ORIGINAL STUDY

acta orthopaedica belgica, 2023, 89, 381-392

doi.org/10.52628/89.3.11201

How to spot the recurring lumbar disc? Risk factors for recurrent lumbar disc herniation (rLDH) in adult patients with lumbar disc prolapse: a systematic review and meta-analysis

ABDEL-RAHMAN ABDEL-FATTAH[1,2], A. IRVING[2], S. BALIGA[2,3], P. K MYINT[1,2], K. R. MARTIN[2,3]

[1]Ageing Clinical and Experimental Research (ACER) Team, Institute of Applied Health Sciences, School of Medicine, Medical Sciences & Nutrition, University of Aberdeen, Aberdeen, UK; [2]University of Aberdeen, School of Medicine, Medical Sciences & Nutrition, University of Aberdeen, Aberdeen, UK; [3]Aberdeen Centre for Arthritis & Musculoskeletal Health, University of Aberdeen, Aberdeen, UK; [4]Department of Trauma & Orthopaedics, Aberdeen Royal Infirmary, Aberdeen, UK.

Correspondence at: Abdel-Rahman Abdel-Fattah, School of Medicine, Medical Sciences and Nutrition, Foresterhill, Aberdeen, AB25 2ZD, Scotland, UK, Email: a.abdelfattah.17@abdn.ac.uk

Despite a fast-growing evidence-base examining the relationship of certain clinical and radiological factors such as smoking, BMI and herniation-type with rLDH, there remains much debate around which factors are clinically important. We conducted a systematic review and meta-analysis to identify risk factors for recurrent lumbar disc herniation (rLDH) in adults after primary discectomy. A systematic literature search was carried out using Ovid-Medline, EMBASE, Cochrane library and Web of Science databases from inception to 23rd June-2022. Observational studies of adult patients with radiologically-confirmed rLDH after ≥3 months of the initial surgery were included, and their quality assessed using the Quality-In-Prognostic-Studies (QUIPS) appraisal tool. Meta-analyses of univariate and multivariate data and a sensitivity-analysis for rLDH post-microdiscectomy were performed. Twelve studies (n=4497, mean age:47.3; 34.5% female) were included, and 11 studies (n=4235) meta-analysed. The mean follow-up was 38.4 months. Mean recurrence rate was 13.1% and mean time-to-recurrence was 24.1 months (range: 6-90 months). Clinically, older age (OR:1.04, 95%CI:1.00-1.08, n=1014), diabetes mellitus (OR:3.82, 95%CI:1.58-9.26, n=2330) and smoking (OR:1.80, 95%CI:1.03-3.14, n=3425) increased likelihood of recurrence. Radiologically, Modic-change type-2 (OR:7.93, 95%CI:5.70-11.05, n=1706) and disc extrusion (OR:12.23, 95%CI:8.60-17.38, n=1706) increased likelihood of recurrence. The evidence did not support an association between rLDH and sex; BMI; occupational labour/driving; alcohol-consumption; Pfirmann-grade, or herniation-level. Older patients, smokers, patients with diabetes, those with type-2 Modic-changes or disc extrusion are more likely to experience rLDH. Higher quality studies with robust adjustment of confounders are required to determine the clinical bearing of all other potential risk factors for rLDH.

Keywords: Risk factors, lumbar disc, disc herniation, recurrence, microdiscectomy.

INTRODUCTION

Lower back pain (LBP) is the leading cause of disability globally and is a major public health concern affecting one-in-six people [1]. More than 75% of those with LBP are older than 35-years and almost 30% are above-65[1]. LBP has considerable implications on quality-of-life (QoL) including poorer functional ability and social exclusion due to inability-to-work, as well as serious mental-health complications including clinical depression and anxiety[2].

A common cause of LBP is disc herniation which has a lifetime incidence of 13-40% peaking in the fifth decade of life[2]. The prevalence of disc herniation in men is twice that of women, which has been attributed to a greater proportion of smokers and those in physically- demanding jobs[3]. Recurrence after surgical treatment has been reported to be as often as five to 15% after primary discectomy[3,4].The primary operation is either a traditional open-microdiscectomy or one of the novel surgical-approaches such as percuta-neous-endoscopic-lumbar-discectomy (PELD)[5-7]. For patients, reoperation reintroduces surgical risks such as: haematoma, infection and dural-injury. Whilst for surgeons, a reoperation is more technically-challenging due to scarring and fibrosis[4-8]. Reoperation also costs approximately 15-times more than conservative treatment[9].

Despite the increasing wealth of literature examining the relationship of certain clinical and radiological factors such as smoking, BMI and herniation-type with rLDH, there remains much debate around which factors are clinically-important[10-13]. Previous studies have reported that smoking is an independent risk factor for rLDH[10,11]. However, other studies suggested that additional factors such as BMI are necessary to support this association[12,13]. A retrospective cohort study in 2010 of 75 patients with rLDH found that those with BMI ≥30 were 12-times more likely to have a recurrence and 30-times more likely to require reoperation compared with non-obese individuals[12]. Conversely, more recent literature suggests that the opposite may be true[14,15].

Our study aimed to identify the clinical and radiological factors which increase the risk of developing rLDH in adult patients with radiologically-confirmed disc herniation. To achieve this, we conducted a comprehensive review of the best available evidence, including all the novel factors in recent literature which have not yet been pooled into a meta-analysis. This will serve to help clinicians identify the higher risk patient and thence individualise care accordingly, as well as, to better inform secondary prevention protocols for patients with LDH.

MATERIALS AND METHODS

A systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement guidance[16].

The inclusion and exclusion criteria are detailed in Table 1. Observational studies (cohort or case-control studies) of adult patients (≥18 years) admitted to hospital with radiologically confirmed rLDH (on magnetic resonance imaging or computed tomography) were included. rLDH was defined as an ipsilateral or contralateral herniation of the nucleus pulposus at the same disc level, in (symptomatic or asymptomatic) patients who had a postoperative pain-free interval of >3 months following primary discectomy. Studies assessing any risk factor for rLDH of interest, irrespective of aetiology of initial disc herniation or geographical setting, were included. No restriction to type of disc-herniation, geographical region or language of published article was applied. Studies which included patients with a postoperative follow-up period of <6 months were excluded. Case-reports and conference abstracts were excluded. Studies which assessed risk factors for rLDH in a specific sub-population such as patients with Crohn's disease were also excluded.

