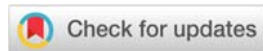


ORIGINAL ARTICLE

Discordance Between Biological and Chronological Age as a Predictor of In-Hospital Functional Decline

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**ABSTRACT**

Background: Biological age may reflect physiological reserve more accurately than chronological age. This study evaluated whether discordance between biological and chronological age predicted in-hospital functional decline among older medical inpatients.

Methods: This prospective observational cohort study included 120 patients aged 60 years or older admitted to a medical ward of General Hospital Lahore between February 2024 and February 2025. Biological age was estimated using the PhenoAge model based on chronological age and nine routine biomarkers. Age discordance was calculated by subtracting chronological age from biological age. Functional status was assessed using the Barthel Index before admission and at discharge. Functional decline was defined as a reduction of at least 10 points. Multivariable logistic regression identified independent predictors.

Results: The mean chronological age was 69.1 ± 6.8 years, while the mean biological age was 74.0 ± 9.4 years. Functional decline occurred in 39 patients (32.5%). Patients with decline had greater age discordance than those without decline (9.4 ± 7.0 versus 2.7 ± 5.4 years; $p < 0.001$). Functional decline occurred in 11.8% of patients without acceleration, 26.3% with moderate acceleration, and 52.1% with marked acceleration. Each five-year increase in age discordance independently increased the odds of functional decline by 56% (adjusted odds ratio 1.56; 95% confidence interval 1.22–2.00; $p < 0.001$).

Conclusion: Positive biological-age discordance independently predicted in-hospital functional decline. Biological-age estimation may improve early identification of vulnerable older patients and support geriatric, nutritional, mobility, and discharge interventions.

Keywords: biological age; chronological age; PhenoAge; functional decline; older adults; hospitalization

INTRODUCTION

Population ageing has substantially increased the number of older adults requiring acute medical hospitalization¹. While for some, admission is essential for the care of an infection, cardiovascular disease, metabolic disturbance and other acute illnesses, hospitalization itself may lead to a loss of independence. Functional decline during admission can be manifested by a loss or decrease in

mobility, self-care, need for help with activities of daily living or new caregiver need. This breakdown continues to be observed in some patients after they leave the hospital and is associated with longer rehabilitation, readmission, institutionalization and reduced survival².

In-hospital functional decline is a complex process involving the interplay of acute illness and pre-existing underlying physiological vulnerability³. Adverse functional

outcomes are associated with frailty, multimorbidity, cognitive impairment, malnutrition, delirium, polypharmacy, immobility, and prolonged hospital stay. These factors, however, can't account for the fact that patients of the same age and with the same severity of their disease can have very different outcomes. Some older adults return to their previous level of functioning, while others end up with significant disability even though the precipitating problem was treated⁴.

The probability of adverse outcomes is generally greater with increasing chronological age, and thus clinical risk assessment is often based on chronological age⁵. However, calendar age is only a partial indicator of physiological reserve. The inflammatory activity, metabolic control, kidney function, nutritional status, immune competence, haematological stability and cumulative organ damage can vary considerably between two persons of the same chronological age. Thus, chronological age by itself may not be an adequate measure to distinguish healthy ageing from more rapid physiological deterioration⁶.

Biological age has become a possible more valuable measure of ageing process⁷. Biological age is a measure of how much wear and tear a person's body has experienced due to aging, rather than counting years. Various strategies have been devised based on molecular, epigenetic, physiological and clinical data. Of these, phenotypic age (or PhenoAge) stands out as being particularly well adapted for hospital based research as it can be calculated via chronological age and blood markers that are normally available⁸.

The PhenoAge model includes mean corpuscular volume, red-cell distribution width, total white-cell count, serum creatinine, glucose, albumin and C-reactive protein, as well as the percentage of lymphocytes⁹. All of these variables are related to inflammatory, metabolic, renal, hepatic, immune, nutritional and haematological status. The resulting value is an age equivalent measure of the physiological state of an individual and could be a better overall indicator of an individual's vulnerability to health than just chronological age¹⁰.

Biological age and chronological age are different, this is called age discordance¹¹. Positive discordance means that the biological age is older than the chronological age, which could mean faster ageing, lower levels of homeostatic reserve or more cumulative physiological damage. Negative discordance occurs when biological age is lower than chronological age and may reflect relatively preserved physiological function. Positive age discordance may make a person more susceptible to acute stress, and to a lesser ability to bounce back after an illness or hospitalization¹².

