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Quantitative analysis of intraspinal cerebrospinal fluid flow in normal adults★

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Abstract

The present study quantitatively analyzed intraspinal cerebrospinal fluid flow patterns in 19 normal adults using fast cine phase-contrast magnetic resonance imaging. Results showed increased downward flow velocity and volume compared with upward flow, and the average downward flow volume of intraspinal cerebrospinal fluid decreased from top to bottom at different intervertebral disc levels. Upward and downward cerebrospinal fluid flow velocity reached a peak at the thoracic intraspinal anterior region, and velocity reached a minimum at the posterior region. Overall measurements revealed that mean upward and downward flow volume positively correlated with the subarachnoid area. Upward peak flow velocity and volume positively correlated with spinal anteroposterior diameter. However, downward peak flow velocity and volume exhibited a negative correlation with spinal anteroposterior diameter. Further flow measurements showed that flow velocity in upward and downward directions was associated with subarachnoid anteroposterior diameter, respectively. The present experimental results showed that cerebrospinal fluid flow velocity and volume varied at different intraspinal regions and were affected by subarachnoid space area and anteroposterior diameter size.

Key Words

cerebrospinal fluid; fast cine phase-contrast magnetic resonance imaging; flow; thoracic spinal canal; quantitative; subarachnoid space; neural regeneration

Abbreviations

CSF, cerebrospinal fluid; SAS, subarachnoid space; PC-MRI, phase-contrast magnetic resonance imaging; T2WI, T2-weighted image; FSE, fast spin echo

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INTRODUCTION

Normal cerebrospinal fluid (CSF) circulation is crucial for optimal performance in the central nervous system. Cine phase-contrast magnetic resonance imaging (PC-MRI) has been widely applied in recent years, allowing for quantitative study of CSF flow[1-15]. Existing quantitative and qualitative studies have analyzed CSF flow under physiological conditions and have primarily focused on the aqueduct of midbrain and upper cervical vertebra[16-21]. In addition, intraspinal CSF flow velocity and volume have been introduced in a variety of PC-based measurement models[22-24], which only estimated CSF flow velocity and volume. A computer-based online literature retrieval from the PubMed database between 1980 and 2011 showed little evidence for the quantitative evaluation of CSF flow in normal adults.

The fast PC method collects multi-phase signals within a cardiac cycle, and the imaging time is shorter than conventional PC method[25]. In addition, quantitative results of CSF flow show no significant difference among conventional PC methods[26-27].

In the present study, the correlation between intraspinal CSF cycle pattern, flow direction, flow volume, and spinal anatomical structure in normal adults was quantitatively determined using the fast PC method to provide a detailed understanding of thoracic spinal CSF flow.

RESULTS

Quantitative analysis of subjects

A total of 19 healthy adult humans were included in the present study and in the final results and analyses.

Baseline information

Baseline data from the included 19 healthy adults are shown in Table 1.

Table 1 Baseline information from 19 subjects

Case	Age (year)	Gender	Height (cm)	Weight (kg)
1	23	F	158	62
2	22	M	178	56
3	25	F	166	57
4	24	F	155	46
5	69	F	160	53
6	34	F	150	47
7	22	M	173	125
8	42	F	160	51
9	22	M	176	61
10	72	M	176	80
11	39	M	177	90
12	53	F	155	56
13	24	M	186	87
14	56	M	170	70
15	38	F	160	61
16	39	F	161	65
17	31	F	153	50
18	52	M	170	75
19	68	F	163	70

M: Male; F: female.

CSF image using the fast PC method

Normal CSF circulation is associated with the cardiac cycle and exhibits a regular bilateral flow, demonstrated by flow to the caudal end during the systolic stage and to the head during the diastolic stage[28-29]. CSF signals labeled with white indicated CSF flow to the caudal end; CSF signals labeled with black indicated CSF flow to the head (Figure 1).