Both clinical prognostic factors and radiological parameters were assessed. The novel clinical factors included: occupational heavy labour, occupational driving, history-of-spinal-trauma, degree of pre-

Table I — PICOTS framework for prognostic studies

PICOTS	*Inclusion criteria*	*Exclusion criteria*
Population	Adult patients ≥ 18 years who had radiologically confirmed lumbar disc herniation.	Studies with participants who have disc disease with another systemic illness e.g., Crohn's disease patients or sarcopenia.
Index prognostic factors *Novel factors in this systematic review*	Hypertension, spine trauma history, occupation, pre-operative function, details of the herniation (type, side, level), Modic change, Disc degeneration (Pfirmann grading), hospital complications and adverse events.	Studies which focus on recurrence which was not radiologically proven.
Comparator prognostic factors *To compare with findings of previous systematic review*	Age, sex, BMI, smoking status, diabetes mellitus.	
Outcome	Adult patients ≥ 18 years who had radiologically confirmed recurrence of their lumbar disc herniation (rLDH) with a pain-free interval of ≥3 months after their primary disc surgery.	Recurrence defined symptomatically or recurrence after non-operative management e.g., period of physiotherapy, analgesia, or spinal nerve root injections. Studies which consider recurrence managed conservatively as cases of non-recurrence.
Time	Prognostic factors measured before the diagnosis of rLDH and prognostic of recurrence in patients with a confirmed radiological diagnosis. Minimum follow-up of patients was 6 months after their primary disc surgery.	
Setting	Patients admitted to hospital or emergency departments with recurrence or an equivalent healthcare facility with access to imaging to radiologically confirm rLDH diagnosis.	

Table II — Characteristics of included studies

Papers (N=12)	Type of study	Population (N=4 497)	%Female (Mean 34.5%)	Age, in years (Mean ± SD) (47.3 ± 11.1)	Type of operation	Region	FU in months (Mean ± SD) (38.4 ± 14.3)	Data period	Prognostic factors of interest
Kim, 2021	Case-control	71	18.3	61.9 ± 13.4	One-level microdiscectomy	Korea	36.9 ± 12.2	Jan 2013 to Dec 2015	Age, sex, smoking status, DM, BMI, level of herniation, discectomy side, herniation type, Modic change, Disc degeneration (Pfirmann grading)
Li, 2021	Case-control	1706	41.0	47.0 ± 15.4	PELD	China	76.3 ± 13.0	2012 to 2015	Age, sex, BMI, smoking status, DM, hx of trauma, hx of intense physical labour, hypertension, pre-operative function by VAS and ODI, level of herniation, herniation type, Modic change, Disc degeneration (Pfirmann grading)
Paracino, 2021	Cohort	262	28.5	46.5 ± 2.5	Microdiscectomy	Italy	Median (range) 24 (13-43)	Jan 2013 to Jun 2018	Age, sex, BMI, smoking status, level of herniation, post-operative ODI score
Yu, 2020	Case-control	484	47.5	48.2 ± 9.7	PELD	China	22.2 ± 8.1	Oct 2014 to Jun 2018	Age, sex, BMI, smoking status, DM, hx of trauma, hypertension, alcohol consumption, time to return to work, Modic change, Disc degeneration (Pfirmann grading)
Dobran, 2019	Case-control	209	40.2	44.6 ± 11.8	Microdiscectomy	Italy	12 months	2013 to 2018	Age, sex, BMI, smoking status, post-operative ODI, pre-operative VAS, level of herniation
Li, 2018	Case-control	321	48.6	35.7 ± 9.9	Discectomy with laminotomy, laminectomy or laminectomy and fusion	China	Median (range) 98 (72-150)	Jun 2005 to Jul 2012	Age, sex, BMI, smoking status, hx of trauma, occupational lifting, occupational driving, type of herniation, alcohol consumption, sport activity, pre-operative function by VAS score, Disc degeneration (Pfirmann grading)
Yaman, 2017	Case-control	126	40.0	50.6 ± 12.3	L4/5 open or microdiscectomy	Turkey	10.8 months	Aug 2004 to Sep 2009	Age, sex, BMI, smoking status, DM, herniation type, Modic change, Disc degeneration (Pfirmann grading)
Yurac, 2016	Nested case-control	218	6.0	37.8 ± 8.2	Loupe-assisted microdiscectomy	Chile	> 12 months	Jun 1994 to May 2011	Age, sex, smoking status, occupational lifting, level of herniation, herniation type, duration of operation, length of hospital stay, time to return to work
Kim, 2014	Case-control	467	n/a	n/a	L5/S1 microdiscectomy	Korea	51.1 ± 22.9	n/a	Age, sex, smoking, DM, herniation type
Miwa, 2012	Case-control	298	28.9	49.0 ± 16.3	Microdiscectomy	Japan	39.0 ± 11.5	Apr 2005 to Mar 2008	Age, sex, BMI, smoking status, alcohol consumption, sport activity, occupational lifting, occupational driving
Oh, 2012	Case-control	178	46.1	51.5	Open single-level discectomy	Korea	22.2 months	May 2006 to Dec 2009	Age, sex, smoking status, level of herniation, herniation type, hx of trauma, pre-operative VAS, Disc degeneration (Pfirmann grading)
Kim, 2009	Case-control	157	n/a	n/a	L4/5 microdis-cectomy	Korea	56.4 ± 18	n/a	Age, sex, smoking, DM

*FU= follow-up, PELD= Percutaneous Endoscopic Lumbar Discectomy, DM= diabetes mellitus, BMI= body mass index, Hx = History, VAS= visual analog scale, ODI= Oswestry Disability Index, n/a= no study data was available for data extraction.

operative pain, measured by Visual-Analogue-Scale (VAS) and degree-of-disability measured by Oswestry-Disability-Index (ODI), sporting ability, alcohol consumption, hypertension, and time-off-work. The radiological factors included: type and level-of-herniation, Modic-change and degree-of-degeneration (measured by Pfirmann-grade).

The comparator prognostic factors were age, sex, BMI, smoking and diabetes-mellitus. These factors have been assessed in a previous systematic review in 2016[5].

Two authors (AA and AI) independently performed a literature search using the databases: Ovid Med-line, EMBASE, Cochrane Library and Web-of-Science, from inception to 23rd-June-2022. In addition, a manual search through reference lists of relevant reviews and their included studies was conducted to identify any further relevant literature. Limitations to 'humans' and 'adults' were delayed to the screening stage to avoid missing recent papers which had not yet been assigned appropriate database-specific tags. Relevant search terms were selected (by AA, SB and KRM) and corroborated by a medical statistician. The MeSH headings included "intervertebral disc", "diskectomy", "risk factors" and "recurrence". The detailed search strategies for each database are found in Supplementary File 1.

Titles and abstracts were independently screened in accordance with the PICOTS criteria (Table 1) by two authors (AA and AI) using a pre-defined screening tool, after deduplicating and exporting citations to Microsoft Excel. All potentially eligible full-text articles were independently screened and assessed for eligibility. Following cross-screening, a senior author (KRM) resolved any discrepancies at title, abstract and full-text screening stages. Data extraction was carried out using the Checklist for critical-Appraisal and data-extraction for systematic-Reviews of prediction-Modelling-Studies (CHARMS) checklist, the tool recommended by Cochrane for prognostic studies[17]. Data extracted included basic study characteristics as shown in Table 2. Primary authors of all eligible studies were contacted to request missing data. When two articles for the same study were found, the more recent article was considered.

