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Serum cholesterol, body mass index and smoking status do not predict long-term cognitive impairment in elderly stroke patients

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1 **Title:** Serum cholesterol, body mass index and smoking status do not predict long-term cognitive
2 impairment in stroke elderly patients

3
4 **Running title:** Stroke, Cardiovascular Factors and Cognition

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26
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32 University Hospital in Gothenburg for assistance with data collection. A small portion of the data
33 was presented in this paper was presented in a poster at EuroHeartCare 2017

34 **ABSTRACT**

35 **Objectives:** Older stroke survivors are at risk of long-term cognitive impairment, which is
36 associated with a number of modifiable and non-modifiable factors. We aimed to assess the
37 association between the modifiable risk factors, serum cholesterol, low density lipoprotein, high
38 density lipoprotein, serum triglycerides, body mass index (BMI) and smoking status on cognitive
39 function, while controlling for the non-modifiable factors, acute functional impairment, diabetes
40 status and age.

41 **Methods:** A cross-sectional study from a metropolitan University Hospital in Sweden involving
42 older adults (n=149). Assessments occurred at 20 months post-stroke, using the Mini Mental State
43 Examination and serum blood levels of cholesterol, low density lipoprotein, high density
44 lipoprotein and serum triglycerides,.

45 **Results:** Hierarchical linear regression showed that only acute functional impairment significantly
46 contributed to long-term cognitive impairment in stroke survivors. Only 12% of the sample
47 showed healthy cholesterol levels while the remaining patients showed borderline or high
48 cholesterol levels. In terms of BMI, only 2% of the sample were underweight, 38% were within
49 healthy range and 26% were overweight/obese. Only eight women and four men were smokers,
50 therefore our sample of smokers was likely too small to detect any differences between smokers
51 and non-smokers in regard to cognitive outcomes.

52 **Conclusion:** Serum cholesterol, low density lipoprotein, high density lipoprotein, serum
53 triglycerides, BMI or smoking status did not influence cognitive outcomes in older stroke
54 surviving individuals. These findings suggest that modification of these factors may not influence
55 cognitive outcomes in stroke-surviving individuals however should be interpreted as preliminary
56 given limitations in the current study.

57 **Introduction**

58 Ischemic stroke is a leading cause of death and disability worldwide, affecting 15 million people
59 every year¹. The societal cost of stroke is €27 billion annually in the European Union alone[1].
60 Stroke results in long-term impairments in a range of abilities, such as cognitive capacity[2].
61 Cognitive impairment affects over two thirds of stroke survivors, while dementia is present in one
62 third of stroke survivors[2]. Aside from the impact of cognitive impairment on quality of life, it is
63 associated with poorer recovery and functional capacity[3], including increased mortality[4]. In
64 order to achieve the best outcomes for stroke survivors, it is important to understand if modifiable
65 factors may mediate post stroke cognitive outcomes.

66 Many modifiable risk factors are associated with long term cognitive impairment following stroke,
67 including lifestyle factors such as diet, nutrition[5] and smoking status[6] which may provide
68 possible avenues to moderate the risk of long term cognitive impairment following ischemic
69 stroke.

70 In non-stroke affected populations, high density lipoprotein (HDL) is associated with better
71 cognitive function, including a lower prevalence of dementia, and less Alzheimer pathology[7].
72 HDL cholesterol levels have been found to be significantly associated with cognitive function, as
73 measured using the Mini Mental State Examination (MMSE), in approximately 700 Dutch
74 individuals aged 85 years or older[8]. In a subsample of individuals who had previously
75 experienced stroke (n=56), both serum HDL cholesterol concentration and cognitive function
76 were lower, indicating that HDL cholesterol levels may be related to cognitive function
77 following stroke[8]. Further research demonstrates that levels of LDL cholesterol are positively
78 associated with an increased risk of dementia following stroke in 122 individuals aged 65 and
79 above from the United States[9].

