI is a 7-item questionnaire assessing the insomnia. The usual recall period is the "last month." A 5-point Likert scale is used to rate each item (eg, 0 = no problem and 4 = very severe problem), yielding a total score ranging from 0 to 28. The total score is interpreted as follows: absence of insomnia (0–7), subthreshold insomnia (8–14), moderate insomnia (15–21), and severe insomnia (22–28).[16]

Frailty was assessed in 2019, before the onset of the COVID pandemic by using a validated 37-item frailty index (FI) ranging from 0 to 1.[17] Each variable included in the FI was coded with a value of 1 when a deficit was present and 0 when it was absent. Missing values were removed from both the numerator and the denominator of the FI.[18] The FI for each patient visit was calculated as the ratio between the number of deficits present and the total number of deficits assessed. Each FI was computed when a minimum of 80% of valid data for the health variables was available. The FI score was categorized as fit (<0.25) or frail (>0.25).[17,18]

Resilience was assessed using the Connor Davidson Resilience Scale (CD-RISC-25). The questionnaire covers the following issues: personal competence, standards and tenacity, trust in its instincts, tolerance of negative effect,

TABLE 1. Demographic, Anthropometric and HIV Characteristics, Comorbidities, and Patient-Reported Outcomes According to 4 Frailty–Resilience Phenotypes

	Fit and Resilient N = 69 (12%)	Fit and Nonresilient N = 242 (42.1%)	Frail and Resilient N = 50 (8.7%)	Frail and Nonresilient N = 214 (37.2%)	Total	P
Demographic and anthropometric characteristics						
Age, yr, mean (±SD)	52.9 (8.6)	52.7 (7.5)	56.9 (7.6)	56.5 (6.3)	54.5 (7.5)	<0.001
Male sex, N (%)	58 (84.1%)	189 (78.1%)	43 (86.0%)	156 (72.9%)	446 (77.6%)	0.09
BMI, kg/m^2, median (IQR)	23.8 (21.9–25.5)	23.31 (22.0–25.2)	25.9 (23.0–27.7)	24.7 (22.1–27.5)	24.0 (22.1–26.4)	<0.001
No physical activity, N (%)	16 (23.2%)	82 (33.9%)	28 (56.0%)	142 (66.4%)	268 (46.6%)	<0.001
HIV characteristics						
HIV duration, mo, median (IQR)	246.0 (138.5–306.5)	263.0 (152.0–334.0)	290.5 (207.3–347.5)	326.0 (267.0–386.0)	292.0 (201.3–357.0)	<0.001
Nadir CD4 cell count, c/μL, median (IQR)	250.0 (161.5–360.5)	261.0 (126.8–350.0)	202.5 (84.8–363.5)	190.5 (66.3–284.8)	222.0 (100.0–322.0)	<0.001
Current CD4 cell count, c/μL, median (IQR)	698.0 (525.3–857.0)	717.5 (559.8–906.0)	660.0 (484.0–918.0)	720.0 (518.5–900.3)	716.0 (534.0–905.5)	0.77
Current exposure to NNRTI, N (%)	16 (23.2%)	46 (19.0%)	8 (16.0%)	36 (16.8%)	106 (18.4%)	0.65
Current exposure to PI, N (%)	9 (13.0%)	32 (13.2%)	10 (20.0%)	36 (16.8%)	87 (15.1%)	0.51
Current exposure to INSTI, N (%)	29 (42.0%)	86 (35.5%)	21 (42.0%)	103 (48.1%)	239 (41.6%)	0.06
Undetectable HIV RNA viral load, N (%)	68 (98.6%)	240 (99.2%)	49 (98.0%)	208 (97.2%)	565 (98.3%)	0.45
Multimorbidity and geriatric syndromes						
Multimorbidity, N (%)	52 (75.4%)	163 (67.4%)	46 (92%)	199 (92.9%)	460 (80.0%)	<0.001
Falls, N (%)	3 (4.4%)	25 (10.3%)	3 (6.0%)	37 (17.3%)	68 (11.8%)	0.008
Polypharmacy, N (%)	17 (24.6%)	71 (29.3%)	29 (58.0%)	121 (56.5%)	238 (41.4%)	<0.001
Frailty index, mean (±SD)	0.17 (0.05)	0.17 (0.05)	0.33 (0.07)	0.33 (0.07)	0.24 (0.1)	<0.001
Loneliness, N (%)	7 (10.1%)	53 (21.9%)	4 (8%)	59 (27.6%)	123 (21.4%)	0.002

