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Cerebrospinal fluid opening pressure: The effect of body mass index and body composition

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A B S T R A C T

Objectives: Idiopathic intracranial hypertension (IIH) is strongly related to obesity. The relationship between intracranial pressure, body mass index (BMI), percentage body fat and distribution of body fat in non-IIH pa- tients remains less clear. The aim of this study was to examine the relationship between intracranial pressure and body type in non-IIH patients.

Patients and Methods: Lumbar puncture manometry was used to measure cerebrospinal fluid opening pressure (CSF_{OP}). BMI, in addition to neck, waist and hip circumferences were calculated. Air displacement plethysmo- graphy (BODPOD) was used to assess body composition.

Results: Data was collected from 100 subjects. 11 subjects with conditions known to cause raised intracranial pressure were excluded from analysis. According to Pearson correlation factors displaying a significant re- lationship with CSF_{OP} included: BMI ($R = 0.635$, $p < 0.0001$); waist circumference ($R = 0.498$, $p < 0.0001$), hip circumference ($R = 0.513$, $p < 0.0001$) and percentage body fat ($R = 0.435$, $p < 0.001$). Multivariate analysis indicated that BMI was the only independent factor which predicted CSF_{OP}. Sub-analysis according to gender indicated that BMI was predictive in females and percentage body fat was predictive in males. We did not identify any differences in BMI, percentage body fat or distribution of body fat in 7 IIH patients and 7 wt- matched non-IIH patients.

Conclusion: BMI and percentage body fat both positively correlated with CSF_{OP}, but BMI was more predictive in women and percentage body fat was more predictive in men. We did not find a relationship between distribution of body fat and CSF_{OP}

1. Introduction

The relationship between body mass index (BMI) and intracranial pressure remains controversial, [[1], [2], [3]] although several studies indicate that raised BMI is associated with raised intracranial pressure [4,5].

Rarely, obese females may develop symptoms and signs of raised intracranial pressure in the absence of any abnormalities on brain imaging. Such patients can be diagnosed with idiopathic intracranial hypertension (IIH) [6]. Although the exact cause of IIH remains unknown, it has been postulated that cerebrospinal fluid (CSF) dynamics are somehow influenced by metabolically active compounds, including hormones and cytokines, produced in the adipose tissue of some obese females [7]. Moreover >90 % of women with IIH have a body mass index (BMI) > 30 kg/m^2 [7], and intracranial pressure appears to reduce in some patients who lose weight [8].

Accurate intracranial pressure readings can be made by measuring CSF opening pressure (CSF_{OP}) by lumbar puncture manometry [9]. The normal range for CSF_{OP} is accepted as 10–25 cm CSF [1]. Diagnosis of IIH requires CSF_{OP} > 25 cm CSF [10]. It remains unknown whether metabolically active compounds and therefore percentage body fat also have an effect on intracranial pressure in women who do not fulfil diagnostic criteria for IIH.

Although it is assumed that BMI is closely associated with body fatness, [11] this is not always the case [12]. A body builder for example, may be overweight according to BMI definitions, but may have normal or low body fatness. The opposite may occur in some individuals who have a normal BMI, but display a high body fatness.

Air displacement plethysmography, using the BODPOD measurement system, is a validated densitometry method used to measure body density and can be used with a high degree of accuracy to calculate percentage body fat [13].

In this study we aimed to evaluate the relationship between CSF_{OP} as measured by lumbar puncture manometry and certain body characteristics, including BMI and percentage body fat.

2. Patients and methods

This prospective study was conducted in the neurology out-patients department at Gloucestershire Royal Hospital and the School of Sport and Exercise Science, University of Gloucestershire. The study was approved by the local ethics committee (IRAS: 164,528).

Consecutive patients over the age of 18-years-old undergoing routine diagnostic lumbar punctures were recruited between July 2015 and December 2018. Informed consent was obtained from all study participants. Data regarding various demographics (age, gender) and previous medical conditions were entered into a prospective database.

