1 Comparison of multifrequency bioimpedance measured lean mass to that
2 calculated from anthropomometric measurements in patients with chronic kidney
3 disease
4
5 Sarju Raj Singh Maharjan[1] MRCP, Keruo Jiang[2] MSc, Adrian Slee[3] PhD, Andrew
6 Davenport[1] FRCP
7
8 [1] UCL Department of Nephrology, Royal Free Hospital, University College London
9 London NW3 2PF, UK
10 [2]UCL Clinical and Public Health Nutrition
11 [3]UCL Division of Medicine, Faculty of Medical Sciences, Gower Street, London
12 WC1E 6BT
13
14
15 Sarju Raj Singh Maharjan   srsingh9@hotmail.com
16 Keruo Jiang   nicolejkr8899@gmail.com
17 Adrian Slee   a.slee@ucl.ac.uk
18 Andrew Davenport   andrewdavenport@nhs.net
19
20
21
22 Address for correspondence
23 contact   andrewdavenport@nhs.net   orchid 0000-0002-4467-6833
24 UCL Department of Nephrology, Royal Free Hospital, University College London,
25 Rowland Hill Street, London NW3 2PF
26 tel   44-2074726457   fax   44-2073178591
27
28
29 short title   measuring muscle mass in patients with chronic kidney disease
30
31 key words   chronic kidney disease   triceps skin fold thickness
32 hand grip strength   mid-arm circumference   bioimpedance
33
34 the authors have no conflicts of interest
35
36 word count   abstract   150
37   body   1000
38   figures   1
39   tables   1
40   references 10
41
42
45

46   <u>Abstract</u>

47

48   Patients with chronic kidney disease (CKD) are at increased risk of sarcopenia.

49   Previous studies have proposed equations to estimate muscle mass based on

50   triceps skin fold thickness and mid upper arm circumference, with or without

51   adjustment for hand grip strength (HGS). We wished to evaluate their

52   usefulness compared to multifrequency segmental bioimpedance (MFBIA)

53   measured appendicular lean mass (ALM). We audited 160 CKD patients attending

54   outpatient clinics, 65.6% male, median age 73 (62-81.5) years. We calculated

55   muscle mass using six proposed equations based on anthropometric

56   measurements. These equations over estimated muscle mass compared to

57   MFBIA with a mean bias ranging from 3.4 to 35.9 kg. Apart from one equation,

58   there was a systematic bias, with bias increasing with increasing fat mass

59   (ranging from $r = 0.17$, $p=0.044$ to $r=0.65$, $p<0.001$). For CKD patients we found

60   that most of the previously proposed equations based on anthropometric

61   equations over-estimated muscle mass compared to MFBIA.

62

63

64

65   <u>Body</u>

66   Patients with chronic kidney disease (CKD) are at increased risk of

67   muscle loss due to multiple factors, including dietary restrictions, metabolic

68   acidosis, inflammation, urinary protein losses and vitamin D deficiency [1].

69   Pathological loss of muscle mass, termed sarcopenia is associated with increased

70   mortality. Thus, rapid low-cost screening tests are required to detect

71   sarcopenia to allow for early intervention.

72   Several equations are used to estimate skeletal muscle mass based on

73   anthropometric measurements of height, weight, and either triceps skin fold

74   thickness (TSF), mid upper arm circumference (MUAC), mid arm muscle

75   circumference (MAMC), or hand grip strength (HGS). These models differ in

76   validating anthropometric estimates of muscle mass by computerized axial

77   tomography (CT) [2], magnetic resonance (MRI) [3] or dual-energy X-ray

78   absorptiometry (DXA) [4,5] imaging. None of these imaging techniques are

79   routinely available for patients attending out-patient clinics. Whereas,

80   multifrequency bioelectrical impedance (MFBIA) devices are now available for

81   clinic use. Previous studies have validated MFBIA measurements of muscle mass

82   with DXA in dialysis patients [6,7]. Over time definitions of body composition

83   have changed with the introduction of newer imaging techniques, and so we

84   wished to retrospectively compare appendicular lean mass (ALM) and the

85   equivalent skeletal muscle mass estimated from anthropometric measurements

86   and HGS.

