Diffusion Tensor Imaging in Idiopathic Normal Pressure Hydrocephalus: Evaluation Between Shunt Responsive and Shunt Non-Responsive Groups in Siriraj Hospital

Chanon Ngamsombat, M.D.*, Anassaya Jaiyasawadi, M.D.*, Theerapol Witthiwej, M.D., Panida Charnchaowanish, B.Sc.*, Orasa Chawalparit, M.D.***

**Department of Radiology, **Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.*

ABSTRACT

Objective: Patient evaluation for the treatment of idiopathic normal pressure hydrocephalus (iNPH) with noninvasive investigation is helpful. Diffusion tensor imaging (DTI) can evaluate the microstructural change in brain parenchyma. The aim of this study was to compare diffusion tensor parameters in the brain before treatment in shunt responsive and shunt non-responsive iNPH patient groups to identify any difference between groups.

Methods: Total 16 subjects with iNPH, 13 overall shunt responsive patients, and three overall shunt non-responsive patients were recruited and underwent MRI study (3-Tesla), including DTI with 32 gradient directions. Patients were scanned before cerebrospinal fluid tap test (CSF-TT) and shunt surgery. Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) between 2 groups were assessed by manual region of interest (ROI) method with FA color support. DTI parameters were correlated with the surgical outcome by clinical assessment.

Results: No statistically significant difference between overall outcome with FA and ADC in all ROIs was found. However, among the overall shunt responsive group, FA was higher, and ADC was lower than the overall shunt non-responsive group in almost all ROIs, except splenium of the corpus callosum (SPL). The difference was seen predominately at the body of the corpus callosum (CCbo) and genu of corpus callosum (GENU), but less at corticospinal tract pathway (CST), including corona radiata, posterior limb of internal capsule, and corticospinal tract at pons level (CR, PLIC, and Po). Subgroup analysis also showed the same tendency in the gait shunt responsive group, urinary symptom shunt responsive group, and cognitive shunt responsive group.

Conclusion: DTI can investigate white matter microstructural change in the iNPH patient. The overall shunt responsive group tends to have higher FA and lower ADC than the overall shunt non-responsive group in almost all ROIs, except SPL. However, no statistically significant difference was found. Further study and comparison between pre and post shunt placement surgery in iNPH patients will be helpful.

Keywords: Normal pressure hydrocephalus; diffusion tensor imaging (Siriraj Med J 2017;69: 198-210)

Abbreviations: iNPH : idiopathic normal pressure hydrocephalus, **DTI:** diffusion tensor imaging; **FA:** fractional anisotropy; **ROI:** region of interest, **ADC :** apparent diffusion coefficient; **CSF-TT :** cerebrospinal fluid tap test, **SPL :** splenium of the corpus callosum, **GENU :** genu of corpus callosum, **CCbo :** body of corpus callosum, **CST :** corticospinal tract, **CR :** corona radiata, **PLIC :** posterior limb of internal capsule and **Po :** corticospinal tract at pons

Correspondence to: Orasa Chawalparit
E-mail: orasa.cha@mahidol.ac.th
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INTRODUCTION

Normal pressure hydrocephalus (NPH) is one of the treatable causes of dementia, and the patients have typical clinical symptoms including gait disturbance, cognitive impairment, and urinary incontinence. CSF shunt surgery can improve clinical symptoms in about 60% of NPH patients.[1,2] NPH can be categorized into idiopathic NPH (iNPH) which is no demonstrable cause can be found, and secondary NPH, which the patients had previous intracranial cause such as traumatic brain injury, subarachnoid hemorrhage or meningitis.

Mechanism to clarify about shunt responsive patients, especially in iNPH is still unclear. Many supplementary tests are used to identify which patients will have most benefit after shunt surgery. The most supportive evidence in this period is CSF-TT and long-term intracranial pressure monitoring.[3] These supplemental tests can increase predictive accuracy for prognosis to greater than 90%.[4] However, these methods may be associated with potentially serious complications[5], including central nervous system infection and hemorrhage.

White matter abnormality is supposed to be pathological findings of iNPH. Pressure effect due to ventricular dilatation, ischemic demyelination, and microinfarction can be demonstrated.[6] MRI is a noninvasive diagnostic tool which can demonstrate ventricular dilatation, disproportionately enlarged subarachnoid space hydrocephalus (DESH feature)[7], white matter signal intensity change, and aqueduct flow void in NPH, but the role of structural neuroimaging in selecting surgical candidates for shunt placement surgery is still limited.[8,9]

DTI is an advanced imaging study and diffusion parameters such as principal diffusivities (parallel and perpendicular to the fibers), apparent diffusion coefficient (ADC) and the fractional anisotropy (FA) can be used to evaluate the early microstructural change in the brain parenchyma.[10,11] Several roles of DTI in NPH are purposed, and some studies evaluate DTI to discriminate NPH and other causes of dementia that can present with the same symptoms, including Alzheimer's disease (AD), Parkinson's disease, and vascular dementia.[12,13] However, there are only a few studies about DTI to identify a shunt responsive patient before surgery.

The aim of this study was to compare diffusion tensor parameters in the brain before treatment in shunt responsive and shunt non-responsive iNPH patient groups to identify any difference between groups.

MATERIALS AND METHODS

A total of 16 subjects with iNPH, 13 overall shunt responsive patients and three overall shunt non-responsive patients were recruited to retrospective review from data base of MRI CSF flow study records from May 2007 until July 2013 (Totally 173 patients, of which only 25 patients were compatible with possible iNPH criteria[14] and had been treated with shunt insertion. Unfortunately, 9 of them had lost DTI data and could not undergo post-processing analysis). Demographic data, underlying disease of the patients, preoperative Evan's index, and abnormal high signal intensity on T2 weighted image (T2WI) or FLAIR (Fluid-attenuated inversion recovery) white matter lesions according to Fazekas scale were also collected.

All 16 subjects were compatible with; 1. Diagnosis criteria of possible iNPH (according to Japanese clinical guideline in idiopathic NPH[14]) which included - Individuals who develop symptoms in their 60's or older. More than one of the clinical triads: gait disturbance, cognitive impairment, and urinary incontinence. CSF pressure of 200 mmH_2O or less and normal CSF content. Above-mentioned clinical symptoms cannot be completely explained by other neurological or non-neurological disease. Preceding diseases possibly causing ventricular dilation are not obvious, including subarachnoid hemorrhage, meningitis, head injury, congenital hydrocephalus, and aqueduct stenosis.; 2. All of the cases underwent surgical intervention, LP or VP shunt.; 3. All of them had DTI data before surgical intervention at Siriraj Hospital.; 4. Clinical evaluation after shunt insertion showing maximal clinical improvement during follow-up after 1 year. In the present study, the overall shunt responsiveness group was defined as an improvement by one point or more on the iNPH grading scale (iNPHGS) within one year of shunt placement surgery, which was a validated scale for evaluation of iNPH symptom severity.[15] The scale was shown in Table 1. The scales of each patient were given by neurosurgeon after review of record data and physical examination.

