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Dietary rhythms and biological aging risk across multiple organs

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The effects of dietary rhythms on organ-specific biological aging remain unclear. This study analyzed 14,012 adults from NHANES to assess associations between dietary rhythms and biological aging of the body, heart, liver, and kidneys. Earlier last meals, specifically before 9 p.m., were linked to lower aging risks for the body, heart, and liver but not kidneys. The strongest protective effects were seen with meals between 3 and 5 p.m. for the body and heart, and 5–7 p.m. for the liver. Conversely, later first meals and longer feeding durations (>8 h) linked to higher aging risks. These associations were modified by age, gender, disease status, caloric intake and dietary quality, with effects more pronounced in individuals over 40, males, and those without existing diseases or with low calorie intake. Delayed first and earlier last meal remained significantly associated with body and liver aging in the healthy diet group, whereas heart aging showed stronger associations with meal time in the unhealthy diet group. This study revealed optimal meal timing and duration differ for biological aging across different organs, ages, genders, disease status, energy intake, and dietary quality, highlighting a critical food-nutrient-timing synergy, and the need for personalized nutritional guidance and population-specific dietary strategies.

As the global population ages, finding effective, low-cost anti-aging strategies becomes crucial. One promising approach is to modify dietary behaviors, particularly through chrono-nutrition, which links eating patterns, circadian rhythms, and health outcomes[1,2]. Inappropriate dietary patterns, such as skipping breakfast or late-night eating, have been shown to significantly elevate the risk of developing obesity, cardiovascular disease, and metabolic syndrome[3–11]. Shift workers with disrupted dietary and circadian rhythms are particularly vulnerable to chronic diseases[12–16]. Time-restricted eating (TRE), limiting food intake to specific windows to extend overnight fasting, has gained attention for its metabolic health benefits[17–21]. While some research has linked TRE to aging and lifespan, findings remain conflicting. One study suggests TRE extends lifespan in fruit flies[22], whereas compelling human data indicate that TRE does not significantly reduce all-cause or cancer mortality, and may even be associated with an increase in cardiovascular disease mortality[23].

While Chronological Age (CA) serves as a simple measure of time, it does not fully reflect an individual's aging rate. Biological Age (BA) is an emerging and superior biomarker of aging because it integrates multiple physiological markers. To better assess aging rate of a person or organ, the concept of BA was developed[24]. A series of methods have been developed to calculate BA[25,26] and the Klemera and Doubal method (KDM)[27] has been shown to predict mortality[28] and health status[25] effectively. Studies have shown that a healthy lifestyle, including regular, balanced diets, is linked to lower BA[29–31]. Moreover, aging rates also vary across diverse organs, with heart biological age closely correlating with CA, while the liver biological age and digestive system exhibit weaker correlations[32–36].

Previous studies on dietary rhythms and health focused on metabolic markers and diseases. However, research exploring the impact of dietary rhythms on biological aging, particularly from the perspective of organ-specific biological aging, is still lacking. To address this gap, we utilized the National Health and Nutrition Examination Survey (NHANES) database to construct biological body and organ age models and investigated associations between various dietary rhythms and the risk of biological aging in the body as well as specific organs (heart, liver, and kidneys). By exploring the potential differences in the associations, we aimed to identify healthy dietary

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rhythms associated with lower biological aging risks across populations stratified by age, gender, and disease status.

Results

Characteristics of the enrolled participants

A total of 14,012 participants were enrolled in this study. Figure 1 illustrates the process of data collection. The clinical characteristics of the study population are summarized in Table 1 and Supplementary table 1. The mean age of the participants in the overall population was 46 years old. Significant differences in several clinical characteristics were observed between participants with accelerated and decelerated biological aging of the body and three organs. Among participants with two recalls, the median absolute differences between Day 1 and Day 2 for key meal-timing variables were modest (Supplementary table 2), indicating reasonable within-person consistency.

Association between biological age, chronological age and mortality

The performance and validation of the newly developed biological age models are presented in Fig. 2. Our new body BA model demonstrated excellent performance, showing a strong correlation with CA ($R = 0.97$) and a low Mean Absolute Error (MAE) of 3.42. It also outperformed the model based on the original features described by Levine et al.[40]. ($R = 0.96$, MAE = 3.62). The organ-specific BA models also showed high performance. The metrics were as follows: heart ($R = 0.93$, MAE = 4.83), kidney ($R = 0.92$, MAE = 5.57), and liver ($R = 0.83$, MAE = 8.47).

As indicated in Supplementary Table 3, individuals with accelerated body biological aging had an increased risk of all-cause mortality (HR = 1.34, 95% CI: 1.22, 1.48, $P < 0.001$). Individuals with accelerated heart biological aging exhibited an increased risk of heart disease-related mortality. (HR = 1.48, 95% CI: 1.20, 1.83, $P < 0.001$). Additionally, each one-year increase in kidney biological age (BA minus CA) was associated with a higher risk of nephrosis-related mortality (HR = 1.02, 95% CI: 1.01, 1.03, $P < 0.001$). Due to the unavailability of liver disease mortality data, Cox proportional hazards analyses for body and organ-specific aging in relation to liver disease mortality were not performed.

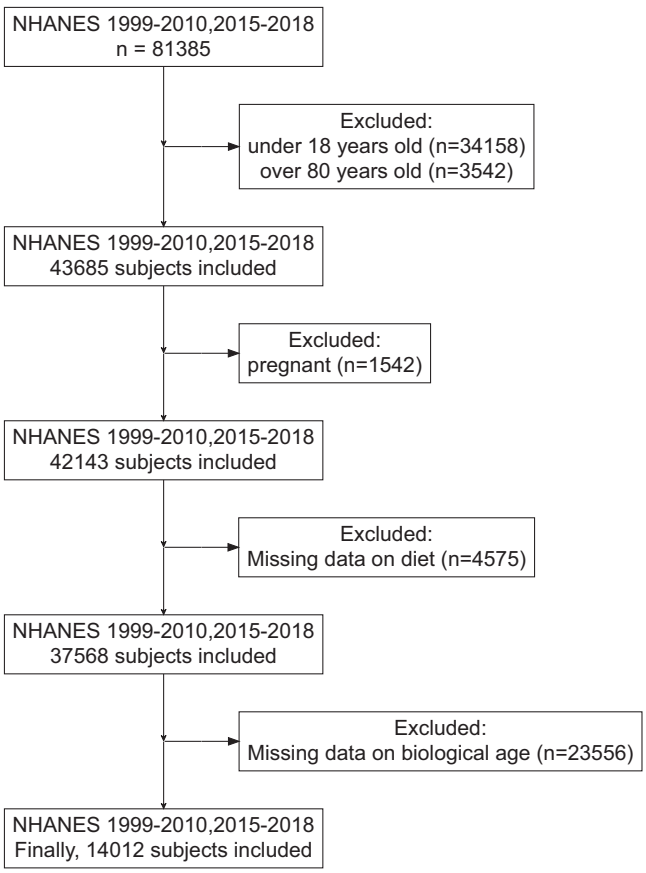

Fig. 1 | Flowchart of study population.

Association of dietary rhythms with the risks of body and organ biological aging

We performed logistic regression to explore the relationship between dietary rhythms and risk of body and organ biological aging. We found that the optimal timing for the last meal varied depending on whether the outcome was whole-body or organ-specific biological aging. In the fully adjusted model, as illustrated in Fig. 3A, compared to eating after 9 p.m., consuming the last meal between 3 p.m. and 5 p.m. was associated with a significantly lower risk of biological aging for both the body (OR = 0.65, 95% CI: 0.43, 0.98, $P = 0.038$) and the heart (OR = 0.43, 95% CI: 0.27, 0.68, $P < 0.001$). A last meal between 5 p.m. and 7 p.m. was associated with a 25% reduction in liver aging risk (OR = 0.75, 95% CI: 0.64, 0.89, $P < 0.001$). Additionally, as shown in Model 2 of Supplementary Table 4, a bidirectional effect of last meal timing on heart and liver biological aging risk was observed.While eating before 3 p.m. was associated with an increased risk for both the heart (OR = 1.27, 95% CI: 1.03, 1.57, $P = 0.023$) and liver (OR = 1.24, 95% CI: 1.01, 1.53, $P = 0.043$), consuming the last meal between 5 p.m. and 7 p.m. was associated with a significant protective effect. (Heart OR = 0.75, 95% CI: 0.63, 0.90, $P = 0.002$; Liver OR = 0.6, 95% CI: 0.51, 0.71, $P < 0.001$).

A consistent trend across all three models revealed that later timing of the first meal was associated with higher risk of biological aging for the body, heart, and liver; however, this association was not observed for kidney biological aging (Fig. 3A and Supplementary Table 4). Particularly, compared to eating before 8 a.m., eating after 12 p.m. was associated with increased aging risk for the body (OR = 1.61, 95% CI: 1.22, 2.11, $P < 0.001$), heart (OR = 1.44, 95% CI: 1.14, 1.83, $P = 0.003$), and liver (OR = 1.61, 95% CI: 1.24, 2.08, $P < 0.001$) (Fig. 3B).

Compared to a feeding duration of less than 8 h, extended feeding duration (over 16 h), was significantly associated with increased biological aging risks for the body (OR = 2.11, 95% CI: 1.35, 3.29, $P = 0.001$), heart (OR = 1.95, 95% CI: 1.40, 2.72, $P < 0.001$), and liver (OR = 1.67, 95% CI: 1.06, 2.64, $P = 0.028$) but not the kidneys (Supplementary Table 5). The results were consistent with individuals with a fasting duration over 16 hours (Supplementary Table 5).

Differences by age

Age-stratified analyses showed that the impact of dietary rhythms on body and organ biological aging risk varied by age group (Table 2). The last meal's effect on body aging was not significant in individuals under 40 but was notable in individuals over 40. For example, in the 40–60 age group, participants who ate their last meal between 3 p.m. and 5 p.m. had a 62% lower risk of body aging (OR = 0.38, 95% CI: 0.19, 0.78, $P = 0.009$) compared to those who ate after 9 p.m. Similarly, in the 40–60 and over 60 age groups, the risk of liver aging was reduced for individuals who ate between 5 p.m. and 7 p.m. Notably, individuals over 60 who ate between 3 p.m. and 5 p.m. had a 63% lower kidney aging risk (OR = 0.37, 95% CI: 0.16, 0.85, $P = 0.02$).