87   A single observer made anthropometric measurements in CKD patients

88   attending outpatient clinics. MUAC and TSF were determined using a non-

89   stretch tape measure and the Harpenden skinfold calliper (HSB-BI, Baty

90   International Ltd, West Sussex, UK). The midpoint of the left upper arm

91   between the lateral acromion and distal olecranon was marked with the left arm

92   bent at 90 °, and MUAC measured to the nearest 0.1 cm. TSF was measured by

93   vertically pulling out the skinfold one inch above the midpoint and calliper jaws

94   applied in the centre of the standard mid-point, and the mean of three

95   recordings taken. Corrected mid-upper arm muscle area (CMUAMA) was derived

96   from MUAC and TSF [2]. HGS was measured using the grip-D strength

97   dynamometer (Takei Scientific Instruments Co, Nigata, Japan). Patients were

98   instructed to use the strength gauge, and measurements made according to the

99   manufacturer's recommendations with patients asked to make three maximal

100   voluntary exertions with the dominant (stronger) arm, with the maximum value

101   recorded.

102   MFBIA were made with an 8 electrode multi-frequency segmental

103   bioimpedance device (InBody 720, Seoul, South Korea) using a standardised

104   protocol [6,7]. The bioimpedance machine was regularly serviced and calibrated.

105   Our retrospective audit complied with the UK National Health Service (NHS)

106   guidelines for clinical audit and service development with all patient data

107   anonymised and complied with UK National Institute for Clinical Excellence

108   (NICE) best practices,

109   www.nice.org.uk/media/796/23/bestpracticeclinicalaudit.pdf.

110   Patient demographics of the 160 CKD patients are reported in table 1.

111   ALM measured with MFBIA was significantly lower compared to all models

112   (Kruskal Wallis p<0.001), apart from total body muscle mass estimated by the

113   equation proposed by Lee at al [4]. We then compared estimates of muscle mass

114   by Bland Altman (Figure 1). Apart from the Lee equation (Figure 1b), all other

115   models not only over estimated muscle mass, but demonstrated a systematic

116 bias, with increasing difference as muscle mass increased (Figure 1a, 1c,

117 1d,1e,1f). Analysing the differences between ALM and muscle mass derived from

118 anthropometric equations: the median difference between MFBIA measured

119 ALM and Lee equation 2.2 (-0.13 to 2.88) kg was significantly less compared to

120 the differences with the other equations; Heymsfeld 37.7 (35-40.6),Tian 23.4

121 (18.8-25.7), Noori 29.3 (26.6-31.8), Noori HGS 30.4 (27.5-32), all p<0.001, and

122 Tian HGS 22 (18.7-24.6), p=0.01.

123 There was no association with estimated glomerular filtration rate, ratio

124 of extracellular to total body water (ECW/TBW) or age, but as fat mass

125 increased, then the difference between MFBIA-ALM and anthropometric

126 derived estimates of muscle mass increased for the models using TSF and

127 MUAMC (Spearman correlation: Heymsfield [2]; r=0.17, p=0.044; Lee [3] r=0.26,

128 p=0.000; Noori [4] r=0.63, p<0.001; Tian [5] r=0.27, p=0.000), and also for those

129 models using HGS (Noori [4] r=0.65, p<0.001; Tian [5] r=0.51, p<0.001).

130 Our results would suggest that apart from the equation proposed by Lee

131 at al [3], based on MRI measurements of muscle mass, the other models used to

132 estimate muscle mass all appear to significantly over estimate muscle mass, and

133 as fat mass increased then the difference between MFBIA measured ALM and

134 these anthropometric estimates of muscle mass rose. MRI is better at

135 estimating fat content than CT, as demonstrated by Figueroa-Bonaparte et al

136 using different radiofrequency pulse sequences then MRI can estimate

137 intracellular fat content due to different precession frequencies of hydrogen in

138 fat molecules compared to water [9]. As muscle from CKD patients contains

139 more intra and extracellular fat [1], then CT scanning will over estimate muscle

140 mass compared to MRI [9].

