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Original Research Article

Diagnostic Performance of MR Imaging Using Unenhanced Axial CISS for Detection of Small Lesions in Cerebellopontine Angle

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Abstract: ***Background*:** Although contrast-enhanced T1-weighted MR imaging is the standard of reference for diagnosing tumour in the cerebellopontine angle (CPA), high-resolution T2-weighted imaging may show more details of the seventh and eighth cranial nerve branches, resulting in more accurate tumour volume measurements. ***The Aim of Study***: Was to evaluate the value of diagnostic accuracy of an unenhanced MR imaging protocol using unenhanced axial 3D constructive interference in steady state (CISS) in detection of small internal auditory canal lesions (IAC). ***Patients and Methods*:** cross-sectional study carried out over a period from April 2018 to February 2019 in the MRI department of Al-Imamain Al-Kadhemain medical city, included 38 patients (76 internal auditory canals), whom presentation with clinical features of (sensorineural hearing loss, tinnitus or vertigo) with suspicion of IAC lesions, sent by specialist after clinical examination. All patients were examined with axial T1WI, axial T2WI, coronal FLAIR, axial 3D-CISS sequence for evaluate its accuracy in detecting abnormalities of the CPA, IAC and inner ear. Each sequence assessed carefully for detection of any lesion within IAC, inner ear and CPA cistern, the statistical analysis is assessed for the sensitivity, specificity and accuracy. ***Results*:** 38 patients (76 IACs /CPA cisterns) met the inclusion criteria, included 18 (47.4 %) patients with radiological evidence of IACs /CPA cistern lesions, 20 (52.6%) patients without lesions, considered as the control group which confirmed by IAC/CPA cistern routine sequences in addition to confirmation by 3D-CISS sequence. Thus 76 IACs are examined 18 with lesions, 58 IACs without significant pathology. The sensitivity, specificity and accuracy of 3D CISS sequence and axial T2WI are estimated separately and both together. 9 lesions (50 %) found intracanalicular 4 fundal (22.2%) and 5 (27 %) within CPA cistern. The number of lesions in diseased group showing true positive results by 3D-CISS sequence were 17 (94.4 %) of detected lesions while one lesion (5.6%) showing false negative result by CISS sequence because it was arachnoid cyst not clearly identified. While the number of lesions in control group showing false positive results were 2 (10.0 %) due to volume averaging artifact, the true negative lesions were 18 (90.0 %), (P-value 0.0001). The number of lesions in diseased group showing true positive results by T2WI sequence were 15 (83.3%) of detected lesions while 3 lesions showing false negative result by T2WI sequence representing (16.7%). Whereas the number of lesions in control group showing false positive results were 4 (20.0%) due to artifact, the true negative lesions were 16 representing (80.0%) (P-value 0.0001). The Sensitivity of axial 3D-CISS sequence was (94.4%), specificity (90%) and accuracy (92.1%). The Sensitivity of axial T2WI sequence was (83.3%), specificity (80%) and accuracy (81.6%). ***Conclusion*:** 3D CISS sequence is supply high topographic resolution, with high contrast to noise ratio that highly beneficial for defining the exact location of the lesion and follow the vascular structures and nerves with clarity. It shows high sensitivity and specificity in detection of lesions of IACs and CPA cistern. Elderly patients and patients with allergy to gadolinium contrast agent can get benefit from using a 3D CISS sequence as screening and diagnostic tools and for follow up.

Keywords: Cerebellopontine Angle Tumour, CISS, Internal Auditory Canal Lesions.

INTRODUCTION

Three-dimensional (3D) constructive interference in steady state (CISS) is a fully refocused steady-state gradient-echo MRI sequence. This sequence is now available and is frequently used in MRI to investigate a wide range of pathologies when routine MRI sequences do not provide the desired anatomic information [1].

Three-dimensional CISS is routinely used in the assessment of cerebellopontine angle lesions, inner ear structures and the internal auditory canal (IAC) [2]. With this sequence the fine structure of the cranial nerves VII

and VIII and the membranous labyrinth of the internal ear can be clearly demonstrated. This has facilitated detection of small intracanalicular lesions and diagnosis of the nerve of origin depending upon exact location in the IAC. This helps to precisely diagnose schwannomas arising from the cochlear nerve [3].

