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Contribution of automated hippocampal volume measurements to radiological diagnosis in cases of mesial temporal sclerosis

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ABSTRACT

Aims: Epilepsy, particularly drug-resistant epilepsy in adults, is often caused by mesial temporal sclerosis (MTS), which can develop after brain injury from febrile illnesses or trauma. Magnetic resonance imaging (MRI) is crucial for diagnosing MTS, although challenges such as patient movement and mild or bilateral hippocampal atrophy can complicate the diagnosis. T1-weighted hippocampal volume measurements are effective in detecting MTS, with recent software advancements enabling automatic hippocampal segmentation. This study compared the hippocampal volumes and indices between adults with MTS and a control group of similar age and sex in the Turkish population. This study aimed to highlight structural differences in the hippocampus associated with MTS.

Methods: This study involved a retrospective review of cranial MRIs scans from patients with MTS, confirmed through histopathological examination after epilepsy surgery. To ensure unbiased comparisons, a control group was selected using propensity score matching by age and gender. Two experienced neuroradiologists independently assessed the MRIs findings for MTS without knowledge of hippocampal volumetric data. Hippocampal volumes were measured using FreeSurfer software and standardized using the hippocampal volume index (HVI) and hippocampal asymmetry index (HAI).

Results: In our study of 38 patients, MTS was found in 55.2% of patients on the right side and in 44.8% of patients on the left side, with no bilateral cases. Visual MRI analysis identified MTS in 84.2% of patients, with an area under of curve (AUC) of 0.921. Automatic volumetry detected MTS in 23 patients with an AUC of 0.791. Combining both methods, MTS was diagnosed in 33 patients, with an AUC of 0.922.

Conclusion: Automated volumetric analyses have been shown to enhance the detection of hippocampal volume loss in patients with MTS.

Keywords: Mesial temporal sclerosis, hypocampus volume, automated segmentation

INTRODUCTION

Epilepsy is a significant health issue that affects both adults and children. In adults, the most common cause of drug-resistant epilepsy is mesial temporal sclerosis (MTS).[1] Many patients with MTS have a history of brain injury due to various factors, such as febrile illnesses or trauma. After an asymptomatic period, patients often develop refractory epilepsy.[2] The primary pathological changes that lead to seizure activity are epileptogenic foci in the mesial temporal region, which result from processes such as neuronal loss, hippocampal sclerosis, and axonal reorganization.[3,4] These changes can occur in isolation or in conjunction with other cortical malformation.

Patients diagnosed with MTS are usually treated with medications. However, approximately one-third of these patients do not respond to antiepileptic drugs. In such cases, surgery is a crucial option.[5] After determining the affected side of the brain, the most common surgical procedure involves removing the anterior part of the temporal lobe and mesial structures.[6] Magnetic resonance imaging (MRI) is widely

used to diagnose MTS. Typical MRI findings of MTS include hippocampal volume loss, increased signal intensity in the hippocampus on T2-weighted and FLAIR sequences, volume loss in the ipsilateral temporal lobe, reduced distinction between white and gray matter in the temporal lobe, and enlargement of the ipsilateral temporal horn.[7]

Different studies have reported varying MTS detection rates. Even expert radiologists sometimes find it challenging to identify MTS through radiological assessments, especially in cases of hippocampal degeneration.[8] Factors such as patient movement during imaging, signal intensity changes, or mild or bilateral hippocampal atrophy can complicate the diagnosis and lateralization of MTS, sometimes necessitating invasive monitoring.[9]

T1-weighted hippocampal volume measurements have long been proven effective in detecting MTS.[10] No significant differences exist between the hippocampal volume data obtained from 1.5T and 3T MRIs.[11] Previously volumetric data for hippocampal volume were obtained by manually segmenting consecutive slices, which is time-consuming and requires specialized expertise.[12] However, recent advances have enabled automatic hippocampal segmentation and volume measurement using various software packages, producing results comparable to those of manual methods in adult patients.[13] These software tools have simplified hippocampal volume measurement and are now used for diagnosing MTS, showing promising results, with sensitivity ranging from to 87-95%, specificity from to 57-94%, and accuracy from 82-89% to in clinical practice.[14] Furthermore, the hippocampal volume index (HVI) and hippocampal asymmetry index (HAI), used alone or together, have improved MRI's sensitivity, specificity, and predictive value of MRI in MTS diagnosis compared with other analytical techniques.[14]

Our study aimed to contribute to the literature by comparing hippocampal volumes, HAI, and HVI indices between individuals with histopathologically confirmed MTS and a control group of similar age and sex within the adult Turkish population.

