

Systematic Review



Incidence of Spontaneous Resorption of Lumbar Disc Herniation: A Meta-Analysis

Ming Zhong, MD^{1,2}, Jin Tao Liu, MD², Hong Jiang, MD, PhD², Wen Mo, PhD¹, Peng-Fei Yu, MD², Xiao Chun Li, MD², and Rui Rui Xue, MD¹

From: ¹Longhua Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, China; ²Department of Orthopaedic Surgery, Suzhou Hospital of Traditional Chinese Medicine, Jiangsu, China

Address Correspondence: Hong Jiang, MD, PhD
Department of Orthopaedic Surgery, Suzhou Hospital of Traditional Chinese Medicine
889 Wuzhongxi Rd
Suzhou, Jiangsu 215009, China
E-mail: doctorhong@yeah.net

Disclaimer: This study was supported by the National Natural Science Funds of China (Grant #81473691).

Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 05-25-2016

Revised manuscript received: 06-28-2016

Accepted for publication: 08-16-2016

Free full manuscript: www.painphysicianjournal.com

Background: Lumbar disc herniation (LDH), a common disease, is often treated conservatively, frequently resulting in spontaneous resorption of the herniated disc. The incidence of this phenomenon, however, remains unknown.

Objective: To analyze the incidence of spontaneous resorption after conservative treatment of LDH using computed tomography and magnetic resonance imaging.

Study Design: Meta-analysis and systematic review of cohort studies.

Setting: The work was performed at The Suzhou Hospital of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine.

Methods: We initiated a search for the period from January 1990 to December 2015 using PubMed, Embase, and the Cochrane Library. Two independent reviewers examined the relevant reports. The references from these reports were also searched for additional trials using the criteria established in the PRISMA statement.

Results: Our results represent the pooled results from 11 cohort studies. The overall incidence of spontaneous resorption after LDH was 66.66% (95% CI 51% – 69%). The incidence in the United Kingdom was 82.94% (95% CI 63.77% – 102.11%). The incidence in Japan was 62.58% (95% CI 55.71% – 69.46%).

Limitations: Our study was limited because there were few sources from which to extract data, either in abstracts or published studies. There were no randomized, controlled trials that met our criteria.

Conclusions: The phenomenon of LDH reabsorption is well recognized. Because its overall incidence is now 66.66% according to our results, conservative treatment may become the first choice of treatment for LDH. More large-scale, double-blinded, randomized, controlled trials are necessary to study the phenomenon of spontaneous resorption of LDH.

Key words: Lumbar, disc herniation, spontaneous resorption, conservative treatment, incidence, country, meta-analysis, systematic review, observational studies, study designs

Pain Physician 2017; 20:E45-E52

Lumbar disc herniation (LDH) is the most common type of degenerative discogenic disease. It is mainly treated surgically or with conservative measures (1-3). Studies of acute LDH have found that 2 and 5 years after diagnosis there was little difference

between patients who underwent surgery and those who did not (4-5). The literature has shown that conservative treatment of LDH has unique advantages, with the clinical symptoms of most patients diminished or even completely gone within a few weeks (6).

Since 1990 magnetic resonance imaging (MRI) and computed tomography (CT) have provided evidence that conservative treatment allows resorption of the herniated disc (7-8). Although there have been numerous reports on this phenomenon, and researchers dedicated to determining how the resorption takes place, there has been little if any research on its incidence.

The aim of the present study was to analyze the incidence of spontaneous resorption after LDH, as observed by MRI and/or CT, with conservative treatment in a meta-analysis of cross-sectional studies. We searched a large quantity of relevant references and selected several publications in accordance with our requirements. We then assessed the quality of the studies (risk of bias) using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool and finally selected 5 studies and utilized the RevMan Version 5.3.5 software for the meta-analysis (9). Subgroup analyses were also performed at various follow-up times.

METHODS

Literature Search Strategy

Two of the authors independently performed a literature search in December 2015 without restriction to regions, publication types, or languages. The primary sources were the electronic databases of PubMed, Embase, and the Cochrane Library. The following MeSH terms and their combinations in English were searched in the [Title/Abstract]: lumbar disc herniation, herniated lumbar disc, LDH, conservation, conservative, non-operation, spontaneous regression, resorption, absorption. The related article function was also used to broaden the search. The computer search was supplemented with manual searches of reference lists of all retrieved studies, review articles, and conference abstracts. When multiple reports describing the same population were published, the most recent or complete report was used.

