Scientific Research

Optimal Adiposity Measurement and Risk Stratification in Established Ischaemic Stroke

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Abstract

Background: Prevention strategies post-stroke should target risk factor reduction which includes consideration of weight, diet and lipoprotein profiles. Limited data informs the optimal adiposity measurement post-stroke to target those at highest recurrent risk. This study aims to identify adiposity measurement/s post-stroke that best predict cardiovascular and co-morbid risk. Subjects and Methods: 142 stroke patients (100 males, 42 females; mean age 63 years) participated. Adiposity and metabolic profiles included BMI, waist circumference, waist to height ratio (WHR), triglyceride levels and hypertriglyceridemic waist. The predictive ability of these measures with indices of cardiovascular risk (Cardiovascular Risk Score) and co-morbidity (Charlson's co-morbidity index) were examined. Results: In hierarchical multiple regression models, age and gender controlled, waist ($p = 0.002$), triglyceride levels ($p = 0.006$), BMI and WHR ($p = 0.014$), uniquely and significantly contributed to the variance in cardiovascular risk, in their models. Only one combination of measures (waist and triglyceride levels) improved the predictive ability of waist in cardiovascular risk stratification ($p = 0.001$). In men, waist ($p = 0.013$) and in women triglyceride levels ($p = 0.012$) performed as the best predictors of cardiovascular risk respectively. No combination of measures was superior to triglyceride levels in women or waist circumference measures in men in predicting cardiovascular risk. With Charlson's co-morbidity index as the dependent variable, triglyceride levels significantly contributed to variance of the model with age and gender influences controlled ($p = 0.047$). No combination of measures improved the predictive ability of triglyceride levels for co-morbidity. Conclusion: Waist circumference and triglyceride levels should form a minimum dataset for adiposity when considering cardiovascular and comorbid risk post-stroke.

Keywords

Stroke, Adiposity, Obesity, Abdominal, Measurement, Risk Factors

1. Introduction

Recent improvements in stroke care have significantly improved survival rates [1] [2], resulting in increasing prevalence of those at risk of recurrent vascular events [3]. Patients who survive a stroke or transient ischaemic attack are at particularly high risk for recurrent stroke or subsequent cardiovascular events, including myocardial infarction and death from vascular causes [4]. The 5-year major cardiovascular event rate after an index stroke is estimated to be 24% [5]. Case fatality rates for recurrent stroke are twice those of first stroke [6] [7] with cardiac disease accounting for as many deaths as recurrent stroke [8]. This highlights the increasing need for disease management and targeted secondary prevention interventions. Obesity is associated with higher cardiovascular event rates including stroke [9]. However, in subjects with established stroke and higher cardiovascular risk, patient specific approaches to assessment and management are required.

In stroke, systemic hypertension and obesity, major cardiovascular risk factors, have an interactive relationship [10]. While body mass index (BMI) is established as an independent risk factor for all cardiovascular disease (CVD), attention has recently been drawn to alternate measures of adiposity that provide information about patterns of body fat distribution [11]. It is recognized that abdominally obese individuals (android obesity) tend to have increased risk of hypertension, dyslipidaemia, CVD and premature death compared with individuals with gynoid or gynecoid obesity (fat distributed in the hip and thigh) [12]. Therefore abdominal obesity should represent a better marker of CVD risk and recurrent events post-stroke [13].

Studies addressing adiposity measures and their association with stroke, to date, yield conflicting results. One study in men found a high BMI was associated with a higher risk for stroke [14]; however in a similar study with women, no significant association was demonstrated [15]. Measures of abdominal obesity including waist circumference, waist-to-height ratio found a significant association with the risk of stroke and a stronger association than BMI alone [16] [17]. Studies have not looked in depth at obesity issues in those with established stroke. In one recent study, visceral adiposity as a percentage of total body adipose tissue demonstrated potential as an epidemiological marker, showing high correlations with established markers of cerebrovascular disease in patients with MRI-proven hyper-acute ischaemic stroke [18]. However MRI or CT imaging techniques required are not recommended by the American Heart Association (AHA) as clinically useful measures due to limitations of cost, availability and technical skill [11]. In another study considering BMI and waist to height ratios post stroke, only extreme waist to height ratios (<0.3 or >0.8) were an independent predictor of 12 month mortality in a Mexican mestizo population with acute ischaemic stroke [19].