METHODS

Study Design

Our study was conducted by retrospectively reviewing the cranial MRIs of patients diagnosed with mesial temporal sclerosis (MTS) through histopathological examination following surgery for refractory epilepsy. These patients presented to the epilepsy outpatient clinic of the neurology department at our institution between January 2019 and June 2024. The study was approved by the İstanbul University-Cerrahpaşa Clinical Researches Ethics Committee (Date:18.09.2024, Decision No: 1090171). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patient Enrollment

We included patients who had undergone surgery for refractory epilepsy, had histopathologically confirmed diagnoses, and whose medical records and imaging data were available at our institution. Patients were excluded if the retrospective review of the pathological results revealed any conditions that could cause epilepsy, such as intracranial malignancy, encephalomalacia, previous intracranial surgery, cortical malformations, or cortical dysplasia. A total of 52 patients met the inclusion criteria. However, upon reviewing their radiological images within our institution's PACS system (Extreme PACS, Ankara), 14 patients were excluded because they did not have MRI scans that adhered to the epilepsy protocol. Consequently, 38 patients were included in the final study.

To avoid bias when compared to the MTS group, we applied propensity score matching by age and sex to select a control group. After matching, 42 control subjects with regular radiological reports and T1 volumetric sections suitable for automatic segmentation using our PACS system were included.

Magetic Resonance Imaging Protocols

All patients underwent MRI scans using a 3T Intera Achieva scanner (Philips Healthcare, Best, Netherlands) following the epilepsy imaging protocol, which included: Coronal images perpendicular to the long axis of the hippocampus, identified on the sagittal plane: 1) T2-weighted imaging (3 mm slice thickness, no gap, voxel size=0.89 x 1 x 3 mm, TR=3300 ms, TE=30/60/90/120/150 ms, matrix=200x180, FOV=180x180, TSE factor=5; EPI factor=5, flip angle=90°); 2) T1-weighted inversion recovery (3 mm slice thickness, no gap, voxel size=0.75x0.75x3 mm, TR=3550 ms, TE=15 ms, TI=400 ms, matrix=240x229, FO=180x180, TSE factor=7); 3) FLAIR (spectral-attenuated inversion recovery, fat suppression power=1, 4 mm slice thickness, section gap=1 mm, voxel size=0.89x1.1x2.4 mm, TR=12,000 ms, TE=140 ms, TI=2850 ms, matrix=180x440, FOV=200x200). Axial images parallel to the long axis of the hippocampus: FLAIR (fat-suppressed spectral-attenuated inversion recovery, 4 mm slice thickness, section gap=1 mm, voxel size=0.89x1.1x2.4 mm, TR=12,000 ms, TE=140 ms, TI=2850 ms, matrix=224x160, FOV=200x200). T1-weighted volumetric images: isotropic voxels of 1 mm, acquired in the sagittal plane (1 mm slice thickness, no gap, flip angle=8°, TR=7.0 ms, TE=3.2 ms, matrix=240×240, FOV=240×240). T2-weighted volumetric images: isotropic voxels of 1.5 mm, acquired in the sagittal plane (no gap, TR=1800 ms, TE=340 ms, matrix=140x140, FOV=230x230, TSE factor=20; flip angle=90°; geometry corrected).

Imaging Analysis

Two board-certified neuroradiologists with 12 and 20 years of experience (S.A. and O.K.) independently reviewed the MRIs, blinded to the hippocampal volumetric data. They assessed the presence of MTS findings, such as hippocampal atrophy, gliosis, and signal changes in the mesial temporal region. If other abnormalities were observed in the mesial temporal structures, they were asked to note them. In cases of disagreement, a final decision was reached through a consensus after a joint review.

Hippocampal Volume Measurement

Hippocampal volume measurements were performed using T1-weighted images on a personal computer equipped with an AMD Ryzen 5 Pro 3.7 GHz processor, 16 GB RAM, and Windows 10, using FreeSurfer software (version 7.4.1; http://surfer.nmr.mgh.harvard.edu), which performs automatic reconstruction and segmentation. The procedures included removing non-brain tissue using a hybrid watershed algorithm,

automatic transformation to the Talairach reference space, and segmentation of subcortical white matter and deep gray matter structures. The entire hippocampal formation was segmented using a standard procedure and a probabilistic brain atlas. The estimated intracranial volume (ICV) was calculated for each subject[15] (**Figure 1**).

