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Development and testing of tools to stratify prognosis of older patients with frailty in different clinical settings

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SUMMARY

Maintaining functional independence with advancing age is an important goal for individuals and society. Older people with frailty are at risk of adverse outcomes, including loss of independence. Thus, identification of frail older persons and, more broadly, prognostic stratification of older persons is essential in order to guide clinical decision-making and to apply appropriate interventions in all clinical settings, either in urgent or subacute-chronic situations, with the ultimate goals of preventing or postponing disability. The evaluation of the Silver Code effectiveness in improving clinical outcomes of frail older persons accessing the emergency department will be a first research area. A second area of research activity will be the prognostic stratification of frail older persons in an outpatient clinic setting, with the aim of integrating more conventional approaches (Comprehensive Geriatric Assessment and Short Physical Performance Battery) with data provided by wearable devices for automatic assessment of physical performance. The two research venues have the common scope of improving our ability to understand factors leading to frailty and from frailty to poor health outcomes in older persons.

BACKGROUND AND AIM

Vulnerability and Frailty

In everyday language, the term “vulnerable” refers to someone or something that can be hurt, injured or damaged. Common to many fields, even in the medical literature the concept of vulnerability is broad and embraces several patients and / or different situations, from the newborn to patients with cancer. In medicine, identifying vulnerable patients is necessary to conduct risk stratification and to correctly plan a diagnostic and therapeutic pathway [Palermo S, 2021; Slaets JP, 2006].

In the geriatric field, the vulnerable patient was defined as someone aged 65 years and over at an increased risk of functional decline or death within two years [Saliba D, 2001]. How can vulnerable patients be identified? Tools for the prognostic stratification in the older population are abundant in the recent medical literature. To this purpose, many tools have been proposed: it should be pointed out that, even with the same scope and sharing common domains of investigations, these tools may substantially differ, as they highlight diverse aspects of older people that can negatively influence prognosis, such as multimorbidity, functional loss, depressive symptoms, and social distress. Thus, each tool in its own way identifies a subtype of vulnerable older adult [Saliba D, 2001; Kim LD, 2016; Teh R, 2018; Sheikh JI, 1986; Ragusa FS, 2022].

In medical practice, older adults are considered as vulnerable when they exhibit clinical complexity, mostly in terms of multimorbidity. This also stems from the longstanding habit of orienting medical practice, and teaching, towards single diseases as separate entities: therefore, the complex patient is the one with several diseases at the same time. However, this approach does not allow for a thorough understanding of a patient's overall health status, nor of the prognostic determinants that arise from it. Many studies show that the most important predictor of adverse outcomes in older adults is the presence and the severity of disability, independent of the number and type of coexistent diseases [Ferrucci L, 1991; Landi F, 2010]. Thus, we may say that disability is the major determinant of vulnerability in older adults. On the other hand, the same degree of disability is not predicted by the sum of the diseases alone, but is the result of complex interactions between biological, environmental, and clinical factors. The prognostic relevance of functional status has also been demonstrated in non-disabled older people, again independently of the severity of multimorbidity: non-disabled older adults with reduced physical performance are more susceptible to new onset disability, in the domain of mobility as well as in that of basic activities of daily living (BADL) [Guralnik JM, 1995; Di Bari M, 2006]. At the same time, similarly to what had been observed with overt disability [Ferrucci 1991], initially non-disabled older persons with poor physical performance have higher mortality [Di Bari M, 2006; Studenski S, 2011; Pavasini R, 2016], independent of coexisting pathologies. For this reason, evaluation of physical performance has assumed central importance in geriatrics, both as a clinical tool to develop clinical pathways and evaluate its effects and as a prognostic tool.

Within the area of vulnerability, older adults who are not disabled, but are at an increased risk of adverse outcomes, disability, can therefore be legitimately identified and defined as frail. In other terms, frailty is an age-related condition, in which a decline in the function of multiple physiological systems is accompanied by increased vulnerability to internal and external stressors, stemming from a progressive inefficiency of the mechanisms responsible for maintaining biological homeostasis. Frailty is therefore better characterized by evaluations of integrated and complex functions, which may be compromised by diseases, as well as by a wide range of physical, psychological, cognitive, and social factors. Dr. Linda Fried's model is the one that best corresponds to this view of frailty. Based on data from the Cardiovascular Health Study, it postulates the existence of a frailty phenotype and classifies an individual as frail when three or more of the following five physical components are present: shrinking (unintentional weight loss of 4·5 kg or more in the last year), weakness (low grip strength), exhaustion (self-reported), slowness (slow walking speed), and low physical activity [Fried L, 2001]. This model offers measurable parameters to identify frailty, and each of these parameters is the result of complex and multifactorial interactions [Rubbieri G, 2013]. Thus, according to the phenotype model, frailty is clearly distinct from comorbidity and disability, and it would rather be a precursor of disability.

Another common frailty instrument used in research and in clinical practice was developed by the Canadian school, led by Dr. Kevin Rockwood, and is based on the principle of accumulation of deficits. From an operational point of view, this approach has led to the development of two tools for the identification of “frailty”, the Frailty

Index (FI) and the Clinical Frailty Scale (CFS). The FI is based on a list of at least 30 deficits, including signs and symptoms, specific pathologies, functional dependence and laboratory or imaging alterations: a patient with deficits in at least a quarter of the listed conditions is defined as frail [Rockwood K, 2007]. The CFS classifies older adults into 9 categories, from “very fit” to “terminally ill”, according to the severity of multimorbidity and disability.

Given the absence of a codified gold standard, in research and clinical practice the phenotype and the accumulative deficits models of frailty are both considered valid in the recognition of frailty [Dent E, 2022; Hoogendik EO, 2019]. The accumulation of deficits model certainly offers the advantage of a greater simplicity of application, as both the FI and the CFS can be compiled even only on the basis of clinical history information. Conversely, Fried's model requires to perform tests (handgrip, walking speed) that are not part of standard clinical practice; moreover, it provides information only on patient’s current status and cannot be used retrospectively, to infer the frailty status prior to the index event. However, beyond their ease of application, the two instruments are profoundly different: the phenotype model seems to identify older adults at risk of disability and, therefore, refers to non-disabled subjects, while the deficit accumulation model incorporates disability as a possible item to estimate the severity of frailty. Thus, we might argue that Fried’s scale is to be properly considered a tool for identifying frailty, while the FI and CFS are improperly defined as instruments of frailty and should be more appropriately seen as measures of complexity or, even better, vulnerability.

In general, most medical research focused on the comparison between these two tools in terms of predictive ability, whereas a few studies tried to analyse the differences between the populations identified by the two tools. There is evidence that the populations identified by the two tools differ substantially. Indeed, in the same, large (n=5,362) cohort of older persons from the Cardiovascular Heart Study the prevalence of frailty was similar (7.0% with Fried’s model and 8.3% with the FI), but with a very poor agreement between them (only 12%). The concordance between the different tools was greater in subjects with a high burden of comorbidities and disabilities, whereas the agreement was very poor exactly in those subjects in whom the identification of frailty would be more important, that is the non-disabled. It should also be noted that the FI more easily identifies patients with greater multimorbidity burden as frail, which is not surprising given how the instrument itself is structured [Xue QL, 2020].

In conclusion, different tools of frailty identify different populations. “Frailty” as a condition of increased risk of adverse events in older non-disabled persons is expressed more rigorously by Fried's model. Rockwood’s model and its resulting tools identify vulnerable older adults, at risk for adverse events, but to a large extent already disabled.

Acute Care Setting – The Dynamic Silver Code

Older frail persons presenting in an urgent situation to the Emergency Department (ED) are often extremely challenging [Beland F, 1991]. They usually have multiple diseases with unusual clinical presentations [Grosmaitre P, 2013], require polypharmacy (which makes treatment particularly complex and exposes to the risk of adverse drug events) [Hohl CM, 2001], and may fail to receive adequate care when admitted to the ED, especially in the presence of cognitive impairment, communication difficulties, or poor social support [Hustey FM 2002; Schumacher JG, 2006]. Not surprisingly, vulnerable older patients are therefore at high risk for multiple hospital admissions and adverse health outcomes, such as functional or cognitive decline, or death [Hastings SN, 2007]. Rapid identification of older persons at risk is therefore of major importance in the ED. To this purpose, tools for prognostic stratification should ideally be accurate, efficient, and easy-to-apply, in order to allow for quick identification of subjects requiring specialized care [Havard D, 2012]. The Dynamic Silver Code (DSC), a prognostic stratificator purely based on administrative data, can satisfy these needs [Balzi D, 2019]. Whereas its parent tool, the Silver Code, was based on one single moment of observation [Di Bari M, 2010; Di Bari M, 2012], the DSC considers, for each individual, the dynamics of events occurring across time. The new tool is implemented into the software routinely used in the ED of several hospitals in Tuscany, Italy, to provide automated, real-time risk stratification of older patients. As soon as an eligible patient is triaged, the repository of healthcare data of the Local Health Unit is queried to provide, thanks to on-demand linkage of the different archives involved, the information required to obtain the DSC: age, gender, number of drugs prescribed in the previous 3 months, days from previous hospital admission, and its associated main diagnostic group (**Table 1**).

Table 1. Variables included in the Dynamic Silver Code with corresponding scores, obtained from Cox regression model predicting 1-year death in 90,039 subjects aged 75+ years [Balzi D, 2019].

Variable	**Score**
Age (years)	
75-79	0
80-84	8
85+	23
Gender	
Female	0
Male	5
Number of drugs in previous 3 months	
0-3	0
4-5	1
6-8	2
9+	6
Main diagnostic group in previous (6 months) hospital admission	
No admission	0
Cardiovascular disease / Others	19
Cancer	42
Respiratory disease	28
Days from previous (6 months) hospital admission	
No admission	0
30-180	8
0-30	0

The score is then in real time calculated and shown, together with the corresponding risk class (class I: score 0-10; class II: score 11-25; class III: score 26-34; class IV: score 35+), onto the computer screen. The lag time between occurrence of events contributing to the DSC (hospitalizations and drug prescriptions) and their registration in the healthcare data repository is approximately 2 weeks. As suggested in the Anziani in DEA (AIDEA) study, designed by the Department of Clinical and Experimental Medicine, at the University of Florence and sponsored by the Italian Ministry of Health and by the Tuscany Region, the DSC evaluates the individual background risk of death at 7 and 30 days and 1 year, irrespective of the event leading to ED admission [Balzi D, 2019].

This first research area focuses on evaluation of the effects of large-scale application of the DSC in the ED, as a guide to optimal management of older patients requiring hospitalization for medical reasons.

Ambulatory Setting

In non-urgent conditions, such as when older persons are seen in an outpatient clinic, assessment of physical performance represents a crucial clue to identify frail older subjects, who may then be targeted for interventions aiming at the prevention of overt disability and other clinical correlates of frailty. Identification of frailty and related prognostic assessment can and should be based on a completely different approach, compared to the kind of assessment lead in an acute setting. Comprehensive Geriatric Assessment (CGA) has been developed as the gold standard to this purpose [Stuck AE, 1993], especially if complemented with objective evaluation of physical performance with appropriate testing, such as the Short Physical Performance Battery (SPPB) [Chiarantini D, 2010; Legrand D, 2016]. However, widely-accepted tools for objective, automated, and unobtrusive assessment of physical performance and frailty are lacking and this limits the application of preventive interventions on a large scale. In recent years, the widespread adoption of wearable devices equipped with inertial sensors has brought to the development of innovative approaches to monitor health and wellbeing in several health conditions [Amiri AM, 2017; Jovanov E, 2015; Tison GH, 2018]. We hypothesize that sensor-based automated assessment may prove a useful integration to conventional clinical assessment for the detection of frail older persons, and it might even represent an alternative, at least in some settings and circumstances.

This second area of research activity considers the prognostic stratification of frail older persons in an outpatient clinic setting, with the aim of integrating more conventional approaches (CGA and SPPB) with data provided by wearable devices for automatic assessment of physical performance.

Community Setting

Although it will not be part of the present study project, for the sake of completeness we mention that the possibility of easily identifying a population at risk of functional decline and adverse clinical events is of great importance also in the community setting. In this context, the goal is to promote health in old age, implement effective interventions to reduce disability and adverse events in frail older adults at home, and reduce the human and economic burden of care for the elderly.

For identifying frail older adults in the general population, many tools have been proposed in the literature in recent years, without one having been identified with ideal characteristics [Faller JW, 2019]. Many of these provide for a clinical evaluation of the subjects or the administration of structured questionnaires, limiting their diffusion and applicability at the level of population screening.

One of the most used tools for this purpose is the Short Physical Performance Battery (SPPB), which, through the timed assessment of balance, walking speed and ability to get up from a chair without the help of the arms [Guralnik JM, 1994], provides a measure of lower limb performance that has been shown to be a powerful predictor of disability and mortality over the years [Vasunilashorn S, 2009; Di Bari M, 2006].

In terms of ease of use, self-report tools have a clear advantage, as they can be administered in an agile way to a large population, even without providing for direct contact. The most used of these self-report questionnaires are the PRISMA-7 and the Groningen Frailty Indicator, which however, despite the excellent accuracy shown in detecting the presence of frailty [Ambagtsheer RC, 2020], are calibrated to identify a population which, in addition to frailty, has a more or less advanced degree of disability [Raîche M, 2008]. On the other hand, in the INTERFRAIL study, coordinated by the Regional Health Agency of Tuscany in collaboration with the Geriatrics of the University of Florence and the USL Toscana Centro, a short self-report questionnaire was developed, administered by mail, which demonstrated a good diagnostic accuracy in identifying the presence of the physical frailty phenotype according to Fried, excluding cases of overt disability in the basic activities of daily living (BADL), and a good ability to predict the risk of death, hospitalization, access to Emergency Department and institutionalization at 12 months [Di Bari M, 2014; Mossello E, 2016].

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Further Validation of the Dynamic Silver Code

Although important, the predictive validity of a prognostic score may not be sufficient to advocate its application in clinical practice. Indeed, patients with similar prognosis may exhibit diverse features, suggesting prevalent physical frailty or cognitive impairment: although tightly interconnected and often coexisting, these conditions require different care approaches, within the overarching geriatric approach of comprehensive geriatric assessment (CGA) [Xue QL, 2020]. Thus, comparing the characteristics of patients across the DSC classes, that is, assessing the concurrent validity of the tool against those features characterizing the geriatric patient, would be an important complement and a further stimulus to its application. This represents the primary aim of this study. Accessorily, we examined whether time spent in the ED and subsequent disposition differed across DSC classes, as these 2 immediate outcomes had not been reported in previous DSC studies. To these purposes, we analyzed data collected in the Anziani in DEA (AIDEA) study, standing for “Older Persons in the ED,” where the predictive validity of the tool has been already ascertained [Balzi D, 2019].

Methods

Study Design and Data Source

The AIDEA project was sponsored by the Italian Ministry of Health and by the Tuscany Region [Balzi D, 2019]. After approval by the local Ethics Committee (976/13_AOUC), the study was conducted in 2 hospitals in Florence (Italy), the Azienda Ospedaliero-Universitaria Careggi (AOUC), an academic tertiary hospital, and the Ospedale Santa Maria Annunziata (OSMA), a community hospital. Data were collected between June and August 2016 and again between February and March 2017 in the AOUC, and between August and September 2016 in the OSMA, for a total of 22 weeks. In these separate time windows, all patients aged ≥75 years accessing the ED of the participating hospitals were consecutively enrolled, with the only exclusion of those residing outside the Florence metropolitan area, or seeking care only because of ophthalmologic problems. For the purpose of this study, in the case of repeated ED access, only the first one was considered.

As previously described, the DSC was obtained with a software incorporated into the application routinely used by ED clinicians, which has now been definitively implemented in all the hospitals in the Azienda Sanitaria Toscana Centro area and in the AOUC [Balzi D, 2019].

As detailed below, face-to-face, direct or proxy interviews were conducted during the period of stay in the emergency room, with participants signing the informed consent by the AIDEA project's staff, which included trained health care workers and physicians fellows of the School of Geriatrics. Interview data and DSC classification were compared in a cross-sectional study design, whereas ED length of stay and disposition were considered as possible outcomes of the DSC classification, according to a short-term cohort study design.

Variables

Variables abstracted from the ED clinical records included time of access, DSC class, presence of a proxy, arrival by ambulance, triage color code, time spent in the ED, and disposition, dichotomized as discharge vs death or hospitalization.

The interview, based on the principles of CGA, focused on health and functional status prior to the index event leading to ED access, investigating symptoms of physical frailty (inability to walk 400 m, complete inability to walk, history of falls, and unintentional weight loss of ≥4.5 kg in the previous year) and cognitive decline (severe memory loss in the previous 5 years and previous diagnosis of dementia, referred by the proxy). The Identification of Senior at Risk (ISAR) score [McCusker J, 1999] was also applied, which classifies as at-risk patients scoring 2 or more. The 4AT, a screening test for cognitive disorders and delirium [Bellelli G, 2014], was administered to the participant to detect the possible presence of delirium, indicated by a score of 4+.

Analytic Procedures

Statistical analysis was performed with SPSS for Mac, version 25 (IBM Corp, Armonk, NY), and Stata, version 15.1 (StataCorp, College Station, TX). Interval variables were expressed as mean ± standard error (SEM) or median and interquartile range, depending on the distribution, and categorical variables as percentages.

The Student *t* and the Mann-Whitney U tests were used to compare normally and non-normally distributed interval variables, and the χ^2 test to compare relative frequencies, between individuals included and not included in the study. To assess concurrent validity, bivariate comparisons across the 4 DSC risk classes of each interview variable (with exclusion of age, gender, previous hospitalization, and number of drugs, directly related to the generation of the DSC itself) were conducted with the χ^2 test for trend. The same test was applied to analyze differences in the proportion of participants being hospitalized or dying in the ED, whereas the Kruskal-Wallis test was used to compare the non-normally distributed duration of ED stay, always across the DSC classes.

A multinomial logistic regression model was then built, to assess the risk of being in DSC class II vs I, III vs I, and IV vs I, as odds ratio (OR) and 95% confidence interval (CI), on the basis of all the variables that, at bivariate comparisons, differed across the 4 classes. Although this approach does not account for the ordinal structure of the data, it was chosen because it allows to overcome violation of the proportionality assumption [Yee TW, 2010; Agresti A, 2013], which was indeed revealed for some independent variables by the Brant test ($p < .001$). Being a nursing home resident and having an abnormal ISAR score were not included in this analysis, because these were considered as summary variables, more than descriptors of specific clinical abnormalities. The variable "inability to walk 400 meters" was not included in this analysis, given its potential collinearity with the variable "total inability to walk." We also excluded the presence of possible delirium, as indicated by the 4AT score, because we focused on conditions preceding ED access, whereas the time of onset of delirium could not be ascertained.

Protection against type I error was set at alpha level of 0.05.

Results

Of a total of 6743 records of patients aged ≥75 years accessing the 2 EDs in the time periods considered, 565 were excluded because they referred to repeated ED access. An additional 544 patients were excluded because they resided outside the Azienda Sanitaria Toscana Centro area, 679 because they accessed the ED only for ophthalmologic problems, and 303 because the triage code or the DSC were unavailable because of temporary software problems. Of the remaining 4652 patients, 3439 consented to the interview and were potentially eligible. Another 81 patients were excluded because of missing data in key variables (disposition after ED access, ISAR score, ability to walk 400 m, report of exhaustion, unintentional weight loss, severe loss of memory), leaving a final sample of 3358 AIDEA participants for the present study.

Patients who were or were not included had comparable mean age (83.2 ± 0.10 vs 84.0 ± 0.68; $p = .197$) and gender distribution (proportion of men among those included 44.1%, vs 43.2% among those not included; $p = .873$). The 2 subgroups had comparable distribution by DSC class (**Figure 1**) and median (interquartile range) ED length of stay [included: 356 (222, 807) vs not included: 330 (213, 486) minutes; $p = .277$], but differed in terms of triage color code (**Figure 2**).