Normal CSF values from measurements in normal adults at varying levels

Overall measurements of normal CSF flow velocity and volume are shown in Table 2. Downward flow velocity and volume were greater than upward flow ($P < 0.01$). Downward and upward average flow volumes at five intervertebral disc levels (T_{2-3}, T_{4-5}, T_{6-7}, T_{8-9}, and T_{10-11}) are shown in Table 3. Downward CSF flow volume gradually decreased along with intervertebral disc placement (top to bottom), but there was no significant difference in average flow volume between T_{2-3}, T_{4-5}, T_{6-7}, and T_{8-9} segments ($P > 0.05$). Downward flow volumes at T_{2-3}, T_{4-5}, and T_{6-7} were greater than at the T_{10-11} level ($P < 0.05$ or $P < 0.01$). Upward flow volumes at T_{2-3}, T_{4-5}, T_{6-7}, and T_{8-9} levels were greater than at T_{10-11}, although differences were only significant between T_{6-7} and T_{10-11} ($P < 0.05$).

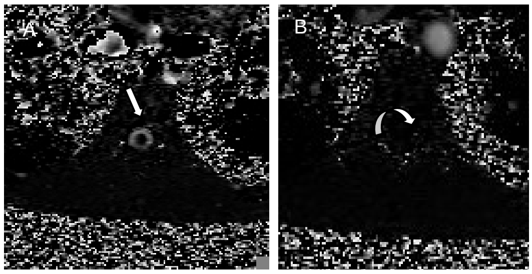

Figure 1 Cerebrospinal fluid (CSF) signals of normal adults using fast cine phase-contrast magnetic resonance imaging.

(A) White signals (straight arrow) indicate caudal CSF flow.

(B) Black signals (curved arrow) indicate cranial CSF flow.

Table 2 Cerebrospinal fluid flow velocity (cm/s) and flow volume (mL/s) in normal adults

Flow direction	Flow velocity		Flow volume	
	Maximum	Average	Maximum	Average
Downward	1.95±0.52	1.09±0.31	1.78±0.58	1.00±0.35
Upward	1.02±0.89[a]	0.62±0.27[a]	0.95±0.98[a]	0.57±0.29[a]

Data are expressed as mean ± SD from 19 subjects. [a]$P < 0.01$, *vs.* downward flow (*t*-test).

Table 3 Comparison of cerebrospinal fluid average flow volume (mL/s) at different intervertebral disc levels in normal adults

Average flow volume	T_{2-3}	T_{4-5}	T_{6-7}	T_{8-9}	T_{10-11}
Downward	1.14±0.31[b]	1.10±0.40[a]	1.02±0.23[a]	0.91±0.36	0.79±0.34
Upward	0.52±0.20	0.63±0.37	0.65±0.27[a]	0.60±0.35	0.47±0.26

Data are expressed as mean ± SD from 19 subjects. [a]$P < 0.05$, [b]$P < 0.01$, *vs.* T_{10-11} level (*t*-test).

Normal CSF values and differences in normal adults

Downward and upward flow peak velocity, as well as mean velocity, were measured in four directions (anterior, posterior, left, and right), obtaining a total of 380 data sets. In a single direction, posterior CSF flow (*i.e.*, CSF flow did not vary with systolic and diastolic changes during a cardiac cycle) was observed in 20 data sets, which accounted for 5.2% of overall measurements. The anterior CSF flow in a single direction occurred in 2 data sets and accounted for 0.5%. However, this flow direction was not observed at the left and right sides. Statistical analysis revealed significantly greater mean flow velocity of anterior upward and downward CSF than in posterior, left, or right ($P < 0.01$). Mean flow velocity and peak flow velocity was at a minimum in the posterior upward and downward CSF. Statistical analysis showed significant differences in peak flow velocity between downward and upward, as well as left and right ($P < 0.01$). In addition, there was a significant difference in mean flow velocity compared with left and right CSF ($P < 0.05$ or $P < 0.01$). Mean flow velocity in left and right CSF was stable, with no significant difference ($P > 0.05$; Table 4).

Table 4 Comparison of cerebrospinal fluid mean flow velocity (cm/s) from four regions in normal adults

Site	Downward peak velocity	Upward peak velocity	Downward mean velocity	Upward mean velocity
Anterior	2.88±1.08	1.52±0.78	1.71±0.70	1.01±0.53
Posterior	1.90±1.15	1.00±0.88	1.07±0.70[a]	0.62±0.58[a]
Left	2.35±0.88	1.23±0.72	1.35±0.53[ac]	0.79±0.39[ab]
Right	2.58±0.76[b]	1.33±0.58[b]	1.44±0.44[ac]	0.83±0.37[ac]

Data are expressed as mean ± SD from 19 subjects. Each subject was measured in five disc levels. [a]$P < 0.01$, *vs*. anterior; [b]$P < 0.05$, [c]$P < 0.01$, *vs*. posterior (*t*-test).