This discordance in biological age might be particularly important in older medical inpatients¹³. Acute

illness leads to raised metabolic needs, inflammation, disturbed nutrition and sleep and often extended bed rest. Patients may not have enough physiological reserve to meet these demands without losing strength, mobility or independence, particularly if they are biologically older than chronologically. Biological age could thus help identify those who are at high risk despite being seemingly similar based on calendar age alone¹⁴.

Although there is increasing interest in biological ageing, little is known about the association with short term functional decline during general medical hospitalisation¹⁵. Previous studies have primarily examined mortality, chronic disease, frailty, or physical performance over the long-term but not the functional loss between admission and discharge. The establishment of this relationship may have significant clinical implications as PhenoAge can be obtained from laboratory tests which are already regularly taken during hospitalization¹⁶.

Identification of the biologically older patients at an early stage could facilitate timely comprehensive geriatric assessment, mobilization, nutritional intervention, prevention of delirium, physiotherapy, medication review and individual discharge planning¹⁷. Biological-age assessment can also be used alongside the more traditional methods as chronological age, comorbidity scores, frailty scales and baseline functional status¹⁸.

Thus, the aim of the present study was to assess whether biological and chronological age discordance was related to functional decline in hospital among older medical inpatients¹⁹. The hypothesis was that there would be a stronger association between biological age and functional decline in patients with a higher biological age than chronological age and that this relationship would be independent of frailty, burden of chronic disease, baseline function, delirium, and duration of hospital stay²⁰.

MATERIALS AND METHODS

Study setting and place of study

This prospective observational cohort study was conducted in the Department of Medicine at General Hospital Lahore Punjab, Pakistan over a one-year period from February 2024 to February 2025. The researchers assessed the potential of using discordance between biological and chronological age as a predictor of functional decline during hospitalization of older medical inpatients. All participants were recruited within 24 hours of admission, and then followed up by prospective observation until discharge.

Study Population

One hundred and twenty medical patients sixty years or older consecutively admitted were included. Participants

were admitted via the emergency department or outpatient service to a general medical ward, were at least 48 hours old and had adequate clinical and laboratory data available for biological-age estimation. Before the onset of the present illness, patients had to be documented or reliably reported as having a functional independence.

Patients were excluded who had terminal illness (expected survival less than 3 months), severe cognitive impairment without a caregiver, were completely dependent in activities of daily living prior to admission, died before functional reassessment, or had incomplete laboratory or functional data. Patients who were transferred to other hospital not assessed prior to discharge were also excluded.

Sampling Technique and Sample Size

A non-probability consecutive sampling technique was used. Eligible patients who presented for admission during the study were approached and included in the study until the desired sample size of 120 patients was attained. The selected sample was deemed to be sufficiently large to assess the association of biological-age discordance with functional decline in hospital and to adjust for major clinical confounders.

Data Collection Procedure

A structured data collection form was used to collect demographic and clinical information within 24 hours of admission. Chronological age, sex, body mass index, smoking status, the primary diagnosis on admission to hospital, comorbid conditions, number of regularly taken medicines, previous hospitalisations, and baseline functional status were all recorded. Delirium, transfer to intensive care, decreased mobility and requirement for physiotherapy were all recorded as clinical events relevant during the hospital stay.

Charlson Comorbidity Index was used to measure the burden of comorbidities. Frailty was assessed using the Clinical Frailty Scale, which uses the pre-acute illness health and functional status. Polypharmacy was considered to be the use of 5 or more drugs regularly. Routine clinical nutritional assessment at admission identified the nutritional risk.

Laboratory Assessment

Biological-age was determined from venous blood samples collected as part of standard clinical care within 24 hours of admission to hospital. The serum albumin, creatinine, glucose, C-reactive protein, alkaline phosphatase, percentage of lymphocytes, mean corpuscular volume, red-cell distribution width, and total white-cell count were measured as biomarkers. Laboratory analysis was carried out in the central laboratory of the hospital using

standardized automated method with routine quality control procedures.

Assessment of Biological Age

Biological age was estimated using the PhenoAge model, which is derived from nine routinely measured clinical biomarkers and chronological age. The values of the biomarkers were then fed into the existing mathematical algorithm to produce an age-equivalent estimate that represents the patient's physiological state.

Biological–chronological age discordance was determined as estimated biological age – chronological age. Positive values meant the patient was biologically older than the calendar age, negative values meant that the patient was biologically younger. For categorical analysis, participants were split into three groups: no biological-age acceleration (discordance of 0 or less than 5 years); moderate biological-age acceleration (discordance 5 years or less); and marked biological-age acceleration (discordance > 5 years). Age discordance was also analysed as a continuous variable.

