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LITERATURE REVIEW

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Association of Annular Defect Width After Lumbar Discectomy With Risk of Symptom Recurrence and Reoperation

Systematic Review and Meta-analysis of Comparative Studies

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Study Design. Systematic review and meta-analysis of comparative studies.

Objective. To characterize the association of annular defect width after lumbar discectomy with the risk of symptom recurrence and reoperation.

Summary of Background Data. Large annular defect width after lumbar discectomy has been reported to increase risk of symptom recurrence. However, this association has not been evaluated in a systematic manner.

Methods. A systematic literature search of MEDLINE and EMBASE was performed to identify comparative studies of large *versus* small annular defects following lumbar discectomy that reported symptom recurrence or reoperation rates. Main outcomes were reported with pooled odds ratios (OR) and 95% confidence intervals (CIs). Sensitivity analyses were performed to assess the robustness of the meta-analysis findings.

Results. After screening 696 records, we included data from 7 comparative studies involving 1653 lumbar discectomy patients, of whom 499 (30%) had large annular defects and 1154 (70%) had small annular defects. Methodological quality of studies was good overall. The median follow-up period was 2.9 years. The risk of symptom recurrence (OR = 2.5, 95% CI = 1.3–4.5, $P = 0.004$) and reoperation (OR = 2.3, 95% CI = 1.5–3.7, $P < 0.001$) was higher in patients with large *versus* small annular defects. Publication bias was not evident. The associations between annular defect width and risk of symptom recurrence and reoperation remained statistically significant in all sensitivity analyses.

Conclusion. Annular defect width after lumbar discectomy is an under-reported modifier of patient outcome. Risk for symptom recurrence and reoperation is higher in patients with large *versus* small annular defects following lumbar discectomy.

Key words: annulus, comparative studies, disc herniation, discectomy, fragment type, lumbar, meta-analysis, microdiscectomy, reherniation, systematic review.

Level of Evidence: 2

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Lumbar discectomy is performed on nearly 500,000 patients per year in the United States.[1] While this procedure is successful in most patients, symptom recurrence related to reherniation is reported in 7% to 18% of patients.[2–4] Recurrent symptomatic herniation is associated with poor clinical outcome and often requires a technically demanding reoperation.[5] Commonly reported risk factors for recurrence include disc degeneration,[6] age,[7] sex,[6] and body mass index.[8] However, the influence of surgery-related factors on recurrence risk is unclear. Carragee *et al*[9] identified postsurgical annular defect size as a risk factor for symptom recurrence. In this study, patients with large *versus* small annular defects had higher rates of symptom recurrence and reoperation. However, the association of postsurgical annular defect width with symptom recurrence risk has not been evaluated in a systematic manner. The purpose of this systematic review and meta-analysis was to characterize the association of annular defect width after lumbar discectomy with the risk of symptom recurrence and reoperation.

MATERIALS AND METHODS

Study Selection

This study was performed according to the guidelines specified in the Preferred Reporting Items for Systematic Reviews

TABLE 1. MEDLINE Search Strategy

Anatomic search terms
1. Lumbar
Therapeutic search terms
2. Discectomy
3. Fragmentectomy
4. Fragment excision
5. Herniotomy
6. Microdiscectomy
7. Nucleotomy
8. Sequestrectomy
9. Subtotal
Annular defect search terms
10. Anular (annular) competence
11. Anular (annular) defect
12. Carragee
13. Fragment-contained
14. Fragment-defect
15. Fragment-fissure
16. Fragment type
17. No fragment-contained
18. Penfield probe
Combination search terms
19. or/1
20. or/2–9
21. or/10–18
22. and/19–21

and Meta-analyses Statement.[10] Two researchers independently searched MEDLINE and EMBASE for studies of lumbar discectomy that reported postsurgical annular defect width using a combination of anatomic-, therapeutic-, and annular defect-specific keywords. The details of the MEDLINE search strategy are listed in Table 1. The syntax for EMBASE was similar, but adapted as necessary. We also reviewed all studies that cited the study of Carragee *et al.*[9] Finally, searches were conducted using the Directory of Open Access Journals, Google Scholar, and the reference lists of included papers and relevant meta-analyses. No date limits were applied to the searches. The final search was performed on June 30, 2017. Main inclusion criteria included prospective or retrospective studies of single-level lumbar discectomy without use of additional stabilization or annular closure devices; primary diagnosis of lumbar disc herniation; mean follow-up period at least 1 year; at least one main outcome compared by post-surgical annular defect width; and publication in an English-language journal. When multiple studies included overlapping series of patients, only the study with the largest sample size was included. Study selection discrepancies between the two researchers were resolved by discussion and consensus.

