HIZ's relation to axial load and low back pain: investigated with axial loaded MRI and pressure controlled discography

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Abstract

Purpose The aims were to investigate if the detection of high-intensity zones (HIZ) is affected by axial load, and to study the correlation between HIZ and discogenic pain provoked with pressure controlled discography (PCD).

Methods 41 consecutive patients with chronic low back pain, referred for discography, were included. Each patient underwent PCD, CT, MRI, and axial loaded MRI (aLMRI) within 24 h. 35 patients completed all MRI sequences (140 discs). The detection of HIZ was compared between conventional MRI and aLMRI. PCD was performed in 119 of the discs examined at MRI. Provoked pain at PCD was classified into four categories (none/unfamiliar/similar/exact), with the patients' daily pain as reference, and correlated with presence of HIZ.

Results aLMRI did not affect the detection of HIZ compared with conventional MRI. No significant correlation between HIZ and the 4-graded pain response at discography was found ($p = 0.34$), neither when combining similarly/exactly reproduced pain ($p = 0.08$). The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of HIZ in detecting discs with exactly reproduced pain were 49, 69, 39 and 76 %. When

combining similarly/exactly reproduced pain, PPV was higher but still only 70 %.

Conclusions The detection of HIZ was not influenced by axial load. With strict PCD, discogenic pain can neither be confirmed when having HIZ (PPV 39 %) nor ruled out in discs without HIZ (NPV 76 %). Larger PCD studies including quantification of HIZ at conventional and aLMRI are needed, before any dynamic component affected by axial load can be ruled out completely.

Keywords Discography · HIZ · Intradiscal pressure · Discogenic low back pain · Axial loaded MRI · Lumbar intravertebral disc

Introduction

High-intensity zones (HIZ), identified at T2-weighted MRI sequences within the posterior annulus [1], have been reported as reliable markers of discogenic pain [2, 3]. However, the diagnostic role of HIZ is limited due to low sensitivity [4–8]. The importance of HIZ in discogenic low back pain (LBP) remains therefore unclear. Pressure controlled discography (PCD), now criterion standard, has not been used in the majority of the numerous studies correlating HIZ and discogenic pain [1–7, 9–16] making previous results dubious, since discography without pressure registration can induce false positive responses [17, 18].

Histology of HIZ lesions, in discs believed to be painful, showed that they are composed of vascularised granulation tissue [2]. A dynamic component in the appearance of HIZ has been suggested by Alyas et al. [19], who reported that HIZ was unmasked by upright extension MRI in one patient with LBP and that HIZ appeared differently in another patient at the upright MRI compared with conventional

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sequences. The authors hypothesized that the load induced extrusion of fluid from the nucleus into the annular tear.

In order to investigate if HIZ constitutes dynamic tissue, affected by axial load, our primary aim was to compare if axial loaded MRI (alMRI) effects the detection of HIZ compared with conventional MRI. A secondary aim was to evaluate the relation between HIZ and discogenic pain with strict PCD.

Materials and methods

41 consecutive patients referred for preoperative lumbar discography were included between April 2007 and March 2010. They all had at least 6 months duration of LBP that had failed conservative therapy. Patients unable to undergo MRI or with allergies to contrast media were not eligible. With approval from the ethics committee, each patient underwent MRI, alMRI, discography and CT within 24 h. First, all were interviewed regarding the character and localisation of their symptoms. Then, MRI was performed with a 1.5 T equipment (Siemens Magnetom Symphony Maestro Class, Erlangen, Germany). T1 (TR 541 ms/TE 1 ms) and T2 (TR 4,000 ms/TE 124 ms) weighted sagittal images (4 mm/FoV 300 mm) were obtained and 4 mm T2 (TR 5,000–6,970 ms/TE 114–116 ms) axial sections were generated. AlMRI was performed with a non-magnetic compression device, and a harness according to Fig. 1 (DynaWell, Dynawell diagnostics AB, Las Vegas, Nevada USA) [20]. In addition to the sequences at the conventional MRI, 4 mm T1-weighted axial images (TR 500 ms/TE 15 ms) were added.