Functional Assessment

Functionality was assessed by the Barthel Index of function which included 10 domains of activities: feeding, bathing, grooming, dressing, bowel and bladder control, toilet use, transfers, mobility and stair climbing. The total score is from 0 to 100, with higher scores representing higher functional independence.

Baseline function was assessed within 24 hours of admission by questioning the patient/carer about the patient's ability to carry out activities of daily living in the 2 weeks before the acute illness. A trained and blinded investigator repeated the functional assessment within 24 hours prior to discharge from hospital when feasible.

Study Outcome

In-hospital functional decline was the primary outcome. This was taken as a decrease of at least 10 points in Barthel Index score from the pre admission assessment to the assessment at the time of discharge. Patients with a decrease of less than 10 points, no change in score or improvement in score were classified as not having a functional decline. Secondary outcomes assessed were: absolute change in Barthel Index score, new dependence in mobility assistance, need for caregiver assistance and length of hospital stay.

Evaluation of potential confounders

Potential confounding factors included chronological age, sex, baseline Barthel Index, frailty, number of comorbidities, polypharmacy, nutritional risk, delirium, admission diagnosis, and hospital stay. Delirium was evaluated in hospital through the use of the Confusion

Assessment Method in conjunction with routine clinical evaluation. The length of hospital stay was defined as the time from admission to discharge from the hospital.

Data Quality Control

All data were obtained from investigators who have been trained in the use of the study instruments. Completed forms were checked on a daily basis for missing and inconsistent information. Laboratory parameters were compared with the hospital information system and functional data was rechecked prior to data entry. The data was stored in a password protected database, with a random sample of the data being checked against the original form to reduce error in filling in the data.

Statistical Analysis

The data were analysed using SPSS version 27.0. Descriptive statistics of the continuous variables were expressed as mean $\pm$ SD or as median (IQR). For categorical variables, frequencies and percentages were used. Analyses of the continuous variables were carried out using the independent-samples t test or the Mann–Whitney U test between those patients with and without functional decline. Categorical variables were analyzed using chi-square or Fisher exact test.

Pearson or Spearman correlation tests were used to assess the correlation between chronological age, biological age, age discordance and the change in Barthel index. Factors associated with functional decline were first identified by univariable logistic regression. Multivariable logistic regression was used for all variables which were clinically important or had a p-value < 0.10 in univariable analysis.

Both categorical and continuous age discordance (in 5-year increments) were analyzed. Adjusted Odds Ratios and 95% Confidence intervals were provided. Appropriate goodness of fit testing and receiver operating characteristic curve analysis were used for model calibration and discrimination. Prior to building final models, multicollinearity was checked. Two-sided p-values of < 0.05 were regarded as statistically significant.

Ethical Considerations

Ethical clearance has been granted by the Institutional Review Board. All participants or their legally authorized representatives signed informed consent forms prior to enrollment. All of the information collected was confidential, anonymised prior to analysis and used solely for research purposes.

RESULTS

Study Population

One hundred and thirty-two older medical inpatients were screened for the study during the study period. Twelve

patients were not included due to insufficient laboratory data, lack of functional data prior to admission, referral to another health care facility or no functional assessment at discharge. Finally, 120 participants were included in the analysis.

The age range for the studied population was 60–86 years and the mean chronological age was 69.1 ± 6.8 years. There were 64 women (53.3%) and 56 men (46.7%). The mean biological age was 74.0 ± 9.4 years and the mean difference between biological and chronological age was 4.9 ± 6.8 years. 86 participants (71.7%) had a biological age that was higher than their chronological age.

Mean pre admission Barthel Index was 88.4 ± 11.5 points and mean discharge Barthel index was 80.8 ± 16.2 points. Of the 39 participants with a decrease of at least 10 points, 32.5% experienced functional decline in hospital. The other 81 patients (67.5%) had a decrease in functional status of less than 10 points or no change in functional status.

The mean chronological age was not significantly different between the group of patients with and without functional decline. But the gap between the two types of age was far greater than the gap between the two ages. The mean biologic age was 81.3 ± 8.5 years among the patients with functional decline, and 70.5 ± 7.7 years among the patients who did not decline.

The biological – chronological age discordance was also significantly higher for the functional-decline group. Among patients with functional deterioration, the difference between biological age and chronological age was 9.4 ± 7.0 years, while among the patients without functional deterioration, the difference was 2.7 ± 5.4 years.