acceptance of change, feeling of control, and spiritual influences. The responses were evaluated on a 5-point Likert scale ranging from 0 to 4: not true at all (0), rarely true (1), sometimes true (2), often true (3), and true nearly all of the time (4). These ratings result in a number between 0 and 100. For the purpose of our study, resilience was defined as CD-RISC-25 score >75.7.[19,20]

According to our preplan analyses, 4 frailty–resilience phenotypes were built: "fit/resilient," "fit/nonresilient," "frail/resilient," and "frail/nonresilient," based on previously reported cutoffs for both scores.[17–20]

Outcome Measures

Outcomes of the study were HR-QoL, assessed by the EQ-5D5L questionnaire and by Short Form 36 (SF-36) Health Survey Questionnaire. EQ-5D-5L evaluated the following domains: mobility, self-care, anxiety and depression, pain and discomfort, and usual activity. Each question has 5 possible answers: no problems, slight problems, moderate problems, severe problems, and extreme problems. The EuroQol-visual analogue scale recorded the respondent's self-rated health from 0 to 100 on a 20 cm Visual Analog Scale with endpoints labeled "the best health you can imagine" and "the worst health you can imagine." The optimal HR-QoL was defined as a score of EQ5D5L >89.7%, as described in the Spanish general population and according to the EQ-5D Guide.[21,22] Spain was chosen as a country with similar socioeconomic characteristics as Italy.

Short Form 36 (SF-36) Health Survey Questionnaire is a 36-item scale, which measures 9 domains of health status: physical functioning (10 items), physical role limitations (4 items), bodily pain (2 items), general health perceptions (5 items), energy/vitality (4 items), social functioning (2 items), emotional role limitations (3 items), mental health (5 items), and health change (1 item). A scoring algorithm is used to convert the raw scores into the 9 dimensions listed above. The scores are transformed to range from zero where the respondent has the worst possible health to 100 where the respondent is in the best possible health. For each domain, an outcome measure is defined as the score below and above the average that was previously standardized.[23,24] The original interpretation describes separately all 9 domains.

TABLE 2. Univariate Analysis That Identifies the Predictors of Impaired Psychological Resilience

	OR	95% CI	*P*
Demographic characteristics and lifestyles			
Age >50 yrs	1.64	1.04 to 2.61	**0.03**
Female sex	1.81	1.05 to 3.11	**0.03**
Migrant status	0.38	0.06 to 2.32	0.59
Employed	1.0	0.65 to 1.55	0.99
Education >13 yrs	1.14	0.68 to 1.92	0.62
Alcohol consumption	1.12	0.70 to 1.79	0.63
Smoking	1.27	0.81 to 1.99	0.29
Physical activity	0.61	0.40 to 0.92	**0.02**
HIV characteristics			
CDC—C group	1.35	0.81 to 2.25	0.26
Nadir CD4 <350	1.53	0.97 to 2.43	0.07
HIV Duration >20 yrs	1.48	0.98 to 2.24	0.06
CD4/CD8 ratio <1	1.17	0.78 to 1.77	0.44
HIV risk—IDU	1.69	0.96 to 2.95	0.07
Social characteristics and frailty			
Health costs difficulties	1.47	0.70 to 3.09	0.31
Loneliness	3.20	1.66 to 6.16	**<0.001**
Family and social support	0.31	0.12 to 0.80	**0.01**
Falls	2.96	1.25 to 7.03	**0.01**

Bold entries represent statistically significant odds ratios.