Vestibular schwannoma; Acoustic schwannomas are benign tumours (WHO grade 1) which usually arise from the intracanalicular segment of the vestibular portion of the vestibulocochlear nerve (CN VIII) [4], accounts for approximately 85% of all cerebellopontine angle masses [5], and it is the most common cause of unilateral sensorineural hearing loss that diagnosed by magnetic resonance imaging (MRI) [6, 7]. However, only 2.7% to 4.7% of case could be diagnosed using contrast-enhanced MRI [8, 9].

Early detection of IAC lesions such as vestibular schwannomas is essential to decrease morbidity of the treatment as larger tumors can lead to more complications [10]. Early detection is vital especially if the surgery is performed to protect from hearing loss; as the size of the mass is related to hearing outcomes [11, 12], though gadolinium-enhanced MRI is the gold standard and embraced by many, as it need longer scan time in comparison to T2 only, more discomfort to the patients, and possible risk of allergic reactions, minimizing health care costs, and adoption of a less expensive tests now become an important factor in decision-making [6]. Therefore aim of this study was to evaluate the value of diagnostic accuracy of an unenhanced MR imaging protocol using unenhanced axial 3D-CISS (constructive interference in steady state in detection of Vestibular Schwannoma.

PATIENTS AND METHODS

Patient's Population

A Cross sectional study carried out from April 2018 to February 2019 in the MRI department of Al-Imamain Al-Kadhemain medical city and included 38 patients (76 IACs); whom presentation with clinical features of (sensorineural hearing loss, tinnitus or vertigo) attributable to a lesion of IAC (Internal Auditory Canal), CPA cistern and inner ear sent by ENT specialist after clinical examination, who submitted to conventional MRI sequences protocol for IAC/CPA cistern in addition to 3D-CISS sequence.

Inclusion Criteria Was: Any patient presented with clinical features of (sensorineural hearing loss, tinnitus or vertigo).

Exclusion Criteria Were:

Inadequate diagnostic quality secondary to motion or other artefacts, large lesion post operation, any lesion located in the cochlea other in semicircular canal that were readily seen on routine sequences and the study concentrate on IAC lesions, an any contraindication to MRI (e.g Patient with claustrophobia).

METHODS

Machine

The MRI examination were performed using 3T superconducting system Philips (Achieva 3 – Philips medical system, Netherlands) via 8 channel standard head matrix coil.

Technique

All patients were examined in supine position and were submitted to an institution rules, thin slice MRI protocols CPA cistern and IAC which include: axial T2-FSE, axial 3D- CISS sequence, axial T1-FSE, coronal FLAIR.

Protocol

The following MRI Sequences with Their Parameters Were Done for All Patients

1. T2 weighted images in axial plane, with following parameters: field of view (FOV) = (230/184/119) mm, matrix =400X225, TR/TE = 3000/80 (msec), flip angle= 90 degree and an acquisition time of 1 min plus 48 sec.
2. 3D-CISS in axial plane, with following parameters: FOV = (180/180/38) mm, matrix = 308x307, voxel size (0.586 /0.586 / 0.5) mm, TR/TE = 6/2.4 msec, flip angle= 45 degree, number of signal averaged=2 and an acquisition time of 3 min plus 46 sec.
3. T1 weighted images in axial plane, with following parameters: FOV = (230/214/143) mm, matrix =400 x 298, voxel size (0.575 /0.72) mm, TR/TE = (255/4.6) msec, flip angle= 80 degree, number of signal averaged =1 and an acquisition time of 1 min plus 17 sec.
4. T2 FLAIR coronal plane, with following parameters: FOV = (230 /183/119) mm, Matrix = 240 x 138, Voxel size (0.65 / 0.87) mm, TR/TE=(11000/2800) msec, number of signal averaged = 1, Flip angle= 120 degree and an acquisition time of 1 min plus 39 sec.
5. DWI axial plane, with following parameters: field of view (FOV) = (230/ 230 / 144) mm, matrix = 152 x121, voxel size (1.5 /1.89) mm, TR / TE = (4045/ 98) msec, number of signal averaged = 1, flip angle=90 degree and acquisition time of 1 min plus 30 sec.