80 Body mass index (BMI) is also reported to influence cognitive function. In a sample of over
81 7,000 individuals from the United States, higher BMI in later life predicts a lower risk of
82 dementia[10]. Accordingly, in another study of approximately 2800 community dwelling adults
83 from the United States, underweight individuals (BMI <20) aged >65 years had an increased risk
84 of developing dementia[11]. In both of these studies however, only a proportion of the sample
85 were stroke survivors (2% and unreported, respectively)[11, 12]. In stroke survivors specifically,
86 dementia risk has been reported to be decreased in individuals with higher BMI, however this
87 was seen in a small sample of 53 individuals[13], and therefore the association between post
88 stroke cognitive outcomes and BMI is yet to be compressively explored.

89 Cigarette smoking also appears to influence cognitive function. In approximately 1700 older
90 German adults, cigarette smoking has been reported to be associated with poorer cognitive
91 function[14]. Similarly, in a longitudinal study of approximately 9,000 participants aged >65
92 years, cognitive function was seen to decline more in smokers compared to non-smokers, as
93 measured using the MMSE[15].

94 No study has been designed to measure the impact of the modifiable cardiovascular risk factors,
95 cholesterol, low density lipoprotein, HDL, serum triglycerides, smoking and body mass index on
96 cognition following stroke. In previous studies, only a proportion of the participating individuals
97 were stroke survivors, the time since stroke was either variable or not reported[8, 9]. Given this
98 these risk factors are modifiable, it is important to assess if they contribute to ongoing post stroke
99 cognitive impairment. Therefore, in the current study we aimed to assess if cholesterol, BMI, and
100 smoking status are associated with cognitive impairment long term after stroke onset, after
101 controlling for non-modifiable factors known to influence long term cognitive outcome, following
102 stroke[3].

103 **Methods**

104 **Participants**

105 Eligible individuals were patients admitted to a stroke unit or medical ward of a metropolitan
106 University Hospital in Gothenburg, Sweden between February 1, 1993, and May 17, 1994. While
107 this data was collected some time ago, the senior author of the current manuscript designed the
108 process and also investigated all patients, ensuring that all of the information was collected reliably
109 and consistently across patients. Eligible patients were aged 70 years or older with no upper age
110 limit, so as to counteract the fact that previous cohorts were biased towards being younger than
111 the typical stroke population. Patients were presenting with an acute cerebrovascular neurological
112 deficit that was diagnosed by routine investigations by the physician on call and an acute computer
113 tomography (CT) scan. Exclusion criteria were coma, extracerebral or subarachnoid haemorrhage,
114 previous cerebral lesion requiring ongoing care, cerebral tumour, or a requirement for care for a
115 specific neurological disorder that cannot be handled in a medicine ward, symptoms for more than
116 7 days prior to admission, or residing in a nursing home at the time of admission. Patients were
117 only excluded if they were severely cognitively impaired or could not be placed in the stroke unit
118 or medical wards because they required particular facilities that precluded the randomization of
119 the patient to either ward. Thus patients were not excluded if co-morbidities were present, such as
120 diabetes, myocardial infarction, Parkinson's Disease or Multiple Sclerosis. Eligible patients were
121 assessed and included in the study at admission, at the emergency unit of the hospital. The study
122 was naturalistic and the patients received all components of the hospital's standard care including
123 any form of therapy addressing any speech/language/cognitive impairments exhibited post stroke.

124 **Study protocol**

125 The protocol for the follow-up investigation has been detailed previously[2]. In brief, participating
126 individuals ($n=149$) were contacted initially by mail and later by telephone to arrange hospital
127 appointments. The patients were contacted by the primary investigator or a study nurse. In cases
128 when the participant was unable to visit the hospital ($n=15$, 10%), appointments were offered to
129 take place in patients' homes. All outcomes measured were collected at 20 months following
130 stroke, in order to assess the impact of the modifiable biomarkers on long-term cognitive outcomes
131 following stroke. Written and verbal information was provided to all individuals or their nearest
132 relative when relevant, prior to obtaining informed consent. Ethics approval was granted by The
133 Ethics Committee for Medical Research, at the University of Gothenburg.