The first meal's impact on body aging was significant in the 40–60 age group (OR = 1.36, 95% CI: 1.08, 1.71, $P = 0.009$ for 8 a.m.-9 a.m. group) and over 60 age group (OR = 2.04, 95% CI: 1.14, 3.65, $P = 0.017$ for after 12 p.m. group). Heart aging risk was significant only in the 40–60 age group (OR = 1.31, 95% CI: 1.01, 1.70, $P = 0.043$ for 9 a.m.-12 p.m. group), while liver aging risk was significant for individuals under 40 years (OR = 1.46, 95% CI: 1.00, 2.13, $P = 0.049$ for after 12 p.m. group).

Supplementary table 6 highlights that, in the 40–60 age group, longer feeding duration (OR = 2.54, 95% CI: 1.41, 4.59, $P = 0.002$ for >16 h) and shorter fasting duration (OR = 2.03, 95% CI: 1.08, 3.82, $P = 0.029$ for < 8 hours) were linked to higher body aging risk, with similar trends for heart aging. In participants over 60 years, longer feeding (OR = 2.5, 95% CI: 1.10,

Table 1 | Characteristics of the included participants

Characteristic	Overall	Body age			Heart age		
		+BA[a]	-BA[a]	p-value[b]	+BA[a]	-BA[a]	p-value[b]
Number[c]	14,012	8781 (57%)	5231 (43%)	NA	7344 (49%)	6668 (51%)	NA
Age, years[c]	46 (32, 58)	42 (27, 58)	48 (38, 59)	<0.001	42 (27, 56)	48 (37, 60)	<0.001
Gender[c]							
Female	6979 (51%)	4312 (50%)	2667 (52%)	0.028	3415 (48%)	3564 (53%)	<0.001
Male	7033 (49%)	4469 (50%)	2564 (48%)		3929 (52%)	3104 (47%)	
Race[c]							
Non-Hispanic White	6061 (69%)	3337 (64%)	2724 (77%)	<0.001	2878 (66%)	3183 (73%)	<0.001
Non-Hispanic Black	2908 (11%)	2231 (14%)	677 (6.2%)		1746 (13%)	1162 (8.8%)	
Mexican American	2801 (8.3%)	1822 (9.4%)	979 (6.6%)		1599 (9.6%)	1202 (6.9%)	
Other Hispanic	1179 (4.9%)	726 (5.4%)	453 (4.3%)		577 (5.1%)	602 (4.8%)	
Other Race	1063 (6.6%)	665 (7.0%)	398 (6.1%)		544 (6.7%)	519 (6.5%)	
Poverty ratio[a]	3.01 (1.50, 5.00)	2.50 (1.29, 4.56)	3.65 (1.92, 5.00)	<0.001	2.72 (1.35, 4.74)	3.39 (1.69, 5.00)	<0.001
Education Level[c]							
Below High School	3736 (16%)	2531 (19%)	1205 (13%)	<0.001	2109 (18%)	1627 (14%)	<0.001
High School	3454 (26%)	2332 (29%)	1122 (22%)		1918 (28%)	1536 (24%)	
Above High School	6822 (58%)	3918 (53%)	2904 (65%)		3317 (54%)	3505 (62%)	
Drinking[c]							
Non-drinker or <1 drinks/month	4532 (28%)	3036 (31%)	1496 (25%)	<0.001	2376 (29%)	2156 (28%)	0.2
1–5 drinks/month	6563 (46%)	4111 (47%)	2452 (44%)		3361 (44%)	3202 (47%)	
5–10 drinks/month	1081 (9.6%)	672 (9.4%)	409 (9.8%)		611 (9.9%)	470 (9.2%)	
10+ drinks/month	1836 (16%)	962 (13%)	874 (21%)		996 (17%)	840 (16%)	
Smoking[c]							
Never smoker	7542 (52%)	4726 (52%)	2816 (53%)	<0.001	3923 (52%)	3619 (53%)	<0.001
Former smoker	3277 (25%)	1940 (24%)	1337 (27%)		1613 (24%)	1664 (26%)	
Current smoker	3,193 (23%)	2,115 (24%)	1078 (21%)		1808 (25%)	1385 (21%)	
BMI, kg/m^2							
Underweight(<18.5)	230 (1.8%)	120 (1.3%)	110 (2.4%)	<0.001	106 (1.6%)	124 (1.9%)	<0.001
Normal(18.5 to <25)	4092 (31%)	2288 (26%)	1804 (37%)		2070 (28%)	2022 (33%)	
Overweight(25 to <30)	4668 (33%)	2702 (30%)	1966 (37%)		2305 (31%)	2363 (35%)	
Obese(30 or greater)	5022 (35%)	3671 (42%)	1351 (24%)		2863 (39%)	2159 (30%)	
COPD[c]							
No	13,067 (93%)	8153 (92%)	4914 (94%)	0.064	6848 (93%)	6219 (93%)	0.9
Yes	945 (7.0%)	628 (7.5%)	317 (6.4%)		496 (7.0%)	449 (7.1%)	
Liver Disease[c]							
No	13,429 (96%)	8406 (96%)	5023 (96%)	0.4	7052 (96%)	6377 (96%)	0.8
Yes	583 (4.1%)	375 (4.3%)	208 (3.8%)		292 (4.0%)	291 (4.2%)	
Cancer[c]							
No	12,963 (92%)	8162 (92%)	4801 (91%)	0.019	6895 (93%)	6068 (90%)	<0.001
Yes	1049 (8.4%)	619 (7.7%)	430 (9.3%)		449 (6.7%)	600 (10%)	
Cardiovascular disease[c]							
No	12,743 (92%)	7873 (91%)	4870 (94%)	<0.001	6685 (92%)	6058 (92%)	>0.9
Yes	1269 (7.8%)	908 (9.2%)	361 (5.9%)		659 (7.8%)	610 (7.8%)	
Hypertension[c]							
No	9574 (70%)	5637 (66%)	3937 (77%)	<0.001	4774 (67%)	4800 (74%)	<0.001
Yes	4438 (30%)	3144 (34%)	1294 (23%)		2570 (33%)	1868 (26%)	
Diabetes[c]							
No	12,230 (90%)	7264 (86%)	4966 (96%)	<0.001	6155 (87%)	6075 (93%)	<0.001
Yes	1782 (9.9%)	1517 (14%)	265 (3.9%)		1189 (13%)	593 (6.8%)	
Kidney Disease[c]							
No	13,635 (98%)	8474 (97%)	5161 (99%)	<0.001	7128 (98%)	6507 (98%)	0.2

Table 1 (continued) | Characteristics of the included participants

Characteristic	Overall	Body age			Heart age		
		+BA[a]	-BA[a]	p-value[b]	+BA[a]	-BA[a]	p-value[b]
Yes	377 (2.0%)	307 (2.9%)	70 (0.8%)		216 (2.2%)	161 (1.8%)	
Meal count/day[c]	5.00 (4.00, 6.00)	5.00 (4.00, 6.00)	5.00 (4.00, 6.50)	<0.001	5.00 (4.00, 6.00)	5.00 (4.00, 6.00)	<0.001
Calorie, kcal/kg[c,d]	25 (19, 33)	25 (18, 32)	26 (20, 34)	<0.001	25 (18, 33)	26 (20, 33)	0.002
Protein, g/kg[c,e]	0.96 (0.72, 1.29)	0.94 (0.69, 1.28)	0.99 (0.74, 1.31)	<0.001	0.95 (0.70, 1.29)	0.98 (0.73, 1.29)	0.005
Carbohydrate, g/kg[c f]	3.00 (2.18, 4.04)	2.87 (2.07, 3.91)	3.20 (2.34, 4.21)	<0.001	2.93 (2.13, 3.98)	3.09 (2.26, 4.10)	<0.001
Fat, g/kg[c,g]	0.96 (0.68, 1.30)	0.94 (0.66, 1.27)	0.99 (0.70, 1.34)	<0.001	0.94 (0.65, 1.28)	0.98 (0.70, 1.32)	0.005
Fiber, g/kg[c,h]	0.19 (0.12, 0.27)	0.17 (0.11, 0.25)	0.20 (0.14, 0.29)	<0.001	0.18 (0.12, 0.25)	0.19 (0.13, 0.28)	<0.001
Feeding duration, hour[c]	12.50 (11.00, 14.00)	12.25 (10.75, 13.75)	12.75 (11.25, 14.00)	<0.001	12.25 (10.75, 13.75)	12.50 (11.25, 14.00)	<0.001
Fasting duration, hour[c]	11.50 (10.00, 13.00)	11.75 (10.25, 13.25)	11.25 (10.00, 12.75)	<0.001	11.75 (10.25, 13.25)	11.50 (10.00, 12.75)	<0.001
First meal time[c,i]	8.13 (7.25, 9.50)	8.50 (7.46, 10.00)	8.00 (7.00, 9.00)	<0.001	8.50 (7.38, 9.88)	8.00 (7.00, 9.00)	<0.001
Last meal time[c,i]	20.5 (19.3, 21.6)	20.5 (19.1, 21.8)	20.5 (19.3, 21.5)	0.073	20.5 (19.2, 21.8)	20.5 (19.3, 21.5)	0.6
Sleep time/day, hour[c,j]	7.00 (6.00, 8.00)	7.00 (6.00, 8.00)	7.00 (6.00, 8.00)	0.025	7.00 (6.00, 8.00)	7.00 (6.00, 8.00)	0.2
MET, min.W[c,k]	1680 (280, 4823)	1920 (280, 6000)	1440 (300, 3840)	<0.001	1920 (360, 5760)	1440 (240, 4320)	<0.001
Sedentary time/day, min[c,k]	300 (180, 480)	300 (180, 480)	300 (180, 480)	0.2	300 (180, 480)	300 (180, 480)	0.2

BMI body mass index, *COPD* Chronic Obstructive Pulmonary Disease, *MET* Metabolic.

[a]+BA means accelerated biological aging (A positive difference of chronological age minus biological age);-BA means normal/decelerated biological aging (A zero or negative difference of chronological age minus biological).

[b]Showed continuous variables as medians and interquartile ranges [M (Q1, Q3)]; Showed categorical variables as counts and weighted proportions N (%).

[c]Wilcoxon rank-sum test for complex survey samples; chi-squared test with Rao & Scott's second-order correction.

[d]Dietary calorie intake per kilogram of body weight.

[e]Dietary protein intake per kilogram of body weight.

[f]Dietary carbohydrate intake per kilogram of body weight.

[g]Dietary fat intake per kilogram of body weight.

[h]Dietary fiber intake per kilogram of body weight.

[i]All meal times were converted to numerical values. For example, if the first meal was consumed at 8:30 AM, it was recorded as 8.5, and if the last meal was consumed between midnight and 5 AM, it was recorded as a value greater than 24 (e.g., 1:00 AM was recorded as 25).

[j]Sleep information was available for 10,298 participants.

[k]Physical activity and sedentary time information was available for 8503 participants.

