Biological age for chronic kidney disease patients using index model

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Abstract

Estimation of biological age (BA) facilitates an advantage of embedding information on the health being in addition to an individual lifetime. Factors that contribute towards profiling the human biological age can be diverse. Therefore, this study focuses on developing a BA model for patients with Chronic Kidney Disease (CKD). The procedure commences with the selection of significant biomarkers using a correlation test. Appropriate weightage is then assigned to each selected biomarker using the indexing method to produce a BA index. The BA index is matched to age variation within the sample to acquire additional terms for the chronological age leading ultimately to the estimated BA. From a sample of 190 patients (133 trained data and 57 testing data) obtained from the University of Malaya Medical Centre (UMMC), Malaysia, the magnitude of the difference for the BA is found to be between 3 to 9 years from the chronological age. Visual observations further validate the high similarities between the training and testing data sets.

Introduction

40

41   Estimation of biological age (BA) is becoming increasingly popular as an asymptotic
42 measure to understand changes in physical functionality as well as the ageing process of a living
43 being. Over the chronological age (CA), which exhibits an exact figure signifying the period
44 between birth and present time of an individual, the BA is widely used to indicate the healthy
45 and unhealthy ageing through variables that contribute to healthspan.[1] Furthermore, BA shows
46 the health state of each individual and serves as a comparative measure between individuals of
47 the same age and gender.[2] Thus, it describes one lifetime behaviour informatively provided the
48 common premise that physical functionality decline is parallel to deterioration of health
49 condition and age increment.

50   Unhealthy individuals demonstrate only decreased function in CA, but functional BA is
51 intended to represent different stages of ageing.[3] Group of individuals that perceived ill-health
52 exhibited higher biological ages compared to the healthier groups. In this respect, those with
53 more significant functional biological age have a higher chance of death because they reached a
54 more advanced ageing stage earlier than others. Thus, the traditional approach in measuring
55 individual health according to CA is less appealing in today's highly dynamic and rapidly
56 changing global lifestyle.

57   Researchers have recently employed several statistical techniques to develop the BA
58 model, primarily by incorporating multiple relevant biomarkers into the model. The BA model
59 does not only predict ageing-related diseases but also considers the functional status during
60 ageing.[4] Several articles have been published on the measurement of BA using statistical
61 methods. Multiple Linear Regression (MLR) remains one of the most widely used methods for
62 calculating BA.[5-13] Nevertheless, MLR has been criticized for the multicollinearity risk besides
63 the potential for estimates to regress toward the mean.[6] These suggest the MLR equation
64 underestimates the individual BA in the older age while overestimating the younger age.[12]
65 Principal Component Analysis (PCA) was proposed to overcome the disadvantage of MLR in
66 the development of the BA formula.[2,6,7,9-12] However, the PCA cannot avoid some of the
67 statistical deficiencies of MLR.[14] An alternative to this, Klemera & Doubal Method (KDM)
68 provides better precision in estimating BA than MLR and PCA methods.[6,7,9,10] Although KDM
69 gives the most reliable estimates in BA prediction, it involves complex calculations.[6]

70   This study focuses on developing the BA model for patients with Chronic Kidney
71 Disease (CKD). The public-health effect from mortality due to this disease has not been fully
72 assessed.[15] Furthermore, CA does not give a good reflection on the time-dependent changes in
73 kidney function.[16] To better understand an individual degree of ageing or life span and how CKD
74 influences an individual degree of ageing, a new approach needs to be developed.

75   In this study, we develop the BA using the indexing method. An index number is the
76 most common statistical method to measure changes in a set of data points besides summarizing
77 and ranking a particular data set. Moreover, measuring BA by examining the index number
78 keeps track of the original representation of the data and thus ensures the output resembles the
79 empirical structure closely. During this indexing process, each selected biomarker is given a

80 unique treatment corresponding to its severity level. Visual observations are also presented to
81 justify the appropriateness of the method used.
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83

Materials & Methods

85

IRB/Ethics approval

87

88 The data used in this study was approved by The Medical Research Ethics Committee,
89 University of Malaya Medical Centre (MREC ID NO 2018428-6258). The committee granted
90 permission to carry out the study within its facilities with common terms including; to adhere the
91 instruction, guidelines and requirement by the committee. The Patient Information Sheet and
92 Consent Form were waived by the committee. This retrospective study uses the data based on the
93 earlier initiated and completed studies in a new outlook.
94

Measure of correlation

96 The strength between two variables can be measured using Pearson's correlation
97 coefficient.[17] A representative measure for this, the r-value, signifies both the magnitude and
98 direction of the strength, that is, a closer value to ± 1 indicate high strength in the positive or
99 negative direction. The r-value can be computed as:

$$r = \frac{n \sum_{i=1}^{n} x_i y_i - \left(\sum_{i=1}^{n} x_i \sum_{i=1}^{n} y_i \right)}{\sqrt{\left(n \sum_{i=1}^{n} x_i^2 - \left(\sum_{i=1}^{n} x_i \right)^2 \right) \left(n \sum_{i=1}^{n} y_i^2 - \left(\sum_{i=1}^{n} y_i \right)^2 \right)}} \tag{1}$$

100 where x and y are the value for the two variables and n is the total number of samples.
101 This study considers ten biomarker relationships with the CA; height, weight, gender,
102 BMI, creatinine, e-GFR, PB Systolic, BP diastolic, CTCA calcium score and CKD stage from
103 CKD patients. BA biomarkers that have an absolute r-value greater than 0.15 were selected for
104 inclusion in BA calculation.[7,12]
105

Weighted average method

107 This study proposes a weighted average method to estimate the weight for each
108 significant biomarker. Note that the weight ranges from 0 to 1. Higher weight signifies a higher
109 association between the health biomarkers to the BA index. The weight for biomarker i is
110 computed as follows:

$$w_i = \frac{|r_i|}{\sum_{j=1}^{n} |r_j|} \quad (2)$$

111 where r_i is the correlation coefficient of the ith biomarker computed using equation (1) and n is
112 the total number of significant biomarkers. Note that the sum for all w_i's equals to one,
113 $\sum_{i=1}^{n} w_i = 1$.