Inclusion and Exclusion Criteria

We selected all peer-reviewed cohort studies on LDH with conservative treatment published from January 1990 to December 2015 that used MRI or CT as a measure to assess the size of the lumbar disc protrusion. The number of LDH patients and the number of resorptions had to be displayed in the outcomes. Reports that failed to provide sufficient information for the data analysis were excluded. Two of the authors indepen-

dently screened the titles and abstracts of the articles that were retrieved and applied the selection criteria to identify the relevant material to be read in full. The reviewers' selections were compared and, in cases of disagreement, decisions were made by consensus. The reviewers independently read the complete articles and applied the selection criteria to determine whether the studies would be included in the meta-analysis. The selections were again compared and, in cases of disagreement, decisions were made by consensus.

Quality Assessment

Articles that met the selection criteria were assessed by the authors independently for quality (risk of bias) using the QUADAS-2 tool (10). In accordance with the QUADAS-2 user guidelines (11), items were modified for this study (12). In domain 1 (Patient selection), the item "Was a case-control design avoided?" was omitted. In domain 2 (Index test), the items "Were the index test results interpreted without knowledge of the results of the reference standard?" and "If a threshold was used, was it pre-specified?" were substituted with the item "Was the method of imaging tests described?". This substitution was made because we included articles regardless of the technique used to test for LDH. In domain 3 (Reference standard), the items "Is the reference standard likely to correctly classify the target condition?" and "Were the reference standard results interpreted without knowledge of the results of the index test?" were omitted. In domain 4 (Flow and timing), the item "Was there an appropriate interval between index test and reference standard?" was omitted, and the item "Did all patients receive the same reference standard?" was substituted with the item "Were all patients tested with MRI or CT?". In accordance with the QUADAS-2 guidelines, articles were assessed for each item according to the following rating scale: high risk of bias, low risk of bias, or unclear. We also graded each study based on the Oxford Centre for Evidence Based Medicine Table (13).

Data Extraction

Relevant data were extracted from the selected studies using a standard form that included information about the following items: country, age of patients, length of follow-up, method of imaging test, number of LDH patients tested with MRI or CT, and number of LDH patients with spontaneous resorption according to MRI or CT results.

Statistical Analysis

Data analysis was conducted using RevMan Version 5.3.5 software provided by the Cochrane Collaboration. For categorical variables analyses, results were expressed as numbers with percentages. Also for categorical variables, weighted risk ratios and their 95% confidence intervals (CIs) were calculated using RevMan 5.3.5 software according to the inverse variance method. Heterogeneity was quantified using a χ^2 heterogeneity statistic and by means of an I^2 statistic for each analysis. A fixed-effects model was used if there was no evidence of heterogeneity between studies. If there was evidence of heterogeneity, a random effects model was used for the meta-analysis.

RESULTS

The literature search initially yielded 779 relevant trials from PubMed, Embase, and the Cochrane Library. We deleted 304 articles because of duplicate data. Review of the references found 2 other articles. After reading the titles and abstracts, 13 articles (14-26) were selected for complete reading. Two studies of these articles reported by Autio et al (16,17) were excluded because they did not count the number of the patients with spontaneous resorption. Thus, the remaining 11 trials were used in the meta-analysis. The study selection process and reasons for exclusion are summarized in Fig. 1.