So, 76 IAC/CPA cistern examined of 38 patients,18 with lesions and 58 without lesions, all their sequences are seen carefully and specifically by conventional, routine MRI sequences for looking for any lesions within IACs / CPA cisterns, further evaluation done by other advanced sequence, through using 3D-CISS sequence.

Absence of pathology was determined in following the vestibulocochlear (VIII) and facial (VII) nerves from their root entry to the fundus of IAC without neighboring mass.

After reading all sequences and imaging carefully, interpretation was compared the T2WI with 3D-CISS sequence to confirm the presence or the absence of the lesions. The measurement was done by taken the maximum diameter 3D-CISS sequence. In general, the axial 3D CISS sequence was 2 minutes 45 seconds to 4 minutes 30 seconds in acquisition time; the average total scan time was 10 minutes 2 seconds to 10 minutes 43 seconds.

Statistical Analysis

Statistical package for social sciences version 22 (SPSS v22) was used for data input and analysis. Continuous variables presented as numbers and percentages while discrete variables presented as mean with standard deviation. The statistical analysis of our research included: the assessment of sensitivity specificity and accuracy of the axial 3D CISS sequence in comparison with axial T2WI sequence and both sequences together. Level of significance was set at <0.05.

RESULTS

76 IACs examined 18 with lesions 58 without significant pathology; 38 patients had undergone the screening, included 18(47.4%) patients with radiological evidence of IACs/CPA cistern lesions and 20 (52.6%) patients without lesions considering the control group which confirmed by IAC/CPA cistern routine sequences in addition to confirmation by 3D-CISS sequence.

The ages of patient ranged from 9 years to 75 years mean±SD 38.71±15.96, median 42, and range 66. The age of diseased groups arranged from 18 years to 62 years with mean ± SD 38.56±13.62, median 42.50, range of 44, while the control group age arranges from 9 years to 75 years; mean ± SD 38.85± 18.17, median 41, range 66 with statistically non-significant results as shown in table 1.

Table 1: Age of group subtypes

Groups type	N	Mean	SD	P-value
Diseased	18	38.56	13.62	0.95
control	20	38.85	18.17	
Total	**38**	**38.71**	**15.96**	

The diseased group including 12 female 66.7 %, 6 male 33.3% while, the control group including 14 female 70%, and 6 male 30% with statistically non-significant results as shown in table (2)

Table 2: Gender distribution between diseased and control groups

	Groups type				P-value
	Diseased		Control		
Male	6	33.3%	6	30.0%	**0.8**
Female	12	66.7%	14	70.0%	
Total	**18**	**100.0%**	**20**	**100.0%**	

The number of patients that showing bilateral complaining were 6 in diseased group that represent 33.3%, while in control group were 4, that represent 20.0%. The number of the patients that showing unilateral illness were 12 in diseased group that represent 66.7%, while in control group were 16 that represent 80.0%, p-value (0.35) as shown in table 3.

Table 3: Site of illness between diseased and control groups

	Groups type				P-value
	Diseased		Control		
Unilateral	12	66.7%	16	80.0%	**0.35**
Bilateral	6	33.3%	4	20.0%	
Total	**18**	**100.0%**	**20**	**100.0%**	

The number of patients complaining from the right side tinnitus in diseased group was 10 that representing 55.6%, while in control group were 14 (70.0%). The number of patients complaining from the left side tinnitus in diseased group were 8 (44.4%0, while in control group were 6 930.0%), p-value (0.35) as shown in table 4.

Table 4: Side of illness between diseased and control groups

	Groups type				P-value
	Diseased		Control		
Right	10	55.6%	14	70.0%	**0.35**
Left	8	44.4%	6	30.0%	
Total	**18**	**100.0%**	**20**	**100.0%**	

The duration of complaining for diseased patients group ranged from 1 month to 36 months, mean ±SD 18±10.74, median 24 months. While the control patients group ranged from 1 month to 84 months, mean±SD 15.55±23.72, the median 5.5, as shown in table 5.

Table 5: Duration of illness of group patients by months

	N	Mean	SD	P-value
Diseased	18	18.08	10.7	0.69
Control	20	15.55	23.72	

The IAC lesions divided according to Koos stage [13], intracanicular and fundal in location, therefore 9 was intracanicular representing 50% and 4 was fundal representing 22.2%, while lesions that seen purely within the CPA cistern which were 5 expressed by other representing 27.8 %.

