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Review Article

The rate of fusion for stand-alone anterior lumbar interbody fusion: a systematic review

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Abstract

BACKGROUND: Anterior lumbar interbody fusion (ALIF) has been used for treatment of a variety of spinal conditions including degenerative disc disorders and low-grade spondylolisthesis. Expected fusion rate of stand-alone ALIF constructs is currently unclear. The aim of this study was to examine the fusion rate for ALIF without supplemental posterior fusion or instrumentation (stand-alone ALIF).

METHODS: We queried the MEDLINE, COCHRANE, and EMBASE databases for all literature related to spine fusion rates using a stand-alone ALIF procedure with a publication cutoff date of July 19, 2018. Supplementary combinations of search terms included spine, fusion, fixation, rate (s), and arthrodesis. ALIF surgery was considered stand-alone when not paired with supplemental posterior fusion or posterior spinal instrumentation. Nonhuman and non-English publications were excluded. Cohort fusion rate differences were calculated using Student *t* test with significance assigned if p value was less than .05.

RESULTS: Title and abstract level review required assessing 840 unique publications. Across the 55 studies that met the inclusion criteria of this systematic review, 5,517 patients and 6,303 vertebral levels were fused. The overall weighted average patient fusion rate following stand-alone ALIF was 88.2% (range: 16.6%−100%). In the 31 studies with at least 50 subjects, the weighted average fusion rate following stand-alone ALIF was 88.6% (range: 57.5% −99.0%). Use of anterior fixation plate devices yielded a fusion rate of 94.2%. Newer zero-profile interbody implants had a fusion rate of 89.2%. Fusion rates were lower in studies with 50% or more subjects having positive smoking and worker's compensation status, however these results were found to be statistically insignificant (p>.05). Fusion rate for subjects in the eight rhBMP-2 study groups was 94.4% (n=889) compared with 84.8% (n=3,102) in 38 study groups without rhBMP-2 used.

FDA device/drug status: Not applicable.

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CONCLUSIONS: Based on the available data, stand-alone ALIF procedures yield high fusion rates overall. Fusion failure and pseudoarthrosis rates are higher in study populations involving a high percentage of smokers or positive workers compensation status. Allograft utilization does not significantly improve fusion rate when compared with autograft in stand-alone ALIF constructs.

Keywords: Anterior lumbar interbody fusion; Cage; Fusion rate; rhBMP-2; Stand-alone; Systematic review

Introduction

Anterior lumbar interbody fusion (ALIF) was first described in the early 1930s by Capener and Burns [1,2]. This procedure is indicated for treating conditions including, but not limited to, spondylosis, spondylolisthesis, and degenerative disc disorders [3,4]. The shift towards minimally invasive surgery techniques and vascular surgery access assistance has led to significantly decreased rates of complications and improved clinical and surgical outcomes which has established ALIF as a common approach for spinal interbody fusion today [5].

Pedicle screw fixation with or without posterior spinal fusion is often used by surgeons to stabilize fused levels following ALIF procedures [6]. ALIF surgery is, in general, considered stand-alone when not paired with pedicle screw fixation or supplemental posterior fusion. Biomechanical studies examining ALIF with supplementary posterior spinal fusion compared with stand-alone ALIF have indicated that there is greater reduction in facet load on the operated level and reduced stress on adjacent levels in stand-alone ALIF surgical approach which leads to load sharing comparable to an intact spine [7−9]. Other benefits of a stand-alone ALIF procedure include not disturbing the posterior paraspinal musculature and associated superficial tissues, reduction of disc herniation risk at the operated level, as well as efficient restoration of disc interspace height, and decompression of the associated posterolateral intervertebral foramens [10].

Currently, there is no single systematic review that specifically addresses two points: (1) the mean fusion rate of the stand-alone ALIF procedure and (2) the association of stand-alone ALIF fusion rate with smoking status, workers compensation status, and BMP utilization. This systematic review was designed to identify stand-alone fusion rates relative to these areas of interest.

Materials and methods

A systematic query was developed to search MEDLINE, COCHRANE, and EMBASE to identify published studies that reported stand-alone ALIF procedure fusion rates. The cutoff date for studies considered for inclusion was July 19, 2018. This search was conducted using supplementary combinations of other search terms including: “anterior interbody lumbar fusion,” “fusion rate,” “fusion rates,” “fixation rate,” “fixation rates,” “rate of arthrodesis,” “arthrodesis rate,” “spinal fusion,” “fusion,” and “fixation.” Nonhuman and non-English publications were excluded in the database queries. Table 1 summarizes the complete inclusion and exclusion criterion for the 840 articles considered for this review. Articles selected for full review were aggregated using an online systematic review system (Covidence Software, Veritas Health Innovation, Melbourne, Australia, available at www.covidence.org) and examined by two independent reviewers (MKM and SSV). In instances when there was disagreement between the reviewers, the senior author (SAQ) reviewed and finalized inclusion decisions. This