Since the first publication describing the hypertriglyceridemic waist concept [20], studies such as that conducted by Kahn and Valdez (2003), have illustrated advantages of using this simple screening phenotype of enlarged waist combined with elevated triglycerides (EWET) to identify individuals with lipid over-accumulation [21]. In support, recent observations continue to indicate that obesity and lipid-related components together can provide a better indicator of atherogenic trends [22]-[24]. EWET has demonstrated utility as a predictor of cardiovascular disease for up to 12 years when other risk factors are controlled [25] and only the simultaneous presence of elevated waist girth and triglyceride concentrations have shown an association with coronary artery disease (CAD) assessed by angiography [20]. As a measure it warrants consideration in stroke.

Clinical adiposity indices need to be evaluated further to refine risk stratification and better target weight loss interventions in the stroke population. While evidence exists that waist circumference is better at risk stratifying those with stroke than BMI [16], a better understanding of the association between fat distribution and lipoprotein profiles in people with known cerebrovascular disease may help inform the clinical pathway to address metabolic risk factor burden. The aim of this study was 1) to perform and examine measurements of adiposity and metabolic risk in patients with established stroke and 2) to examine the relationship of these measures with indices of cardiovascular risk and co-morbidity.

2. Materials and Methods

Data collected in this study form part of the baseline data collection from the cardiac rehabilitation adapted for TIA and stroke (CRAFTS) trial (Current Controlled Trials ISCTRN90272638). Subjects with ischaemic stroke were recruited from an outpatient Stroke Rehabilitation Unit, from 4 community based Volunteer Stroke Scheme support groups and TIA subjects were recruited from a TIA clinic in a tertiary hospital in the greater Dublin area. Information leaflets were distributed to potential subjects fulfilling the inclusion criteria. Subjects contacted the principle researcher to indicate interest in participation. All subjects were over 18 years of age, of either gender

and medically stable >3 months post TIA or minor stroke with consent from their consultant neurologist or >1 year post ischaemic stroke with G.P. consent from community services.

2.1. Ethical Considerations and Confidentiality

The study was approved by University College Dublin Human Research Ethics Committee (Ref HREC-19-06-Blake) and Saint James's Hospital SHJ/Adelaide, Meath and National Children's Hospitals AMNCH Research Ethics Committee (Ref REC: 2008/07/03). All participants were volunteers and informed consent was sought. Participants were given a code on entering the study to ensure anonymity.

2.2. Anthropometric Measurements

Subjects wore light clothing and removed footwear during testing. A digital scale was used to measure weight to the nearest 0.1 kg. Height was measured to the nearest 0.1 cm using an anthropometer. BMI was calculated using the formula kg/m^2. Waist circumference was measured in accordance with the ACSM's guidelines for testing. Subjects standing upright and relaxed with a horizontal measure taken at the greatest anterior extension of the abdomen with a flexible yet inelastic tape [26]. Waist to height ratios (WHtR) were calculated with the above measures of waist (cm)/height (cm).

2.3. Fasting Lipids

Fasting lipids were measured from blood samples obtained by venipuncture following an overnight fast of greater than 12 hours by subjects. Serum was analysed using standard enzymatic techniques for total cholesterol and triglycerides. High density lipoprotein (HDL) cholesterol was determined from plasma, low density lipoprotein (LDL) cholesterol using the Friedewald Equation [27]. Elevated triglyceride levels were defined as ≥1.7 mmol/L, validated as a cut-off for the risk of cardiovascular disease [28] (Expert Panel of Detection Evaluation and Treatment of High Blood Cholesterol in Adults, 2001). Participants below this were labelled normal (NTg) and those at or above this level as elevated (ETg). Hyper-Triglyceridemic waist (EWET), a classification determined by combined elevated fasting triglyceride levels (>1.7 mmol/L) and elevated waist girth (>88 cm for women and >102 cm in men).