The risk of bias for all eligible studies was assessed using the Quality-In-Prognostic-Studies (QUIPS) tool, based on Cochrane recommendations[17]. Funnel plots were used to measure publication bias where ≥10 studies were included in the meta-analysis[18]. The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology was used to assess the weight-of-evidence from the meta-analysis[19].

Study heterogeneity was examined by assessing the study and participant characteristics to determine if there was sufficient homogeneity of data pool. Where study homogeneity was sufficient, a meta-analysis was then carried out. Meta-analysis results were expressed as weighted-mean-differences (MD) and 95% confidence intervals (CI), and dichotomous variables from case-control studies were reported as odd ratios (ORs) and 95% CI. Results were considered statistically significant if p-values were less than 0.05. Statistical heterogeneity was measured using the I^2 statistic which was also used to confirm data homogeneity. A fixed-effects model was implemented due to homogeneity of the included studies. The meta-analysis was conducted using RevMan version 5.4[20]. A sensitivity-analysis of studies assessing recurrence after conventional microdiscectomy only (the most commonly performed type of disc surgery[21]) was conducted by excluding data for all other types of disc surgery.

RESULTS

The literature search generated 2070 records (**Figure 1**). Full-text articles were reviewed for 141 studies. Twelve studies were eligible for inclusion in the systematic review.

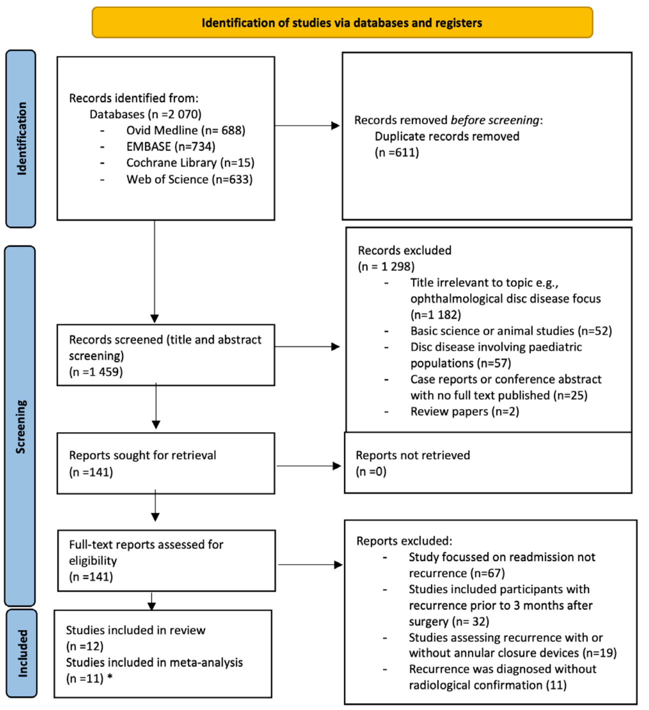

Figure 1

. * Paracino et al., 2021 was the only study to report hazard ratios. All other studies reported odds ratios. Since these two effect estimates cannot be considered equal for pooling in the same meta-analysis, this study's data was excluded from meta-analysis.

Table III — Characteristics of the recurrence in the included studies

Papers (N=12)	No. of patients recurred (%) 553/4497(13.1%)	Time to recurrence in months, Mean ± SD (range in months) (24.1 ± 16.0, 6-90)	Definition of recurrence
Kim, 2021	15/71 (21.2)	17.5 ± 11.2 (8-46)	Symptoms at same-level, or on the ipsilateral or contralateral side, ≥6 months after primary operation, confirmed by MRI imaging
Li, 2021	177/1706 (10.4)	27.4 ± 18.7 (6-72)	Relief of symptoms by ≥50% after surgical treatment followed by recurrence of back and radicular leg pain ≥6 months after surgery caused by nucleus pulposus protrusion at same segment, reconfirmed by imaging
Paracino, 2021	46/262 (17.6)	Most of the patients recurred within 24 months after surgery	Disc herniation at same level and side of previous microdiscectomy after a period free of post-operative pain for ≥3 months, confirmed by MRI imaging
Yu, 2020	46/484 (9.5)	12 – 48 months	Herniation at L5-S1 level confirmed by MRI or CT, nerve root pain with distribution confirming with imaging with no short-term recurrence (<3 months)
Dobran, 2019	20/209 (9.6)	12 months	Herniation at the same level and side of previous microdiscectomy after 3 months postoperative pain-free period, confirmed by MRI imaging
Li, 2018	58/321 (18.1)	32.3 ± 16.5 (7–90)	Herniation at the same level, regardless of ipsilateral or contralateral herniation, in patients who had pain-free interval of ≥6 months after surgery, confirmed by MRI imaging
Yaman, 2017	25/126 (19.8)	8 (6.3-42.0)	Radiologically confirmed re-herniation in patients with a pain-free interval of pain ≥6 months after the primary surgery
Yurac, 2016	109/218 (50) * *Nested case-control*	n/a	Radiologically confirmed re-herniation in patients with a pain-free interval of pain ≥6 months after the primary surgery
Kim, 2014	39/467 (8.4)	39.4 ± 17.9 (7-90)	Symptoms at same-level, or on the ipsilateral or contralateral side, ≥6 months after primary operation, confirmed by MRI imaging
Miwa, 2012	32/298 (10.7)	14.6 months	Symptoms at same-level, or on the ipsilateral or contralateral side, ≥6 months after primary operation, confirmed by MRI imaging
Oh, 2012	18/178 (10.1)	18.7 (6-61)	Radiologically confirmed re-herniation in patients with a pain-free interval of pain ≥6 months after the primary surgery
Kim, 2009	14/157 (8.9)	40.8 ± 15.5 (7-70)	Repeated disc herniation at a previously operated disc level in patients who experienced a pain-free interval of ≥6 months after surgery, confirmed by MRI imaging

*Not the true proportion of recurrences from the original study population due to the study design (nested case-control) therefore, result not included in the overall mean recurrence calculation. n/a= no study data was available for data extraction.

Table 2 illustrates the characteristics of included studies. Twelve studies (n=4497, mean-age: 47.3; 34.5% female) were included. Mean follow-up was 38.4-months (standard- deviation [SD]:14.3). Eleven studies (n=4235), all of which were case-control studies, had appropriate data for pooling into the meta-analysis. One study was a cohort study and reported their data in hazard ratios (HRs) and therefore was not included in meta-analysis[22]. Eight studies were from East Asia (four Korean, three Chinese and one Japanese), one study from West Asia (one Turkish), two studies from Europe (both Italian) and one study from South America (Chilean).