Correlation between overall CSF measurements and corresponding anatomical structures of the spinal canal in normal adults

In the normal adults, measured values of the spinal canal anatomical structure are shown in supplementary Table 1 online. Pearson correlation analysis revealed a significant positive correlation in normal adults between CSF downward and upward mean flow volume, as well as subarachnoid space (r = 0.452 69, 0.384 17, $P < 0.01$), although flow velocity did not relate to area. There was no correlation between CSF flow velocity and flow volume with the spinal area and subarachnoid anteroposterior diameter, although a positive correlation was observed between upward peak flow velocity and flow volume in the low and spinal anteroposterior diameter (r = 0.294 14, 0.311 19, $P < 0.01$). However, downward peak flow volume and mean flow volume negatively correlated with spinal anteroposterior diameter (r = −0.242 78, −0.224 39, $P < 0.05$).

Correlation between partial CSF measurements and corresponding anatomical structure of the spinal canal in normal adults

Pearson correlation analysis revealed a positive correlation between downward peak flow velocity and mean flow velocity in the anterior CSF of normal adults with the anterior diameter, but a negative correlation with the posterior diameter ($P < 0.01$). In contrast, downward peak flow velocity and mean velocity of the posterior CSF negatively correlated with the anterior diameter, but positively correlated with the posterior diameter ($P < 0.01$). Upward peak flow velocity and mean flow velocity of the anterior and posterior CSF negatively correlated with the subarachnoid anteroposterior diameter ($P < 0.01$), which was consistent with correlations verified by overall measurements (Table 5). CSF flow at the left and right sides did not correlate with the anatomical structures.

Table 5 Correlation (r) between cerebrospinal fluid partial measurements and corresponding anatomical structures of the spinal canal

Parameter	Anterior diameter (cm)	Anteroposterior diameter (cm)	Posterior diameter (cm)
Anterior			
Downward peak velocity	0.449 74[a]	0.225 31[b]	−0.587 43[a]
Upward peak velocity	−0.336 73[a]	−0.227 36[b]	−-0.508 60[a]
Downward mean velocity	0.391 25[a]	0.210 56[b]	−0.498 24[a]
Upward mean velocity	−0.348 07[a]	−0.226 30[b]	−0.496 93[a]
Posterior			
Downward peak velocity	−0.511 66[a]	−0.381 54[a]	0.475 58[a]
Upward peak velocity	−0.480 48[a]	0.301 31[a]	0.420 43[a]
Downward mean velocity	−0.448 81[a]	−0.358 70[a]	0.424 52[a]
Upward mean velocity	−0.433 44[a]	0.302 71[a]	−0.393 76[a]

[a]$P < 0.01$, [b]$P < 0.05$.

DISCUSSION

In the present study, fast PC examination showed an upward and downward change in CSF flow, which was related to cardiac cycle. In overall CSF measurements, downward mean flow volume gradually decreased, but remained greater than upward mean flow volume. CSF flow gradually decreased from top to bottom in the spinal canal, but little is known about the remaining CSF flow. CSF arising from the lateral and third ventricles may flow into the fourth ventricle along the midbrain aqueduct. Indeed, CSF flows into the subarachnoid space *via* median and lateral apertures of the fourth ventricle, while some CSF also flows downward, which is crucial for CSF exchange and pressure compensation[30]. Due to the lumbar venous plexus, the vertebral canal volume expands[30] and functions as a large storage tank, so it is possible that downward CSF flow is greater than upward flow. When CSF flows downward along the canal, with the exception of the vertical direction, some CSF flows in bilateral directions along the nerve root axis, which is clearly visualized in magnetic resonance myelography coronal images[31]. To determine whether CSF returns, Steer *et al* [32] injected a blue suspension solution into the pig and sheep spinal subarachnoid space, revealing blue particles in the brachial plexus, sacral nerve plexus and branches, thoracic nerve, and nerve-innervating muscles at 4–21 days post-injection. These results demonstrate that CSF flows peripherally along the spinal nerve. If CSF did flow into the surrounding area along the spinal nerve, CSF flowing from the intracranial region into the spinal canal should be partially refluxed. In this scenario, CSF flow volume would decrease and downward mean flow volume would become greater than upward flow, which was confirmed by results from the present study. Results from partial measurements demonstrated a negative correlation between anterior and posterior upward mean flow velocity and the subarachnoid anteroposterior diameter.