Charlson Comorbidity Index and Clinical Frailty Scale scores were higher for patients with functional decline. These patients were also more likely to receive polypharmacy, be at nutritional risk, experience delirium during the hospitalization, and have a history of hospitalization in the year prior to the hospital stay. Sex distribution, pre admission Barthel index and body mass index were not found to be significantly different among them. As shown in Table 1, the mean length of the hospital stay was significantly higher in patients who had functional decline.

Distribution of Biological-Age Discordance

Participants were split into three groups based on their difference between their biological age and chronological age. Thirty-four patients (28.3%) did not show any biological-age acceleration: biological age was equal to or lower than chronological age. Moderate acceleration (0.1–5.0 years) was found in 38 patients (31.7%) and marked acceleration (more than five years) was found in 48 patients (40.0%).

There was a corresponding gradient of in-hospital functional decline with each of the three levels of biological age. There was functional decline in 4 of 34 patients (11.8%) without biological-age acceleration; in 10 of 38 patients (26.3%) with moderate acceleration; and in 25 of 48 patients (52.1%) with marked acceleration. Statistically significant difference was found between the groups.

There were no significant differences among the three groups in pre-admission Barthel Index scores, but there were significant differences in discharge scores. The mean Barthel Index scores for patients without biological-age acceleration, moderate-acceleration, and marked-acceleration groups were 89.2 ± 10.6 points, 82.7 ± 14.3 points, and 71.8 ± 17.4 points, respectively.

The mean decrease in Barthel Index was 1.8 ± 5.9 for patients without acceleration, 6.4 ± 8.7 for patients with moderate acceleration, and 14.1 ± 12.6 for patients with marked acceleration. These results showed that the extent of this biological-age acceleration was related to the degree of functional decline in a graded manner.

Delirium in-hospital was found in 2.9% of the without acceleration group, 10.5% of the moderately accelerated group and 20.8% of the markedly accelerated group. Likewise, the need for new mobility assistance and caregiver support at discharge was more often the higher the biological age discordance. Table 2 also indicates that the mean length of stay in hospital also rose steadily in the three categories.

Correlation Between Age Measures and Functional Change

There was a weak positive correlation with chronological age and the decrease in Barthel Index score, suggesting that functional decline slightly increased with age. The correlation coefficient between chronological age and Barthel Index reduction was 0.24 and P value is 0.008.

Biological age was found to be more associated with functional deterioration. The biological age and Barthel Index reduction had a correlation coefficient of 0.46, and the p value was <0.001. Biological–chronological age discordance showed the highest relationship with reduction in functional status with a correlation coefficient of 0.49 and a p-value of <0.001.

The results showed that the association between biological age and age discordance was more tightly coupled to the functional decline in hospital than chronological age alone.

Univariable Analysis

Every one year increment in chronological age was independently associated with functional decline by an additional 9% in univariable logistic regression analysis. This means that for every five-year difference between

biological–chronological age, there was a 78% higher risk of functional decline.

Patients with moderate biological-age acceleration were 2.68 times more likely to have functional decline than patients without biological-age acceleration, but this was not statistically significant. The patients with extreme biologic-age acceleration had over eight times the risk of functional deterioration, in contrast.

Clinical Frailty Scale scores and Charlson Comorbidity Index scores were significantly associated with a decline in function. In the univariable analyses, the use of polypharmacy, nutritional risk, delirium and prolonged hospitalization were also each associated with increased odds of functional deterioration.

Multivariable Analysis

A multivariable logistic regression model was constructed to test if there was an independent association between biological–chronological age discordance and functional decline. The following were included in the model: age discordance, chronological age, sex, Clinical Frailty Scale, Charlson Comorbidity Index, in-hospital delirium, and length of hospital stay.

Biological–chronological age discordance was an independent predictor of functional decline after these variables were accounted for. For each 5-year difference in age discordance, there was 56% higher adjusted odds of functional deterioration.

Biological-age acceleration, as a categorical predictor, was also studied. The more a patient's biological age was older than their chronological age, the higher the adjusted odds of functional decline were, with the odds being 3.89 times higher in patients with biological-age acceleration of more than five years.

Each increment in the Clinical Frailty Scale was an independent predictor, with a 54% increase in the adjusted odds of functional decline for every point increase. The adjusted odds of functional deterioration rose by 2.84 times with each additional day of hospitalization and those who developed delirium in hospital.