The measurement of largest diameter of the lesions in diseased group range from 0-30 mm, mean±SD 9.28± =9.405, median 8. The 0 refers to vascular looping of AICA which responsible for some patient's symptom.

The number of lesions in diseased group showing true positive results by 3D-CISS sequence were

17 (94.4%) of detected lesions while one lesion showing false negative result by CISS sequence because it was arachnoid cyst no clearly identified representing 1 (5.6%). While number of the lesions in control group showing false positive results were 2 (10.0%) due to volume averaging artifact, the true negative lesions were 18 (90.0%). (P-value <0.001), as shown in table 6.

Table 6: Detection of lesions by 3D-CISS

	Groups type				P-value
	Diseased		Control		
Positive	17	94.4%	2	10.0%	**<0.001***
Negative	1	5.6%	18	90.0%	
Total	**18**	**100.0%**	**20**	**100.0%**	

The result was significant at P-value <0.05

The number of lesions in diseased group showing true positive results by T2WI sequence was 15 (83.3%) of detected lesions while 3 (16.7%) lesions showing false negative result by T2WI sequence. While the number of lesions in control group showing false positive results were 4 (20.0%) due to artifact, the true negative lesions were 16 (80.0%), (P-value <0.001), as shown in table 7.

Table 7: Detection of lesions by T2W2

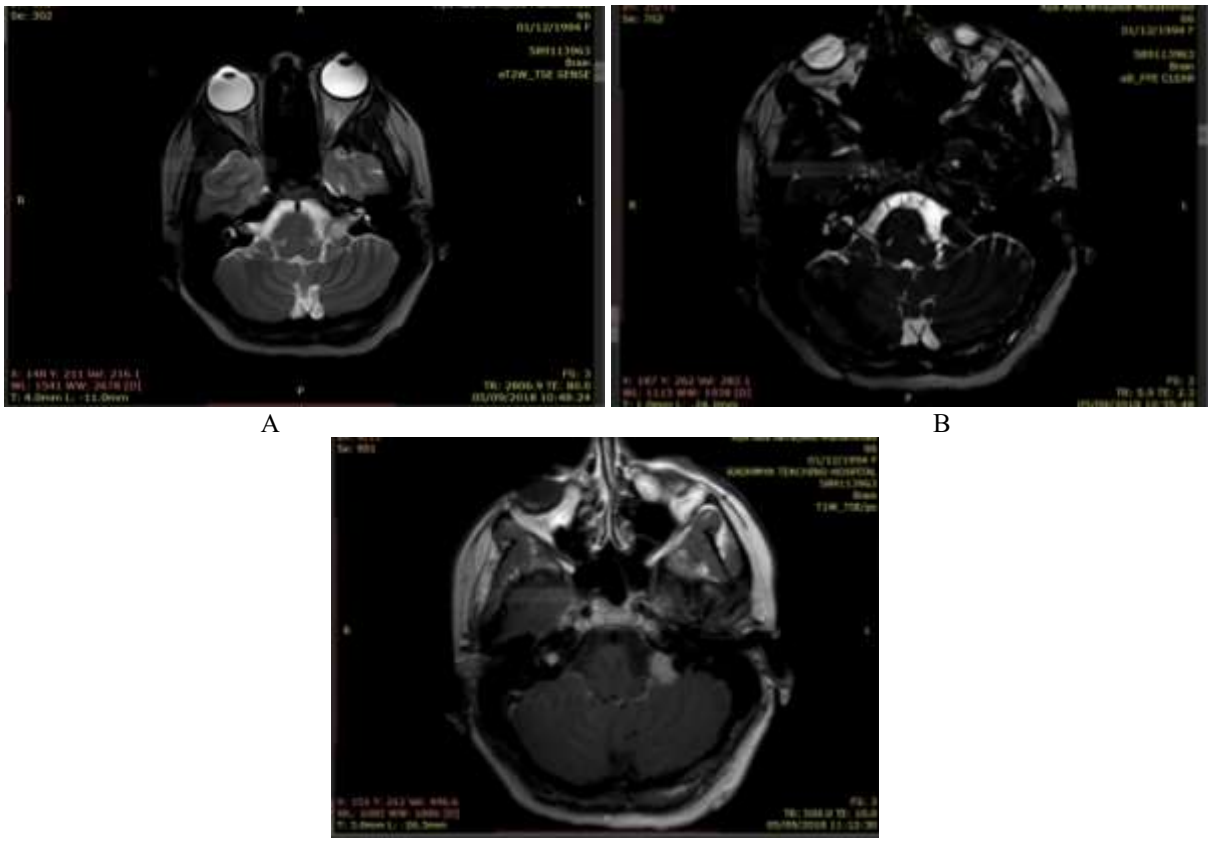
	Groups type				P-value
	Diseased		Control		
Positive	15	83.3%	4	20.0%	**<0.001***
Negative	3	16.7%	16	80.0%	
Total	**18**	**100.0%**	**20**	**100.0%**	