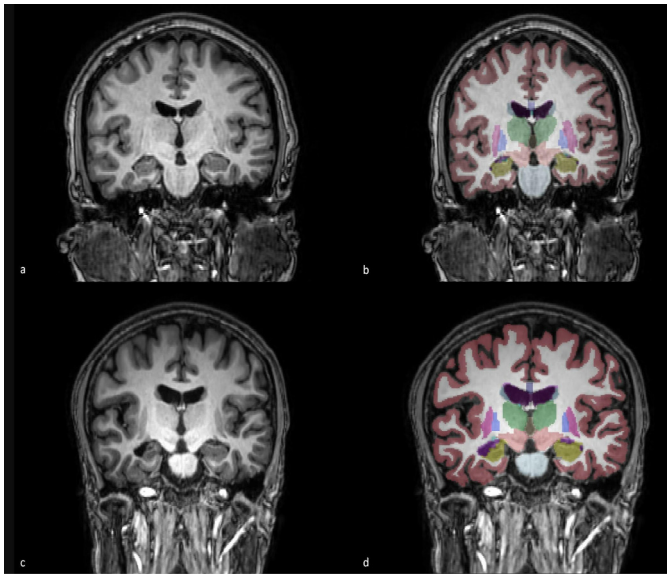

Figure 1. a,b. A 38-year-old healthy individual. **a.** Cranial MRI T1-weighted images (T1WI) in coronal sections displaying both hippocampi. **b.** FreeSurfer segmented image illustrating brain cortical and subcortical structures, with both hippocampi highlighted in yellow and the lateral ventricular temporal horn in purple. **c,d**. A 28-year-old male patient diagnosed with right mesial temporal sclerosis (MTS). MR imaging volumetry revealed a significant reduction in the volume of the right hippocampus. **c.** T1WI showing both hippocampi, which appear normal upon visual inspection. **d.** FreeSurfer volumetry images with the hippocampi marked in yellow. The right hippocampus is notably smaller than the left, and the right lateral ventricular temporal horn (purple) is visibly wider than the left.

Data Analysis

Volumetric values were standardized using the hippocampal volume index (HVI), which is the ratio of the hippocampal volume to the total intracranial volume (TIV) (HVI=hippocampal volume/TIV×100). Separate values were obtained for the right hippocampus (HVIR) and the left hippocampus (HVIL). Interhemispheric comparisons were performed using the hippocampal asymmetry index (HAI), defined as the difference between the left and right hippocampal volumetric indices, and the sum of these indices (HAI=[HVIL-HVIR]/[HVIR+HVIL]). Atrophy was considered if there was a difference of more than 2 SD between the measured volumetric values and indices and the mean values of the controls. In addition, we combined the performance of neuroradiologists with automatic volumetric measurements. A patient was considered to have MTS if either or both the methods yielded positive results.

Statistical Analysis

Categorical data were presented as numbers and percentages (N, %) and compared using Pearson's Chi-square or Fisher's exact test, where appropriate. Numerical values are presented as mean and standard deviation. Two independent-sample t-tests were used to determine whether the parametric values showed a statistically significant difference. The Shapiro-Wilk test was used to ensure that the data were normally distributed. The specificity and sensitivity of the values were calculated and ROC curve analysis was performed for each lateralization assessment. Statistical significance was considered two-tailed ($p<0.05$). Statistical analysis was conducted using IBM Statistical Package for the Social Sciences (SPSS) version 22.0 for Windows.

RESULTS

In our study, 29% (5/17) of cases were excluded due to lack of imaging studies,; another 29% (5/17) were excluded due to accompanying pathologies such as focal cortical dysplasia, 24% (4/17) were excluded due to extensive tissue loss caused by preoperative changes such as encephalomalacia and infarction, and 18% (3/17) were excluded due to the detection of intracranial malignancy. A total of 38 patients met the inclusion criteria (**Table 1**).

MTS was detected on the right side in 21 patients (55.2%) and on the left side in 17 (44.8%). There were no cases of bilateral MTS. The patient group consisted of 21 females (55.3%) and 17 males (44.7%), with an average age of 34.29±10.02 years. The control group consisted of 42 individuals, 21 females (50%) and 21 males (50%), with an average age of 34.62±11.01 years (**Table 2**).