MRI procedure:

All cases were scanned with a 3-Tesla MRI system (Achieva, Philips Healthcare) and DTI was performed in an axial orientation using a single-shot EPI sequence (Echo planar imaging) with 32 diffusion-encoding directions (B value 0 and 800 mm^2/s). The axial orientation was chosen to cover the entire brain from vertex to medulla oblongata. The data acquisition matrix=112x112; field of view=220x220 mm; TR=10448 and TE =54.

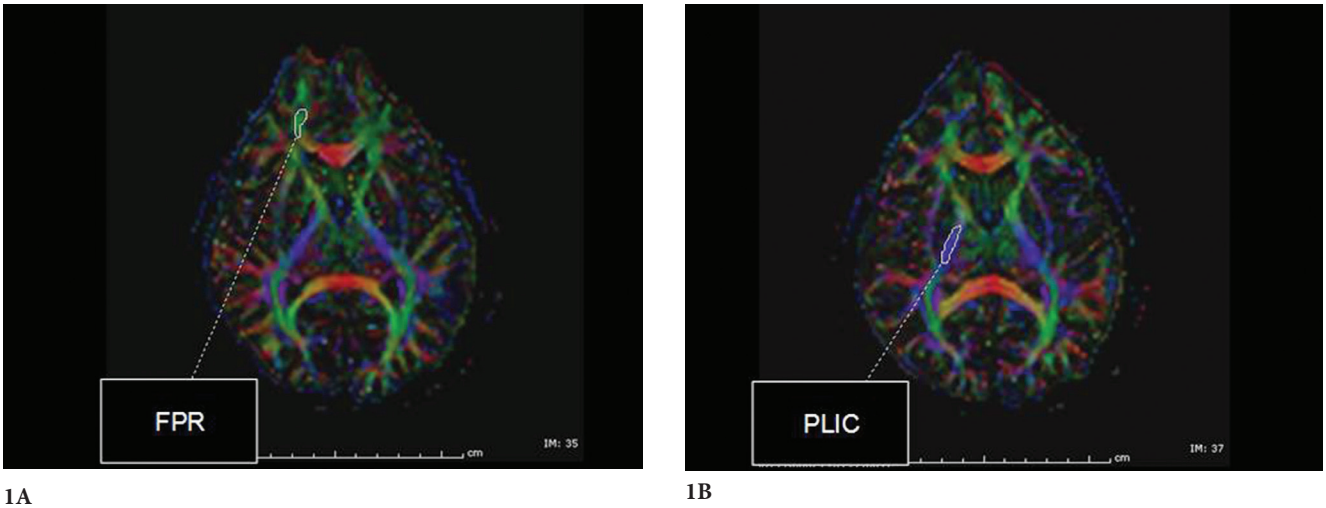
DTI processing:

DTI data was transferred to a commercially available work station (Extended MR Work Space Release 2.6.3.5,

TABLE 1. Idiopathic normal pressure hydrocephalus grading scale (iNPHGS).[15]

Symptoms	Grade	Definition
Cognitive impairment	0	Normal
	1	Complaints of amnesia or inattention but no objective memory and attention impairment
	2	Existence of amnesia or inattention but no disorientation of time and place
	3	Existence of disorientation of time and place but conversation is possible
	4	Disorientation for the situation or meaningful conversation impossible
Gait disturbance	0	Normal
	1	Complaints of dizziness of drift and dysbasia but no objective gait disturbance
	2	Unstable but independent gait
	3	Walking with any support
	4	Walking not possible
Urinary disturbance	0	Normal
	1	Pollakiuria or urinary urgency
	2	Occasional urinary incontinence (1–3 or more times per week but less than once per day)
	3	Continuous urinary incontinence (1 or more times per day)
	4	Bladder function is almost or completely deficient

2013 Philips medical systems, the Netherlands) to evaluate FA and ADC at ROI, including frontal periventricular region (FPR), posterior limb of internal capsule (PLIC), corona radiata (CR), and corticospinal tract at the pons level (Po), the genu of the corpus callosum (GENU), the splenium of the corpus callosum (SPL), and body of the corpus callosum (CCbo). We used FA color maps to support manual ROI placement and locate the white matter structure and each parameter was averaged from both sides of ROI. (Fig 1-5).



1A 1B

Fig 1. Region of interest selection in a patient by location of FPR (A) and PLIC (B) were determined on axial image near pineal body level that well seen the interested region.

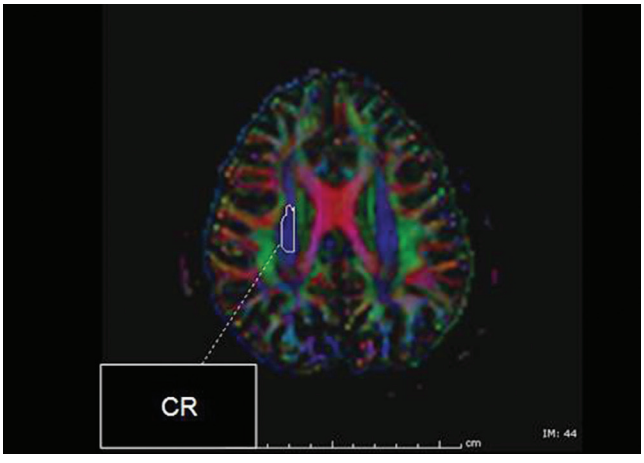


Fig 2. Location of CR was decided above 9-15mm from FPR and PLIC.

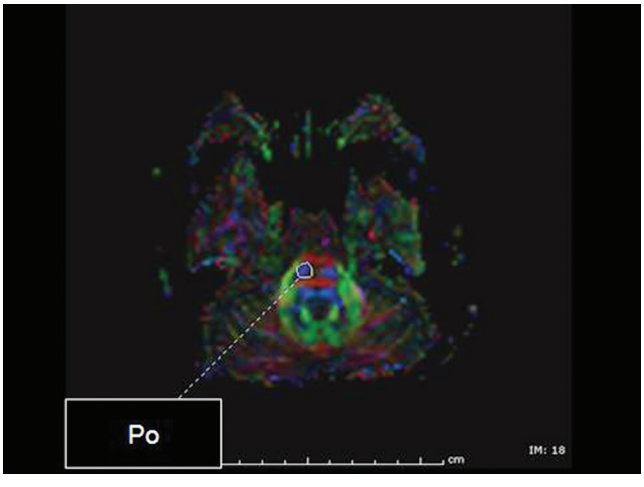
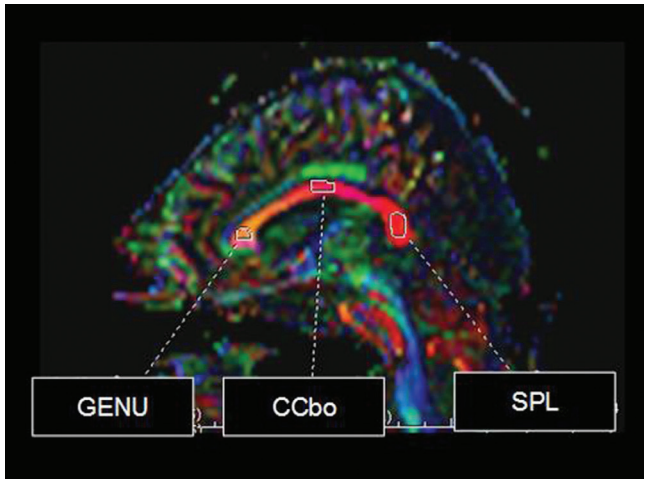


Fig 3. Location of corticospinal tract at pons level (Po) was demonstrated.



