Lumbosacral Cerebrospinal Fluid Volume in Humans Using Three-Dimensional Magnetic Resonance Imaging

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BACKGROUND: The clinical response to spinal anesthesia is influenced by lumbosacral cerebrospinal fluid (CSF) volume, which is highly variable among patients.

METHODS: Lumbosacral magnetic resonance images were obtained in 71 patients using a long echo time (TE = 198 msec), fast spin echo sequence with fat suppression. Three-dimensional images were created and lumbosacral CSF volume was estimated using a threshold-based region growing algorithm.

RESULTS: A validation experiment using a water bath and cadaveric spinal cord demonstrated that the technique was accurate (1.4 ± 0.4% difference between estimated and measured). The coefficient of variance was 0.42% among the three estimated CSF values per subject. The mean calculated volume was 35.8 ± 10.9 mL with a range of 10.6–61.3 mL. Lumbosacral CSF volume was widely variable among patients and was inversely proportional to body mass index ($r = -.276$, $P = 0.02$). Mean calculated lumbosacral CSF volumes were smaller in the group of subjects that had radiographic diagnoses of spinal stenosis when compared with subjects with no diagnosis (mean difference −8.4 mL, 95% CI of the difference, −16.1 to −0.8 mL, $P = 0.03$) and were not different when compared with those with herniated disk disease (mean difference −6.4 mL, 95% CI of the difference −14.7 to 1.9 mL, $P = 0.19$).

CONCLUSIONS: Application of this technique to clinical investigations may further enhance our understanding of spinal anesthesia.

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Factors associated with the variable clinical response to spinal anesthesia are local anesthetic dose, baricity, patient positioning, site of injection, body habitus, speed of injection, and age (1). Interindividual variability in lumbosacral cerebrospinal fluid (CSF) volume may be an under-estimated factor associated with variation in the spread of intrathecal local anesthetic. This volume cannot be accurately predicted on the basis of physical characteristics such as height and weight (2,3). Accurate noninvasive estimation of CSF volume using imaging technology depends on the ability to differentiate CSF from surrounding tissue. This allows calculation of intrathecal volume and subtraction of the spinal cord and nerve root volumes that reside within the CSF space.

Advances in radiographic imaging and computer processing techniques have contributed greatly to our ability to accurately estimate CSF volume. Hogan et al. estimated lumbosacral CSF volume based on digitally assisted, segmental measurements of the anterior–posterior intrathecal and spinal cord dimensions using two-dimensional magnetic resonance imaging (MRI) (4). They demonstrated significant interindividual variation in lumbosacral CSF volume. Applying this technique to healthy volunteers who received hyperbaric lidocaine or isobaric bupivacaine spinal anesthesia, subsequent investigators found a strong inverse relationship between lumbosacral CSF volume and peak sensory cephalad blockade height and anesthetic duration (2,3). Similarly, in patients randomized to receive hyperbaric bupivacaine either in the lateral or sitting position, lumbosacral CSF volume is inversely correlated with the spread, onset, and duration of anesthesia (5).

Lee et al. reported a technique using a three-dimensional fast spin echo(FS) MRI sequence to measure CSF volume in four healthy volunteers (6). One millimeter contiguous sagittal plane images were used to formulate a three-dimensional view of the CSF column, and CSF volume was calculated with a post-processing computer algorithm. The calculated error of this technique using an *in vitro* validation experiment was 4.1%. The investigators used this methodology to measure the impact of hyperventilation and abdominal compression on CSF volume change in four healthy volunteers.

The purpose of our study was to use an improved three-dimensional FS MRI volume analysis technique to define the lumbosacral CSF volume variability in