No significant differences were found between patients and controls in terms of sex and age distribution (sex, $p=0.661$; age, $p=0.502$). No significant relationship was found between the sex of the patient and the side of the lesion ($p=0.796$). Regarding sex, no significant differences were found in the adjusted HVIR and HVIL values in control subjects (HVIR, $p=0.091$; HVIL, $p=0.107$) (**Table 2**).

Neuroradiologists' Evaluation

Excellent concordance was observed among the neuroradiologists. In evaluating the MTS, both radiologists provided positive interpretations for 30 patients. In contrast, in one patient, the O.K. was negative, S.A. was positive, O.K. was positive, and S.A. was negative. In these two patients, a decision favoring the disease was made based on a joint assessment. The results showed that 32 individuals (84.2%) were consistent with MTS in the visual analyses on MRI. Despite the presence of MTS in the visual analysis, MTS was not detected in 6 patients (15.8%). The area under the curve for joint neuroradiologist assessment was 0.921 (standard error 0.036, $p<0.001$; 95% CI).

Automated Volumetry

In the control group, the average right hippocampal volume was 4236.36±452.32 mm^3, while the average left hippocampal volume was 4102.83±422.11 mm^3. The mean HVIR was 0.301±0.031, and 0.292±0.031 in the control and HVIL groups, respectively. For controls, the mean HAI index in absolute terms was 0.027±0.018. Automatic volume measurement revealed physiological asymmetry between the right and left hippocampal volumes in the control group, with the right hippocampal volume being 3.3% larger than the left ($p<0.001$). In the patient group, the average right hippocampal volume was 3755.41±802.51 mm^3, while the average left hippocampal volume was 3899.12±610.49 mm^3. The mean HVIR in the patient group was 0.457±0.28, and the mean HVIL was 0.426±0.29. The mean HAI index in the patients was 0.840±0.370, which was significantly higher than that in the control group ($p<0.001$). Right hippocampal volumes were significantly reduced in patients with right MTS compared to those without right MTS ($p<0.001$). Similarly, left hippocampal volumes were significantly reduced in patients with left MTS compared to those without left MTS ($p=0.006$).

Table 1. MTS group

Patient	Age (years)	Sex	MTS	Hippocampus (R)	Hippocampus (L)	TVI	HVIR	HVIL	HAI
1	41	M	R	1822.6	3991.7	1370900.3	0.21	0.29	0.14
2	34	F	R	2098.8	4102	1208412.1	0.36	0.33	-0.03
3	19	F	R	1298.6	3.642	956790.83	0.37	0.38	0.00
4	56	F	R	1752.4	3604.9	1389013.7	0.20	0.25	0.11
5	28	F	L	1126.9	2861.4	1050819.5	0.37	0.27	-0.16
6	28	M	R	2059.1	4544.6	1701792.3	0.20	0.26	0.13
7	32	F	R	2151.5	4305.5	1034469.3	0.45	0.41	-0.04
8	23	F	R	1796.7	4015.9	1548279.2	0.20	0.25	0.10
9	49	F	L	2116.8	4058.1	1640752.9	0.31	0.24	-0.12
10	23	F	R	2127.4	4597.3	1445610.6	0.34	0.31	-0.04
11	32	F	R	2072.2	3834.6	1169270.2	0.34	0.32	-0.02
12	24	M	L	2116.1	4470.2	1643794	0.27	0.27	0.00
13	35	F	L	1895.1	4337.9	1314324.7	0.34	0.33	-0.02
14	34	M	L	2094.6	4868.2	1641647.8	0.30	0.29	-0.01
15	28	M	R	1878.8	4652.1	1183510.2	0.30	0.39	0.12
16	21	M	R	1900.5	4145.9	1599950.2	0.19	0.25	0.13
17	41	F	L	1844.5	4116.3	1415082.4	0.30	0.29	-0.02
18	29	F	L	1835.7	2559.9	1252275.6	0.31	0.20	-0.21
19	35	F	R	1407.5	3371.6	791471.61	0.35	0.42	0.09
20	46	M	R	1971.4	4180	1474052.8	0.25	0.28	-0.04
21	48	F	L	1586.3	4354.8	1395354.1	0.32	0.31	-0.01
22	48	M	L	1832.7	4141.1	1820314.1	0.25	0.22	-0.05
23	57	F	R	1752.9	3707.8	994663.37	0.33	0.37	0.05
24	37	M	L	1590.1	2630.2	1380438.2	0.19	0.19	-0.02
25	32	F	L	1359.5	3133.7	1079315.7	0.30	0.29	-0.02
26	40	M	L	1374.6	3428.9	1092095.6	0.30	0.31	0.01
27	26	M	R	1676.2	4128.3	1491270.7	0.18	0.27	0.18
28	45	F	L	2253.1	3122.3	1254046.5	0.37	0.24	-0.20
29	47	F	L	1215.7	3728.3	1182686.6	0.30	0.31	0.01
30	25	M	R	649.3	4381.6	1846007.9	0.15	0.23	0.21
31	37	M	R	2515	4971.3	1540049.3	0.28	0.32	0.06
32	33	F	R	1255.9	4048.2	1412347.7	0.20	0.28	0.16
33	29	M	L	2009.3	3064.6	1286119.9	0.29	0.23	-0.10
34	33	F	R	1886.7	4293.5	1444513.1	0.26	0.29	0.06
35	18	M	R	481.4	4245.4	1455397.5	0.12	0.29	0.40
36	25	M	L	1992.7	3619.6	1687706.2	0.26	0.21	-0.10
37	40	F	R	1507.1	4108.7	1353613	0.19	0.30	0.21
38	25	M	L	1448.9	2798.5	1497254.9	0.26	0.18	-0.16