Indexing method

115   This study uses the indexing method for BA calculation. The index produced from this
116 method represents the amount of change with respect to the base value. For each biomarker, the
117 base value is set to be the normal value or the favourable health condition. Thus, each biomarker
118 has a unique indexing assignment based on the medical measurement they carry. In brief,

$$Index_{(i)} = \left| \frac{Measured\ value\ i - Normal\ value\ i}{Normal\ value\ i} \right| \quad (3)$$

119 where measured value is the current health reading of the patient while the normal value is the
120 normal reading level for health biomarker i. Table 1 summarizes several common reading levels
121 based on the standard clinical practice as well as work carried out in literature studies. The health
122 biomarkers are categorized into several reading levels based on the severity of the postulated
123 measurements.

124   Index equations are then developed based on Table 1. Note that the normal reference
125 value is taken as the mid-point of the normal reading level. The index equation for the BMI is
126 given by:

$$Index_{BMI} = \begin{cases} 1 - \left[\frac{4}{13}(x - 18.5) \right], & if\ 18.5 \leq x \leq 21.75, \\ 1 + \left[\frac{4}{33}(x - 30) \right], & if\ 21.75 < x \leq 30, \\ 1, & otherwise. \end{cases} \quad (4)$$

127 The index equation for the systolic blood pressure is given by:

$$Index_{SBP} = \begin{cases} 1 - \left[\frac{1}{5}(x - 120) \right], & if\ 120 \leq x \leq 125, \\ 1 + \left[\frac{1}{15}(x - 140) \right], & if\ 125 < x \leq 140, \\ 1, & otherwise. \end{cases} \quad (5)$$

128 The index equation for the diastolic blood pressure is given by:

$$Index_{DBP} = \begin{cases} 1 - \left[\dfrac{1}{2}(x-80)\right], & if\ 80 \leq x \leq 82, \\ 1 + \left[\dfrac{1}{8}(x-90)\right], & if\ 82 < x \leq 90, \\ 1, & otherwise. \end{cases} \tag{6}$$

129 The index equation for the eGFR is given by:

$$Index_{eGFR} = \begin{cases} 1, & if\ x \leq 15, \\ \dfrac{90-x}{75}, & if\ 15 < x < 90, \\ 0, & if\ x \geq 90. \end{cases} \tag{7}$$

130 The index equation for the CTCA is given by:

$$Index_{CTCA} = \begin{cases} 0, & if\ x \leq 100, \\ \dfrac{x-100}{300}, & if\ 100 < x < 400, \\ 1, & if\ x \geq 400. \end{cases} \tag{8}$$

131 Equations (4) to (8) formulate the framework for BA index calculation similar to medical
132 practices for six biomarkers to detect the severity level.
133   Figure 1 (a) to (e) show the aforementioned state graphically. Note that the health
134 biomarkers index ranges from 0 to 1 where 0 indicates a favourable level of the health
135 biomarker, index value from 0 to 1 indicates deteriorating health condition, while index value of
136 1 indicates a critically ill stage. The medical measures for each of the biomarkers are unique.
137 Therefore, the index value can be a useful comparative tool across these measurements.
138   In order to produce the biological index for each individual, each health biomarker index
139 is multiplied by its corresponding weight. The weight proportionately signifies the contribution
140 of each biomarker index to the BA index. Mathematically, the overall index for individual x is
141 computed as follows:

$$I_{BioAge\ for\ x} = w_1 Index_{1,x} + w_2 Index_{2,x} + \ldots + w_n Index_{n,x} \tag{9}$$

142 where w_i and $Index_{i,x}$ are the weight and index for the ith health biomarker of individual x,
143 respectively.
144
145 **BA Estimation**
146   Several methods have been proposed to estimate the BA. Among these are the multiple
147 linear regression (MLR) [9] and principal component analysis (PCA) [11]. PCA method is derived
148 from MLR and it reduces the effects of underestimated or overestimated BA.[9] Both methods
149 show a linear relationship between BA and health parameters.

150   BA index models developed for predicting BA in this study also follow a linear
151   relationship for individual general health status. It is developed based on the mathematical
152   settings of the index method. The method suggests combining all individual subcomponents
153   indices in one principal component (in this case, all health biomarkers into a single BA index).
154   The subcomponent index measures the changes for each representative group of the biomarkers
155   from the CA. Note however that the value of the index is not in year term. A common approach
156   translating it into meaningful year-unit is by equation $BA_x = (I_{BioAge\ for\ x}$
157   $\times\ standard\ deviation) + mean\ of\ CA$. Because the sample data focuses on the individual
158   kidney patients, the following adjustment was made to the BA_x.

$$BA_x = (I_{BioAge\ for\ x} \times SD) + CA_x \tag{10}$$

159   where BA_x and CA_x are the biological age and chronological age for individual x, respectively.
160   The standard deviation SD is computed based on the chronological age of the sample.