To estimate overall HR-QoL using SF-36, we considered the contribution of each domain to the total mean score, for example, physical functioning comprises 10 items of 36, that equals to 27.8%, emotional well-being and general health comprise 5 items each of 36 that equals to 13.9%, role limitations due to physical health and energy/fatigue comprise 4 items each of 36 that equals to 11.1%, role limitations due to emotional problems comprise 3 items that equals to 8.33%, social functioning and pain comprise 2 items each of 36 that equals to 5.56%, and, finally, health change comprises only 1 item of 36 that equals to 2.78%. Using the standardized means[23] for each domain and previously described percentages, a standard total mean score for HR-QoL was estimated based on the following calculation:

$$
\begin{aligned}
\text{Standard total mean score} = {} & 0.278 \times 70.61 + 0.139 \times 65.78 \\
& + 0.139 \times 56.99 \\
& + 0.111 \times 52.97 \\
& + 0.111 \times 52.15 \\
& + 0.083 \times 70.38 \\
& + 0.056 \times 78.77 \\
& + 0.056 \times 70.77 \\
& + 0.028 \times 59.14 \\
= {} & 64.40
\end{aligned}
$$

The total mean scores in PLWH were calculated using the same formula. HR-QoL above the mean was defined as a score of SF-36 > 64.40.

Statistical Analysis

Data were expressed as mean ± SD for normally distributed continuous variables, as median and interquartile range (IQR) for non-normally distributed continuous variables, and as frequencies and percentages for categorical variables. Student *t* test and analysis of variance were performed to identify statistical differences for the normally distributed continuous variables, whereas Mann–Whitney and Kruskal–Wallis tests were used for not normally distributed continuous variables. The $\chi2$ test was applied for categorical variables. Characteristics of PLWH were described according to resilience and frailty separately and according to resilience–frailty phenotypes.

Univariate analysis was conducted to explore factors associated with impaired resilience, using predictors such as demographics, lifestyles, HIV, and social and frailty variables. Statistically significant variables were further explored in the multivariable logistic regression. Multivariable logistic regressions were also built to investigate predictors of HR-QoL with particular attention on frailty–resilience phenotypes.

The statistical analysis was performed in Python. This study was approved by the University of Modena and Reggio Emilia Ethics Committee according to the Declaration of Helsinki.

RESULTS

Of 800 PLWH reached by mail, 575 (72%) completed the questionnaires. The mean age was 54.5 (SD = 7.5), and the median HIV duration was 24.3 (IQR = 16.8–29.8) years, respectively. The median current CD4 cell count was 716 (IQR = 534–955)/µL, and 98.3% had HIV RNA below the limit of detection. All participants were ART experienced. Major ART core classes were NNRTI 18.4%, boosted PI 15.1, and INSTI 41.6%. PLWH who did not respond to questionnaires were not different regarding age and frailty when compared with the study population (mean age = 54.5 years and mean frailty index = 0.24). However, PLWH with more than 13 years of education were more likely to respond to online questionnaires (32.2% vs. 21.3%, $P < 0.001$).

Prevalence of frailty using 37-FI cutoff >0.25 was 45.9%. Table 1, Supplemental Digital Content, http://links.lww.com/QAI/B761, details demographic, anthropometric HIV, and clinical variables in people with a without frailty. As expected, frail PLWH were significantly older (56.6 vs. 52.7), had lower CD4 nadir (191 vs. 254 µL), higher BMI (25.0 vs. 23.5 kg/m²), and higher multimorbidity (91.8% vs. 69.1%). Regarding geriatric syndromes, higher burden of polypharmacy (56.8% vs. 28.3%) and falls (15.2% vs. 9.0%) was observed, whereas there was no difference in loneliness (23.9% vs. 19.3%).