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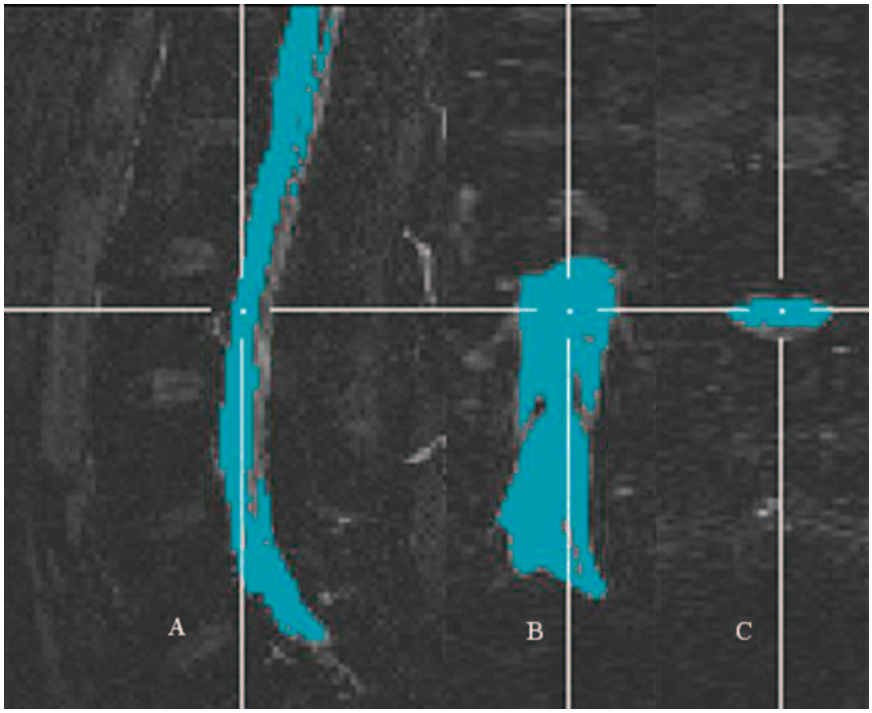

Figure 1. Two dimensional lumbosacral magnetic resonance images with highlighted cerebrospinal fluid (A = sagittal; B = coronal; and C = axial planes).

two patient populations (18 to 45-year-old females and 50 to 80-year-old males) and examine the relationship of estimated volume to physical characteristics. Subjects with a known diagnosis of lumbar spinal disease were included to evaluate the impact on the lumbosacral CSF volume.

METHODS

In Vitro Validation Experiment

Prior to initiating the investigation in human subjects, an *in vitro* experiment was conducted to validate the accuracy and precision of the volume measurement technique. A dissected cadaveric spinal cord with intact cauda equina was placed in a plastic basin. A known volume of water (1500.0 mL measured with a 1500 mL graduated cylinder) was poured into the basin over the dissected cadaveric specimen. MRIs of the cadaveric spinal cord were obtained using a long echo time (TE = 198 msec) FS echo sequence with fat suppression. This sequence produced 1 mm contiguous sagittal images with an in-plane resolution of 0.73 mm and a high degree of contrast between the water and the spinal cord and nerve roots.

A three-dimensional rendering of the water in the basin was created which excluded the cadaveric spinal cord and nerve roots (Brain Voyager 2000, V 4.9.6.0, Brain Innovation BV, Maastricht, The Netherlands). The digital images were converted to 8-bit data (0–255) and the initial threshold settings included intensities between 190 and 255. Using this technique, an initial seed was placed within the region of interest by a single investigator and all contiguous voxels (the three-dimensional geometric counterpart of the two-dimensional pixel) within a defined intensity range were identified. The number of labeled voxels was calculated and multiplied by the voxel volume to obtain the total volume of the CSF.

Human Subject Experiment

IRB approval was obtained for subsequent human investigation. Eighty-five patients scheduled for lumbosacral spine MRI at an outpatient facility between January and July 2004, who met inclusion criteria (females aged 18–45 and males aged 50–80 yr old) were recruited and gave written informed consent to participate in the investigation. Exclusion criteria were defined as the presence of a known space-occupying lesion of the spinal canal or scoliosis. Patients were included who had symptoms of low back pain, with or without radiculopathy, and spinal stenosis. Patient demographics, including gender, age, self-reported height, and indications for MRI (reported by the referring physician) were recorded. Patient weight was measured by one of the investigators. Lumbosacral MRIs were obtained using the same methodology described in the *in vitro* experiment. Radiographic diagnoses made by neuroradiologists were recorded. Lumbar pathology was classified into three groups: no diagnosis, herniated disk disease, and spinal stenosis.

