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ABSTRACT

BACKGROUND AND PURPOSE: Imaging features of spine degeneration are common in symptomatic and asymptomatic individuals. We compared the prevalence of MR imaging features of lumbar spine degeneration in adults 50 years of age and younger with and without self-reported low back pain.

MATERIALS AND METHODS: We performed a meta-analysis of studies reporting the prevalence of degenerative lumbar spine MR imaging findings in asymptomatic and symptomatic adults 50 years of age or younger. Symptomatic individuals had axial low back pain with or without radicular symptoms. Two reviewers evaluated each article for the following outcomes: disc bulge, disc degeneration, disc extrusion, disc protrusion, annular fissures, Modic 1 changes, any Modic changes, central canal stenosis, spondylolisthesis, and spondylolysis. The meta-analysis was performed by using a random-effects model.

RESULTS: An initial search yielded 280 unique studies. Fourteen (5.0%) met the inclusion criteria (3097 individuals; 1193, 38.6%, asymptomatic; 1904, 61.4%, symptomatic). Imaging findings with a higher prevalence in symptomatic individuals 50 years of age or younger included disc bulge (OR, 7.54; 95% CI, 1.28–44.56; $P = .03$), spondylolysis (OR, 5.06; 95% CI, 1.65–15.53; $P < .01$), disc extrusion (OR, 4.38; 95% CI, 1.98–9.68; $P < .01$), Modic 1 changes (OR, 4.01; 95% CI, 1.10–14.55; $P = .04$), disc protrusion (OR, 2.65; 95% CI, 1.52–4.62; $P < .01$), and disc degeneration (OR, 2.24; 95% CI, 1.21–4.15, $P = .01$). Imaging findings not associated with low back pain included any Modic change (OR, 1.62; 95% CI, 0.48–5.41, $P = .43$), central canal stenosis (OR, 20.58; 95% CI, 0.05–798.77; $P = .32$), high-intensity zone (OR = 2.10; 95% CI, 0.73–6.02; $P = .17$), annular fissures (OR = 1.79; 95% CI, 0.97–3.31; $P = .06$), and spondylolisthesis (OR = 1.59; 95% CI, 0.78–3.24; $P = .20$).

CONCLUSIONS: Meta-analysis demonstrates that MR imaging evidence of disc bulge, degeneration, extrusion, protrusion, Modic 1 changes, and spondylolysis are more prevalent in adults 50 years of age or younger with back pain compared with asymptomatic individuals.

Low back pain affects up to two-thirds of adults at some point in their lives.[1] Back pain–related disability has significant economic consequences due to consumption of health care resources and loss of economic productivity.[2] Increased use of MR imaging and CT in the evaluation of patients with back pain consumes a large amount of health care resources.[3] Imaging findings such as disc bulge and disc protrusion/extrusion are often interpreted as causes of back pain, triggering both medical and surgical interventions.[4] Furthermore, prior studies have demonstrated that imaging findings of spinal degeneration associated with back pain are present in a large proportion of both symptomatic and asymptomatic individuals, thus limiting the diagnostic value of these findings.[5-7]

Numerous studies have examined and compared the prevalence of degenerative spine findings in symptomatic and asymptomatic populations. Given the large number of adults who undergo advanced imaging to help determine the etiology of their back pain, it is important to know whether these findings are indeed more prevalent in symptomatic-versus-asymptomatic patients. Such information will help radiologists, referring clinicians, and patients interpret the importance of degenerative findings noted in radiology reports. The purpose of this meta-analysis of case-control studies was to compare the prevalence of MR imaging features of lumbar spine degeneration in adult individuals

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50 years of age or younger with and without self-reported low back pain.

MATERIALS AND METHODS

Data Sources and Searches

We performed a comprehensive search for studies describing relevant imaging findings as described below by using MEDLINE and EMBASE. To identify studies on imaging of symptomatic and asymptomatic spinal disorders, a medical librarian searched Ovid MEDLINE, Ovid EMBASE, and the Web of Science through April 24, 2014 (week 16). EMBASE was searched beginning in 1988 to April 24, 2014, and MEDLINE was searched beginning in 1946 through April 24, 2014. The Web of Science is text-word-based, but it tends to be more current and multidisciplinary, so studies may be discovered that are not included in the other data bases. The search strategy is further detailed in the On-line Tables 1 and 2. The initial search terms included spinal diseases or disorders affecting the spine: intervertebral disc degeneration or displacement, spondylolysis, low back pain, or specific vertebrae and joints (eg, lumbar vertebrae). This search term was combined with diagnostic imaging techniques (MR imaging) and the terms "symptomatic," "pain," "undetected," "asymptomatic," and "asymptomatic disease" (subject heading available in EMBASE, but not MEDLINE). Studies identified from the literature search underwent further evaluation for inclusion in the meta-analysis. We also searched references from the studies included in this meta-analysis to find any additional case-control studies that reported lumbar spine MR imaging findings. This systematic review was not registered with the Cochrane Collaborative.

