Resilience is associated with frailty and older age in hospitalised patients

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Abstract

Background: Little is known about resilience in an internal medicine setting. We aimed to assess the relationship between resilience and frailty and other clinical and sociodemographic characteristics in a cohort of prospectively enrolled hospitalised patients.

Methods: In 2017–2019, we consecutively enrolled patients in our internal medicine wards. We selected all patients who filled in the 25-item Connor-Davidson resilience scale (CD-RISC). Mean resilience was evaluated according to baseline demographic (i.e., age, sex, marital and socioeconomic status) and clinical (i.e., Cumulative Illness Rating Scale [CIRS], Edmonton Frail Scale [EFS], Barthel index, Short Blessed test, length of stay [LOS]) data. A multivariable analysis for assessing factors affecting resilience was fitted.

Results: Overall, 143 patients (median age 69 years, interquartile range 52–79, 74 females) were included. Resilience was significantly lower in frail (p = 0.010), elderly (p = 0.021), dependent (p = 0.032), and more clinically (p = 0.028) and cognitively compromised patients (p = 0.028), and in those with a low educational status (p = 0.032). No relation between resilience and LOS was noticed (p = 0.597). Frail patients were significantly older (p < 0.001), had a greater disease burden as measured by CIRS comorbidity (p < 0.001) and severity indexes (p < 0.001), were more dependent (p < 0.001), more cognitively impaired (p < 0.001), and displayed a lower educational level (p = 0.011) compared to non-frail patients. At multivariable analysis, frailty (p = 0.022) and dependency (p = 0.031; according to the Barthel index) were associated with lower resilience in the age groups 18–64 and ≥ 65 years, respectively.

Conclusions: Low resilience was associated with frailty and dependency with an age-dependent fashion. Studies assessing the impact of this finding on important health outcomes are needed.

Trial registration: Clinical Complexity in Internal Medicine Wards. San MATteo Complexity Study (SMAC); NCT03439410. Registered 01/11/2017.

Keywords: Ageing, Clinical complexity, Elderly, Multimorbidity

Background

Resilience is a key variable that is rising an ever-great interest among clinicians [1, 2] and consists of a process of negotiation, adaptation or management of stressors, encompassing a broad spectrum of personal abilities that allow bouncing back despite adversities [1, 3]. At present, most of the available data about resilience derive from disease-specific settings, such as psychiatric disorders, HIV, neoplasic diseases, and intestinal diseases [4–10], whereas little is known about resilience on a patient-centred basis, particularly in a hospital setting. Given its nature, resilience is multifactorial, and it has been shown to be affected by several factors, both patient- and

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environmental-related [1]. Remarkably, it can be enhanced through specific interventions, such as cognitive-behavioural therapy [11], and an increased resilience was found to be a predictor of recovery and quality of life in individuals living with chronic conditions [12–14].

Another factor that may theoretically affect resilience is frailty, which develops as a consequence of age-related decline in physiological systems, underlying a vulnerable state of health due to poor homeostatic resources [15, 16]. Indeed, frailty is associated with an increased risk of hospitalisation and mortality [17], and it can be reversed only at an early stage [18] through physical activity and nutritional interventions [19], as well as by using drugs targeting fundamental pathways of senescence [20]. Additionally, extra-biological factors, such as low family income, low educational level, and belonging to ethnic minorities, may represent, besides older age, additional contributors to this condition [21].

In clinical settings, both resilience and frailty can be assessed by means of internationally validated tools, such as the 25-item Connor-Davidson resilience scale (CD-RISC) [3] and the Edmonton Frail Scale (EFS) [22], but, disappointingly, their bidirectional relationship has never been studied. Hence, we aimed to assess the relationship between resilience and frailty and other clinical and sociodemographic characteristics in a cohort of prospectively enrolled hospitalised patients.