161   **Bland-Altman analysis**
162   It is vital to observe the mean values to understand the nature of a prediction model. It
163   follows that the degree of dispersion from the mean indicates the fitness of individual BA
164   values.[8] Degrees of dispersion between BA and CA are commonly presented using the Bland-
165   Altman plots. Bland-Altman plots the difference of CA and BA against the mean of the two
166   measurements where it is easier to measure the magnitude, spot outlier, and see the data trend.[18]
167   If the differences are normally distributed, the mean differences should lie between $\overline{d}$
168   $-1.96s\ and\ \overline{d} + 1.96s$ (95% confidence interval) where $\overline{d}$ is the estimated mean difference and
169   s is the standard deviation for the differences [19].
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173   **Results and Discussion**
174   **Data**
175   The study population consists of 190 patients subject to stage 1 to stage 4 CKD. Patients
176   were recruited from the inpatient clinic, University of Malaya Medical Center (UMMC), Kuala
177   Lumpur, Malaysia. Chronological age varied from 35 to 82 years, comprising males (115
178   patients) and females (75 patients). The age range was chosen to ensure that the population is old
179   enough to be experiencing age-related changes in biomarkers.
180   Physical measurements include gender, height, weight, body mass index (BMI), systolic
181   blood pressure (SBP), diastolic blood pressure (DBP), CTCA Calcium Score (CTCA),
182   Creatinine, CKD stage and eGFR. It is observed that the CKD stage for the data involved is
183   between 2 and 5. More specifically, 4% are in stage 2, 50% are in stage 3, 38% are in stage 4 and
184   8% are in stage 5. Table 2 shows the mean result, standard deviation (SD) and data range of
185   CKD patients. For validation purposes of the BA model, 70 percent of the data are used as the
186   training set (i.e., 133 data) while the remaining 30 percent for the testing set (i.e., 57 data).
187

Findings

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189   Development of BA using the indexing method involves several sequences; correlation

190 analysis, computation of weighted average for selected health biomarkers, construction of BA

191 indices from the index equations and estimation of BA based on sample variations.

192   Biomarkers that show an absolute correlation coefficient value exceeding 0.15 are

193 selected for BA estimation. An associated significance test that examine the correlation between

194 the biomarkers and the chronological age for the training data set is summarized in Table 3.

195 Seven biomarkers are found significant for inclusion in the BA estimation. It is observed that

196 creatinine, weight, BMI, eGFR, BP systolic and BP diastolic decrease as age increases, while

197 only the CTCA Calcium increases with age. Height, CKD stage and gender have a low

198 correlation with age and are thus excluded from the BA estimation.

199   Note that some biomarker features have almost similar clinical implications and express

200 high inter-correlation. It indicates the existence of redundancy. To cater for this redundancy, one

201 biomarker with more substantial significance is selected. It is observed from Table 4 that weight

202 and BMI have an absolute correlation coefficient of more than 0.15 (-0.234 and -0.173,

203 respectively) and both show high correlation with each other (0.787). Due to the marginal

204 difference in their correlation with age and clinical significance of the BMI, it is selected for BA

205 estimation. Furthermore, BMI is more reliable to indicate the individual weight, either normal,

206 overweight or obese [20]. Similar procedure is used for selection between the creatinine and eGFR.

207 Both biomarkers represent the renal function. Creatinine and eGFR show mild inter-correlation

208 (0.641) in addition to the absolute correlation coefficient of more than 0.15 (-0.202 and -0.233,

209 respectively). Therefore, eGFR is selected for the BA estimation. With respect to its significance,

210 measurement of eGFR is the most reliable assessment of renal function in CKD [21] where it is

211 used as an index of renal function in clinical practice [22].

212   The weight for each parameter is derived based on the correlation analysis. The higher

213 the correlation, the higher the weighted for the BA parameters. As shown in Table 5, BP

214 Diastolic, CTCA and eGFR are the three highest contributors to the index value for predicting

215 the BA.

216   Accordingly, five biomarkers including BMI, CTCA calcium, eGFR, BP systolic and BP

217 diastolic are selected to estimate the BA index. The weightage for each of the selected

218 biomarkers is then computed using equation (2) to arrive at the following BA index:

219

$$I_{BioAge} = 0.1422I_{BMI} + 0.2046I_{CTCA} + 0.1915I_{eGFR} + 0.1241I_{BPSystolic}$$
$$+ 0.3377I_{BPDiastolic} \tag{11}$$

220   Table 6 summarizes the estimated BA based on the BA index of equation (11). It is

221 evident that all estimated BAs are higher than their corresponding CAs for CKD patients. Note

222 however that the increase in BA varies for patients with identical CKD stages, acknowledging

223 other competing factors that compensate for the difference. It is observed that the gain in BA for

224 the 133 training data set ranges from 3 to 9 years with a mean of 7 years.

225   Overall, the BA for patients suffering kidney disease increased by 5% to 16% from its
226   CA. Figure 2 shows that about 65% of kidney patients in stage 3 and stage 4 increase 9% to 12%
227   from their CA. It indicates that on average the CKD patients at these stages gain between 5 to 9
228   years from their CA biologically.
229   Bland-Altman plot in Figure 3 exhibits the differences in CA and BA against the mean
230   with a 95% confidence interval. All plots are shown below the zero value because this study
231   utilizes data for patients diagnosed with CKD. Note however, the plot does not indicate whether
232   the limits are acceptable or not. The judgment is based on clinical necessity. It is observed that
233   most of the plots lie between the 95% confidence interval (CI), that is, they are inside the limit of
234   agreement (LOA).
235   To explain further, the differences between CA and BA are plotted against the z-score of
236   a standard normal distribution in Figure 4. It is observed that the majority of the plots fall along
237   the straight line, which suggests the difference between CA and BA to follow the normal
238   distribution. Furthermore, the correlation is found to be 0.9715 and the bell test using kurtosis
239   test (0.170) indicates the degree of tailedness in the frequency is close to perfect normal
240   distribution. In addition, the skewness test gives a value of 0.395 where the test value is between
241   -0.5 and 0.5 or nearly zero, which justifies the assumption of normal distribution.
242   To further validate the BA index model, the testing dataset with 57 CKD patients is
243   examined. Figure 5 shows the proximity between BA for the testing dataset and BA for the
244   training dataset. BA of CKD patients increases as the CA increase due to the severity of the
245   biomarkers measurements. On average, the age for patients diagnosed with CKD (stage 1 to
246   stage 4) increases by seven years from their CA (64 years old) to BA (71 years old).
247   Nevertheless, we conceived the small size of the sample and its representation of the population
248   as the limitation of the study.
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Conclusions