2.4. Cardiovascular Risk Score

Cardiovascular Risk Score (CRS) was calculated as the 10 year risk of a fatal cardiovascular event. This is an algorithmic score based on age, resting blood pressure, smoking status, diabetic status, total cholesterol and HDL scores [29].

2.5. The Charlson Comorbidity Index

The Charlson comorbidity index (CCI) was calculated for each patient. This index can predict the ten-year mortality risk for patients who may have a range of co-morbid conditions [30].

2.6. Data Analysis

Baseline characteristics were summarised using descriptive statistics of mean (sd) and frequency. Independent t-tests and chi squared tests identified gender differences in measures of adiposity and cardiovascular risk and co-morbidity scores. Pearson's and point biserial correlation co-efficients examined the linear relationship between continuous and dichotomous measures of adiposity and cardiovascular and co-morbidity risk scores respectively. Hierarchical regression models were employed to analyse how well individual measures of adiposity predicted cardiovascular and co-morbidity scores when age and gender were controlled. Each adiposity measure was tested in a separate model and its significance established, with F tests, comparing the full model with the adiposity measure to the nested model with only age and gender. The relative contribution of each adiposity measure was explored by means of standardised regression coefficients and the change in R^2 attributable to each measure. Combinations of unrelated measures *i.e.* waist, BMI and triglycerides were further explored to determine if a more optimal model could predict cardiovascular and co-morbid risk with age and sex controlled. Ancillary analysis explored differences between the performance of adiposity results in men and women, in sepa-

rate hierarchical regression models (controlling for age).

3. Results

From a total of 473 invited to participate by letter and following 4 information talks at community stroke support groups, a total of 142 subjects (96 ischaemic stroke; 46 TIA), with a mean age of 63 years, consented to participate. Baseline characteristics are summarised in **Table 1**. No weight measurement was recorded in two cases (subjects 67 & 73). Participants were unable to stand on the scales due to balance difficulty and alternate means of measurement were unavailable. Lipoprotein results are missing for three subjects (subjects 15, 36 and 38)

Table 1. Baseline characteristics and obesity profiles of participants.

	Men (n = 100)		Women (n = 42)		*p* value
	Mean	(sd)	Mean	(sd)	
Age	62.94	12.9	63.38	12.8	0.852
Waist Girth(cm)	101.45	12.0	96.83	13.6	0.047
Weight (kg)	83.66	13.6	71.54	14.6	<0.001
Height (cm)	171.94	7.1	159.63	7.4	<0.001
BMI (kg/m^2)	28.40	4.8	28.23	6.6	0.187
Waist (cm)/Height (cm) Ratio	0.59	0.1	0.61	0.1	0.015
Cardiovascular Risk Score (CRS)	5.54	4.8	2.90	3.2	0.002
Charlson Co-Mobidity Index	2.27	1.5	1.86	1.0	0.077
Total Cholesterol (mmol/L)	3.99	1.0	4.50	0.9	0.006
High Density Lipoprotein (mmol/L)	1.31	0.4	1.47	0.4	0.036
Low Density Lipoprotein (mmol/L)	2.08	0.9	2.45	0.8	0.021
Triglyceride (mmol/L)	1.37	0.8	1.40	1.2	0.829
	n	(%)	n	(%)	
Smokers	13	13%	10	24%	0.111
Diabetics	16	16%	4	10%	0.311
BMI Categories					0.858
Healthy ≤ 25	27	27%	13	32%	
Over Weight > 25 ≤ 30	45	45%	17	41%	
Obese >30	27	27%	11	27%	
Fasting Triglyceride ≥ 1.7 mmol/L	23	23%	10	24%	0.846
Statin Use	86	86%	38	90%	0.464
Elevated Waist Girth[*]	40	40%	32	76%	<0.001
Elevated Waist/Height (>0.5)	90	90%	37	88%	0.463
Waist/triglyceride Combinations					0.002
Normal Waist/Normal Triglycerides	45	45%	10	24%	
Elevated Waist/Normal Triglycerides	31	31%	22	52%	
Normal Waist/Elevated Triglycerides	12	12 %	0	0%	
Elevated Waist/Elevated Triglycerides	12	12%	10	24%	