In univariable analyses, chronological age and Charlson Comorbidity Index were significantly associated with functional decline but were not independently associated with functional decline after accounting for biological-age discordance, frailty, delirium and length of stay. The results of the regression are shown in table 3.

Predictive Performance

The area under the receiver operating characteristic (ROC) curve for a conventional clinical model was 0.73 and included chronological age, sex, clinical frailty scale, Charlson comorbidity index, in hospital delirium, and length of stay.

Biological–chronological age discordance added 0.02 to the area under the curve, which reflects better discrimination between patients who experienced functional decline and those who did not.

A biological-age discordance threshold > 5 years revealed a sensitivity of 64.1% and specificity of 71.6% for the identification of patients who developed functional decline. Positive predictive value = 52.1% and negative predictive value = 80.6%.

Principal Findings

About one-third of the population experienced in-hospital functional decline. Biological age and positive discordance between biological and chronological age was significantly

higher in patients with functional deterioration as compared to patients who did not deteriorate in function.

There was a well-defined age-discordance continuum. Biological-age acceleration was associated with a gradient of increased frequency and severity of functional decline, delirium, needs for mobility support, caregiver support and hospital length of stay.

Even when accounting for chronological age and sex as well as frailty, comorbidity burden, delirium and length of hospitalization, biological–chronological age discordance was still independently associated with functional decline. It also enhanced the performance of the classical clinical model.

Table 1: Baseline and Clinical Characteristics According to In-Hospital Functional Decline

Variable	No functional decline (n=81)	Functional decline (n=39)	p-value
Chronological age, years	67.8 ± 6.3	71.8 ± 7.0	0.002
Female sex, n (%)	41 (50.6%)	23 (59.0%)	0.389
Male sex, n (%)	40 (49.4%)	16 (41.0%)	0.389
Biological age, years	70.5 ± 7.7	81.3 ± 8.5	<0.001
Biological–chronological age discordance, years	2.7 ± 5.4	9.4 ± 7.0	<0.001
Body mass index, kg/m ²	25.8 ± 4.2	24.9 ± 4.5	0.279
Charlson Comorbidity Index	2.7 ± 1.5	4.1 ± 1.8	<0.001
Clinical Frailty Scale	3.7 ± 1.1	5.0 ± 1.3	<0.001
Pre-admission Barthel Index	89.8 ± 10.4	85.6 ± 13.0	0.058
Polypharmacy, n (%)	39 (48.1%)	27 (69.2%)	0.030
Nutritional risk, n (%)	19 (23.5%)	19 (48.7%)	0.005
In-hospital delirium, n (%)	5 (6.2%)	10 (25.6%)	0.002
Previous hospitalization within one year, n (%)	21 (25.9%)	18 (46.2%)	0.026
Length of hospital stay, days	6.0 ± 2.7	8.8 ± 3.8	<0.001

Table 2: Functional and Clinical Outcomes According to Biological-Age Discordance

Outcome	No acceleration, ≤0 years (n=34)	Moderate acceleration, 0.1–5.0 years (n=38)	Marked acceleration, >5 years (n=48)	p-value
Functional decline, n (%)	4 (11.8%)	10 (26.3%)	25 (52.1%)	<0.001
Pre-admission Barthel Index	91.0 ± 9.3	89.1 ± 10.7	85.9 ± 13.1	0.073
Discharge Barthel Index	89.2 ± 10.6	82.7 ± 14.3	71.8 ± 17.4	<0.001
Reduction in Barthel Index	1.8 ± 5.9	6.4 ± 8.7	14.1 ± 12.6	<0.001
In-hospital delirium, n (%)	1 (2.9%)	4 (10.5%)	10 (20.8%)	0.038
New mobility assistance at discharge, n (%)	2 (5.9%)	7 (18.4%)	17 (35.4%)	0.003
New caregiver requirement, n (%)	3 (8.8%)	8 (21.1%)	18 (37.5%)	0.009
Length of hospital stay, days	5.5 ± 2.4	6.7 ± 2.9	8.3 ± 3.8	<0.001

Table 3: Logistic Regression Analysis of Predictors of In-Hospital Functional Decline