134 **Biomarkers collection**

135 Table 1 shows the timeline for collection for data collection. Serum cholesterol, LDL, HDL, and
136 serum triglycerides were collected 20 months post-stroke from peripheral venous blood samples
137 during the hospital appointment. Other biomarkers were also collected at this time, including the
138 acute phase reactant C-reactive protein and the amino acid homocysteine that have been reported
139 elsewhere[16, 17]. Samples were collected into 5ml gel tubes, inverted >5 times, left to
140 coagulate, centrifuged (10 min) and assessed by photometry. Collection and analysis was
141 conducted in an accredited university hospital pathology laboratory, in in the patients' home
142 when necessary. The healthy range of human serum cholesterol is <5mmol/L in adults[18].
143 Individuals were classified as having healthy (<200 mg/dl), borderline (200-239 mg/dL) or high
144 cholesterol levels (>240 mg/dl).

145 **Cognitive assessments**

146 Cognitive assessments were conducted by a neurologist/psychiatrist according to Mini Mental
147 State Examination (MMSE) at a single time point, 20 months post stroke, selected to reflect
148 cognitive impairments at long term following stroke onset. To ensure the screening tool was
149 consistently administered in the same manner, the same person evaluated all the patients. Before
150 commencing, co-assessments and calibrations were done with researchers who were experienced
151 with the method. Diagnoses were reviewed in a three-physician conference. MMSE scores are
152 compiled based on information obtained from eight criteria: orientation to time and place;
153 registration; attention and calculation; recall; language; repetition; and complex commands.
154 Individuals are given a score for each of these measures that is compiled into an overall cognition
155 score out of 30, with lower scores indicating greater cognitive impairment. A score of 25-30 is
156 considered normal cognition; 21-24 is considered mild cognitive impairment, 10-20 is considered
157 moderate cognitive impairment and <10 is considered severe cognitive impairment[19]. The
158 neurologist/psychiatrist conducting the assessment was unaware of the type, size and location of
159 the index stroke throughout the diagnostic and assessment procedure.

160 **Acute functional impairment assessment**

161 Functional impairment was assessed as either improved or unchanged using the Barthel Index at
162 3 days following stroke. The Barthel Index consists of 10 items that measure a person's daily
163 functioning as assessed by the ability to perform activities, including feeding, bathing, grooming,
164 dressing, bowel movements, bladder movements, toilet use, transfers from one location to another,
165 mobility, and stair walking, with lower scores indicating higher disability and higher scores
166 indicating less disability[20].

167 **Body mass index (BMI)**

168 BMI was calculated by dividing body weight in kilograms by body height in meters squared.
169 Individuals were classed as either underweight (<18.5), healthy (18.5-25), overweight (25-30) or
170 obese (>30).

171 **Statistical methods**

172 Statistical analyses were conducted using the SPSS version 20 package. Exploratory analyses
173 were used to determine means and standard errors for acute functional impairment, age, diabetes
174 status, BMI, mean serum cholesterol, LDL, HDL, serum triglycerides, smoking status (as
175 measured using a self-report questionnaire), and MMSE scores. Independent sample *t tests* were
176 used to determine differences in outcomes measures between female and males. Hierarchical
177 linear regression was used to assess the predictive value of acute functional impairment, age,
178 diabetes, serum cholesterol, LDL, HDL, serum triglyceride, BMI and smoking status on MMSE
179 scores. For the purpose of multiple regression analysis and descriptive statistics, raw continuous
180 MMSE scores were used. Outliers were screened using box plots. Multicollinearity was checked
181 using collinearity statistics, variance inflation and tolerance. Independence of errors was checked
182 using the Durbin-Watson test. Histograms and The Shapiro-Wilk Test were used to assess
183 normality.