Prevalence of impaired resilience using CD-RISC-25 cutoff <75.7 was 79.3%. Table 2, Supplemental Digital Content, http://links.lww.com/QAI/B761, details demographic, anthropometric HIV, and clinical variables in people with and without resilience. PLWH with impaired resilience had similar age (54.5 vs. 54.6), had lower CD4 nadir (222.5 vs. 221 µL), BMI (23.8 vs. 24.6 kg/m²), and multimorbidity (79.4% vs. 82.4%). Regarding geriatric syndromes, similar
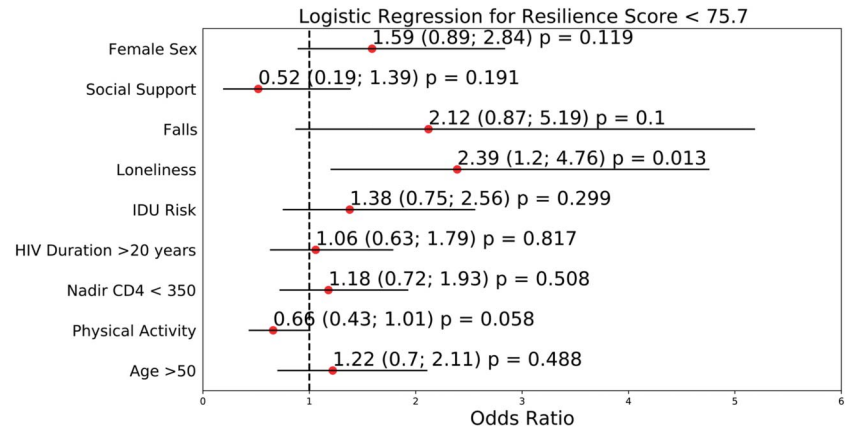
FIGURE 1. Predictors of impaired resilience in the multivariable logistic regression model.

burden of polypharmacy (42.1% vs. 38.7%) we observed while there were significant difference in falls (13.6% vs. 5.0%) and loneliness (24.6% vs. 9.2%).

The relationship between resilience and frailty was explored in a linear regression model, depicting a weak correlation between the 2 measures (r = −0.02, P = 0.65) (see Figure 1, Supplemental Digital Content, http://links.lww.com/QAI/B761).

Table 1 shows 4 frailty–resilience phenotypes in PLWH. Groups included 69 (12%) "fit and resilient," 242 (42.1%) "fit and nonresilient," 50 (8.7%) "frail and resilient," and 214 (37.2%) "frail and nonresilient." The "frail and resilient" were the oldest with the mean age of 56.9 years.

The "frail and nonresilient" had the lowest nadir CD4 (190.5 µL) and the highest prevalence of multimorbidity (92.9%), falls (17.3%), and loneliness (27.6%).