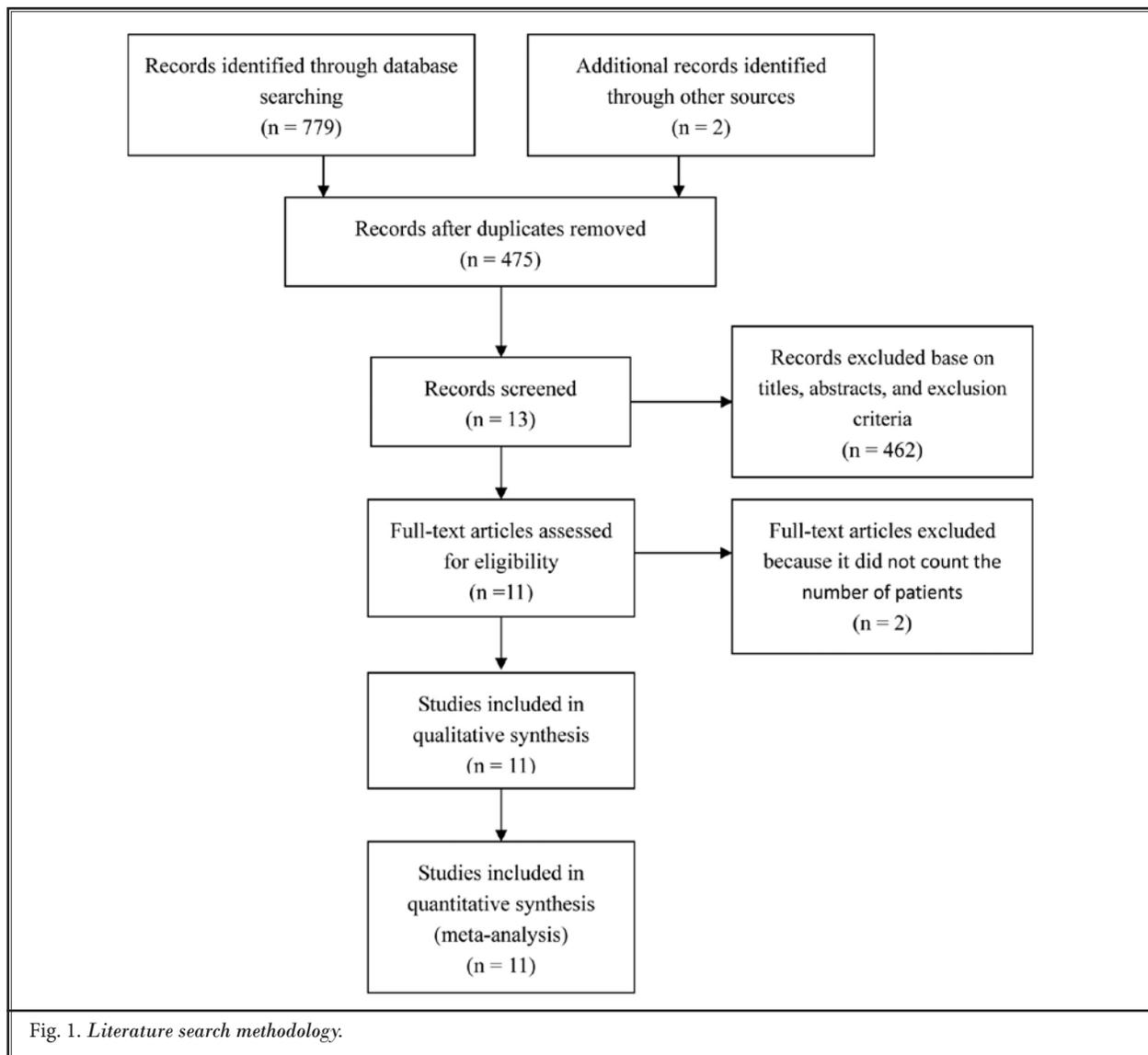


Fig. 1. Literature search methodology.

The 11 trials selected represented a total of 587 LDH patients managed conservatively, 380 of whom experienced resorption. The studies accepted for the meta-analysis are shown in Table 1.

Two reviewers independently assessed the methodological quality of the included trials with the QUADAS-2 tool. The outcomes are summarized in Table 2. No significant publication bias was found, and significant heterogeneity between these studies was observed.

Our meta-analysis showed that the overall incidence of spontaneous resorption after LDH was 66.66% (95% CI 55.12% – 78.21%) as shown in Fig. 2 in the forest plot. The funnel plot shows that the publication bias was minimal, and we were able to evaluate the overall rate of absorption with the meta-analysis (Fig. 3). In all, 11 articles were from United Kingdom, Japan, France, Korea, and Italy, although most were from the United Kingdom and Japan. The meta-analysis showed that