Lumbosacral CSF volume was determined between a perpendicular plane established at the cephalic edge of the T12-L1 intervertebral disk and the terminal thecal sac (Fig. 1). The operator identified the T12-L1 disk plane and created a cut plane to restrict measurement of area caudal to this level. The same initial parameters for intensity thresholds (190–255) were applied to each subject. If there were areas of CSF-equivalent signal intensity, noncontiguous with the central spinal canal, then the lower signal intensity threshold was increased incrementally until these

Table 1. Subject Characteristics

	Male	Female	*P*
Number of Subjects	42	43	
Age (yr)	63 ± 8	34 ± 7	<0.01
Height (cm)	176 ± 8	166 ± 7	<0.01
Weight (kg)	87 ± 13	73 ± 17	<0.01
Body mass index (kg/m^2)	28.0 ± 4.6	26.4 ± 6.0	0.21
Indication for scan			0.43
Low back pain	23	27	
Sciatica/radicular pain	13	9	
Rule out metastatic disease	1	4	
Multiple myeloma	3	1	
Degenerative disk disease	2	2	

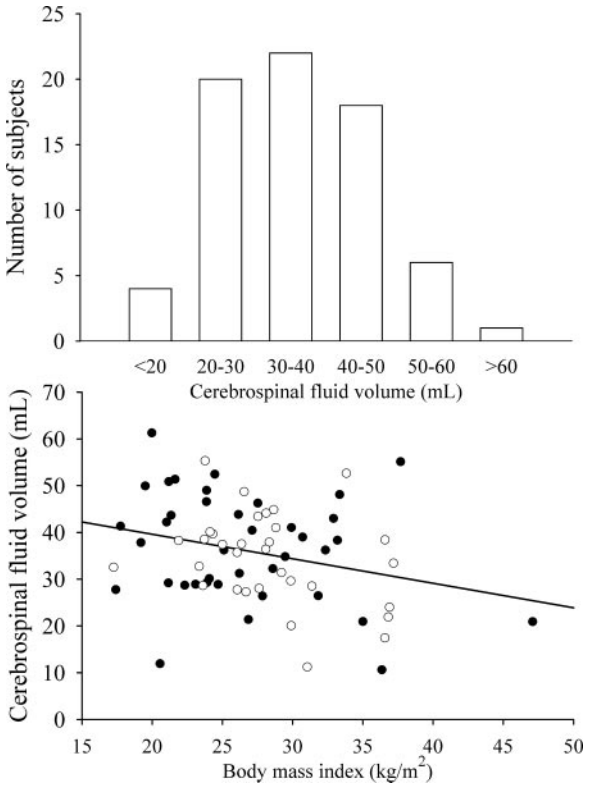

Figure 2. Top panel: histogram of estimated cerebrospinal fluid volume. Bottom panel: scattergram and linear regression of estimated cerebrospinal fluid volume versus body mass index ($r = -276$, $P = 0.02$) (○ = males ● = females).

ectopic signals disappeared, but central canal signal was preserved. If, during the intensity threshold adjustment, the central spinal canal signal was altered before resolution of ectopic signal, then the data from the patient were excluded from analysis. Three volume calculations were conducted on the images from each subject for internal validation.

Data Analysis

The accuracy of the *in vitro* experiment was determined by calculating the difference between the measured and the three digital estimations of water volume. The coefficient of variance was determined from the average of the calculated estimates. The minimum number of subjects for this study (35 males and 35 females) was determined to achieve power = 0.9 to detect a difference of −0.4 in the correlation coefficient between estimated lumbosacral CSF volume and body mass index (BMI) at $\alpha = 0.05$. Estimated CSF volumes were compared with BMI using linear regression analysis. Calculated CSF volumes were tested for normality using the Shapiro–Wilk *W*-test. Mean volumes between genders were compared with the Student's *t*-test. The relationships between CSF volumes and radiographic diagnoses were evaluated using one way-ANOVA. *Post hoc* comparisons were made using the Bonferroni method. A $P < 0.05$ was required to reject the null hypothesis.

Table 2. Distribution of Subject Characteristics and Estimated Cerebrospinal Fluid Volumes with Radiographic Diagnoses of Lumbar Spine Pathology

	No diagnosis	Spinal stenosis[a]	Herniated disc	*P*
Gender				0.43
Male	13	10	9	
Female	19	7	13	
Age (yr)	45 ± 13	51 ± 18*	42 ± 16	0.03
Body mass index (kg/m^2)	27.2 ± 6.0	28.2 ± 5.8	26.9 ± 5.5	0.89
Estimated CSF volume (mL)	38.4 ± 11.4	30.0 ± 10.5†	36.3 ± 8.9	0.03

[a] Two subjects had both herniated discs and spinal stenosis and are included in the stenosis group.