184 Insert table 1 here

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191 **Results**192 **Characteristics of the cross sectional study population**

193 A detailed loss-to-follow-up-analysis has been previously reported elsewhere[2]. Table 2 shows
194 mean values of acute functional impairment, age, diabetes status, serum cholesterol, LDL, HDL,
195 serum triglyceride, BMI and MMSE scores at 20 months following stroke onset. The mean level
196 of serum cholesterol was clinically elevated (healthy range <5mmol/L in adults)[18], 13% (n=19)
197 of patients had healthy cholesterol levels (<200mg/dL), 28% (n=41) had borderline high
198 cholesterol (200-239 mg/dL) and 35% (n=52) had high cholesterol (>240mg/dL) [21] In 25%
199 (n=37) of patients, cholesterol outcomes were unable to be collected. The mean level of
200 triglycerides in patients was 1.84 mmol/L, which is clinically elevated [30], indeed, only 54% of
201 patients had triglyceride levels considered clinically desirable. The mean LDL levels in patients
202 with a history of coronary artery disease or diabetes (n=39) was 4.08 mmol/L which is considered
203 to be high [30]. In patients without a history of coronary artery disease or diabetes (n=66) mean
204 LDL levels were 3.90 mmol/L which is considered to borderline high [30]. The mean level of HDL
205 was 1.31 mmol/L for men (n=35) and 1.46 mmol/L for women (n=74), which is considered to be
206 clinically normal [30]. The mean MMSE scores indicated mild cognitive impairment (21–24
207 points)[19], 65 individuals (43.6%) had normal cognition, 40 (26.8%) had mild cognitive
208 impairment, 40 (10.7%) had moderate cognitive impairment and 1 (0.7%) had severe cognitive
209 impairment (data was missing for 27 of the 149 individuals). Individuals with cognitive
210 impairment did not differ from individual without cognitive impairment on any of the modifiable
211 risk factors assessed, serum cholesterol, $t(110)=-0.62, p=0.53$; triglycerides, $t(109)=-1.52, p=0.13$;
212 HDL, $t(107)=1.71, p=0.08$; LDL, $t(103)=-0.70, p=0.48$; BMI, $t(97)=-1.00, p=0.32$; smoker,
213 $t(93)=-0.44, p=0.66$. Individuals with cognitive impairment were however found to more

214 functional impairment, $t(147)=-4.75$, $p=0.00$ (no impairment M Barthel Index =2.8, $SD=0.47$,
215 impairment M Barthel Index =2.1, $SD=0.8$). Eight women (8.2%) and four men (7.7%) were
216 smokers. In terms of BMI, 2% ($n=3$) of individuals were underweight, 38% ($n=57$) were within
217 healthy range, 20% ($n=29$) were overweight and 7% were obese ($n=10$). In 34% ($n=50$) of
218 individuals, BMI was unable to be collected as morphometry could not be done when house-
219 visiting or when the patients were bed-ridden. Independent sample t tests showed that men and
220 women did not differ on any of the reported outcomes: acute functional impairment, $t(147)=-0.27$,
221 $p=0.77$; age at follow up, $t(147)=3.12$, $p=0.35$; serum cholesterol, $t(110)=2.23$, $p=0.77$;
222 triglycerides, $t(109)=0.45$, $p=0.66$; HDL, $t(107)=1.73$, $p=0.09$; LDL, $t(103)=0.77$, $p=0.44$; BMI,
223 $t(97)=-0.10$, $p=0.23$; MMSE scores, $t(120)=-1.57$, $p=0.46$. Spontaneous recovery in terms of
224 physical and cognitive function during the first year following stroke has been previously
225 measured and reported elsewhere [2, 22]

226 Inset table 2 here

227

228 **The modifiable risk factors cholesterol, BMI and smoking status are not associated with**
229 **cognitive impairment at 20 months after stroke**

230 To explore the factors affecting MMSE scores long-term after stroke, hierarchical multiple
231 regression was conducted with MMSE scores as the dependent variable and acute functional
232 impairment, diabetes status, age, serum cholesterol, LDL, HDL, serum triglyceride, BMI and
233 smoking status and as predictor variables, at 20 months following stroke. Acute functional
234 impairment (as collected at 3 days post stroke) age and diabetes status were entered into the first
235 block as these were considered to be non-modifiable risk factors. After controlling for these, serum
236 cholesterol, LDL, HDL, serum triglyceride levels, BMI and smoking status were entered into the