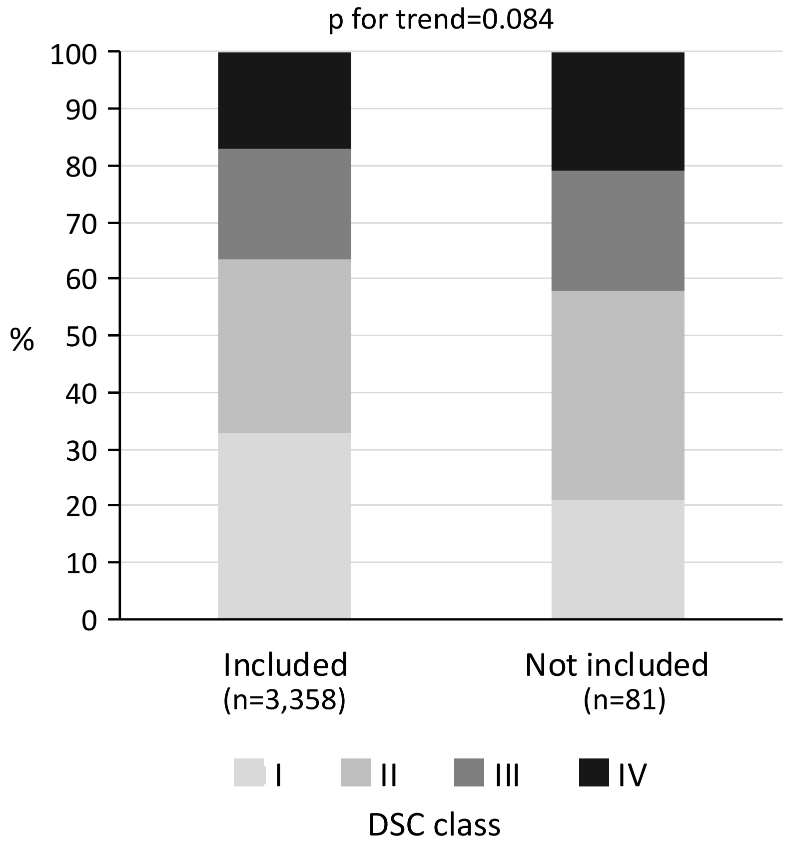

Figure 1. Comparison of the distribution of the AIDEA participants across Dynamic Silver Code (DSC) classes, by inclusion in the present study. Cutoff scores for DSC classes were I: 0-10, II: 11-25, III: 26-34, and IV: 35+.

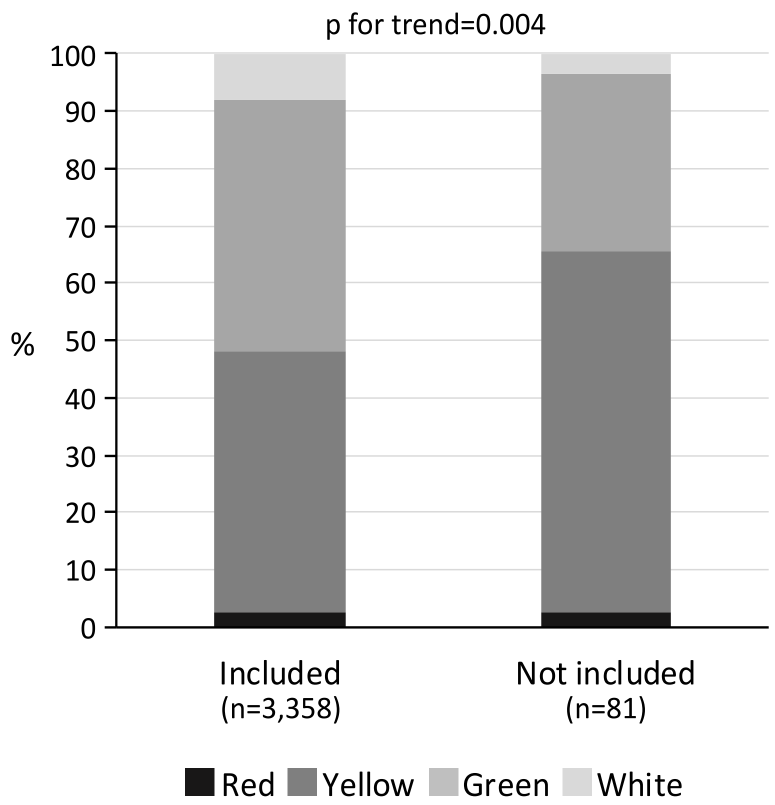

Figure 2. Comparison of the distribution of the AIDEA participants across triage color codes, by inclusion in the present study.

Characteristics of the Sample, As a Whole and by DSC Classes

Of the 3358 participants, 1034 (30.8%) were younger than 80 years and 1326 (39.5%) were aged ≥85 years. More than 40% of the interviews were conducted with a proxy. The DSC score ranged from 0 to 84, with a median (interquartile range) of 23 (8, 29) and a mean of 21.8 ± 0.30. A total of 1106 participants (32.9%) were in DSC class I, 1019 (30.3%) in class II, 656 (19.5%) in class III, and 577 (17.2%) in class IV. Most participants were triaged with green (n = 1471, 43.8%) or yellow code (n = 1524, 45.4%), whereas only few of them were assigned white (n = 275, 8.2%) and red (n = 88, 2.6%) codes. The distribution of color triage codes differed across the DSC risk classes ($p < .001$), with participants triaged with white or green code prevailing in DSC class I and being less represented in class IV (**Figure 3**).

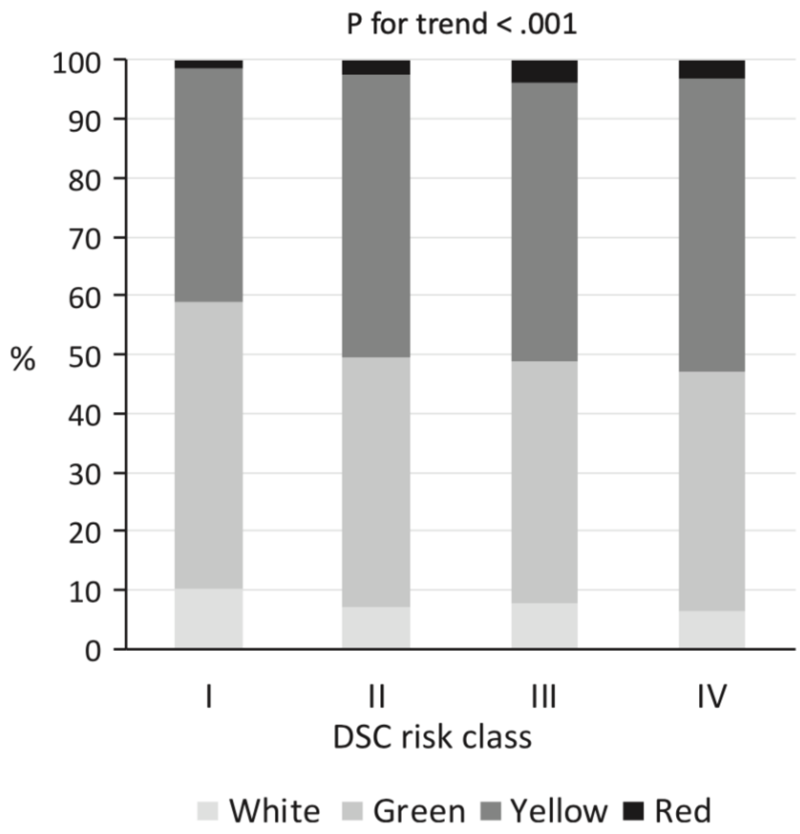

Figure 3. Distribution of the study participants across triage color codes, by DSC risk classes. Cutoff scores for DSC classes were I: 0-10, II: 11-25, III: 26-34, and IV: 35+.

Overall, 111 participants (3.3%) were nursing home residents, 348 (10.7% of the 3249 in whom this information was available) had 24-hour home assistance by salaried personnel, and 2194 (65.3%) arrived at the ED by ambulance. According to several markers, functional status prior to ED access was moderately to severely impaired: 1838 participants (54.7%) reported feeling of exhaustion, 1874 (55.8%) had an ISAR score of 2 or greater, 1554 (46.4%) could not walk 400 m, 359 (10.7%) were completely unable to walk; finally, 1009 participants (30.0%) reported significant unintentional weight loss and 508 (15.1%) 1 or more falls requiring ED access in the previous year.

According to their proxy informant, 716 (21.3%) study participants had substantial memory loss or a formal diagnosis of dementia in the previous 5 years. A score of 4 + at the 4AT test, administered during ED stay to 3188 participants, suggested the presence of possible delirium in 422 participants (13.2%).

As shown in **Table 1**, the prevalence of preadmission abnormal functional and cognitive conditions, as well as that of delirium, increased progressively across DSC classes. In particular, an almost 10-fold increase was observed, from class I to class IV, in the prevalence of total inability to walk.

Table 1
Comparison of Study Participants' Characteristics Across DSC Risk Classes

Characteristic	Class I (n = 1106)	Class II (n = 1019)	Class III (n = 656)	Class IV (n = 577)	*P* for Trend
Nursing home resident	17 (1.5)	33 (3.3)	32 (4.9)	29 (5.1)	<.001
Self-report of exhaustion	515 (46.6)	566 (55.6)	371 (56.6)	386 (66.9)	<.001
ISAR score 2+	389 (35.2)	578 (56.7)	414 (63.1)	493 (85.4)	<.001
Unable to walk 400 m	440 (39.8)	580 (56.9)	371 (56.6)	413 (71.6)	<.001
Totally unable to walk	32 (2.9)	106 (10.4)	86 (13.1)	135 (23.4)	<.001
Weight loss ≥4.5 kg in previous year	255 (23.1)	272 (26.7)	194 (29.6)	288 (49.9)	<.001
Fall with ED access in previous year	119 (10.8)	137 (13.4)	106 (16.2)	146 (25.3)	<.001
Severe memory loss and diagnosis of dementia	158 (14.3)	245 (24.0)	165 (25.2)	148 (25.6)	<.001
Probable delirium, 4AT score 4+	81 (7.5)	140 (14.6)	103 (16.5)	98 (18.6)	<.001

Data are n (%).

Table 2 reports findings from the multinomial logistic regression model, where DSC classes II, III, and IV were contrasted to DSC class I as far as variables primarily representing preadmission functional and cognitive impairments. In this model, the ORs for being in a higher DSC class were greater for the variable "total inability to walk" than for the other variables, and increased from the first (class II vs class I) through the last (class IV vs class I) comparison; thus, this variable was the strongest predictor of being in progressively worse DSC classes. The variable "exhaustion" increased the risk of being in a higher class almost homogeneously for all comparisons. Reporting of an ED-requiring fall contributed only to assignment to classes II and III vs class I, whereas the variable "weight loss" contributed only to assignment to class IV vs class I. Finally, the presence of severe memory loss or a diagnosis of dementia gave a significant contribution only to being in class II vs class I.

Table 2
Multinomial Logistic Regression Model Testing the Multivariable Association Between DSC Class and Selected Markers of Physical Frailty and Cognitive Decline

Marker	Or (95% CI)		
	Class II vs I	Class III vs I	Class IV vs I
Self-report of exhaustion	1.28 (1.08, 1.53)	1.29 (1.05, 1.57)	1.67 (1.34, 2.09)
Totally unable to walk	3.03 (1.99, 4.6)	3.90 (2.53, 6.03)	7.45 (4.88, 11.38)
Weight loss ≥4.5 kg in previous year	1.08 (0.88, 1.32)	1.21 (0.96, 1.51)	2.61 (2.09, 3.27)
Fall with ED access in previous year	1.18 (0.91, 1.54)	1.45 (1.09, 1.94)	2.39 (1.80, 3.17)
Severe memory loss or diagnosis of dementia	1.52 (1.20, 1.92)	1.48 (1.14, 1.92)	1.05 (0.79, 1.39)

Short-Term Outcomes

The time spent in the ED increased significantly across the DSC risk classes (**Figure 4, top panel**). Overall, 1059 participants (31.5%) were hospitalized and 11 (0.3%) died in the ED. The proportion of hospitalizations or deaths in the ED increased substantially across the 4 DSC risk classes (**Figure 4, bottom panel**).

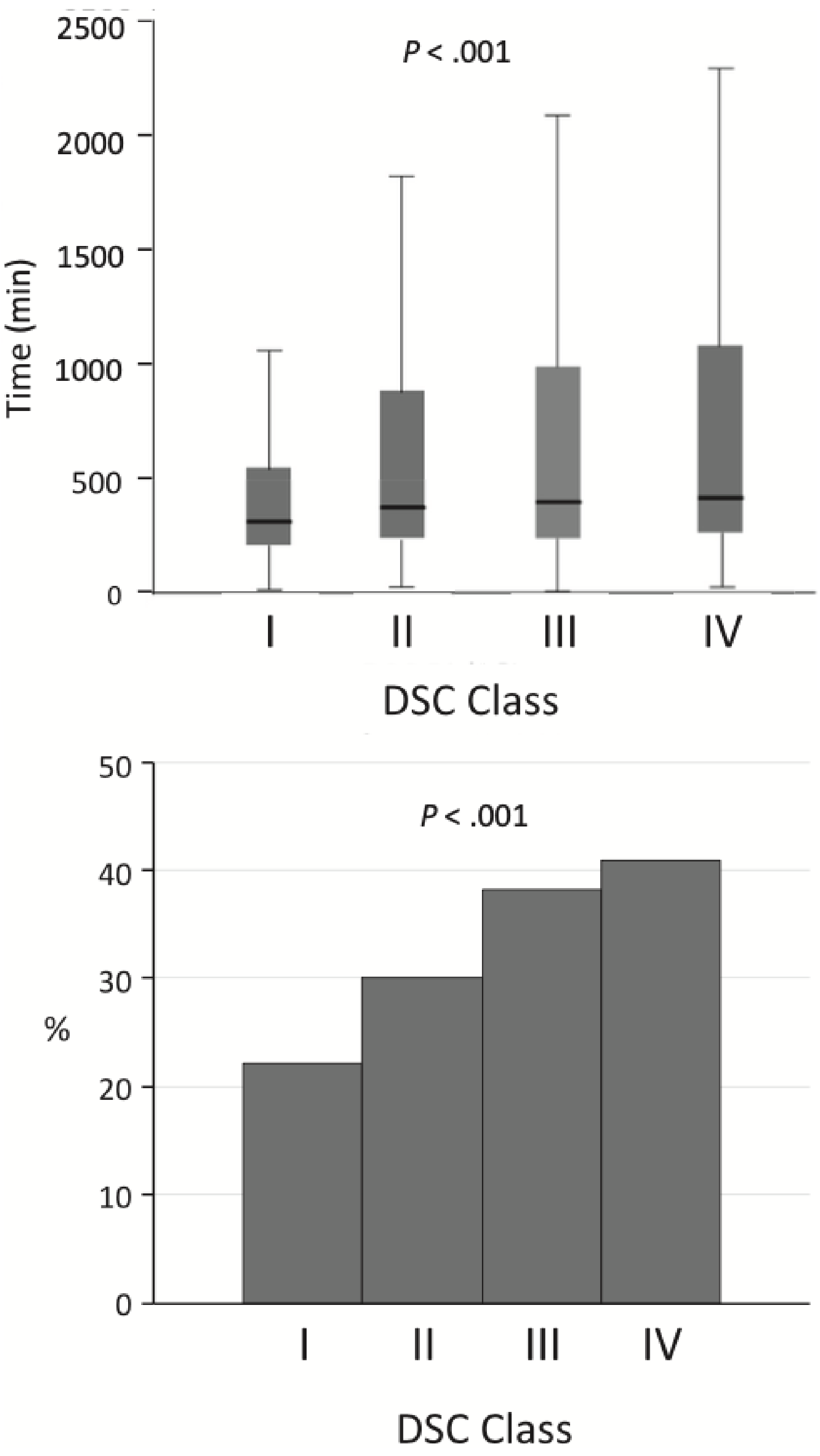

Figure 4. Time spent in the ED (top panel) and proportion of participants admitted to the hospital or dying in the ED (bottom panel), across DSC risk classes.

Discussion

In this large cohort of older adults admitted to the ED, the definition of the risk status provided by the DSC was associated with previous participant's frailty status, as documented by several indicators, whose prevalence, as well as that of delirium, increased progressively across DSC classes. In particular, inability to walk and, with weaker associations, exhaustion were the 2 variables that more consistently predicted assignment to progressively worse DSC classes. Other markers of poor physical status and the presence of cognitive impairment contributed to this outcome, although to a lesser extent.

It has been previously shown that the DSC could identify older patients at an increased risk of death, independent of the acute condition leading to ED access [Balzi D, 2019]. However, those studies could not indicate which features distinguished patients across risk classes. This study fills this knowledge gap, demonstrating that the higher the DSC risk class, the greater the prevalence of 2 summary markers of pre-existing vulnerability, such as living in a nursing home and having an ISAR score of 2 or higher, of some of Fried's hallmarks of physical frailty [Fried LP, 2001], and of cognitive impairment. Thus, the DSC is associated with well-known aspects of age-related functional and cognitive decline, which often remain undetected in the busy routine of the ED. Notably, its strong association with inability to walk is consistent with previous studies, showing that walking speed is a major predictor of death in older persons [Studenski S, 2011].

Assessment of pre-existing functional status must be part of prognostic judgment in older patients. When this background information is ignored, grim consequences may derive in the 2 opposite directions of futility and undertreatment: many older patients with a limited disability-free life expectancy receive therapies of questionable appropriateness [Walter LC, 2001], whereas others with a reasonably good prognosis are denied effective treatments because they are considered too old [Mehta KM, 2010]. Previous investigations where simple administrative data were assembled to predict survival in older persons [Di Bari 2010; Clegg A, 2018; Gilbert T, 2018; Bertini F, 2018; McIsaac DI, 2019; Soong JTY, 2019] usually did not explore associations with Fried's markers of frailty [Fried LP 2001]. The only exception is probably represented by the Hospital Frailty Risk Score (HFRS), which was developed to predict 30-day mortality using a clustering of diagnoses [Gilbert T, 2018]. Unfortunately, agreement of the HFRS with Fried's frailty phenotype, but also with Rockwood cumulative deficit model [Rockwood K, 2007], was disappointingly low, as shown by kappa statistics of 0.22 and 0.30, respectively [Gilbert T, 2018]. Thus, we believe that our study offers a positive contribution on an issue that, to our knowledge, remained unsolved in previous studies.

Cognitive impairment may severely compromise personal independence and life expectancy in old age [Di Bari M, 2006; Wang MC 2020]. Accordingly, in our bivariate comparisons, the proportion of patients with severe memory loss or diagnosis of dementia increased from DCS class I to IV. However, such a diagnosis was only marginally associated with worsening DSC risk classification in the multinomial model. This may possibly reflect the limited accuracy of our diagnostic criteria for cognitive impairment, or it may suggest that, as a prognostic marker, cognitive impairment has some independent value in older individuals whose overall health status and function is still preserved, whereas it is largely surpassed by measures of functional status in the presence of poor health and reduced life expectancy.

A few other findings deserve comments. First, the DSC classes were also associated with triage color codes, with participants triaged as white or green codes prevailing in DCS class I and being less represented in class IV. The statistical significance of such an association should not obscure that, in fact, the 2 classification systems resulted in markedly different distributions: indeed, the study sample was fairly homogeneously distributed across the 4 DSC classes, whereas it was almost completely concentrated in the 2 intermediate color code classes. Thus, in spite of the statistically significant association, the 2 tools convey quite different information. Second, the study shows that also the prevalence of delirium increased progressively across DSC classes. This may simply reflect the association with previous cognitive impairment, discussed above: as a screening test, indeed, the 4AT tool might not discriminate completely delirium from pre-existing dementia [Bellelli G, 2014; O’Sullivan D, 2018]. On the other hand, this association may be due to the frequent occurrence of delirium in frail older persons with poor health status, even in the absence of known cognitive decline. Finally, the DSC classification was shown to be strongly associated with the time spent in the ED and the proportion of hospitalizations or deaths in the ED; thus, besides long-term survival, short-term outcomes also can be predicted by the tool, a finding further supporting its value.