Lumbar Puncture: All lumbar punctures (LPs) were carried out using a standardized protocol by RW in the LP clinic. Patients were placed in the left-lateral position. CSF opening pressure (CSF_{OP}, cm of CSF or water), were measured using a standard LP manometer.

Hemodynamic data: Systolic (sBP) and diastolic (dBP) blood pressures were measured using an automatic blood pressure cuff 5-minutes before the procedure and used to calculate pulse pressure (PP) and mean arterial blood pressure (MAP).

Body composition: Height (m) and body mass (kg) were determined in order to calculate BMI. Measurements were also made of hip, waist and neck circumference using a standard tape measure. Air displacement plethysmography, using the BODPOD measurement system [11] was used to determine percentage body fat.

Statistics: Patients' demographic and baseline variables were analysed descriptively. Pearson correlation coefficients were calculated between CSF pressure and body fat, pre-measurement MAP, age, waist, neck and hip circumferences and body mass index. Multiple regressions were then performed with CSF pressure as dependent variable and the other variables as predictors. These analyses were carried out for both genders together, and again for males and females separately. All statistical analyses were performed by using SPSS version 20 (IBM Inc.).

3. Results

We identified a study group of 100 subjects. 11 subjects were removed from analysis as they were subsequently diagnosed with IIH or other neurological conditions, which would be predicted to cause raised intracranial pressure. Of the remaining 89 subjects, 48 (54 %) were female and 41 (46 %) male.

3.1. Baseline characteristics

Baseline clinical and demographic data are presented in Table 1. Briefly median age was 51 years (range 18–81 years) in females and 52 years (range 30–74 years) in males. Median CSF opening pressure was 14 cm (range 10–22 cm) for females and 14 (range 10–24 cm) in males. Median BMI was 26.4 kg/m^2 (range 19.1–47.6 kg/m^2) in females and 28.4 kg/m^2 (range 19.6–38.7 kg/m^2) in males. Median percentage body fat (n = 29; high body fat = 11, excess body fat = 9, moderately lean = 8, lean = 1, ultra lean = 0) was 35.7 % (range 22.2–52.5 %) in females and 27.1 % (range 7.4–45.2) in males (n = 29; high body fat = 9, excess body fat = 14, moderately lean = 3, lean = 2, ultra lean = 1)

Table 1. Baseline clinical and demographical data for study population (n = 97).

Variable / median (range)	Female	Male	IIH
n	48	41	8
Age / years	51 (18 – 81)	52 (30 – 74)	34 (18 – 55)
Weight / kg	71.7 (45.8 – 119.7)	83.6 (63.4 – 113.3)	109.7 (81.7 – 129.5)
Height / m	1.61 (1.53 – 1.74)	1.73 (1.63 – 1.94)	1.59 (1.55 – 1.71)
BMI / kg/m^2	26.4 (19.1 – 47.6)	28.4 (19.6 – 38.7)	42.1 (27.9 – 51.9)
Neck circumference / m	0.34 (0.15 – 0.41)	0.40 (0.27 – 0.48)	0.40 (0.33 – 0.43)
Waist circumference / m	0.90 (0.70 – 1.23)	1.00 (0.80 – 1.29)	1.12 (0.79-1.28)
Hip circumference / m	1.02 (0.85 – 1.75)	1.01 (0.56 – 1.24)	1.32 (1.04 – 1.55)
% body fat	35.7 (22.2 – 52.5)	27.1 (7.4 – 45.2)	48.1 (35.7 – 52.5)
Pre-MAP	94 (64 – 128)	94 (73 – 124)	93.3 (60 – 123)

There was no significant difference between CSF opening pressure, age, BMI, hip circumference or preMAP between males and females. Neck circumference and waist circumference were significantly higher in males, but percentage body fat was higher in females.