due to difficulty drawing bloods. Subsequently triglyceride levels, triglyceridemic waist and Cardiovascular Risk indices are missing for these subjects.

Between sex differences in characteristics were tested initially and summarised in **Table 1**. Men, who are weighted more heavily in the cardiovascular risk algorithmic score, demonstrated an expected higher CRS (t = 3.24, *p* = 0.002). No significant difference was noted for the Charlson co-morbidity index. Despite no significant difference between groups in statin prescription (85% in men and 90% in women), women presented with higher lipoprotein profiles for total cholesterol, HDL and LDL levels (t = 2.80, *p* = 0.006; t = 2.12, *p* = 0.036; t = 2.34, *p* = 0.021 respectively). No significant gender difference in triglyceride levels was observed. When measures of adiposity were considered, men presented with higher waist scores (t = 2.01, *p* = 0.047) and higher waist to height ratios (t = 2.47, *p* = 0.015). Despite significant differences in weight and height measures, no gender difference in BMI scores or when categorised into healthy, overweight or obese categories was noted. A significantly higher proportion of women relative to men were noted in the elevated waist girth category (Chi square 13.52, *p* < 0.001) and interestingly, despite no significant gender differences in triglyceride scores observed, when categorised by hypertriglyceridemic waist categories, a significantly higher proportion of women were observed in the elevated waist/elevated triglyceride category and differences were significant (Chi square 14.75, *p* = 0.002).

The relationship between continuous and categorical measures of adiposity (BMI, Waist girth, Waist to height ratio, triglyceride levels and hypertriglyceridemic waist category) and the Cardiovascular Risk Score and Charlson co-morbidity index was explored initially using Pearsons correlation and Point Biserial correlation co-efficients respectively. Results are summarised in **Table 2**. Using classification by Cohen (1988), coefficient values of ≥0.3 and ≥0.5 were considered to indicate moderate and large strength relationships. Although both cardiovascular and comorbidity risk scores demonstrated moderate relationship to each other (r = 0.33, *p* < 0.001) and waist and triglyceride levels also approached a moderate relationship with each other (r = 0.25; *p* = 0.003), no measure of adiposity demonstrated a moderate or strong relationship with the risk indices. Of note, waist girth demonstrated the strongest linear relationship in relation to cardiovascular risk (r = 0.26, *p* = 0.002).

Cardiovascular risk scores and Charlson co-morbidity index were tested individually with hierarchical multiple regression models to identify how much variance in each index was explained by a measure of adiposity

Table 2. Correlation of adiposity measures with Cardiovascular and Charlson risk scores.

Pearson's correlation		Cardiovascular Risk	Charlson Co-Morbidity Index
Cardiovascular Risk	Pearson's r	------------	0.330**
	Significance (2-tailed)	------------	<0.001
Charlson Co-Morbidity Index	Pearson's r	0.330**	------------
	Significance (2-tailed)	<0.001	------------
Waist (cm)	Pearson's r	0.262**	0.194*
	Significance (2-tailed)	0.002	0.021
BMI kg/m^2	Pearson's r	0.092	0.036
	Significance (2-tailed)	0.282	0.674
Triglyceride mmol/L	Pearson's r	0.018*	0.169*
	Significance (2-tailed)	0.033	0.047
Waist/Height Ratio	Pearson's r	0.143	0.064
	Significance (2-tailed)	0.094	0.454
Point Biserial Correlation			
Elevated Waist/Elevated Triglycerides (Yes/No)	Pearson's r	0.035	0.058
	Significance (2-tailed)	0.677	0.496