5.70, $P = 0.03$ for > 16 h) and shorter fasting durations (OR = 2.36, 95% CI: 1.09, 5.10, $P = 0.03$ for <8 h) showed increased kidney aging risk. Generally, dietary rhythms are associated with body and organ biological aging risk for the population over 40 years old.

Differences by gender

Dietary rhythms were associated with biological aging risks in a gender-specific manner (Table 3). The timing of the last meal had a stronger effect on body and heart aging in males. In males, eating the last meal between 7 p.m. and 9 p.m. was linked to lower body aging risk (OR = 0.74, 95% CI: 0.62, 0.90, $P = 0.002$), meals between 3 p.m. and 5 p.m. were associated with reduced heart aging risk (OR = 0.29, 95% CI: 0.15, 0.53, $P < 0.001$), and meals between 5 p.m. and 7 p.m. were associated with reduced liver aging risk (OR = 0.72, 95% CI: 0.57, 0.91, $P = 0.007$). In females, the timing of the last meal did not significantly affect body aging risk. Additionally, males who had their first meal between 9 a.m. and 12 p.m. showed a higher risk of heart aging (OR = 1.44, 95% CI: 1.16, 1.79, $P = 0.001$), whereas females did not.

Feeding and fasting durations significantly impacted body and kidney aging risks in females but not in males (Supplementary Table 7). Longer feeding durations showed increased risk of body (OR = 2.68, 95% CI: 1.50, 4.78 for >16 h) and kidney (OR = 2.05, 95% CI: 1.21, 3.49 for >16 hours) aging, while shorter fasting durations were similarly associated with higher body (OR = 2.07, 95% CI: 1.11, 3.86 for <8 h) and kidney (OR = 2.03, 95% CI: 1.20, 3.43 for <8 h) aging risks.

Differences by disease status

Dietary rhythms showed different risks of body and organ-specific biological aging in individuals with and without diseases (Table 4). Last meal time significantly influenced body aging only in the non-diseased group. Specifically, individuals eating between 7 p.m. and 9 p.m. had a lower risk (OR = 0.75, 95% CI: 0.64, 0.88, $P < 0.001$) compared to those eating after 9 p.m. Conversely, a significant effect on liver aging was observed only in the diseased group, where individuals eating last meal between 5 p.m. and 7 p.m. experienced a reduced risk (OR = 0.75, 95% CI: 0.56, 0.99, $P = 0.046$). Later first meal time was significantly associated with an increased body (OR = 1.27, 95% CI:1.04, 1.53, $P = 0.019$ for 8 a.m.-9 a.m. group; OR = 1.71, 95% CI: 1.19, 2.47, $P = 0.005$ for after 12 p.m. group) and heart (OR = 1.38, 95% CI: 1.13, 1.68, $P = 0.002$ for 9 a.m.-12 p.m. group; OR = 1.4, 95% CI: 1.02, 1.93, $P = 0.038$ for after 12 p.m. group) aging risk only in the non-diseased group. Shorter fasting duration was significantly associated with increased body (OR = 2.51, 95% CI: 1.35, 4.64, $P = 0.004$ for less than 8 h group) and heart (OR = 2.26, 95% CI: 1.33, 3.85, $P = 0.003$ for less than 8 h group) aging risks only in the diseased population (Supplementary Table 8).

Differences by caloric intake

Associations between dietary rhythms and biological aging varied by caloric intake. Among participants with low caloric intake, dietary rhythms were consistently associated with body and organ-specific biological aging, whereas these associations were weaker or less evident in participants with high caloric intake.

In the low caloric intake group, the optimal timing of the last meal varied across body and organ-specific aging, a pattern consistent with the main analysis (Fig. 4A). Compared with individuals consuming their last meal after 9:00 p.m., those eating between 3:00 and 5:00 p.m. exhibited lower risks of body biological aging (OR = 0.58, 95% CI: 0.35, 0.96, $P = 0.035$) and heart biological aging (OR = 0.38, 95% CI: 0.22, 0.65, $P < 0.001$). Additionally, consuming the last meal between 5:00 and 7:00 p.m. was associated with a reduced risk of liver biological aging (OR = 0.75, 95% CI: 0.59, 0.96,

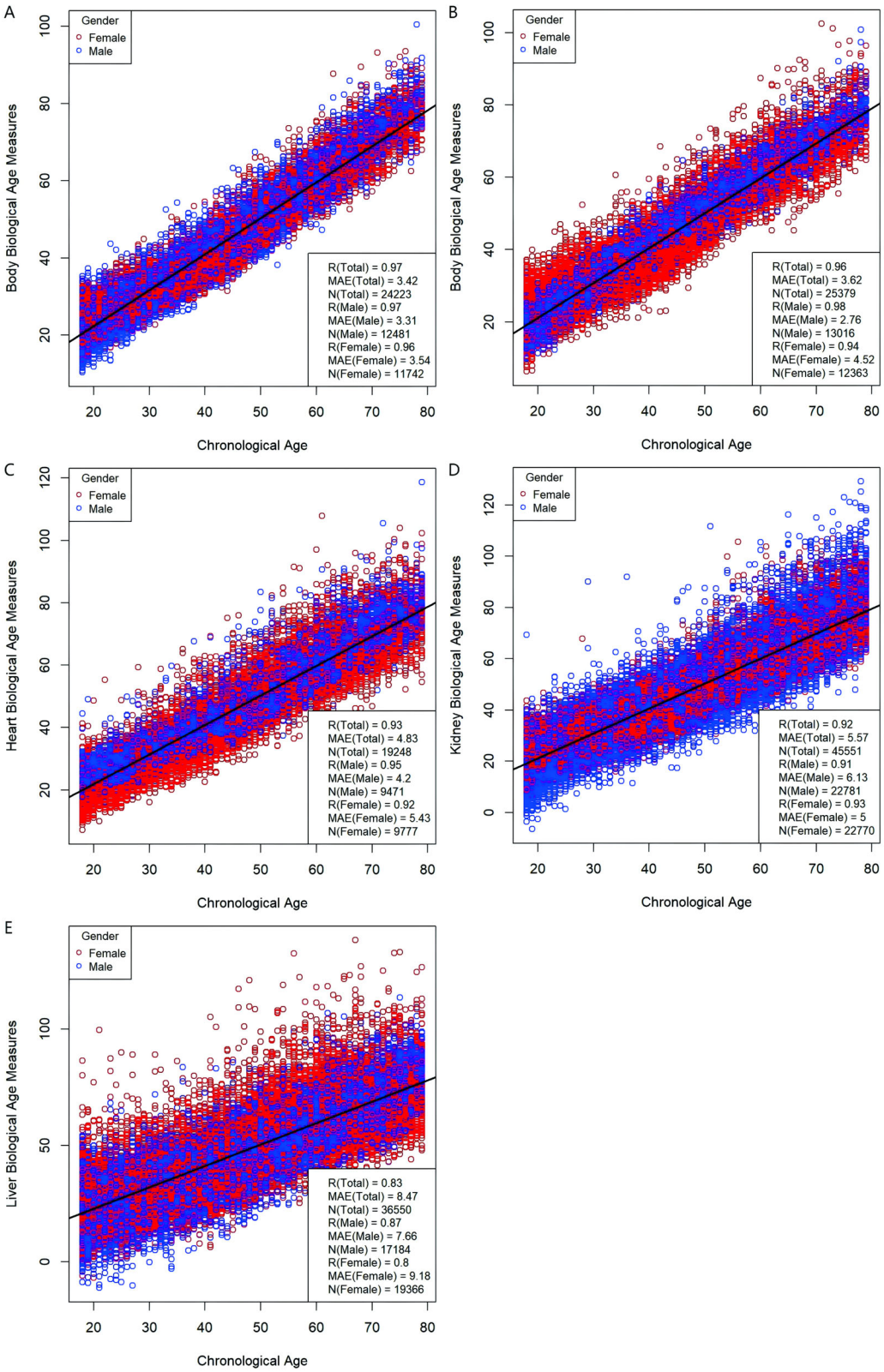

Fig. 2 | Correlations between chronological age and calculated biological ages. Each panel displays a scatter plot of chronological age (x-axis) versus a specific biological age (y-axis) for the entire dataset. The solid black line in each panel represents the linear regression line of best fit. **A** Body biological age calculated using the newly developed 13-biomarker model. **B** Body biological age calculated using the original features from Levine et al.[41]. **C** Heart biological age. **D** Kidney biological age. **E** Liver biological age. The specific biomarkers used for each model are detailed in Supplementary Table 1. Abbreviations: R Pearson correlation coefficient, MAE mean absolute error in years, N sample size.