Study Selection and Data Extraction

To be included in our review, a study needed to be published in English and report the prevalence of degenerative findings on spine MR imaging in both asymptomatic and symptomatic individuals. Case-control and cross-sectional studies were included in this analysis. Patient symptomatology was generally determined at the time of the MR imaging findings. We defined asymptomatic individuals as those with no history of back pain and symptomatic individuals as those with any history of back pain, which included axial back pain and/or sciatica or radiculopathies. The age range for included individuals was 15–50 years. Any studies reporting the prevalence of degenerative findings in patients older than 50 years of age were reviewed to determine whether they stratified outcomes by age so that findings in individuals 50 years of age or younger could be abstracted. Inclusion criteria, including age cutoffs, were agreed on by the authors by consensus. One reviewer examined abstracts of studies identified from the literature search to determine whether the studies met the inclusion criteria and to exclude any studies that were not relevant to the topic being studied (ie, neck pain, studies correlating CT or radiographs and low back pain, review articles, and so forth).

For each study that met inclusion criteria, we used a standard form to abstract imaging technique, sample sizes, and the prevalence rates for the following imaging findings: central spinal canal stenosis, disc degeneration, annular fissure (including high-intensity zones), high-intensity zones (a subgroup of annular fissures defined as "annular fissures with a focal area of increased T2 signal"), disc bulge, disc protrusion, disc extrusion, Modic changes (type 1 Modic changes and all Modic changes), spondylolisthesis, and spondylolysis. These entities are defined in detail by the combined task forces of the American Society of Neuroradiology, American Society of Spine Radiology, and North American Spine Society.[8] Each study that met the initial inclusion criteria was abstracted by 2 reviewers. Any differences in data abstraction were resolved by having a third, independent reviewer arbitrate the findings. There were 6 studies that, when further reviewed during data abstraction, were not thought to meet the inclusion criteria. These studies were sent to an independent reviewer to verify that they did not meet the inclusion criteria.

Quality Assessment

We performed quality assessment of the studies by using the Newcastle-Ottawa Scale. This tool is used for assessing the quality of nonrandomized studies included in systematic reviews and/or meta-analyses. Each study is judged on 8 items categorized into 3 groups: 1) selection of the study groups, 2) comparability of the study groups, and 3) ascertainment of the outcome of interest.[9]

Statistical Analysis

From each study, we extracted a 2×2 table for binary outcomes. Random-effects meta-analysis was used for pooling across studies.[10] The I^2 statistic was used to express the proportion of inconsistency that was not attributable to chance.[11] I^2 values of $>50\%$ indicated substantial heterogeneity of the observed odds ratios. Meta-analysis results were expressed as odds ratios for binary outcomes with respective 95% confidence intervals. $P < .05$ was statistically significant. To further explore heterogeneity and the effect of confounding by age, in addition to conducting subgroup analysis based on age, we conducted meta-regression. In the regression model, the dependent variable is the log of the odds ratio and the independent variable is age as a continuous outcome. We conducted the meta-analysis by using Comprehensive Meta-Analysis, Version 2.2 (Biostat Inc, Englewood, New Jersey). We also reported the mean prevalence and 95% CI for each imaging finding. The mean prevalence was determined by using a pooled analysis. We provide these data for reference but did not use them for statistical comparison.

RESULTS

Literature Search

On-line Table 3 summarizes the included studies, and Fig 1 summarizes the search and selection process. Our initial search yielded 280 unique studies. On the basis of the abstracts of these studies, we excluded 243 studies (86.8%) that did not meet our review inclusion criteria. Of the remaining 37, we excluded 17 (45.9%) because they either did not separate the prevalence of findings by symptomatic status, did not include a truly asymptomatic cohort, or had ambiguous symptomatic status of the patients. We excluded an additional 6 case-control studies because they either did not include patients 50 years of age or younger or findings of patients 50 years of age or younger could not be differentiated from those of the rest of the cohort. In total, 14 (5.0%) studies comprising 3097 patients met the inclusion criteria. Asymptomatic individuals composed 38.6% of the overall cohort

(1193 individuals), and symptomatic individuals composed 61.4% of the overall cohort (1904 individuals).