**Correlation is significant at the 0.01 level (2-tailed); *Correlation is significant at the 0.05 level (2-tailed).

when age and gender influences were controlled. The measure of adiposity which significantly contributed to the model, generated the highest R^2 change and the largest standardised regression coefficient (beta value), thus making the greatest contribution to the hierarchical model, was considered to be the best predictor of Cardio-vascular risk or co-morbidity. Results are summarised in **Table 3**.

Table 3. Hierarchical multiple regression models.

Dependent Variable	Model 1		Model 2		Contribution of Adiposity Measure	
	Independent Variables	R^2	Independent Variables	R^2	R^2 Change	Standardised Coefficient for Adiposity Measure (Beta)*
Cardiovascular Risk Score	Age & Sex	0.509	**Waist** and Model 1	0.541	0.032	0.182
	$F_{(2,137)} = 70.94$;			$F_{(3,136)} = 53.40$;	$F_{(1,136)} = 9.51$	
	$p < 0.001$			$p < 0.001$	$p = 0.002$**	
		0.519	**BMI** and Model 1	0.54	0.021	0.146
	$F_{(2,135)} = 72.80$;			$F_{(3,134)} = 52.43$;	$F_{(1,134)} = 6.14$	
	$p < 0.001$			$p < 0.001$	$p = 0.014$**	
		0.509	**WHR** and Model 1	0.53	0.021	0.147
	$F_{(2,137)} = 70.94$;			$F_{(3,136)} = 51.11$;	$F_{(1,136)} = 6.14$	
	$p < 0.001$			$p < 0.001$	$p = 0.014$**	
		0.509	**EWET** and Model 1	0.52	0.011	0.107
	$F_{(2,137)} = 70.94$;			$F_{(3,136)} = 49.08$;	$F_{(1,136)} = 3.15$	
	$p < 0.001$			$p < 0.001$	$p = 0.078$	
		0.508	**Triglyceride** and Model 1	0.535	0.027	0.164
	$F_{(2,136)} = 70.18$;			$F_{(3,135)} = 51.73$;	$F_{(1,135)} = 7.08$	
	$p < 0.001$			$p < 0.001$	$p = 0.006$**	
Charlson Co-Morbidity INDEX	Age & Sex	0.082	**Waist** and Model 1	0.106	0.025	0.159
	$F_{(2,139)} = 6.175$;			$F_{(3,138)} = 5.47$;	$F_{(1,138)} = 3.80$	
	$p = 0.003$			$p = 0.001$	$p = 0.053$	
		0.08	**BMI** and Model 1	0.083	0.003	0.054
	$F_{(2,137)} = 5.926$;			$F_{(3,136)} = 4.08$;	$F_{(1,136)} = 0.43$	
	$p = 0.003$			$p = 0.008$	$p = 0.512$	
		0.082	**WHR ratio** and Model 1	0.102	0.020	0.143
	$F_{(2,139)} = 7.175$;			$F_{(3,138)} = 5.21$;	$F_{(1,138)} = 3.10$	
	$p = 0.003$			$p = 0.002$	$p = 0.080$	
		0.082	**EWET** and Model 1	0.09	0.009	0.094
	$F_{(2,139)} = 6.175$;			$F_{(3,138)} = 4.56$	$F_{(1,138)} = 1.30$	
	$p = 0.003$			$p = 0.004$	$p = 0.257$	
		0.076	**Triglyceride** and Model 1	0.083	0.027	0.163
	$F_{(2,136)} = 5.59$;			$F_{(3,135)} = 5.15$;	$F_{(1,135)} = 4.10$;	
	$p = 0.005$			$p = 0.002$	$p = 0.047$**	

BMI: body mass index; WHR: waist to height ratio; EWET: elevated waist, elevated triglycerides; *This is standardised regression coefficient where the predictors have been standardised to have mean of 0 and variance of 1; **Significant contribution to variance in the dependent variable, in addition to age and gender.