**Methods**

The present research is part of the still ongoing San Matteo Complexity (SMAC) study (NCT03439410), which is a prospective cohort study with the aim of validating a clinical complexity index, the general frame of which has already been described elsewhere [23, 24]. In brief, all adult patients (age > 18 years) admitted to our internal medicine ward, regardless of the cause, were consecutively enrolled from November 2017 to November 2019 according to the study protocol and are still currently being followed-up through a phone call. The San Matteo hospital Foundation is a tertiary referral, academic hospital located in Northern Italy, serving a population of roughly 500,000 people, and has a 24-h A&E access. Most patients (> 95%) who are admitted to our internal medicine ward have been first assessed by the emergency department that is in charge of sorting the admission to the various specialty wards.

Patients with a prognosis < 48 h and denial of informed consent were the only exclusion criteria. In case of advanced dementia, the informed consent was requested to the closest relative, caregiver or next of kin. We initially excluded those patients admitted with a severe or ominous condition (due to either the severity of a specific disease or the overall compromised clinical picture), with an expected prognosis of less than 48 h, according to the treating physician. If this was not the case, we eventually included these patients, after the 48-h observation. All the research staff involved into the project were specifically trained for collecting all data within the study [25].

For the specific purposes of the present study resilience was assessed in all consecutive patients, regardless of the admitting diagnosis, since 7th January 2019 onwards, with the CD-RISC, a self-reported questionnaire that was translated and validated into Italian [3, 26]. The CD-RISC comprises of 25 items, each rated on a 5-point scale (0–4), with higher scores reflecting greater resilience [3]. According to the original scale [3], five areas are explored, namely personal competence, high standards, and tenacity (a); trust in one’s instincts, tolerance of negative affect, and strengthening effects of stress (b); positive acceptance of change and secure relationships (c); control (d); and spiritual influences (e). Only patients who were unable (i.e., due to severe dementia, altered state of consciousness, linguistic barrier) or unwilling to complete the questionnaire, were excluded. A total of 143 patients (median age 69, IQR 52–79, 74 females), whose characteristics will be described later, were eventually included.

Frailty, according to the main study protocol, was assessed in the same 143 patients using a validated, and broadly used scale [22] that was translated into Italian. The EFS was initially designed as an easily available questionnaire to measure frailty in the elderly, both in a hospital and in an outpatient setting [22]. It consists of nine items that investigate cognition, health status, functional dependence, social support, medication use, nutrition, mood, continence, and functional performance. The score ranges from 0 to 2 per each item, with higher scores reflecting greater frailty [27]. A score of > 5 defines a frail state, and accordingly, we used this cut off for defining a patient as being frail.

All the causes of admission were collected according to the International Classification of Diseases (ICD)—9th revision. Categories with less than 10 cases were pooled into the category “others”. Additionally, the overall burden of medical and psychiatric conditions was calculated by using the Cumulative Illness Rating Scale (CIRS) comorbidity and severity indexes [28]. While the CIRS comorbidity index reflects the burden of the number of diseases within the same patient, the severity index reflects how severe are the diseases on a 5-point scale (from 1, absence of the disease, to 5, life-threatening on a short term). Both indexes are calculated through a standardised algorithm [28].

Other relevant demographic or clinical data, as reported later, were retrieved from the dedicated REDCap database of the SMAC study, in which patients’ data were entered in a pseudo-anonymised format.
The primary aim of the study was to assess whether any relationship between resilience and frailty existed. As a secondary outcome, we assessed whether this relationship depended on a set of variables chosen a priori by the clinicians according to their relevance, namely age, sex, CIRS indexes, BMI, Barthel index (which assesses functional dependency) [29], income (categorised according to the limit of 1000€/month net salary below which people can be eligible for public subsidies in Italy), living alone, schooling (categorised into ≤ 8 or > 8 years of education, which reflects the compulsory education in Italy), the Short Blessed Test (which assesses cognitive impairment) [30], and length of stay (LOS). For the Barthel index, a cut off of < 60 was used for indicating moderate-to-severe dependency, as previously reported [31], while a cut off of ≥ 9 was used for the Short Blessed Test for indicating any grade of cognitive impairment, as originally reported in the validation study [30]. All the scales were assessed by the study investigators for each patient. Of the scales used in this research, only the CD-RISC is under license. The license was obtained from the scale owner (Prof. Davidson), by paying a fee for its use in an academic setting, in up to 1000 individuals.