Table 1. *Study characteristics.*

Study	Number of LDH Patients Tested by MRI or CT	Number with Spontaneous Resorption	Country	Measure Method	Age Range (years)	Review Time	Therapy
Ahn et al (14)	36	25	Korea	MRI or CT	17–74		Bed rest, oral steroids, NSAIDs, massage, physical therapy
Autio et al (15)	74	68	UK	MRI	19–78	3–28 weeks	Conservative
Bozzao et al (18)	69	45	Rome	MRI	23–65	6–15 months	Conservative
Bush et al (19)	111	71	UK	CT	17–72	12 months	Prescribed analgesics, NSAIDs, bed rest, manual techniques
Cribb et al (20)	15	14	UK	MRI	24–73	5–56 months	Conservative
Delauche-Cavallier et al (21)	21	14	France	CT	20–64	6–27 months	Conservative
Iwabuchi et al (22)	34	21	Japan	MRI		Every 3 months	Conservative
Komori et al (23)	77	49	Japan	MRI	18–86	2–40 months	Conservative
Komori et al (24)	48	32	Japan	Gd-MRI	20–75	3–6 months	Conservative
Splendiani et al (25)	72	25	Italy	MRI	21–68	–	Conservative
Yukawa et al (26)	30	16	Japan	MRI	14–69	2–40 months	Conservative

Table 2. *Modified QUADAS-2.*

Study	Was a consecutive or random sample of patients enrolled?	Did the study avoid inappropriate exclusions?	Was the method of imaging tests described?	Were all patients tested with MRI or CT?
Ahn et al (13)	Yes	Yes	Yes	Yes
Autio et al (14)	Unclear	Yes	Yes	No
Bozzao et al (17)	Yes	Yes	Yes	Yes
Bush et al (18)	Yes	Yes	Yes	Yes
Cribb et al (19)	Yes	Yes	Yes	Yes
Delauche-Cavallier et al (20)	Yes	Yes	Yes	Yes
Iwabuchi et al (21)	Yes	Yes	Yes	Yes
Komori et al (22)	Yes	Yes	Yes	Yes
Komori et al (23)	Yes	Yes	Yes	Yes
Splendiani et al (24)	Unclear	Yes	Yes	Yes
Yukawa et al (25)	Yes	Yes	Yes	No

QUADAS-2, Quality Assessment of Diagnostic Accuracy Studies.

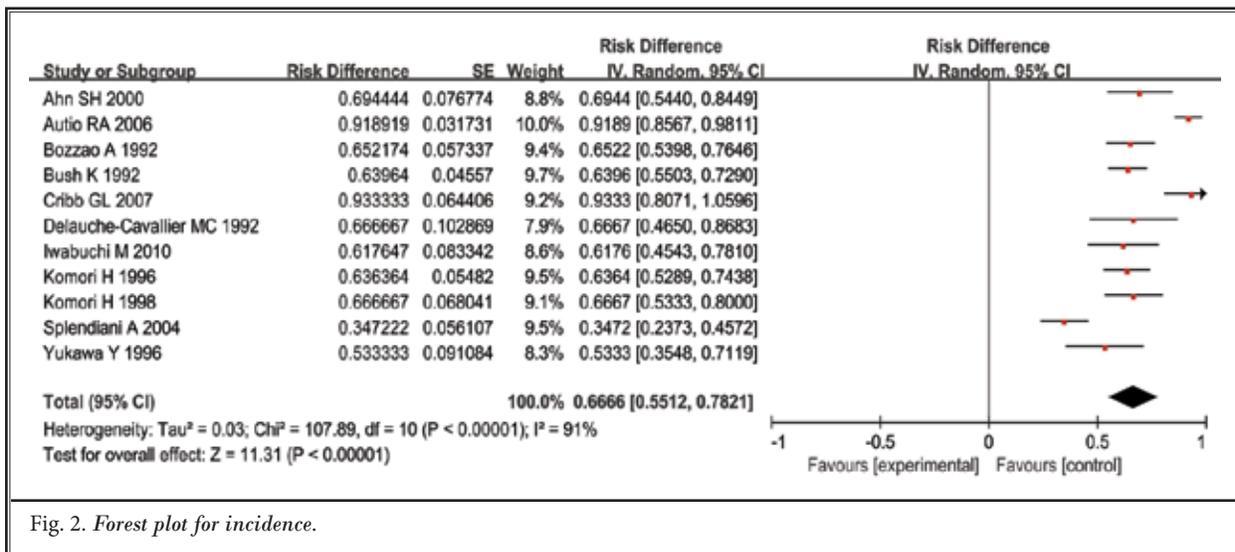


Fig. 2. Forest plot for incidence.

the incidence of spontaneous resorption in the United Kingdom was 82.94% (95% CI 63.77% – 102.11%) (Fig. 4), whereas the incidence in Japan was 62.58% (95% CI 55.71% – 69.46%) (Fig. 4).