Data Extraction

An initial database was developed, pilot-tested, and refined to ensure consistency with outcomes reported in the literature. Data were independently extracted from eligible peer-reviewed articles by two researchers. Data extraction discrepancies were resolved by discussion and consensus. The types of data recorded in the standardized data extraction forms included general manuscript information, study design, patient characteristics, study characteristics, study quality, and main outcomes. For articles in which data were unclear or not reported, we attempted to contact the corresponding author of the study in question.

Definitions and Outcomes

Studies were selected for inclusion contingent on reporting annular defect width measured in the medial-lateral direction following lumbar discectomy. Postsurgical annular defect width was typically assessed with a number-1 Penfield probe (6 mm). Fragment-defect herniation (Carragee type 2), no fragment-contained herniation (Carragee type 4), or annular defect $\geq$6 mm width were classified as large annular defects. Fragment fissure herniation (Carragee type 1), fragment-contained herniation (Carragee type 3), or annular defect <6 mm width were classified as small annular defects. One study used a threshold of 5 mm for defining large annular defects and corresponding herniation types.[11] Although Carragee type 4 herniation was originally described as "no defect,"[9] surgical treatment involves extensive annulotomy, which ultimately results in a large postsurgical annular defect. Main outcomes of this meta-analysis were symptom recurrence and reoperation for recurrence following lumbar discectomy. The definitions used to classify large *versus* small postsurgical annular defects and terminology used to characterize symptom recurrence and reoperation for recurrence were generally consistent among studies (Table 2).

Methodological Study Quality Assessment

Study quality was assessed using the methodological index for nonrandomized studies.[12] When applied to nonrandomized comparative studies, this instrument consists of 12 items, each scored as 0 if the item is not reported, 1 if the item is inadequately reported, and 2 if the item is adequately reported. The scores for each item were summed to yield a global score ranging from 0 to 24 where higher scores represented higher methodological quality.

Data Analysis

For each main outcome, the pooled estimate and 95% confidence interval (CI) were calculated. The risk of a given outcome in large *versus* small postsurgical annular defects was reported with the odds ratio (OR), where OR greater than 1 indicates higher risk in large defects. Forest plots were used to illustrate individual study findings and pooled meta-analysis results. We used the I^2 statistic to estimate heterogeneity of outcomes among studies.[13] Significant heterogeneity was identified by a Cochran Q test $P < 0.1$ or $I^2 > 50\%$. When significant heterogeneity existed, a DerSimonian and Laird random effects model was used; otherwise, a Mantel-Haenszel fixed effects model was used.[14] Potential for publication bias was visually examined with funnel plots and evaluated with Egger regression

TABLE 2. Methodological Quality and Risk of Bias Among Studies

Study	Global MINORS Score	Key Definitions		
		Large *Versus* Small Annular Defect*	Symptom Recurrence	Reoperation for Recurrence
Bono *et al*, 2017[15]	18/24	Carragee type 2 or 4 *vs.* type 1 or 3	Described as "symptoms of reherniation"; no definition provided and imaging confirmation not specified	Reoperation for reherniation
Boyaci, 2016[17]	17/24	Carragee type 2 *vs.* type 1 or 3†	MR confirmed reherniation in patients with self-reported symptoms	Reoperation for MR confirmed symptomatic reherniation
Carragee *et al*, 2003[9]	18/24	Carragee type 2 or 4 *vs.* type 1 or 3	MR confirmed reherniation in patients with self-reported symptoms	Reoperation for MR confirmed symptomatic reherniation
Kim *et al*, 2015[6]	14/24	Annular defect width ≥6 mm *vs.* <6 mm	Described as "recurrent lumbar disc herniation"; no definition provided and imaging confirmation not specified	Not reported
McGirt *et al*, 2009[4]	18/24	Annular defect width ≥6 mm *vs.* <6 mm	MR and CT confirmed reherniation in patients with self-reported symptoms	Reoperation for MR and CT confirmed symptomatic reherniation
Wera *et al*, 2008[18]	12/24	Carragee type 2 or 4 *vs.* type 1 or 3	Not reported	Reoperation for reherniation
Zhou *et al*, 2016[19]	14/24	Annular defect width ≥6 *vs.* <6 mm	Described as "recurrent lumbar disc herniation"; no definition provided and imaging confirmation not specified	Not reported