Study limitations must be acknowledged. We had a relatively high proportion of nonparticipation: nearly a quarter of those potentially eligible for the study did not consent to the interview or gave incomplete answers. This was mostly due to difficulties in performing a face-to-face interview with older patients in an unstable or critical status: red and yellow triage color codes, indeed, prevailed among patients not included in the study. In a way, this finding corroborates the value of the DSC score, which may provide valuable information even in patients unable to collaborate. Furthermore, as discussed above, evaluation of previous cognitive status was fairly imprecise, yet it reflected the approach usually applicable in the ED, where in-depth cognitive evaluation is commonly precluded. We did not compare the DSC with the Clinical Frailty Scale, which has been recently validated also for application in the ED [Kaeppeli T, 2020], neither with laboratory markers of frailty, such as hemoglobin and albumin. However, it should be pointed out that the Clinical Frailty Scale provides a summary evaluation of frailty status and does not consent to analytically recognize and score individual physical and cognitive components of frailty, as indeed we aimed doing. Moreover, laboratory markers are less appropriate to identifying frail individuals in the setting of the ED, because they may be commonly altered as an effect of the acute disease leading to ED access.

Conclusions and Implications

This study shows that the DSC reflects well-known components of frailty, and functional impairment in particular, a finding that may justify the good prognostic ability of the tool. We believe that the evidence provided increases the confidence in the DSC and supports its potential for clinical utilization.

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Dynamic Silver Code and long-term survival after discharge from Geriatrics or Internal Medicine Units

Hospitalization, or even only access to an Emergency Department (ED), represents a destabilizing event in older patients, in whom it may increase the risk of negative outcomes, including functional or cognitive decline, adverse drug reactions, or death, above and beyond that deriving from acute illness [Aminzadeh F, 2002]. The term “posthospital syndrome” has been introduced to indicate the increased vulnerability after acute hospitalization and failure to recover to baseline functioning [Van Seben R, 2020]. This condition may be enhanced by chronic multimorbidity, cognitive impairment, mobility problems, and functional dependency [Hastings SN, 2007].

Randomized clinical trials (RCTs) and meta-analyses show that, compared to Internal Medicine, admission to acute Geriatrics wards, where personalized therapeutic and management programs based on comprehensive geriatric assessment are applied, may improve survival and functional outcomes of frail older patients needing hospitalization [Ekerstad N, 2017; Saltvedt I, 2002; Ellis G, 2017]. Rather than simply because of an advanced age, participants in these studies were usually selected based on some explicit criteria, pointing towards an intermediate level of severity: subjects at the opposite extremes of the spectrum, that is, those who are too well or too sick, are indeed considered unable to draw substantial benefit from admission to a specialized geriatric setting [Tanderup A, 2018].

In the present study, we compared long-term prognosis of older patients admitted to acute care Geriatrics or Internal Medicine hospital wards, after stratification for background risk of long-term mortality, as represented by the DSC, and across a variety of discharge diagnoses.

Methods

Study Design

Data used in this study were derived from the “Silver Code National Project (SCNP),” sponsored by the Centre for Disease Control of the Italian Ministry of Health in 2008 [1s]. Aim of the SCNP was to evaluate innovative interventions to managing older persons transitioning from the community to the hospital and vice versa. Within this overarching purpose, a non-concurrent cohort study was conducted, to develop and validate a prognostic score for older persons accessing the hospital, using only administrative data. Accordingly, a database was assembled combining the administrative archives of two Italian Regions, Tuscany and Lazio, which deliver health care services to more than 9.6 million persons. The database included information on demographics, hospitalizations, drug prescriptions, and deaths of beneficiaries aged 75+ years, residing in the area where the study was conducted and admitted via the ED to Geriatrics or Internal Medicine hospital wards between April 2004 and December 2009. The specific features of the Geriatrics and Internal Medicine wards scrutinized were not reported in the database: however, the differences between the two settings are described in an official document of the Italian Ministry of Health [1s]. Briefly, unlike Internal Medicine wards, Geriatrics wards in Italy apply systematically comprehensive geriatric assessment, value a multidisciplinary and multiprofessional approach of care, prioritize functional recovery and early mobilization, and offer some degree of continuity of care after discharge.

Data were linked using a numeric unique identifier, allowing preservation of beneficiaries' confidentiality thanks to anonymized data processing. Universal health care coverage in Italy warrants completeness and comprehensiveness of the databases, which have been used in previous studies [Di Bar M, 2010] and have been certified to be 100% complete and 95% accurate [2s]. In contrast with the original publication on the development and validation of the DSC [Balzi D, 2019], in the case of multiple hospitalizations only the first admission was considered in the present study.

Ethics

Following the Italian legislation on observational studies using administrative databases in place when data were acquired, Ethics Committee approval and participants' subscription of informed consent were waived, because only anonymized administrative data were extracted.

Variables

Discharge diagnoses classified according to the International Classification of Diseases, ninth edition codes, were grouped into unique disease categories according to the Clinical Classifications Software (CCS) [3s]. CCS codes of interest were selected and eventually combined into broader groups through a consensus process among investigators. To obtain stable ratios, only grouped CCS codes associated, in participants admitted to Geriatrics, to at least 50 deaths in 1 year were considered.

We applied the DSC to minimize possible biases due to unbalanced background risks between participants admitted to Geriatrics or Internal Medicine [Balzi D, 2019].

Analytic Procedures

Statistical analysis was performed with STATA v. 15.1 (StataCorp. 2017, Stata Statistical Software: Release 15, StataCorp LLC, College Station, TX). Student's *t*-test was used to compare means of interval variables between two groups and the χ^2 test to compare relative frequencies, considering trends as appropriate. Because the DSC had been validated on 1-year survival, this was chosen as our primary outcome when comparing participants admitted to Internal Medicine (reference category) and Geriatrics. To this purpose, Cox proportional hazards models with hazard ratio (HR) and 95% confidence interval (CI) were built, adjusting for DSC and region of hospital admission. Interaction between DSC and assignment to Internal Medicine or Geriatrics was checked. Further analyses were then conducted within DSC classes, in the entire cohort and separately in subgroups identified by discharge diagnosis group of CCS codes, as described above. The assumption of proportionality of hazards over time was verified with Schoenfield's residuals and comparing the survival functions for each covariate pattern; the fitting of the models was evaluated using Cox-Snell's residuals. To explore whether unmeasured confounding led to selection bias in favor of Geriatrics, and following also recommendations for reporting effects at prespecified times over a prolonged follow-up [Stensrud MJ, 2020], mortality was compared between the two hospital settings in two separate time windows, that is, in the first 30 days and from 90 to 365 days post-discharge. These two distant periods were selected in the assumption that short-term mortality might be more reflective of hospital care than later-only mortality, which would therefore represent a negative control outcome [Arnold BF, 2016]. A two-tailed *p* value less than .05 was considered statistically significant.

Results

General Characteristics of Participants

The study cohort included 180,079 participants, of whom 10,362 were admitted to Geriatrics and 169,717 (94.2%) to Internal Medicine. Mean age was 84 ± 5.5 years and 83 ± 5.6 years in participants admitted to Geriatrics and Internal Medicine, respectively ($p < .001$); conversely, the proportion of women was similar (57.0% vs 56.8%; $p = .611$). The distribution of participants across the four DSC classes was 29.1, 37.8, 21.7, and 11.4% in Geriatrics and 33.4, 36.3, 19.2, and 11.1% in Internal Medicine (p for trend $< .001$).

The grouped CCS codes associated, among participants admitted to Geriatrics, to at least 50 deaths in 1 year were, in a descending order of frequency: cerebrovascular diseases (CCS codes 109, 111, 112), respiratory diseases (CCS codes 122, 127, 131, 133), heart failure (CCS code 108), malignancies (CCS codes 11–43), renal diseases (CCS codes 157, 158, 159), and cognitive disorders (CCS code 653) (**Table 1**). All together, these six CCS codes collected 96,599 participants, 53.6% of the entire cohort.

Table 1. Total number and 1-year mortality of participants who had their first admission to Internal Medicine or Geriatrics wards, for all discharge diagnoses and separately by grouped Clinical Classifications Software (CCS) codes. The p values reported refer to χ^2 tests comparing mortality between participants initially admitted to Internal Medicine or Geriatrics.

	Total		**Internal Medicine**		**Geriatrics**		**p**
	Patients	**Deaths, N (%)**	**Patients**	**Deaths, N (%)**	**Patients**	**Deaths, N (%)**	
All discharge diagnoses	180,079	60,703 (33.7)	169,717	57,377 (33.8)	10,362	3,326 (32.1)	<0.001
Cerebrovascular diseases (CCS codes 109, 111, 112)	29,091	8,745 (30.1)	27,322	8,279 (30.3)	1,769	466 (26.3)	<0.001
Respiratory diseases (CCS codes 122, 127, 131, 133)	25,368	9,503 (37.5)	23,895	8,918 (37.3)	1,473	585 (39.7)	0.066
Heart failure (CCS code 108)	20,188	7,362 (36.5)	19,194	7,009 (36.5)	994	353 (35.5)	0.522
Malignancies (CCS codes 11-43)	11,472	8613 (75.1)	11,022	8267 (75.0)	450	346 (76.9)	0.002
Renal diseases (CCS codes 157, 158, 159)	6,584	2,58 (39.3)	6,193	2,444 (39.5)	391	145 (37.1)	0.350
Cognitive disorders (CCS code 653)	3,896	1,545 (39.7)	3,370	1,385 (41.1)	526	160 (30.4)	<0.001

Their distribution differed between Geriatrics and Internal Medicine ($p < .001$): the diagnoses of heart failure and malignancies prevailed slightly among discharges from Internal Medicine, those of cerebrovascular diseases and cognitive disorders in participants discharged from Geriatrics, whereas the diagnosis of respiratory diseases had a comparable frequency between the two settings (**Figure 1**).

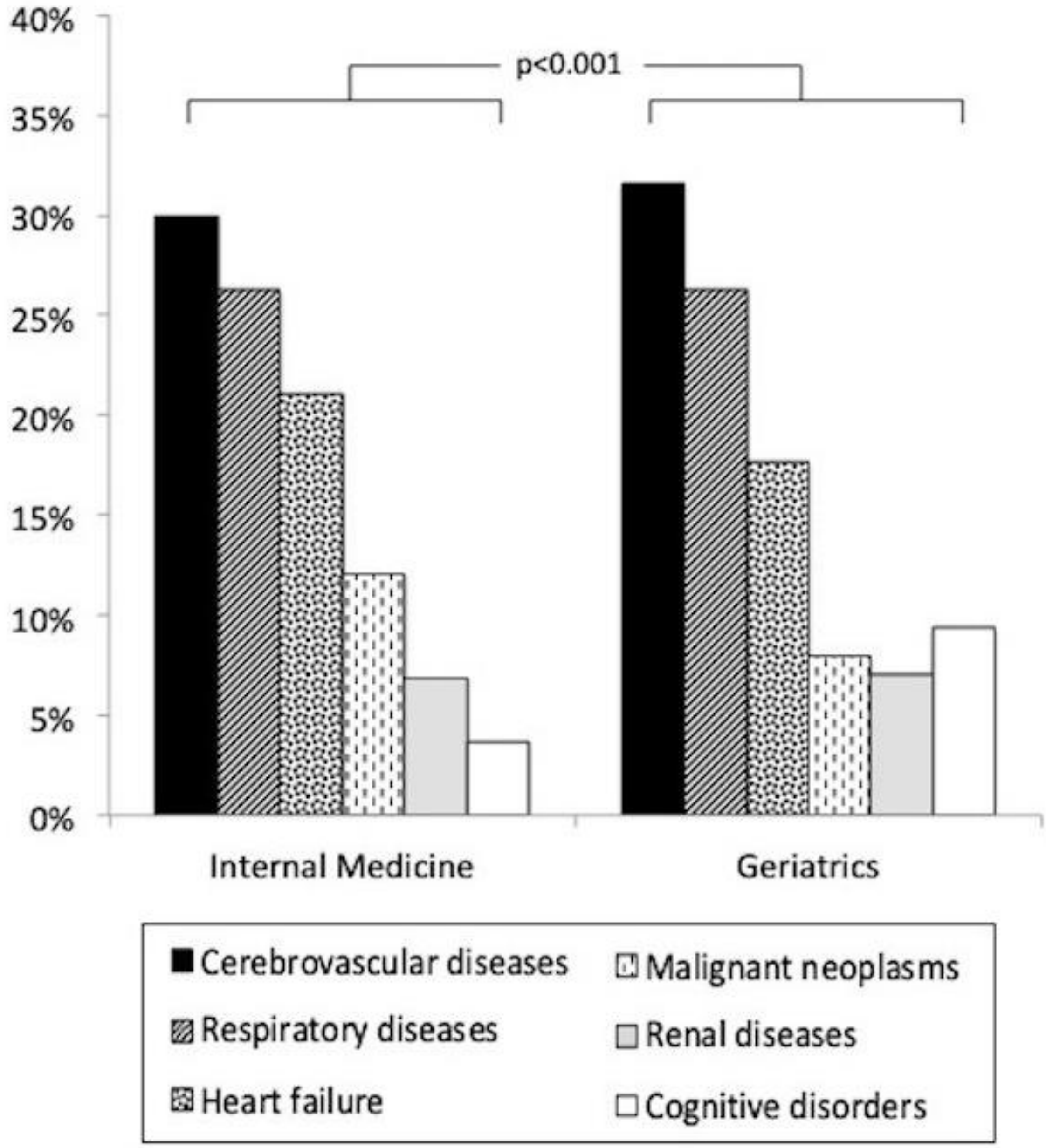

Figure 1. Distribution of grouped discharge diagnosis Clinical Classifications Software (CCS) codes between Internal Medicine and Geriatrics wards.

Mortality

In the entire cohort, 1-year mortality was 33.7% (n = 60,703), lower in participants admitted to Geriatrics than in those assigned to Internal Medicine wards (32.1% vs 33.8%; $p < .001$) (**Table 1**). When comparisons between the two settings were conducted separately in the six grouped CCS codes previously identified, survival was significantly better in participants admitted to Geriatrics wards and discharged with a diagnosis of cerebrovascular diseases or cognitive disorders, comparable between the two settings in those receiving a diagnosis of heart failure, renal diseases, or respiratory diseases, and better in those admitted to Internal Medicine and discharged with a diagnosis of malignancies (**Table 1**).

Independent of the discharge diagnosis, Cox regression confirmed a better survival in participants admitted to Geriatrics, adjusting for DSC class and region of hospital admission (HR 0.89, 95% CI 0.86–0.93) and with no interaction between ward of admission and DSC class (p = .465). Because mortality is strongly dependent on background mortality risk, which has been shown to increase with DSC class, comparisons were conducted separately within DSC classes, again adjusting for region of hospital admission. In these analyses, the prognostic advantage associated with admission to Geriatrics was negligible in the lowest risk class, became highly significant in DSC class II and III, and decreased slightly, yet remaining statistically significant, in DSC class IV (**Figure 2** and **Table 2**).

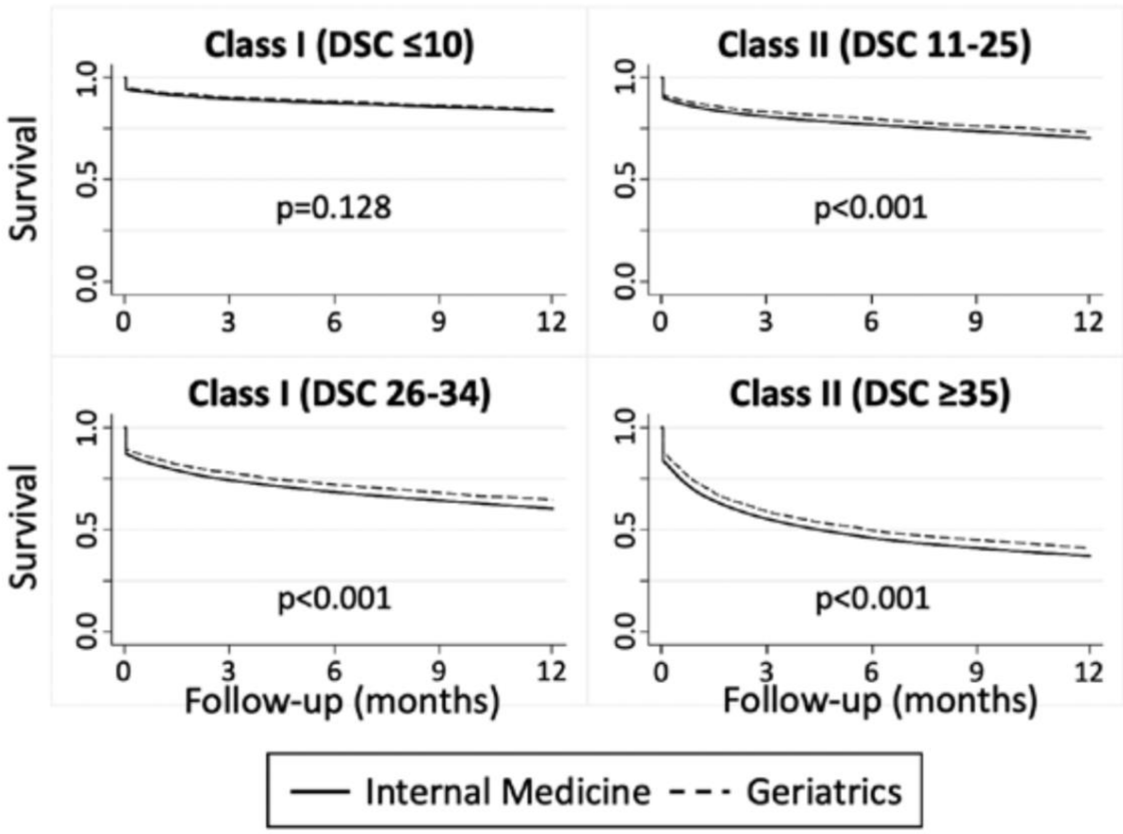

Figure 2. One-year survival curves for the entire cohort of participants initially admitted to Internal Medicine vs Geriatrics wards for all discharge diagnoses.

Table 2. Comparison of the risk for 1-year mortality between participants initially admitted to Geriatrics or to Internal Medicine wards, in the entire cohort and separately by discharge diagnosis Clinical Classifications Software (CCS) codes. Cox regression models, adjusted for Region of residence, with Internal Medicine as the reference category.

	Class I (DSC ≤10)		**Class II (DSC 11-24)**		**Class III (DSC 26-34)**		**Class IV (DSC ≥35)**	
	HR (95% CI)	**p**	**HR (95% CI)**	**p**	**HR (95% CI)**	**p**	**HR (95% CI)**	**p**
All discharge diagnoses	0.93 (0.84-1.02)	0.128	0.88 (0.83-0.94)	<0.001	0.86 (0.80-0.92)	<0.001	0.92 (0.86-0.97)	0.005
Cerebrovascular diseases (CCS codes 109, 111, 112)	0.83 (0.65-1.07)	0.146	0.72 (0.61-0.84)	<0.001	0.72 (0.60-0.88)	0.001	0.81 (0.68-0.96)	0.016
Respiratory diseases (CCS codes 122, 127, 131, 133)	1.07 (0.83-1.38)	0.588	1.11 (0.95-1.30)	0.206	1.06 (0.89-1.25)	0.522	0.99 (0.86-1.14)	0.859
Heart failure (CCS code 108)	1.11 (0.80-1.54)	0.528	1.01 (0.83-1.22)	0.920	0.74 (0.59-0.93)	0.009	0.90 (0.76-1.08)	0.271
Malignancies (CCS codes 11-43)	1.10 (0.86-1.41)	0.435	0.88 (0.72-1.08)	0.222	1.01 (0.78-1.30)	0.955	1.13 (0.94-1.35)	0.201
Renal diseases (CCS codes 157, 158, 159)	0.82 (0.47-1.44)	0.492	1.04 (0.77-1.41)	0.799	0.82 (0.59-1.13)	0.227	0.91 (0.69-1.22)	0.545
Cognitive disorders (CCS code 653)	0.69 (0.45-1.07)	0.094	0.52 (0.37-0.72)	<0.001	0.55 (0.39-0.77)	0.001	0.86 (0.65-1.14)	0.288

When the analyses stratified for DSC class were repeated in the subgroups identified by the grouped CCS codes, the survival benefit associated with admission to Geriatrics was evident in participants in DSC class II, III, and IV discharged with a diagnosis of cerebrovascular diseases, in those in DSC class II and III discharged with a diagnosis of cognitive disorders, and in those in DSC class III with a discharge diagnosis of heart failure. The apparent benefit, suggested by bivariate comparisons for participants with malignancies admitted to Internal Medicine, was not confirmed in stratified analyses: within DSC classes, survival was indeed comparable between Internal Medicine and Geriatrics (**Table 2)**.