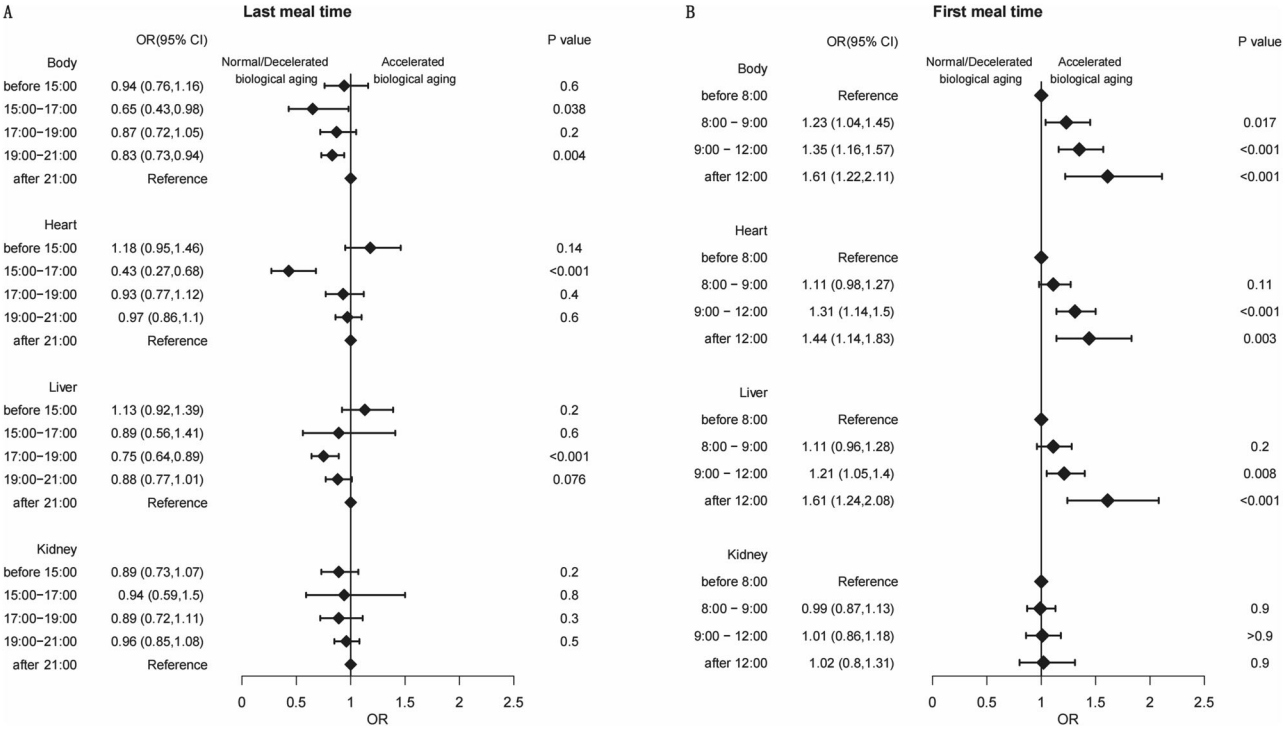

Fig. 3 | . Association of last meal time (**A**) and first meal time (**B**) with the biological aging risk of the body and organs. Number = 14,012. OR indicates odds ratio. CI indicates confidence interval; Ref indicates reference. The multivariate logistic regression models adjusted for feeding duration (continuous), age (continuous), gender (male or female), race (non-Hispanic White, non-Hispanic Black, Mexican American, or other Race), poverty ratio (continuous), education level (below high school, high school or above high school), drinking status (non-drinker or <1 drinks/month, 1–5 drinks/month, 5–10 drinks/month or 10+ drinks/month), smoking status (never smoker, former smoker or current smoker), body mass index (underweight (<18.5), normal (18.5 to <25), overweight (25 to <30) or obese (30 or greater)), self-reported chronic obstructive pulmonary disease (yes or no), self-reported liver disease (yes or no), self-reported cancer (yes or no), self-reported cardiovascular disease (yes or no), self-reported hypertension (yes or no), self-reported diabetes (yes or no), self-reported kidney disease (yes or no), meal count (continuous), caloric intake, carbohydrate intake, fat intake, protein intake, and dietary fiber intake per kilogram of body weight (continuous).

$P = 0.021$). In contrast, these protective associations were not evident in the high caloric intake group. Later timing of the first meal was associated with increased risks of body and organ-specific biological aging in both low and high caloric intake groups, consistent with the findings of the primary analysis (Fig. 4B).

Feeding and fasting durations showed differential associations with biological aging across caloric intake levels (Supplementary Fig. 1). In the low caloric intake group, longer feeding duration (>16 h) was consistently associated with higher risks of body (OR = 2.17, 95% CI: 1.09, 4.35, $P = 0.028$) and heart (OR = 2.71, 95% CI: 1.58, 4.64, $P < 0.001$) biological aging. In contrast, these associations were weakened in the high caloric intake group (Supplementary Fig. 1A). Similar patterns were observed for fasting durations exceeding 16 h (Supplementary Fig. 1B).

Differences by dietary quality

Stratified analyses by dietary quality, assessed using the Alternate Mediterranean Diet (aMED) score, demonstrated differential associations between dietary rhythms and organ-specific biological aging.

For first and last meal time, associations with body and liver biological aging were more pronounced among individuals with healthy diet patterns. In this group, delayed first meal was associated with increased risks of body (OR = 1.97, 95% CI: 1.26, 3.08 for after 12:00 p.m.) and liver (OR = 2.11, 95% CI: 1.37, 3.22 for after 12:00 p.m.) biological aging, while earlier last meal was associated with reduced risks of body (OR = 0.71, 95% CI: 0.59, 0.86 for 7:00–9:00 p.m.) and liver (OR = 0.67, 95% CI: 0.52, 0.87 for 5:00–7:00 p.m.) biological aging. These associations were weaker or not statistically significant in the unhealthy diet group. Conversely, heart biological aging showed stronger associations with later first and last meal time in the unhealthy diet group (Fig. 5).

Longer feeding duration was significantly associated with increased risk of heart biological aging in both healthy and unhealthy diet groups. For body biological aging, feeding duration showed more evident associations in the healthy diet group, particularly when feeding duration exceeded 16 h (OR = 3.50, 95% CI: 1.74, 7.05). Similar trends were observed for fasting duration. In contrast, kidney biological aging exhibited stronger associations with both feeding duration and fasting duration among individuals with unhealthy dietary pattern (Supplementary Fig. 2).

Sensitivity analysis

The associations observed in the main analyses remained robust across sensitivity analyses, including various exclusions and analytical adjustments, such as exclusion of participants with atypical meal time (Supplementary Table 9), restriction to participants reporting usual dietary intake (Supplementary Table 10), and additional adjustment for Metabolic Equivalent of Task (MET), sedentary time, and sleep duration. Expectedly, insignificant associations were observed in models using the negative control outcome or exposure (Supplementary Tables 11 and 12).

Discussion

This is the first study, to our knowledge, to examine the associations between dietary rhythms and biological aging of the human body and its organs. Previous studies in both animals and humans have shown that dietary habits, including TRE, influence metabolic processes across organ systems[3,4,8–11,18,21,37,38]. More importantly, aging is driven by metabolic changes and different organs age at varying rates[34–36]. Consequently, we hypothesized that dietary rhythms exert distinct effects on the biological aging of the body and its organs, a theory this study successfully supports.

Our findings suggest that meal timing may be a powerful modulator of biological aging. Specifically, later first and last meals, as well as

Table 2 | Association of first meal time and last meal time with the biological aging risk of the body and organs by age. Number = 14,012

Characteristic	Body biological aging		Heart biological aging		Liver biological aging		Kidney biological aging	
	OR (95% CI)[a]	p-value	OR (95% CI)[a]	p-value	OR (95% CI)[a]	p-value	OR (95% CI)[a]	p-value
First meal time								
Under 40 years old (*N* = 5708)								
before 8:00	Ref	NA	Ref	NA	Ref	NA	Ref	NA
8:00–9:00	1.03(0.79, 1.35)	0.8	1.07(0.83, 1.36)	0.6	1.14(0.88, 1.47)	0.3	0.82(0.67, 1.02)	0.078
9:00–12:00	1.21(0.92, 1.58)	0.2	1.22(0.96, 1.55)	0.10	1.08(0.86, 1.37)	0.5	0.84(0.67, 1.04)	0.11
after 12:00	1.47(0.92, 2.34)	0.11	1.33(0.91, 1.95)	0.14	1.46(1.00, 2.13)	0.049	0.89(0.62, 1.26)	0.5
Between 40 and 60 years old (*N* = 4648)								
before 8:00	Ref	NA	Ref	NA	Ref	NA	Ref	NA
8:00–9:00	1.36(1.08, 1.71)	0.009	1.21(0.96, 1.52)	0.10	1.14(0.92, 1.41)	0.2	1.01(0.80, 1.27)	>0.9
9:00–12:00	1.32(1.04, 1.67)	0.022	1.31(1.01, 1.70)	0.043	1.26(0.98, 1.61)	0.073	0.90(0.72, 1.12)	0.3
after 12:00	1.14(0.72, 1.81)	0.6	1.20(0.77, 1.86)	0.4	1.57(0.99, 2.51)	0.056	0.89(0.57, 1.39)	0.6
Over 60 years old (*N* = 3656)								
before 8:00	Ref	NA	Ref	NA	Ref	NA	Ref	NA
8:00–9:00	1.11(0.82, 1.51)	0.5	0.90(0.70, 1.16)	0.4	0.98(0.75, 1.28)	0.9	1.06(0.79, 1.43)	0.7
9:00–12:00	1.11(0.79, 1.56)	0.5	1.11(0.86, 1.43)	0.4	1.17(0.95, 1.45)	0.15	1.25(0.92, 1.71)	0.15
after 12:00	2.04(1.14, 3.65)	0.017	0.75(0.44, 1.28)	0.3	1.08(0.63, 1.84)	0.8	1.64(0.74, 3.64)	0.2
Last meal time								
Under 40 years old (*N* = 5708)								
after 21:00	Ref	NA	Ref	NA	Ref	NA	Ref	NA
before 15:00	1.02(0.75, 1.37)	>0.9	1.20(0.85, 1.71)	0.3	1.18(0.86, 1.62)	0.3	0.88(0.69, 1.13)	0.3
15:00–17:00	1.50(0.55, 4.10)	0.4	0.39(0.15, 1.03)	0.056	0.89(0.35, 2.25)	0.8	2.28(0.91, 5.68)	0.076
17:00–19:00	1.16(0.81, 1.66)	0.4	0.81(0.59, 1.09)	0.2	0.95(0.69, 1.29)	0.7	1.08(0.80, 1.47)	0.6
19:00–21:00	0.93(0.75, 1.15)	0.5	1.07(0.89, 1.28)	0.5	0.98(0.81, 1.18)	0.8	0.99(0.83, 1.17)	>0.9
Between 40 and 60 years old (*N* = 4648)								
after 21:00	Ref	NA	Ref	NA	Ref	NA	Ref	NA
before 15:00	1.00(0.73, 1.36)	>0.9	1.40(0.97, 2.04)	0.074	1.18(0.83, 1.67)	0.4	0.91(0.61, 1.36)	0.7
15:00–17:00	0.38(0.19, 0.78)	0.009	0.51(0.23, 1.12)	0.091	0.92(0.44, 1.94)	0.8	0.82(0.36, 1.84)	0.6
17:00–19:00	0.79(0.56, 1.11)	0.2	1.09(0.76, 1.56)	0.7	0.70(0.52, 0.94)	0.019	0.81(0.57, 1.15)	0.2
19:00–21:00	0.85(0.68, 1.05)	0.13	1.12(0.88, 1.44)	0.4	0.91(0.74, 1.12)	0.4	0.96(0.79, 1.17)	0.7
Over 60 years old (*N* = 3656)								
after 21:00	Ref	NA	Ref	NA	Ref	NA	Ref	NA
before 15:00	0.75(0.44, 1.27)	0.3	0.81(0.52, 1.26)	0.3	1.00(0.60, 1.65)	>0.9	0.95(0.61, 1.47)	0.8
15:00–17:00	0.53(0.28, 1.01)	0.053	0.51(0.23, 1.10)	0.086	0.99(0.46, 2.11)	>0.9	0.37(0.16, 0.85)	0.020
17:00–19:00	0.86(0.57, 1.29)	0.5	1.15(0.82, 1.60)	0.4	0.71(0.52, 0.96)	0.028	0.79(0.56, 1.11)	0.2
19:00–21:00	0.94(0.71, 1.24)	0.7	0.95(0.73, 1.24)	0.7	0.85(0.65, 1.10)	0.2	1.04(0.81, 1.34)	0.7

OR Odds Ratio, *CI* Confidence Interval, *Ref* Reference, *N* Number, *NA* Not applicable.