Alperin *et al* [33] hypothesized that reliability of PC-MRI in fluid quantitative studies is dependent on consistency within the luminal border. To avoid errors, the present study maintained consistency in overall and partial measurements. In annular measurements of each disc dimension, the axial spinal cord area was determined based on measured data and the spinal contour equal to axial T2-weighted fast spin echo (T2WI FSE) sequences was subsequently outlined on the corresponding PC-magnitude diagram to determine the inner boundary of annular measurements, as well as the window width and level. According to the axial subarachnoid area, the outside boundary represented by the axial T2WI FSE sequence was outlined in the corresponding PC-magnitude diagram. Therefore, the errors of measured value were reduced to a minimum.

Previous studies have explored CSF circulation patterns[34-35], but little is known about intraspinal CSF flow patterns. In the present study, in addition to intraspinal CSF flow analyses, CSF flow was also evaluated in four directions. Results showed that CSF flowed in all four sites, with stable flow at left and right sides. Significant differences in flow were observed between anterior and posterior, which was possibly associated with subarachnoid space changes resulting from frequent bending. CSF may be affected by the subarachnoid diameter line, which leads to changes in flow velocity, as well as subarachnoid anteroposterior diameter. To ensure normal intraspinal CSF flow velocity and volume, CSF flow in the subarachnoid space at left and right sides was stably maintained. Results demonstrated that flow velocity and volume from overall measurements did not correlate with spinal cord and subarachnoid areas, but did significantly correlate with the spinal anteroposterior diameter.

In normal adults, intraspinal CSF flow velocity and volume were quantitatively measured using the fast PC method. Results demonstrated that CSF flow velocity and volume were greater in the downward fashion than in the upward fashion, and flow gradually decreased from top to bottom. Between four sites of CSF flow, flow velocity was slowest in the posterior site, but stable in the left and right sides, and intraspinal CSF flow was affected by the spinal arachnoid subarachnoid area and anteroposterior diameter size.

SUBJECTS AND METHODS

Design

A clinical, neuroimaging observation.

Time and setting

Experiments were performed from February 2010 to May 2011 at the Department of Medical Imaging, Second Hospital of Hebei Medical University, China.

Subjects

A total of 19 healthy adult volunteers were selected from the Department of Medical Imaging at the Second Hospital of Hebei Medical University, China between February 2010 and May 2011, including 8 males and 11 females. The subjects were aged 22–72 years, with an average of 39.7 years. MRI examination confirmed that all subjects had no vertebral or spinal deformities or affections, no spinal cord inflammation or degeneration, and no syringomyelia.

All experimental procedures complied with ethical requirements stated in the *Declaration of Helsinki*, and all subjects provided signed, informed consent.

Methods

MR scan

The subjects were scanned using a Signa Excite HD3 T high-field MR scanner (GE, Bethesda, MD, USA). First, sagittal T2WI FSE sequence scanning was performed utilizing the following parameters: repetition time = 2 500 ms, echo time = 107 ms, 3.0-mm thickness, 0.5-mm space, 38 mm × 38 mm field of view, 384 × 224 matrix, number of excitations = 2; and 2 minutes and 22 seconds scanning time. Sagittal T2WI FSE sequences were obtained from T_{2-3}, T_{4-5}, T_{6-7}, T_{8-9}, and T_{10-11} segments for fast cine-PC sequence and axial T2WI FSE sequence scanning, and the scan line was vertical and corresponded with the subarachnoid long axis. Fast cine-PC sequence scanning parameters were as follows: minimum value echo time; 4 mm slice thickness; 0 mm space; 20° flip angle; 31.25 bandwidth; 26 mm × 26 mm field of view; 256 × 128 matrix; number of excitations = 2; 15 cm/s velocity encoding; encoding direction was from cranial to caudal area; 40-second scan time. Axial T2WI FSE sequence scanning parameters were as follows: 2 920 ms repetition time; 107 ms echo time; 5.0 mm slice thickness; 1 mm layer space; 20 mm × 20 mm field of view; 288 × 192 matrix; number of excitations = 2; 1 minute and 42 seconds scanning time. Subjects were quietly breathing during scanning.