*Annular defect width ≥6 mm for Carragee type 2 or 4 herniation and <6 mm for Carragee type 1 or 3 herniation, unless otherwise specified.[9]
†Carragee type 2 herniation defined as ≥5 mm width.
CT indicates computed tomography; MINORS, methodological index for nonrandomized studies; MR, magnetic resonance.

test.[15] In studies reporting symptom recurrence but not reoperation, or vice-versa, we imputed missing values by assuming that 78% of patients with symptom recurrence underwent reoperation in each group based on the meta-analysis findings of Ran *et al*.[5] We tested the robustness of this assumption in sensitivity analyses. A one-study removed sensitivity analysis was also performed, which recalculated the meta-analysis after removing one study at a time to explore the influence of individual studies on main outcomes. *Post hoc* analyses were performed to compare main outcomes among subgroups. All tests were two-sided; an alpha level of 0.05 was chosen for significance. Statistical analyses were performed using Comprehensive Meta-analysis version 3.3 (Biostat, Englewood, NJ).

RESULTS

Our initial database search retrieved 687 titles and abstracts; hand searching relevant bibliographies identified 9 additional records. After screening records for inclusion criteria, 98 full-text articles were reviewed for eligibility. The primary reason for study exclusion was lack of annular defect width reporting (64 studies). We contacted corresponding authors of three studies[4,16,17] where postsurgical annular defect width data were collected, but main outcome data were not reported by large *versus* small annular defect width. After a maximum of two requests per author, two authors responded and provided additional outcome data[4,16]; the remaining study was excluded.[17] Ultimately, we included 7 studies[4,6,9,11,16,18,19] involving 1653 lumbar discectomy patients, of whom 499 (30%) had large postsurgical annular defects and 1154 (70%) had small postsurgical annular defects. A flow diagram of study identification and selection is shown in Figure 1.

Methodological quality of studies was good overall; the median methodological index for nonrandomized studies global score was 17 (Table 2). Study and patient characteristics are reported in Table 3. Among seven studies (four prospective), the median patient age was 45 years, and 60% of patients were men. Surgical technique consisted of sequestrectomy only in three studies, subtotal discectomy only in two studies, and mixed techniques in two studies. The median follow-up period was 2.9 years (range: 1.2–8.1 yr).

In the base case analysis for recurrence, seven studies provided data (six as reported, one imputed from reoperation rates) for a random effects meta-analysis. The risk of

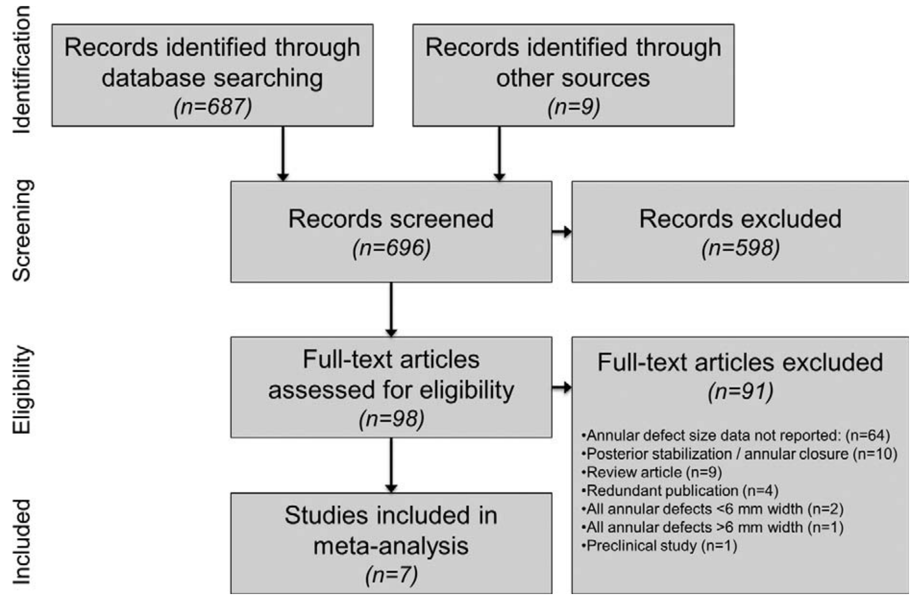

Figure 1. PRISMA flow diagram of study selection process.