Nine studies defined outcome as recurrence of symptoms at the same level (ipsilateral or contralateral) in patients with pain-free interval ≥6 months after primary operation, confirmed by MRI imaging. Three studies used a shorter pain-free interval of ≥3 months[22,24,25]. Nine studies assessed rLDH in patients who underwent a traditional microdiscectomy whereas two studies focussed on those who underwent PELD[23,24]. The mean recurrence-rate was 13.1% (n=553/4497 patients), 10.0% after PELD and 13.8% after micro-discectomy, and the mean time-to-recurrence was 24.1 months (Table 3).

All studies were single-centre observational studies with sample populations ranging from 71 and 1706 patients. Ten studies including more than 20 patients in the recurrence arm[22-25,28-33]. Kim et al. and Oh et al. had only 15 and 18 patients with recurrence, respectively.[26,27]. In addition, Oh et al. had a large number of patients lost to follow-up in both arms which may have resulted in underreporting of rLDH cases[27]. All patients underwent preoperative and postoperative MRI or CT imaging[22-33].

Seven studies reported on the surgical technique and data were mostly consistent in all of them[22-24,28-30,32]. All patients in the study by Paracino et al. and over two-thirds of patients in Li et al. underwent partial or total laminectomy[22,28]. In all other studies the discectomy was accompanied by a laminotomy alone[23,24,29,30,32]. An open discectomy approach was used in five studies[22,28-30,32] whereas Yu et al. and Li et al. used an endoscopic approach[23,24]. A sensitivity analysis excluding these two studies was conducted to minimise confounding. Five studies did not disclose details of the operation[25-27,31,33]. In the study by Miwa et al. the operations were conducted by two specific experienced surgeons[32]. In all other studies, the operations were carried out by any experienced spinal surgeon in the respective hospital department[22-24,29,30,32]. In all reporting studies, the operation was conducted using the same standardised technique for all patients however, inter-surgeon variability remains a source of bias. Nine studies included recurrence at any lumbar disc level [22-28,30,32] however, Yaman et al. and Kim et al. (2009) focussed on L4/5 recurrence alone, and Kim et al. (2014) focussed on L5/S1 recurrence alone[29,31,33]. Kim et al. (2014) and Yaman et al. included patients which were followed up for less than 12 months which limits our understanding of the prognostic significance of individual factors in the longer term[29,31]. The study by Kim et al. (2021) was limited by a small sample size (n=71) increasing the imprecision of its findings. The majority of included studies undertook a retrospective analysis of all eligible patients who underwent a discectomy within a prespecified time period[22-29,31-33]. However, Yurac et al. only included compensated patients under the workforce compensation program, hereby reducing the generalisability of their findings[30].

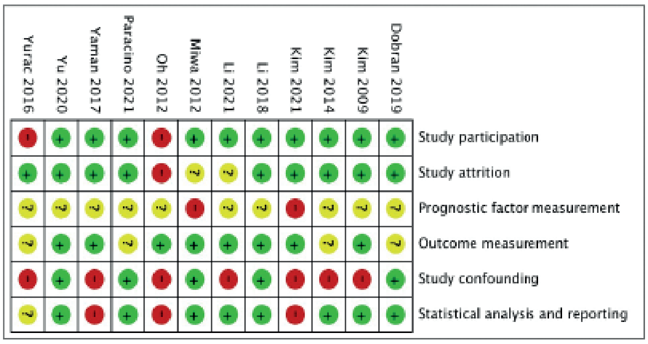

Figure 2

Due to the younger mean age (recurrences: 35.1 ± 7.5 years and non-recurrence: 40.4 ± 8.9 years), patients in this study had a higher rate of subligamentous disc herniations (92.6% of recurrences, compared to 25.9% of recurrences in other studies[25]). Similarly, in the study by Miwa et al., the study sample was 71.1% male and 28.9% female[32]. Therefore, the unadjusted data should be interpreted with caution due to unbalanced sex ratio which may have influenced the prognostic significance of sex on rLDH.

Ten of 12 studies (83.3%) reported sufficient information on their study participants with detail regarding study characteristics and criteria used (Figure 2). Similarly, a low attrition-bias was found, with nine studies (75%) reporting good response rate from both recurrence and no-recurrence groups. The definition of recurrence (outcome measurement) was clear, with detailed methods of the applied radiological criteria reported in eight studies (66.7%). Only four studies (33.3%) adequately considered all relevant variables which could influence recurrence outcome. Finally, despite eight studies using a multivariate statistical model, many of these studies did not perform adjusted analyses on all the included factors.

All studies were similar in design (case-control, nested case-control, or cohort) and reported on similar risk factors of interest (low methodological and clinical diversity). Data variables on age, sex, smoking and DM were included in all studies[22-33]. Analysis of age, sex and BMI was largely consistent across the studies (Supplementary Table 1). Five studies reported a thorough biomechanical analyses with consistent measurement methods of disc height, sagittal range of motion, disc degeneration (Pfirmann grading) and endplate changes (Modic change)[23-24,26-28] A narrow age range was used in nine studies (mean age 35-50 years[22-26,28-30,32]). The surgical technique was largely consistent within and across all studies (Supplementary Table 2), and both studies which used a different technique were accounted for by sensitivity analysis.

Table 4 — Summary table of meta-analysis and sensitivity analysis results illustrating the relationship between specific risk factors and recurrence in adults (over 18 years) after primary disc surgery at mean follow-up of 38.4 months (recurrence, n=553, no recurrence, n=3944, total N=4497); mean difference (MD) or odds ratio (OR) with 95% confidence intervals (CI)