Table 2: Control group

Patient	Age (years)	Sex	MTS	Hippocampus (R)	Hippocampus (L)	TVI	HVIR	HVIL	HAI
1	35	F	0	3304.2	3177	1107147.9	0.29	0.28	-0.01
2	23	M	0	4341.7	4159	1350956.2	0.31	0.30	-0.02
3	21	F	0	3964	3890.3	1429430.9	0.27	0.27	0.00
4	34	M	0	5020.2	4348.9	1524919.7	0.32	0.28	-0.07
5	26	F	0	4139.8	4524.3	1474817.2	0.28	0.30	0.04
6	28	F	0	4131.6	4091.6	1314065.8	0.31	0.31	0.00
7	32	F	0	4898.6	4638.6	1447987.2	0.33	0.32	-0.02
8	33	F	0	3804.9	3664.8	1061439.7	0.35	0.34	-0.01
9	19	M	0	4391.7	3911.3	1635988.5	0.26	0.23	-0.05
10	19	M	0	4796.2	5044.1	1695725.3	0.28	0.29	0.02
11	35	M	0	4802.8	4473	1648093.6	0.29	0.27	-0.03
12	38	F	0	3331.5	3389.4	1333834.4	0.24	0.25	0.00
13	43	M	0	4815.1	4414.7	1372317.9	0.35	0.32	-0.04
14	50	F	0	3727.7	3644.3	1460117	0.25	0.24	-0.01
15	56	F	0	4186.9	3942.3	1361931.9	0.30	0.28	-0.03
16	46	M	0	4310.1	4027.3	1536389.8	0.28	0.26	-0.03
17	45	M	0	4108.6	4566.1	1563843.8	0.26	0.29	0.05
18	39	F	0	3421.8	3301.7	1045933.7	0.32	0.31	-0.01
19	32	F	0	4413	4263.5	1209318	0.36	0.35	-0.01
20	31	F	0	4733.9	4275.8	1517097.7	0.31	0.28	-0.05
21	28	M	0	4397.8	4365	1482867.8	0.29	0.29	0.00
22	23	M	0	4823.3	4569.8	1636038.5	0.29	0.27	-0.02
23	23	M	0	4074	4175	1477876.1	0.27	0.28	0.01
24	26	M	0	4735	4119.5	1689085.7	0.28	0.24	-0.06
25	29	M	0	4114.6	4338.8	1323723.1	0.31	0.32	0.02
26	30	M	0	4462.3	4249.1	1574831.4	0.28	0.26	-0.02
27	35	F	0	4321	3849.5	1351729.5	0.31	0.28	-0.05
28	35	M	0	4462.3	4249.1	1574831.4	0.28	0.26	-0.02
29	42	M	0	4420.8	4138	1572328.1	0.28	0.26	-0.03
30	48	M	0	4283.3	4259	1461063	0.29	0.29	0.00
31	58	F	0	3778.5	3935.1	1393277.6	0.27	0.28	0.02
32	29	M	0	4688.6	5074.7	1495213.7	0.31	0.33	0.03
33	43	F	0	3786.3	3596.8	1316671.7	0.28	0.27	-0.02
34	45	F	0	4045.3	3820.2	1338679.1	0.30	0.28	-0.02
35	37	F	0	4851.3	4371.7	1653291.2	0.29	0.26	-0.05
36	50	F	0	3747.6	3606.3	1316642.8	0.28	0.27	-0.01
37	22	F	0	4087.3	3992.3	1094632.8	0.37	0.36	-0.01
38	57	F	0	3551.7	3529.7	1135889.3	0.31	0.31	0.00
39	28	M	0	3533.7	3666.4	1426506.9	0.24	0.25	0.01
40	19	M	0	4255	3875.8	1295258.8	0.32	0.29	-0.04
41	18	F	0	4440.6	4426.7	1188054.3	0.37	0.37	0.00
42	44	M	0	4422.6	4362.4	1599046.9	0.27	0.27	0.00