The sensitivity analysis showed that I² changed from 91% to 0% after removing 3 articles (15,20,25) that were of low quality. The incidence of spontaneous resorption after LDH changed from 66.66% to 64.20% (Figs. 3,5). Thus, the outcome changed very little, showing that the consolidated result was credible.

DISCUSSION

Spontaneous regression of disc herniation at repeat epidurography has been described since 1945 (27). In 1990, an article was published in Spine in which Saal et al (7) first identified the phenomenon of spontaneous resorption as observed by MRI and CT. This phenomenon showed us that LDH could be treated conservatively.

LDH is a common disease with a high recurrence rate (28,29). It has a serious impact on quality of life. There is a general consensus among contemporary orthopedists that, for most patients with LDH, an initial trial of conservative treatment is preferable to surgical intervention. MRI and CT have proved to be excellent tools for following up patients with LDH who undergo conservative treatment. In most studies, however, patients were followed up with MRI or CT because of persisting symptoms after conservative treatment (30-32). Thus, it is difficult to research those measured by MRI or CT.

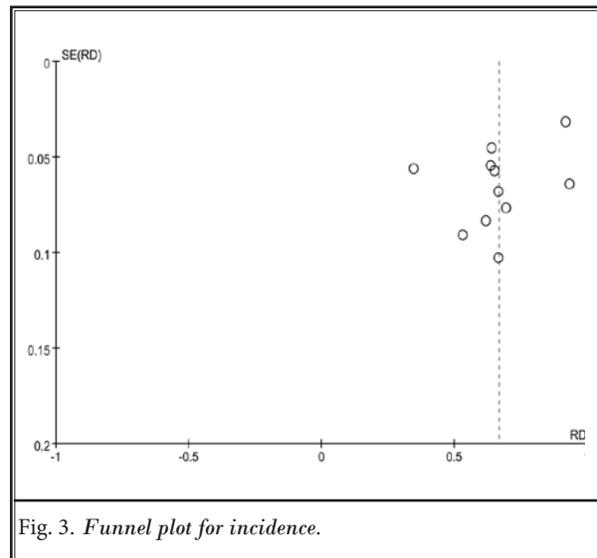


Fig. 3. Funnel plot for incidence.

We collected the articles for the meta-analysis without language limitation. After analyzing the selected literature, we found that the overall incidence of LDH reabsorption was around 66.66%. In Japan, the resorption rate was 62.58%, which is close to the average level. In the United Kingdom, the incidence was much higher, at 82.94%. The medical standards of the countries may have an impact on the incidence of LDH reabsorption with conservative treatment. The United Kingdom, as a developed country, has an excellent health care system. Conservative treatment could reduce complications, lighten the suffering, reduce the