Summary results from meta-analysis				
Clinical risk factors				
	Primary analysis		**Sensitivity analysis**	
	Univariate	**Multivariate**	**Univariate**	**Multivariate**
Age	**MD 3.99 (2.87, 5.11) N= 3064**	**OR 1.04 (1.00, 1.08) N=1014**	**MD 4.07 (2.52, 5.63) N=874**	**OR 1.04 (1.00, 1.08) N=530**
Sex (male)	OR 1.02 (0.82, 1.26) N=3336	OR 0.78 (0.44, 1.38) N=747	**OR 1.43 (1.05, 1.96) N= 1421**	n/a
BMI	**MD 1.07 (0.70, 1.45) N=2720**	OR 1.10 (0.89, 1.36) N=693	**MD 1.31 (0.40, 2.21) N=530**	OR 1.09 (0.88, 1.36) [ò] N=484
Smoking status	**OR 3.19 (2.59, 3.92) N=3611**	**OR 1.80 (1.03, 3.14) N=3425**	**OR 1.69 (1.27, 2.25) N=1421**	OR 1.18 (0.41, 3.38) N=1719
DM	**OR 5.78 (3.88, 8.60) N=2387**	**OR 3.82 (1.58, 9.26) N=2330**	OR 1.76 (0.75, 4.11) N=197	OR 1.34 (0.26, 6.94) N=624
Occupational lifting/ Heavy labour	**OR 4.74 (3.44, 6.54) N=2543**	OR 1.48 (0.18, 12.43) N=2004	**OR 2.79 (1.84, 4.23) N=837**	OR 1.40 (0.16, 12.53) [ò] N=298
Occupational driving	OR 1.95 (0.95, 4.01) N=619	OR 1.20 (0.36, 4.03) [ò] N=298	n/a	n/a
History of spine trauma	**OR 4.59 (3.26, 6.46) N=2689**	n/a	**OR 5.90 (3.50, 9.95) N=499**	n/a
Alcohol consumption	OR 1.22 (0.81, 1.85) N=1103	OR 1.18 (0.55, 2.54) N=298[ò]	OR 1.20 (0.70, 2.04) N=619	n/a
Hypertension	**OR 3.62 (2.58, 5.07) N=2190**	n/a	n/a	n/a
Pre-operative back pain (VAS)	**MD 0.53 (0.40, 0.66) N=2236**	n/a	MD 0.10 (-0.15, 0.34) N=530	n/a
Pre-operative leg pain (VAS)	**MD 0.49 (0.36, 0.63) N=2027**	n/a	MD -0.04 (-0.32, 0.24) [ò] N=321	n/a
Time to return to work	MD 0.07 (-0.15, 0.30) N=702	n/a	MD 0.18 (-0.14, 0.49) [ò] N=218	n/a
Athleticism (sport activity)	OR 1.15 (0.66, 2.00) N=619	n/a	n/a	n/a
Radiological risk factors				
	Primary analysis		**Sensitivity analysis**	
	Univariate	**Multivariate**	**Univariate**	**Multivariate**
Modic Change				
Type 0	**OR 0.19 (0.14, 0.25) N=1903**	n/a	OR 0.52 (0.25, 1.07) N=197	n/a
Type 1	OR 1.07 (0.53, 2.15) N=1903	n/a	OR 1.58 (0.53, 4.72) N=197	n/a
Type 2	**OR 5.32 (3.95, 7.17) N=1903**	**OR 7.93 (5.70, 11.05) N=1706** [ò]	OR 1.12 (0.53, 2.37) N=197	n/a
Type 3	OR 0.68 (0.26, 1.77) N=1903	n/a	**OR 7.33 (1.52, 35.47) N=197**	n/a
Pfirmann Grade (Disc degeneration)				
Grades I and II	**OR 0.64 (0.42, 0.97) N=1098**	n/a	OR 0.57 (0.31, 1.04) N=570	n/a
Grades III and IV	**OR 1.75 (1.26, 2.43) N=2760**	OR 1.39 (0.70, 2.77) N=2190	OR 1.54 (0.96, 2.47) N=570	n/a

Type of disc herniation				
Protrusion	**OR 0.47 (0.32, 0.69) N=2620**	OR 1.32 (0.68, 2.57) ò N=1706	**OR 0.57 (0.38, 0.85) N=914**	n/a
Extrusion	**OR 4.39 (3.43, 5.60) N=2620**	**12.23 (8.60, 17.38) ò N=1706**	**OR 1.73 (1.20, 2.48) N=914**	n/a
Sequestration	OR 1.14 (0.73, 1.78) N=2402	n/a	OR 1.04 (0.61, 1.75) N=696	n/a
Level of herniation				
L2/3	OR 1.08 (0.13, 8.69) ò N=1706	n/a	n/a	n/a
L3/4	OR 1.50 (0.89, 2.52) 2133	n/a	OR 1.77 (0.82, 3.84) N=427	n/a
L4/L5	OR 0.84 (0.65, 1.07) N=2382	OR 0.88 (0.41, 1.88)ò N=209	OR 0.94 (0.63, 1.40) N=676	n/a
L5/S1	OR 1.09 (0.84, 1.41) 2311	n/a	OR 0.87 (0.56, 1.35) N=605	n/a
MD= Mean difference, OR= Odds Ratio, CI= Confidence interval DM= Diabetes Mellitus, VAS= Visual analogue scale. n/a= No study data was available for data extraction.ò Results from one study only.				

Therefore, despite heterogeneity in certain risk factors such as occupational level and history of spinal trauma, the studies were similar in the characteristics of study participants; exclusion criteria; strict case definition and, method of surgical intervention (Table 3 and Supplementary Table 2).

A summary of the results from all meta-analyses is shown in Table 4. Results from analysis of univariate data showed that older age (MD:3.99, 95%CI:2.87-5.11, N=3064, GRADE:high), higher BMI (MD:1.07, 95%CI:0.70-1.45, N=2720, GRADE:moderate), current smoker (OR:3.19, 95%CI:2.59-3.92, N=3611, GRADE:moderate), diabetes-mellitus (DM) (OR:5.78, 95%CI:3.88-8.60, N=2387, GRADE:low) and occupational heavy-labour (OR:4.74, 95%CI:3.44-6.54, N=2543, GRADE:low) increased the odds of rLDH. However, once these variables were adjusted in a multivariate analysis, only age (OR:1.04, 95%CI:1.00-1.08, n=1014, GRADE:moderate), smoking (OR:1.80, 95%CI:1.03-3.14, N=3425, GRADE:low) and DM (OR:3.82 95%CI:1.58-9.26, N=2330, GRADE:low) were associated with increased odds of rLDH. Both occupational driving and alcohol consumption were not associated with increased odds of rLDH in univariate or multivariate analyses, respectively. Only univariate data was available for the following variables: history of spinal-trauma (OR:4.59, 95%CI:3.26-6.46, N=2689, GRADE:moderate), hypertension (OR:3.62, 95%CI:2.58-5.07, N=2190, GRADE:low), pre-operative back (MD:0.53, 95%CI:0.40-0.66, N=2236, GRADE:low) and leg pain (MD:0.49, 95%CI:0.36-0.63, N=2027, GRADE:low) assessed by visual-analogue-scale (VAS) score, which were found to increase the likelihood of rLDH. Whereas, no relationship was found between rLDH and degree of sport activity or time-off work.

Results from sensitivity-analysis of univariate data illustrated that older age (MD:4.07, 95%CI:2.52-5.63, N=874, GRADE:high), male-sex (MD:1.43, 95%CI:1.05-1.96, N=1421, GRADE:low), higher BMI (MD:1.31, 95%CI:0.40-2.21, N=530, GRADE: moderate), current smoker (OR:1.69, 95%CI:1.27-2.25, N=1421, GRADE:moderate), and occupational heavy-labour (OR:2.79, 95%CI:1.84-4.23, N=837, GRADE:moderate) increased odds of rLDH. However, once these variables were adjusted in a multivariate analysis, only age (OR:1.04, 95%CI:1.00-1.08, n=530, GRADE:moderate) was associated with an increased likelihood of rLDH. Results for the relationship of rLDH with history of spinal-trauma were concordant with that of primary-analysis (OR:5.90, 95%CI:3.50-9.95, N=499, GRADE:moderate). No relationship was found between rLDH and alcohol consumption, pre-operative back and leg pain or time-off work.