Study Quality

All included studies had a high-quality as assessed by the New Castle–Ottawa Scale. All included studies demonstrated a high degree of comparability based on variables such as race/ethnicity, demographic groups, and age. Outcomes were clearly reported in all included studies. Three included studies were at risk for selection bias because they studied the prevalence of degenerative findings in elite athletes.

Degenerative Spine Findings by Symptomatic Status in Individuals 50 Years of Age and Younger

In order of decreasing OR, imaging findings with a higher prevalence in individuals with low back pain 50 years of age or younger compared with asymptomatic individuals 50 years of age or younger included disc bulge (OR, 7.54; 95% CI, 1.28–44.56; $P = .01$), spondylolysis (OR, 5.06; 95% CI, 1.65–15.53; $P < .01$), disc extrusion (OR, 4.38; 95% CI, 1.98–9.68; $P < .01$), Modic 1 changes (OR, 4.01; 95% CI, 1.10–14.55; $P = .04$), disc protrusion (OR, 2.65; 95% CI, 1.52–4.62; $P = .03$), and disc degeneration (OR, 2.24; 95% CI, 1.21–4.15; $P = .01$).

Imaging findings not associated with low back pain included any Modic change (OR, 1.62; 95% CI, 0.48–5.41; $P = .43$), central canal stenosis (OR, 20.58; 95% CI, 0.05–798.77; $P = .32$), high-intensity zone (OR, 2.10; 95% CI, 0.73–6.02, $P = .17$), annular fissures (including patients with and without high-intensity zones) (OR, 1.79; 95% CI, 0.97–3.31; $P = .06$), and spondylolisthesis (OR, 1.59; 95% CI, 0.78–3.24; $P = .20$). These data, including the prevalences and 95% CIs of each of these findings, are summarized in the Table.

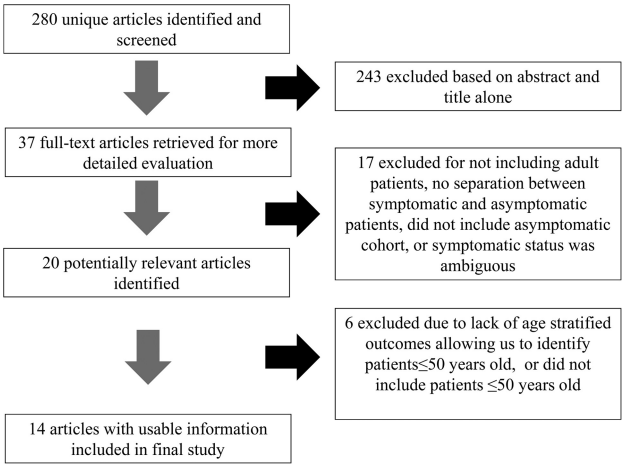

FIG 1. Search strategy.

Meta-Regression Results

Meta-regression based on age was possible only in 2 outcomes (disc degeneration and protrusion, with 12 and 9 studies, respectively). The number of studies evaluating the remaining outcomes was too small to do a meaningful meta-regression. We were unable to demonstrate a statistically significant association between age and these 2 outcomes (P values for the model of .22 and .49; respectively). This is likely due to low power and the small number of available studies and should not be interpreted as lack of effect of age on these 2 outcomes.

Study Heterogeneity

Meta-analysis of the following findings demonstrated I^2 values of <50%, indicating a lack of substantial heterogeneity in reported ORs: Modic 1 changes (0%), disc extrusion (0%), spondylolisthesis (0%), and spondylolysis (0%). Meta-analysis of the following findings demonstrated I^2 values of >50%, indicating substantial heterogeneity of reported ORs: central spinal canal stenosis (94%), disc bulge (90%), disc degeneration (89%), high-intensity zones (72%), disc protrusion (62%), annular fissure (59%), and any Modic changes (65%).

DISCUSSION

This meta-analysis of 14 high-quality case-control studies including >3000 individuals demonstrates that many degenerative spine findings have a higher prevalence in individuals 50 years of age or younger with self-reported low back pain compared with asymptomatic individuals. Disc findings, including disc bulge, disc degeneration, and disc extrusion and protrusions, had significant associations with low back pain. Type 1 Modic changes and spondylolysis also demonstrated a significant association with low back pain. While these findings do not prove that disc- and endplate-related imaging and spondylolysis are pain generators, they do suggest that evidence of these findings could be explored as candidates for biomarkers of low back pain.