All patients provided written informed consent prior to study enrolment and the study protocol was approved by the local Ethics Committee (IRCCS Policlinico San Matteo, 3 July 2017, Protocol number 2017/0019414).

Statistical analysis
Continuous data were described with the mean and standard deviation or the median and interquartile range (IQR) and compared between EFS groups (<5/>5) with the Student t test or the Mann Whitney U test, respectively, depending on the distribution. The distribution of continuous variables was assessed graphically by plotting the quantiles of the variable against the quantiles of normal distribution. Categorical data were reported as counts and percent and compared with the Fisher exact test. Univariable generalised linear models were then fitted for resilience, where the choice of covariates was decided a priori based on clinical considerations. Candidates were the most relevant patient clinical characteristics and the socioeconomic status. Variables with a p-value < 0.10 at the univariable model were included in the multivariable models. These were fitted in two predefined subgroups: adult patients (aged 18–64 years) and elderly patients (aged ≥ 65 years), according to the current WHO classification for developed countries. Spearman’s rho was used for assessing the relation between resilience (continuous variable) and LOS. The software Stata 16 (StataCorp, College Station, TX, USA) was used for all computations. The study follows the STROBE recommendations for quality assurance.

Results
Table 1 reports the main demographic and clinical characteristics of the 143 enrolled patients. Of note, the majority of patients were aged ≥ 65 years, displayed a high multimorbidity burden, as measured by the CIRS, and roughly one third of them was frail, as measured by the EFS.

In Table 2 we reported the demographic and clinical variables in relation to resilience as a continuous variable. Resilience was significantly lower in frail (p = 0.010), elderly patients (p = 0.021), in those lacking functional autonomy (p = 0.032), in those with a higher CIRS severity index (p = 0.028) and in more cognitively impaired patients (p = 0.028), and in those with a low educational level (p = 0.032). No relation between resilience and sex, BMI, admission diagnosis, income, living alone, and LOS (Spearman’s rho -0.0445; p = 0.597) was found.

Demographic and clinical variables in relation to frailty are reported in Supplementary Table 1. Similarly to what found for resilience, also frail patients (EFS > 5) were significantly older (p < 0.001), had a greater disease burden as measured by CIRS comorbidity (p < 0.001) and severity indexes (p < 0.001), were more dependent (p < 0.001), more cognitively impaired (p < 0.001), and displayed a lower educational level (p = 0.011) compared to non-frail patients. Notably, BMI, LOS, lower household income and living alone were not statistically different between frail and non-frail patients (data not shown in Table).

In a multivariable analysis for factors affecting resilience according to different age groups (Table 3), after the exclusion of variables which turned out to be collinear, we found that frailty as measured by the EFS (p = 0.022) and dependency according to the Barthel index (p = 0.031) were the only statistically significant factors related to lower resilience in the age groups 18–64 and ≥ 65 years, respectively. Although only a minority of patients had a Barthel index < 60, we could not use this variable as continuous due to a relevant ceiling effect (i.e., the first tertile and the first quartile cut-offs were 88 and 95, respectively). Given that at univariable analysis there was no association of admission diagnosis and resilience, this variable was not included in the multivariable analysis.

Discussion
We herein found that, in an internal medicine setting comprising of a majority of elderly patients with a great disease burden, resilience and frailty were inversely correlated and both associated with ageing, dependency, cognitive impairment, and low educational level. These correlations seem to be a feature of this setting as a whole, as they turned out not to be dependent on the admission diagnosis. The fact that, in our study, the mean resilience level (60.6) turned out to be rather low when
compared to other available settings, such as that of geriatric outpatients (66.2) [32], corroborates the importance of the clinical context. As we mentioned, resilience was lower in frail, elderly, dependent, multimorbid patients, in whom it has been poorly addressed in the past [33], as well as in those with a low educational level. Of note, at multivariable analysis, resilience was significantly and inversely related to frailty in adults (aged 18–64 years), and to dependency in older patients (≥ 65 years). We hypothesise that this may reflect the “natural history” of frailty which initially compromises main organ system functions and subsequently determines dependency, which both may severely affect resilience. Indeed, dependency is often preceded by a state of reduced capacity to respond to stressors due to a decline in functional reserves, i.e., frailty [34]. At any rate, we should highlight that our study was not designed for testing the directionality of these observed correlations, the explanation of which may be provided by future, ad hoc, longitudinal studies. Additionally, it should be noted that only a minority of patients in our study fell into the category of a Barthel index < 60 (seven cases), and this variable could not be used as continuous due to the substantial ceiling effect.