Image measurement

The scanned image was measured using the fast-cine

PC sequence, and all subjects maintained stable breathing prior to scanning. A total of 60 frame images of CSF flow during a cardiac cycle were obtained from a single scan. The first 30 frames represented the phase image, while the latter 30 frames represented the magnitude image. Thirty phases from each cardiac cycle represented the fluid measurements of bidirectional flow. The region of interest was outlined in the CSF flow magnitude-velocity image using track balls, then the region of interest was copied to phase-velocity image and the range was subsequently determined. The number of pixels in the region of interest in each image was analyzed using Function Tool software (GE) on an Advantage workstation 4.2 to obtain CSF flow direction and velocity from each scanning during a cardiac cycle. Flow velocity values were expressed as data and as a graph to indicate CSF flow. Flow volume was the multiple of flow velocity and area. Because the encoding direction was from cranial to caudal end, the positive value in a cardiac cycle was the head-to-caudal direction (downward), while the negative value was the caudal-to-head direction (upward).

CSF flow parameter measurement

Using fast-cine PC sequences, image measurements from each disc level were divided into overall and partial measurements.

Overall measurement: CSF flow was measured in the entire subarachnoid space. First, the spinal cord area at the axial dimension was measured twice by two physicians, and the average value was calculated. Accordingly, window width and level were adjusted in the corresponding levels of fast-cine PC sequence magnitude diagram to clearly outline the image. The measured spinal cord area was the same as the axial area, and the window width was determined at 480/80 Hu. Prior to measurements, the spinal cord was outlined and served as the inner boundary of the measurement. The outside boundary of the subarachnoid space was subsequently drawn (underlined region did not exceed the subarachnoid space boundary). The upward and downward peak flow velocity and mean flow velocity of CSF were measured from five intervertebral disc levels under a cardiac cycle, and then the corresponding flow volume was calculated. The CSF flow difference was determined between five intervertebral disc levels; correlations between CSF peak flow velocity and flow volume, as well as mean flow velocity and flow volume, with spinal cord area, spinal anteroposterior diameter, subarachnoid space area, and subarachnoid anteroposterior diameters were analyzed.

Partial measurement: the circular subarachnoid area in the spinal canal was divided into four parts – anterior, posterior, left, and right. According to window width and level in the fast cine-PC sequence magnitude diagram, the spinal cord boundary was outlined, and a straight line was drawn along four directions of the spinal cord to form a “井” shape. The measurement range was then determined along the lines, and CSF flow velocity was measured in each region. Measured parameters included CSF upward and downward peak flow velocity and mean velocity within a cardiac cycle, and the difference in flow velocity among the four regions was compared. In addition, correlations between CSF flow velocity in the four regions with subarachnoid anteroposterior diameter and spinal anteroposterior diameter were analyzed.

Normal anatomical structure parameter measurements

The following parameters were separately measured for each disc dimension using axial T2WI FSE sequences: subarachnoid area, spinal cord area, spinal anteroposterior diameter, anterior spinal subarachnoid diameter line, and posterior spinal subarachnoid diameter line.

Statistical analysis

Data were statistically analyzed using SAS 8.0 software (SAS Software Institute, Kerry, North Carolina, USA) and were expressed as mean ± SD. CSF flow velocity and volume from overall and partial measurements were compared using the *t*-test. Correlation analyses between flow velocity, flow volume, and anatomical structures were performed using Pearson correlation analysis. $P < 0.05$ was considered statistically significant.

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Author contributions: Leka Yan was responsible for data acquisition, integration, and statistical analysis, and also drafted the manuscript, revised the study, and performed statistical analyses. Huaijun Liu had full access to the study concept and design. Hua Shang assisted in data integration.

Conflicts of interest: None declared.

Ethical approval: The present study was approved by the Ethics Committee at the Second Hospital of Hebei Medical University in China.

Supplementary information: Supplementary data associated with this article can be found in the online version, by visiting www.nrronline.org, and entering Vol. 7, No. 15, 2012 after selecting the “NRR Current Issue” button on the page.

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