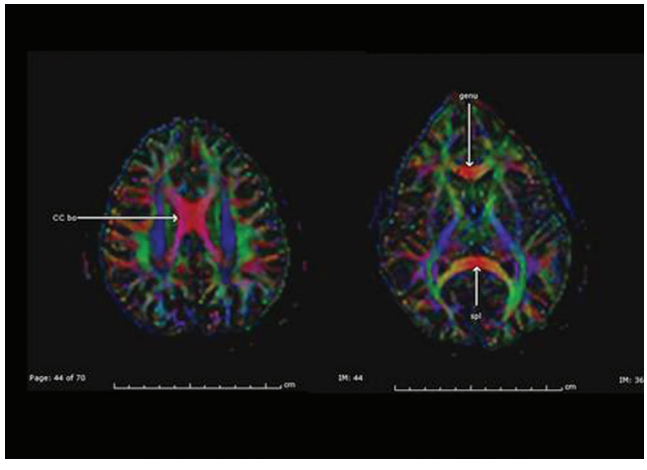


Fig 4 & 5. ROIs in the corpus callosum in three segments of the corpus callosum (genu, body, splenium) were determined on sagittal and correlate to axial views.

Statistical analysis

Statistical analysis was performed using PASW(SPSS) version 18. Statistical analysis between the two groups was performed by Mann-Whitney's *U* test. The FA and ADC analysis in overall shunt responsive and overall shunt non-responsive patients in each group were performed by Wilcoxon signed-rank tests. Statistical significance was preset at $p < 0.05$.

RESULTS

All patients had symptomatic gait abnormality, and pretreatment scoring was at least 1 point. The 14 patients had complete clinical triad, and two patients had no urinary incontinence. In the patient groups, mean age was 75.38+/-5.45 years. Cardiovascular risk factors were as follows: hypertension (HT) (n = 13), CAD (Coronary Artery Disease)/Stroke (n = 5), dyslipidemia (DLP) (n=8), and DM (diabetes mellitus) (n=5). Median disease duration was two years (range approximately about 1-5 years). The data are summarized in Table 2.

There were 13 overall shunt responsive and three overall shunt non-responsive patients. Subgroup data analysis showed gait shunt responsive 12 patients, urinary symptom shunt responsive ten patients and cognitive shunt responsive five patients.

The mean of FA and ADC values at all ROIs before shunt insertion were summarized in Tables 3-4. FA value was highest at SPL, CCbo and GENU and lowest at FPR in overall shunt responsive and shunt non-responsive groups. ADC value showed lowest at CR in both groups. ADC at CCbo and GENU tended to be higher than other areas.

There was no statistically significant difference between overall outcomes with FA and ADC in all ROIs. Among the overall shunt responsive group, FA was higher, and ADC was lower than the overall shunt non-responsive group in almost all ROIs, except SPL. The difference of FA and ADC values was seen predominantly at CCbo and GENU, but less at part of CST pathway (CR, PLIC, Po). Subgroup analysis also showed the same tendency in the gait shunt responsive group, urinary symptom shunt responsive group, and cognitive shunt responsive group (Fig 6-7).

TABLE 2. Demographic data, duration of symptoms, iNPHGS, overall outcome of improvement after shunt surgery, associated findings (Evan's index, white matter lesion as Fazekas score), type of surgery and time of maximal improvement after surgery.

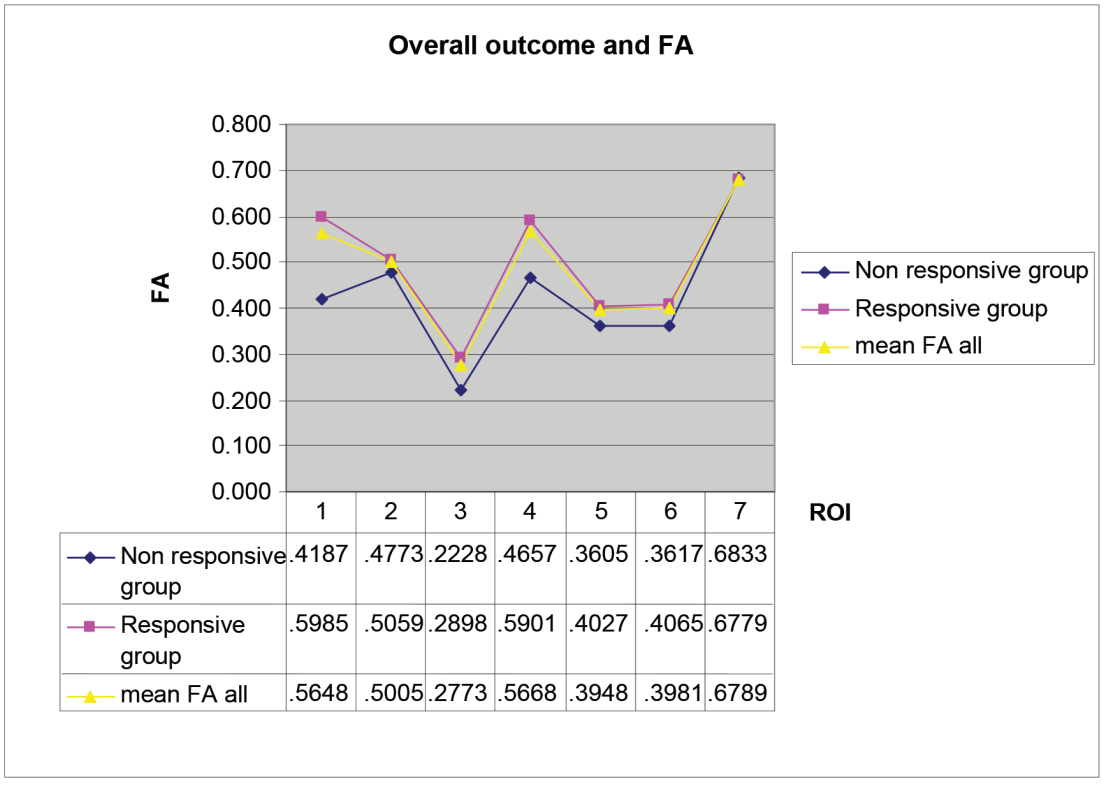
case	Sex (m=male, f= female)	age	Underlying disease(s)	Approximation duration of symptoms (year(s)) (G=Gait, U=Urinary, C=Cognitive)	Pre-operative iNPHGS G/U/C	Post-operative iNPHGS G/U/C	Overall outcome of improvement	White matter lesion	Evan's index	VP or LP shunt	Month(s) of maximal improve	Note
1	m	80	DM, HT, CA prostate	G/5, U/1	3/4/4	3/3/2	yes	1	0.37	LP	2	S/P TURP (Transurethral resection of the prostate) in follow up period
2	f	76	HT	G/2, U/2, C/1	4/3/3	3/2/2	yes	2	0.3	VP	4	Spinal stenosis also causes gait symptom.
3	m	75	HT, CAD, Stroke	G/1, U/1, C/3	3/3/2	1/1/1	yes	1	0.3	VP	12	
4	m	78	DM, CAD, DLP, PD (Parkinson's disease)	G/2, C/3	2/0/3	1/0/2	yes	2	0.33	VP	2	PD disturb gait.
5	f	67	PD, hypothyroidism	G/5, M/5, U/4	4/4/4	3/4/2	yes	2	0.35	VP	6	Neurogenic bladder
6	f	74	HT, PD, DLP	G/2, U/1	3/3/2	2/1/2	yes	2	0.3	VP	6	
7	m	76	DM, HT, DLP	G/2, U/1	3/4/3	2/1/2	yes	4	0.34	VP	12	
8	m	78	HT, Prostatic CA	G/1, U/1, C/1	2/3/3	0/0/2	yes	0	0.33	VP	11	post operation 2 months with SDH (subdural hemorrhage)
9	m	79	DM, HT, DLP	C/2	3/0/2	2/0/1	yes	2	0.3	VP	9	post operation 2 months with SDH
10	m	77	Small cavernous schwannoma	G/1, U/1, C/1	2/2/2	1/1/2	yes	1	0.34	VP	2	
11	f	76	HT	G1, U/1, C/1	2/2/2	1/1/1	yes	3	0.31	VP	3	
12	m	76	Arrhythmia, HT	G/2, U/1, C/1	3/4/3	2/1/2	yes	2	0.42	VP	8	
13	m	71	HT, DLP, Stroke	U/2, C/2	1/4/3	2/2/2	yes	2	0.35	VP	4	Stroke causes weakness and gait disturbance.
14	f	85	HT, CAD, DLP	G/4, U/1, C4months	4/4/4	4/4/4	no	4	0.42	VP	12	
15	f	61	DM, TIA, HT, DLP	G/1, U/1, C/1	3/4/2	2/4/3	no	2	0.28	VP	6	
16	m	77	HT, PD, DLP	G/4, U1, C/1	3/1/2	4/1/2	no	0	0.31	VP	1	Post operative bleeding then bed ridden.