F: Famale, M: Male, MTS: Mesial Temporal Sclerosis, HVIR: Right hippocampus, HVIL: Left hippocampus, HAI: Hippocampal asymmetry index

Table 3. Demographic characteristics

	Patients (n:38)	Controls (n:42)	p value
Age (years)	34.29±10.02	34.62±11.01	0.502
Gender (male)	44.7% (n: 17)	50% (n:21)	0,661
Side of MTS	Left: 44.8 (n:17) Right: 55.2% (n:21)		

MTS: Mesial temporal sclerosis

The threshold for diagnosing MTS was set at a difference of 0.059 or higher for the HAI. Additionally, values of 0.239 or lower for HVIR and 0.231 or lower for HVIL were considered significant for the MTS. Based on the HVI values, 16 patients were diagnosed with MTS, with no misdiagnoses in the control group. In the HVI analysis, an area under the curve (AUC) of 0.711 was obtained for the diagnosis and lateralization of patients with MTS, with a sensitivity of 42.0% and specificity of 100.0% (standard error 0.060, p=0.001; 95% CI). HAI correctly identified 21 patients with MTS using the automatic method but incorrectly diagnosed one control as MTS. The predictive values were better with the HAI. For the HAI values, an area under the curve of 0.764 was obtained, with a sensitivity of 55.00% and specificity of 97% (standard error 0.056, p<0.001; 95% CI). Among the seven patients identified with MTS based on HAI values, the HVI values were within normal limits, and two patients with average HAI values had HVI values consistent with MTS. In 14 patients, both HAI and HVI values consistently indicated MTS, whereas 15 patients were within normal limits for both indices. In the automatic volumetric analysis, MTS was detected in 23 patients based on the overall performance of the HVI or HAI indices. The area under the curve for automatic volumetry was 0.791 (standard error 0.054; p<0.001; 95% CI).

Overall Performance

Visual inspection and automatic volumetry detected mesial temporal sclerosis (MTS) in 22 patients. However, both methods missed MTS in 5 patients, resulting in false-negative outcomes. Overall, the two methods were in agreement in 27 of the 38 cases. Among the ten patients with visually identified MTS, 95% had average volumetric indices, whereas 13% of those with visually averaged MRI results showed hippocampal atrophy through volumetric analysis. MTS was diagnosed in 33 patients when both methods were combined. The area under the curve (AUC) for the combined effectiveness of visual assessment and automatic volumetry was 0.934 (standard error 0.033, p<0.001; 95% CI) (**Figure 2**).

DISCUSSION

MTS is the primary cause of refractory epilepsy. According to the literature, 55.5% of these patients show findings consistent with MTS, based on tests and examinations.[16,17] MRI is beneficial and commonly used for identifying epilepsy-related pathologies, such as MTS.[18] Furthermore, detecting MRI findings of hippocampal sclerosis, the primary pathology in MTS, is crucial for determining lateralization in drug-resistant MTS patients and for guiding surgical treatment.[19] Typical imaging findings of MTS include signal changes in T2-weighted sequences and decreased hippocampal size.[20] Additionally, hippocampal volume data are recognized as reliable surrogate markers for hippocampal sclerosis, the primary pathological basis of MTS.[21]