Mortality was further compared between the two settings in the first 30 days and, separately, from 90 to 365 days post-discharge, the latter possibly representing a negative control outcome of an exposure (admission to Geriatrics) that would presumably act mainly close to hospital admission. In the entire cohort, mortality was

15.4% (n = 27,812) in the first 30 days, lower in participants admitted to Geriatrics than in those assigned to Internal Medicine wards (13.8% vs 15.5%; $p < .001$), and 15.5% (n = 21,857) from 90 to 365 days post-discharge, comparable in participants admitted to either setting (15.1% vs 15.5%). As shown in **Table 3**, the 30-day HRs for death were significantly in favor of Geriatrics in the entire cohort and in all DSC classes (in particular, in class II and III) and greater than those detected over the entire 1-year follow-up, whereas they did not reach statistical significance in the latest follow-up, neither in the whole cohort nor within DSC classes.

Table 3. Comparison of the risk of death between participants initially admitted to Geriatrics or to Internal Medicine wards in two separate time windows after hospital discharge.

	30-Day Mortality				Mortality From Day 90 to 365			
	Internal Medicine	Geriatrics			Internal Medicine	Geriatrics		
DSC Class (score)	Deaths, *N* (%)	Deaths, *N* (%)	HR (95% CI)	*p*	Deaths, *N* (%)	Deaths, *N* (%)	HR (95% CI)	*p*
All classes	26,386 (15.5)	1,426 (13.8)	0.86 (0.81–0.91)	<.001	20,602 (15.5)	1,255 (15.1)	0.97 (0.92–1.03)	.305
I (≤10)	4,600 (8.1)	219 (7.3)	0.87 (0.76–1.00)	.046	2,704 (6.1)	149 (6.3)	0.99 (0.84–1.17)	.931
II (11–25)	9,026 (14.7)	498 (12.7)	0.84 (0.77–0.92)	<.001	5,310 (12.2)	325 (11.5)	0.94 (0.84–1.05)	.250
III (26–34)	6,191 (19.0)	354 (15.8)	0.79 (0.71–0.88)	<.001	4,733 (19.2)	291 (17.3)	0.89 (0.79–1.00)	.055
IV (≥35)	6,569 (34.8)	355 (30.0)	0.84 (0.75–0.93)	.001	7,855 (38.0)	490 (34.9)	0.91 (0.83–1.00)	.052

CI = confidence interval; DCS = Dynamic Silver Code; HR = hazard ratio. Cox regression models, adjusted for region of residence, with Internal Medicine as the reference category.

Discussion

In this large cohort of older subjects admitted to wards of Geriatrics or Internal Medicine, admission to Geriatrics was associated with lower long-term mortality, more evident in subjects at a moderate- to high-background risk. Survival was better after admission to Geriatrics in DSC class III participants, in particular with discharge diagnoses of cerebrovascular diseases, cognitive disorders, or heart failure. Conversely, survival was comparable between Geriatrics and Internal Medicine across all DSC classes for respiratory or renal diseases. Interestingly, whereas in crude comparisons assignment to Geriatrics was associated with worse prognosis in subjects with malignancies, in DSC stratified analyses survival was comparable between the two settings, suggesting that Geriatrics wards commonly admit cancer patients with a greater background risk.

RCT and meta-analyses demonstrated that, when patients at an intermediate risk are selected, geriatric care models improve clinical outcomes in frail elderly patients [Ekerstad N, 2017; Saltvedt I, 2002; Ellis G, 2017]. Conversely, the few trials where the target population was selected solely by chronological age reported no discernible advantages from admission to Geriatrics over Internal Medicine [Harris RD, 1992; Asplund K, 2000]. Our observational study, while echoing findings from the majority of RCT, offers the advantage of a large, population-based cohort of older patients, representing the “real world” of clinical practice and service delivery better than the relatively small samples of strictly selected participants enrolled in those RCT.

Geriatricians frequently care for older patients with cognitive disorders and neurological diseases, including cerebrovascular diseases [Lo Coco D, 2016], that in our sample were more frequently documented as discharge diagnoses from Geriatrics than from Internal Medicine (**Figure 1**). Comprehensive geriatric assessment programs are successfully applied to patients with these conditions, which were sometimes reported as inclusion criteria in RCT exploring the effectiveness of geriatric care models [Saltvedt I, 2002]. Moreover, older patients with acute heart failure are frequently frail, with multiple impairments in physical and cognitive functioning that may contribute to their poor outcomes [Chiarantini D, 2010] and remain frequently unrecognized outside of the geriatric arena [Reeves GR, 2016]: it has been shown that patients with heart diseases may specifically benefit from application of interventions guided by comprehensive geriatric assessment [Rubenstein LZ, 1988]. Thus, the advantage that we observed from admission to Geriatrics of subjects with these discharge diagnoses is not surprising.

Implications of our findings should be highlighted. They confirm the validity of the DSC as a prognostic tool to identify older patients at risk in an acute hospital setting and perform risk adjustment, when comparing clinical interventions or health care models. The tool may be used in the ED to select patients who are likely to benefit the most from geriatric care, specifically in the presence of some clinical conditions such as cerebrovascular diseases, cognitive impairment, or heart failure. Even though our analyses were based on discharge and not on admission diagnoses, all these three clinical conditions are often promptly identifiable on ED presentation.

We recognize that the study has several limitations. Data available were collected some years ago and comparisons between Geriatrics and Internal Medicine should be confirmed in more recent databases. Hospital discharge diagnoses may sometimes be distorted by economic issues associated with reimbursement procedures. Information on comorbidities and on hospital of admission was not available and, therefore, risk adjustment was performed only on the basis of the DSC. However, the DSC and its parent tool have been used in previous studies on different cohorts, being always proven to offer an acceptable level of risk stratification [Balzi D, 2019; Di Bari M, 2010; Di Bari 2012; Di Bari, 2014]. The SCNP database did not report outcomes such as cognitive and functional decline, which are very relevant in geriatric patients, neither other possible negative control outcomes, which would allow checking the risk for selection bias or other unmeasured confounding. In observational studies, selection bias may lead to erroneously attribute to the condition under investigation a positive effect that is in fact due to an unbalanced distribution of other favorable factors. On the other hand, admissions to Geriatrics wards appeared to have been possibly biased negatively towards patients with a mildly to moderately increased risk of death (DSC Class II and III). In cancer patients, this unbalanced admission policy led, in crude comparisons, to an apparently increased risk of death for patients admitted to Geriatrics, which was corrected after stratification by the DSC. Moreover, mortality was comparable between the two settings in the latest follow-up, a finding that may represent a negative outcome control of an exposure acting mainly close to hospitalization [Arnold BF, 2016]. Explicit information on the characteristics of the Geriatrics and Internal Medicine wards in the study was lacking and could only be inferred in general terms from official statements issued by the Italian Ministry of Health [1s]. The proportion of subjects admitted to Geriatrics (<6%) was limited: although this figure is consistent with the Italian national scenario [1s; Fracchia S, 2015], it might generate uncertainty on applicability of our findings to countries where this proportion is greater.

Conclusions and Implications

In conclusions, frail older persons at moderate- to high-risk, the ideal target for application of the geriatric model of care, can be recognized in the ED with the DSC. The tool, now available in real-time in Tuscany hospitals [Balzi D, 2019], may therefore greatly facilitate the procedures for patients' assignment to the most appropriate setting in the ED. In conjunction with the DSC, identification of features of specific clinical conditions may further improve selection of patients that can benefit the most from admission to Geriatrics.

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Effects of the Implementation of the Dynamic Silver Code in the Emergency Department

Older patients represent an increasing share of Emergency Department (ED) visitors worldwide [Pines 2013]. Because of their complex medical and social problems, older patients in the ED require longer clinical evaluation times and increased resources compared to younger adults [Aminzadeh 2002]. For the most vulnerable, ED use represents per se a destabilizing event, which may be independently associated with suboptimal outcomes. Therefore, risk stratification screening instruments have been proposed to identify vulnerable subjects in the ED setting with the goal of improving patient management and outcomes, while allowing for faster and more focused use of time and resources [Salvi F, 2012]. However, the prognostic accuracy and applicability of these tools are limited [Carpenter CR, 2015].

The DSC has been implemented in software for routine management of ED patients and is now available in real-time across all the hospitals in the healthcare district of Florence, Italy [Di Bari M, 2022]. This study describes the effects of the DSC implementation that were observed in the Ospedale Santa Maria Annunziata (OSMA), a community-based facility in the metropolitan area of Florence. To this purpose, indicators of the clinical management of patients admitted before and after the implementation of the DSC were compared.

Methods

Study Design and Data Source

This is an ancillary study of the Anziani in DEA (AIDEA) study, also known as "Older Persons in the ED", sponsored by the Italian Ministry of Health and by the Tuscany Region [Balzi D, 2019]. Approval by the local Ethics Committee was obtained (976/13_AOUC). To evaluate the effects of the DSC implementation, we used a pre-post comparison of anonymized data collected in all subjects aged 75+ years, accessing the OSMA ED before and after the software for DSC scoring was fully implemented. The period between April 2017 and March 2018 was the pre-DSC phase, whereas the post-DSC phase lasted from April to August 2018.

Implementation and Clinical Application of the DSC

As previously described [Balzi D, 2019] the DSC was obtained using software incorporated into the application routinely used by ED clinicians in all the hospitals of the area. In the pre-DSC phase, the score remained unknown to ED staff, whereas in the second phase it became promptly available onto the computer screen soon after triage, together with the corresponding risk class.

In the post-DSC implementation phase, physicians in the ED and in the Internal Medicine and Geriatrics wards in the OSMA were trained on its use and agreed upon its application in a clinical decision tree, limited to patients admitted with conditions not requiring surgery or admission to Intensive Care. Specifically, the evidence from a previous study [Di Bari M, 2021] was valued, that the greatest survival benefit could be expected in class III patients assigned to Geriatrics vs. Internal Medicine, whereas similar mortality rates are expected between the two wards in class I patients [Di Bari M, 2021]. Therefore, following the decision for admission made by the ED physician, patients in class I or II were directly assigned to Internal Medicine and those in class III directly to Geriatrics with no further geriatrics workup, whereas those in class IV would require additional criteria and in-person evaluation by a consulting geriatrician before final assignment (**Figure 1**).

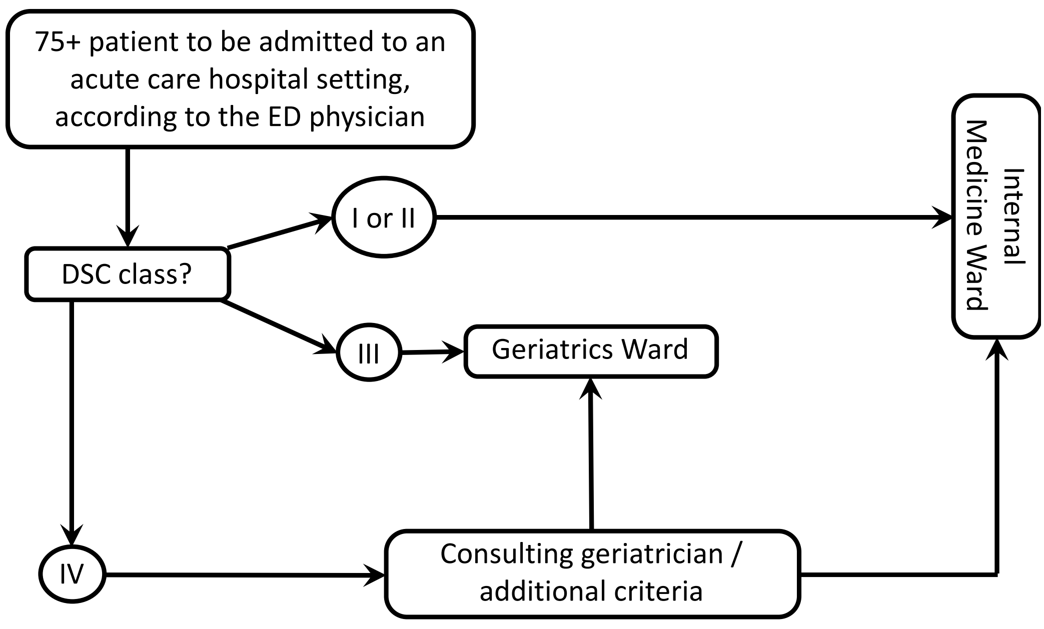

Figure 1. Clinical decision tre**e** for admission to Interna Medicine or Geriatric ward.

Outcome Measures

ED length of stay (LOS) was compared between the pre-DSC and the post-DSC phase as the main outcome measure, in the entire sample as well as in the subsample of patients who were admitted to Internal Medicine or Geriatrics. Furthermore, we also compared the ED LOS between the two time periods in another community hospital (Ospedale San Giovanni di Dio) of the same health district as the OSMA, where the DSC was implemented in the ED software but remained always masked to the staff.

Other outcomes, limited to patients admitted to Geriatrics, were represented by weight of the Diagnosis Related Groups (DRG) on discharge, total hospital LOS, and hospital mortality.

Analytic Procedures

Statistical analysis was performed with SPSS for Mac, version 25 (IBM Corp, Armonk, NY), and Stata, version 15.1 (StataCorp, College Station, TX). Due to non-normal distribution, interval variables were expressed as median and interquartile range, and categorical variables as percentages.

The Mann-Whitney U test was used to compare interval variables and the χ^2 test to compare relative frequencies, considering trends when appropriate. Logistic regression was used to analyze factors associated with binary outcomes, using the "Enter" method to handle variables in the models. The strength of the association was expressed by calculating ORs and their 95% CIs. The goodness-of-fit was checked with the Hosmer–Lemeshow test.

Protection against type I error was set at alpha level of 0.05.

Results

Overall, 7,270 75+ year-old patients were enrolled in the pre-DSC phase and 4,725 in the post-DSC phase in the OSMA, for a total of 11,995, after exclusion of 17 patients with incomplete data. Technical issues with the informatic procedure for data linkage and DSC calculation occurred during the run-in period of the pre-DSC phase, making the score unavailable at random in some weeks: the monthly median [IQR] number of patients in whom the score was obtained was 633 [288, 921] in the pre-DSC and 914 [903, 1007] in the post-DSC phase (p=0.079). Demographics were comparable between the two periods: median age was 84 [79, 89] and 84 [80, 88] years (p=0.510) and the proportion of men 42% and 41% in the pre-DSC and in the post-DSC period, respectively (p=0.357). The distribution across triage color classes differed significantly, with a lower prevalence of white and green codes in the pre-DSC (white: n=1,040, 14.3%; green: n=3,230, 44.4%; yellow: n=2,788, 38.4%; red: 212, 2.9%) than in the post-DSC phase (white: n=824, 17.4%; green: 2,335, 49.4%; yellow: 1,455, 30.8%; red: 111, 2.4%; p for trend<0.001). Conversely, no statistically significant difference was observed in the distribution across DSC classes between the pre-DSC (class I: n=1,256, 17.3%; class II: n=1,992, 27.4%; class III: 1,967, 27.1%; class IV: 2,055, 28.3%) and the post-DSC phase (class I: n=775, 16.4%; class II: 1,378, 29.2%; class III: 1,243, 26.3%; class IV: 1,329, 28.1%; p for trend=0.166).

In the overall sample, the ED LOS decreased from a median of 380 [206, 958] in the pre-DSC to 318 [178, 655] min in the post-DSC period (p<0.001). In a logistic regression model adjusted for color triage code and DSC class, the OR (95% CI) for an ED LOS below the median was significantly in favor of the post-DSC period (0.73, 0.68-0.78; p<0.001). In the subsample of patients eventually admitted to Internal Medicine or Geriatrics, the decline in the ED LOS was even greater, from a median of 975 [418, 1,419] min in the pre-DSC to 537 [324, 1,166] min in the post-DSC phase (p<0.001). In this subsample, the odds for an ED LOS below the median was again significantly in favor of the post-DSC phase (OR 0.50, 0.42-0.59; p<0.001), adjusting for color triage code and DSC class in a logistic regression model; the fitting of the model was good (p=0.940). Across the same months, in the other hospital where the DSC has a masked implementation, the ED LOS in patients eventually admitted to Internal Medicine was 1,057 [461, 1,520] min in the first period and 659 [380, 1,330] in the second one: no statistically significant difference was observed between the two periods in the odds of LOS above the median in a logistic regression model, adjusting for triage code (OR 1.09, 0.62-1.56; p=0.663), again with a good fitting of the model (p=0.260).

A total of 550 patients in whom the DSC was available were admitted to Geriatrics and 1,928 to Internal Medicine across the two periods. As shown in **Figure 2**, the distribution of admissions to Geriatrics across DSC classes differed significantly between the two phases: class III covered the largest share of admissions when the DSC-based clinical decision tree was applied in the post-DSC period (57.7%), compared to only 38.3% in the pre-DSC phase (p<0.001).

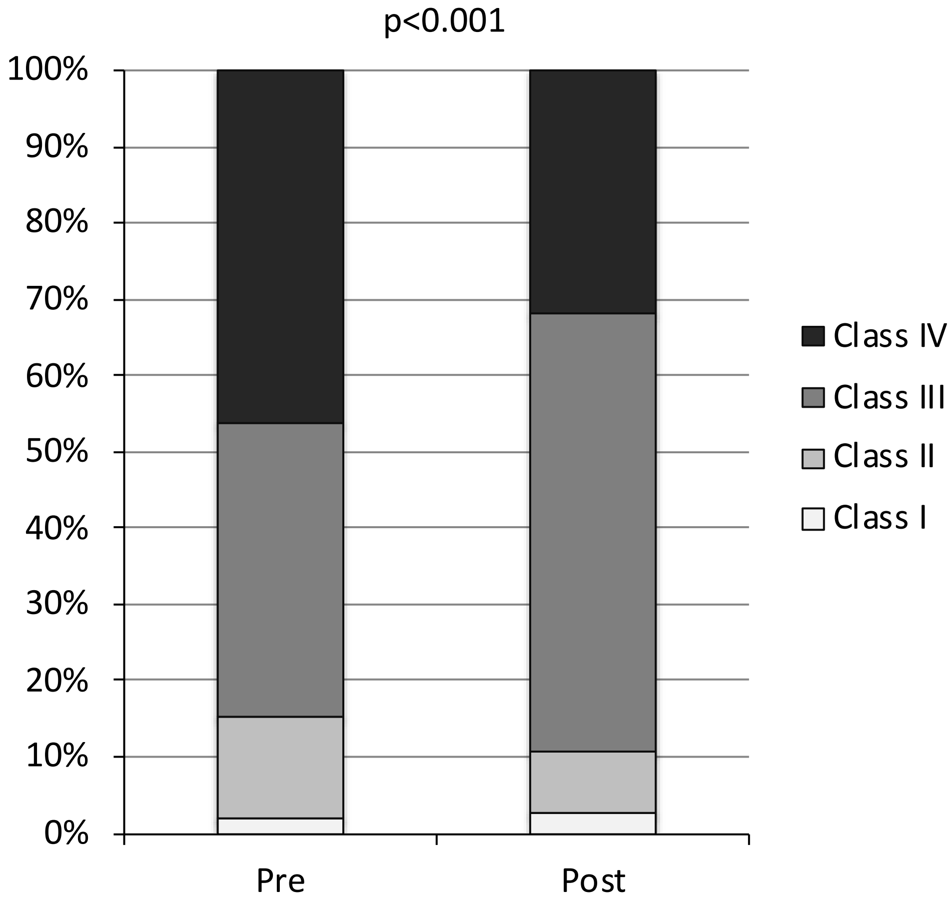

Figure 2. Comparison of admissions to Geriatrics across the DSC classes between the pre-DSC and the post-DSC phase.

In a logistic regression model adjusted for color triage code and length of ED staying, factors independently associated with admission to Geriatrics were DSC and phase of the study (**Table 1**), always with a good fitting of the model (p=0.329). Patients seen in the post-DSC phase were twice as likely to be admitted to Geriatrics as those in the pre-DSC; at the same time, compared to DSC class I, being in DSC class III and IV was associated to an almost four- and two-times greater odds of being admitted to Geriatrics, respectively, independent of age, color triage code, and ED LOS (**Table 1**).