253   Recent studies have shown the importance of assessing the functional biomarkers for
254   predicting ageing-related diseases. Ageing-related disease influences the BA of a person. Several
255   statistical approaches have been observed in constructing the BA model, namely, the MLR, the
256   PCA and the KDM.[10] Each method owns its deficiency in the measurement of BA. Therefore,
257   the indexing method is proposed to address issues, especially with redundant biomarkers
258   (through manual examination of redundant biomarkers and selection of the relevant biomarker
259   by experience), over or underestimated BA for a particular age group (by concentration to a
260   particular disease group), and complicated calculations (through a tractable computation for each
261   biomarker).
262   Estimation of BA using the indexing method proposed in this study facilitates a tractable
263   form for each health biomarker. The initially calculated BA index represents the illness severity
264   level for the CKD patients which contributes to proportionate gain in the BA. The level of

265 severity is categorized into high risk, normal risk and at risk so that each patient may be assessed
266 individually. Ten biomarkers have been examined to see their appropriateness for inclusion in
267 the BA estimation.

268   The results of this study show that patients with CKD between stage 2 to stage 5
269 experience gain in BA between 3 to 9 years. This finding may serve the medical practitioners a
270 precaution for treatment in addition to current measurement facilities as it provides a
271 comprehensive reading of the manifold biomarkers. The result is further validated with trained
272 data and visual observations. Notwithstanding, increasing the sample size for the study and
273 inclusion of diverse population may enhance the reliability of the end result.

274   Besides its practicality in the medical field, BA can be potentially useful in many areas,
275 including the insurance industry where age and health play a central role in the premium
276 calculation. Mortality projection based on the BA can be an exciting exploration of human
277 lifetime behaviour that incorporates health biomarkers. In addition, an interesting future work is
278 to develop methods which enables a fair comparison between the various biological age
279 approaches.

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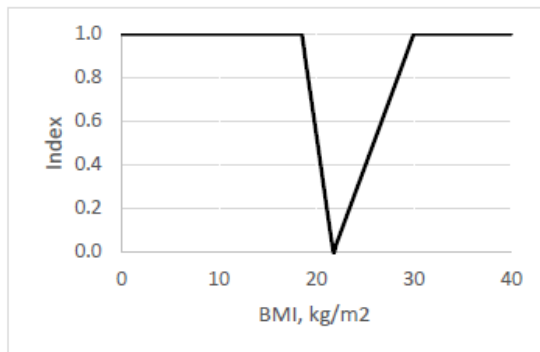
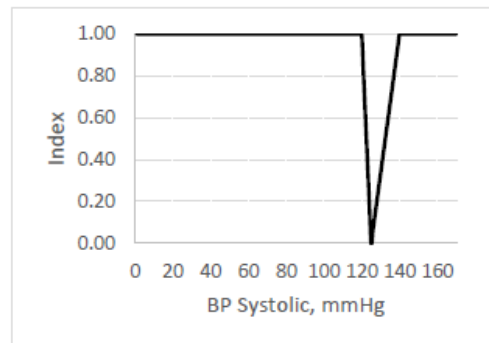
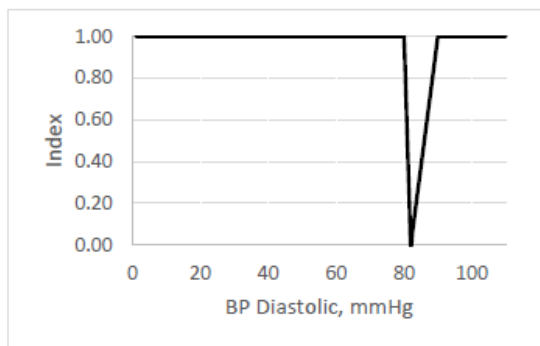
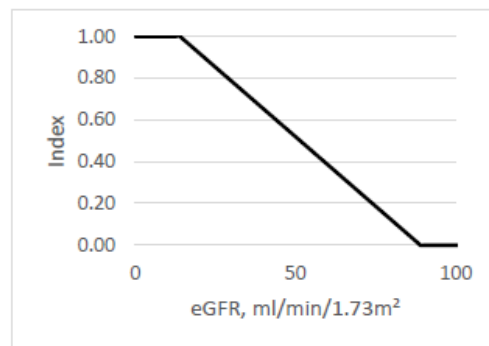
Figure 1