Consistently with previous observations, we found that also in an internal medicine setting advanced age [15, 35], multimorbidity [36], dependency [37], severe cognitive impairment [38], and low level of schooling [39, 40] were all associated with frailty. Of note, household income did not differ between frail and non-frail patients, and this might be explained by the universal public healthcare coverage which, at least partially, reduces socioeconomic differences in Italy. Additionally, the LOS did not differ between frail and non-frail patients, due to the allegedly higher in-hospital mortality in the former [16, 41, 42].

The results of the present study seem to point at the need for early detection of both low resilience and frailty, so to plan and prescribe ad hoc interventions for improving patients’ health. Since both resilience and frailty can be improved [43–46], corrective actions may potentially constitute a therapeutic advantage. For example, physical activity and nutritional interventions help improving both physical and mental functioning and are key for preventing frailty [19, 47, 48]. Resilience can be implemented through other interventions, including cognitive behavioural therapy [11] and, of note, according to a recent systematic review, resilience-promoting interventions have been attempted in twelve studies involving patients living with chronic conditions, including cancer, cardiovascular diseases, and diabetes [49]. Although the heterogeneity of the included studies partly affects the strength and generalisability of the findings, resilience enhancement programmes turned out to be of benefit on depression, anxiety, and quality of life, helping patients to recognise the changes in their lives and to improve adherence to the treatment plans [49].

To summarise, we have here provided further evidence about the necessity of integrating in clinical medicine the

| Table 1 | Main demographic and clinical characteristics of the cohort of patients |
| --- | --- |
| Total number of patients, n | 143 |
| Age (years), median (IQR) | 69 (52–79) |
| Age groups (years), n (%) | 18–64 60 (42.0) ≥ 65 73 (58.0) |
| Sex, n (%) | M 69 (48.3) F 74 (51.7) |
| CIRS comorbidity index, median (IQR) | 3 (2–4) |
| CIRS severity index, median (IQR) | 1.6 (1.4–1.8) |
| CIRS comorbidity index ≥ 3, n (%) | No 86 (60.1) Yes 57 (39.9) |
| BMI class, n (%) | < 18.5 15 (10.5) 18.5–24.9 71(49.6) 25–29.9 34 (23.8) ≥ 30 23 (16.1) |
| Admission diagnosis, n (%) | Circulatory ICD9 chapter 30 (21) Respiratory ICD9 chapter 22 (15) Gastroenteric ICD9 chapter 18 (13) Symptoms ICD9 chapter 43 (30) Others 30 (21) |
| Resilience, mean (SD) | 60.6 (19.1) |
| Edmonton > 5, n (%) | No 94 (66.2) Yes 49 (33.8) |
| Barthel index, mean (SD) | 92.5 (12.7) |
| Income < 1000 €/mon, n (%) | No 85 (59.4) Yes 58 (40.6) |
| Living alone, n (%) | No 107 (74.8) Yes 36 (25.2) |
| Schooling ≤ 8, n (%) | No 102 (71.3) Yes 41 (28.7) |
| SBT ≥ 9, n (%) | No 113 (79.6) Yes 29 (20.4) |

Abbreviations: CIRS Cumulative Illness Rating scale, ICD9 International Classification of Diseases 9.th revision, IQR Interquartile range, SD Standard deviation
evaluation of resilience and frailty as it has been recently proposed by Hale and colleagues [50]. In this conceptual paper, the authors postulate that frailty can be considered as a phenotype of patients who lost resilience, and both factors may be potentially improved by taking actions on several other external or environmental determinants of health, such as the socioeconomic status and the level of education, this latter being correlated to both resilience and frailty in our study. The clinician has a central and active role in this process, being involved into the recognition of more vulnerable patients who may benefit from tailored interventions based on their specific needs.