Table 1. Logistic regression model of factors associated with admission to Geriatrics in the two study periods, adjusted for age, color triage code, and ED length of stay (LOS).

	OR (95% CI)	**p value**
Post-DSC vs. pre-DSC study phase	1.99 (1.62-2.45)	<0.001
DSC class III vs. I	3.76 (2.66-5.31)	<0.001
DSC class IV vs. I	1.91 (1.34-2.73)	<0.001

Two hundred sixty-five patients in whom the DSC was available were admitted to Geriatrics in the pre-DSC and 285 in the post-DSC phase. Among them, hospital LOS decreased by one day, from 7 [5, 11] to 6 [5, 9] days (p=0.006) between the two study periods. The odds of a post-DSC hospital LOS below the median were significant, after adjusting for color triage code (OR 0.67, 0.46-0.98; *p*=0.041). At the same time, the weight of the DRG increased slightly but significantly between the pre-DSC and the post-DSC phase (**Figure 3**). Fifty patients (19%) died in-hospital in the pre-DSC and 61 (21%) in the post-DSC phase (*p*=0.459).

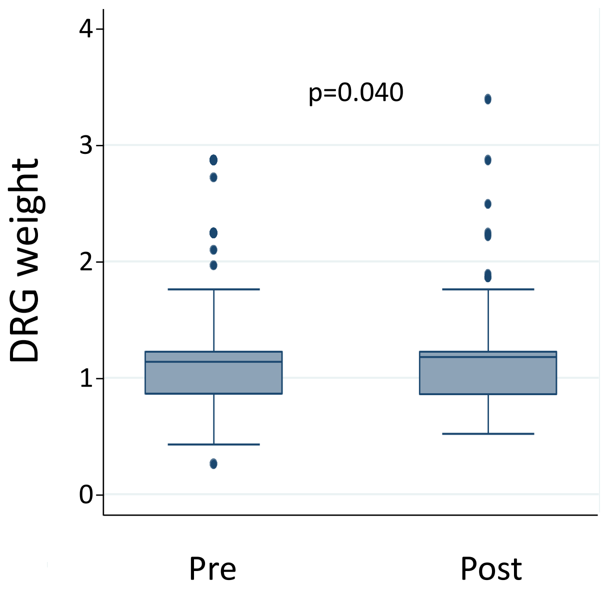

Figure 3. Comparison of weight of the DRG between the pre-DSC and the post-DSC phase in patients admitted to Geriatrics.

Discussion

This study shows that the DSC, a prognostic score based on simple administrative data, contributed to improved patient flow and better overall clinical management of older patients in the ED, as suggested by decreased ED LOS, especially in patients eventually admitted to Internal Medicine and Geriatrics wards. Moreover, implementation of the DSC and of a DSC-derived clinical decision tree for assignment to a specific ward appeared to improve appropriateness of admissions to Geriatrics: in fact, in the post-DSC phase this ward received mostly patients at an intermediate risk (DSC class III), with greater clinical complexity but more chances for improvement and recovery, leading to shorter hospital LOS.

Instruments for risk stratification of older patients in the ED have been developed, but their performance has been poor [Carpenter CR, 2015]. More recently, the Clinical Frailty Scale (CFS) was validated for use in the ED in patients aged 65+, with area under the receiver operating characteristic curve of 0.81 and 0.77 for 30-day and 1-year mortality, respectively [Kaeppeli T, 2020; Rueegg M, 2022; Huh JY, 2022]. However, this tool is complex and requires in-person evaluation, which is difficult to implement because of time constraints and lack of trained personnel in the busy routine of an ED.

Despite their inherent limitations, simple administrative data are an attractive contribution to prognostic assessment of older patients, because they are accurate, objective, easily available at a low cost, and are applicable also in patients unable to cooperate with care plan due to comorbidity [Dagan N, 2017; Simpson AN, 2018]. These characteristics should be particularly valued in the ED, where extensive application of complex assessment procedures may be problematic [Asomaning N, 2014]. Also, addition of a mobility status as a frailty indicator did not improve the accuracy of a computerized triage system [Chien CY, 2022]. To our knowledge, the DSC is the only real-time electronic tool for risk stratification of older persons developed for the ED. With this study, we provide evidence suggesting that the availability of prognostic information, based on background risk status, together with standardized clinical decision rules for assignment to a specific ward, may expedite procedures in the ED, ultimately reducing waiting time and ED LOS. The importance of this finding should be underlined, because previous studies have shown that older patients stay longer than younger ones in the ED [Rossi PD, 2010], and such an increased LOS may by itself contribute to ED-associated complications [Aminzadeh F, 2002].

Randomized clinical trials (RCTs) and their meta-analyses reported that, compared to Internal Medicine, admission to acute Geriatrics wards may improve survival and functional outcomes of frail older patients requiring hospitalization [Ekerstad N, 2017; Saltvedt I, 2002; Ellis G, 2017] thanks to the delivery of personalized care based on comprehensive geriatric assessment. Participants enrolled in these studies were usually at an intermediate level of clinical severity, whereas those who were too well or too sick were considered unable to draw substantial benefit from admission to a specialized geriatric setting [Tanderup A, 2018]. Our non-randomized intervention study is coherent with the available evidence from RCTs. The clinical decision tree based on the DSC allowed to select patients for direct admission to Geriatrics as those at an intermediate risk (DSC class III), whereas those with low background risk (DSC class I and II) were candidates for Internal Medicine, and an individualized assessment was devised for those at greater risk (class IV). Our findings indicate that this decision tree was indeed correctly applied, therefore improving patients' selection and ultimately increasing the efficiency of the Geriatrics ward. In fact, the combination of greater DRG weight and shorter LOS, with unchanged hospital mortality, suggests that patients admitted to Geriatrics in the post-DSC phase could recover faster than those in the pre-DSC phase, even in the face of an increased clinical complexity.

This study has numerous limitations. We are aware that the pre-post study design is intrinsically weak, as many other variables besides the intervention can modify the outcomes considered. However, a randomized study design would be difficult, if not impossible, to apply when examining changes affecting the delivery of care in an entire healthcare facility, such a whole hospital. To limit the chances of bias, we adjusted our pre-post comparisons for some indicators of complexity, such as the triage color code and the DSC class. Moreover, we also verified that no such a difference in ED LOS was observed in another community-based hospital, similar to the OSMA, across the study period. In the pre-DSC phase, availability of the score was erratic and, in fact, the number of patients enrolled monthly was lower, although not significantly, than in the post-DSC phase. For the same reason, patients observed in the Geriatric ward were less in the pre-DSC than in the post-DSC phase, despite longer enrollment period. However, these fluctuations were random, and we are, therefore, confident they have not biased our findings. Variables in the DSC are very simple and cannot convey the whole spectrum of conditions that make an older patient susceptible to poor outcomes. However, the DSC is a population management tool, and its simplicity intentionally facilitates its broad application, especially in Italy, where the National Healthcare System warrants universal delivery of services and, at the same time, availability of consistent information to compile the score. This metric and its value need to be tested in emergency departments outside the Italian healthcare system. Finally, only a few indicators (LOS and DRG weight) were available to assess changes in the pre-post comparisons, but these are reliable, important, and easily obtainable from administrative archives.

Conclusions and Implications

In conclusion, application of the DSC in the ED of a community hospital was associated with shorter ED LOS of older patients and provided a standardized method identifying older patients most appropriate for admission to a Geriatric inpatient unit. This enhanced the value and efficiency of clinical management of patients admitted to this ward. Further studies should be performed to obtain a more rigorous and extensive assessment of the effects of the implementation of the DSC.

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DSC predicts the Need for Post-Acute Care Services

Hospitalization may represent a tipping point in the clinical history of older patients, as it is often followed by serious negative health outcomes, such as functional and cognitive decline, delirium, and even death [Sager MA, 1996; Siddiqi N, 2006]. In particular, because of prolonged bed rest, reduced calories and protein intake, and lack of physical therapy, many hospitalized older patients fail to regain their pre-admission functional status and remain severely disabled at discharge, independent of the severity of the index disease that brought to hospitalization [Peel NM, 2019; Kang MC, 2018]. Thus, it is often necessary to develop and implement an individualized discharge planning for these patients such as delivery of home healthcare services or discharge to skilled nursing (SNF) or rehabilitation facilities [Wang YC, 2019; Balaban RB, 2008; Gonçalves-Bradley DC, 2022]. It should be noted that discharge to post-acute care facilities is increasing in recent years, reflecting both the growing complexity of older patients [Burke RE, 2015; White HK, 2019] and a broader view of post-acute care, which may offer an opportunity to assess, and respond to, specific needs in view of returning home, rather than simply trying to recover previous functioning [Jenq GY, 2015]. On the other hand, accurate selection of patients to be discharged towards post-acute care is mandatory: indeed, it has been suggested that, at least in trauma patients, discharging to post-acute care might represent an independent risk factor for long-term institutionalization and mortality [Hakkarainen TW, 2016; Middleton A, 2018; Claridge JA, 2010]. Therefore, patients whose discharge may eventually prove to be complex should be identified as accurately and early as possible, ideally even on admission, with the two aims of optimizing hospital care and to plan in advance post-acute care, with the ultimate goal of reducing long-term institutionalization post discharge [Gonçalves-Bradley DC, 2022; Naylor MD, 1999].

In the Azienda Ospedaliero-Universitaria Careggi (AOUC) in Florence, Italy, an academic tertiary care hospital, the Agency for the Hospital-Community Continuity Care (Agenzia per la Continuità Ospedale Territorio - ACOT) is responsible for the connection between hospital wards and healthcare services in the community. Patients who may have nursing, rehabilitation, or assistance needs at the time of discharge, are referred by physicians in the individual hospital wards to ACOT, which then activates the post-discharge services required, including those offering residential care when the patient is not able to return directly home.

In the ED of the AOUC and of all the hospitals in the Central District for Healthcare Services of Tuscany (Azienda USL Toscana Centro, ATC), the Dynamic Silver Code (DSC) is in place to predict short- and long-term survival of subjects aged 75+ years accessing the Emergency Department (ED) [Balzi D, 2019].

Aim of this study was to evaluate if the DSC predicts referral to ACOT and the actual discharge to post-acute care facilities.

Methods

Study design and data source

A non-concurrent cohort study design was applied, using data obtained from the administrative archives of the AOUC, pseudonymized in order to prevent personal identification. We considered all the subjects aged 75+ accessing the AOUC ED and then hospitalized with medical or surgical diagnoses from November 1, 2020, to December 31, 2021. Patients dying in hospital and those admitted with stroke, severe acquired brain injury, or trauma, all conditions that require mandatory ACOT referral for activation of specific discharge projects, were excluded. We also excluded patients with COVID-19, who were referred to ACOT to find a facility for quarantining.

Variables

In all participants, vulnerability status was estimated with the DSC. Primary discharge diagnoses, classified according to the International Classification of Diseases, ninth edition codes, were grouped into unique disease categories according to the Clinical Classifications Software (CCS) [1s]. CCS codes of interest were selected and eventually combined into broader groups through a consensus process among investigators. To further estimate the burden of comorbidity, the number of non-primary diagnoses, listed in the hospital discharge archive, was calculated in each participant.

Two outcome variables were considered: 1) referral to ACOT and 2) discharge to a post-acute care facility, as reported in the ACOT archive.

Statistical analysis

Statistical analysis was performed with SPSS for Mac V.28.0.1.0 (IBM Corp., Armonk, NY, USA). Interval variables were expressed as mean standard error (SEM) or median and interquartile range, depending on the distribution, and categorical variables as percentages. The Student *t* and the Mann-Whitney U tests were used to compare normally and non-normally distributed interval variables, and the χ^2 test to compare relative frequencies, between individuals reported and not reported to ACOT and between individuals discharged and not discharged to low-care facilities. The bivariate association between the four DSC risk classes and the outcomes was analyzed with the χ^2 test for trend. Separate binomial logistic regression models were built to assess the risk of being referred to ACOT and to be actually discharged to a post-acute care facility as a function of DSC, contrasting class II, III, and IV with class I and adjusting for CSS and the number of comorbidities; from these models, odds ratios (OR) and 95% confidence interval (CI) were calculated. Age and gender were not entered into the models, because they contributed to the generation of the DSC itself. We also did not include hospital length of stay, because it may be influenced by the waiting list for obtaining a SNF bed and, therefore, it might bias the causal relationship. The goodness-of-fit of the model was assessed using the Hosmer-Lemeshow method.

Results

Out of 6,252 subjects enrolled, 49.7% were women; mean age was 83±0.07 years. The distribution of participants across the four DSC classes was 25.4, 32.2, 21.3, and 21%, respectively. The most frequent discharge diagnoses are listed in **Table 1**. A total of 1,467 (23.5%) subjects were referred to ACOT and 629 (10.1%) were eventually discharged to a post-acute care facility.

Table 1. Baseline characteristics of participants in the entire sample (n=6252).

Variable	N (%) or mean (SEM) or median [IQR]
Gender F	3108 (49.7)
Age (years)	83.4 (0.07)
DSC	
Class I	1590 (25.4)
Class II	2014 (32.2)
Class III	1332 (21.3)
Class IV	1316 (21.0)
Discharge diagnoses	
Heart failure (CCS code 108)	769 (12.3)
Respiratory diseases (CCS codes 103, 122, 126-131, 133-134)	1064 (17.0)
Cognitive disorders (CCS code 653)	85 (1.4)
Gastrointestinal bleeding (CCS code 153)	58 (0.9)
Renal diseases (CCS codes 156-158)	160 (2.6)
Sincope (CCS code 245)	132 (2.1)
Malignancies (CCS codes 11-43)	89 (1.4)
Infections (CCS codes 1-3, 6-8, 76, 77, 123, 135, 148, 159, 197, 201)	772 (12.3)
Lenght of stay (days)	8 [5-13]
Number of comorbidities	
1	862 (13.8)
2	1265 (20.2)
3	1250 (20.0)
4	1134 (18.1)
5+	1741 (27.8)
Patients reported to ACOT	1467 (23.5)
Discharged with activation of home services	654 (10.5)
Transfer to rehabilitation facilities	184 (2.9)
Transfer to low-care facilities	629 (10.1)

Participants who were referred to ACOT were significantly older than those who were not (83±0.78 vs. 84±0.14 years; p<0.001); they had a greater proportion of women (52.6% vs. 48.8%, p = 0.013) and a significantly longer hospital stay (7 [IQR 5-11] vs. 12 [IQR 8-18] days, p<0.001). The proportion of ACOT referral increased from DSC class I to II-IV, where the group in DSC class III had the higher percentage of cases referred (class I: n=309, 19.4%; class II: n=483, 24%; class III: n=345, 25.9%; class IV: n=330, 25.1%; p for trend <0.001) **(Table 2)**.

Subjects who were discharged to a post-acute care facility were older than those who were not (85±0.21 vs. 83±0.07 years; p <0.001); they had a greater proportion of women (55.0 vs. 49.1%; p = 0.005) and a longer length of hospital stay (12 [IQR 8-18] days vs. 8 [IQR 5-12]; p<0.000). Overall, discharge to a post-acute care facility occurred in 10.1% of cases, again with a significant difference across DSC classes (class I: 116, 7.3%; class II: n=214, 10.6%; class III: n=157, 11.8%; class IV: n=142, 10.8%; p for trend <0.001) **(Table 2)**.

Table 2. Distribution of study participants referred to ACOT and discharged to a post acute care facility, across DSC classes.

	Referred to ACOT N (%)	*p* for trend	Discharged to post-acute care facility, N (%)	*p* for trend
DSC		<0.001		<0.001
Class I	309 (19.4)		116 (7.3)	
Class II	483 (24.0)		214 (10.6)	
Class III	345 (25.9)		157 (11.8)	
Class IV	330 (25.1)		142 (10.8)	

In multivariable analysis, being in DSC class II-IV resulted in a 28 to 38% significantly greater risk of ACOT referral, adjusting for CCS and number of comorbidities; both covariates gave a significant contribution to the prediction of this outcome (**Table 3**). According to the Hosmer-Lemeshow test, the fitting of the model was suboptimal (p=0.004). Similar findings were obtained in the logistic regression model predicting actual discharge to post-acute care, with a 42 to 61% significantly greater risk in DSC class II to IV compared to class I, always adjusting for CCS (which contributed to the prediction of the outcome) and comorbidities (**Table 3**); this model resulted well calibrated, according to the Hosmer-Lemeshow test (p=0.161).

Table 3. Logistic regression models testing the association between DSC and referral to ACOT and discharge to a post-acute care facility, adjusted for discharge diagnosis and number of diseases.

	Referred to ACOT		Discharged to SNFs	
DSC	OR (95% CI)	p	OR (95% CI)	p
Class I	Ref.		Ref.	
Class II	1.28 (1.08-1.50)	0.003	1.47 (1.16-1.87)	0.001
Class III	1.38 (1.16-1.65)	<0.001	1.61 (1.25-2.08)	<0.001
Class IV	1.29 (1.07-1.54)	0.006	1.42 (1.10-1.84)	0.008
Discharge diagnosis	1.02 (1.00-1.04)	0.013	1.01 (0.98-1.03)	0.646
Number of diseases	1.34 (1.29-1.41)	<0.001	1.29 (1.21-1.38)	<0.001

Discussion

In this large cohort of older subjects admitted to a large academic hospital for medical or surgical problems, being in a DSC risk class > 1 resulted in an increase of up to 46% of being referred to ACOT for the implementation of post-acute care services, and up to 70% of being discharged to a post-acute care facility, regardless of the discharge diagnosis. Only the model testing the predictors for discharge to post-acute care, resulted as well calibrated, according to the goodness of fit test. For both outcomes, the ORs were slightly greater in DSC class III than in class II and IV, which showed comparable values.

Many older patients have unique difficulties with recovering from surgery or injury, because the physiologic homeostatic reserve, which provides tolerance to adverse events, declines with aging, and is particularly compromised in vulnerable subjects [Gupta S, 2019]. Consequently, it is more difficult for vulnerable older patients to recover, regain independence, and return home after hospital discharge. It is therefore not surprising that the DSC, as a proxy of the vulnerability status of older adults, was shown to be correlated to the augmented need of post-acute care services and of discharge to a skilled nursing facility (SNF). In fact, previous studies showed that patient factors associated with discharge to SNF included advanced age, female sex, longer length of stay, and a variety of comorbidities [Allen LA, 2011]. Furthermore, performance measures were modestly lower for patients discharged to SNF [Allen LA, 2011].

Participants who were referred to ACOT and those discharged to post-acute care facilities had a significantly longer hospital stay. This can be explained by the increased clinical complexity and the greater risk for in-hospital complications. In addition, the waiting lists for the beds in the SNF may further increase hospitalization stay, with augmented risk for short-term negative outcomes [Ghazalbash S, 2022]. For these reasons, the discharge planning must be as early as possible, and every effort must be done to avoid intrahospital complications [Gonçalves-Bradley DC, 2022; Balentine CJ, 2016].

The multivariate analysis showed that subjects in DSC class III have the highest OR for our outcomes, especially the discharge to SNF, compared to DSC class II and

IV. Reasons for not being discharged home are many and common to all risk classes. However, fit subjects (DSC class II) have shorter recovery times, and greater probability of returning home. On the other hand, functionally dependent patients, such as those in DSC class IV, may be already organized at home for the assistance they need, resulting in a lower rate of discharge to SNF. This emphasizes the need for individualized assessments and for the implementation of patient-tailored post-acute care projects.

The DSC was developed using death as an outcome and, indeed, it is mainly a mortality stratifier. Thus, this is the first study showing that it can also predict other outcomes, which are proxies of functional decline. Other tools helping physicians in the discharge planning have been reported in medical literature. Most of them focused on patients with a specific disease, such as stroke or hip surgery [Casertano LO, 2022; Ortiz D 3rd, 2022]. Conversely, only few studies are geared to the geriatric population. The majority were scores assessed by hospital workers, such as nurses, at the time of the admission in the hospital ward, such as the BRASS Index and the ESDP score [Holland DE, 2006; Ortiz D 3rd, 2022]. Compared to these tools, DSC has the advantage of being based only on administrative data, which can be easily and promptly available on admission with no need for human resources for data collection. We found one study where administrative data were used in the identification of complex discharges in patients who underwent elective surgery, but the resulting score was calculated only retrospectively, not in real time [Stubbs DJ, 2019]. It has to be noted that all the tools listed above, including the DSC, share a high sensitivity compared to their specificity, with the implication of identifying a too large group of patients. Those results certainly enrich medical literature, but their use in clinical practice is limited to identify a group of patients requiring specific attention by physicians and other healthcare professionals, both for the intrahospital route and the discharge planning.