TABLE 3. Outcome of improvement after surgery (overall outcome, gait outcome, urinary symptom outcome and cognitive outcome) and mean FA value in each ROIs.

Shunt Outcome/ Mean FA ROI	CC bo FA	CR FA	FPR FA	Genu FA	PLIC FA	PO FA	SPL FA
Overall non responsive group (n=3)	.4186	.4773	.2228	.4657	.3605	.3617	.6833
Overall responsive group (n=13)	.5985	.5059	.2898	.5901	.4026	.4065	.6778
Gait non responsive group (n=4)	.4762	.5098	.2956	.4840	.3930	.3734	.6965
Gait responsive group (n=12)	.5943	.4975	.2711	.5943	.3953	.4064.	6730
Urinary non responsive group (n=6)	.5023	.4846	.2455	.5077	.3663	.3766	.6841
Urinary responsive group (n=10)	.6023	.5101	.2963	.6022	.4118	.4111	.6757
Cognitive non responsive group (n=5)	.5258	.5109	.2366	.5458	.3676	.3838	.6926
Cognitive responsive group (n=11)	.5825	.4958	.2957	.5763	.4071	.4046	.6726
Mean FA all (N=16)	.5648	.5005	.2772	.5668	.3947	.3981	.6788

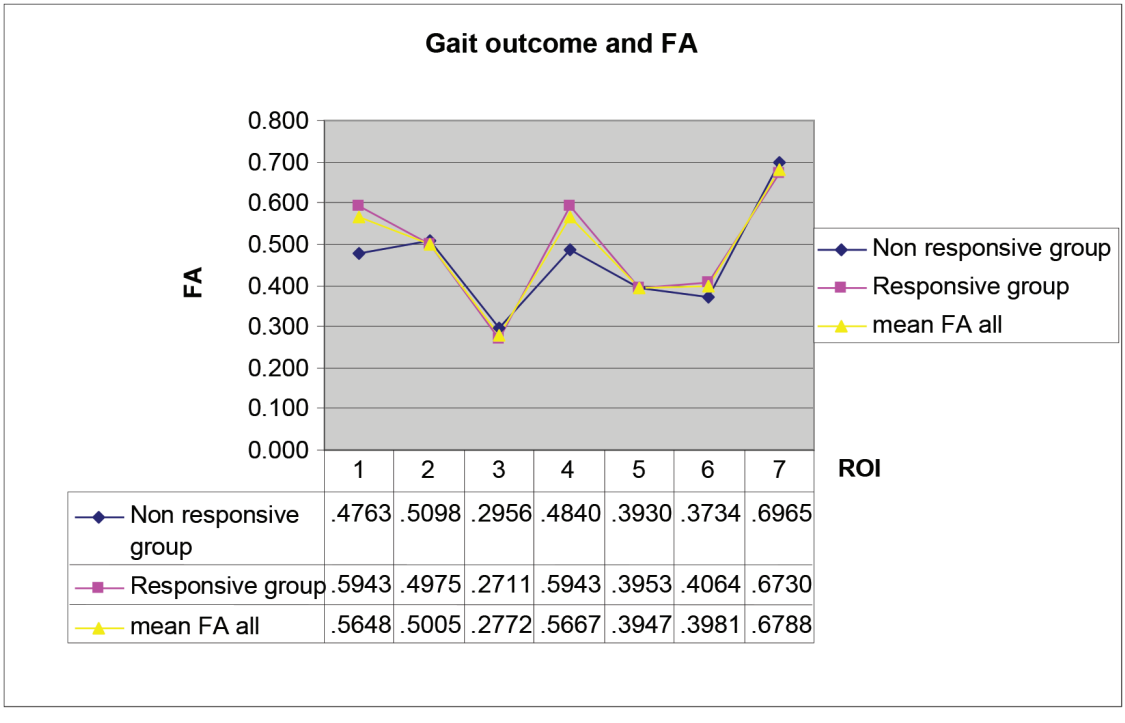
TABLE 4. Outcome of improvement after surgery (overall outcome, gait outcome, urinary symptoms outcome and cognitive outcome) and mean ADC value (x 10^{-3} mm^2/s) in each ROIs.