Waist, BMI, waist to height ratios and triglyceride levels were all seen to uniquely contribute to the variance in cardiovascular risk, in their respective models. Age and sex accounted for 51% of the variance, while waist measures explained an additional 3.2% of the variance in the cardiovascular risk index (R^2 change 0.032; $F_{(1, 136)}$ = 9.51; $p = 0.002$). Triglyceride levels explained an additional 2.7% of the variance in cardiovascular risk ($F_{(1, 135)}$ = 7.08, $p = 0.006$). BMI and waist height ratios each explained an additional 2.1% of the variance in their individual models achieving statistical significance at $p = 0.014$ levels.

With the Charlson co-morbidity index as the dependent variable, triglyceride levels were observed to significantly contribute to their model. Age and gender accounted for 7.6% of the variance in the dependent variable and triglyceride levels contributing an additional 2.7% of the overall variance in the index (R^2 change 0.027; $F_{(1, 135)}$ = 4.00; $p = 0.047$). Waist circumference accounted for an additional 2.5% variance to the 8.2% attributed to age and sex in the co-morbidity index. The contribution of waist measurement did not reach statistical significance (R^2 change 0.025; $F_{(1, 138)}$ = 3.80; $p = 0.053$).

Ancillary analysis, with models run again for each gender with the influence of age controlled, generated interesting results. In men, waist (3.1% increase; $p = 0.013$), BMI (2.1% increase; $p = 0.042$), waist to height ratios (2.7% increase; $p = 0.023$) and triglyceride levels (2.3% increase; $p = 0.037$) continued to significantly and uniquely contribute to the variance in cardiovascular risk scores. However no measure of adiposity with the exception of triglyceride levels (8.5% increase; $p = 0.012$) contributed significantly to the variance in the dependent cardiovascular risk index in women.

With co-morbidity as the dependent variable, triglyceride levels in men were the only variable that made a unique additional contribution (2.3% increase; $p = 0.032$) to the variance observed when the influence of age was controlled. No measure of adiposity uniquely contributed to the variance in comorbidity index in females when the influence of age was controlled.

Combinations of adiposity items were tested, controlling for age and sex, to see if an optimal data set of adiposity measures for risk determination could be established. One combination improved the predictive ability of waist alone in cardiovascular risk. While waist contributed an additional 3.2% of the variance observed in cardiovascular risk score with the influence of age and sex controlled ($p = 0.002$), waist and triglyceride levels in combination contributed an additional 4.7% of the variance in cardiovascular risk score ($p = 0.001$).

When this combined waist and triglyceride model was tested in men and women separately, controlling for the influence of age, it continued to significantly contribute to the variance observed in the cardiovascular risk index. This is summarised in **Table 4**. However, of note, the model was not superior to triglyceride levels alone in women or waist circumference measures in men. No combination of adiposity measures improved the predictive ability of triglyceride levels for co-morbidity scores, with age and sex influences controlled.

4. Discussion

Clinical measures of adiposity, fat distribution and lipoprotein profiles were employed post-stroke to test their utility in targeting those at increased vascular and co-morbid risk. Warranting consideration first, is the feasibility of these measures in routine clinical practice. Weight and height and therefore BMI are the most common anthropometric measures captured clinically [31]. This was not always feasible in the post-stroke population

Table 4. Combination of adiposity measures in hierarchical multiple regression models.