Study limitations must be acknowledged. The DSC can be calculated only for patients residing in the florentine area, limiting the transferability of our data; however, this is a large cohort of real-world older adults hospitalized for many different medical and surgical conditions. The goodness of fit test showed that the model testing the predictors of referral to ACOT was not well calibrated. Indeed, the referral to ACOT in the AOUC is necessary for the implementation of any post-acute care services, even specific and single nursing needs, such as management of bladder catheter or medication of surgical wounds, that may be independent from the vulnerability status of a patient. Hospital discharge diagnoses may sometimes be distorted by economic issues associated with reimbursement procedures.

Conclusions and Implications

The DSC has proven again to be an indicator of vulnerability in hospitalized older patients. Because of its prompt, real-time availability at triage in the ED, it can effectively identify possible difficult discharges even before hospitalization. Shedding a light on those patients is the first step for early discharge planning, by identifying subjects in need of post-acute care, who would eventually be assessed and referred to an array of different patient-tailored projects.

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COVID -19, Vulnerability, and Long-Term Mortality in Hospitalized and Non-hospitalized Older Persons

Since its beginning, the SARS-CoV-2 pandemic has severely hit older patients, in whom COVID-19 mortality reaches stunning proportions [1s; 2s; Islam N, 2021]. An advanced age has been identified as a major negative prognostic determinant in the course of COVID-19, independent of disease-specific predictors [Williamson EJ, 2020; Parohan M, 2020; Palmieri L, 2020]. Specifically, an exceeding COVID-19 mortality has been reported in subsets of older patients at an increased background risk of death, generically defined as frail [Andrés-Esteban EM, 2021; Hewitt J, 2020; Marengoni A, 2021; Blomaard LC, 2021; De Smet R, 2020; Gilis M, 2021; Koduri G, 2021; Sablerolles RSG, 2021]. Consequently, recommendations have been issued to consider frailty in the decision-making process on whether or not to increase the level of care in older patients with COVID-19 [3s]. However, in the given context the use of the term frailty may be questioned because assessment of an increased risk status was based on tools, such as the Clinical Frailty Scale (CFS), that rely on comorbidities and dependency more than on the construct of frailty as a predisability condition, accepted in most current literature [Hoogendijk EO, 2019; Pilotto A, 2021; Rockwood K, 2005; Dent E, 2019]. Therefore, the term vulnerability will be used hereinafter, even when frailty had been used in the original reports.

Other studies showed that CFS-assessed vulnerability did not contribute to predicting death in older persons hospitalized with COVID-19 [Owen RK, 2021; Miles A, 2020]. Yet, the evidence provided so far is unsatisfactory. Most of the studies considered only hospitalized patients and were limited to hospital mortality [Andrés-Esteban EM, 2021; Hewitt J, 2020; Marengoni A, 2021; Blomaard LC, 2021; De Smet R, 2020; Gilis M, 2021; Koduri G, 2021; Sablerolles RSG, 2021], providing no information on the role of vulnerability in individuals not requiring hospitalization nor on long-term survival. Moreover, they usually lacked non-COVID-19 comparators and, finally, assessed vulnerability a posteriori on the basis of some operator-dependent tool, such as the CFS. Assessing the excess risk associated with COVID-19 in vulnerable older patients is, therefore, a substantially unsolved issue.

In the community hospitals of the Central District for Healthcare Services of Tuscany (Azienda USL Toscana Centro, ATC) and in the Azienda Ospedaliero-

Universitaria Careggi (AOUC), an academic hospital caring for adult patients in Florence, real-time, automated prognostic stratification of persons aged 75+ years accessing the emergency department (ED) is provided by the Dynamic Silver Code (DSC). Using only administrative data, the tool is able to predict short- and long-term survival [Balzi D, 2019]: more recently, it has been shown to also reflect pre-existing functional status, specifically inability to walk [Di Bari, 2022]. Thus, although not a direct measure of frailty, the DSC expresses an increased vulnerability to adverse outcomes strictly associated with poor physical functioning.

This study was conducted to evaluate the role of pre-existing vulnerability, as represented by the DSC, on long-term mortality in a large cohort of older persons seeking care in the ED during the pandemic, separately in hospitalized and not hospitalized persons, comparing patients diagnosed with COVID-19 to those with other diagnoses.

Methods

Study Design and Data Source

A concurrent cohort study design was applied, using data obtained from the administrative archives of the ATC and the AOUC and the database of the Italian National Health Institute (Istituto Superiore di Sanità, ISS) of individuals diagnosed with COVID-19.

The ATC serves a population of approximately 1.6 million residents in central Tuscany, where the AOUC and 13 community hospitals are located. From the ATC and AOUC archives collecting all ED accesses and hospital discharges, we selected patients age 75+ years whose ED database record reported the DSC, accessing an ED in the area between March 1 and November 15, 2020. In addition, we also consulted the local demographics registry to obtain mortality data.

The ISS database [4s] is the national registry of all the confirmed cases of COVID-19, based on reverse transcriptase–polymerase chain reaction testing. It reports when, but not where (ie, hospital, community clinic, or patient's home), the diagnosis was made.

Assembly of Study Cohorts

Two different approaches were applied to select eligible patients, depending on whether ED access was followed or not by hospital admission.

Hospitalized patients were identified by linking the ED database with the hospital discharge database, using a unique identifier that does not allow personal identification. Linkage was limited to cases accessing the ED not earlier than 2 months prior hospitalization; in case of multiple ED access, the one closest to admission was kept. Elective hospitalizations were excluded. In this database, diagnoses are coded following the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). The diagnosis of COVID-19, deriving from a positive reverse transcriptase–polymerase chain reaction testing, was adjudicated when an ICD-9-CM code 078.89 was reported as primary or secondary discharge diagnosis, or as a subsequent diagnosis when the primary diagnosis was consistent with an acute respiratory disease or a viral infection (ICD-9-CM codes 484.8, 466, 490, 519.8, 518.82, 518.81, 518.84, 480, 480.8, 480.9, 487.0, or 480.3). These hospitalized COVID-19 (HC+) patients were compared with all other nonelective, non-COVID-19 admissions (HC-).

Among patients registered in the ED database but not admitted to the hospital, those with COVID-19 (nonhospitalized COVID-19 cases, NHC+) were identified by linkage, using again the anonymous identifier, with the ISS database. When a participant had more than 1 ED access, the closest to the date of COVID-19 diagnosis was considered. ED records not linking with the ISS database were considered for comparison, as referring to nonhospitalized patients without COVID-19 (NHC-) patients.

Assessment of Vulnerability

Vulnerability was assessed with the DSC.

Mortality Ascertainment

Vital status was ascertained from the ATC demographics registry as of March 31, 2021.

Analytic Procedures

Statistical analysis was performed with STATA v 16.1 (StataCorp, 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC). Interval variables were expressed as mean ± standard error (SEM) or median and interquartile range (IQR), depending on the distribution, and categorical variables as percentages.

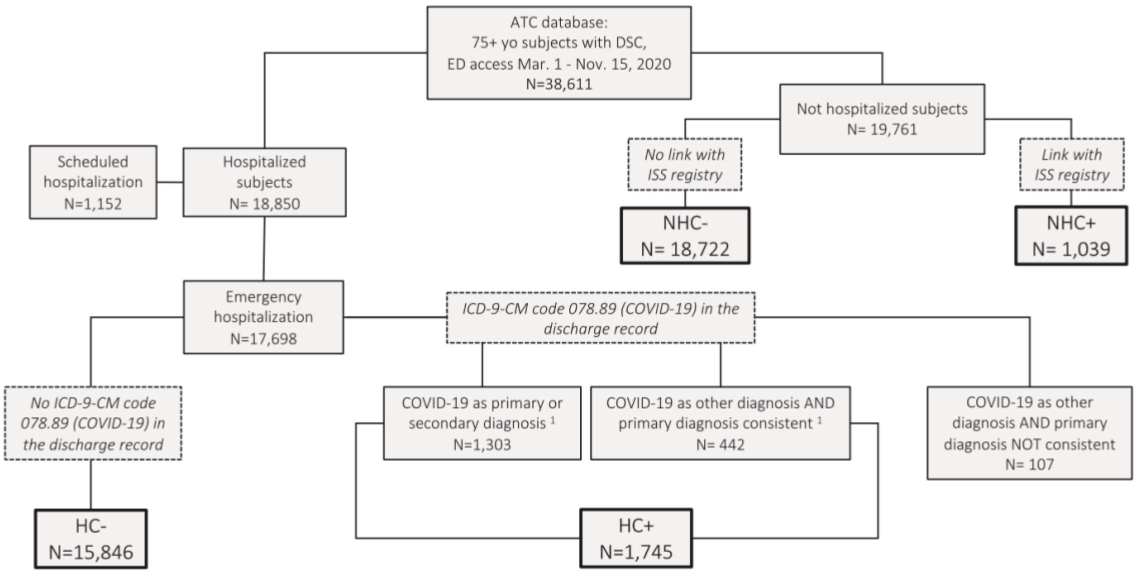
Main analyses were performed separately in hospitalized and nonhospitalized participants. The student *t*-test was used to compare normally distributed variables between 2 groups, the Mann-Whitney test for non-normally distributed variables, and the χ^2 test to compare relative frequencies, considering trends as appropriate. Survival analysis was performed with Cox proportional hazards models with hazard ratio (HR) and 95% CI, to compare mortality across DSC classes, separately in individuals with and without COVID-19, and between persons with and without the disease within DSC classes. The assumption of proportionality of hazards over time was verified with the Schoenfeld residuals and comparing the survival functions for each covariate pattern; the fitting of the models was evaluated using the Cox-Snell residuals. Interaction between diagnosis of COVID-19 and DSC class was tested with Wald test. Because the DSC incorporates demographics and some data on comorbidities, these variables were not entered in multivariable analyses, to prevent over-correction.

Protection against type I error was set at alpha level of 0.05.

Results

Figure 1 reports the study cohort assembly, after exclusion of repeated ED accesses. A total of 38,611 patients age 75+ years had at least 1 ED access between March 1 and November 15, 2020 registered in the ATC and AOUC archives, from which the DSC could be extracted. Of them, 17,698 had emergency hospitalization, 1152 elective hospitalization, and 19,761 were not hospitalized. Among patients with emergency hospitalization, those with an ICD-9-CM code 078.89 as their primary or secondary diagnosis, together with those in whom this code was a subsequent diagnosis and the primary diagnosis reported an ICD-9-CM code consistent with acute respiratory disease or viral infection, represented the group of hospitalized participants with adjudicated diagnosis of COVID-19 (HC+, n = 1745). The HC+ group was compared with patients whose emergency hospitalization was not due to COVID-19 (HC-, n = 15,846).

Of the 19,761 patients whose ED access was not followed by hospital admission, 1039 could be linked to records in the ISS registry of COVID-19 cases and represented the group of nonhospitalized COVID-19 (NHC+) participants, whereas 18,722 could not be linked and were considered as nonhospitalized non-COVID-19 (NHC-) comparators.



[1] The diagnosis of COVID-19 was adjudicated when the ICD-9-CM code 078.89 was reported as primary or secondary discharge diagnosis or as a subsequent diagnosis when the primary diagnosis reported a clinical condition consistent with the disease (ICD-9-CM codes 484.8, 466, 490, 519.8, 518.82, 518.81, 518.84, 480, 480.8, 480.9, 487.0, or 480.3).

Figure 1. Flow-chart of the study cohort assembly. HC+ and HC- are hospitalized participants with/without adjudicated diagnosis of COVID-19, based on discharge records. NHC+ and NHC- are nonhospitalized participants with/without diagnosis of COVID-19, based on linkage with the ISS registry.

Overall Assessment of Mortality Risk

Over the entire follow-up, 8134 (21.8%) participants died. Increasing DSC class, the diagnosis of COVID-19, and hospital admission predicted independently the risk of death (**Table 1**).

Table 1. Mortality and Risk of Death by DSC Class, COVID-19 Diagnosis, and Hospitalization

	Participants N = 37,352	Deaths (%) n = 8134 (21.8)	HR (95% CI)
DSC score			
DSC class I (score ≤10)	13.725	1347 (9.8)	1
DSC class II (score 11–25)	13.750	3194 (23.2)	2.25 (2.11–2.4)
DSC class III (score 26–34)	6.918	2354 (34)	3.32 (3.1–3.55)
DSC class IV (score ≥35)	2.959	1239 (41.9)	3.83 (3.55–4.14)
COVID-19 diagnosis			
No	34.568	6998 (20.2)	1
Yes	2.784	1136 (40.8)	2.17 (2.04–2.31)
Hospitalization			
No	19.761	1917 (9.7)	1
Yes	17.591	6217 (35.3)	3.69 (3.5–3.88)

Hospitalized Participants

The characteristics of HC+ and HC- participants are shown in Table 1. HC+ participants were younger than HC-, with a similar proportion of men. The distribution across DSC classes and the duration of hospital stay differed significantly between the 2 groups. The 10 most common discharge diagnoses in HC- are reported in **Table 2**.

Table 2. The 10 Most Common Discharge Diagnoses in the 15,846 COVID-19-Free Hospitalized Participants

ICD-9 Codes	Description	n	%
518.81	Acute respiratory failure	1163	7.34
428.0	Congestive heart failure	428	2.70
434.01	Cerebral thrombosis with cerebral infarction	392	2.47
428.1	Left heart failure	365	2.30
518.84	Acute and chronic respiratory failure	362	2.28
820.20	Closed fracture of trochanteric section of neck of femur	357	2.25
410.71	Subendocardial infarction, initial episode of care	281	1.77
995.91	Sepsis	270	1.70
486	Pneumonia, organism unspecified	262	1.65
820.02	Closed fracture of midcervical section of neck of femur	235	1.48

Over a median follow-up duration of 206 (86–293) days, 48.4% of the HC+ and 33.9% of the HC- participants died (**Table 3**). Interaction between DSC class and the diagnosis of COVID-19 was slightly significant (p = .034). In HC+ participants, mortality increased from 27.5% in DSC class I to 51.1% in class II and 65.3% in class III, then it declined mildly (64.0%) in class IV, with 2-fold to 3-fold greater hazards of death in class II–IV vs class I. In HC- patients, the absolute risk of death was always lower than in HC+ within each DSC class and increased progressively across DSC classes, from 19.9% in class I through 51.1% in class IV. HRs had a similar stepwise increase, from 1.9 to 2.9 (**Table 4**). Thus, in analyses stratified by DSC class, the excess mortality associated with COVID-19, although always significant, was comparable within each DSC stratum, with HRs ranging between 1.6 and 2.2 (**Figure 2**).

Table 3. Comparison of the Characteristics of Participants Who Were or Were Not Diagnosed With COVID-19 Separately in Those Who Were or Were Not Hospitalized

	HC + (n=1745)	HC – (n=15,846)	*p* Value	NHC + (n=1039)	NHC- (n=18,722)	*p* Value
Age (y)	84 ±5.6	85 ± 5.7	<.001	84 ± 6.1	83 ± 5.5	<.001
Male sex	852 (48.8)	6839 (43.1)	<.001	417 (40.1)	7751 (41.4)	.432
DSC class (Score)			<.001			<.001
I (<10)	541 (31.0)	4599 (29.0)		352 (33.9)	8233 (44.0)	
II (11-25)	616 (35.3)	6270 (39.6)		396 (38.1)	6468 (34.6)	
III (26-34)	360 (20.6)	3525 (22.2)		199 (19.2	2834 (15.1)	
IV (≥ 35)	228 (13.1)	1452 (9.2)		92 (8.6)	1187 (6.3)	
Length of stay (day)	11 [6, 19]	7 [5, 11]	<.001	/	/	/
Mortality	845 (48.4)	5372 (33.9)	<.001	291 (28.0)	1629 (8.7)	<.001

Table 4. Mortality and Risk of Death by DSC Class Separately in Participants Who Were or Were Not Hospitalized and Were or Were Not Diagnosed With COVID-19

	Hospitalized			Non-hospitalized		
	Participants	Deaths (%)	HR (95% CI)	Participants	Deaths(%)	HR (95% CI)
All COVID-pos	1745	845(48.4)	/	1039	291(28.0)	/
DSC class I	541	149(27.5)	1	352	50(14.2)	1
DSC class II	616	315(51.1)	2.24(1.84-2.72)	396	114(28.8)	2.25(1.62-3.14)
DSC class III	360	235(65.3)	3.37(2.75-4.14)	199	84(42.2)	3.5(2.46-4.96)
DSC class IV	228	146(64.0)	3.08(2.45-3.87)	92	43(46.7)	3.72(2.47-5.59)
All COVID-neg	15,846	5372(33.9)	/	18,722	1626(8.7)	/
DSC class I	4599	913(19.9)	1	8233	235(2.9)	1
DSC class II	6270	2131(34.0)	1.88(1.74-2.03)	6468	634(9.8)	3.55 (3.05-4.12)
DSC class III	3525	1587(45.0)	2.65(2.45-2.88)	2834	448(15.8)	5.86(5.00-6.86)
DSC class IV	1452	741(51.0)	2.85(2.59-3.15)	1187	309(26.0)	9.7(8.18-11.49)

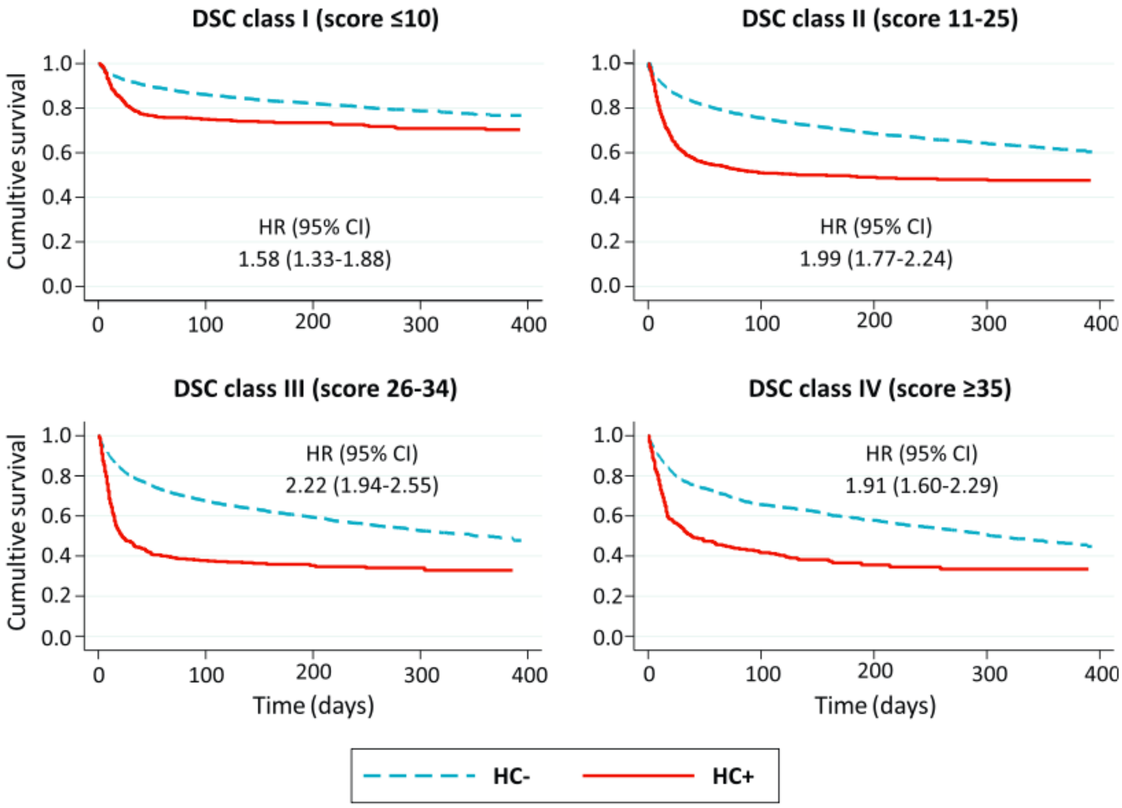


Figure 2. Survival curves of hospitalized COVID-19 vs non-COVID-19 (HCþ, HC-) participants, separately in each DSC class.