Shunt Outcome/ mean ADC ROI	CC bo ADC	CR ADC	FPR ADC	Genu ADC	PLIC ADC	PO ADC	SPL ADC
Overall non responsive group (n=3)	1.6826	.8968	1.2255	1.5570	1.1133	1.5178	.9877
Overall responsive group (n=13)	1.1939	.8783	.9203	1.1960	.9442	1.4508	1.026
Gait non responsive group (n=4)	1.5165	.8868	1.0721	1.5555	1.0560	1.5221	.9675
Gait responsive group (n=12)	1.2085	.8801	.9460	1.1664	.9492	1.4438	1.0363
Urinary non responsive group (n=6)	1.4653	.9108	1.0935	1.3732	1.0543	1.5097	.9852
Urinary responsive group (n=10)	1.1776	.8644	.9080	1.1980	.9289	1.4356	1.0395
Cognitive non responsive group (n=5)	1.4172	.8826	1.1104	1.3472	1.0402	1.4806	.9712
Cognitive responsive group (n=11)	1.2256	.8814	.9171	1.2257	.9467	1.4555	1.0409
Mean ADC all (N=16)	1.2855	.8818	.9775	1.2637	.9759	1.4634	1.0191



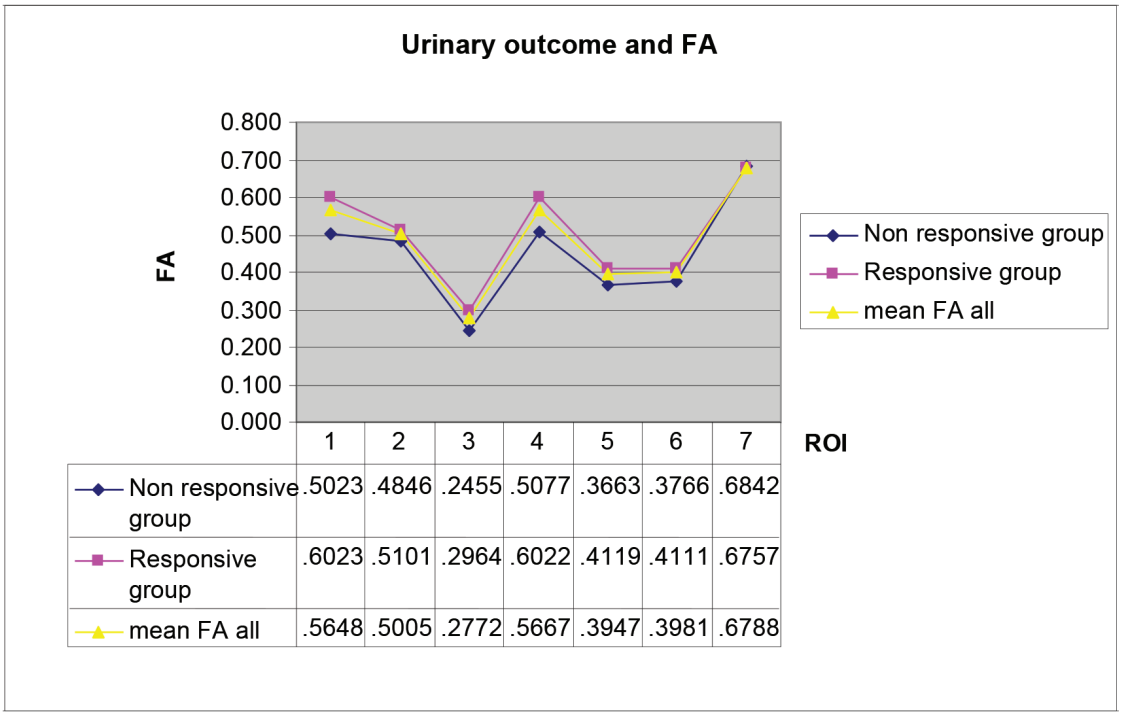
	1	2	3	4	5	6	7
Non responsive group	.4187	.4773	.2228	.4657	.3605	.3617	.6833
Responsive group	.5985	.5059	.2898	.5901	.4027	.4065	.6779
mean FA all	.5648	.5005	.2773	.5668	.3948	.3981	.6789

A. Overall outcome/FA ROI	1 CCbo	2 CR	3 FPR	4 Genu	5 PLIC	6 Po	7 SPL
p-value	**.296**	**.439**	**.364**	**1.000**	**.611**	**.057**	**1.000**



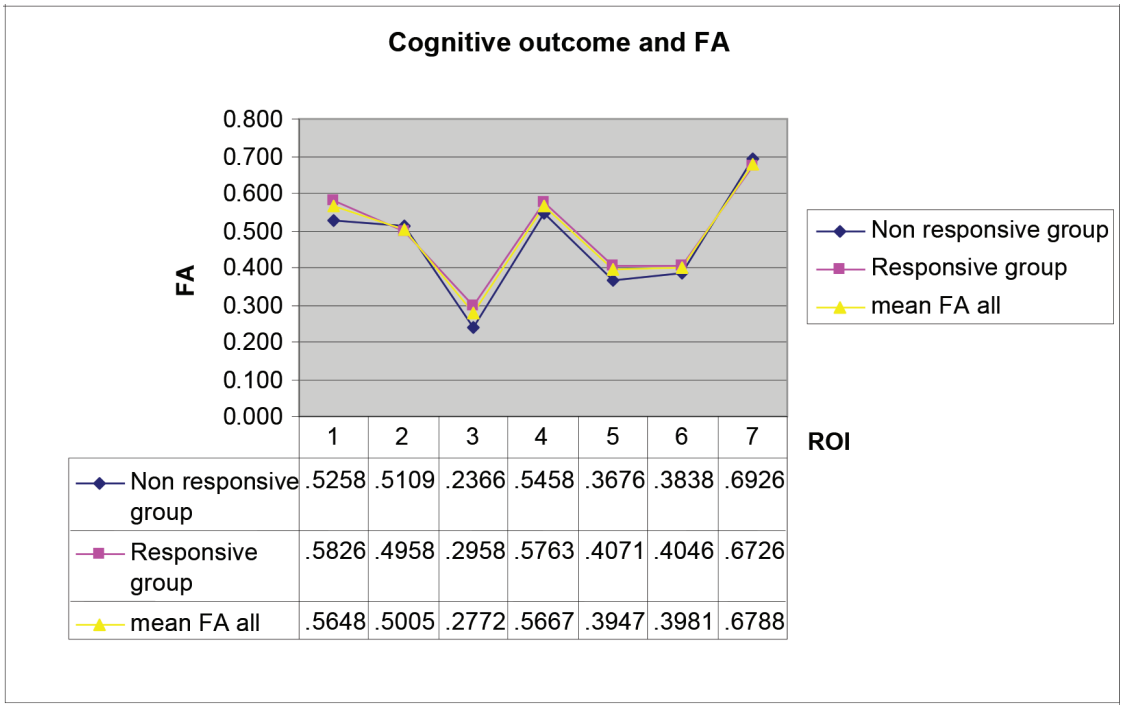
	1	2	3	4	5	6	7
Non responsive group	.4763	.5098	.2956	.4840	.3930	.3734	.6965
Responsive group	.5943	.4975	.2711	.5943	.3953	.4064	.6730
mean FA all	.5648	.5005	.2772	.5667	.3947	.3981	.6788