Biomarkers severity index

(a) BMI severity

(b) BP Systolic severity

(c) BP Diastolic severity

(d) eGFR severity

(e) CTCA calcium score severity

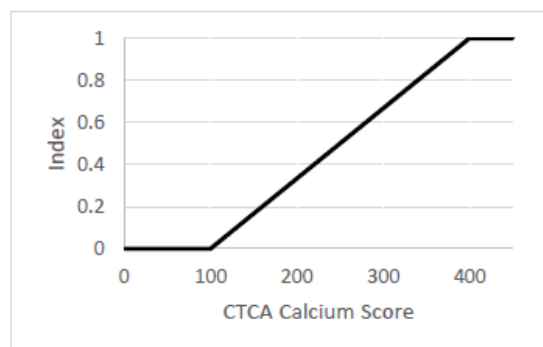



Figure 2

BA increment from CA by CKD stage

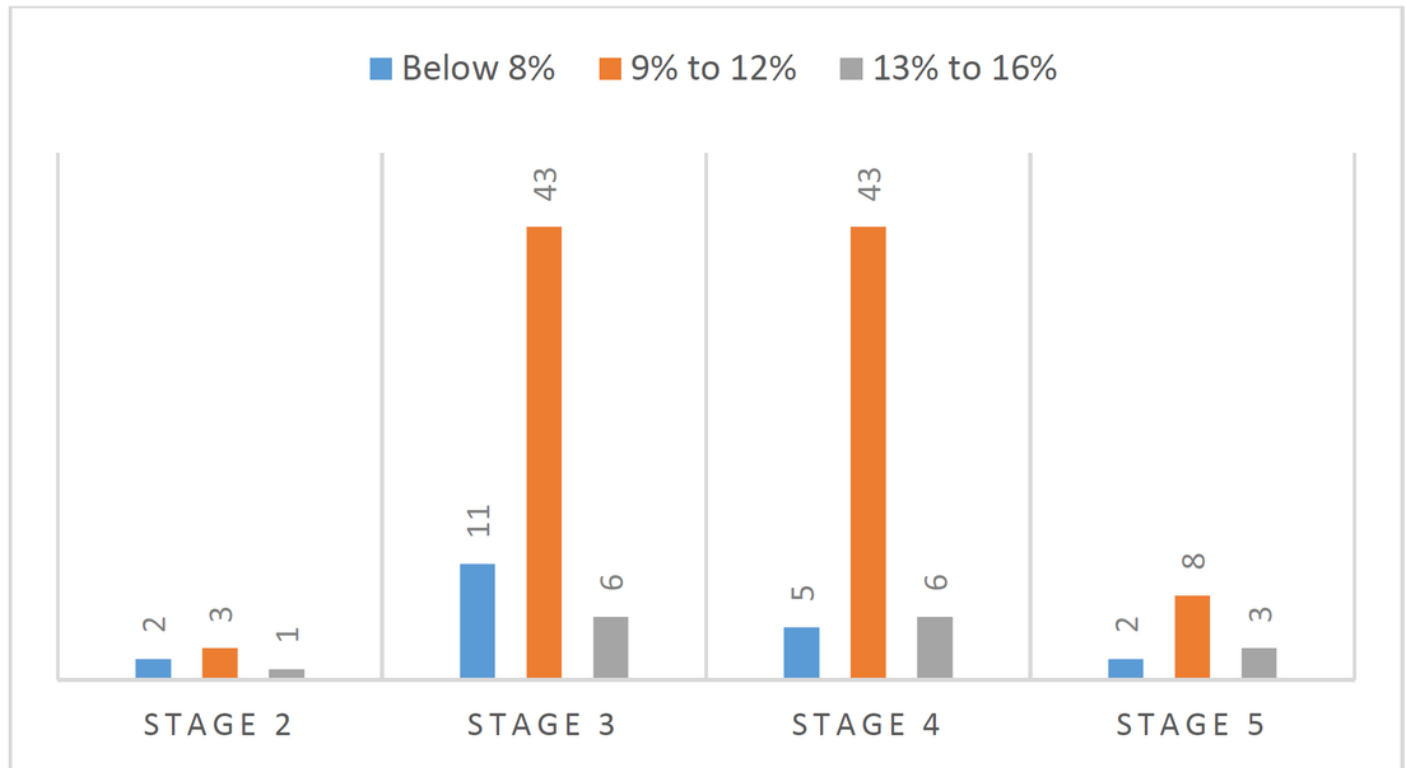



Figure 3

Bland-Altman plot

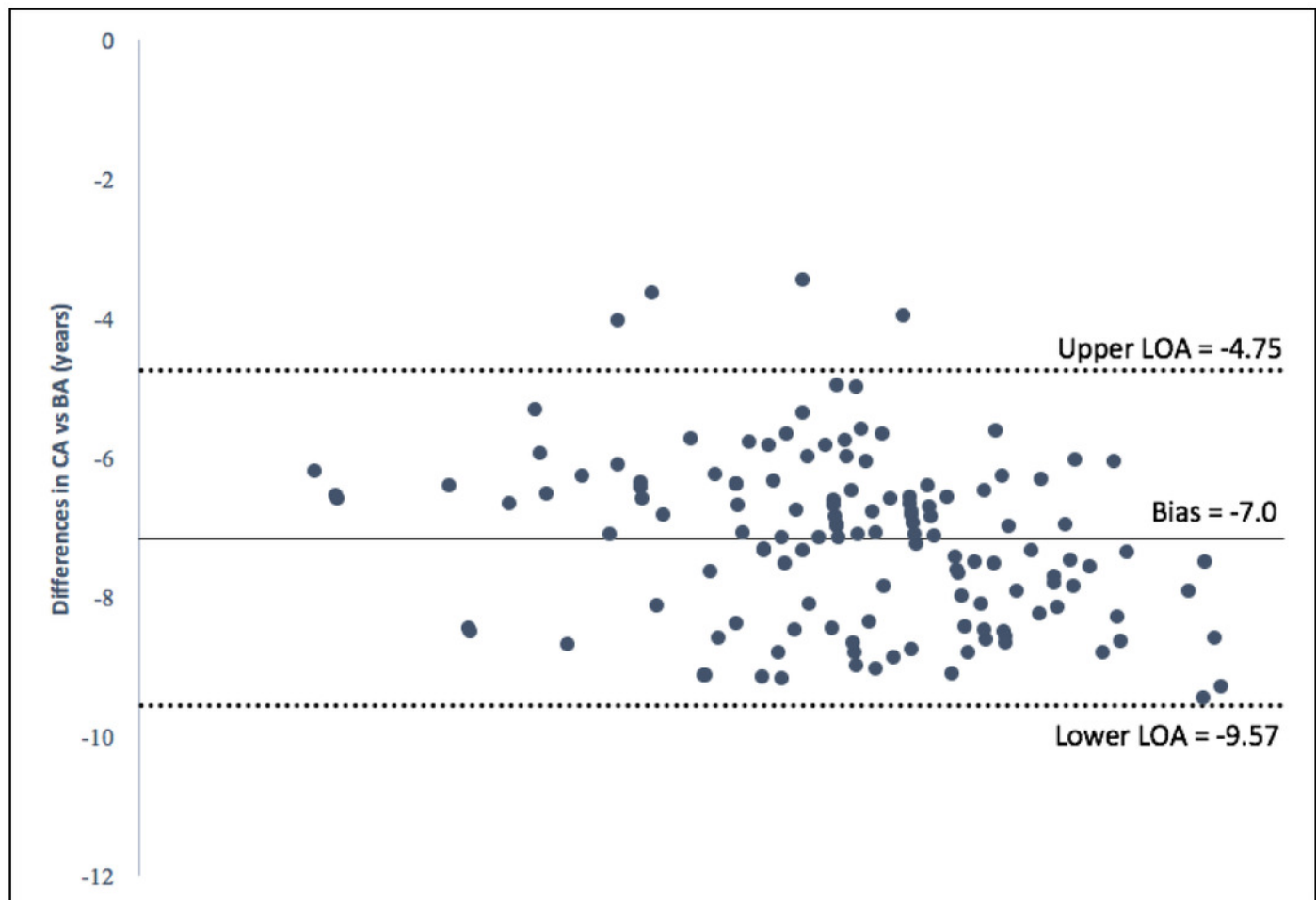



Figure 4

Scatter plot for differences between CA and BA versus the Z-score

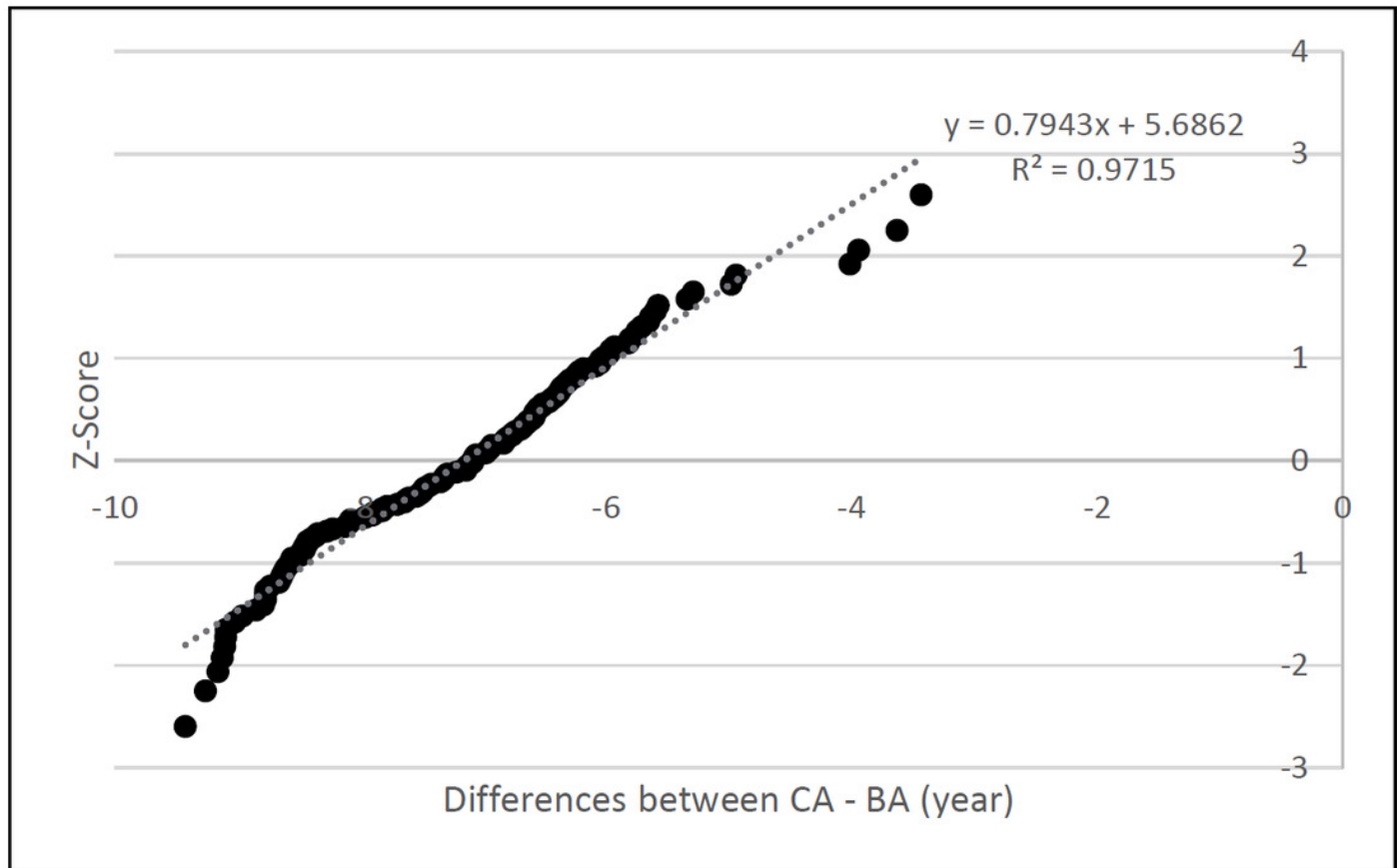
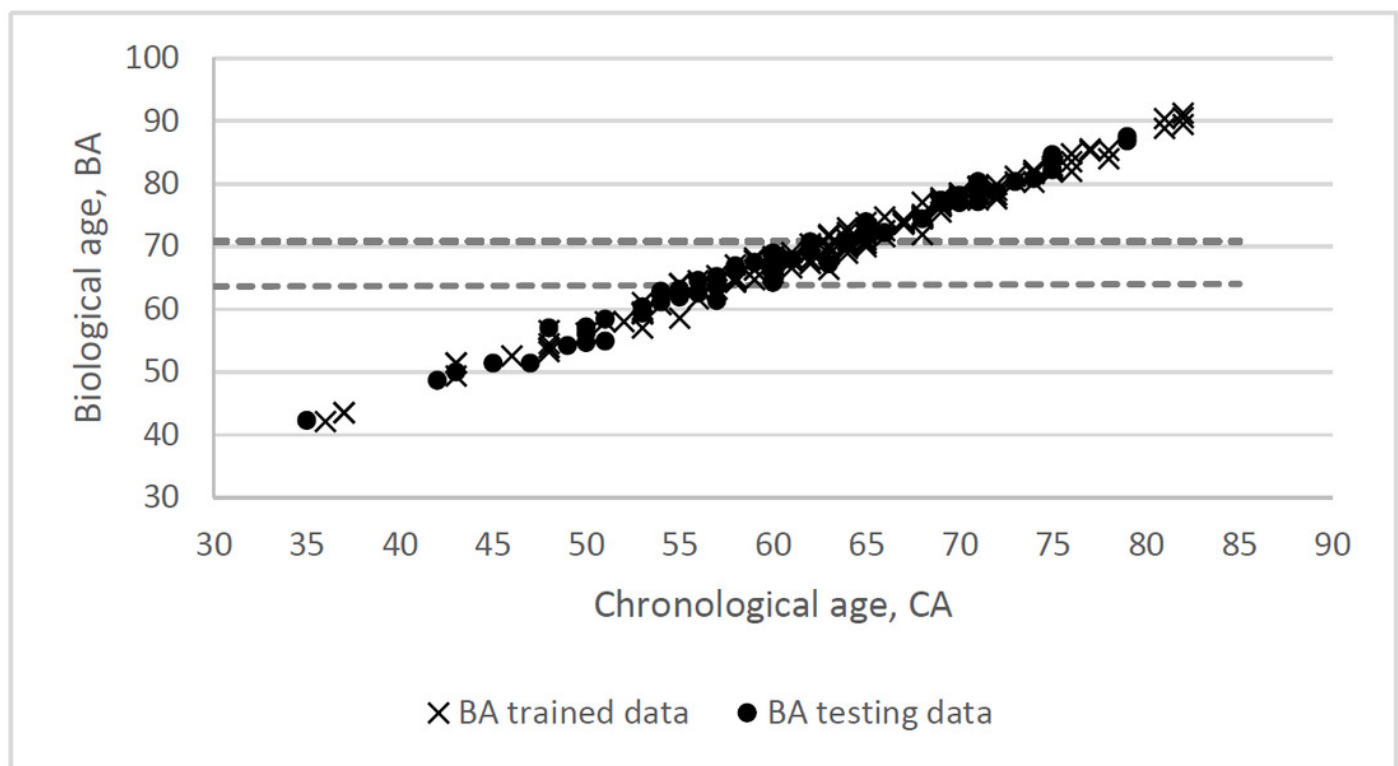