Dependent Variable	Model 1		Model 2		Contribution of Model 2
	Independent Variables	R^2	Independent Variables	R^2	R^2 Change
Cardiovascular Risk Score					
All	Age & Sex	$0.508 F_{(2,136)} = 70.18$; $p < 0.001$	**Waist** and Triglyceride Levels with Model 1	$0.555 F_{(4,134)} = 41.78$; $p = 0.002$	$0.047 F_{(2,134)} = 7.09$; $p = 0.001$**
Male	Age	$0.494 F_{(1,96)} = 93.74$; $p < 0.001$	**Waist** and Triglyceride Levels with Model 1	$0.537 F_{(3,94)} = 36.40$; $p < 0.001$	$0.043 F_{(1,94)} = 4.40$; $p = 0.015$**
Female	Age	$0.452 F_{(1,39)} = 32.21$; $p < 0.001$	**Waist** and Triglyceride Levels with Model 1	$0.538 F_{(3,37)} = 14.36$; $p < 0.001$	$0.086 F_{(1,37)} = 3.42$; $p = 0.043$**

**Significant contribution to variance in the dependent variable, in addition to age and gender or age.

without specialised equipment, as issues of balance and mobility can limit testing both height and weight. However, waist circumference proved a quick and easy measure, feasible for all participants in this current study and has shown high reliability in testing [32].

Additionally, waist circumference represented the best individual index of adiposity for prediction of cardiovascular risk post-stroke. This concurs with findings from a case controlled study by Winter *et al.*, 2008, identifying superior risk stratification by waist girth and waist to height ratios compared to BMI [16]. However that study failed to look at the contribution of lipoprotein measures to risk stratification. Considering a comparator population of peripheral arterial disease, a systematic review identified waist circumference as the strongest, most consistent predictor of cardiovascular event rates compared with BMI and waist to hip ratios [33]. In addition waist circumference has demonstrated high correlation with abdominal obesity assessed by imaging methods [34] and is associated with increased risk for all adiposity-related morbidity and mortality [35].

Triglyceride levels delivered the next best predictive ability of cardiovascular risk above measures of BMI and waist to height ratios and, of note, was the only index included in this study that demonstrated predictive ability of cardiovascular risk in both men and women when considered separately. Combining waist measures and triglyceride levels in regression analysis demonstrated the highest overall predictive ability of cardiovascular risk, when age and gender were controlled. This combination also made a significant contribution to the vascular risk score in both men and women when genders were considered separately. It was not superior to waist circumference in men or triglyceride levels in women for predicting cardiovascular risk.

Contrary to that initially considered, the potential utility post-stroke of the dichotomous hypertriglyceridemic waist nomenclature (EWET) demonstrated no predictive ability of cardiovascular risk in the regression models employed in this study. Considering both measures as continuous variables appears to be the optimal, minimal criteria for considering cardiovascular risk overall post stroke applicable males and females. When considered within gender, waist girth should be more heavily weighted in males and triglycerides in females.

Triglyceride levels were the only measure that demonstrated predictive ability of co-morbidity. Again this measure performed differently across the genders when considered in separate models. No measure of adiposity contributed to the variance observed in co-morbidity models in women alone. Triglyceride levels significantly contribute to the variance in co-morbidity scores in men. No combination of triglyceride levels and unrelated adiposity measure including waist circumference improved the predictive ability of this measure.

BMI and Waist to height ratio (WHtR) did demonstrate a weaker predictive ability of cardiovascular risk, when the influence of age and sex were controlled. These remained significant contributions to the variance in cardiovascular risk in men only but failed to perform as a predictive index in women. A study of 12 month mortality risk following acute ischaemic stroke demonstrated no predictive ability of BMI tested either as continuous or stratified variable. However a U-shaped relationship was observed in the study between baseline waist to height ratio and mortality. On multivariate analysis, baseline WHtR ≤ 0.300 or >0.800 independently predicted all-cause mortality (hazard ratio 1.91, 95% confidence interval 1.04 - 3.51) [19]. WHtRs in this study were considered a continuous variable and extremes of this measure were not tested. Interestingly a Japanese study noted that WHtR was useful in identifying specific age brackets of middle-aged men and women aged 50 - 69 years of age at higher risk of CVD and was a better predictor than waist circumference of cardiovascular disease, especially in men [36]. This finding was not upheld in this current study, although the specific age bracket (50 - 69 years) was not considered in isolation due to limited sample sizes available.