[a]Multivariate logistic regression models adjusted for feeding duration (continuous), age (continuous), gender (male or female), race (non-Hispanic White, non-Hispanic Black, Mexican American, or other Race), poverty ratio (continuous), education level (below high school, high school or above high school), drinking status (non-drinker or <1 drinks/month, 1–5 drinks/month, 5–10 drinks/month or 10+ drinks/month), smoking status (never smoker, former smoker or current smoker), body mass index (underweight (<18.5), normal (18.5 to <25), overweight (25 to <30) or obese (30 or greater)), self-reported chronic obstructive pulmonary disease (yes or no), self-reported liver disease (yes or no), self-reported cancer (yes or no), self-reported cardiovascular disease (yes or no), self-reported hypertension (yes or no), self-reported diabetes (yes or no), self-reported kidney disease (yes or no), meal count (continuous), caloric intake, carbohydrate intake, fat intake, protein intake, and dietary fiber intake per kilogram of body weight (continuous).

prolonged feeding durations, were associated with accelerated aging, particularly of the body, heart, and liver. This aligns with the fundamental principles of chrononutrition[2]. The body's circadian system, governed by a central clock in the brain's suprachiasmatic nucleus (SCN) and synchronized by light, orchestrates daily rhythms in metabolism and repair. Peripheral organs, however, contain their own clocks, which are powerfully entrained by feeding signals[1]. A conflict between the SCN's light-driven schedule and the metabolic cues from late meals can lead to circadian misalignment, a state increasingly linked to metabolic dysfunction and accelerated aging[3–11,39–42].

The timing of the first meal sets the metabolic tone for the day. A delayed first meal prolongs the overnight fast but may also disrupt the cortisol awakening response and blunt the morning peak of insulin sensitivity. This can lead to larger glycemic excursions and a greater metabolic load on the heart and liver upon the first nutrient intake[43–45]. Conversely, a late last meal forces metabolic activity during the biological night, a period programmed for rest and cellular repair (e.g., autophagy)[46–49]. This inopportune timing can lead to elevated nocturnal insulin levels[50,51], promoting inflammation and anabolic processes at a time when catabolic, restorative functions should dominate. Interestingly, our study identified nuanced

Table 3 | Association of first meal time and last meal time with the biological aging risk of the body and organs by gender. Number = 14,012

Characteristic	Body biological aging		Heart biological aging		Liver biological aging		Kidney biological aging	
	OR(95% CI)[a]	p-value	OR(95% CI)[a]	p-value	OR (95% CI)[a]	p-value	OR (95% CI)[a]	p-value
First meal time								
Female (*N* = 6979)								
before 8:00	Ref	NA	Ref	NA	Ref	NA	Ref	NA
8:00–9:00	1.34(1.07, 1.67)	0.011	1.15(0.95, 1.39)	0.2	1.02(0.84, 1.23)	0.8	1.11(0.93, 1.33)	0.2
9:00–12:00	1.36(1.10, 1.70)	0.006	1.18(0.97, 1.44)	0.10	1.07(0.88, 1.29)	0.5	1.15(0.92, 1.44)	0.2
after 12:00	1.87(1.25, 2.79)	0.003	1.3(0.94, 1.78)	0.11	1.55(1.11, 2.16)	0.011	1.31(0.87, 1.96)	0.2
Male (*N* = 7033)								
before 8:00	Ref	NA	Ref	NA	Ref	NA	Ref	NA
8:00–9:00	1.12(0.89, 1.41)	0.3	1.04(0.88, 1.24)	0.6	1.18(0.96, 1.45)	0.12	0.89(0.73, 1.08)	0.2
9:00–12:00	1.36(1.09, 1.71)	0.008	1.44(1.16, 1.79)	0.001	1.29(1.02, 1.64)	0.036	0.87(0.71, 1.08)	0.2
after 12:00	1.53(1.05, 2.24)	0.028	1.39(0.97, 1.99)	0.074	1.59(1.10, 2.30)	0.014	0.91(0.63, 1.30)	0.6
Last meal time								
Female (*N* = 6979)								
after 21:00	Ref	NA	Ref	NA	Ref	NA	Ref	NA
before 15:00	0.99(0.68, 1.44)	>0.9	1.14(0.88, 1.47)	0.3	1.38(1.01, 1.87)	0.041	1(0.74, 1.36)	>0.9
15:00–17:00	0.57(0.27, 1.20)	0.13	0.8(0.45, 1.43)	0.4	0.92(0.51, 1.66)	0.8	0.75(0.42, 1.35)	0.3
17:00–19:00	0.87(0.65, 1.16)	0.3	1.08(0.82, 1.40)	0.6	0.76(0.60, 0.97)	0.026	0.85(0.64, 1.12)	0.3
19:00–21:00	0.89(0.73, 1.09)	0.3	1.16(0.97, 1.39)	0.094	0.94(0.78, 1.13)	0.5	0.95(0.80, 1.14)	0.6
Male (*N* = 7033)								
after 21:00	Ref	NA	Ref	NA	Ref	NA	Ref	NA
before 15:00	0.91(0.69, 1.19)	0.5	1.16(0.88, 1.53)	0.3	0.95(0.70, 1.27)	0.7	0.82(0.62, 1.07)	0.14
15:00–17:00	0.66(0.39, 1.14)	0.13	0.29(0.15, 0.53)	<0.001	0.92(0.46, 1.83)	0.8	1.18(0.56, 2.47)	0.7
17:00–19:00	0.86(0.64, 1.15)	0.3	0.81(0.59, 1.10)	0.2	0.72(0.57, 0.91)	0.007	0.9(0.68, 1.18)	0.4
19:00–21:00	0.74(0.62, 0.90)	0.002	0.86(0.70, 1.06)	0.2	0.85(0.71, 1.02)	0.079	0.94(0.80, 1.09)	0.4

OR Odds Ratio, *CI* Confidence Interval, *Ref* Reference, *N* Number, *NA* Not applicable.

[a]Multivariate logistic regression models adjusted for feeding duration (continuous), age (continuous), race (non-Hispanic White, non-Hispanic Black, Mexican American, or other Race), poverty ratio (continuous), education level (below high school, high school or above high school), drinking status (non-drinker or <1 drinks/month, 1–5 drinks/month, 5–10 drinks/month or 10+ drinks/month), smoking status (never smoker, former smoker or current smoker), body mass index (underweight (<18.5), normal (18.5 to <25), overweight (25 to <30) or obese (30 or greater)), self-reported chronic obstructive pulmonary disease (yes or no), self-reported liver disease (yes or no), self-reported cancer (yes or no), self-reported cardiovascular disease (yes or no), self-reported hypertension (yes or no), self-reported diabetes (yes or no), self-reported kidney disease (yes or no), meal count (continuous), caloric intake, carbohydrate intake, fat intake, protein intake, and dietary fiber intake per kilogram of body weight (continuous).

"optimal" windows for the last meal, which differed by organs: 3 p.m.–5 p.m. for the heart and 5 p.m.–7 p.m. for the liver. This suggests that simply eating "early" is not the full story. The earlier window for the heart may reflect its sensitivity to nocturnal metabolic and autonomic stress, benefiting from a longer fasting period before sleep[52,53]. The slightly later window for the liver, the body's metabolic nexus, might represent an optimal balance point, allowing it to efficiently process the day's final nutrient load before shifting to its critical overnight functions of gluconeogenesis and detoxification, processes primarily regulated by hormones such as glucagon[54]. The bidirectional effect we observed, where very early last meals (before 3 p.m.) were also linked to accelerated aging, hints at the complexity of the rhythms and suggests that extreme feeding schedules may also disrupt metabolic homeostasis. The underlying mechanisms, likely involving intricate feedback loops between insulin, glucagon, ghrelin, and core clock genes, require further investigation[54–56].

Moreover, our findings indicated that longer feeding durations and shorter fasting durations were independently linked to increased biological aging risks in the body, heart, and liver. This suggests that adherence to an approximately 8-h TRE regimen may be necessary to delay biological aging. This observation remains consistent with TRE research, where existing evidence shows that the practice improves health status by alleviating insulin resistance, obesity, blood pressure, and metabolic syndrome risk[17,18,21,57–59].

We found differential sensitivity of organs to dietary rhythms. Our results suggest that dietary rhythms, including meal timing and feeding and fasting durations, were primarily associated with biological aging of the heart and liver but not the kidneys. This finding aligns with existing animal literature, which demonstrated that the liver exhibits the fastest response to changes in feeding times, followed by the heart, while the kidneys adjust the slowest[60]. The heart and liver are heavily regulated by the circadian clock, which governs daily fluctuations in their metabolic activities and repair processes[61,62]. In contrast, kidney functions, filtration, reabsorption, and excretion, showed less diurnal variation and were more influenced by hemodynamic and endocrine signals, like aldosterone[63], making them less sensitive to dietary rhythm changes. This could explain its relative insensitivity to the timing of single meals, although it did show a response to the overall feeding duration in older adults, suggesting a sensitivity to cumulative daily metabolic load.