Predictor	Unadjusted odds ratio (95% confidence interval)	p-value	Adjusted odds ratio (95% confidence interval)	p-value
Biological–chronological age discordance, per five-year increase	1.78 (1.41–2.25)	<0.001	1.56 (1.22–2.00)	<0.001
Marked biological-age acceleration, >5 years	8.15 (2.52–26.37)	<0.001	3.89 (1.37–11.03)	0.011
Chronological age, per year	1.09 (1.03–1.16)	0.003	1.03 (0.96–1.10)	0.412
Female sex	1.40 (0.66–3.00)	0.389	1.24 (0.52–2.94)	0.627
Clinical Frailty Scale, per point	2.15 (1.55–2.99)	<0.001	1.54 (1.10–2.16)	0.012
Charlson Comorbidity Index, per point	1.63 (1.30–2.04)	<0.001	1.19 (0.93–1.53)	0.168
In-hospital delirium	5.24 (1.68–16.36)	0.004	2.84 (1.01–8.02)	0.048
Length of hospital stay, per day	1.30 (1.15–1.47)	<0.001	1.11 (1.01–1.23)	0.032

DISCUSSION

The present study revealed strong association between discordance between biological and chronological age, and functional decline among older medical patients in hospital¹. About one-third of the subjects had a clinically significant decrease in the Barthel Index score during their hospital stay. Patients with functional decline were significantly older and were more positively age discordant than patients who were able to maintain function².

Biological-age acceleration and functional deterioration were clearly related³. Few patients with biological age equal or less than chronological age experienced functional decline. The frequency was higher in the moderate acceleration group and the highest in the group whose biological age was more than 5 years older than their chronological age. This suggests a spectrum of physiological vulnerability to biological age discordance and not just a dichotomy of risk⁴.

In the unadjusted analysis, but not statistically significant after taking into account biological-age discordance, frailty, delirium, comorbidity and length of stay, chronological age was associated with functional decline⁵. This discovery shows that age alone cannot be used to evaluate older patients. Some may have a high inflammatory load, while others may have low inflammatory load; some may be well nourished, while others may not have a very good nutritional status; some may be in a much better kidney condition, while others may not be as good; some may be in a more stable metabolic state, while others may not; some may be immune competent while others may not; and some may have a very stable hematological profile while others may not. Biological age may better reflect these differences and thus offer a more true measure of the patient's tolerance to an acute illness⁶.

The biological-age model applied in this study included laboratory measures of multiple physiological systems which were routinely collected⁷. Low albumin is a potential sign of malnutrition, inflammation, liver diseases, or low protein reserve. Creatinine is a marker of renal function, and high C-reactive protein and abnormalities in white-cell counts are markers of inflammatory activation. The glucose, alkaline phosphatase, lymphocyte percentage, mean corpuscular volume and red-cell distribution width offer further details of metabolic, hepatic, immune, and haematological health. The reason for this stronger relationship of a functional decline with biological age than chronological age alone may be the integration of these variables in a single age-equivalent measure⁸.

There was also a higher reduction in Barthel index scores for discharge, longer hospital stay, more delirium and more mobility and caregiver support needed in patients with marked biological-age acceleration⁹. The results suggest that biological ageing could be a modifier of the functional decline and of its clinical severity and impact. These patients may be less physiologically capable and may have impaired abilities to tolerate periods of bed rest, acutely inflamed tissues, nutritional deprivation, sleep impediments, and other stressors present with hospital admission¹⁰.

In the adjusted model, frailty was independently associated with functional decline¹¹. This was not surprising as frailty is defined as a decreased ability to withstand physiological stress and is closely linked to disability. Still, the effect of biological age discordance was found to be significant even when frailty was taken into account. The two indicators can thus reflect some of the same, but not necessarily all components of vulnerability. Biological age reflects laboratory evidence of multisystem physiological deterioration, while frailty is the primary measure of clinical performance, dependence and overall health status¹².

Also, the independence of the association of delirium and functional decline was clinically important¹³. Delirium may result in decreased patient engagement with mobility, feeding, rehabilitation, and self-care. May also be a sign of serious acute illness or underlying neurological sensitivity. Biological-age acceleration might be a useful indicator of an especially high-risk population if along with delirium, these patients would benefit from intensive multidisciplinary treatment¹⁴.

An additional independent predictor of functional decline was longer hospital stay¹⁵. Longer stays can be the cause of prolonged periods of immobility, muscle wasting, sleep disturbances, inadequate nutrition, and hospital-acquired complications, as well as being an opportunity for older adults to become exposed to these risks. But the association could also go the other way—patients who have functional decline might need longer hospital stays for rehabilitation and discharge planning¹⁶.