Our study has some limitations that should be mentioned. The sample size is rather small, and it should be kept in mind that resilience can only be assessed in patients without severe cognitive impairment. Also, only

**Table 2** Demographic and clinical variables in relation to resilience as a continuous variable (generalised linear regression model, univariable analysis)

|                           | N (%) | Mean ± SD | Difference | 95% CI       | p-value |
|---------------------------|-------|-----------|------------|---------------|---------|
| Edmonton frail scale and resilience |       |           |            |               | 0.010   |
| Edmonton ≤ 5              | 94 (65.7) | 63.41 ± 17.96 | 0 (base)   |               |         |
| Edmonton > 5              | 49 (34.3) | 54.69 ± 20.38 | -8.73      | -15.32 to -2.13 |         |
| Sex and resilience        |       |           |            |               | 0.652   |
| M                         | 69 (48.3) | 61.32 ± 18.48 | 0 (base)   |               |         |
| F                         | 74 (51.7) | 59.86 ± 19.88 | -1.45      | -7.81 to 4.90  |         |
| Age group and resilience  |       |           |            |               | 0.021   |
| 18–64                     | 60 (42.0) | 66.25 ± 18.41 | 0 (base)   |               |         |
| ≥ 65                      | 73 (58.0) | 56.91 ± 18.21 | -9.34      | -17.32 to -0.78|         |
| BMI class and resilience   |       |           |            |               | 0.785   |
| < 18.5                    | 15 (10.5) | 60.47 ± 19.93 | 0 (base)   |               |         |
| 18.5–24.9                 | 71 (49.6) | 62.15 ± 18.58 | 1.69       | -9.15 to 12.53 | 0.759   |
| 25–29.9                   | 34 (23.8) | 58.59 ± 20.54 | -1.88      | -13.70 to 9.95 | 0.754   |
| ≥ 30                      | 23 (16.1) | 58.65 ± 19.22 | -1.81      | -14.48 to 10.85| 0.777   |
| Admission diagnoses       |       |           |            |               |         |
| *Circulatory ICD9 chapter  | 30 (21.0) | 56.63 ± 18.68 | 0 (base)   |               |         |
| *Respiratory ICD9 chapter  | 22 (15.4) | 61.73 ± 20.71 | 5.09       | -5.60 to 15.79 | 0.348   |
| *Gastroenteric ICD9 chapter| 18 (12.6) | 64.83 ± 17.20 | 8.20       | -3.16 to 19.56 | 0.156   |
| *Symptoms ICD9 chapter     | 43 (30.0) | 61.53 ± 19.49 | 4.90       | -4.16 to 13.97 | 0.287   |
| *Other ICD9 chapters       | 30 (21.0) | 59.70 ± 19.62 | 3.07       | -6.77 to 12.91 | 0.539   |
| Barthel index              |       |           |            |               | 0.032   |
| Barthel ≥ 60               | 136 (95.1) | 61.35 ± 18.66 | 0 (base)   |               |         |
| Barthel < 60               | 7 (4.9) | 45.43 ± 24.01 | -15.92     | -30.41 to -1.42|         |
| CIRS; CIRS severity and resilience |       |           |            |               | 0.028   |
| CIRS < 3                   | 86 (60.1) | 63.42 ± 17.74 | 0 (base)   |               |         |
| CIRS ≥ 3                   | 57 (39.9) | 56.26 ± 20.55 | -7.16      | -13.54 to -0.77|         |
| Income and resilience      |       |           |            |               | 0.073   |
| Income ≥ 1000 €            | 85 (59.4) | 62.94 ± 18.84 | 0 (base)   |               |         |
| Income < 1000 €            | 58 (40.6) | 57.09 ± 19.27 | -5.85      | -12.26 to 0.55 |         |
| Living alone and resilience|       |           |            |               | 0.519   |
| No                        | 107 (74.9) | 61.17 ± 18.88 | 0 (base)   |               |         |
| Yes                       | 36 (25.1) | 58.78 ± 20.16 | -2.39      | -9.71 to 4.92  |         |
| Schooling and resilience   |       |           |            |               | 0.032   |
| Schooling > 8 years        | 102 (71.3) | 62.75 ± 19.02 | 0 (base)   |               |         |
| Schooling ≤ 8 years        | 41 (28.7) | 55.15 ± 18.65 | -7.60      | -14.51 to -0.68|         |
| Short blessed test and resilience |       |           |            |               | 0.028   |
| SBT < 9                   | 113 (79.0) | 62.68 ± 18.94 | 0 (base)   |               |         |
| SBT ≥ 9                   | 30 (21.0) | 54.17 ± 16.28 | -8.51      | -16.10 to -0.92|         |