Interestingly, if dietary rhythms have the most pronounced impact on the liver's circadian clock, followed by the heart and then the kidneys, it might be expected that an earlier last meal time might have a more significant effect on the liver. However, our observations indicate that the optimal last meal time for delaying liver aging occurred later (5 p.m. to 7 p.m.), while the best time for delaying heart aging was earlier (3 p.m. to 5 p.m.). The underlying mechanisms responsible for this differential optimal timing require further investigation. Importantly, our results indicate

Table 4 | Association of first meal time and last meal time with the biological aging risk of the body and organs by disease. Number = 14,012

Characteristic	Body biological aging		Heart biological aging		Liver biological aging		Kidney biological aging	
	OR (95% CI)[a]	p-value	OR (95% CI)[a]	p-value	OR (95% CI)[a]	p-value	OR (95% CI)[a]	p-value
First meal time								
Non-diseased population[b] (*N* = 7717)								
before 8:00	Ref	NA	Ref	NA	Ref	NA	Ref	NA
8:00–9:00	1.27(1.04, 1.54)	0.019	1.15(0.97, 1.37)	0.11	1.17(0.97, 1.41)	0.10	0.88(0.74, 1.05)	0.14
9:00–12:00	1.5(1.26, 1.80)	<0.001	1.38(1.13, 1.68)	0.002	1.24(1.01, 1.53)	0.043	0.97(0.79, 1.19)	0.8
after 12:00	1.71(1.19, 2.47)	0.005	1.4(1.02, 1.93)	0.038	1.66(1.18, 2.34)	0.004	0.96(0.70, 1.32)	0.8
Diseased population[c] (*N* = 6295)								
before 8:00	Ref	NA	Ref	NA	Ref	NA	Ref	NA
8:00–9:00	1.22(0.95, 1.57)	0.12	1.1(0.92, 1.30)	0.3	1.01(0.82, 1.24)	>0.9	1.12(0.91, 1.38)	0.3
9:00–12:00	1.14(0.88, 1.47)	0.3	1.21(0.95, 1.52)	0.12	1.17(0.98, 1.40)	0.088	1.01(0.82, 1.24)	>0.9
after 12:00	1.38(0.91, 2.09)	0.13	1.34(0.90, 2.00)	0.15	1.5(1.00, 2.25)	0.050	1.14(0.74, 1.76)	0.5
Last meal time								
Non-diseased population[b] (*N* = 7717)								
after 21:00	Ref	NA	Ref	NA	Ref	NA	Ref	NA
before 15:00	1.11(0.81, 1.52)	0.5	1.21(0.91, 1.61)	0.2	1.15(0.88, 1.51)	0.3	0.98(0.76, 1.26)	0.9
15:00–17:00	0.59(0.32, 1.07)	0.082	0.45(0.21, 0.97)	0.042	0.8(0.39, 1.65)	0.5	0.99(0.51, 1.91)	>0.9
17:00–19:00	0.83(0.64, 1.09)	0.2	0.74(0.57, 0.94)	0.016	0.77(0.58, 1.03)	0.073	1(0.74, 1.34)	>0.9
19:00–21:00	0.75(0.64, 0.88)	<0.001	0.89(0.76, 1.04)	0.2	0.87(0.72, 1.05)	0.2	1.01(0.85, 1.20)	>0.9
Diseased population[c] (*N* = 6295)								
after 21:00	Ref	NA	Ref	NA	Ref	NA	Ref	NA
before 15:00	0.75(0.55, 1.02)	0.070	1.08(0.80, 1.47)	0.6	1.09(0.80, 1.48)	0.6	0.8(0.61, 1.06)	0.11
15:00–17:00	0.81(0.43, 1.54)	0.5	0.5(0.29, 0.87)	0.014	0.98(0.51, 1.86)	>0.9	0.96(0.45, 2.03)	>0.9
17:00–19:00	0.96(0.70, 1.32)	0.8	1.24(0.91, 1.69)	0.2	0.75(0.56, 0.99)	0.046	0.81(0.61, 1.07)	0.13
19:00–21:00	0.94(0.77, 1.15)	0.5	1.06(0.85, 1.31)	0.6	0.91(0.74, 1.12)	0.4	0.92(0.78, 1.10)	0.4

OR Odds Ratio, *CI* Confidence Interval, *Ref* Reference, *N* Number, *NA* Not applicable.

[a]Multivariate logistic regression models adjusted for feeding duration (continuous), age (continuous), race (non-Hispanic White, non-Hispanic Black, Mexican American, or other Race), poverty ratio (continuous), education level (below high school, high school or above high school), drinking status (non-drinker or <1 drinks/month, 1–5 drinks/month, 5–10 drinks/month or 10+ drinks/month), smoking status (never smoker, former smoker or current smoker), body mass index (underweight (<18.5), normal (18.5 to <25), overweight (25 to <30) or obese (30 or greater)), meal count (continuous), caloric intake, carbohydrate intake, fat intake, protein intake, and dietary fiber intake per kilogram of body weight (continuous).

[b]Non-diseased population: all of the following disease were 'no': self-reported chronic obstructive pulmonary disease, self-reported liver disease, self-reported cancer, self-reported cardiovascular disease, self-reported hypertension, self-reported diabetes, self-reported kidney disease.

[c]Diseased population: any of the following disease was 'yes': self-reported chronic obstructive pulmonary disease, self-reported liver disease, self-reported cancer, self-reported cardiovascular disease, self-reported hypertension, self-reported diabetes, self-reported kidney disease.

different meal timing may have different effects on patients with organ-specific diseases.

Our stratified analyses reveal that the relationship between dietary rhythms and biological aging was not uniform, but was modulated by age, sex, and disease status. In younger populations (under 40), dietary rhythms did not significantly affect biological aging across organs, likely due to their robust physiological functions and adaptability. However, in the 40–60 age group, dietary rhythms notably impacted body and heart aging. In the over 60 age group, the effect on kidney aging became more pronounced, possibly because kidney circadian gene regulation is less efficient compared to the liver and heart[60,64]. As individuals aged, the kidney's compensatory ability declined, making it more susceptible to the effects of dietary rhythms. With increasing age, the circadian system becomes less robust and more prone to disruption[65,66]. This "chrono-decline" can lead to a dampened amplitude of hormonal rhythms and a reduced ability to synchronize peripheral clocks, making older individuals more vulnerable to the disruptive effects of circadian challenges like a late meal. The heightened sensitivity of the kidneys to feeding duration in individuals over 60 supports this, suggesting that as intrinsic organ resilience wanes, external synchronizers like diet become increasingly important.

The observed sex differences—with males appearing more sensitive to meal timing and females to feeding/fasting duration, may be rooted in the sexual dimorphism of the circadian system and metabolic regulation, which is partly governed by sex hormones[67,68]. Estrogen, for example, is known to influence clock gene expression and energy homeostasis, potentially conferring different sensitivities to dietary inputs[69,70]. Further research is needed on the gender-specific effects.

Furthermore, the impact of dietary rhythms was modulated by disease status. The finding that liver aging was more strongly affected by last meal timing in the diseased group suggests that existing disease may alter organ metabolism and inflammation, potentially heightening the liver's sensitivity to dietary rhythm regulation of aging[22]. Conversely, the stronger effect of meal timing on systemic Body Age in the healthy group suggests that in the absence of overt disease, dietary rhythms may be a more prominent regulator of the overall aging process. Our findings highlight that, the interplay between health status and dietary habits could play a crucial role in the aging process, often accelerating the progression of existing diseases. These results establish the necessity of personalized nutritional guidance, suggesting that dietary rhythms should be tailored based on an individual's specific gender, age, and disease status to optimize aging outcomes.

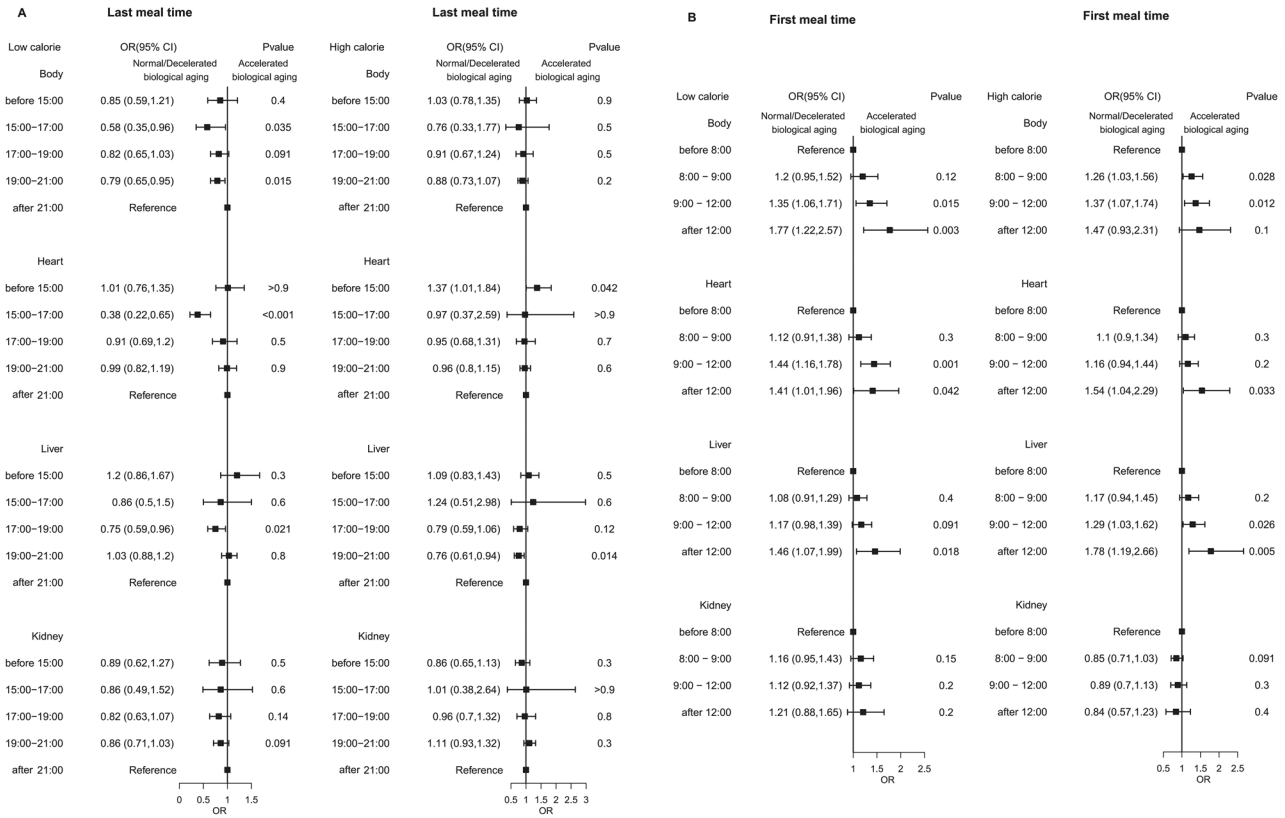

Fig. 4 | . Association of last meal time (**A**) and first meal time (**B**) with the biological aging risk of the body and organs by caloric intake. Number = 14,012. OR indicates odds ratio. CI indicates confidence interval; Ref indicates reference. The multivariate logistic regression models adjusted for feeding duration (continuous), age (continuous), gender (male or female), race (non-Hispanic White, non-Hispanic Black, Mexican American, or other Race), poverty ratio (continuous), education level (below high school, high school or above high school), drinking status (non-drinker or <1 drinks/month, 1–5 drinks/month, 5–10 drinks/month or 10+ drinks/month), smoking status (never smoker, former smoker or current smoker), body mass index(underweight (<18.5), normal (18.5 to <25), overweight (25 to <30) or obese (30 or greater)), self-reported chronic obstructive pulmonary disease (yes or no), self-reported liver disease (yes or no), self-reported cancer (yes or no), self-reported cardiovascular disease (yes or no), self-reported hypertension (yes or no), self-reported diabetes (yes or no), self-reported kidney disease (yes or no), meal count (continuous), carbohydrate intake, fat intake, protein intake, and dietary fiber intake per kilogram of body weight (continuous).