Analysis of data on radiological factors showed that type-2 Modic-changes and extrusion-type disc herniation increased the likelihood of recurrence (OR:5.32, 95%CI:3.95-7.17, N=1903, GRADE: moderate and OR:4.39, 95%CI:3.43-5.60, N=2620, GRADE:moderate, respectively). This was also true when the data were adjusted for possible confounders (OR:7.93, 95%CI:5.70-11.05, N=1706, GRADE=moderate and OR:12.23, 95%CI:8.60-17.38, N=1706, GRADE=moderate, respectively). Grade III and IV disc-degeneration (Pfirmann-grading) was found to increase the odds of rLDH (OR:1.75, 95%CI:1.26-2.43, N=2760, GRADE: moderate). However, adjusted data showed this relationship was no longer true (OR:1.39, 95%CI:0.70-2.77, N=2190, GRADE=moderate). Data from univariate analyses showed that type-0 Modic-change, Grade I and II disc-degeneration and protrusion-type disc herniation decreased the odds of rLDH (OR:0.19, 95%CI:0.14-.0.25, N=1903, GRADE:moderate, OR:0.64, 95% CI:0.42-0.97, N=1098, GRADE:moderate and OR:0.47, 95%CI:0.32-0.69 M=2620, GRADE:moderate, respectively). However, no multivariate data were available to comment on the clinical significance of these findings. Level-of-herniation was not associated with recurrence in both primary and sensitivity-analyses. Multivariate data was only available for L4/5 level which showed no relationship with recurrence (OR:0.88, 95%CI:0.41-1.88, N=209, GRADE:low).

The results from univariate data showed that extrusion-type disc herniation increased the odds of rLDH (OR:1.73, 95%CI:1.20-2.48, N=914, GRADE:moderate) whilst protrusion decreased odds of rLDH (OR:0.57, 95%CI:0.38-0.85, N=914, GRADE:moderate). Type-3 Modic-change was also found to increase likelihood of rLDH (OR:7.33, 95%CI:1.52-35.47, N=197, GRADE:moderate). No relationship between rLDH and types 0, 1 or 2 Modic-change or Pfirmann-grading was found on sensitivity-analysis. Not enough data was available to synthesise any multivariate sensitivity-analysis findings from that which were available.

DISCUSSION

This systematic review is a comprehensive review of the most up-to-date evidence adding to the findings of a previous review in 2016[5]. The results of this review indicate that the likelihood of recurrence increases 4% by older age, almost twice by smoking and almost four-fold in people with diabetes. Radiologically, the likelihood of recurrence increases almost eight-fold in patients with type-2 Modic-changes and twelve-fold in those with extrusion-type herniations. Sensitivity-analysis of microdiscectomy patients alone indicated that older age is the only prognostic factor for rLDH. Meta-analysis of unadjusted data show that history of spine trauma, hypertension, high pre-operative pain scores, as well as Pfirmann-grade III/IV are also potentially prognostic.

The previous systematic review of 17 studies conducted by Huang et al. in 2016 also reported positive associations between rLDH, and smoking (OR:1.99, 95%CI:1.53–2.58) and a weaker association with diabetes (OR:1.19, 95%CI:1.06–1.32)[5]. Regarding herniation-type, opposing conclusions were drawn for protrusions between our meta-analysis (OR:0.47, 95%CI:0.32-0.69) and that by Huang et al (OR:1.79, 95%CI:1.15–2.79)[5]. Nevertheless, concordant results were found for BMI, gender or occupational-work[5]. Notably, their systematic review had several limitations. Most pertinently, there was little restriction to recurrence definition resulting in patients readmitted for complications of the primary operation e.g., epidural-haematoma or infection, included in the recurrence arm. In addition, the lack of distinction between unadjusted and adjusted data in their meta-analyses makes it difficult to draw clinically useful conclusions as the effect estimates do not uniformly account for confounders. Furthermore, a limited number of risk factors were considered, therefore a systematic review taking a more comprehensive approach was warranted.

More recent evidence also supports the relationship between older age, BMI and smoking, and rLDH with concordant findings reported by Ono et al. in 2022 (n=909)[43], Noh et al. in 2021 (n=6300)[44] and Fuentes et al. in 2021 (n=6901)[45]. Several recent studies also highlight the prognostic significance of the novel factors examined[46-49]. However, some heterogeneity in the literature exists surrounding these conclusions. For example, a post-hoc subgroup analysis of data from the Spine-Patients-Outcome-Research Trial (SPORT) of 810 patients found younger patients to be at greater risk of rLDH, with recurrence rate decreasing 4% per year (HR:0.96, 95%CI:0.94-0.99, p=0.002)[50]. This finding was also supported by another three older observational-studies[34-36]. Our results for radiological risk factors were also consistent with current literature. A large retrospective analysis of 1807 patients who underwent PELD between 2012-2015 constructed a multiple logistic regression prediction model for recurrence including type-2 Modic-changes (OR:7.93, 95%CI:5.70-11.05), Pfirmann-grading type-III (OR:4.92, 95%CI:3.56-6.80) and extrusion-type herniation (OR:12.23, 95%CI:8.60-17.38), with an overall predictive accuracy of 97.6%[23].

Several underlying mechanisms for the increased risk of recurrence in older people, smokers, and people with diabetes have been proposed. In older patients, degenerated discs exhibit microtears and annular collagen changes which limit the capacity of the external-annulus to reform post-operatively[37,38]. Similarly, smoking has a negative effect on the regenerative capacity of the nucleus pulposus after primary surgery[39,40]. In people with diabetes, an increased risk of rLDH is hypothesised to be due to lower sulfation rate resulting in fewer proteoglycans, which is the main constituent of the intervertebral-disc[41].

This systematic review and meta-analysis has several strengths. It is a comprehensive review of the most up-to-date literature including the wealth of recent studies assessing risk factors for rLDH (since previous systematic review in 2016[5]). The highest quality evidence for prognostic factor studies (case-control and cohort studies) were included[42]. Unadjusted and adjusted data were analysed separately, and a sensitivity-analysis carried out to examine the effect of operation type on the relationship between risk factor and rLDH[21]. All relevant clinical and radiological risk factors routinely assessed in clinical practice were included. In addition, several novel factors were examined, such as: pre-operative pain scores, history-of-spine trauma, occupational-driving, alcohol-consumption, hypertension, sport-activity and time-to-return-to-work as well degree of Modic-change, degree-of-disc-degeneration (Pfirmann-grading) and level-of-herniation which had not previously been pooled in a meta-analysis. Strict definitions of recurrence were adhered to, ensuring recurrence was due to reherniation of disc at the same level and not a complication of the primary operation[23,24,34].