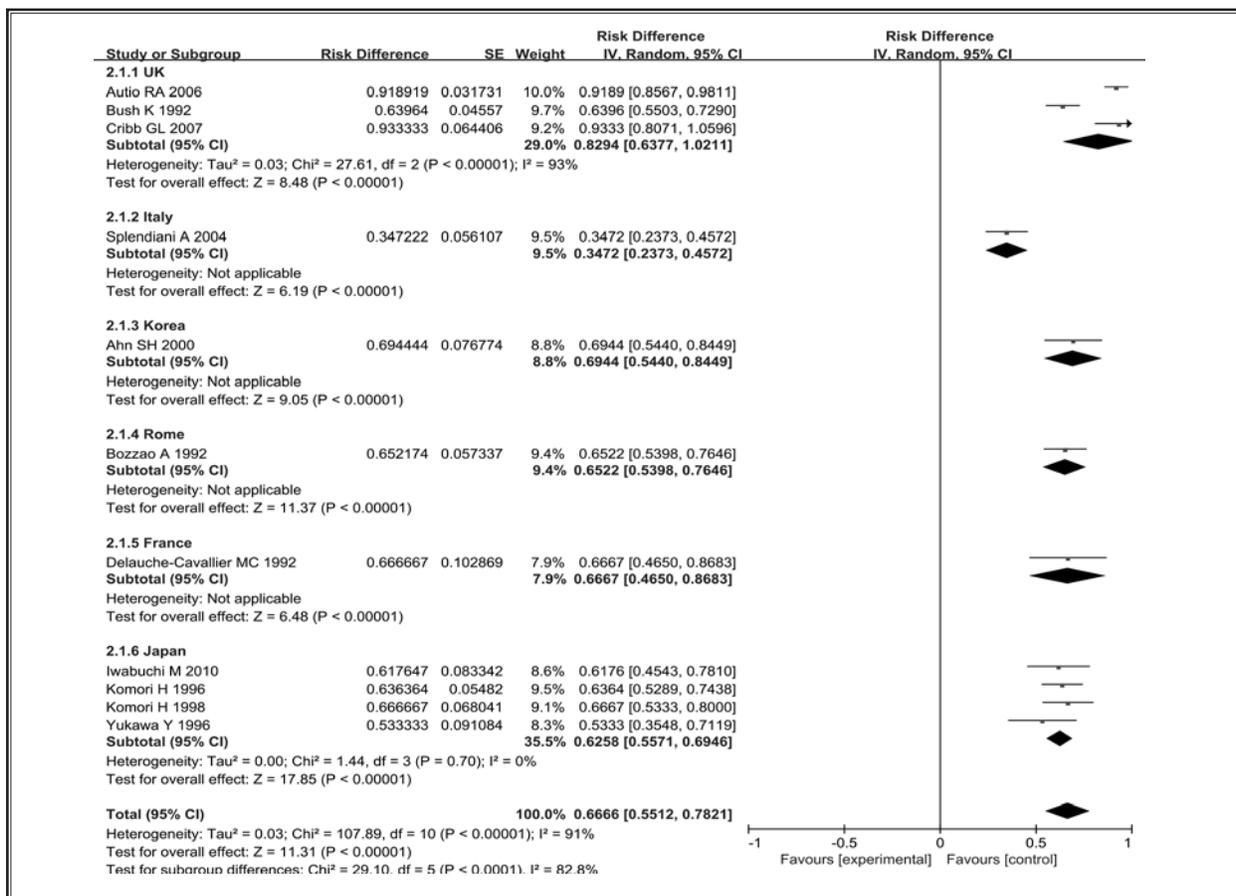


Fig 4. Forest plot for incidence in various countries.

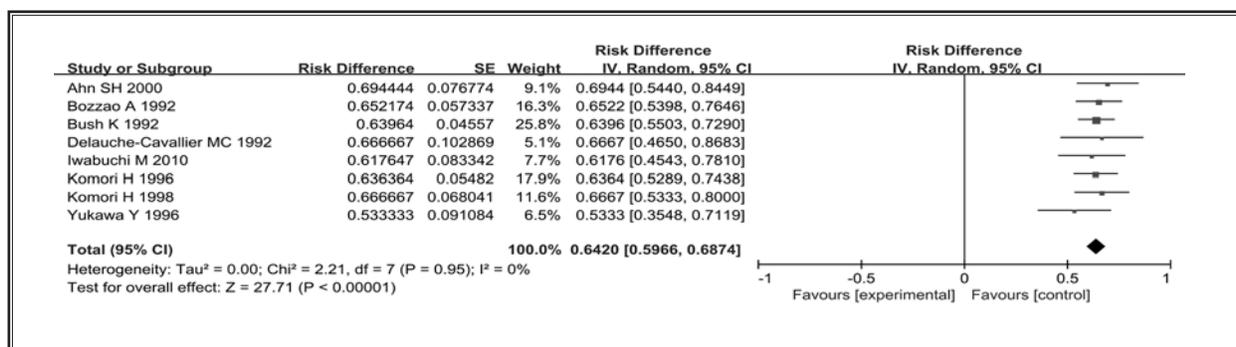


Fig 5. Forest plot for incidence after removing three low-quality studies.

economic burden for patients, and elevate their quality of living (5,33,34).