3.2. Correlation of clinical and demographic data with CSF_{OP}

Age, pre-MAP, BMI, percentage body fat, neck / waist and hip circumference were correlated in 89 subjects with CSF_{OP} (Table 2). Correlations were also performed in males and females separately and in 58 subjects that underwent percentage body fat measurements (Table 3). According to Pearson correlation factors displaying a significant relationship with CSF_{OP} included: BMI ($R = 0.635$, $p < 0.0001$); waist circumference (0.498, $p < 0.0001$), hip circumference ($R = 0.513$, $p < 0.0001$) and percentage body fat ($R = 0.435$, $p < 0.001$). In both females and males there was a positive relationship between CSF_{OP} and BMI (females n = 29, $R = 0.771$, $p < 0.0001$, males n = 29, $R = 0.635$, $p < 0.0001$) and percentage body fat (females n = 29, $R = 0.480$, $p < 0.0001$, males n = 29, $R = 0.572$, $p < 0.0001$). The correlation between CSF_{OP} and BMI, waist and hip circumference was stronger in females compared to males (Fig. 1). The correlation between percentage body fat and CSF_{OP} was stronger in males. Age was only significant when correlating all subjects ($R = -0.262$, $p = 0.013$) and was not significant when performed in males and females separately or in subjects that had percentage body fat measurements.

Table 2. Pearson Correlation Coefficient with Cerebrospinal Fluid Opening Pressure.

	All (n = 89)		Female (n = 48)		Male (n = 41)	
	R	p	R	p	R	p
Age	−0.262	0.013	−0.370	0.10	−0.127	0.431
BMI	0.635	<0.0001	0.712	<0.0001	0.543	<0.0001
Neck	0.176	0.100	0.251	0.085	0.157	0.334
Waist	0.498	<0.0001	0.637	<0.0001	0.394	0.012
Hip	0.513	<0.0001	0.642	<0.0001	0.368	0.020
% body fat	0.435	0.001	0.480	0.008	0.572	0.001
Pre-MAP	−0.11	0.921	0.129	0.381	−0.138	0.391

Table 3. Pearson Correlation Coefficient with Cerebrospinal Fluid Opening Pressure (BODPOD only).

	All (n = 58)		Female (n = 29)		Male (n = 29)	
	R	p	R	p	R	p
Age	0.078	0.560	0.19	0.924	0.260	0.173
BMI	0.607	<0.0001	.771	<0.0001	0.635	<0.0001
Neck	−0.104	0.443	.194	0.314	0.292	0.131
Waist	0.459	<0.0001	.792	<0.0001	0.686	<0.0001
Hip	0.720	<0.0001	0.824	<0.001	0.662	<0.0001
% body fat	0.435	0.001	0.480	0.008	0.572	0.001
Pre-MAP	0.010	0.942	0.073	0.708	0.041	0.835