HIZ was evaluated by an experienced radiologist, blinded to the discography result, according to the criteria by Aprill and Bogduk [1]. PCD was performed, by one of two experienced radiologists, under standardized conditions. In all patients, discograms were performed of at least L4–L5 and L5–S1 and in addition 1–2 disc levels above these to include one negative control disc. Intravenous cefuroxime 1.5 g $\times$ 1 and midazolam 10 mg $\times$ 1 rectally was

Fig. 1 Compression device used at the alMRI. The alMRI was performed with a non-magnetic compression device in an out-stretched leg position, with an axial load of 50 % of the total body weight to simulate an upright position. The compression device is composed of a patient harness attached to a footplate with adjustable side straps. The external load was adjusted by loosening or tightening the straps

administered before the patients were placed for a prone posterolateral approach. 5–10 ml carbocain 10 mg/ml was administered locally before a 22-Gauge needle was introduced into each disc under fluoroscopy guidance. At the L5–S1 level, an 18-Gauge introduction needle was used. Contrast (Omnipaque, GE, Healthcare) was injected with a twist-manometer (Stryker Discmonitor[®], Kalamazoo Michigan, USA), until one of the following endpoints was reached: pain intensity $\geq 5/10$, pressure 100 pounds per square inch (psi), contrast volume 3.5 ml or a steady state in the pressure/volume curve (i.e., further pressurization impossible due to high resistance or epidural leak). 0.1–0.2 ml was injected at each twist, resulting in an injection speed of approximately 0.03 ml/s. Absolute intradiscal pressure was registered by the pressure limits including the intrinsic hydrostatic disc pressure. The patients were asked to relate any provoked pain in relation to their daily LBP and classify it into one of the four grades: none or pressure sensation, unfamiliar, similar and exact pain. During injection, the patient's pain response was registered directly by the second radiologist. Discs were only graded as similarly or exactly reproduced, if the pain intensity was $>5/10$ on a numerical rating scale (0 = no pain and 10 = worst experienced pain). The patients were awake, alert and could respond adequately when asked about their pain experience. The subsequent CT was performed within an hour after the contrast injection, and the annular disruptions was graded according to a modified Dallas discogram description (DDD) [21].

Statistics

Wilcoxon rank sign test was used to compare HIZ before and after axial load. Chi-square test, Fisher's exact test and logistic regression analysis were used to analyze associations between HIZ and pain/annular disruptions. To correlate the grade of annular disruption with pain, contrast volumes and disc pressures, non-parametric Spearman test was used. The intra- and inter-observer agreement of HIZ was tested with kappa-coefficient. Kappa values >0.75 represent excellent agreement beyond chance, 0.60–0.74 good agreement, 0.40–0.59 moderate agreement and <0.40 poor agreement [22]. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated considering discography as a reference standard. A p value of <0.05 was considered statistically significant. The statistical analyses were performed with SPSS software.

Results

Of 41 patients, initially included 35 (19 female and 16 male, age 26–64 years, mean 46.9 years) completed all

required MRI sequences. The reasons for incomplete examinations were in four cases handling errors with incomplete sequences, and in the remaining two patients due to motion artifacts. In the remaining 35 patients, 140 discs were examined with both conventional and alMRI. No significant difference in the detection of HIZ before and during axial load was found. 48 discs (34 %) displayed HIZ at MRI and 49 (35 %) at alMRI. However, in three discs, HIZ appeared at axial loaded sequences (two at L4–L5, one at L5–S1), whereas at four levels HIZ was detected before but not after axial load (two at L3–L4, two at L5–S1). Kappa value for intra- and inter-observer agreement of the 164 discs at the conventional MRI was 0.87 and 0.84, respectively. Intra- and inter-observer agreement of HIZ at the 140 discs at the alMRI was 0.82 and 0.80, respectively.

Of the 164 discs examined with conventional MRI, PCD was performed at 124 discs. Due to anatomic unfavorable positioning of 5 L5–S1 discs, 119 discs were successfully injected. The distribution of disc levels injected and their pain response is shown in Table 1. Maximal pressure, total contrast volume and both pressure and contrast volume at the initial evoked pain are displayed in Table 2. Since the absolute pressure was used in this study, the opening pressure (i.e., the intrinsic hydrostatic pressure) was estimated to 14 psi, the mean opening pressure found by Derby et al. [23] when using manometry. Mean maximal pressure in the current study was 43 psi, subtracting the estimated opening pressure results in a mean maximum pressure of 29 psi above opening pressure in the current study. Low pressure positive disco grams, i.e., positive at ≤ 15 psi above opening pressure [23] were 14 % for exactly reproduced pain, and 23 % for similar/exact pain in combination. Seven patients had exact pain at two or more discs.