The result was significant at P-value <0.05

Assessment of sensitivity, specificity and accuracy were calculated for both sequence axial 3D-CISS and axial T2WI. The sensitivity of axial 3D-CISS sequence 94.4%, specificity 90%, accuracy 92.1%, AUC 0.92, positive likelihood ratio 9.4, negative likelihood Ratio 0.062, positive predictive value 89.47% and negative predictive value 94.73%. While the sensitivity of axial T2WI sequence 83.3%, specificity 80 %, accuracy 81.6 %, AUC 0.817, positive likelihood ratio 4.16, negative likelihood ratio 0.208, positive predictive value 78.94 % and negative predictive value 84.2%, as shown in table 8.

Table 8: The sensitivity, specificity and accuracy for T2WI and 3D CISS

	Sensitivity	Specificity	Accuracy
T2	83.3%	80.0%	81.6%
CISS	94.4%	90.0	92.1%



A B C

Figure 1: A 24 year old young female presented with tinnitus of Lt. ear (A) axial T2WI image displays subtle ill-defined hypointense signal lesion at medial aspect of right IAC, (B) axial 3D CISS confirmed a well-defined hypointense lesion about the fundus of Rt. IAC (arrow) which is more established after IV contrast (picture C : axial T1WI / PC), to be an enhancing 4 mm, well defined mass lesion within Rt. IAC picture consisting with vestibular schwanoma, Lt. vestibular schwanoma diagnosed previously as the patient is a known case of NF2

DISCUSSION

Vestibular schwannoma is a relatively common tumor with a clinical incidence of 10–15 per million [14], most lesions occur in patients between 40 and 60 years of age [15].

Three-dimensional constructive interference in steady-state (CISS) MR imaging is a slow version of fully refocused steady-state sequence [16], provides a high spatial resolution image with clear contrast between fluid and other structures and is reported to have high sensitivity for detecting IAC lesions and cerebellopontine angle (CPA) lesions without additional contrast agents [2].

There is a difficulty to obtain histological sample from IACs, so the necessity to have a neuroradiologically methods to establish diagnosis. So this study inquiring for two questions first we estimate the diagnostic accuracy of 3D CISS sequence and comparison with the standard conventional routine sequence including T2WI to look for small lesions by sensitivity, specificity and accuracy.

The detection of vestibular schwannomas and other small lesions of IAC as early as possible so vital due to complication of large tumor size as mass effect on adjacent structure in CPA cisterns (brain stem, posterior fossa) and treatment complication regarding fascial nerves outcome [17]. Early detection is so important for hearing preservation and if there is attempt for surgery as hearing outcome correlate frankly with size of tumour [17,18].

As trend fashion using convention MRI sequences for examining the IACs and CPA cisterns small percentage of exam will be positive for detection of small lesions even though Gd enhanced MR imaging considered the gold standard in detection small IAC and CPA cisterns lesions but in our study we proved the role of unenhanced high resolution MR imaging in detection small subcentimeter lesions of IAC.

In the present study the mean age of patients 38.71±15.96 years; the mean of diseased group 38.56±13.62 years, the mean of control group 38.85± 18.17. The current study shows slight predominance female incidence; thus (female:male 2:1).