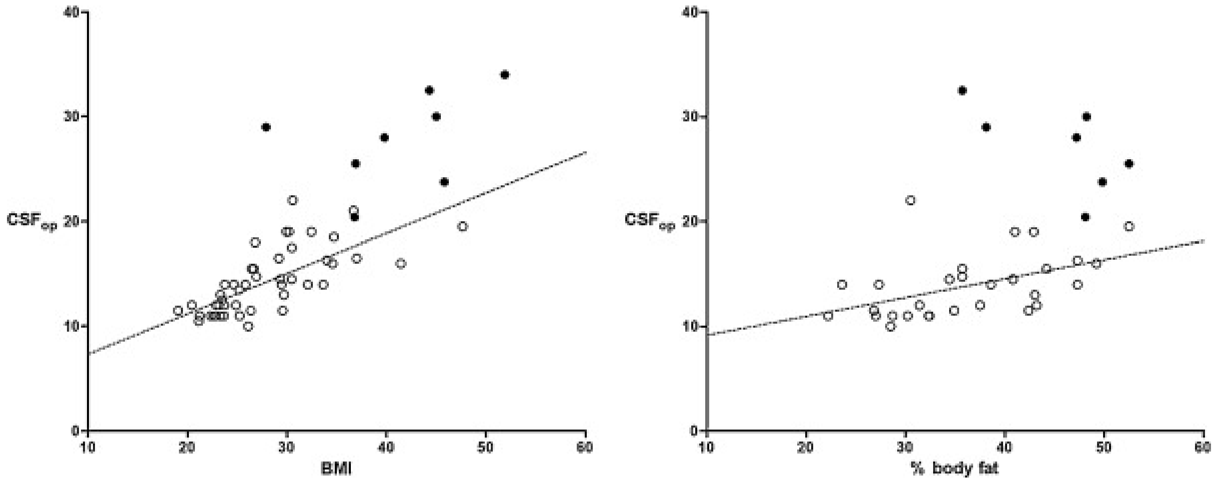

Fig. 1. CSF_{OP} (cm CSF) according to BMI (kg/m^2) and percentage body fat (%) in non-IIH female patients (open circles). According to Pearson correlation there were significant relationships between CSF_{OP} and BMI ($R = 0.712$, $p < 0.0001$) and CSF_{OP} and percentage body fat ($R = 0.480$, $p < = 0.008$). IIH patients (closed circles) were not included in analysis, but demonstrated significantly higher CSF_{OP} than predicted by BMI or percentage body fat in non-IIH female patients.

3.3. Multivariate analysis of factors associated with change in CSF_{OP}

Factors (age, BMI, neck and waist circumference and percentage body fat) demonstrating significant associations ($p < 0.05$) with CSF opening pressure on univariate analysis were evaluated using linear regression (Table 4). Overall BMI was the only independent factor which predicted CSF opening pressure. Sub-analysis according to gender indicated that BMI was predictive in females and percentage body fat was predictive in males.

Table 4. Multivariate Analysis of Factors Associated with Change In Cerebrospinal Fluid Opening Pressure.

Model	**Variable**	**B (95% CI)**	**p**
Males and females	BMI	0.605 (0.251 – 0.527)	<0.0001
Males only	% body fat	0.583 (0.102 – 0.363)	0.001
Females only	BMI	0.681 (0.196 – 0.485)	<0.0001

3.4. Correlation of clinical and demographic data with CSF_{OP} in patients with IIH

Of the 100 subjects recruited into this study, 8 females were excluded because they had a known or suspected diagnosis of idiopathic intracranial hypertension. Baseline clinical and demographic data for these subjects are presented in Table 1.

Median age among 8 female subjects with IIH was significantly less than the 48 female subjects without IIH (34.5 vs. 51.0 years, p = 0.012). IIH subjects when compared to non-IIH females were also heavier (109.7 vs. 71.7 kg, p < 0.0001), and displayed greater BMI (42.1 vs. 26.4 kg/m^2, p < 0.0001), neck circumference (0.40 vs 0.34 m, p = 0.005), waist circumference (1.11 vs 0.90 m, p = 0.0013), hip circumference (1.32 vs 1.02 m, p = 0.0003) and percentage body fat (48.1 vs 35.7 %).

There was no significant correlation between age, BMI, neck circumference, waist circumference, hip circumference or percentage body fat and CSF_{OP} in subjects with IIH. There was no correlation between BMI and percentage body fat and CSF_{op}. IIH patients demonstrated significantly higher CSFop than predicted by BMI or percentage body fat in non-IIH female patients (Fig. 1).

4. Discussion

In this study we compared features of body type with CSF_{OP} and showed that subjects with raised BMI and percentage body fat were more likely to have raised CSF_{OP}. In women BMI was most predictive and in men percentage body fat was most predictive.

In healthy individuals CSF_{OP} ranges between 10 and 25 cm [1]. The positive relationship between CSF_{OP} and BMI remains controversial [[1], [2], [3], [4], [5]]. In the largest retrospective study of over 4000 patients CSF_{OP} was shown to have a positive linear relationship with BMI [4].