symptom recurrence was higher in large *versus* small postsurgical annular defects (OR = 2.5, 95% CI = 1.3–4.5, $P = 0.004$) (Figure 2). Moderate heterogeneity was observed among studies ($I^2 = 51\%$, $P = 0.05$) and publication bias was not evident (Egger test $P = 0.88$; Figure 3). In the base case analysis for reoperation, seven studies provided data (five as reported, two imputed from recurrence rates) for a fixed effects meta-analysis. The risk of reoperation was higher in large *versus* small postsurgical annular defects (OR = 2.3, 95% CI = 1.5–3.7, $P < 0.001$) (Figure 4). Low heterogeneity was observed among studies ($I^2 = 20\%$, $P = 0.28$) and publication bias was not evident (Egger test $P = 0.96$; Figure 5).

The associations between post-surgical annular defect width and risk of symptom recurrence and reoperation were robust to various assumptions as comparisons remained statistically significant in all sensitivity analyses (Table 4). In subgroup analysis, no variable significantly modified these associations; however, this analysis had limited ability to detect such differences due to the small number of studies within each subgroup (Table 5).

TABLE 3. Study and Patient Characteristics

Study	Study Design	No. Patients by Defect Width (Large-Small)	Male Sex	Mean Age (yr)	Surgery Type	Treatment Period	Follow-up Duration (yr)
Bono *et al*, 2017[15]	P	41–59	56%	43	Sequestrectomy	2011–2013	1.2
Boyaci, 2016[17]	P	64–106	52%	46	Sequestrectomy (46%), subtotal discectomy (54%)	2006–2010	2.9
Carragee *et al*, 2003[9]	P	49–131	[67%]*	38	Sequestrectomy	[1989]–1999*	6.0
Kim *et al*, 2015[6]	R	61–406	60%	45	Sequestrectomy	2004–2010	4.3
McGirt *et al*, 2009[4]	P	52–16	67%	41	Sequestrectomy, subtotal discectomy†	2003–2006	2.1
Wera *et al*, 2008[18]	R	146–113	[71%]*	50	Subtotal discectomy	1980–2005	8.1
Zhou *et al*, 2016[19]	R	86–323	59%	46	Subtotal discectomy	2013–2015	[2.0]*

*Bracketed value represents estimate.
†Distribution of surgical types not specified.
BMI indicates body mass index; P, prospective; R, retrospective.

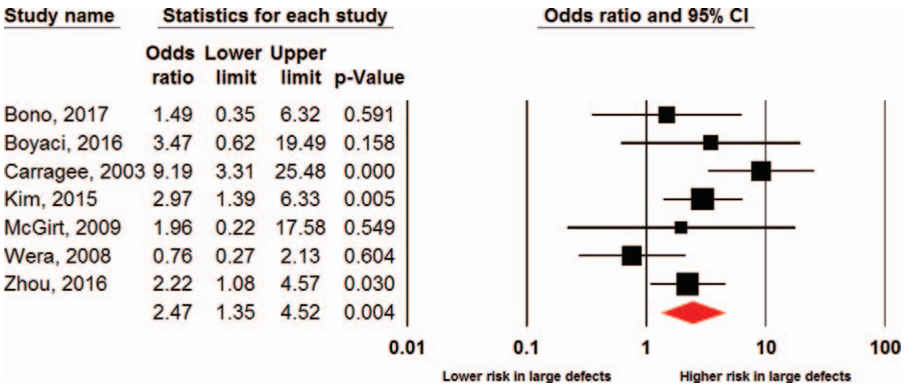

Figure 2. Meta-analysis of reherniation risk in large *versus* small annular defects after lumbar discectomy. The odds ratio and 95% confidence interval is plotted for each study. The pooled odds ratio (diamond apex) and 95% confidence interval (diamond width) is calculated using a random effects model. Pooled odds ratio of more than 1 suggests higher risk of reherniation in large annular defects. Pooled odds ratio of less than 1 suggests lower risk of reherniation in large annular defects. Pooled odds ratio = 2.5, $P = 0.004$. Heterogeneity: $I^2 = 51\%$, $P = 0.05$. CI indicates confidence interval.