Our study also found that the impact of dietary rhythms on biological aging is not uniform but is significantly modulated by caloric intake and diet quality, revealing a complex interaction between "when to eat," "how much to eat," and "what to eat."

We observed that the protective associations of optimal meal time (e.g., earlier last meal) were stronger in individuals with low caloric intake but weaker in the high calorie intake group. One possible interpretation is that the circadian rhythms regulate energy expenditure. Human studies suggest that diet-induced thermogenesis (also known as the thermic effect of food, or the specific dynamic action of food) is approximately 50% lower in the evening compared to the morning, independent of behavioral cycles[71,72]. This implies that consuming the same amount of calories later in the day may leads to an energy surplus and reduced metabolic efficiency. In our study, this mechanism may explain why later meal time was associated with accelerated biological aging, particularly in metabolically sensitive organs such as the liver and heart. Furthermore, for individuals with high caloric intake, the evening reduction in diet-induced thermogenesis may further exacerbate the metabolic burden, diminishing the protective effects of optimal meal timing. Our results indicate that moderating calorie intake may help maximize the benefits of dietary rhythms.

Stratified analysis by dietary quality showed interesting organ-specific interactions, extending the current understanding of how nutrition impacts aging. A recent study demonstrated that high-quality dietary patterns are fundamentally linked to decelerated biological aging across multiple organs[73]. Based on this, our study highlights the time of meals could influence, or even diminish, the protective effects of a healthy diet.

For body and liver biological aging, the detrimental effects of delayed meals were more apparent in participants with healthier diets. This may reflect the strong sensitivity of the liver and body metabolism to feeding time: even a high-quality diet cannot fully offset the impact of eating at the suboptimal time. It suggests that "when you eat" is an independent determinant of health, separate from "what you eat"[74]. Mechanistically, a healthy diet improves insulin sensitivity and metabolic flexibility, but the liver's peripheral clock is strongly adjusted by feeding signals[75]. Late or irregular meals may desynchronize the liver clock from the central circadian system, disturbing downstream metabolic pathways regardless of nutrient quality. Thus, following regular dietary rhythm seems essential to get the full anti-aging benefits of a healthy diet.

In contrast, the associations between meal time and heart biological aging were stronger in the unhealthy diet group. This suggests that the heart may be particularly affected by a combination of poor diet quality and irregular meal time, potentially accelerating heart biological aging. The cardiovascular system is highly sensitive to circadian fluctuations in inflammation and oxidative stress, so when the protective effects of a high-quality diet are absent, late eating may have a stronger deleterious impact[76].

Taken together, these results suggest that a nutrient-focused approach alone may be insufficient for healthy aging. Effective dietary strategies should combine proper meal time, moderate energy intake, and high-quality foods, rather than focusing on any single aspect in isolation.

This study has several strengths. First, this study is the first to evaluate associations between various dietary rhythms and biological aging across different organs, accompanied by stratified analyses. Second, we accounted for potential confounding factors, including other dietary rhythms, and

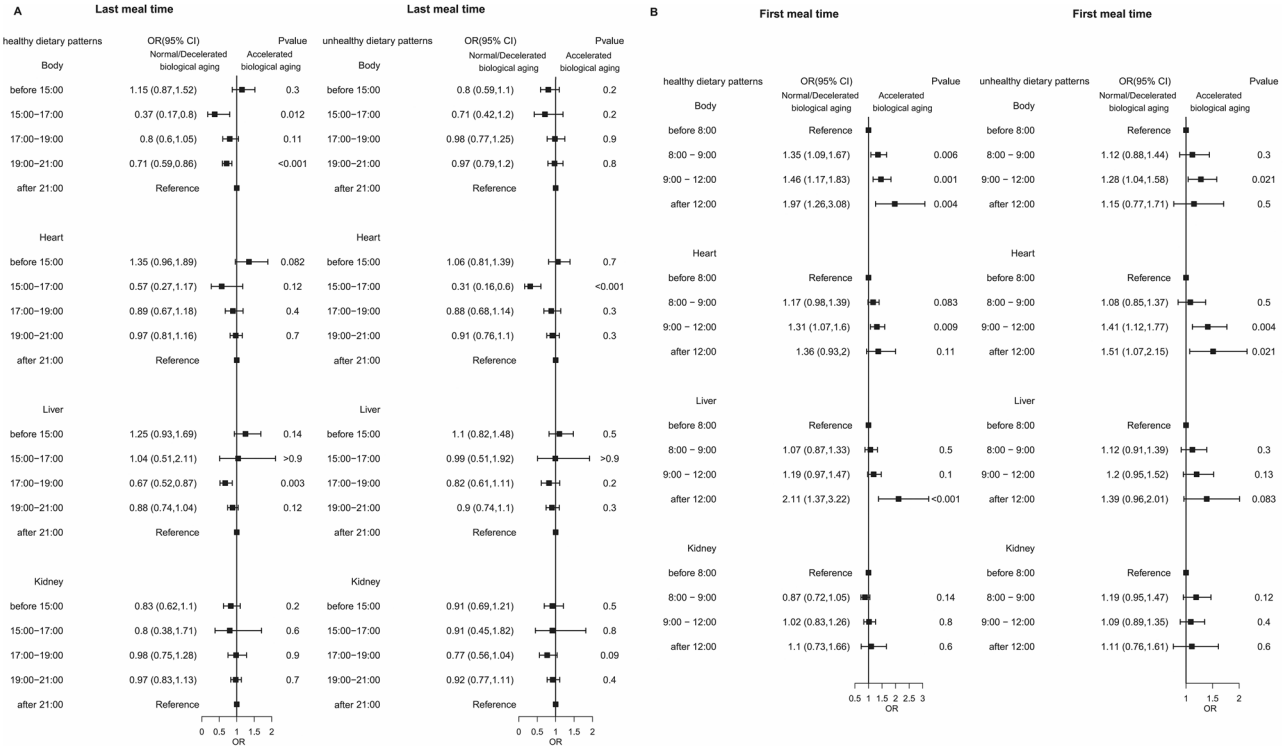

Fig. 5 | . Association of last meal time (**A**) and first meal time (**B**) with the biological aging risk of the body and organs by alternate Mediterranean diet (aMED) score. Number = 14,012. OR indicates odds ratio. CI indicates confidence interval; Ref indicates reference. The multivariate logistic regression models adjusted for feeding duration (continuous), age (continuous), gender (male or female), race (non-Hispanic White, non-Hispanic Black, Mexican American, or other Race), poverty ratio (continuous), education level (below high school, high school or above high school), drinking status (non-drinker or <1 drinks/month, 1–5 drinks/month, 5–10 drinks/month or 10+ drinks/month), smoking status (never smoker, former smoker or current smoker), body mass index (underweight (<18.5), normal (18.5 to <25), overweight (25 to <30) or obese (30 or greater)), self-reported chronic obstructive pulmonary disease (yes or no), self-reported liver disease (yes or no), self-reported cancer (yes or no), self-reported cardiovascular disease (yes or no), self-reported hypertension (yes or no), self-reported diabetes (yes or no), self-reported kidney disease (yes or no), meal count (continuous).

confirmed the robustness of our findings through sensitivity analyses. Third, we used a large, nationally representative database, minimizing measurement bias and increasing sample size by combining data from eight cycles.

However, there were several limitations. First, the cross-sectional design of our study limited the ability to infer causality and underlying biological mechanisms between dietary rhythms and biological aging, and reverse causation, where health status influences dietary habits, cannot be fully excluded. Second, dietary data were derived from 24-h recalls, which are subject to recall bias and day-to-day variability. Although among participants with two days of recall data median absolute differences between days were modest. Future studies with more precise and long-term dietary timing data are warranted. Third, although we adjusted for a wide range of covariates, including sleep duration and physical activity in sub-analyses, potential residual confounding remains possible. Specifically, Objective chronotype measures (e.g., dim light melatonin onset) and longitudinal sleep regularity were unavailable for the full cohort of NHANES. Nevertheless, future longitudinal studies incorporating objective circadian markers are needed to disentangle the complex interactions between chronotype, sleep regularity, other circadian-related behaviors and dietary rhythms. Fourth, our analysis is restricted to data from NHANES because other large-scale cohorts representing different populations, such as the UK Biobank (European) and the China Health and Retirement Longitudinal Study (Asian), currently lack the detailed meal timing data required to investigate dietary rhythms. Therefore, the findings may not be generalizable to populations as potential geographic and ethnic differences in dietary patterns and circadian characteristics may influence the observed associations.

In total, this cross-sectional study demonstrates that dietary rhythms are associated with biological aging across different organs to varying extents. Later first or last meal times, longer feeding duration or shorter fasting duration were associated with increased risk of biological aging, although the optimal meal timing differed for the whole body and individual organs. The dietary patterns exhibited varying association with the biological aging of the body and different organs, influenced by factors such as age, gender, disease status, energy intake, and dietary quality. In addition, these findings suggest a complex relationship between when to eat, how much to eat, and what to eat. Rather than focusing on nutrient composition alone, dietary guidance for healthy aging may benefit from considering dietary rhythms alongside diet quality and energy balance. Our findings may provide insight into developing targeted dietary strategies for diverse populations.

Methods

Data source and study population

This cross-sectional observational study utilized data from NHANES, a nationally representative survey of the U.S. population that collects demographic, socioeconomic, dietary, and health-related data through interviews, physical examinations, and laboratory tests[77,78].

To ensure analytical accuracy and comparability, we included only NHANES cycles with consistent biomarker measurements and survey methods. C-reactive protein (CRP), required for calculating body BA, was not measured during the 2011–2014 cycles. According to the National Center for Health Statistics[79], NHANES field operations were suspended in 2018 due to the COVID-19 pandemic, and the 2017-March 2020 Pre-pandemic File was a combined dataset with distinct design and weighting methods. Because of its methodological differences from the standard 1999–2018 cycles, including this dataset could introduce bias. Furthermore, biochemical data from the NHANES 2020–2023 cycles were not yet

available at the time of our data extraction, precluding the calculation of biological age for this period. Therefore, data from the 1999–2010 and 2015–2018 cycles were used in this study. Adults aged 18–80 years with complete dietary data, parameters required to calculate body and organ-specific BA, and survey weight data were included. Participants under 18 or over 80 were excluded due to NHANES recording limitations or puberty-related changes. Pregnant women and individuals with missing relevant data were also excluded, resulting in a final sample of 14,012 participants (Fig. 1).

The analysis of U.S. NHANES was approved by the U.S. NHANES institutional review board and National Center for Health Statistics Research ethics review board. The following protocol approval numbers of U.S. NHANES were provided by the NCHS Research Ethics Review Board (ERB) for the presented surveys years of 1999–2010 and 2015–2018: Protocol #98-12, Protocol #2005-06, Continuation of Protocol #2005-06, Continuation of Protocol #2011-17, Protocol #2018–01. Participants were de-identified and from public database. All the participants provided with informed consent. The present study was conducted in accordance with the Declaration of Helsinki.