The conventional clinical model was enhanced by the incorporation of the biological-age discordance, which increased the discriminatory ability of the clinical model¹⁷. This indicates that biological age may be of prognostic value in addition to the age, comorbidity, frailty, and acute clinical events. The negative predictive value of the five-year discordance threshold was also relatively high, suggesting that patients who do not have a marked acceleration may be less likely to have functional decline. However, biological age discordance should not be used alone as a diagnostic

test. It may be best suited as part of a comprehensive risk assessment program¹⁸.

Routine laboratory variables are used, which makes this approach clinically practical¹⁹. Biological age could be determined automatically, for example in hospital information systems, and without the use of molecular testing or special equipment. Patients that were biologically older than their chronological age might be offered early geriatric assessment, medication review, nutritional support, delirium prevention, physiotherapy, structured mobilisation and individual discharge planning²⁰.

This study had several strengths⁴. It was prospective, it included all consecutive admissions to hospital for medical conditions, it used a standard instrument to assess functional status and it looked at biological-age discordance both as a continuous and categorical variable. Other key factors, such as frailty, comorbidity, delirium, baseline function and length of hospital stay, were also taken into account¹¹.

There are some drawbacks to take into account⁷. The study was performed in one centre and the sample was relatively small and this may restrict the generalizability and precision of the findings. Some baseline Barthel Index scores were based on patient/carer reported scores and thus could have been influenced by reporting bias. Laboratory measurements were made during acute illness and the age obtained was biological age, which may also have reflected disease-related variables¹⁶.

Patients who died or were transferred were not included in final functional analysis, as were those who did not have discharge assessments⁹. They may have underestimated the association between biological-age acceleration and poor outcomes as they were not included. Functional status was only measured at discharge and the study did not assess if functional losses continued post hospital. Other disease severity, socioeconomic, rehabilitation intensity or social support factors are also potential sources of residual confounding¹⁴.

These findings should be confirmed in larger and more heterogeneous groups of patients in future multicentre studies⁶. Biological age measurements repeated after clinical stabilization may help to differentiate between chronic biological ageing and the effect of acute illness. More information is also required on longer follow-up to see if age discordance is predictive of persistent disability, readmission, institutionalization and mortality. Interventional trials should be conducted to assess how targeted geriatric care of patients with accelerated biological ageing might lower hospital associated disability^{19,20}.

CONCLUSION

In older patients in medical wards, positive discordance between biological and chronological age was an independent predictor of functional decline in hospital. Those who were biologically older than their chronological age by greater than 5 years had highest biological functional independence loss, longest length of stay and greatest mobility and caregiver support needs. Biological-age discordance alone was a better prognostic variable than chronological age alone and biological-age discordance combined with conventional clinical assessment was a better predictor than chronological age alone. Thus, the use of routine admission biomarkers to calculate a biological age may be a practical approach to identifying vulnerable older people early in the course of hospital admission. Biological-age assessment along with frailty evaluation, delirium screening, nutritional assessment, and baseline functional status may help to provide more personalized care. Structured discharge planning, nutritional intervention, delirium prevention, and early mobilization and rehabilitation are all targets to consider for patients with significant biological-age acceleration. More extensive multicentre studies with documented clinical data are needed to recommend routine use.

DECLARATION

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REFERENCES

1. Iuorio MS, De Vincentis A, Lelli D, Bandinelli S, Ferrucci L, Antonelli Incalzi R, et al. PhenoAge and PhenoAgeAccel do not outperform chronological age in predicting physical performance decline or mortality in community-dwelling older adults. *J Gerontol A Biol Sci Med Sci*. 2026;81(3):glaf285. doi:10.1093/gerona/glaf285.
2. Tay JH, Barros D, Wang W, Wazny VK, Maier AB. Biological age measured by DNA methylation clocks and frailty: a systematic review and meta-analysis. *Lancet Healthy Longev*. 2025;6(10):100773. doi:10.1016/j.lanhl.2025.100773.
3. Anthony NP, Ho KM. Biological age and clinical frailty scale measured at intensive care unit admission as predictors of hospital mortality among the critically ill in Western Australia: a