B. Gait outcome/FA ROI	1 CCbo	2 CR	3 FPR	4 Genu	5 PLIC	6 Po	7 SPL
p-value	**.379**	**.770**	**.521**	**.521**	**.862**	**.078**	**.770**



	1	2	3	4	5	6	7
Non responsive group	.5023	.4846	.2455	.5077	.3663	.3766	.6842
Responsive group	.6023	.5101	.2964	.6022	.4119	.4111	.6757
mean FA all	.5648	.5005	.2772	.5667	.3947	.3981	.6788

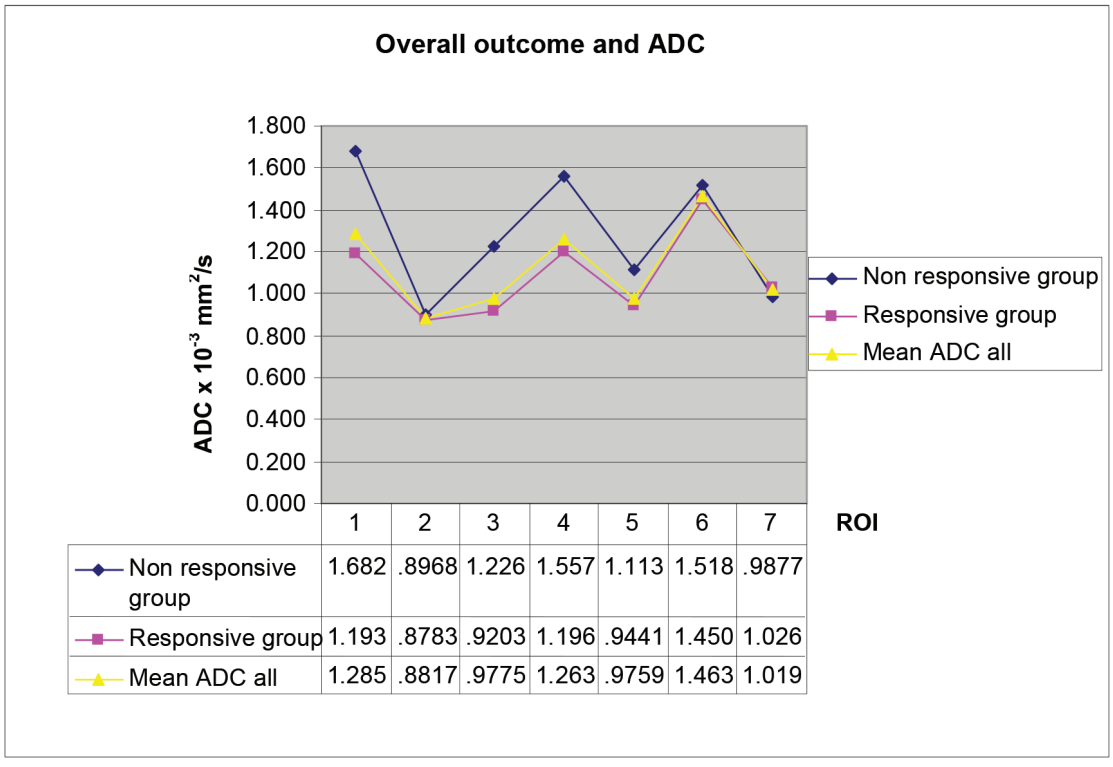
C. Urinary outcome/FA ROI	1 CCbo	2 CR	3 FPR	4 Genu	5 PLIC	6 Po	7 SPL
p-value	**.368**	**.492**	**.263**	**.313**	**.147**	**.073**	**1.000**



	1	2	3	4	5	6	7
Non responsive group	.5258	.5109	.2366	.5458	.3676	.3838	.6926
Responsive group	.5826	.4958	.2958	.5763	.4071	.4046	.6726
mean FA all	.5648	.5005	.2772	.5667	.3947	.3981	.6788

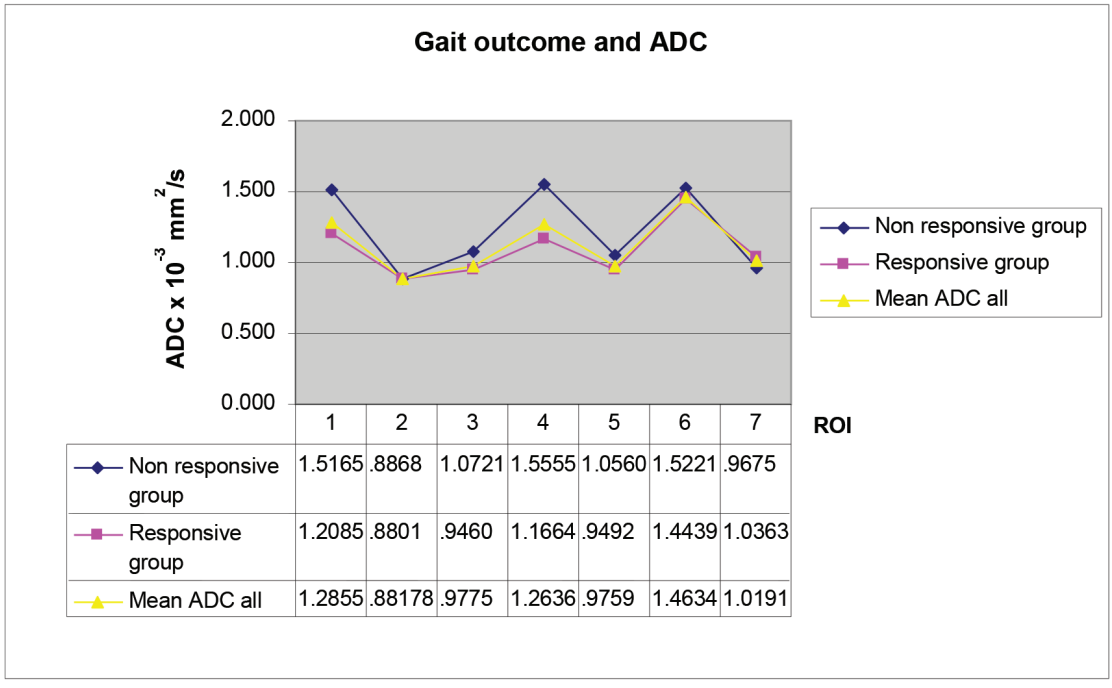
D. Cognitive outcome/FA ROI	1 CCbo	2 CR	3 FPR	4 Genu	5 PLIC	6 Po	7 SPL
p-value	**1.000**	**.827**	**.267**	**.145**	**.377**	**.377**	**.827**

Fig 6. Demonstration of relationship between FA and outcomes (overall outcome-A, gait outcome-B, urinary outcome-C and cognitive outcome-D).