Predictors of impaired resilience were explored in univariable and multivariable analyses. Risk factors of impaired resilience were age >50 years [odd ratio (OR) = 1.64, 95% confidence interval (CI): 1.04 to 2.61], female sex (OR = 1.81, 95% CI: 1.05 to 3.11), loneliness (OR = 3.20, 95% CI: 1.66 to 6.16), and falls (OR = 2.96, 95% CI: 1.25 to 7.03). Protective factors for impaired resilience were physical activity (OR = 0.61, 95% CI: 0.4 to 0.91), self-reported family, and social support (addressing the question "In case of need, can you count on someone close to you?")
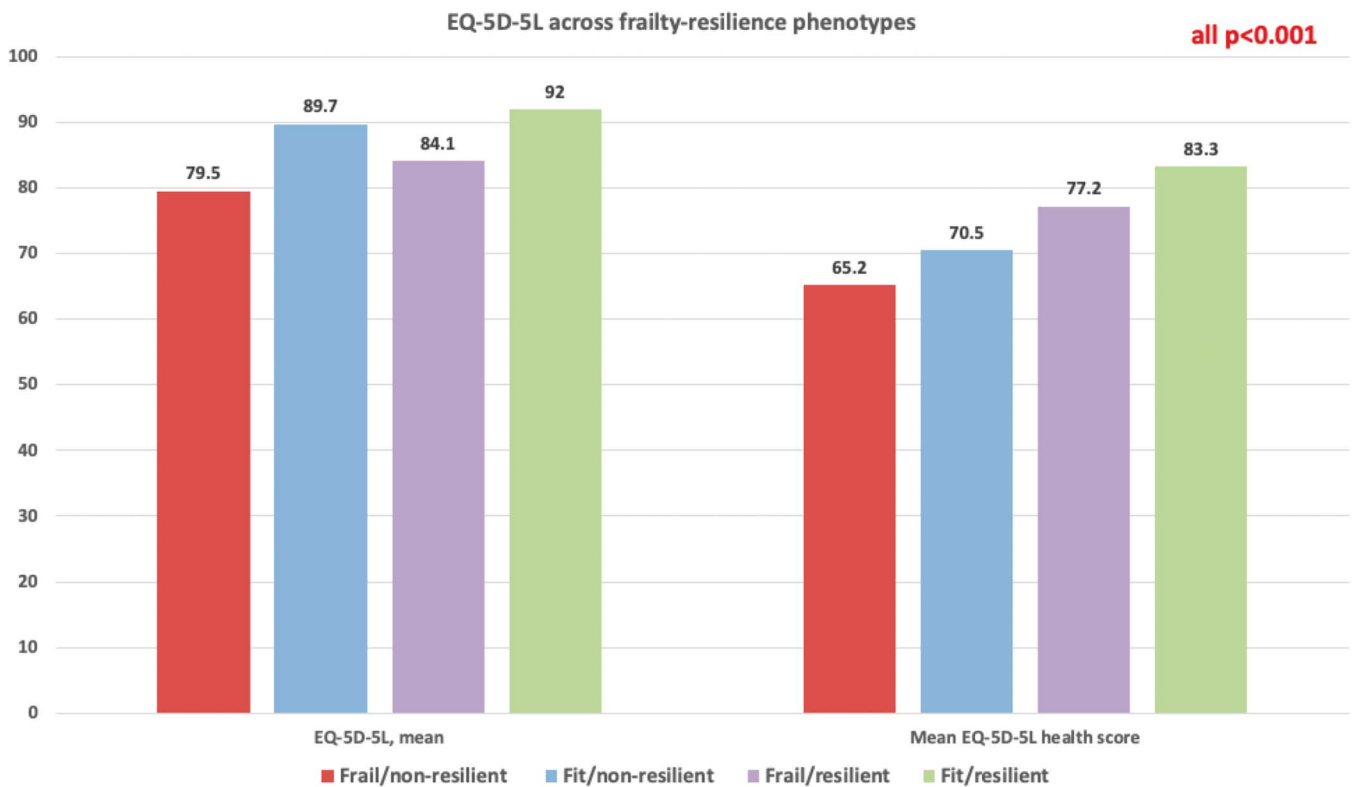