In a recent study distribution of body fat was examined in IIH and non-IIH subjects using Dual-Energy X-ray Absorptiometry Scanning (DEXA) [14]. Interestingly CSF_{OP} correlated positively with % truncal body fat, a measure of truncal obesity, but not with BMI. In our study, in both males and females, we observed a positive correlation between waist and hip circumference and CSF_{OP}, although neither were independent factors and we could not attribute raised CSF_{OP} to distribution of body fat. Obstructive sleep apnoea is associated with raised intracranial pressure, [15] and is often associated with increased neck circumference [16], but we found no significant correlation between neck circumference and CSF_{OP} in any group.

Several studies suggest that central adiposity is associated with raised intracranial pressure [17,18]. Cardiovascular and neuroendocrine mechanisms have been proposed and may be more relevant in certain patient groups. Subjects with raised central adiposity demonstrated higher intraabdominal pressures, which may result in increased cardiac filling and subsequent raised intracranial venous pressures and therefore disturbed CSF drainage [17,18]. Adipose tissue displays neuroendocrine function and produces a number of hormones and cytokines [19]. Although central adiposity is associated with a number of adverse medical conditions, including dyslipidaemia, type-2 diabetes and increased cardiovascular risk, it remains unclear whether this relates to specific neuroendocrine function [[20], [21], [22]]. One hormone produced by adipose tissue, Leptin, is thought to modulate intracranial pressure, but does not appear to be raised in patients with IIH [23].

We did not assess patients for presence of obstructive sleep apnoea, which in some patients may have cause raised intracranial pressure [24]. Furthermore, obstructive sleep apnoea is more prevalent in morbidly obese (BMI > 40 kg/m^2) patients [25]. In the present study 2 non-IIH female subjects had BMI > 40 kg/m^2, but neither displayed CSF_{OP} > 25 cm CSF.

Other factors at the time of LP, including levels of anxiety, Valsalva maneuver [26] and positioning [27], may also contribute to accuracy of CSF_{OP}. Where possible physiological variability was minimized by asking subjects to control their breathing and avoid Valsalva maneuver. We found no relationship between MAP and CSF_{OP}. One study showed that increasing age in adulthood after the age of 60-years is associated with reduced CSF_{OP} [28]. Overall we observed a weak negative correlation in CSF_{OP} with increased age, but this was lost in subjects who had BODPOD measurement. In our study technical variability was minimized by ensuring that LPs were carried out using identical equipment and procedural methodology by the same experienced consultant nurse.

Finally we examined any potential differences between 7 patients diagnosed with IIH and 7 wt matched female non-IIH patients. In keeping with a larger study we found no differences in BMI, percentage body fat or distribution of body fat between IIH and weight-matched non-IIH patients [14]. Patients with IIH appeared to have significantly higher CSF_{op} than would be predicted by the relationships between CSF_{op} and BMI and percentage body fat we identified in non-IIH patients.

5. Conclusions

This is the first study to compare whole body composition using air displacement plethysmography (BODPOD) with CSF opening pressure. BMI and percentage body fat both positively correlated with CSF_{OP}, but BMI was more predictive in women and percentage body fat was more predictive in men. Although fat distribution did not correlate with CSF_{OP}, there is mounting evidence to suggest that increased central adiposity is likely to play a role in raised CSF_{OP}. The exact mechanism underpinning this association remains unknown, but may relate to the cardiovascular effects of central adiposity on intracranial venous pressure and the neuroendocrine function of adipose tissue on CSF production and reabsorption. Other mechanisms are likely to be important in patients with very raised intracranial pressure diagnosed with IIH.

Contributions

Richard Warner, Matthew Cole and Keeron Stone collected data. Mara Sittampalam, Benjamin Wakerley and Chris Foy analysed data. Benjamin Wakerley drafted manuscript and supervised study.

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Declaration of Competing Interest

BRW, RW, MC, KS, CF and MS have no competing interests.

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