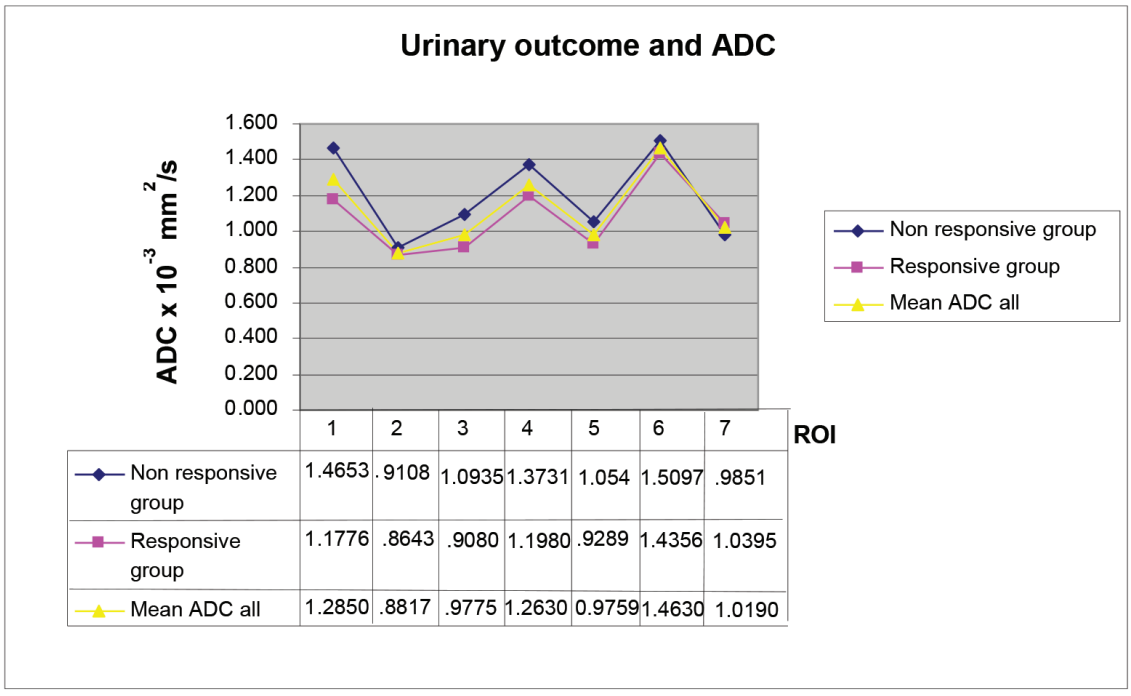
	1	2	3	4	5	6	7
Non responsive group	1.682	.8968	1.226	1.557	1.113	1.518	.9877
Responsive group	1.193	.8783	.9203	1.196	.9441	1.450	1.026
Mean ADC all	1.285	.8817	.9775	1.263	.9759	1.463	1.019

A. Overall outcome/ADC ROI	1 CCbo	2 CR	3 FPR	4 Genu	5 PLIC	6 Po	7 SPL
p-value	**.521**	**.800**	**.296**	**.521**	**.521**	**.611**	**.704**



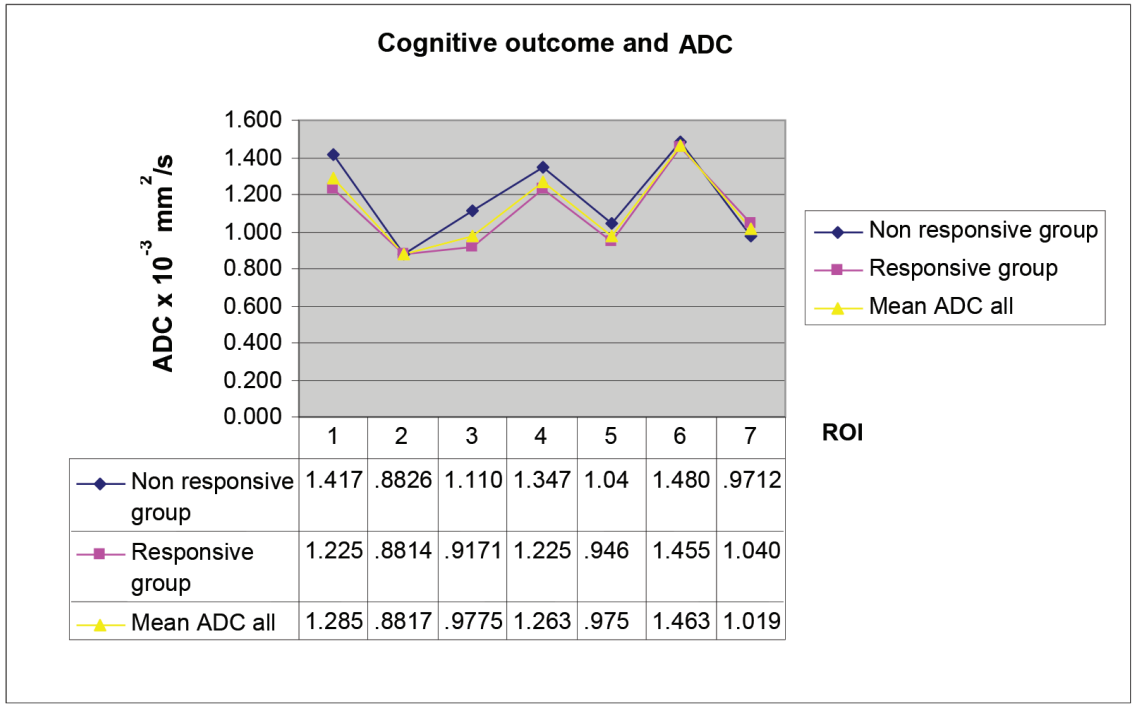
	1	2	3	4	5	6	7
Non responsive group	1.5165	.8868	1.0721	1.5555	1.0560	1.5221	.9675
Responsive group	1.2085	.8801	.9460	1.1664	.9492	1.4439	1.0363
Mean ADC all	1.2855	.88178	.9775	1.2636	.9759	1.4634	1.0191

B. Gait outcome/ADC ROI	1 CCbo	2 CR	3 FPR	4 Genu	5 PLIC	6 Po	7 SPL
p-value	**.684**	**1.000**	**.316**	**.379**	**.862**	**.862**	**.770**



	1	2	3	4	5	6	7
Non responsive group	1.4653	.9108	1.0935	1.3731	1.054	1.5097	.9851
Responsive group	1.1776	.8643	.9080	1.1980	.9289	1.4356	1.0395
Mean ADC all	1.2850	.8817	.9775	1.2630	0.9759	1.4630	1.0190

C. Urinary outcome/ADC ROI	1 CCbo	2 CR	3 FPR	4 Genu	5 PLIC	6 Po	7 SPL
p-value	**.492**	**.562**	**.118**	**.958**	**.368**	**.492**	**.713**



	1	2	3	4	5	6	7
Non responsive group	1.417	.8826	1.110	1.347	1.04	1.480	.9712
Responsive group	1.225	.8814	.9171	1.225	.946	1.455	1.040
Mean ADC all	1.285	.8817	.9775	1.263	.975	1.463	1.019

D. Cognitive outcome/ADC ROI	1 CCbo	2 CR	3 FPR	4 Genu	5 PLIC	6 Po	7 SPL
p-value	**1.000**	**.827**	**.377**	**.090**	**.583**	**.913**	**.377**

Fig 7. Demonstration of relationship between ADC and outcome (overall outcome-A, gait outcome-B, urinary outcome-C and cognitive outcome-D).