Because the overall incidence of spontaneous resorption after LDH is high, more research is needed on spontaneous regression after LDH with conservative treatment.

Limitations

Our study was limited because there were few sources from which to extract data, either in abstracts or published studies. There were no randomized, controlled trials that met our criteria. Obvious confounding

variables were the use of different inclusion and exclusion criteria and the treatment modalities employed. A random-effects model was therefore chosen to account for this heterogeneity.

CONCLUSIONS

Whether LDH should be treated conservatively or surgically remains a source of controversy. The phenomenon of LDH reabsorption has been recognized, and its overall incidence has reached 66.66%, according to our results. Conservative treatment may therefore become

the first choice for treating LDH. The cost reduction thereby achieved should benefit patients and society. Research on spontaneous resorption is still sparse. Future studies with a similar design in prospective, randomized, controlled trials are required to study the phenomenon of spontaneous resorption of LDH.

Acknowledgment

This study was supported by the National Natural Science Funds of China (grant number 81473691).

REFERENCES

- Freeman BJ, Ludbrook GL, Hall S, Cousins M, Mitchell B, Jaros M, Wyand M, Gorman JR. Randomized, double-blind, placebo-controlled, trial of transforaminal epidural etanercept for the treatment of symptomatic lumbar disc herniation. *Spine* 2013; 38:1986-1994.
- Kamper SJ, Ostelo RW, Rubinstein SM, Nellensteijn JM, Peul WC, Arts MP, van Tulder MW. Minimally invasive surgery for lumbar disc herniation: A systematic review and meta-analysis. *Eur Spine J* 2014; 23:1021-1043.
- Oliphant D. Safety of spinal manipulation in the treatment of lumbar disk herniations: A systematic review and risk assessment. *J Manip Physiol Ther* 2004; 27:197-210.
- Lurie JD, Tosteson TD, Tosteson AN, Zhao W, Morgan TS, Abdu WA, Herkowitz H, Weinstein JN. Surgical versus non-operative treatment for lumbar disc herniation: Eight-year results for the spine patient outcomes research trial. *Spine* 2014; 39:3-16.
- Matsumoto M, Chiba K, Ishikawa M, Maruiwa H, Fujimura Y, Toyama Y. Relationships between outcomes of conservative treatment and magnetic resonance imaging findings in patients with mild cervical myelopathy caused by soft disc herniations. *Spine* 2001; 26:1592-1598.
- Gautschi OP, Stienen MN, Schaller K. [Spontaneous regression of lumbar and cervical disc herniations - a well established phenomenon]. *Praxis* 2013; 102:675-680.
- Saal JA, Saal JS, Herzog RJ. The natural history of lumbar intervertebral disc extrusions treated nonoperatively. *Spine* 1990; 15:683-686.
- Haro H. Translational research of herniated discs: Current status of diagnosis and treatment. *J Orthop Sci* 2014; 19:515-520.
- Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* [updated March 2011]. The Cochrane Collaboration, 2011.
- Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, Leeflang MM, Sterne JA, Bossuyt PM. QUADAS-2: A revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011; 155:529-536.
- QUADAS-2 manual. University of Bristol, Bristol, UK, 2011. www.bris.ac.uk/quadas/quadas-2/.
- Sobanski V, Dauchet L, Lefevre G, Lambert M, Morell-Dubois S, Sy T, Hachulla E, Hatron PY, Launay D, Dubucquoi S. Prevalence of anti-RNA polymerase III antibodies in systemic sclerosis: New data from a French cohort and a systematic review and meta-analysis. *Arthritis Rheum* 2014; 66:407-417.
- OCEBM Levels of Evidence Working Group. The Oxford Levels of Evidence 2. *Oxford Centre for Evidence-Based Medicine*. www.cebm.net/index.aspx?o=5653
- Ahn SH, Ahn MW, Byun WM. Effect of the transligamentous extension of lumbar disc herniations on their regression and the clinical outcome of sciatica. *Spine* 2000; 25:475-480.
- Autio RA, Karppinen J, Niinimäki J, Ojala R, Kurunlahti M, Haapea M, Vanharanta H, Tervonen O. Determinants of spontaneous resorption of intervertebral disc herniations. *Spine* 2006; 31:1247-1252.
- Autio RA, Karppinen J, Kurunlahti M, Haapea M, Vanharanta H, Tervonen O. Effect of periradicular methylprednisolone on spontaneous resorption of intervertebral disc herniations. *Spine* 2004; 29:1601-1607.
- Autio RA, Karppinen J, Niinimäki J, Ojala R, Veeger N, Korhonen T, Hurri H, Tervonen O. The effect of infliximab, a monoclonal antibody against TNF- α , on disc herniation resorption: A randomized controlled study. *Spine* 2006; 31:2641-2645.
- Bozzao A, Gallucci M, Masciocchi C, Aprile I, Barile A, Passariello R. Lumbar disk herniation: MR imaging assessment of natural history in patients treated without surgery. *Radiology* 1992; 185:135-141.
- Bush K, Cowan N, Katz DE, Gishen P. The natural history of sciatica associated with disc pathology. A prospective study with clinical and independent radiologic follow-up. *Spine* 1992; 17:1205-1212.
- Cribb GL, Jaffray DC, Cassar-Pullicino VN. Observations on the natural history of massive lumbar disc herniation. *J Bone Joint Surg Br* 2007; 89:782-784.
- Delauche-Cavallier MC, Budet C, Laredo JD, Debie B, Wybier M, Dorfmann H, Ballner I. Lumbar disc herniation. Computed tomography scan changes after conservative treatment of nerve root compression. *Spine* 1992; 17:927-933.
- Iwabuchi M, Murakami K, Ara F, Otani K, Kikuchi S. The predictive factors for the resorption of a lumbar disc herniation on plain MRI. *Fukushima J Med Sci* 2010; 56:91-97.
- Komori H, Shinomiya K, Nakai O, Yamaura I, Takeda S, Furuya K. The natural history of herniated nucleus pulposus with radiculopathy. *Spine* 1996; 21:225-229.
- Komori H, Okawa A, Haro H, Muneta T,