* Spinal stenosis different from No diagnosis and Herniated disc, $P = 0.05$ (Bonnferoni *post hoc* test).

† Spinal stenosis different from No diagnosis, $P = 0.05$ (Bonnferoni *post hoc* test).

RESULTS

In Vitro Experiment

The mean estimated water volume in the *in vitro* validation experiment was 1478.5 ± 6.5 mL. This represents a 1.4 ± 0.4% difference from the 1500.0 mL measured value.

Human Subject Experiment

Of the 85 subjects enrolled, 14 were excluded due to MRI quality or technical reasons such as poor image quality ($n = 4$), ectopic CSF-equivalent signal intensity unresponsive to threshold adjustment ($n = 3$), terminal thecal sac not included in image series ($n = 3$), unreported scoliosis ($n = 2$), and interference from surgical implants ($n = 2$). No patients were excluded for space-occupying lesions of the spinal canal.

The demographic data of the 71 volunteers included in the analysis are presented by gender in Table 1. Internal validation demonstrated a coefficient of variance of 0.42% among the three estimated CSF values per subject. The mean (±SD) calculated lumbosacral CSF volume was 35.8 ± 10.9 mL, with a median value of 36.4 mL (range 10.6–61.3 mL), and the distribution appeared normal (Shapiro–Wilk $W = 0.99$, $P = 0.82$) (Fig. 2). The relationship between estimated lumbosacral CSF volume and BMI is shown in Figure 2. Estimated lumbosacral CSF volume was

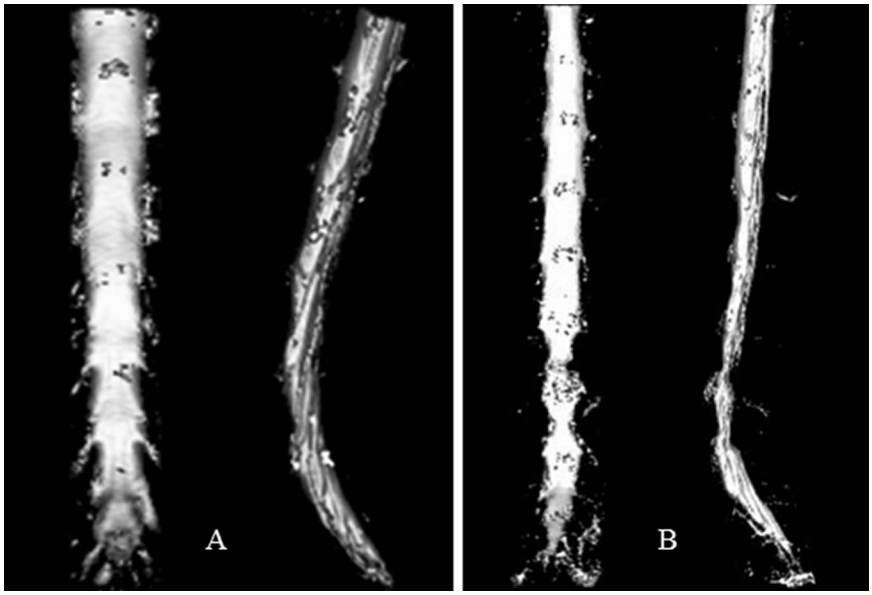

Figure 3. Three-dimensional renderings of lumbosacral cerebrospinal fluid volumes (coronal and sagittal planes). A = subject with no radiographic diagnosis, B = subject with radiographic diagnosis of spinal stenosis.

inversely proportional to BMI ($r = -.276$, $P = 0.02$), however, height ($r = 0.09$, $P = 0.46$) and weight ($r = -.23$, $P = 0.06$) as independent variables did not correlate with the estimated lumbosacral CSF volume.

There was no difference in the distribution of gender, age, or BMI among the groups (Table 2). Mean calculated lumbosacral CSF volumes were smaller in the group of subjects that had radiographic diagnoses of spinal stenosis when compared with subjects with no diagnosis (mean difference −8.4 mL, 95% CI of the difference, −16.1 to −0.8 mL, $P = 0.03$), but were not different when compared with those with a diagnosis of a herniated disk (mean difference −6.4 mL, 95% CI of the difference −14.7 to 1.9 mL, $P = 0.19$). Subjects with a diagnosis of a herniated disk were similar to the group with no diagnosis (mean difference −2.0 mL, 95% CI of the difference −9.1 to 5.1 mL).