237 second block to determine if these significantly explained the variance in MMSE scores. Acute
238 functional impairment (at 3 days post stroke) diabetes status and age explained 23.3% of the
239 variance in MMSE scores and significantly predicted depression scores ($F(3, 63)=6.08, p<0.01$).
240 The addition of serum cholesterol, LDL, HDL, serum triglycerides, BMI and smoking status
241 increased the amount of variance explained to 27.1%, and the model again significantly predicted
242 MMSE scores ($F(9, 63)=2.23, p=0.03$). However, serum cholesterol, BMI and smoking status only
243 increased the amount of variance explained by 3.8%. Table 3 shows the slope of the regression
244 line for each of the individual independent variables. Of these, only acute functional impairment
245 (at 3 days) was found to significantly explain the variance seen in MMSE scores.

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260 **Discussion**

261 This study examined the relationship between the modifiable risk factors serum cholesterol, LDL,
262 HDL, serum triglyceride, BMI, smoking status and cognitive impairment long-term after stroke
263 onset, after controlling for non-modifiable risk factors, acute functional impairment and age, in
264 community dwelling older individuals. In our study, patients showed a mean MMSE score that
265 indicated mild cognitive impairment at 20 months post-stroke. Mean scores of serum cholesterol,
266 triglycerides and LDL were also elevated. This is not surprising given that the vast majority of the
267 sample had borderline or high cholesterol. Indeed, only 13% of the sample had cholesterol in the
268 healthy range. Using hierarchical regression modelling our study demonstrates that acute
269 functional impairment at 3 days post-stroke is associated with worse cognitive outcomes at 20
270 months post-stroke. This result is not unexpected given that previous research indicates that acute
271 cognitive function is a predictor of long-term cognitive impairment[3]. Thus, our study confirms
272 the importance of and prognostic value of early neuropsychological examination in regard to
273 identifying individuals at risk of long-term cognitive impairment in clinical settings, however there
274 are some limitation of the MMSE as discussed below.

275 Interestingly, in this study age was not found to be not associated with cognitive function in stroke
276 survivors; however the sample comprised only older adults, and thus the results could reflect a
277 ceiling effect. Alternately, while multiple studies have previously indicated that increasing age is
278 associated with greater cognitive impairment following stroke[3], a number of other factors have
279 also been demonstrated to be important predictors of longer term cognitive outcomes[3], such as
280 ethnicity, lower social class, left hemispheric stroke, visual field defect, education level and urinary
281 incontinence[3]. A limitation in the current study is that comprised of only elderly Swedish
282 individuals, and did not examine the predictive value of any of the above listed factors such as

283 ethnicity. It is possible that the predictive role of age is more meaningful when studied in
284 conjunction with other relevant predictive factors.

285 Our study did not find an association between serum cholesterol, LDL, HDL, serum triglyceride
286 levels and long-term cognitive function following stroke, indicating that these cardiovascular risk
287 factors are not associated with cognitive outcomes in stroke survivors. This finding is inconsistent
288 with previous research which demonstrates that cognitive impairment is associated with increased
289 serum triglycerides and lipoproteins in non-stroke surviving populations[7]. Indeed, membrane
290 cholesterol has been shown to play a role in the formation and aggregation of amyloid-beta[23,
291 24] the main component of the amyloid plaques that are present in the brains of individuals with
292 Alzheimer's disease[23, 24]. Other studies however have highlighted that decreased cholesterol
293 levels may impair brain function in older individuals, as cholesterol is essential for synapse
294 formation involved in signal transduction as a component of the cell membrane[7]. It appears that
295 when measured in midlife, high cholesterol levels are associated with an increased risk of late-life
296 cognitive decline. However, when measured later in life, high cholesterol levels show no
297 association or an inverse association with cognition decline, whereby low levels of cholesterol are
298 associated with more cognitive impairment[7]. In our sample of older individuals, mean
299 cholesterol levels were clinically elevated at 20 months post stroke (Female M=6.46, SE=0.15,
300 Male M=5.88, SE=0.22). Indeed, only 13% of the sample showed healthy levels of cholesterol,
301 compared to 28% with borderline and 35% with high cholesterol. Therefore the cognitive
302 impairments previously reported to be associated with low cholesterol levels would not likely have
303 been present in the patients who partook in this study, given that most patients had clinically
304 elevated cholesterol levels. This finding is interesting as it indicates that in elderly stroke survivors,
305 that high cholesterol may not contribute to cognitive difficulties[7].