Mean preoperative Evan's index of all patients was about 0.334. Mean preoperative Evan's index of overall shunt responsive was 0.333 and shunt non-responsive was 0.336. Most of the patients, 8 cases had associated abnormal high signal intensity on T2WI or FLAIR white matter lesion grade 2, according to Fazekas scale. There were no significant differences of Evan's index (P-value = 0.800) or abnormal high signal intensity on T2WI, or FLAIR white matter lesions between overall shunt responsive and shunt non-responsive groups and in subgroup analysis (Table 5).

TABLE 5. This table showed no statistically significant difference (p value>0.05) between Evan's index or abnormal high signal intensity on T2WI, FLAIR white matter lesion between of overall shunt responsive and shunt non responsive groups and in subgroup analysis.

Clinical outcome	Overall shunt responsive/ non responsive	Gait shunt responsive/ non responsive	Urinary symptom shunt responsive/ non responsive	Cognitive shunt responsive/ non responsive
Evan's index *(p value)*	0.800	0.780	0.713	0.583
White matter lesion *(p value)*	0.900	0.684	0.713	0.641

DISCUSSION

In comparison with normal control, previous studies showed that patients with chronic idiopathic hydrocephalus had significantly higher mean diffusivity (MD) values in both the periventricular corticospinal tract (CST) and the corpus callosum (CC), whereas FA values were significantly higher in the CST/corona radiata (CR), but lower in the CC.[16] In the CC, the pre-surgery FA values in patients with hydrocephalus were lower than those of control values, and no significant changes were seen following surgery.[17] Another study also showed decreased FA in anterior frontal white matter and elevated ADC were found in genu of corpus callosum and areas of centrum semiovale associated with the precentral area. However, diffusion patterns in these areas did not change after drainage.[18]

About pre and post surgical intervention evaluation and outcome after surgery, the previous study suggested that pre-surgical iNPH had significantly higher FA than all the other groups in the posterior limb of the internal capsule, in which FA was decreased after shunt surgery. Pre-surgical MD of the iNPH group was higher than that in the AD and healthy control groups in the anterior periventricular white matter, the anterior limb of the internal capsule, and the superior longitudinal fasciculus.[13]

The relationship between shunt responsive or CSF-TT positive and DTI was shown in the previous study as ADC values were significantly decreased in the frontal periventricular region and the body of the corpus callosum in the positive group ($p < 0.05$) after CSF-TT, whereas no significant change was shown in the negative group. FA values were significantly increased in the body of the corpus callosum in both groups after CSF-TT ($p < 0.05$). However, the reduction of the CSF after CSF-TT may be too small to change FA values in other regions.[19,20] Another study showed the elevation of the periventricular ADC in the poor outcome group, compared with both controls and the good outcome group despite appearing normal on conventional imaging.[21]

The assumption in our study was based on the previous study that in a normal healthy adult population, the FAs at splenium and CCbo were highest, and ADC at CR was the lowest.[22,23] The iNPH patients should have lower FA values in the CC, FPR and significantly higher FA values in the CST as compared with healthy controls.[16] Changes in DTI parameters of the CST are shown to be correlated with the severity of gait disturbance.[16]

There was no statistically significant differences between overall outcomes with FA and ADC in all ROIs. However, among the overall shunt responsive group, FA was higher, and ADC was lower than the overall shunt non-responsive group in almost all ROIs, except SPL. The differences of FA and ADC values were seen predominately at CCbo and GENU, but less at part of CST pathway (CR, PLIC, Po). Subgroup analysis also showed the same tendency in the gait shunt responsive group, urinary symptom shunt responsive group, and cognitive shunt responsive group.

From the previous study about DTI in iNPH, the mechanical pressure caused higher packing of fibers and increased fiber density per unit area, resulting in increased FA values of CST (CR, PLIC).[16] In contrast to CC and FPR, it is likely to have decreased FA value due to distention, thinning, with axonal degeneration of the CC and FPR.[18,24] These mechanisms may explain our results that our higher FA value and lower ADC result suggested the less degree of white matter damage or degeneration, the better outcome after surgery is possible.

In general, ADC is inversely related to FA.[11] In our study, the mean ADC of CR showed no obvious increase as compared with other ROIs (CCbo, SPL, and FPR) and the ADC of CR was the lowest ADC of each group. These findings could be explained by the different pathology. In chronic hydrocephalus[16], damage secondary to compression mechanism to axonal fibers, including axonal loss and gliotic change may result in later increase of ADC.[25]

In subgroup analysis, we also observed almost no difference in ranking of FA value between shunt responsive and shunt non-responsive groups, except mean values of FA at CR, CCbo, and GENU. In overall shunt non-responsive group and gait shunt non-responsive group, mean FA values of CCbo and GENU tended to be lower than CR. These could imply that more damage to CCbo and GENU, possibly lead to poor outcome.

Multiple limitations of the study were realized.

1. About the subjects:
   - Because there were difficult criteria to set up the accurate diagnosis of iNPH and database of case collection which used CSF flow studies. Some parameters such as CSF flow velocity caused influence in selecting a case for shunt insertion treatment.[8,26]
   - Underlying diseases of the patient's group may interfere with FA and ADC.[6]
   - Underlying diseases of the patient may affect triad symptoms, including Parkinson's disease, hypothyroidism, spinal stenosis, previous stroke, or neurogenic bladder.[27]
2. About techniques:
   - Small sample size, especially in the shunt non-responsive group was noted.
   - The limited spatial resolution, partial volume contamination and image artifacts that occurred during DTI postprocessing analysis.
3. Lack of post shunt insertion study and no matched control case for comparison was noted.
4. There were variations in time for scoring after post-operative follow-up, and some cases had developed other disease attack (new onset of stroke, spinal stenosis, OA knees, fractured femoral neck, depression or TURP (Transurethral resection of the prostate)) or emerging complication after treatment such as subdural hemorrhage.

CONCLUSION

DTI can investigate white matter microstructural change in the iNPH patient. The overall shunt responsive group tends to have higher FA and lower ADC than the overall shunt non-responsive group in almost all ROIs, except SPL. However, no statistically significant difference was found. Further study and comparison between pre and post shunt placement surgery in iNPH patients will be helpful.

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