DISCUSSION

The findings of this study support the previously reported wide interindividual variation of estimated lumbosacral CSF volume and the inverse relationship between CSF volume and BMI. In addition, we found a relationship between the radiographic diagnosis of spinal stenosis and a reduction in the mean calculated lumbosacral CSF volume.

Investigators using two-dimensional methods have reported a wide range of lumbosacral CSF volumes: 28.0–81.1 mL ($n = 25$) (4), 42.7–81.1 mL ($n = 9$) (2), 20.5–61.6 mL ($n = 41$) (3). Our range of estimated lumbosacral CSF volume, 10.6–61.3 mL, is consistent with previous investigations, but also includes some individual estimates below 20 mL. This is likely due to our subject population who were recruited at an outpatient MRI center scheduled for diagnostic scans to assess a variety of physical complaints or diagnoses. These diagnoses included spinal stenosis which is associated with central canal compression. In addition, small differences in the cephalad limits for CSF included in our calculations may have contributed to our smaller observed volumes. We established an arbitrary cephalad anatomical limit of the T12-L1 intervertebral disk. Our caudal limit was the terminal thecal sac. Previous investigators (2,4) included some lower thoracic CSF volume (measured volume from T11-12 disk to terminal thecal sac) in their calculations.

We believe that this investigative methodology provides rapid, accurate, and reproducible approximation of CSF volume because of the improved tissue discrimination, narrow anatomic slicing, and digital summation. Rapid volume estimation is achieved due to the computer automated postprocessing technique. Although the research MRI scan sequence added 4 min and 20 s to the scheduled diagnostic sequence, the computer calculation required minimal training and was conducted in 5–10 min. In addition, several features of this estimation technique may contribute to improved accuracy. The principle advantage is that 1 mm sagittal slicing of three-dimensional MRI scans provide substantially more volume data than earlier two-dimensional techniques which were limited by relatively thick (8 mm) slices. As we observed the shape of the CSF column in our three-dimensional images to be highly irregular (Fig. 3), wider sagittal image spacing may fail to incorporate many of these volume-influencing geometric variations (e.g., the dural sheaths). In addition, narrow radiographic cuts also achieve more accurate subtraction of significant intrathecal volume-occupying structures such as the spinal cord and nerve roots. These methodological advancements may not be appreciated when comparing the accuracies of *in vitro* validation experiments conducted with straight-edged water containers. Another improvement in accuracy may be due to better discrimination between CSF and surrounding fat tissue. Lee et al. identified that poor

discrimination between epidural fat and CSF was a technical problem with the three-dimensional MRI technique, which required operator intervention to resolve (6). FS MRI scanning with longer echo time (TE = 198 msec vs 100 msec reported by Lee et al.) provides improved discrimination between CSF and contiguous anatomical structures, thus substantially reducing the impact of this problem.

We focused our analysis on lumbosacral CSF volume because of previously reported greater interindividual variability at this level (3). This volume is only part of the spinal CSF volume that may influence the clinical outcome of spinal anesthesia (e.g., peak cephalad sensory level). Females of child-bearing age (18–45 yr) and males (50–80 yr) were studied because these populations are the most likely to receive spinal anesthesia at our institution for obstetric and urologic procedures, respectively, and may serve as a target population for subsequent investigations. We excluded from analysis, the data obtained from 14 patients for technical reasons and this may have influenced our results. Data were excluded from three patients who had ectopic CSF-equivalent signal intensity that could not be eliminated with lower intensity threshold adjustment. We excluded data from two patients who had vertebral hardware because it interfered with the acquisition of clear lumbosacral images. However, earlier back surgery itself was not an exclusion criterion and this may influence CSF volume.

In summary, we describe the use of a rapid and accurate method of noninvasively estimating lumbosacral CSF volume using three-dimensional MRI with computer postprocessing. There was a wide range of lumbosacral CSF volume and an inverse relationship between spinal stenosis and lumbosacral CSF volume, for which additional research may be needed to define further. The application of this technique to clinical investigations may further enhance our understanding of spinal anesthesia.

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