306 Body mass index was similarly not found to be not associated with cognitive function in stroke
307 survivors. This is inconsistent with previous research that indicates that higher BMI is associated
308 with less cognitive decline in older individuals (>65 years)[11]. In the current study, we may have
309 failed to demonstrate a relationship between BMI and cognitive function as only 2% (n=3) of
310 patients in the current sample were underweight. On the contrary, 38% of patients (n=57) were
311 within healthy range, 20% (n=29) were overweight and 7% were obese (n=10). The Mean BMI of
312 the entire sample was in the healthy range (Female $M=24.1$, $SE=0.58$, Male $M=24.9$, $SE=0.57$),
313 thus these patients were not vulnerable to the mechanisms underlying the cognitive dysfunction
314 seen among underweight older adults.

315 Finally, smoking status was not found to be associated with cognitive impairment, contrary to
316 previous research demonstrating that cigarette smoking is associated with poorer cognitive
317 outcomes and dementia in older, stroke and non-stroke affected adults[14]. Interestingly, smoking
318 has been reported to be associated with reduced cortical regional grey matter density in brain
319 regions associated with Alzheimer disease, as assessed using voxel-based morphometry[25] and
320 reduced cerebral blood flow, as assessed using single-photon emission computed tomography[26].
321 Indeed, heavy smoking in midlife is associated with 3-fold increased risk of stroke-related
322 cognitive impairment, even after controlling for various potential vascular confounding factors[6].
323 In the present cross-sectional study, the smoking status of patients in midlife was not a studied
324 variable, and would be worthwhile to explore in future research. A limitation of our study is that
325 only eight females and four males were smokers, and thus while there may be an effect, our sample
326 of smokers was likely too small and lacked sufficient power to detect any differences between
327 smokers and non-smokers in regard to cognitive outcomes. Furthermore, smoking status was

328 obtained using self-report and thus it is possible that patients did not accurately report their
329 smoking status.

330 A further limitation of the current study is that the MMSE is often criticized for being biased
331 toward memory and language, as opposed to executive function and abstract thinking, and
332 therefore could be followed by a more formal assessment in order to more thoroughly assess
333 cognitive impairment [27]. For example, the MMSE does not take into account potential language
334 impairments often associated with a hemisphere stroke[28]. Analysis of a more stringent measure
335 of cognitive ability which is more commonly used in the stroke surviving population and sensitive
336 to cognitive impairment in the post stroke population [29], may have provided a more accurate
337 and specific measure of cognitive ability. While we chose to use the MMSE for this study, in future
338 studies it would be valuable to analyse a more stringent measure of cognitive ability, to examine
339 if cognitive change is associated with various risk factors. Finally, the design of this study does
340 not allow us to determine the cause of cognitive impairment and dementia and therefore, it is
341 unclear whether stroke survivors in the current study experience cognitive impairment resulting
342 from stroke and/or cognitive impairments resulting from other causes. The senior author of this
343 paper has however previously assessed the impact of stroke on cognitive impairment[2], by
344 comparing stroke survivors to a population sample, using the same instruments utilized in the
345 current study[2].

346 This study is the first to report that modifiable risk factors, serum cholesterol, LDL, HDL, serum
347 triglycerides, BMI and smoking status do not seem to be associated with long term cognitive
348 outcomes in stroke survivors, after controlling for acute cognitive impairment and age. These
349 findings suggest that modification of these factors may not influence cognitive outcomes in stroke-
350 surviving individuals. In light of the limitations of our study, such as a small sample size of

351 smokers, healthy BMI and elevated serum cholesterol levels among patients, these results should
352 be interpreted with caution. It would be valuable to explore the relationship between BMI, serum
353 cholesterol and cognition in stroke survivors with low BMI and low serum cholesterol levels.