Statistically significant associations were found neither between HIZ and discogenic pain (4 grades) ($p = 0.34$), nor between HIZ and similar/exact pain in combination

Table 1 Distribution of the disc levels and corresponding pain response in the 119 discs examined with pressure controlled discography

	Provoked pain at discography				Total
	None	Unfamiliar	Similar	Exact	
Disc					
L2–L3	6	4	2	1	13
L3–L4	10	15	6	8	39
L4–L5	3	5	18	14	40
L5–S1	1	4	10	12	27
Total	20	28	36	35	119

The positive rate of discograms calculated per disc was 29 % (35/119) for exact provoked pain and 60 % (71/119) when combining similar/exact pain. The pain provoked at discography is correlated with the patients' daily pain

Table 2 Maximal pressure, total contrast volume and both pressure and contrast volume at initial evoked pain at discography

	Disc Nr	Min	Max	Mean	SD
Total contrast volume	107	0.6	3.5	1.8	0.6
Volume at initial evoked pain	96	0.1	2.5	0.7	0.4
Maximal pressure	119	10	127	43	25
Pressure at initial evoked pain	94	3	72	24	16

Due to technical and human factors (invaluable figures, when doubt existed if pain was evoked etc.) all parameters were not registered in every disc. Volume is given in ml and pressure in pounds per square inch (psi)

SD Standard deviation

($p = 0.08$). HIZ's relation to provoked pain, is displayed in Table 3. There was a significant association between HIZ and annular disruption according to DDD ($p < 0.01$). Annular disruptions directly correlated with symptomatic discs when using PCD, both with the 4-graded pain scale ($p < 0.01$, $\kappa = 0.48$), as well as for similar/exact pain in combination ($p < 0.01$). 82 % of the discs with exact pain reproduction had grade 4 disruption according to DDD.

Contrast volume correlated neither with maximal pressure ($p = 0.08$), nor with pain at discography ($p = 0.55$). Significant correlation was found between maximal pressure at discography and provoked pain at discography ($p = 0.01$, $\kappa = -0.25$). There was a strong correlation between annular disruption and maximal pressure ($p < 0.01$, $\kappa = -0.41$), and between annular disruption and contrast volume ($p < 0.01$, $\kappa = 0.42$).

Discussion

The principal findings of this study were that the detection of HIZ did not change between conventional and alMRI, and that HIZ is a poor predictor of discogenic pain provoked by strict PCD. We hypothesized that alMRI, possibly by forcing nuclear material into the annular tear or just by the pressure elevation, may change the flow in the vascularised HIZ tissue, and consequently change its detection. The present study did not reveal any significant change in the appearance of HIZ due to axial load. We found, however a small discrepancy in HIZ between unloaded and loaded position in some of the more than 40 discs presenting with HIZ (Fig. 2).

With a 1.5 T the signal-to-noise ratio ought to be high enough for detecting HIZ, but as Peng et al. [2] pointed out HIZ might be undetected even in 3–4 mm sagittal images if the granulation tissue is too small or less vascularised.

According to Aprill and Bogduks [1] definition HIZ must be as intense as the adjacent CSF, suggesting that less

Table 3 Pain provoked at discography in relation to HIZ

	Provoked pain at discography				Total
	None	Unfamiliar	Similar	Exact	
HIZ					
Absent	18	17	22	18	75
Present	2	11	14	17	44
Total	20	28	36	35	119

Discography was considered reference standard and a discogram positive when pain was either exactly provoked or similarly/exactly provoked. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of HIZ in detecting painful discograms were 49 % (17/35), 69 % (57/84), 39 % (17/44) and 76 % (57/75) for exactly reproduced pain. Corresponding figures for similar/exact pain were 44 % (31/71), 73 % (35/48), 70 % (31/44) and 47 % (35/75)

Fig. 2 T2-weighted sagittal images of one patient at conventional MRI and at axially loaded MRI **a** Conventional MRI. **b** Axially loaded MRI. There is a discrepancy in HIZ between the conventional and axially loaded MRI examination. At the conventional MRI HIZ was observed at L3–L4 and L5–S1 whereas when applying axial load HIZ was not shown at L5–S1. Note the increased lordosis at the aMRI

bright zones, “low intensity zones”, represents less inflamed tears. Carragee et al. [5] used quantitative digital signal analysis in the center of HIZ and classified it into “high-intensity” (HIZ) and “medium-intensity” (MIZ) zones, where MIZ might be more inactive tears. Further

O’Neill et al. [8] classified HIZ into mild, moderate and marked hyper intense zones, also showing that there exist a spectra of intensity variations within HIZ. HIZ was not quantified in the current study which is a limitation. However in consistency with the case report by Alyas et al. [19], the impression was that HIZ often existed at unloaded and loaded MRI examination but varied in intensity/size/shape.