Abbreviations: BMI Body Mass Index, CI Confidence interval, CIRS Cumulative Illness Rating Scale, SBT Short blessed Test, SD Standard deviation
a minority of patients displayed a low Barthel index, and hence this datum should not be overinterpreted. Instead, the strengths of our study include its prospective nature, which was not based on mere administrative data, and the fact that all data have been collected by the same research nurse and physicians who had been specifically trained before study initiation [25], and this ensures the homogeneity of the data. Our results should be interpreted in the light of this specific setting, i.e., that of hospitalised patients in an internal medicine ward, in which most patients are elderly and burdened by multimorbidity.

**Conclusions**

To conclude, resilience and frailty turned out to be inversely related in adult hospitalised patients, while resilience and dependency were inversely related in a more advanced age. Whether frailty occurs before or after the occurrence of low resilience needs to be elucidated. Studies assessing the impact of these findings on important health outcomes are warranted, especially by including more compromised and dependent patients.

**Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s12877-022-03251-9.

**Additional file 1: Supplementary Table 1.** Demographic and clinical variables in relation to frailty (as measured by the Edmonton Frail Scale).

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**Authors’ contributions**

All authors participated in the drafting of the manuscript or critical revision of the manuscript for important intellectual content and provided approval of the final submitted version. Individual contributions are as follows: GRC designed the study; GRC, MV, ASB, and CK organized data collection and drafted the manuscript; all other authors conducted the study and enrolled patients; CK, performed statistical analysis and interpreted data; GRC made the final critical revision for important intellectual content. All authors approved the final version of the paper.

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**Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

### Table 3

Multivariable sub-group analysis (generalised linear regression model) for factors affecting resilience according to age groups (18–64 and ≥65 years)

| Age 18–64          | (model p-value 0.078) | p-value | Age ≥65          | (model p-value 0.240) | p-value |
|--------------------|-----------------------|---------|------------------|-----------------------|---------|
| Edmonton           |                       |         |                  |                       |         |
| Edmonton < 5       | 0 (base)              | 0.022   |                      | 0 (base)              | 0.817   |
| Edmonton > 5       | -14.6                 | -2.17   |                      | 1.2                   | -8.98   |
| Barthel index      |                       |         |                  |                       |         |
| Barthel > 60       | 0 (base)              | 0.192   |                      | 0 (base)              | 0.031   |
| Barthel < 60       | 25.5                  | -64.11  |                      | -17.5                 | -1.63   |
| Short blessed test |                       |         |                  |                       |         |
| SBT < 9            | 0 (base)              | 0.800   |                      | 0 (base)              | 0.664   |
| SBT > 9            | -3.10                 | 21.30   |                      | -2.2                  | -1.17   |
| Income             |                       |         |                  |                       |         |
| Income < 1000 €    | 0 (base)              | 0.015   |                      | 0 (base)              | 0.487   |
| Income < 1000 €    | -6.7                  | 3.05    |                      | -3.1                  | -5.70   |
| CIRS; CIRS severity|                       |         |                  |                       |         |
| CIRS < 3           | 0 (base)              | 0.967   |                      | 0 (base)              | 0.316   |
| CIRS > 3           | 0.26                  | 12.56   |                      | -4.77                 | 6.55    |
| Schooling          |                       |         |                  |                       |         |
| Schooling > 8 years| 0 (base)              | 0.341   |                      | 0 (base)              | 0.685   |
| Schooling < 8 years| -11.7                 | 12.78   |                      | 1.8                   | 68.62   |

**Abbreviations**

CBT: Cognitive behavioural therapy; CD-RISC: Connor-Davidson resilience scale; EFS: Edmonton Frail Scale.
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