FIGURE 2. Mean percentages of PLWH with EQ-5D-5L scores.
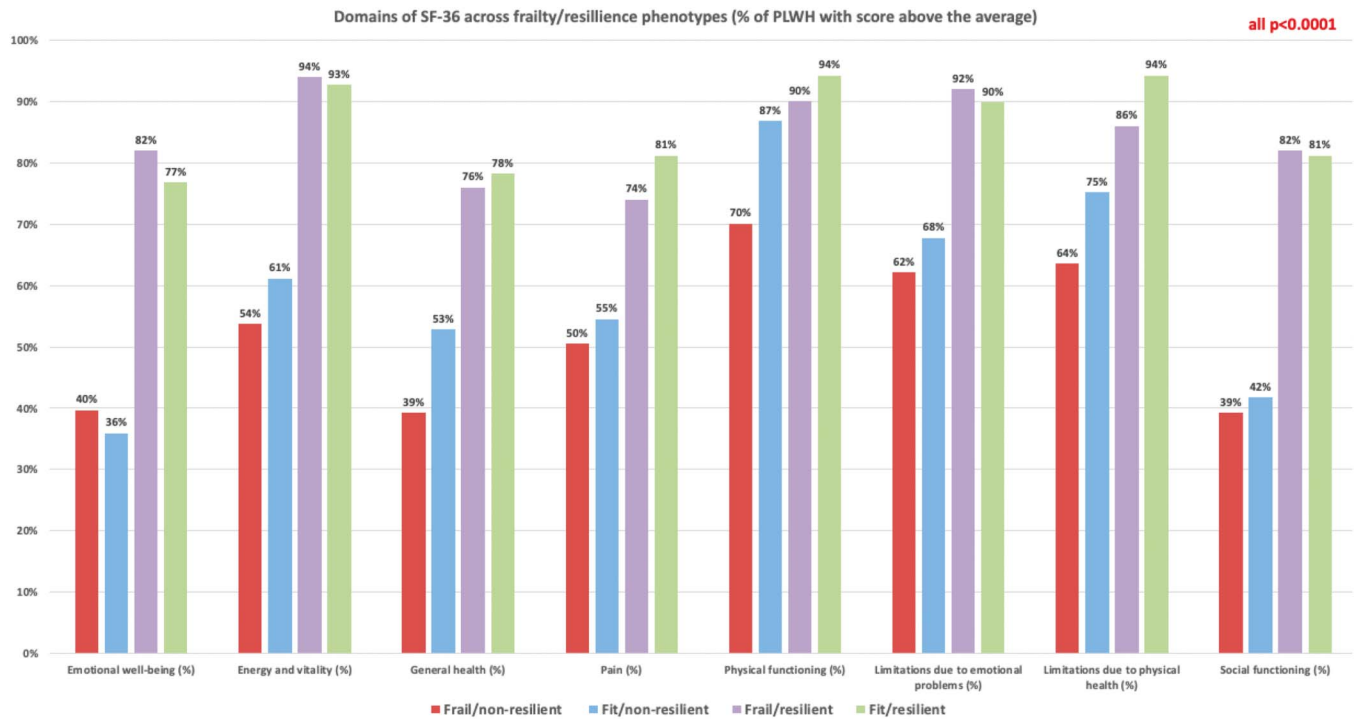
FIGURE 3. Percentage of PLWH with scores above the average.

(OR = 0.31, 95% CI: 0.12 to 0.80) (Table 2). In a logistic regression, impaired resilience was associated with loneliness (OR = 2.39; 95% CI: 1.20 to 4.76, $P < 0.001$), whereas age, sex, HIV risk, HIV duration, and nadir CD4 were not (Fig. 1).

Figures 2 and 3, Supplemental Digital Content, http://links.lww.com/QAI/B761, describe DASS-21 and ISI questionnaire, respectively, according to 4 phenotypes. PLWH with impaired resilience, regardless of frailty, displayed higher burden of depression, anxiety and stress, as well as insomnia.

The study outcome was explored by means of EQ-5D-5L and SF-36 questionnaires. Domains of each questionnaire are detailed in Figures 2 and 3. Figure 2 represents mean percentages of PLWH with EQ-5D-5L scores. Figure 3 represents percentage of PLWH with scores above the average. Apparently, in all explored domains, better HR-QoL was achieved in resilient PLWH regardless of frailty.