Nevertheless, some limitations to the study are important to highlight. Most pertinently, the paucity of multivariate-data confined the interpretation of several factors (such as: pre-operative pain) and their potential clinical bearing on rLDH. Further, measurement of prognostic factors was poor due to inherent heterogeneity in defining and measuring factors such as: smoking-history, alcohol consumption, extent of spinal-trauma or intensity of occupational-labour. Finally, several data were imprecise with large confidence intervals (due to small sample sizes in some studies[26,27,29]) resulting in these data being statistically underpowered in the meta-analysis. This was reflected in the assessment of the strength of the evidence. Therefore, future studies should aim to clearly describe their prognostic factor definitions for methodological reliability. In addition, authors should include a multivariate analysis adjusting for common confounders, to ensure the clinical bearing of each individual variable on risk of recurrence can be deduced.

Clinicians should encourage patients with LBP due to LDH to stop smoking and ensure those with diabetes engage with regular follow-up. Further, public-awareness strategies should highlight the vital role smoking cessation plays in improving prognosis for patients with LDH. Surgeons considering operative management of patients with LDH should conduct a thorough clinical and radiological assessment, paying particular attention to age; diabetes; and smoking status as well as herniation-type and Modic-change to identify patients with higher recurrence risk. Based on the results of this meta-analysis, further predictive modelling research should be conducted to help implement these findings into clinical practice.

CONCLUSION

Older patients, smokers, patients with diabetes, those with type-2 Modic-changes or disc extrusion are more likely to have rLDH. No relationship between rLDH and sex, BMI, occupational labour/driving, alcohol-consumption, Pfirmann-grade, or herniation-level was found. Higher quality studies with robust adjustment of confounders are required to determine the clinical bearing of all other potential risk factors for rLDH.

Funding: AA received the "Wolfson Foundation Intercalated Degree Research Fellowship" from the Royal College of Physicians, England.

Conflict of Interest: The authors have no competing interests to declare that are relevant to the content of this article.

Ethical Approval: None required.

Registration: Review protocol was written up but not registered a priori.

Disclosures: None.

REFERENCES

1. Versusarthritis.org. 2021. Available at: https://www.versusarthritis.org/media/13183/portsmouth-back-pain.pdf
2. Nice.org.uk. 2022. Available from: https://www.nice.org.uk/guidance/ng59
3. Alshehri A, Alshehri T, Alyali S, et al. Awareness of disc herniation among general population in Aseer province, Saudi Arabia. *J Family Med Prim Care* 2019;8:1159-1163.
4. Swartz K, Trost G. Recurrent lumbar disc herniation. *Neurosurg Focus* 2003;15(3):E10.
5. Huang W, Han Z, Liu J, et al. Risk Factors for Recurrent Lumbar Disc Herniation: A Systematic Review and Meta-Analysis. *Medicine (Baltimore)* 2016;95(2):e2378.
6. Giannina L, Ambrossi G, Matthew J, et al. RECURRENT LUMBAR DISC HERNIATION AFTER SINGLE-LEVEL LUMBAR DISCECTOMY: INCIDENCE AND HEALTH CARE COST ANALYSIS, *Neurosurgery* 2009;65(4):574-478.
7. Yadav Y, Parihar V, Namdev H. Endoscopic interlaminar management of lumbar disc disease. *Journal of Neurological Surgery* 2013;74:77-81.
8. Gibson J, Waddell G. Surgical interventions for lumbar disc prolapse: updated Cochrane Review. *Spine (Phila Pa 1976).* 2007;32(16):1735-47.
9. Shin B. Risk factors for recurrent lumbar disc herniations. *Asian Spine J.* 2014;8(2):211-215.