Figure 5

CA versus BA

Reading level for body mass index, blood pressure, eGFR, and calcium score

1   **Table 1:** Reading level for body mass index, blood pressure, eGFR, and calcium score

Health biomarkers	Reading level (Severity level)					Researchers
Body Mass Index (BMI) (in kg/m²)	less than 18.5 (at risk)	18.5 to 24.9 (normal)	25 to 29.9 (moderate risk)		greater than 30 (high risk)	23,24
Blood Pressure (Systolic) (in mmHg)	less than 120 (at risk)	120 to 130 (normal)	130 to 139 (moderate risk)		greater than 140 (high risk)	25
Blood Pressure (Diastolic) (in mmHg)	less than 80 (at risk)	80 to 84 (normal)	85 to 89 (moderate risk)		greater than 90 (high risk)	25
eGFR ml/min/1.73m²	≥ 90 Stage 1 (normal)	60 to 89 Stage 2 (low risk)	30 to 59 Stage 3 (moderate risk)	15 to 29 Stage 4 (moderately high risk)	<15 Stage 5 (high risk)	26
CTCA Calcium Score	0 (no risk)	less than 100 (low risk)	101 to 400 (moderately high risk)		> 400 (high risk)	27,28

General characteristics of the CKD patient biomarkers

1   **Table 2:** General characteristics of the CKD patient biomarkers.

Parameters	Male (n=115)	Female (n=75)	Combined (n=190)
Age (years)	62.88 ± 9.463	61.97 ± 9.988	62.52 ± 9.657
Weight (kg)	76.77 ± 12.305	68.60 ± 14.347	73.54 ± 13.709
Height (m)	1.66 ± 0.0647	1.523 ± 0.060	1.604 ±0.091
BMI (kg/m²)	27.93 ± 0.392	29.469 ± 5.109	28.535 ± 4.6328
CTCA Calcium Score	558.997 ± 733.855	291.853 ± 470.753	453.546 ±654.786
Creatinine (µmol/L)	242.11 ± 130.025	229.59 ± 105.253	237.17 ± 120.718
eGFR (mL/min/1.73m²)	35.513 ± 14.857	28.481 ± 12.432	32.737 ±14.336
BPSystolic (mmHg)	146.88 ± 23.808	148.20 ± 21.075	147.4 ± 22.720
BPDiastolic (mmHg)	76.47 ± 14.906	76.23 ± 13.736	76.37 ± 14.419
CKD Stage	3.41 ± 0.687	3.67 ± 0.081	3.51 ± 0.703

2   **Note:** Mean±SD

p-values for the significance test

Table 3: p-values for the significance test

Parameters	p-values
Weight (kg)	0.003
Height (m)	0.056
BMI (kg/m2)	0.023
CTCA Calcium Score	0.002
Creatinine (μmol/L)	0.010
eGFR (mL/min)	0.004
BPSystolic (mmHg)	0.041
BPDiastolic (mmHg)	0.000
CKD Stage	0.081
GenderT	0.421