Our findings corroborate those of other studies examining the association between disc imaging findings and low back pain. Multiple previous studies have demonstrated a higher prevalence

Outcomes

Outcome	No. of Studies	OR (95% CI)	Prevalence Asymptomatic	Prevalence Symptomatic	*P* Value[a]	I^2 (%)
Annular fissure	6	1.79 (0.97–3.31)	11.3% (9.0%–14.2%)	20.1% (17.7%–22.8%)	.06	59
High-intensity zone	4	2.10 (0.73–6.02)	9.5% (6.7%–13.4%)	10.4% (8.0%–13.4%)	.17	72
Central spinal canal stenosis	2	20.58 (0.05–798.77)	14.0% (10.4%–18.6%)	59.5% (54.9%–63.9%)	.32	94
Disc bulge	3	7.54 (1.28–44.56)	5.9% (3.8%–8.9%)	43.2% (38.2%–48.2%)	.03	90
Disc degeneration	12	2.24 (1.21–4.15)	34.4% (31.5%–37.5%)	57.4% (54.8%–59.8%)	.01	89
Disc extrusion	4	4.38 (1.98–9.68)	1.8% (0.1%–3.7%)	7.1% (5.4%–9.4%)	<.01	0
Disc protrusion	9	2.65 (1.52–4.62)	19.1% (16.5%–22.3%)	42.2% (39.3%–45.1%)	.00	62
Modic changes	5	1.62 (0.48–5.41)	12.1% (9.6%–15.2%)	23.2% (21.7%–27.3%)	.43	65
Modic 1 changes	2	4.01 (1.10–14.55)	3.2% (0.7%–9.4%)	6.7% (4.2%–10.4%)	.04	0
Spondylolisthesis	4	1.59 (0.78–3.24)	3.2% (1.8%–5.8%)	6.2% (4.4%–8.7%)	.20	0
Spondylolysis	2	5.06 (1.65–15.53)	1.8% (0.0%–5.3%)	9.4% (6.6%–12.4%)	<.01	0

[a] *P* values are computed from the meta-analysis of ORs. Prevalence data are provided for reference but are not meant for statistical comparison.

of disc findings in symptomatic-versus-asymptomatic individuals. Disc protrusions are not uncommon in asymptomatic adult populations, with prevalences ranging from 10% to 30%, depending on the studied age group.[12-20] In general, epidemiologic studies demonstrate that the prevalence of disc protrusions in asymptomatic populations increases with age.[12-20] Our study found that nearly 20% of asymptomatic patients 50 years of age or younger had disc protrusion compared with nearly 40% in the symptomatic group. Disc extrusions are rare in asymptomatic populations. The prevalence of disc extrusions ranged from 0% to 4% in asymptomatic patients, with most studies reporting prevalence rates of <2%.[21-24] On the contrary, prevalence of disc extrusions ranged from 5% to 10% in symptomatic populations.[21-24]

One surprising finding from our study was that disc bulge had a strong association with low back pain. Because of the high prevalence in the asymptomatic population, disc bulges are often considered incidental findings and not associated with low back pain. The prevalence of disc bulges in asymptomatic populations ranges from 20% in young adults to >75% in patients older than 70 years of age.[25-30] Our meta-analysis found a prevalence of disc bulges of 6% in asymptomatic populations and 43% of symptomatic populations. All 3 studies included in our meta-analysis assessing the association between disc bulges and pain demonstrated a very strong association between disc bulge with low back pain.[19,21,31] Two of these studies only included patients younger than 30 years of age.[21,31] These findings suggest that the association between disc bulge and low back pain may be more significant in younger adults, in whom the prevalence in the general asymptomatic population is much lower. It is possible that the association between disc bulges and low back pain disappears in older populations, in whom the prevalence of this imaging finding is >90% in the asymptomatic population.[32]

Similar to disc bulge, disc degeneration also has a very high prevalence in asymptomatic individuals, ranging from 30% to 95%, depending on the age group.[5,13,15,18,19,23,27,29,32-36] Some studies have demonstrated no association between disc degeneration and low back pain, especially in older individuals.[37,38] Our meta-analysis on 12 studies found a strong association of disc degeneration and low back pain in individuals 50 years of age or younger, with >30% of asymptomatic individuals and >50% of symptomatic individuals found to have disc degeneration on MR imaging.