- retrospective cohort study. *Acute Crit Care*. 2025;40(2):264-272. doi:10.4266/acc.000200.
4. Félix J, Martínez de Toda I, Díaz-Del Cerro E, González-Sánchez M, De la Fuente M. Frailty and biological age: which best describes our aging and longevity? *Mol Aspects Med*. 2024;98:101291. doi:10.1016/j.mam.2024.101291.
5. Xu X, et al. Association between phenotypic age and the risk of all-cause mortality in patients with heart failure. *Clin Cardiol*. 2024;47(8):e24321. doi:10.1002/clc.24321.
6. Huang Y, Zhou A, Huang Y, Wang Y, Liu X, Liu X. Association between phenotypic age and mortality risk in individuals with obesity: a retrospective cohort study. *Front Public Health*. 2024;12:1505066. doi:10.3389/fpubh.2024.1505066.
7. Weng B, Jin J, Huang L, Tong X, Jiao W, Wang Y, et al. Risk factors associated with functional decline in older hospital survivors with acute lower respiratory tract infections: a prospective cohort study. *BMC Geriatr*. 2024;24(1):208. doi:10.1186/s12877-024-04838-0.
8. Chavarro-Carvajal DA, Vargas-Beltrán MP, Morros-González E, Orjuela-Rolón CA, Cano-Gutiérrez CA, Chacón-Valenzuela E. Factors associated with functional decline in hospitalized patients. *Acta Med Colomb*. 2024;49(1). doi:10.36104/amc.2024.2943.
9. Clotet-Vidal S, Saez Prieto ME, Duch Llorach P, Santos Gutiérrez Á, Casademont Pou J, Torres Bonafonte OH. Malnutrition, functional decline, and institutionalization in older adults after hospital discharge following community-acquired pneumonia. *Nutrients*. 2023;16(1):11. doi:10.3390/nu16010011.
10. Ho KM, Morgan DJ, Johnstone M, Edibam C. Biological age is superior to chronological age in predicting hospital mortality of the critically ill. *Intern Emerg Med*. 2023;18(7):2019-2028. doi:10.1007/s11739-023-03397-3.
11. Drewelies J, Hueluer G, Duezel S, Vetter VM, Pawelec G, Steinhagen-Thiessen E, et al. Using blood test parameters to define biological age among older adults: association with morbidity and mortality independent of chronological age validated in two separate birth cohorts. *Geroscience*. 2022;44(6):2685-2699. doi:10.1007/s11357-022-00662-9.
12. Vetter VM, Kalies CH, Sommerer Y, et al. Relationship between five epigenetic clocks, telomere length, and functional capacity assessed in older adults: cross-sectional and longitudinal analyses. *J Gerontol A Biol Sci Med Sci*. 2022;77(9):1724-1733. doi:10.1093/gerona/glab381.
13. Geyskens L, Jeuris A, Deschodt M, Van Grootven B, Gielen E, Flamaing J. Patient-related risk factors for in-hospital functional decline in older adults: a systematic review and meta-analysis. *Age Ageing*. 2022;51(2):afac007. doi:10.1093/ageing/afac007.
14. O'Shaughnessy I, Robinson K, O'Connor M, Conneely M, Ryan D, Steed F, et al. Effectiveness of acute geriatric unit care on functional decline, clinical and process outcomes among hospitalised older adults with acute medical complaints: a systematic review and meta-analysis. *Age Ageing*. 2022;51(4):afac081. doi:10.1093/ageing/afac081.
15. Ji L, Jazwinski SM, Kim S. Frailty and biological age. *Ann Geriatr Med Res*. 2021;25(3):141-149. doi:10.4235/agmr.21.0080.
16. Wu JW, Yaqub A, Ma Y, Koudstaal W, Hofman A, Ikram MA, et al. Biological age in healthy elderly predicts aging-related diseases including dementia. *Sci Rep*. 2021;11(1):15929. doi:10.1038/s41598-021-95425-5.
17. Tavares JPA, Nunes LANV, Grácio JCG. Hospitalized older adult: predictors of functional decline. *Rev Lat Am Enfermagem*. 2021;29:e3399. doi:10.1590/1518-8345.3612.3399.
18. Hosoda T, Hamada S. Functional decline in hospitalized older patients with coronavirus disease 2019: a retrospective cohort study. *BMC Geriatr*. 2021;21(1):638. doi:10.1186/s12877-021-02597-w.
19. Van Grootven B, Jeuris A, Jonckers M, Devriendt E, Dierckx de Casterlé B, Dubois C, et al. Predicting hospitalisation-associated functional decline in older patients admitted to a cardiac care unit with cardiovascular disease: a prospective cohort study. *BMC Geriatr*. 2020;20(1):112. doi:10.1186/s12877-020-01510-1.
20. Liu Z, Kuo PL, Horvath S, Crimmins E, Ferrucci L, Levine M. A new aging measure captures morbidity and mortality risk across diverse subpopulations from NHANES IV: a cohort study. *PLoS Med*. 2018;15(12):e1002718. doi:10.1371/journal.pmed.1002718.

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