Note: Trained data, n=133

Correlation coefficients (Pearson) between CA and biomarkers

1   **Table 4:** Correlation coefficients (Pearson) between CA and biomarkers

Parameter	Age	CTCA Calcium Score	Creatinine	Weight	Height	BMI	eGFR	BPSystolic	BPDiastolic	CKD Stage	Gender
	1.000	0.249	-0.202	-0.234	-0.138	-0.173	-0.233	-0.151	-0.411	0.122	0.017
		1.000	0.021	0.045	0.106	0.007	-0.056	0.009	-0.134	0.062	0.226
			1.000	0.042	0.113	-0.018	-0.641	0.179	0.021	0.716	0.066
				1.000	0.515	0.787	0.544	0.012	0.095	-0.452	0.369
					1.000	-0.108	0.292	0.087	0.115	-0.287	0.713
Age						1.000	0.399	-0.045	0.023	-0.306	-0.081
							1.000	-0.083	0.203	-0.862	0.276
								1.000	0.542	0.121	-0.016
									1.000	-0.138	0.053
										1.000	-0.259
											1.000

Average weighted for significant BA biomarkers

Table 5: Average weighted for significant BA biomarkers

Parameters	Weightage
Weight	0.142
BMI	0.105
CTCA	0.151
Creatinine	0.122
eGFR (mL/min)	0.141
BP Systolic (mmHg)	0.091
BPDiastolic (mmHg)	0.249

BA estimated using the BA index

1   **Table 6:** BA estimated using the BA index

No.	CA	CKD Stage	BA Index	BA	No.	CA	CKD Stage	BA Index	BA
1	64	4	0.5240	69	68	70	3	0.8971	78
2	60	4	0.6699	66	69	56	3	0.9104	65
3	48	3	0.5611	53	70	64	5	0.9575	73
4	65	4	0.5914	71	71	65	3	0.9392	74
5	67	4	0.7351	74	72	37	3	0.6988	44
6	63	5	0.9507	72	73	53	3	0.6813	59
7	60	5	0.7954	67	74	81	3	0.8380	89
8	59	3	0.7737	66	75	36	2	0.6562	42
9	70	4	0.9129	79	76	73	4	0.8726	81
10	66	3	0.9264	75	77	68	3	0.6789	74
11	61	3	0.7143	68	78	70	4	0.8573	78
12	82	4	0.7948	89	79	74	3	0.6681	80
13	57	5	0.8876	65	80	48	4	0.9191	57
14	48	2	0.6292	54	81	64	3	0.8854	72
15	67	4	0.6962	74	82	61	4	0.7756	68
16	43	3	0.8947	51	83	37	4	0.6919	44
17	81	5	1.0000	90	84	65	4	0.7499	72
18	55	3	0.3852	59	85	78	3	0.7795	85
19	63	3	0.7392	70	86	77	4	0.9145	86
20	63	3	0.7570	70	87	69	4	0.8449	77
21	68	4	0.9649	77	88	58	3	0.7076	65
22	60	4	0.7578	67	89	63	3	0.7245	70
23	67	4	0.7214	74	90	63	3	0.9308	72
24	58	5	0.9680	67	91	70	3	0.7933	77
25	58	4	0.7490	65	92	74	4	0.8170	82
26	56	4	0.8093	64	93	53	4	0.6986	60
27	43	4	0.9002	51	94	67	4	0.7660	74
28	62	4	0.8951	70	95	71	3	0.7973	79
29	75	3	0.8297	83	96	53	5	0.6726	59
30	55	4	0.9661	64	97	52	3	0.6456	58
31	62	4	0.6336	68	98	60	3	0.8970	68
32	63	4	0.7361	70	99	73	3	0.7774	80
33	72	4	0.7405	79	100	61	5	0.5983	67
34	76	4	0.8005	84	101	66	3	0.5996	72

35	43	4	0.6770	49	102	71	4	0.9006	79
36	59	3	0.9323	68	103	78	3	0.6414	84
37	72	3	0.6619	78	104	64	4	0.6862	70
38	64	4	0.6324	70	105	50	3	0.6637	56
39	72	4	0.8376	80	106	68	3	0.7547	75
40	46	3	0.7040	53	107	53	3	0.8595	61
41	75	4	0.7902	82	108	75	3	0.7372	82
42	69	3	0.6955	76	109	63	3	0.9176	72
43	66	4	0.6984	73	110	58	4	0.6760	64
44	68	2	0.4181	72	111	82	4	0.9827	91
45	64	3	0.6099	70	112	68	3	0.7254	75
46	55	4	0.9653	64	113	67	3	0.7050	74
47	63	4	0.7009	70	114	61	5	0.8571	69
48	63	3	0.3643	66	115	51	4	0.7512	58
49	69	4	0.8109	77	116	54	5	0.7234	61
50	69	3	0.8070	77	117	72	3	0.5938	78
51	76	4	0.6379	82	118	67	3	0.7171	74
52	68	4	0.7109	75	119	77	4	0.8781	85
53	65	3	0.5285	70	120	60	3	0.6174	66
54	65	3	0.8299	73	121	64	3	0.7517	71
55	59	3	0.7763	66	122	62	3	0.5667	67
56	69	4	0.8914	77	123	82	4	0.9089	91
57	76	3	0.9309	85	124	74	4	0.8258	82
58	69	4	0.7874	76	125	74	4	0.8620	82
59	63	5	0.6161	69	126	62	3	0.7566	69
60	48	3	0.6912	55	127	63	4	0.7086	70
61	59	5	0.9720	68	128	67	3	0.7509	74
62	53	2	0.4258	57	129	59	3	0.6114	65
63	56	2	0.6054	62	130	71	5	0.9078	80
64	65	2	0.7176	72	131	71	4	0.6842	77
65	69	4	0.9307	78	132	65	3	0.6418	71
66	58	3	0.6751	64	133	71	3	0.9161	80
67	57	3	0.6600	63					