Many neuroradiologists are adept at visually identifying moderate-to-severe hippocampal atrophy when conducting epilepsy MRI protocols. However, detecting MRI abnormalities in patients with MTS relies heavily on both the quality of the MRI protocol and the evaluator's experience in interpreting MRIs in patients with epilepsy. In a particular study, "non-expert" radiologists deemed 61% of specific standard MRIs as normal, whereas "expert" radiologists found that 28% of the same MRIs were technically inadequate and 22% were normal.[22] It has been demonstrated that even expert neuroradiologists can produce false-negative results with qualitative analysis when there are varying conditions related to the imaging technique and patients.[9] Additionally, qualitative MRI readings may miss minor differences in hippocampal volumes, and quantitative volume measurements have been reported to be beneficial in such cases.[23] The strong correlation between the volumes detected by quantitative analysis and histopathology supports this hypothesis.

Recent research has indicated that measuring hippocampal volume can aid qualitative analysis in cases of mild hippocampal volume loss,[24] bilateral hippocampal volume loss with minimal

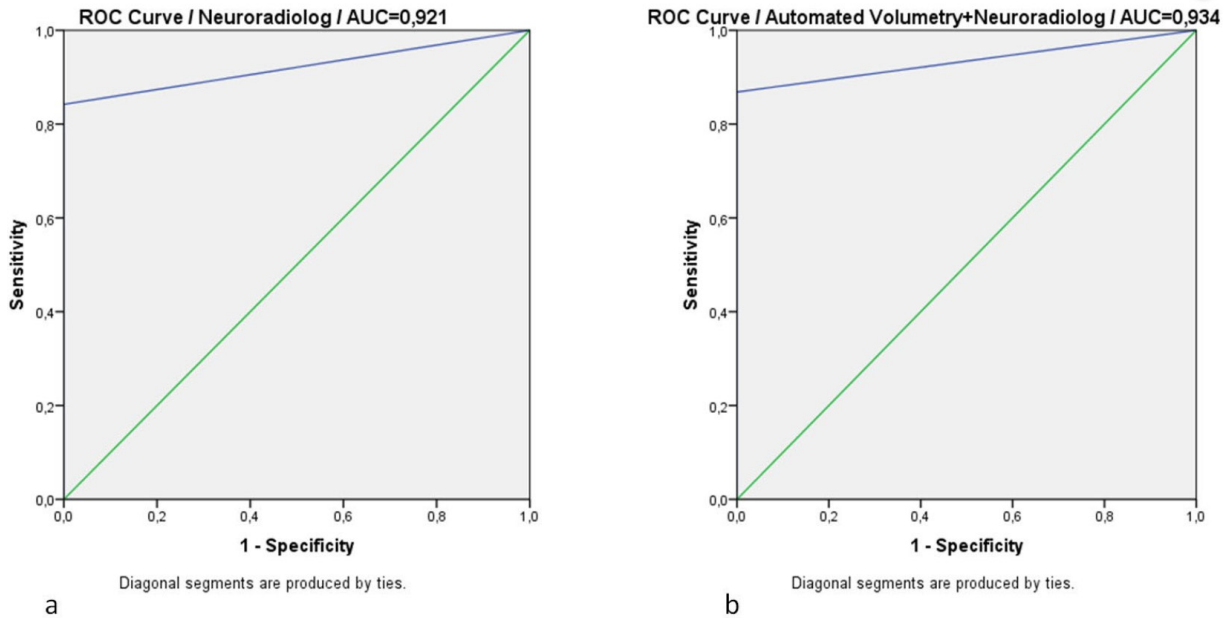

Figure 2. The Receiver Operating Characteristic (ROC) curve analysis for diagnosing mesial temporal sclerosis indicates that combining automated volumetry with visual assessment enhances the area under the curve (AUC). This suggests improved diagnostic accuracy when both methods are used together.

or no asymmetry,[25] and in centers without expertise in epilepsy imaging.[26]

Studies have shown that manually measured hippocampal volumes are more accurate than those measured using automatic methods. However, automatic segmentation is approximately 77% faster than manual segmentation and is less susceptible to different operator biases.[26-28] Additionally, the small size of the hippocampus can lead to significant errors in volume calculation during manual measurements.[21] The literature also suggests that results from FreeSurfer software, which automatically performs cerebral cortex parcellation and subcortical structure segmentation based on probabilistic information from manual segmentation datasets, can be as reliable as those obtained through manual techniques.[14,29] Therefore, we used the FreeSurfer software to obtain hippocampal volume data.