Predictors for EQ-5D5L <89.7% were the phenotypes "frail/nonresilient" (OR = 5.21, 95% CI: 2.62 to 10.33, $P < 0.001$) and "fit/nonresilient" (OR = 5.48, 95% CI: 2.8 to 10.74, $P < 0.001$) after correction for age, sex, HIV duration, and nadir CD4 (Fig. 4). Predictors for SF-36 <64.40 were the phenotypes "frail/nonresilient" (OR = 7.43, 95% CI: 2.57 to 21.22, $P < 0.001$), "fit/nonresilient" (OR = 6.27, 95% CI: 2.17 to 18.16, $P < 0.001$), and HIV duration (OR = 1.0, 95% CI: 1.0 to 1.01, $P < 0.001$) after correction for age, sex, and nadir CD4 (Fig. 5).

DISCUSSION

This study characterized resilience in a large cohort and compared this construct with frailty, providing a new insight into the vulnerability of PLWH. According to the resilience construct complementary to frailty we characterized 4 frailty-resilience phenotypes differently associated with demographic, HIV and geriatric variables and more importantly with different impact on HR-QoL. In detail, resilience and frailty acted as complementary forces which differently contributed to multiple domains of HR-QoL.

We have previously characterized frailty in MHMC,[3,17,18] whereas for the first time, we described a high burden of impaired resilience (79.3%) in this cohort, using a validated cutoff for the general population. Interestingly, resilience was not associated with any of the HIV variables, but with loneliness, that is highly prevalent and known to be associated with aging and stigma.[25] A recent study that comprised 273 PLWH in the United States reported a significant interaction between COVID-19 burden and loneliness in women living with HIV.[26] In our study, women had higher burden of impaired resilience, but sex was not an independent predictor in the multivariable analysis. Dedicated interventions for loneliness may be explored using resilience as a potential study outcome.

We must underline that the CD-RISC-25 questionnaire clearly depicts a measure of psychological and not physical resilience. Moreover, the stress condition that we explored (the lockdown associated with COVID-19 crisis and not COVID-19 disease) was potentially more related to mental rather physical health status. We were able to describe a large spectrum of PROs, in which most of the questions referred to the period between last 2 weeks and last year, identifying consistently the "frail and nonresilient" phenotype as the most vulnerable group. However, our findings should not be
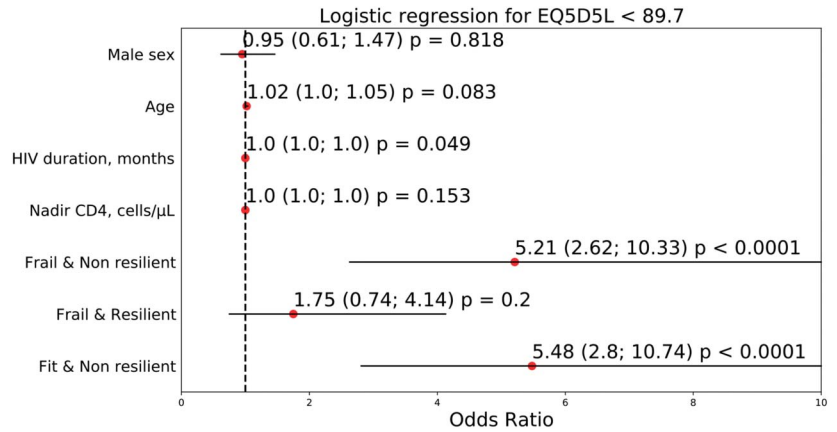
FIGURE 4. Predictors of EQ-5D-5L below the standard mean of general population in the multivariable logistic regression model.

attributed to the pandemic only but should be interpreted as a description of frailty–resilience phenotypes in the context of the COVID-19 era.