Biological age calculation

In line with the methodology used by Kwon D et al.[27], when processing biomarkers for calculating biological age, we excluded outliers by calculating the standard deviation and corrected for changes in measurement methods to ensure data comparability across different years. For example, Creatinine values from the 1999–2000 to 2005–2006 NHANES were corrected according to the analytical notes posted by NHANES (https://www.cdc.gov/nchs/nhanes/index.htm). High sensitivity C-reactive protein assays from the 2015–2016 NHANES were posted in units mg/L and were divided by 10 to match units in previous waves. Measurement methods for plasma fasting glucose changed in the 2005–2006, 2007–2008, and 2015–2016 NHANES. Values were adjusted to be comparable across years using multiple regression equations (https://www.cdc.gov/nchs/nhanes/index.htm).

To provide a multi-dimensional assessment of aging, we calculated Body BA and three organ-specific BAs (Heart, Liver, and Kidney). Data were sourced from the NHANES. Specifically, we used data from the 1999–2010 and 2015–2018 cycles for the Body BA calculation and data from the 1999–2018 cycles for the three organ-specific BAs. All calculations were performed using the KDM implemented in the "BioAge" R package[27,80].

To establish a "normative aging" baseline and create a standardized tool for measuring deviations from this norm in the general population, our approach involved first training our models on a "healthy" reference cohort, and then applying these calibrated models to the entire study cohort to assess aging. This process ensures that the models capture age-related physiological changes, free from the confounding effects of overt disease, rather than signals from specific pathologies. The healthy reference cohort was selected from the full NHANES dataset by excluding participants with pre-existing chronic conditions relevant to the specific aging model being trained. The exclusion criteria were as follows: For the Body Age model: Exclusion of participants with cardiovascular disease (CVD), kidney disease, liver disease, Chronic Obstructive Pulmonary Disease (COPD), malignancies, hypertension, or diabetes. For the Heart Age model: Exclusion of participants with CVD. For the Liver Age model: Exclusion of participants with liver disease, liver cancer, or a history of heavy alcohol consumption. For the Kidney Age model: Exclusion of participants with kidney disease. Finally, 24,223 individuals were included for the calculation of body age, 19,248 individuals were included for the calculation of heart age, 45,551 individuals were included for the calculation of kidney age, and 36,550 individuals were included for the calculation of liver age.

The selection of biomarkers for this study was a systematic, biologically-informed process. For the Body BA, we based our panel on the validated biomarker system proposed by Levine et al.[81], which includes albumin, alkaline phosphatase, blood urea nitrogen, creatinine, C-reactive protein, glycated hemoglobin, uric acid, white blood cell count, lymphocyte percentage, mean corpuscular volume, and red cell distribution width. In addition to this original panel, we incorporated diastolic blood pressure and pulse pressure. This decision was based on the rationale that a true "whole-body" age model should represent multiple systems, including the cardiovascular, hepato-renal, metabolic, and immune systems. While the Levine model covers several of these, it lacks direct variables reflecting cardiovascular health. For the organ-specific BAs, we grouped biomarkers available in NHANES based on their primary association with specific organs, guided by established medical knowledge and the research frameworks of Nie et al. and Tian et al.[32,33]. Only biomarkers that significantly improved model performance were retained in the final models. The final biomarker panels for each model are detailed in Supplementary Table 13.

After data preparation and biomarker selection, we trained the BA models separately for males and females using a five-fold cross-validation method. The newly trained algorithms were then applied to the entire study population to calculate each individual's BA. The difference between an individual's CA and BA reflects the current aging status of the body and organs. A positive difference (BA minus CA) signifies accelerated biological aging, while a negative difference indicates decelerated aging. The risk of biological aging is considered as 1 if BA is larger than CA and 0 if BA is less than CA per individual.

To validate the robustness and accuracy of our newly trained models, we performed a two-tiered validation: Internal Accuracy Validation: Within the healthy reference cohort, we used five-fold cross-validation to assess model performance by calculating the Pearson correlation coefficient and MAE between the predicted BA and chronological age. To assess the real-world applicability of our models, we further tested the ability of age acceleration to predict the risk of all-cause mortality. In detail, we collected data from 1999–2010 and 2015–2018 to establish a Cox proportional hazards model for body biological aging and mortality (a total of 34,371 cases), since CRP, which is used to calculate body biological age, was only measured in those cycles. Data from 1999 to 2018 were used to calculate the Cox proportional hazards models for cardiac biological aging (20,437 cases), liver biological aging (40,894 cases), and kidney biological aging (44,479 cases) in relation to mortality. Mortality data were sourced from linked records extracted from the National Death Index up to 2018. We assessed the associations between body and organ-specific aging and all-cause mortality, cancer mortality, heart disease mortality and nephrosis mortality, over a medium follow-up of 140 months. However, since the NDI did not have mortality data for liver diseases, we did not conduct Cox proportional hazards analyses for body and organ-specific aging in relation to liver disease mortality. The cox proportional hazards models adjusted for age (continuous), gender (male or female), race (non-Hispanic White, non-Hispanic Black, Mexican American, or other Race), poverty ratio(continuous), education level(below high school, high school or above High School), drinking status (non-drinker or <1 drinks/month, 1–5 drinks/month, 5–10 drinks/month or 10+ drinks/month), smoking status(never smoker, former smoker or current smoker), body mass index (underweight (<18.5), normal (18.5 to <25), overweight (25 to <30) or obese (30 or greater)), self-reported chronic obstructive pulmonary disease (yes or no), self-reported liver disease (yes or no), self-reported cancer (yes or no), self-reported cardiovascular disease (yes or no), self-reported hypertension (yes or no), self-reported diabetes (yes or no), self-reported kidney disease (yes or no), caloric intake per kilogram of body weight (continuous). We adjusted sample weights using first-day dietary weight data from NHANES.

Dietary rhythms

We calculated first and last meal times, feeding/fasting duration, and meal count utilizing 24-h dietary recall data from NHANES. First meal times were categorized into four groups: before 8 a.m., 8 a.m.–9 a.m., 9 a.m.–12 p.m., and after 12 p.m. Last meal times were grouped into five categories: before 3 p.m., 3 p.m–5 p.m., 5 p.m–7 p.m., 7 p.m–9 p.m., and after 9 p.m. Feeding/fasting duration was divided into five groups: <8 h, 8–10 h, 10–12 h, 12–16 h, and >16 h.

For participants with two days of data, we averaged the values; if only the first day was available, we used that alone. To assess the reliability of meal-timing variables, we quantified within-individual variability by

calculating the median absolute differences between Day 1 and Day 2 for key dietary rhythm measures among participants with two recalls. The first meal time was defined as occurring after 5 a.m., and the last meal time as occurring before 5 a.m[82]. To facilitate calculation and statistical analysis, all meal times were converted to numerical values. For example, a meal at 8:30 a.m. was recorded as 8.5, and a meal between midnight and 5 a.m. as a value greater than 24 (e.g., 1:00 a.m. as 25).

Dietary quality

To assess diet quality, we calculated the aMED score[83] using the "dietaryindex" R package, a validated tool designed for standardized dietary index computation in epidemiological research[84]. The aMED score ranges from 0 to 9 and is derived from nine components adapted for the U.S. population. Participants received 1 point for intakes above the population median for beneficial components (vegetables, fruits, nuts, whole grains, legumes, fish, and the ratio of monounsaturated to saturated fat) or below the median for the detrimental component (red and processed meats). An additional point was assigned for moderate alcohol consumption (5–15 g/day for women and 10–25 g/day for men). For subsequent analyses, participants were categorized into two groups according to their aMED scores. A score of ≥4 was classified as the "Healthy Mediterranean diet pattern," while a score of <4 was classified as the "Unhealthy Mediterranean diet pattern"[85].

Covariates

Demographic information including age, sex, race/ethnicity, family poverty income ratio (PIR), education level, smoking history, drinking history and BMI were considered as covariates. Participants were identified as having CVD, diabetes, hypertension, cancer, liver disease, kidney disease, or COPD if they answered "yes" to related questions. We also calculated the number of eating occasions, caloric intake, carbohydrate intake, fat intake, protein intake, dietary fiber intake per kilogram of body weight, weekly metabolic equivalent minutes (2007–2018), sedentary time (2007–2018), and sleep duration (2005–2018) for certain years when data is available. Dietary intake estimates were based solely on foods reported in the 24-h dietary recall and did not include dietary supplement intake. All details are shown in Table 1.

Statistical analysis

We applied NHANES first-day dietary sample weights in all analyses. All variables had missing rates below 15%, and missing data were handled using multiple imputation. The number of missing observations for each variable was presented in Supplementary Table 14. Continuous variables were presented as medians and interquartile ranges [M (Q1, Q3)] and compared using the design-based Wilcoxon rank-sum test. Categorical variables were reported as counts and weighted proportions N (%), compared using the Rao & Scott corrected chi-square test.

Survey-weighted logistic regression models were used to assess the association between dietary rhythms and biological aging. We built three models with different numbers of covariates (univariate, adjusted for other dietary rhythms, and fully adjusted for all covariates). Stratified analyses were conducted by age (under 40 years, between 40 and 60 years, over 60 years), gender, health status, caloric intake (low caloric intake, high caloric intake, based on the survey-weighted distributions of daily energy intake per kilogram body weight) and dietary quality (healthy diet, unhealthy diet). Sensitivity analyses were conducted by first excluding participants with atypical meal timing (defined as the first meal after 3 p.m. or the last meal before 12 p.m.). The remaining participants, who possessed complete sleep and physical activity data, were then further adjusted in the models for MET, sedentary time, and sleep duration. To further evaluate potential residual confounding, we also conducted sensitivity analyses using a negative control outcome (positive hepatitis A antibody), a negative control exposure (self-reported crab consumption in the past 30 days), and by restricting the analysis to participants who reported that their intake on the recall day was "usual" based on the NHANES dietary recall questionnaire. All statistical analyses were performed using R software (version 4.1.2). A $P < 0.05$ was considered statistically significant.

This study was reported in accordance with the STROBE-nut reporting guidelines. (Supplementary Table 15)[86].

Data availability

Publicly available datasets were analyzed in this study. The data can be found here: https://www.cdc.gov/nchs/nhanes/index.htm.

Code availability

The underlying code for this study is not publicly available but may be made available to qualified researchers on reasonable request from the corresponding author.

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Competing interests

The authors declare no competing interests.

Additional information

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