Through volume analysis conducted on healthy controls, we found that the hippocampal volumes (right=4236 mm^3, left=4102 mm^3) were consistent with the values obtained in a previous study[19] using a similar software and methodology (right=4179 mm^3, left=3999 mm^3). This consistency indicates the reproducibility of the automatic segmentation. The left dominance observed in our study might be a physiological characteristic of our population; however, more extensive cohort studies are needed to confirm this hypothesis. Furthermore, as reported in the literature, no statistically significant differences were observed in hippocampal values between sexes or HVI values between the right and left hemispheres in the control group.[30]

In previous studies, evaluating hippocampal atrophy using HVI values yielded a sensitivity between 44% and 94% and a specificity between 86% and 96%. When HAI values were utilized, sensitivity ranged from 88% to 96%, and specificity ranged from 87% to 100%. In our study, using threshold values determined by ROC analysis, we achieved sensitivity and specificity for detecting hippocampal volume loss, consistent with the literature, based on both HVI and HAI values. Pathology reports indicated a significant correlation between the side where MTS was detected and the side where volume loss was observed. However, contrary to our expectations, we observed a slight increase in hippocampal volume on the affected side in six patients. This suggests that during the very early stages of the disease, before atrophy develops, the hippocampal volume may temporarily increase due to inflammatory changes.[31] This might be one of the reasons why the sensitivity and specificity of the threshold values calculated in our study are lower than those reported in the literature.

In alignment with a similar study conducted previously in a different population, our research found that the predictive value of HAI was superior. HAI demonstrated a higher true-positive rate and a lower false-negative rate than HVI. Furthermore, the absolute threshold value for HAI identified in this study (0.06) closely matched the absolute threshold value that we determined (0.057). This suggests that the HAI value does not vary significantly across different populations, and is reliable in terms of reproducibility. Physiological asymmetry between hippocampal volumes has been consistently reported in various studies.[9,32]

The neuroradiologist's assessments demonstrated sensitivity and specificity rates comparable to those in other studies with similar goals.[9,20] When automatic volumetric values were evaluated in coordination with neuroradiologists, there was a notable increase in both the sensitivity and specificity. Furthermore, the excellent specificity rate observed in our study supports the clinical application of the workflow proposed in a previous study.[20] The main reason for achieving similar results in both studies might be the difficulty in visually detecting minor volumetric differences.[23]

Limitations

The main limitations of this study are the small cohort size and retrospective nature of the analysis. Second, hippocampal atrophy is only one component of MTS, and signal changes in T2-weighted FLAIR images are among the other findings of hippocampal sclerosis. However, the detection of T2-weighted signal changes in pathologies, such as focal cortical dysplasia and temporal lobe lesions causing epilepsy, apart from MTS, indicates that hippocampal volume loss is a more specific marker for MTS. Additionally, the neuroradiologist interpreting the study might have been biased because of being aware of the patient's clinical diagnosis of epilepsy. However, the quantitative MRI data were blinded to the control subjects and patients. Finally, our dataset was relatively small to determine the optimal threshold values, and there was notable asymmetry in the hippocampal volume ratios within the population we studied. Additionally, differences in hippocampal volume size were observed based on the timing of potential MTS pathology. Therefore, the absolute optimal threshold value may vary with the lateralization of pathology.

Automated volumetric analyses have been shown to enhance the detection of hippocampal volume loss in MTS patients. By incorporating these efficient volumetric methods, which can be identified via MRI, into clinical workflows, radiological assessments can be streamlined. Moreover, with further validation, these methods can evolve into parameters that clinicians can interpret in routine practice. Additionally, combining hippocampal volume measurements with data from other imaging techniques, such as T2 and FLAIR in future studies, which include larger patient and control groups, offers exciting potential for improving the effectiveness of clinical applications.

CONCLUSION

In conclusion, the qualitative analysis of signal changes in T2-weighted and FLAIR imaging, combined with unbiased quantitative volumetric data, facilitates a more comprehensive investigation of the critical findings in hippocampal sclerosis pathology.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Faculty of İstanbul University-Cerrahpaşa Clinical Researches Ethics Committe (Date: 18.09.2024, Decision No: 1090171).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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