A higher proportion of women than men, reaching statistical significance in comparison across genders, presented in the EWET category despite no gender difference in triglyceride levels. This variable has recently been shown to have a higher association with diabetes in people with normal BMI [37] and the findings in this study may point towards a stronger cardiometabolic aetiology of stroke in women [38]. A prospective study over 8.5 years of more than 550 women indicated that survival rates dropped significantly in women with an elevated waist girth and high triglyceride concentrations compared to women without these conditions. Moreover, relative risk for all-cause mortality (hazard ratio: 2.2, 95% CI: 1.3 - 3.6, $p < 0.01$) and cardiovascular death (hazard ratio: 4.7, 95% CI: 2.2 - 9.8, $p < 0.001$) associated with hypertriglyceridemic waist was significant even after adjusting for age, smoking, LDL cholesterol and diabetes [24].

Baseline lipid profiles, which were significantly different between men and women for total cholesterol and LDL cholesterol, suggest less stringent secondary control post-stroke in women. This is borne out in emergent trends in US risk factor control post-stroke. A recent report indicates that despite improvement in cholesterol treatment rates by 10% and 8% in men and women respectively, no improvement in control rates was observed

in women [39]. Sub-optimal control of cholesterol in women may have detrimental consequences, as a recent prospective study has shown poor total, HDL and LDL cholesterol results significantly increases the risk of ischaemic stroke in women only [40].

It is clear from the literature that no one ideal measure of adiposity exists. There is growing evidence that the predictive ability of the measures vary for example between genders, age categories and extremes of the measure [14] [15] [19] [36]. Future prospective studies are required to track the predictive ability of measures of obesity on mortality and cardiovascular event rates post-stroke in men and women of different age categories. This study suggests that waist circumference and triglyceride levels warrant inclusion as a minimum data set of obesity and fat deposition post-stroke and cautions against its use as a dichotomous measure. In addition stroke survivors with an increased waist circumference measure and/or elevated triglyceride levels should receive lifestyle counselling including diet and exercise to reduce their future risk profile.

It is important that equivalent anthropometric measures are utilised [33] across future studies post-stroke to facilitate comparison and meta-analysis.

5. Study Limitations

The CRS algorithm employed in this study underestimates risk in those with known cardiovascular disease, however the true value was not of interest here, rather that of a continuous variable that could identify risk. This score is not validated for non-caucasians (n = 2) and those over 74 years old (n = 25). Analysis, rerun with data from these subjects removed, found no reportable difference in results. Limited numbers of participants were categorised as obese by the BMI (n = 38), however adiposity distribution as distinct from BMI derived categories warrants consideration. Finally, regression analysis in women (n = 42) may have limited statistical power and results should be interpreted with a degree of caution (Stevens (1996) recommends a minimum of 15 subjects per predictor in regression analysis [41]).

6. Conclusion

Waist circumference represented the single best adiposity predictor post stroke of cardiovascular risk as measured by the CRS. It was simple and easy to measure in the clinical setting and superior to weight derived indices. Waist circumference and triglyceride levels combined provided the best overall predictive ability of vascular risk and should form a minimum data set for adiposity to guide future risk reduction strategies. Triglyceride levels provided the single best adiposity predictor of co-morbidity in the post-stroke population and again warrant inclusion in a minimum data set on these grounds. Prospective studies are required to identify optimum gender and age related indices of future risk as results from this study, supported by the literature, suggest measures of adiposity may not generalise well across these categories.

Acknowledgements

Conflict of Interest Statement

The authors declare no financial interests or other conflict of interest in relation to the work submitted.

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