10. Ann H, Silveri C, Simpson J. Comparison of smoking habits between patients with surgically confirmed herniated lumbar and cervical disc disease and controls. *J Spinal Disord.* 1984;7:369–373.
11. Robinson D, Mirovsky Y, Halperin N, et al. Changes in proteoglycans of intervertebral disc in diabetic patients. A possible cause of increased back pain. *Spine (Phila Pa 1976)* 1998;23:849–856.
12. Meredith D, Huang R, Nguyen J, et al. Obesity increases the risk of recurrent herniated nucleus pulposus after lumbar microdiscectomy. *Spine J*. 2010;10:575–580.
13. Kara B, Tulum Z, Acar U. Functional results and the risk factors of reoperations after lumbar disc surgery. *Eur Spine J*. 2005;14:43–48.
14. Rihn J, Kurd M, Hilibrand A. The influence of obesity on the outcome of treatment of lumbar disc herniation: analysis of the Spine Patient Outcomes Research Trial (SPORT*). J Bone Joint Surg Am*. 2013;95:1–8.
15. Quah C, Sye G, Swamy G, et al. Obesity and recurrent intervertebral disc prolapse after lumbar microdiscectomy. *Ann R Coll Surg Engl.* 2014;96:140–143.
16. Moher D, Liberati A, Tetzlaff J, et al. Reprint—Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *Physical Therapy*. 2009;89:873-880.
17. Tools | Cochrane Prognosis [Internet]. Methods.cochrane.org. 2022. Available from: https://methods.cochrane.org/prognosis/tools
18. Recommendations on testing for funnel plot asymmetry. Handbook-5-1.cochrane.org. 2022. Available from: https://handbook-5-1.cochrane.org/chapter_10/10_4_3_1_recommendations_on_testing_for_funnel_plot_asymmetry.htm
19. Schüneman H, Oxman A. G.E. Vist Cochrane handbook for systematic reviews of interventions version 5.1.0. Updated March, 2011 https://training.cochrane.org/cohcrane-handbook-systematic-reviews-interventions
20. RevMan. Training.cochrane.org. 2022. Available from: https://training.cochrane.org/online-learning/core-software/revman
21. Yorimitsu E, Chiba K, Toyama Y, et al. Long-term outcomes of standard discectomy for lumbar disc herniation: a follow-up study of more than 10 years. *Spine (Phila Pa 1976)* 2001 15;26(6):652-7.
22. Paracino R, Mancini F, Lattanzi S et al. Risk Factors and Post-Operative Predictors for Recurrent Lumbar Disc Herniation: A Long-term Follow-up Study. *J Appl. Health Sci.* 2021;7(2):121-126.
23. Li Y, Wang B, Li H et al. Adjuvant surgical decision-making system for lumbar intervertebral disc herniation after percutaneous endoscopic lumber discectomy: a retrospective nonlinear multiple logistic regression prediction model based on a large sample. *Spine J.* 2021;21(12):2035-2048.
24. Yu C, Zhan X, Liu C, et al. Risk Factors for Recurrent L5-S1 Disc Herniation After Percutaneous Endoscopic Transforaminal Discectomy: A Retrospective Study. *Med Sci Monit.* 2020;26:e919888.
25. Dobran M, Nasi D, Paracino R, et al. Analysis of risk factors and postoperative predictors for recurrent lumbar disc herniation. *Surg Neurol Int.* 2019;10:36.
26. Kim Y, Yang J, Kim T. Risk Factors for Recurrence of Disc Herniation After Single-Level Lumbar Discectomy. *Asian J Pain.* 2021;7:1.
27. Oh JT, Park KS, Jung SS, Chung SY, Kim SM, Park MS, Kim HK. Surgical results and risk factors for recurrence of lumbar disc herniation. Korean J Spine. 2012 Sep;9(3):170-5.
28. Li Z, Yang H, Liu M, Lu M, Chu J, Hou S, Hou T. Clinical Characteristics and Risk Factors of Recurrent Lumbar Disk Herniation: A Retrospective Analysis of Three Hundred Twenty-One Cases. Spine (Phila Pa 1976). 2018 Nov 1;43(21):1463-1469.
29. Yaman ME, Kazancı A, Yaman ND, Baş F, Ayberk G. Factors that influence recurrent lumbar disc herniation. Hong Kong Med J. 2017 Jun;23(3):258-63.
30. Yurac R, Zamorano JJ, Lira F, Valiente D, Ballesteros V, Urzúa A. Risk factors for the need of surgical treatment of a first recurrent lumbar disc herniation. Eur Spine J. 2016 May;25(5):1403-1408.
31. Kim KT, Lee DH, Cho DC, Sung JK, Kim YB. Preoperative Risk Factors for Recurrent Lumbar Disk Herniation in L5-S1. J Spinal Disord Tech. 2015 Dec;28(10):E571-7. Erratum in: Clin Spine Surg. 2018 Jul;31(6):268.
32. Miwa S, Yokogawa A, Kobayashi T, Nishimura T, Igarashi K, Inatani H, Tsuchiya H. Risk factors of recurrent lumbar disk herniation: a single center study and review of the literature. J Spinal Disord Tech. 2015 Jun;28(5):E265-9.
33. Kim KT, Park SW, Kim YB. Disc height and segmental motion as risk factors for recurrent lumbar disc herniation. Spine (Phila Pa 1976). 2009 Nov 15;34(24):2674-8.
34. Suk K, Lee H, Moon S, et al. Recurrent lumbar disc herniation: results of operative management. *Spine (Phila Pa 1976)* 2001;26:672–276
35. Cinotti G. Ipsilateral recurrent lumbar disc herniation. A prospective, controlled study. *J Bone Joint Surg Br*. 1998;80(5):825–32
36. Keskimaki I. Reoperations after lumbar disc surgery: a population-based study of regional and interspecialty variations. *Spine (Phila Pa 1976)* 2000;25(12):1500–8.
37. Osti O, Vernon-Roberts B, Fraser R. Volvo Award in experimental studies. Anulus tears and intervertebral disc degeneration. An experimental study using an animal model. *Spine* 1990;15(8):762–767.
38. Gruber H, Hanley E. Jr. Observations on morphologic changes in the aging and degenerating human disc: secondary collagen alterations. *BMC Musculoskelet Disord.* 2002;3:9.
39. Ann H, Silveri C, Simpson J, et al. Comparison of smoking habits between patients with surgically confirmed herniated lumbar and cervical disc disease and controls. *J Spinal Disord.* 1984;7:369–373.
40. Nakahashi M, Esumi M, Tokuhashi Y. Detection of apoptosis and matrical degeneration within the intervertebral discs of rats due to passive cigarette smoking. *PLoS One. 2019*;14(8):e0218298.
41. Robinson D, Mirovsky Y, Halperin N, et al. Changes in proteoglycans of intervertebral disc in diabetic patients. A possible cause of increased back pain. *Spine (Phila Pa 1976).* 1998;23:849–856.
42. Foroutan F, Guyatt G, Zuk V, Vandvik PO, Alba AC, Mustafa R, Vernooij R, Arevalo-Rodriguez I, Munn Z, Roshanov P, Riley R, Schandelmaier S, Kuijpers T, Siemieniuk R, Canelo-Aybar C, Schunemann H, Iorio A. GRADE Guidelines 28: Use of GRADE for the assessment of evidence about prognostic factors: rating certainty in identification of groups of patients with different absolute risks. J Clin Epidemiol. 2020 May;121:62-70. doi: 10.1016/j.jclinepi.2019.12.023. Epub 2020 Jan 23. PMID: 31982539.
43. Ono K, Ohmori K, Yoneyama R, et al. Risk Factors and Surgical Management of Recurrent Herniation after Full-Endoscopic Lumbar Discectomy Using Interlaminar Approach. *J Clin Med*. 2022;11(3):748.
44. Noh S, Cho P, Kim K, et al. Risk factors for reoperation after lumbar spine surgery in a 10-year Korean national health insurance service health examinee cohort. *Sci Rep.* 2022;12(1):4606.
45. Fuentes A, Patil S, Chiu R, et al. Revision Discectomy with or without Fusion for the Treatment of Recurrent Lumbar Disc Herniation: A Nationwide Analysis of Risk Profiles and Short-Term Outcomes. *World Neurosurg.* 2021;148:e346-e355.
46. Fotakopoulos G, Makris D, Kotlia P, et al. Recurrence Is Associated With Body Mass Index in Patients Undergoing a

Single-Level Lumbar Disc Herniation Surgery. *J Clin Med Res.* 2018;10(6):486-492.
47. Kong M, Xu D, Gao C, et al. Risk Factors for Recurrent L4-5 Disc Herniation After Percutaneous Endoscopic Transforaminal Discectomy: A Retrospective Analysis of 654 Cases. *Risk Manag Healthc Policy.* 2020;18(13):3051-3065.
48. Shi H, Zhu L, Jiang Z, et al. Radiological risk factors for recurrent lumbar disc herniation after percutaneous transforaminal endoscopic discectomy: a retrospective matched case-control study. *Eur Spine J.* 2021;30(4):886-892. doi: 10.1007/s00586-020-06674-3.
49. Hong X, Liu L, Bao J, et al. Characterization and risk factor analysis for reoperation after microendoscopic diskectomy. *Orthopedics* 2015;38(6):e490–e496.
50. Abdu W, Pearson A, Zhao W, et al. Reoperation for Recurrent Intervertebral Disc Herniation in the Spine Patient Outcomes Research Trial: Analysis of Rate, Risk Factors, and Outcome. *Spine (Phila Pa 1976)* 2017;42(14):1106-1114.
51. Williams RW. Microlumbar discectomy: a conservative surgical approach to the virgin herniated lumbar disc. Spine (Phila Pa 1976). 1978 Jun;3(2):175-82.