- Yamamoto H, Shinomiya K. Contrast-enhanced magnetic resonance imaging in conservative management of lumbar disc herniation. *Spine* 1998; 23:67-73.
25. Splendiani A, Puglielli E, De Amicis R, Barile A, Masciocchi C, Gallucci M. Spontaneous resolution of lumbar disk herniation: Predictive signs for prognostic evaluation. *Neuroradiology* 2004; 46:916-922.
 26. Yukawa Y, Kato F, Matsubara Y, Kajino G, Nakamura S, Nitta H. Serial magnetic resonance imaging follow-up study of lumbar disc herniation conservatively treated for average 30 months: Relation between reduction of herniation and degeneration of disc. *J Spinal Disord* 1996; 9:251-256.
 27. Key JA. The conservative and operative treatment of lesions of the intervertebral discs in the low back. *Surgery* 1945; 17:291-303.
 28. Shan Z, Fan S, Xie Q, Suyou L, Liu J, Wang C, Zhao F. Spontaneous resorption of lumbar disc herniation is less likely when modic changes are present. *Spine* 2014; 39:736-744.
 29. Haro H, Domoto T, Maekawa S, Horiuchi T, Komori H, Hamada Y. Resorption of thoracic disc herniation. Report of 2 cases. *J Neurosurg Spine* 2008; 8:300-304.
 30. Lutman M, Girelli G. [Spontaneous regression of lumbar disk hernia]. *Radiol Med* 1991; 81:225-227.
 31. Macki M, Hernandez-Hermann M, Bydon M, Gokaslan A, McGovern K, Bydon A. Spontaneous regression of sequestered lumbar disc herniations: Literature review. *Clin Neurol Neurosurg* 2014; 120:136-141.
 32. Martinez-Quinones JV, Aso-Escario J, Consolini F, Arregui-Calvo R. [Spontaneous regression from intervertebral disc herniation. Propos of a series of 37 cases]. *Neurocirugia (Astur)* 2010; 21:108-117.
 33. Monument MJ, Salo PT. Spontaneous regression of a lumbar disk herniation. *CMAJ* 2011; 183:823.
 34. Orief T, Orz Y, Attia W, Almusrea K. Spontaneous resorption of sequestered intervertebral disc herniation. *World Neurosurg* 2012; 77:146-152.