Nonhospitalized Participants

The characteristics of NHC+ and NHC- participants are presented in Table 1. NHC+ participants were older than NHC-, with a similar proportion of men. The distribution across DSC classes was also different between the 2 groups.

Throughout a median (IQR) observation time of 247 (190–302) days, 28% of the NHC+ participants and 8.7% of the NHC- participants died ($p < .001$). Interaction between DSC class and the diagnosis of COVID-19 in nonhospitalized participants was highly significant ($p < .001$). Mortality increased stepwise across DSC classes in both groups, yet more sharply in NHC-, from 14.2% in class I to 46.7% in class IV among NHC+, and from 2.9% in class I to 26% in class IV among NHC- (**Table 4**). Compared with class I, the hazard of death across classes II–IV was 2.3, 3.5, and 3.7 greater in NHC+, and 3.6, 5.9, and 9.7 greater in NHC- (**Table 4**). The excess mortality associated with COVID-19 decreased progressively with advancing DCS class, from an HR of 5.3 in class I to an HR of 2.0 in class IV (**Figure 3**).

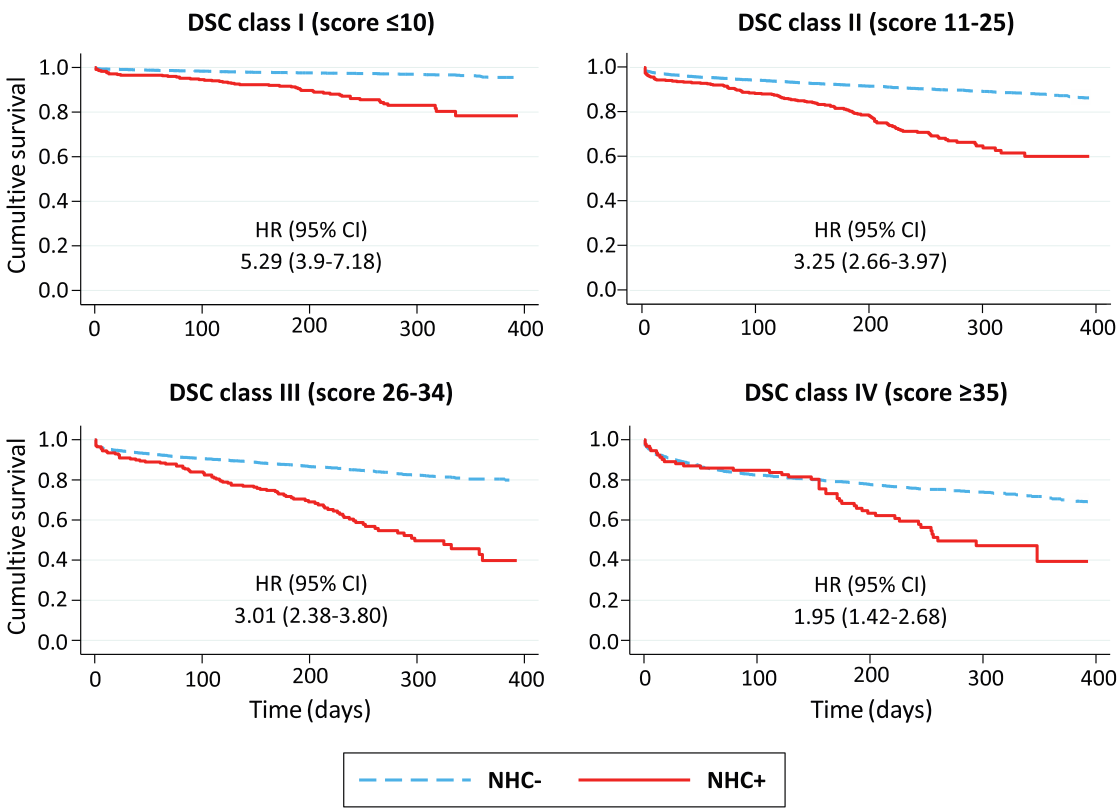


Figure 3. Survival curves of non-hospitalized COVID-19 vs non-COVID-19 (NHCþ, NHC-) participants, separately in each DSC class.

Time Course of Mortality

Mortality gradient between participants with and without COVID-19 had different time courses in hospitalized and nonhospitalized individuals. In HC+ of all DSC classes, the risk of death increased dramatically in the first month after enrollment, plateauing in the following months (**Figure 2**). Conversely, in nonhospitalized participants the survival curves separated progressively in classes I–III and diverged substantially only after the third month in class IV (**Figure 3**).

Discussion

In this large cohort of older patients accessing the EDs of Tuscany, we examined whether vulnerability, expressed by the DSC, modulated the risk of death associated with COVID-19 several months after ED access, separately in individuals who were or were not hospitalized. At the same time, we evaluated the excess risk of death associated with COVID-19, balancing background risk with the DSC. In hospitalized participants, mortality increased 2- to 3-fold with advancing DSC class, similarly in the presence and in the absence of COVID-19. The mild decline in the risk of death observed in DSC class IV HC+ participants compared with class III, can be ascribed to the lower precision of the estimates in the smaller group of HC+ patients. Conversely, in nonhospitalized participants, the diagnosis of COVID-19 increased the risk of death within each DSC class, but to a greater extent in the first than in the last classes (ie, more in individuals with lower background risk).

Several studies [Andrés-Esteban EM, 2021; Hewitt J, 2020; Marengoni A, 2021; Blomaard LC, 2021; De Smet R, 2020; Gilis M, 2021; Koduri G, 2021; Sablerolles RSG, 2021; s3; Hoogendijk EO, 2019; Pilotto A, 2021] and systematic reviews [Dumitrascu F, 2021; Kastora S, 2021] analyzed the relationship between frailty and COVID-19 mortality. However, the tool usually applied for this purpose was the CFS, which incorporates dependency as a measure of "frailty", where in fact dependency is to be considered as an outcome of the frailty status [Hoogendijk EO, 2019]. Therefore, we questioned this use of the term frailty, instead of vulnerability. With few exceptions [Owen RK, 2021; Miles A, 2020], the available evidence suggests that CFS-defined vulnerable individuals have an increased COVID-19 short-term mortality. In particular, a systematic review of 34 articles, with more than 18,000 hospitalized patients, reported that, compared with individuals with CFS of 1-3, mortality was 2-fold and 3-fold greater in those with CFS of 4–5 and 6–9, respectively [Kastora S, 2021]. Nevertheless, in a retrospective cohort study of 1071 patients age 65+ years, increasing vulnerability was associated with greater 30-day mortality in COVID-negative, but not in COVID-positive participants: because the diagnosis of COVID-19 enhanced the risk of death, the authors concluded that the disease strongly influences per se survival, beyond well-established prognostic indicators [Owen RK, 2021]. Consistently with the majority of previous studies enrolling only COVID-19 participants, we found that vulnerability, as estimated from the DSC, increases long-term mortality in older patients hospitalized with COVID-19, but not more than in patients hospitalized with other diagnoses.

The relationship between vulnerability and COVID-19 differed substantially in nonhospitalized patients, as the mortality gradient across DSC classes, although always detectable independent of the diagnosis, was less pronounced in participants with COVID-19 than in others. Thus, COVID-19 had a relatively more severe impact on survival in participants with lower background risk, as shown by decreasing HRs of NHC+ vs NHC- across DSC classes.

We also observed a different time course of COVID-19 mortality in patients who were or were not hospitalized. The brisk decline in survival in HC+ reflects the well-known severity of the disease in its acute phase. Yet, the slowly progressive separation between NHC+ and NHC- survival curves was unexpected and suggested that COVID-19 may eventually lead to a fatal outcome, even when no need for hospitalization was initially devised. It should be emphasized that COVID-negative individuals accessing the ED in the pandemic period probably had more severe conditions, thus, minimizing the difference with COVID-positive individuals, than the average population of ED visitors in nonpandemic times. Overall, our findings alert toward long-term consequences of the disease in otherwise well older patients, whose initial clinical presentation may appear noncritical.

Many patients with COVID-19 recover slowly and remain symptomatic long after the acute phase [Oronsky B, 2021], but long-term sequelae are sometimes unrelated to the initial severity of the disease [Townsend L, 2021]. It has been hypothesized that a “long-COVID” syndrome might affect a fairly large number of patients [Townsend L, 2021]. In a recent series of 958 COVID-19-convalescent, never hospitalized young individuals, first examined in a post-COVID outpatient clinic 6 weeks after the diagnosis, 442 persons were followed-up at 4 months and 353 at 7 months: shortness of breath and fatigue were present in as many as 9%–10% at 4 months and 14%–15% at 7 months [Augustin M, 2021]. Putting this evidence and our findings together, we would speculate that some insidious, possibly undetected, post-COVID syndrome might develop in old age, ultimately increasing the risk of death in the long term.

Most previous studies assessed the relationship between vulnerability and COVID-19 only in hospitalized patients without COVID-negative comparators, and limited to survival until discharge or, at most, at 30 days after admission. Thus, compared with the existing literature, this study has several strengths. We could assess the impact of vulnerability on long-term survival in both hospitalized and nonhospitalized older persons with COVID-19, compared with participants without COVID-19. We assembled a large, population-based sample of individuals older than those in most previous studies. Finally, because the CFS and other vulnerability screening tools are usually applied a posteriori and require some degree of skills, they might present issues of reliability and validity. Furthermore, they largely depend on the quality of the data collected, which may be suboptimal when taking history from an older patient. Conversely, the DSC is objective, completely operator-independent, and can also be obtained in noncollaborating patients.

The study has limitations. We had no other information, besides that conveyed by the DSC, on associated chronic comorbidities. In nonhospitalized participants, we could not ascertain the reason for ED access and its precise timing in relation to COVID-19 diagnosis, as well as the mode and cause of death. Because the DSC is available only following ED access, we could not extend our evaluation to patients with COVID-19 who received care in the community without accessing the ED: in particular, it is possible that extremely vulnerable older persons, such as those living in nursing homes, received neither a diagnosis of COVID-19 nor an ED admission during the months of the pandemic. This might limit the external validity of our findings. Finally, our findings depict the natural history of the disease as it appeared before the widespread application of vaccination programs, which fortunately has dramatically reduced COVID-19 mortality in older individuals.

Conclusions and Implications

In hospitalized patients age 75+ years, the increase in long-term mortality with progressive vulnerability, as documented by the DSC, is similar in presence and in absence of COVID-19. Conversely, in patients who are not hospitalized after ED access, the increase in long-term risk of death associated with worsening DSC class is greater in the absence than in the presence of COVID-19. In other terms, the disease appears to compromise long-term survival of older patients proportionally more when initial clinical status presents as noncritical and hospitalization is not devised. As a consequence, these apparently uncomplicated patients deserve closer clinical monitoring than commonly thought. Further studies are required to understand the pathophysiological mechanisms underlying this epidemiologic evidence.

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The Wearable Sensor-based Personalized Assessment (WeSPA) study

As previously discussed, diverse conceptual models and, consequently, different diagnostic tools have been proposed for frailty. One of the most accredited is the phenotype model, which was developed by Fried et al. [Fried LP, 2001] and considers decline in physical performance as the cornerstone of frailty. Although this tool is simple and of rapid application, it requires some specialized clinical setup and trained personnel. Moreover, it might be hypothesized that exploring physical performance of older subjects in their own environment is more appropriate to capture frailty status, as compared to the somewhat artificial setting needed to apply this and other similar tests. For these reasons, many researchers have focused on the use of wearable, sensor-based technology to gather parameters on motor condition [Dasenbrock L, 2016; Schwenk M, 2015; Mohler MJ, 2014; Abbate S, 2012], thus obtaining an objective, ecological assessment of frailty status in older subjects [Schwenk M, 2014], [Thiede R, 2016]. Furthermore, patient monitoring through wearable technology has the potential for enabling prolonged studies, thus expanding the bulk of data available for evaluation, while reducing healthcare costs and the discomfort that might derive to the patient when the assessment is done within a specific clinical setting.

Among the activities that can be investigated using wearable sensors, gait plays a very important role in identifying age- and frailty-related conditions. Gait analysis has been the subject of several studies in the context of personalized healthcare, and gait-related parameters derived from wearable sensors have already been associated with frailty [Kosse NM, 2016; Pradeep D, 2020]. In a cross-sectional study, Schwenk et al. examined the ability of wearable sensors to evaluate walking, balance, and physical activity as indices of physical frailty during a 24-hour period, to identify sensitive parameters that allow to distinguish the three Fried’s frailty phenotypes (robust, pre-frail, and frail). Gait speed was the most sensitive parameter to identify pre-frailty, whereas stride length and double support time were the most sensitive for classifying frailty level [Schwenk M, 2014]. Compared to those experiences, the technology offers highly interesting advances in the field of automatic information extraction (machine learning), thanks to the massive development of computer models of artificial intelligence, useful for the management of huge amounts of data. Machine learning is a branch of artificial intelligence that uses statistical methods for the construction of algorithms by learning from a set of data, thanks to iterations that allow to progressively improve the performance of the algorithm itself [1s]. Thus, it is possible to obtain reliable predictions through the inductive construction of a recognition model, starting from an initial set of data (training set) whose initial classification (labeled dataset) is known. After the training phase, the generated model is used to automatically classify the new data. Machine learning is increasingly used in those fields of information technology where designing and programming explicit algorithms is impractical: common examples are the filtering of e-mails to avoid spam, the detection of intruders who try to breach data, optical character recognition or search engines [2s]. Machine learning could therefore represent a very useful technique for refining the assessment of the motor performance of the elderly using sensors, in order to more accurately identify frail subjects.

The introduction of physical performance tests into geriatric practice has already represented a significant advancement in our ability to predict major clinical outcomes (onset of disability, falls, institutionalization, or even death) in older subjects, compared to the scales of traditional multidimensional assessment. Therefore, it is possible to hypothesize that an “ecological” monitoring of motor behavior of the elderly, conducted in the home for prolonged times, with the extraction of a huge amount of data, may allow to delineate the performance even more accurately, compared to what can be obtained with traditional tests [Gala´n-Mercant A, 2013; Greene BR, 2014; Zacharaki EI, 2020; Huisingh-Scheetz M, 2016].

The precise procedures and methods to apply this innovative and promising technology in the assessment of frailty are still under investigation, and uncertainties exist on the best position of the sensors, as well as on the parameters to be extracted and the algorithm to process them.

The general goal of the WeSPA Study (Wearable Sensor-based Personalized Assessment), conducted in collaboration between the Unit of Geriatrics, Department of Experimental and Clinical Medicine at the University of Florence and investigators from the Informatic Engineering Department at the University of Pisa, is to develop algorithms, based on machine learning techniques, for the automated identification of the frailty phenotype, using data collected by wearable sensors.

Initially, the general feasibility of the study and the technical quality of the signal were assessed, examining motor behavior of older persons during simple standardized tests. Then, the performance of wearable sensors, positioned in different places of the body, in classifying subjects according to their frailty status was assessed, using a set of gait-related parameters.

Methods

We selected subjects aged 70+ years, independent in basic activities of daily living (BADL) according to Katz [Kats S, 1983] and cognitively intact, who were visiting the outpatients clinic of the Geriatrics Unit of Careggi teaching hospital either as patients or as patients' carers, from July 10th, to August 20th, 2019. Exclusion criteria were dependence in BADL, except for mild, non-urgency urinary incontinence, sensory deficits (blindness), neurological or osteoarticular diseases that impair walking (such as Parkinson disease, severe hip or knee osteoarthritis). Moreover, because the manufacturer of the sensors did not guarantee the absence of radio interference with other electronic devices, pacemaker wearers were also excluded.

Participants were examined by geriatricians and classified as robust, pre-frail, or frail, in agreement with Fried's frailty phenotype [Fried LP, 2001]. As stated above, this tool includes five items: unintentional weight loss, self-reported exhaustion, low energy expenditure, slow gait speed, and weak grip strength. Scoring positive in three or more, one or two, or none of these items classifies older subjects as frail, pre-frail, or robust, respectively [Fried LP, 2001].

They then underwent the Short Physical Performance Battery (SPPB) test [Guralnik JM, 1994] and measurement of 60-m gait speed in two tasks, at usual and fast velocity. The SPPB is a frailty instrument that has been demonstrated to have excellent psychometric properties and is predictive of a broad range of adverse outcomes, including mortality, incident disability, falls, hospitalization, and healthcare utilization (Guralnik JM, 2000). Three tests are administered, examining balance, gait speed, and chair standing. In the balance test, the participant is asked to stand unassisted in three different positions, for ten seconds each: with the feet together, in semi-tandem and in tandem stand. The gait speed test consists in a 4-m timed walk at the usual pace. In the chair stand test, the participant attempts to rise from a chair without using his arms, at first in a single try (this task is not timed during its execution), then in a timed series of five sit-to-stand movements. A summary performance score is created by summation of the scores for the individual tests, each of which is scored from 0 to 4: the final score ranges from 0 (worst performance) to 12 (best performance).

During initial testing, our participants wore three inertial sensors (Shimmer 3), applied to the wrist, to the lumbar area, and to mid-thigh, to obtain movement tracks during each performance test. Shimmer3 is a wearable sensor embedding a tri-axial accelerometer [3s], which was used to collect acceleration samples at 102.4 Hz. Sensors were positioned in the same way in all subjects, so that the directions of the sensor reference system with respect to the subject were consistent throughout experiments. After some trials, the signal obtained from the mid-thigh sensor proved to be very poor: therefore, the subsequent experiments were conducted with only two sensors, positioned at the wrist and at the lumbar region (**Figure 1**).

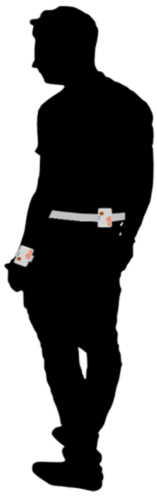


Figure 1. On-body sensors setup.

The clinicians who enrolled the participants and administered the assessment could not see the tracks recorded by the sensors during data collection. Data were eventually transmitted to investigators at the University of Pisa. An ad hoc module in Python language was created for the visualization and analysis of the signals. In particular, the Matplotlib library was used for the visualization of motion traces and statistical analysis, while the Numpy and Pandas libraries were used for exploratory analyses. Finally, the SciPY library was used for the machine learning phase.

A signed, written consent to participate in the study was obtained. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Identifiable information was removed from the collected data to ensure participant anonymity. Ethical approval for this study was obtained from Comitato Etico Regionale per la Sperimentazione Clinica della Regione Toscana (approval n. 14834 oss of May 7, 2019).

Feature extraction, selection, and automated frailty status assessment

Sensor-derived signals were analyzed to compare the ability of the two signals (wrist vs back) in the identification of frailty status. A gait-cycle detection technique was applied to divide each signal into segments made of four gait cycles, which were then used as input to a feature-extraction phase.

The set includes common statistical parameters used in signal processing, such as mean, median, standard deviation, minimum and maximum values, interquartile range (IQR), mean absolute deviation (MAD), root mean square (RMS), kurtosis, skewness and zero-crossing rate (ZCR), calculated on acceleration components or Wavelet coefficients. In addition, we considered some other features previously used in gait analysis and fall detection studies: the cadence, defined as the ratio between duration of the gait segment and the number of performed steps, and the average absolute acceleration variation (AAV), which is computed on consecutive acceleration samples [Cola G, 2014; Cola G, 2017]. Features bringing information in the time-frequency domain were extracted by applying the Continuous Wavelet Transform (CWT) on the acceleration magnitude signal to study variations of power within gait segments.[Daubechies I, 1990].