141   Whereas the equations proposed by Heymsfield [3] and Lee [4] were

142 derived from healthy non-obese patients, those proposed by Tian [5] were based

143 on patents with CKD, and Noori studied haemodialysis patients [4]. Both sets of

144 equations appear to over-estimate muscle mass compared to MFBIA and MRI,

145 with increasing bias with increasing muscle. All imaging techniques will over-

146 estimate muscle mass when patients are volume overloaded, due to the increased

147 water content of muscle [10]. In the study reported by Tian et al, then the mean

148 ratio of ECW/TBW was 0.45 (normal 0.36-0.4) [5], much higher than in our

149 cohort, with >90% of patients having no recorded signs of ECW excess. As their

150 patients had greater ECW then muscle mass would be over-estimated. Although

151 Noori et al did not provide any estimate of volume status, their patients were

152 recruited from eight dialysis centres, with DXA imaging on a non-dialysis day, so

153 patients would be most likely over-hydrated. As such body composition studies

154 should report hydration status.

155   Our retrospective audit in patients with CKD demonstrates that the

156 majority of previously reported equations estimating muscle mass based on

157 anthropometric measurements of TSF and MUAC, appear to over-estimate

158 muscle mass compared to segmental MFBIA, with bias increasing with increasing

159 fat mass. Whereas ALM estimated anthropometric equations based on MRI

160 scanning, which can exclude intracellular fat, most closely correlated with

161 segmental MFBIA measured ALM.

162
163   The authors have no conflict of interest
164

165   References
166   1. Wang XH, Mitch WE. Mechanisms of muscle wasting in chronic kidney
167   disease Nat Rev Nephrol. 2014;10(9):504-16
168   2. Rosenberg IH. Sarcopenia: origins and clinical relevance. Clin Geriatr Med
169   2011; 27:337–339.
170   3. Heymsfield SB, McManus C, Smith J, Stevens V, Nixon DW.
171   Anthropometric measurement of muscle mass: revised equations for
172   calculating bone-free arm muscle area. Am J Clin Nutr. 1982;36(4):680-
173   90
174   4. Lee RC, Wang Z, Heo M, Ross R, Janssen I, Heymsfield SB. Total-body
175   skeletal muscle mass: Development and cross-validation of
176   anthropometric prediction models. Am J Clin Nutr 2000; ;72(3):796-803
177   5. Noori N, Kovesdy CP, Bross R, Lee M, Oreopoulos A, Benner D, et al.
178   Novel equations to estimate lean body mass in maintenance hemodialysis
179   patients. Am J Kidney Dis. 2011;57(1):130-9
180   6. Tian X, Chen Y, Yang ZK, Qu Z, Dong J. Novel Equations for Estimating
181   Lean Body Mass in Patients With Chronic Kidney Disease. J Ren Nutr.
182   2018;28(3):156-164
183   7. Fürstenberg A, Davenport A. Comparison of multifrequency bioelectrical
184   impedance analysis and dual-energy X-ray absorptiometry assessments in
185   outpatient haemodialysis patients. Am J Kidney Dis. 2010;57(1):123-129
186   8. Fürstenberg A, Davenport A. Assessment of body composition in
187   peritoneal dialysis patients using bioelectrical impedance and dual-energy
188   x-ray absorptiometry. Am J Nephrol. 2011;33(2):150-6
189   9. Figueroa-Bonaparte S, Llauger J, Segovia S, Belmonte I, Pedrosa I,
190   Montiel E, et al. Quantitative muscle MRI to follow up late onset Pompe
191   patients: a prospective study. Sci Rep. 2018 8(1):10898
192   10.   Sawant A, House AA, Chesworth BM, Connelly DM, Lindsay R, Gati
193   J, et al. Association between muscle hydration measures acquired using
194   bioelectrical impedance spectroscopy and magnetic resonance imaging in
195   healthy and haemodialysis population. Physiol Rep. 2015;3(1). pii: e12219

196
197
198
199
200
201
202
203

204   Figure 1. Bland Altman graphs comparing multifrequency segmental bioimpedance
205   appendicular lean mass (ALM) and muscle mass estimated by Helmsfield et al [2]
206   (Figure 1a); skeletal muscle mass estimated by Lee at al [3] Figure 1b; lean body

207   mass estimated by Noori at al [4] Figure 1c; lean body mass estimated by Tian et
208   al [5] figure 1d; and anthropomorphic equations including an adjustment for hand
209   grip strength: Noori at al [4] Figure 1e, and Tian et al [5] figure 1f. Graphs show
210   mean bias and 95% limits of agreement (LA).
211
212
213