We described HR-QoL both in continuous and categorical terms, by means of EQ-5D-5L and SF-36 questionnaires. Several studies compared head-to-head these 2 measures in different health conditions. Apparently, using a short form of these questionnaires, in a Chinese study, the EQ-5D-3L had a higher ceiling effect as well a higher level of discriminant validity among different sociodemographic groups, whereas the SF-6D had a lower ceiling effect and higher level of discriminant validity in health condition groups.[27–29] It was out of the purpose of our study to validate the best tool for HR-QoL in PLWH, but these data may pave the way to further studies that may identify best instruments and optimal cutoffs as a measure of the fourth 90% goal.

Several limitations can be acknowledged and are intrinsic to the observational and cross-sectional nature of the study design and the absence of a control group. Interestingly, resilience was not associated with any of HIV variables, but with loneliness, that is highly prevalent and known to be associated with aging and stigma.[25] Interestingly, resilience was not associated with any of HIV variables, but with loneliness, that is highly prevalent and known to be associated with aging and stigma[25] Description of frailty and resilience is a function of the tools that were

used in this study. The 37-FI is more focused on physical health domains, whereas the CD-RISC-25 describes in particular psychological health domains. In the setting of the COVID-19 pandemic and limited resources, it was more challenging to capture biological basis of this construct. The lack of longitudinal data also did not allow describing resilience as the capacity to recover after a stressor returning to the initial or to a new homeostatic equilibrium state. Nevertheless, we captured psychological resilience in the middle of the COVID-19 crisis and hopefully, in the early future, we will still have the opportunity to study the recovery after the stressor and new health equilibrium. However, we did not account for unmeasured confounders that may also have affected resilience in PLWH other than the COVID-19 crisis. Prospective data may allow us to analyze the interaction between damage and repair and explain why some individuals are aging "faster," and studying them jointly may point to the controversial mechanisms of accelerated aging in PLWH.[30–32] Finally, frailty and resilience were not measured at the same time point, as the resilience had not been assessed previously at MHMC, whereas the frailty index could not be assessed during the lockdown.

In summary, these data show that resilience construct also characterizes health status and well being of PLWH during the COVID crisis. We presented frailty and resilience phenotypes as complementary measures in which each one
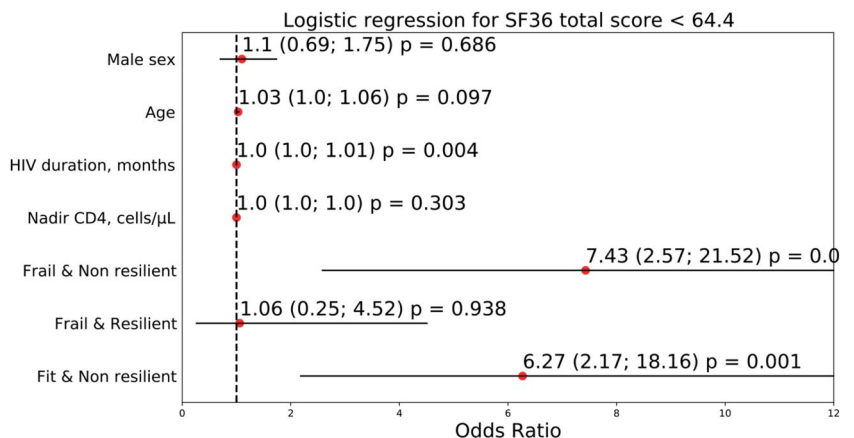

FIGURE 5. Predictors of SF-36 below the standard mean of general population in the multivariable logistic regression model.

depicts different slices of the vulnerability spectrum. The use of both these measures should be encouraged to capture more broad aspects of health of PLWH. By combining these 2 variables into a phenotype, we were able to depict PLWH at a highest risk for negative outcomes and these individuals should be prioritized for dedicated interventions to achieve the fourth 90 goal, that is, optimal HR-QoL.

In conclusion, resilience characterizes the well being of PLWH during the COVID crisis, highlighting that this construct is complementary to frailty in the identification of clinical phenotypes with different impacts on relevant clinical outcomes including HR-QoL.

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