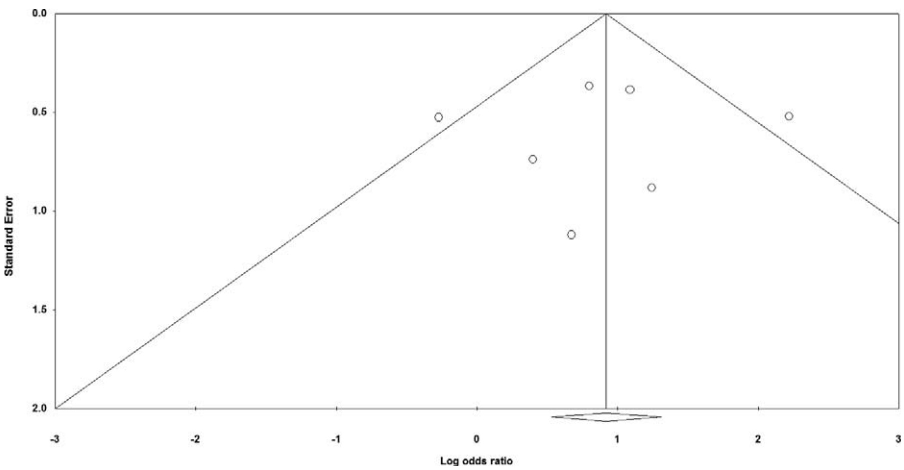

Figure 3. Funnel plot of standard error by log odds ratio for reherniation risk in large *versus* small annular defects after lumbar discectomy. The plot is symmetric about the mean effect, which indicates absence of substantial publication bias. Egger regression P value for publication bias = 0.88.

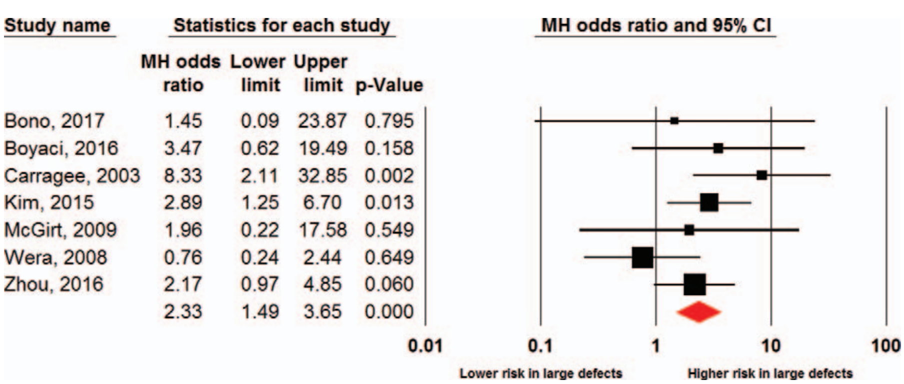

Figure 4. Meta-analysis of reoperation risk in large *versus* small annular defects after lumbar discectomy. The odds ratio and 95% confidence interval is plotted for each study. The pooled odds ratio (diamond apex) and 95% confidence interval (diamond width) is calculated using a fixed effects model. Pooled odds ratio of more than 1 suggests higher risk of reoperation in large annular defects. Pooled odds ratio of less than 1 suggests lower risk of reoperation in large annular defects. Pooled odds ratio = 2.3, $P < 0.001$. Heterogeneity: $I^2 = 20\%$, $P = 0.28$. CI indicates confidence interval.