Frailty status was assessed in a two-stage process by means of a machine learning model. In the first stage, gait instances were classified as non-robust (NR, combining pre-frail and frail) or robust (R). In the second stage, the subject was classified according to a majority voting scheme. In order to maximise the performance of the classifier, we evaluated five different machine learning models: Random Forest, Gaussian naive Bayes, Logistic Regression, Multilayer Perceptron, and Support Vector Machine. Models were tested by means of a Leave-One-Subject-Out cross-validation procedure: at each iteration, the gait instances of one subject were used as testing set, while the gait instances of other subjects were used as training set to build a classification model. A *feature selection* step was performed within the cross-validation procedure. At each Leave-One- Subject-Out iteration, features were selected using only the training set, so that the model was built without any test set information. This led to a different feature set at each iteration, according to the subjects belonging to the training set. The trained model was then used to classify the instances of the left-out subject as NR or R. Finally, subject classification as NR or R was based on the majority voting scheme. This procedure was repeated, each time leaving out a different subject as the testing set.

The Receiver Operating Characteristic (ROC) Area Under the Curve (AUC) was calculated for every model tested, in which NR subjects were considered as positive and R subjects as negative classification results. From the ROC curve, accuracy, sensitivity, and specificity were extracted to evaluate and compare performance of the classification models.

Results

Thirty-six participants were enrolled, aged 74 to 86 years (60% males); of them, 11 (30%) were robust, 15 (42%) pre-frail, and 10 (28%) frail. Two participants were excluded due to the loss of readable recordings. There were no differences between the three groups in terms of age and gender, while the median scores at hand-grip test, SPPB test, and the speed of walking on 4 and 60 m of distance, were progressively lower across the three groups (from robust to frail; **Table 1**).

Table 1. Characteristics of the study population and sample features according to frailty status).

Variables Median [IQR] or n (%)	**Robust (n=11)**	**Pre-frail (n=15)**	**Frail (n=8)**
Age (y)	76 [70-93]	79 [71-87]	86 [73-88]
Female, n (%)	8(73)/3(27)	10(67)/5(33)	3(37)/5(63)
Handgrip (kg)	22 [10-36]	18 [8-32]	10 [1-18]
SPPB mean (tot)	10 [7-12]	9 [6-11]	7 [4-12]
Walk speed on 4 m (m/s)	0.96 [0.77-1.2]	0.8 [0.57-1]	0.66 [0.55-0.99]
Walk speed on 60 m (m/s)	1.2 [0.82-1.38]	0.98 [0.73-1.2]	0.8 [0.64-1.1]

When the number of trials received by each participant was considered, 9 series of recordings (or even less, when a test could not be performed) might be obtained, each containing two tracks (wrist and lumbar area), thus the number of the expected recordings was equal to 9 x n participants. The tracks recorded in the remaining 34 participants were 296, and not 306 as expected, because 7 participants were unable to perform one or more tests, for a total of 10 missing tests. Of the 296 available tracks, 294 were fully interpretable (99%). From these recordings, the duration of each task was obtained manually, also examining the timing recorded by clinicians.

Initially, to obtain a summary validation of the sensor recordings, the correlation between the time for the single chair-standing (a task that is not timed during the execution of the SPPB) and that recorded for the complete chair-standing (that is instead recorded in the SPPB) was analysed, obtaining a Pearson's *r* correlation coefficient equal to 0.831 ($p < .001$, **Figure 2**). This initial finding corroborated the expectation that it is possible to use wearable inertial sensors to achieve measures of the time needed to do standardized performance tests in older subjects with different functional status.

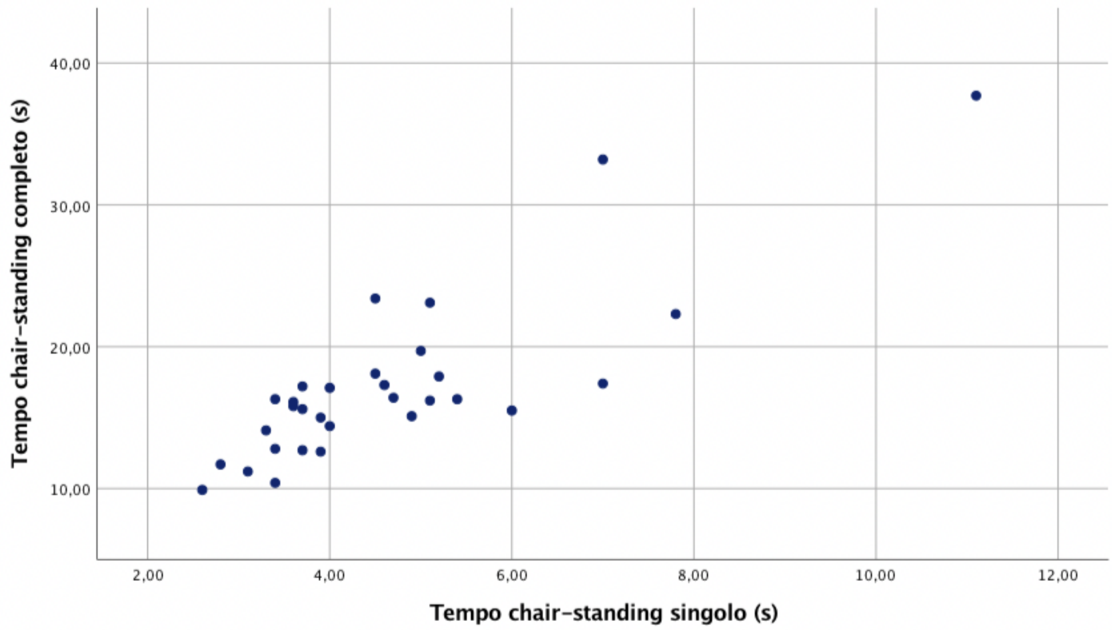


Figure 2. The correlation between the time for the single chair-standing (a task that is not timed during the execution of the SPPB) and that recorded for the complete chair-standing (that is instead recorded in the SPPB): r=0,831, *p*<.001

Features extraction and automated frailty assessment

The analysis of the traces was conducted through the following phases:

- data collection and recognition of the gait cycle detection, for the identification of 4-cycle segments;
- gait segment analysis and features extraction;
- automated assessment of the state of frailty by means of machine learning techniques applied to the features extracted for the segments identified.

The results of the clinical evaluation were used to label the accelerometer signals in the creation of a dataset which, in turn, was used to train, validate and test machine learning techniques. The signals deriving from the two sensors (wrist and lumbar) were analyzed separately to compare the ability of each of them to identify frailty status.

More in detail, a gait-cycle detection technique was applied to divide each signal into segments made of four gait cycles (corresponding to 8 consecutive steps), which were then used as input to a feature-extraction phase. Of the 131 variables extracted, 18 were selected by an automatic process (features selection) to train different machine learning models in order to classify the subjects into robust and non-robust. The output of all models is always represented by a numerical value between 0 and 1, which represents the predicted probability of not being robust; the algorithm also incorporates a decision function to assign the analyzed inputs to one class or another (in our case, robust or not robust), that is, to identify the best discrimination threshold.

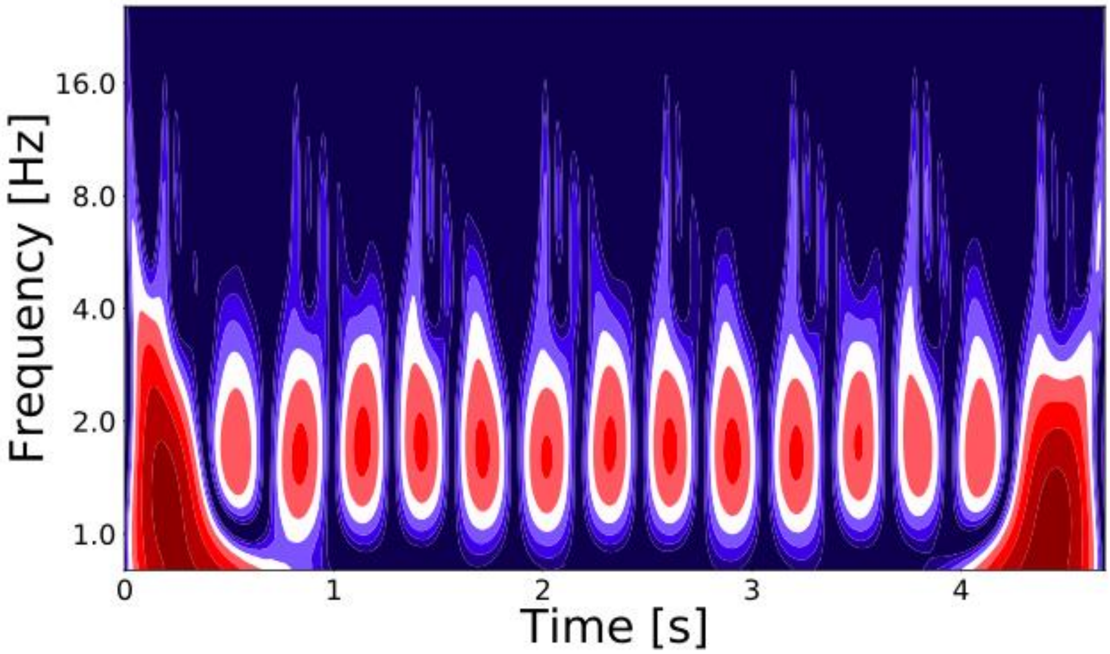
The internal validation procedure of each algorithm is conducted according to the iterative 'leave-one-subject-out' approach. At each “leave-one-subject-out” iteration, features were selected using only the training set, so that the model was built without any test set information. This led to a different feature set at each iteration, according to the subjects belonging to the training set. The trained model was then used to classify the instances of the left-out subject as NR or R. Finally, subject classification as NR or R was based on the majority voting scheme. This procedure was repeated, each time leaving out a different subject as the testing set.

For data extracted from the wrist, all trained models achieved high classification accuracy. Among these, Gaussian Naive Bayes was the best, being able to discriminate non-robust subjects from robust ones with an AUC of 0.87, 91% sensitivity, 82% specificity, and 88% accuracy. The signal extracted from the device worn in the lumbar area also obtained good values, again with the Gaussian Naive Bayes method, although slightly lower than the sensor on the wrist with an AUC of 0.75, sensitivity 87%, specificity 74 %, and 79% accuracy (**Table 2**). The AUC data reported above, in a classification carried out by means of machine learning models, are calculated using the probability value of belonging to one of the two classes.

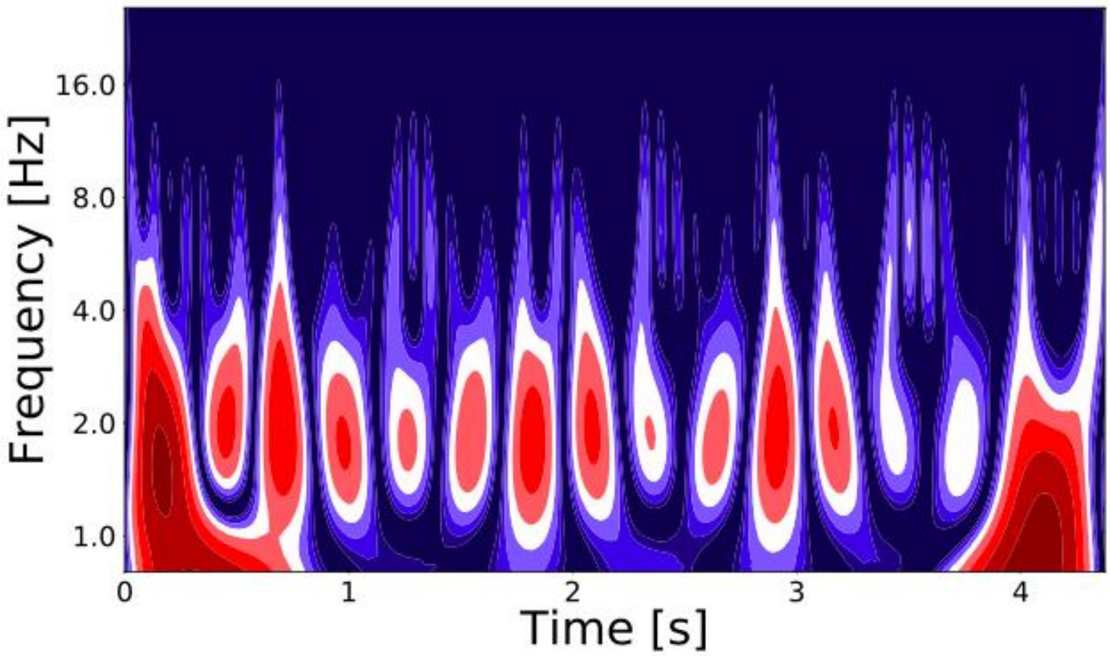
Table 2. Average results of frailty status assessment, both for wrist and lower back.

		WRIST				LOWER BACK			
Features	Model	Acc.	Sens.	Spec.	AUC	Acc.	Sens.	Spec.	AUC
TIME DOMAIN	Gaussian NB	0.82	0.91	0.64	0.77	0.76	0.87	0.55	0.71
	Random Forest	0.74	0.78	0.64	0.71	0.68	0.83	0.36	0.59
	Log. Regression	0.76	0.87	0.55	0.71	0.59	0.70	0.36	0.53
	ML Perceptron	0.71	0.78	0.55	0.66	0.65	0.70	0.55	0.62
	SVM	0.74	0.78	0.64	0.71	0.56	0.61	0.45	0.53
TIME DOMAIN + CWT-BASED	Gaussian NB	0.88	0.91	0.82	0.87	0.79	0.87	0.64	0.75
	Random Forest	0.85	0.96	0.64	0.80	0.76	0.87	0.55	0.71
	Log. Regression	0.79	0.91	0.55	0.73	0.74	087	0.45	0.66
	ML Perceptron	0.76	0.87	0.55	0.71	0.71	0.83	0.45	0.64
	SVM	0.68	0.74	0.55	0.64	0.74	0.83	0.55	0.69
TIME DOMAIN + FFT-BASED	Gaussian NB	0.82	0.91	0.64	0.77	0.76	0.87	0.55	0.71
	Random Forest	0.76	0.91	0.45	0.68	0.71	0.83	0.45	0.64
	Log. Regression	0.71	0.83	0.45	0.64	0.74	0.83	0.55	0.69
	ML Perceptron	0.53	0.48	0.64	0.56	0.50	0.35	0.82	0.58
	SVM	0.74	0.78	0.64	0.71	0.68	0.70	0.64	0.67

In **Figure 3**, we report the outputs of CWT analysis applied to two sample gait segments, in the case of a R and a NR subject, respectively. Signals were recorded by the wrist sensor (similar considerations also apply to the lower back- worn sensor). Here, red areas of scalograms correspond to higher levels of power released during stronger oscillations in gait, within a given frequency range (y-axis values), over a particular time interval (x-axis values). Notably, the scalogram produced by an R subject evidences a certain regularity in the of power released during the gait (**Figure 3, top panel**). The same cannot be said of the gait signal produced by a NR subject, whose scalogram is shown in **Figure 3, bottom panel**. Here, even though red areas still depict a gait activity with a similar level of associated power, it is clear that power is not released with the same regularity.



CWT: R subject



CWT: NR subject

Figure 5. Power spectrum of the CWT (top panel: R subject, bottom panel: NR subject).

Discussion

As this study shows, signals obtained from wearable sensors, processed with machine learning algorithms, can provide valuable information on frailty status in older persons. In particular, the sensor positioned on the wrist correctly identified non-robust subjects with a sensitivity of 91% and a specificity of 82%. The sensor positioned in the lumbar region was less sensitive and specific, with values of 87% and 64%. These findings suggest that the approach adopted is promising towards the automated assessment of frailty in the elderly. We hypothesize that this result is due to the role of the pendular movements of the arm during the walk, to which a wrist-worn device is more exposed, and that the alteration of pendular activity of the upper limb may be an hallmark that enables distinguishing robust from non robust subjects.

Moreover, the CWT analysis showed a certain regularity in the power released during the gait, in R subjects, while power is not released with the same regularity, in NR subjects. These results suggest that a higher level of power distributed regularly along time is associated with better stability during gait. In contrast, an irregular power distribution over time reflects a high gait variability, whose correlation with frailty has already been explored in previous studies. Montero-Odasso et al. demonstrated that a high gait variability is a marker of the loss of complexity in the dynamics of the gait pattern, and it is associated with frailty status [Montero-Odasso M, 2011].

In our experiments, we found that a higher level of power correlates with a more emphasized arm swing, which is also known to be positively related to “global gait stability” [Bruijn SM, 2010]. These findings are also in line with those of Mirelman et al., who reported that aging is associated with decreased arm swing amplitude [Mirelman A, 2015]. Indeed, many conditions may impair the normal pendular activity of arms in older adults. One-sided reduced arm swing may be an early motor sign of Parkinson’s disease, a condition that, indeed, is frequently associated with frailty and, eventually, with an increased risk of disability. Arm swing is correlated with the severity of radiographic adult spinal deformity, osteoporotic changes, and back muscle weakness [Kobayashi T, 2019]. Older adults may also present with a nonspecific "cautious" gait, that is characterized by mildly flexed posture with reduced arm swing and a broadening of the base of support [Lam R, 2011]. In these cases, arm swing may be reduced simply as an adaptation of the body to disease limitations.

The upper extremity function has been already studied as an alternative method to assess frailty status in elderly subjects [Mohammad NS, 2022]. Moreover, in recent years, the spread of the use of sensors for this purpose provided accurate identification of frailty, testing several kinematic and kinetics parameters of elbow flexion (such as speed of elbow flexion, power of movements and speed variation) that only sensors can objectively quantify [Toosizadeh N, 2015; Toosizadeh N, 2016]. However, as far as we know, the pendular movements of the upper limbs while walking has never been investigated as a possible early marker of frailty.

Conclusions and Implications

Our results demonstrate that unobtrusive wearable devices may enable an effective approach in continuous monitoring of human walking, and represent a significant step towards the feasibility of automated frailty status assessment based on machine-learning. Also, from the application point of view, a wrist-worn based implementation of the proposed method may foster user adoption of wearable devices for early detection of the frailty syndrome, as it may be embedded into a smartwatch.

After completion of this pilot study, a new set of experiments was conducted, where participants wore only one sensor at the wrist for 24 h. The findings from the study described here, i.e. the possibility to characterize gait istances as belonging to R or NR subject, will be highly valued in the analysis of 24-h recordings. Thus, the possibility of a completely automated classification of frailty status in older subjects based on the use of wearable sensors seems to be reasonably at hand.

Further developments will be provided by longitudinal studies, where older persons will be assessed with sensors at baseline and subsequently be monitored longitudinally for the development of major clinical outcomes, such as incident or worsening disability, institutionalization, or even death. The machine learning algorithms will then be trained on the basis of these outcomes, rather than on a cross-sectional comparison with their frailty status, as depicted by Fried’s tool. Assessment of the predictive ability of the procedure will complete WeSPA research program, whose initial, ground-breaking activities have been summarized here.

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CONCLUSION

According to Fried's model, "frailty" is a condition of increased risk of adverse events in non-disabled older persons. The broader term of "vulnerability" should be more appropriately used when baseline risk status may include disability. Independent of this semantic distinction, prognostic stratification is essential in older persons to guide clinical decision making and to implement appropriate interventions in different clinical settings, with the ultimate goals of preventing or postponing disability and improving survival.

The studies reported here show that, in hospitalized patients, the DSC reflects well-known components of vulnerability / frailty, in particular of functional impairment, a finding that may justify the good prognostic ability of the tool. Its use as a prognostic stratifier was particularly useful in defining the clinical-care pathways of hospitalized older adults, as older persons at moderate- to high-risk, the ideal target for application of the geriatric model of care, can be recognized in the ED with the DSC. As a prognostic stratifier, the DSC was also particularly useful in risk-adjustment of elderly subjects with COVID-19, both hospitalized and non-hospitalized. Moreover, the application of the DSC in the ED of a community hospital was associated with shorter ED LOS of older patients and provided a standardized method identifying older patients most appropriate for admission to a Geriatric inpatient unit. Finally, in addition to the *quoad vitam* prognosis, the DSC also predicts the need for post-acute care after discharge from the hospital.

We believe that the evidence provided increases the confidence in the DSC and supports its potential for clinical utilization in acute settings.

In non-urgent conditions, our results demonstrated that unobtrusive wearable devices may enable an effective approach in continuous monitoring of human walking, and represent a significant step towards the feasibility of automated frailty status assessment based on machine-learning.