Our study also found that in the adult population of 50 years of age or younger, annular fissures and high-intensity zones had no association with low back pain. The association between annular fissures and low back pain is controversial. A majority of studies in our analysis demonstrated a higher prevalence of annular fissures in symptomatic-versus-asymptomatic patients. However, the largest study in our analysis, which included >500 patients 18–21 years of age, demonstrated no association between annular fissures and low back pain.[25]

Modic 1 changes had a significant association with low back pain in our analysis. However, Modic changes as a whole (Modic 1–3) did not have an association with low back pain. In a systematic review of Modic change prevalence in asymptomatic and symptomatic populations, Jensen et al[39] found that the median prevalence of any type of Modic changes in symptomatic individuals in the literature was 36% compared with 14% in non-back pain populations. However, when considering case-control studies, this analysis demonstrated no association between Modic changes and low back pain. Large cohort studies have demonstrated that type 1 Modic changes are, in fact, strongly associated with low back pain.[40] Spondylolysis was strongly associated with low back pain in patients 50 years of age or younger. These findings are supported in studies from the surgical literature that demonstrate that direct screw repair of pars interarticularis defects provides long-term pain relief and improves the biomechanical function of the lower lumbar spine.[41]

Findings not directly related to the disc such as spondylolisthesis and central canal stenosis demonstrated no association with low back pain in our study. These findings are consistent with what has been previously reported in the literature. Spondylolisthesis is also consistently not associated with low back pain in case-control studies.[6] However, in general, the grade or average grade of spondylolisthesis found in these population-based studies was low, and none of the studies included in our meta-analysis evaluated the presence of dynamic instability. Our finding that central canal stenosis was not associated with low back pain is likely because this entity typically presents with lower extremity rather than back pain (ie, neurogenic claudication). In addition, only the presence rather than the severity of central canal stenosis was evaluated.

Limitations

Our study has limitations. It was limited to individuals 50 years of age or younger; thus, our findings pertain only to this specific population. With the increasing prevalence of some degenerative findings such as degenerative disc and disc bulge with increasing age, it is possible that the association between these entities and low back pain is less significant in older age groups. There was substantial geographic, ethnic, and occupational heterogeneity in the populations included our analysis. Another major limitation is that the studies included in our analysis were published during a broad time period, and not all of the studies used the original or more recent Fardon et al[8] and Fardon and Milette[42] combined task force nomenclature recommendations. Thus, differences in nomenclature and definitions of some entities could affect our results.

Another limitation is that our study defined back pain broadly, including axial, sciatica and radicular pain. Most of the studies did not explicitly define whether patients had axial or radicular symptoms or both. In general, the studies in our analysis included patients with self-reported low back pain, which was confirmed on physical examination at or around the time of the MR imaging examination. Another important limitation is that only the presence of these degenerative findings was considered, not the extent or severity. This is especially important because increased severity and extent of Modic changes, spinal stenosis, and disc degeneration are associated with increased pain.[43] Modic changes could only be analyzed as type 1 changes and combined type 2 and 3 changes because the included studies generally did not differentiate between type 2 and 3 changes. As such, we did not have the opportunity to study whether type 2 or 3 changes were associated with low back pain.

Regarding the study design, our study included primarily case-control and cross-sectional studies but did not include cohort studies. As such, we did not study the association between MR imaging findings and future back pain. Symptomatology was determined at the time of imaging. In addition, we could not perform separate subgroup analyses by decade of life due to a paucity of studies that stratified findings by decade of life. It is possible that the association of pain and degenerative findings is different for patients 30 years of age and younger and those 30–50 years of age. Many of the I^2 values were >50%, suggesting substantial heterogeneity in reported results. The imaging features examined in this study are correlated (ie, a patient with one finding is more likely to have another). Hence, the observed associations are affected by confounding and cannot be used for diagnostic purposes. Last, some of the specific MR imaging finding meta-analyses included as few as 2 studies. All these limitations highlight the need for further studies on the association between MR imaging findings and low back pain. One disadvantage of evaluating only case-control studies is that we excluded the populations included in cohort studies reporting the prevalence of degenerative findings in asymptomatic subjects only.

CONCLUSIONS

This meta-analysis of epidemiologic studies demonstrates that MR imaging evidence of disc bulge, disc degeneration, disc extrusions and protrusions, Modic 1 changes, and spondylolysis had significant associations with low back pain in adult patients 50 years of age or younger. The association between these degenerative findings and pain should not be interpreted as causation. These imaging findings may be considered as candidate biomarkers for low back pain in younger patients (younger than 50 years of age). The role of these findings in determining treatment strategies or prognosis of low back pain has not been established.

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