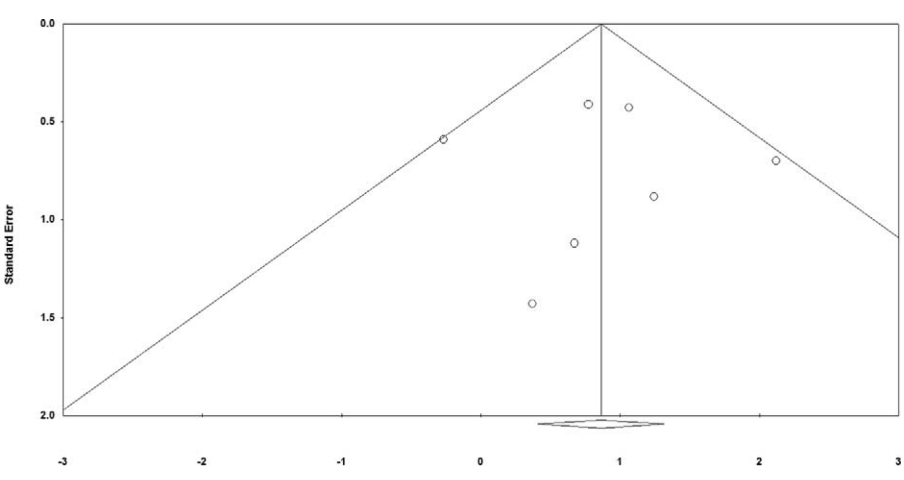

Figure 5. Funnel plot of standard error by log odds ratio for reoperation risk in large *versus* small annular defects after lumbar discectomy. The plot is symmetric about the mean effect, which indicates absence of substantial publication bias. Egger regression P value for publication bias = 0.96.

TABLE 4. Sensitivity Analyses of Symptom Recurrence and Reoperation Risk in Patients With Large *Versus* Small Annular Defects after Lumbar Discectomy

		Symptom Recurrence				Reoperation			
Model	Assumptions	No. Studies	Odds Ratio	95% CI	*P*	No. Studies	Odds Ratio	95% CI	*P*
Base case model	Realistic scenario imputation*	7	2.5	1.3, 4.5	0.004	7	2.3	1.5, 3.7	<0.001
Sensitivity analyses	As reported†	6	3.1	1.9, 5.1	<0.001	5	2.2	1.1, 4.4	0.02
	One study removed analysis, minimum*,‡	6	2.3	1.1, 5.1	0.03	6	2.0	1.2, 3.2	0.007
	One study removed analysis, maximum*,‡	6	3.1	1.9, 5.1	<0.001	6	2.9	1.8, 4.8	<0.001
	Alternative Carragee herniation type assumption*,§	7	2.4	1.6, 3.6	<0.001	7	2.5	1.6, 3.9	<0.001

In studies reporting reoperation but not recurrence or vice versa, we imputed values by assuming 78% of patients with recurrence underwent reoperation in each group based on the meta-analysis of Ran et al.[5]

†*Data reported with no imputation of missing data.*

‡*Data reported as the combination of studies resulting in the minimum or maximum P value after removing one study at a time from the meta-analysis.*

§*Large defect defined as annular defect width ≥6 mm or Carragee type 2 herniation. Small defect defined as annular defect width <6 mm or Carragee type 1, 3, or 4 herniation.*

CI indicates confidence interval.

DISCUSSION

This is the first systematic review and meta-analysis to examine the relationship of annular defect width following lumbar discectomy with risk of symptom recurrence and reoperation. We have shown that patients with large annular defects after lumbar discectomy have higher risk for symptom recurrence and reoperation compared to those with small annular defects.

TABLE 5. *Post hoc* Subgroup Analyses of Symptom Recurrence and Reoperation Risk in Patients With Large *versus* Small Annular Defects After Lumbar Discectomy

	Symptom Recurrence					Reoperation				
Variable	No. Studies	OR	95% CI	Within-Group *P* Value	Between-Group *P* Value	No. Studies	OR	95% CI	Within-Group *P* Value	Between-Group *P* Value
MINORS global score*					0.25					0.16
≥17 (Higher study quality)	4	3.7	1.4, 9.6	0.007		4	4.1	1.6, 10.2	0.003	
<17 (Lower study quality)	3	1.9	0.9, 3.8	0.09		3	1.9	1.1, 3.2	0.02	
Surgery type					0.50					0.19
Sequestrectomy	4	3.0	1.1, 8.0	0.03		4	3.1	1.6, 5.9	<0.001	
Subtotal discectomy	3	1.8	0.6, 5.5	0.30		3	1.8	1.0, 3.4	0.06	
Age*					0.45					0.19
≥45 yr	4	2.0	1.1, 3.7	0.03		4	2.0	1.2, 3.3	0.008	
<45 yr	3	3.5	0.9, 12.9	0.06		3	4.3	1.5, 12.7	0.008	
Male sex*					0.67					0.93
≥60%	4	2.6	0.9, 7.8	0.08		4	2.4	1.3, 4.2	0.004	
<60%	3	2.2	1.2, 4.0	0.01		3	2.3	1.1, 4.6	0.02	
Median surgery year*					>0.99					0.68
2007–2014	4	2.5	1.5, 4.0	<0.001		4	2.5	1.5, 4.3	<0.001	
1993–2006	3	2.5	0.4, 14.7	0.33		3	2.1	0.9, 4.5	0.07	
Follow-up duration*					0.58					0.67
≥2.9 yr	4	2.9	1.0, 8.2	<0.05		4	2.5	1.4, 4.4	0.002	
<2.9 yr	3	2.0	1.1, 3.8	0.02		3	2.1	1.0, 4.3	0.05	

Subgroups defined as values above versus below the median.