AlMRI increases the lordosis [20], and alters the position of nucleus pulposus [25]. These alterations might be another explanation to the discrepancy of HIZ appearance between the examinations in one and the same patient. AlMRI is developed to simulate the loading conditions of the lumbar spine in standing position particularly to the L3–L4-level, where usually the peak of the lumbar lordosis is found. Depending on at what lumbar level the tears are located, their granulation tissue might be more or less prone to react to the changes in the intradiscal pressure, if the peak stress is at the anterior or posterior annulus. At some discs, the axial load might result in a disc pressure that exceeds the intravascular pressure of the vascularised granulation tissue in HIZ, obstructing the vascular supply of the latter. Theoretically this could lead to a reduced signal in the posterior annulus.

Despite above discussed topics, the most probable explanations to the discrepancy in HIZ between the MRI examinations in the current study are partial volume effect and the observers’ validation of HIZ, deciding if zones are as bright as CSF or less. A more detailed investigation is needed to clarify if axial load affects HIZ in terms of intensity/size/shape.

Significant association between HIZ and discogenic pain was not found in contrary to many previous studies [1, 6, 9, 10, 15, 26]. Granulation tissue is likely to change over time rendering this study an edge, since MRI and discography were performed within 24 h. The time interval between the two procedures varied between 4 weeks [5] and 5 months [13] in the previous studies correlating HIZ and discography findings, and could be a possible explanation of the discrepancy with this study. The PPV of HIZ in terms of exactly reproduced pain was only 39 % compared to, between 83 and 95 % [1, 6, 9–11] in studies favoring HIZ as a reliable marker of discogenic pain. Among numerous authors correlating HIZ and discogenic pain [1, 2, 4–13, 15, 26], only Carragee et al. [5] and O’Neill et al. [8] used PCD. The lack of controlled pressure injection can be an important reason to the discrepancy in PPV between the current and previous reports. Uncontrolled high intradiscal pressures and injection speeds have been shown to generate false positive responses [17, 18, 27]. It is likely that the lack of PCD was a strong confounding factor to many of those previous results. The use of 4-graded pain scale instead of three or less [2, 6, 7, 9–11, 15, 21] may also have

influenced our results and that is why we also combined similar/exact pain in our calculations, by doing so PPV became higher though still only 70 %.

As previously shown [2, 21], significant correlation was found between annular disruption and both HIZ and symptomatic discograms. In this study, 97 % of the discs with exactly reproduced pain exhibited grade 3 or higher annular disruptions, indicating that annular tears are important in generating discogenic pain.

Limitations

The general lower pressurization in the current study might have resulted in some false negative discograms. However, since intradiscal pressure during discography potentially is transferred to adjacent discs [28] and consequently might result in false positive diagnosis when pressurizing discs too much, a lower pressurization was used. O'Neill et al. [17] also favors a lower pressurization when reporting 50 % false positive discograms at 25 psi above opening pressure. Further, Derby et al. [18] stated that mean pressure initially evoking pain in positive discograms was 20 psi, also supporting a lower pressure range. The rate of low pressure positive discograms in the current study was in accordance with Derby et al. [23], who showed a rate of 15 % when using manometry. The limitations of not quantifying HIZ have been discussed above. Further limitations are the relatively small number of patients and that an asymptomatic control cohort was not used to evaluate any change in HIZ between the MRI examinations.

Conclusions

There was no significant change in appearance of HIZ between conventional and axial loaded MRI, indicating that the appearance of HIZ is not in any distinct way related to the loading of the spine. HIZ is a poor predictor of discogenic pain using PCD. Discogenic pain can neither be confirmed when having HIZ, nor ruled out in discs lacking the sign. Larger PCD studies, including quantification (size, shape, intensity) of HIZ without and with axial load as well as a likewise study on asymptomatic individuals are needed before any dynamic component affected by axial load completely can be ruled out.

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Conflict of interest None.

Ethical standard Ethical approval was granted by the Ethics Committee of Gothenburg, Sweden.

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