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459 **Tables**460 *Table 1.*461 **Timeline for data collection**

Timeline for data collection	
3 days post stroke	Acute functional impairment - Barthel Index
20 months post stroke	Serum cholesterol Serum LDL Serum HDL Serum Triglycerides MMSE BMI Age Smoking status Diabetes status

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471 *Table 2.*472 **Key descriptive Statistics in Stroke Survivors**

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Descriptive Statistics

	Mean	Std. Deviation	N
Mini Mental State Examination	24.08	3.68	122
Stroke Severity (Barthel) at 3 days	2.32	0.80	149
Age at follow-up	81.04	5.33	149
Diabetes	0.13	0.34	149
s-Cholesterol (mmol/L)	6.26	1.31	112
s-Triglycerides (mmol/L)	1.84	0.95	111
s-High density lipoprotein (mmol/L)	1.41	0.41	109
s-Low density lipoprotein (mmol/L)	3.97	0.98	105
BMI	24.40	4.17	99
Smoker	0.13	0.33	95

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477 The healthy range of human serum cholesterol is <5mmol/L in adults[18]. A desirable triglyceride

478 level is less than 1.7 mmol/L [30]. LDL of 3.4-4.1 mmol/L is borderline high if there is no coronary

479 artery disease and high if there is coronary artery disease[30]. An acceptable level of HDL is

480 between 1.0-1.5 mmol/L for men and between 1.3-1.5 mmol/L for women [30]. Mini Mental State

481 Examination = MMSE; age is shown in years. Lower MMSE scores represent more cognitive

482 impairment. Scores of 25-30 out of 30 are considered normal cognition; 21-24 as mild cognitive

483 impairment, 10-20 as moderate cognitive impairment and <10 as severe cognitive impairment[19].
 484 Means and Standard Errors of acute functional impairment at 3 days post stroke, age, serum
 485 cholesterol, LDL, HDL, serum triglycerides, body mass index and MMSE scores at 20 months
 486 following stroke onset.

487 *Table 3*

488 **Coefficients, Standard Error of the Coefficients, Standardized Beta Values, P Value and**
 489 **Collinearity Statistics of the Regression Model**

Model	Unstandardized Coefficients		Standardized Coefficients	Sig.	Collinearity Statistics	
	B	Std. Error	Beta		Tolerance	VIF
(Constant)	31.141	6.572		<0.01		
1 Stroke Severity at 3 days	1.951	0.523	0.424	<0.01	0.992	1.008
Age at follow-up	-0.143	0.079	-0.207	0.074	0.988	1.012
Diabetes	0.003	1.252	<0.01	0.998	0.986	1.014
(Constant)	35.761	8.966		<0.01		
2 Stroke Severity at 3 days	2.064	0.564	0.448	0.001	0.902	1.109
Age at follow-up	-0.174	0.089	-0.252	0.057	0.807	1.238
Diabetes	-0.088	1.336	-0.008	0.948	0.915	1.093
s-Cholesterol (mmol/L)	-0.640	0.611	-0.229	0.299	0.284	3.524

Stroke, Cardiovascular Factors and Cognition

s-Triglycerides (mmol/L)	0.695	0.603	0.179	0.254	0.559	1.788
s-High density lipoprotein (mmol/L)	0.945	1.319	0.105	0.477	0.631	1.586
s-Low density lipoprotein (mmol/L)	0.079	0.768	0.021	0.918	0.327	3.060
BMI	-0.052	0.119	-0.058	0.667	0.743	1.345
Smoker	-0.234	1.426	-0.021	0.870	0.806	1.240

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492 Dependent Variable: Mini Mental State Examination. Computed using alpha = .05 * is significant

493 at p<0.05.

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