CI indicates confidence interval; MINORS, methodological index for nonrandomized studies.

In 2003, Carragee *et al*[9] reported that the degree of annular competence after lumbar discectomy was associated with symptom recurrence and reoperation rates. Although this study has been widely cited, the influence of annular defect width after lumbar discectomy remains under-reported. In this meta-analysis, six of seven included studies reported higher risk of complications with larger postsurgical annular defects. However, the study of Wera *et al*[18] reported a nonsignificant lower complication risk in larger defects which they attributed to a subtotal discectomy technique. Sequestrectomy is consistently associated with less recurrent pain severity compared to subtotal discectomy; however, the influence of surgical technique on herniation recurrence rates is conflicting.[5,20] We attempted to explore the influence of surgical technique on main outcomes within subgroup analysis. Although it is plausible that large postsurgical annular defects are most problematic in patients undergoing sequestrectomy given the considerable volume of intervertebral disc material that remains,[21] we could not confirm this in subgroup analysis due to insufficient power.

The finding that large postsurgical annular defects increase risk for symptom recurrence and reoperation has strong theoretical underpinnings.[22] A number of animal studies have reported that a compromised annulus fibrosis has limited intrinsic healing ability.[23–25] Collectively, these studies support the hypothesis that annular healing after discectomy occurs slowly and ultimately yields biomechanically inferior fibrous tissue with reduced capacity to accommodate tensile force. Thus, reherniation of disc material may occur under lower biomechanical stresses in patients with large postsurgical annular defects, which comprise approximately 30% of those treated with lumbar discectomy. The association of annular defect width with symptom recurrence and reoperation was not significantly influenced by factors such as surgery type, age, and sex in the current study.

The findings of this meta-analysis suggest that routine measurement of annular defect width after lumbar discectomy may assist in identifying patients at high risk of recurrence. The measurement technique is straightforward and interobserver reliability is high.[9] Classification typically involves comparing annular defect width to a number-1 Penfield probe (6 mm) after completion of the discectomy. Defects that are wider than the probe are classified as large defects. Intraoperative identification of annular competence may assist surgeons in stratifying patients based on recurrence risk, which may warrant more detailed postsurgical discussions.

This meta-analysis was associated with several strengths including a comprehensive literature search with exploration of potential sources of bias and heterogeneity in outcomes reporting. This meta-analysis also has certain limitations that may influence interpretation. First, postsurgical annular defect width and defect type were uncommonly reported within the lumbar discectomy literature. Whether this under-reporting influences the conclusions of this meta-analysis is unclear. Second, given the limited number of comparative studies included in this review, we were unable to evaluate the influence of postsurgical annular defect width within a multivariate model of other known risk factors for recurrence. The only study that evaluated annular defect width within a multivariate framework reported that male sex and large annular defect were the strongest predictors of symptom recurrence.[6] The relative importance of annular defect width compared to other risk factors for recurrence should be explored in future studies. Finally, there was low power to detect significant subgroup interactions and publication bias given the small number of included studies. Variables such as surgery type, techniques for discectomy/annulotomy, study design, and patient age may indeed influence the relationship of annular defect width with risk of symptom recurrence and reoperation. Therefore, subgroup interaction and publication bias data should be interpreted cautiously and considered exploratory only.

CONCLUSION

Annular defect width after lumbar discectomy is an under-reported modifier of patient outcome. Risk for symptom recurrence and reoperation is higher in patients with large *versus* small annular defects following lumbar discectomy.

➢ Key Points

- ❑ Annular defect width after lumbar discectomy has been reported to increase risk of symptom recurrence, but has not been evaluated in a systematic manner.
- ❑ A systematic review and meta-analysis of seven comparative studies (1653 patients) was performed to compare risks of symptom recurrence and reoperation with large *versus* small annular defects after lumbar discectomy.
- ❑ The risks of symptom recurrence (OR = 2.5, $P = 0.004$) and reoperation (OR = 2.3, $P < 0.001$) were higher in patients with large *versus* small annular defects after lumbar discectomy.

Acknowledgments

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