The current screening exam shows high sensitivity, specificity and accuracy regarding 3D CISS sequence consist of (94.4%, 90%, 92.1%) respectively, while T2WI sequence shows sensitivity, specificity and accuracy of (83.3%, 80%, 81.6%) respectively. 9 lesions were intracanalicular and 4 were fundal in location. The false positives were small and recognized due to volume averaging artefact which confirmed by 3D CISS sequence.

These results are in agreement with Abele TA *et al*., [19], who compare between coronal T2WI and axial 3D CISS sequence for detection of small IAC lesions and calculated the sensitivity, specificity and accuracy depending on two observer showing that sensitivity 91%, specificity 98% and accuracy 94% for 1st observer while sensitivity 100% specificity 92% and accuracy 94% for 2nd observer, they found 14 lesions intracanalicular and 9 lesions fundal in location.

Ozgen B *et al*., [20], who study the diagnostic accuracy of axial CISS alone included;18 patients with known VS showing the tumour size measured by CISS was slightly smaller than post contrast T1WI of about (<0.5 mm) but the sensitivity, specificity and accuracy for CISS sequence was 100% also concluded that some tumours internal architecture not so clear because if they were post operation or post radiation.

Adam A *et al*., [21], compare between the diagnostic accuracy of CISS sequence with GDT1, they found the sensitivity of CISS sequence was 93% and specificity was 100 %, they looking for small vestibular schwannoma and assess the neuroradiologist confidence in diagnosis. Hermans *et al*., [22], having similar research of 83 patients from them 18 were positive, size of lesion ranging from (4.0-33) mm, that included comparing axial CISS with axial T1 post-contrast, the sensitivity was from 89%- 94%.

As in searching one previous research found to be with less sensitivity which was by Goebelle *et al*., [23], they were five readers looking at 200 CISS studies in suspicion of VS, the sensitivity was 77.8%, specificity was 97.6% for 31 pathological lesions, and they concluded the CISS sequence should be a complementary to other sequences not a replacement.

In comparing the present study with previous researches support a diagnostic benefit of using axial 3D CISS sequence as screening tool in complementary with other routine sequence, lessen the effect of volume averaging artefact which can be of effect especially at small IACs, in Hermans *et al*., [22], missed 3 mm IAC lesion and 6 mm intralabyrinthine lesion due to volume averaging artefact and suboptimal techniques in Allen *et al*., [24], publication, 2 lesions measuring 2 and 3 mm in maximum diameter were missed likely because of volume averaging because they were specifically noted to be found in small IACs.

One of important advantage of 3D CISS sequence is twice high contrast to noise ratio for CSF and intracanalicular nerves “compared with the 3D recovery fast spin-echo T2WI sequence” [25], however there is a limitation due to banding artefact due to inhomogeneity of magnetic field [26], that can appeared as a pseudolesion which can overcome by T2WI to exclude artifactual lesions.

Fortnum *et al*., [27], concluded that high resolution fluid-sensitive sequences can detect small IAC lesions from 2 mm to more than 20 mm as sensitivities ranging from 96%–98%. They determined high resolution non enhanced sequence can evaluate the eighth and seventh cranial nerves in their course in CPA cisterns and IAC.

While high non contrast sequence consider enough in exclusion lesions of IAC, but still contrast enhanced imaging necessary in some condition as vestibular neuritis, sarciodosis, labyrinthitis and leptomeningeal metastasis therefore here come the role of clinical assessment to judge the condition and requesting the optimum exam.

Limitation of the Study:

1. The people in our community with less education about the importance of hearing problem and necessity of seeing specialist as early as possible.
2. Lack of pathological confirmation in most cases.

CONCLUSION

3D CISS sequence is supply high topographic resolution with high contrast to noise ratio that highly beneficial for defining the exact location of the lesion and follow the vascular structures and nerves with clarity. It offers information that not obtained by other spine echo sequences, this information help widely in deciding management.

Recommendation

As 3D CISS sequence consider high resolution sequence without need a contrast agent, so it is recommended to ENT physician and neuroradiologist to depend on it for screening any patient suspicion for hearing loss or tinnitus and as a diagnostic tool and also for following up patients diagnosed for small asymptomatic lesions or lesions could not be operated on.

Competing Interests: None

Authors' Contributions:

All had confirms responsibility for the following: study conception and design, data collection, analysis and interpretation of results, and manuscript preparation.

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