Table 1
Review inclusion/exclusion criteria

Review criteria	Inclusion	Exclusion
Patient population	Age ≥18 years old Indicated pathologies: • Degenerative disc disease • Spondylosis • Low-grade spondylolisthesis • Group size≥10 subjects	Age <18 years old Out of scope pathologies: • Revision surgery • Tumor, infection, trauma • High-grade spondylolisthesis • Group size<10 subjects
Intervention	Stand-alone ALIF across L2/L3, L3/L4, L4/L5, L5/S1	TLIF, PLIF, LLIF, XLIF, PLF, AxiaLIF, or circumferential/combined anterior-posterior lumbar interbody fusion
Outcome	Reported fusion rate	Unreported fusion rate
Level of evidence	I/II—RCT III—Non-random trials IV—Case-control/cohort	Case reports Reviews
Publication types	English language peer reviewed journal	Letters & abstracts Duplicate patient population studies Feasibility studies Radiologic diagnostic studies Cadaveric studies In vitro studies Nonhuman studies

ALIF, anterior lumbar interbody fusion; TLIF, transforaminal lumbar interbody fusion; PLIF, posterior lumbar interbody fusion; PLF, posterior lumbar fusion; LLIF, lateral lumbar interbody fusion; XLIF, extreme lateral lumbar interbody fusion (NuVasive, San Diego, CA, USA); AxiaLIF, axial interbody fusion (Baxano Surgical, Raleigh, NC, USA).

process matches the recommendations Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) approach [11].

While recording overall fusion rate for each study, the following variables were also recorded: ALIF group size; radiological approach for fusion determination; number of fused levels; average patient age; interbody cage use and type, screw utilization, plate utilization, graft type, and graft location; study design; utilization of rhBMP-2; length of patient follow-up; percent of smoker subjects in the study population; and percent of worker's compensation subjects in the study population.

Methodological quality bias risk was assessed for every study included in this review using the Newcastle-Ottawa Scale (NOS). Specific dimensions examined across these studies included: selection of subjects (patient population, range of diagnoses being treated, and verification that subjects were not being treated with stand-alone ALIF revision surgery), comparability of data (study controls), and outcomes measurement (fusion methodology, follow-up duration, and limited loss-to-follow-up rate). All methodological quality risk bias assessments were performed by one reviewer (MKM).

The primary outcome considered for statistical analysis was mean fusion rate (a binary outcome measurement) for demographic cohorts identified from the included studies. Demographic cohort fusion rates were weighted using ALIF group sizes of the sample patient populations included in each individual study. Meta-analysis was unable to be conducted due to high variability in outcomes, measurement approach, and follow-up periods. Pooled odds ratios (OR) were calculated wherever appropriate. Differences between cohort fusion rates were calculated using Student *t* test (2-tail, unpaired, and assuming unequal variance) and followed up with confirmatory post hoc Tukey's HSD tests. Significance was assigned to differences between cohorts if a resultant p value was less than .05. All statistical analysis and data visualization was generated using Microsoft Excel 2016 Version 1809 (Microsoft Corporation, Redmond, Washington).

Results

After removing 407 duplicates, an initial screening of the 840 unique articles was conducted using only title and abstract which lead to 730 articles being excluded for irrelevance. Full screening was conducted on the remaining 110 papers with 55 being further excluded and 55 papers were included for this review (see Fig. 1). Of the 55 articles excluded, 24 were abstracts, 18 used supplementary posterior pedicle screw fixation in all or most cases, 10 did not report fusion rate, and 3 were based on repeat study populations.

For the 55 studies that satisfied the inclusion criteria after full review, 14 were assessed to have medium risk of bias due to methodological quality based on their NOS score of six or seven with an average of 6.9 out of 9 possible points. The remaining 41 papers were assigned NOS scores of eight or nine with an average of 8.3 out of 9 possible points, indicating low risk of bias (see Table 2). Only three studies were randomized control trials (RCTs) with stand-alone ALIF cohorts. The remaining 52 studies used a comparative observational approach. Primary sources of bias were attributed to study population selection, limited follow-up duration, and inconsistent implant utilization across a cohort. Specifically, 41 studies included proportions of WC status and/or higher age subjects relative to the reported means for these patient demographics observed among all spine fusion surgery cases in the United States [12]. Radiological follow-up periods of less than 12 months and variable utilization of cages, grafts, screws, and/or plating within a study led to lower NOS scores as well. Overall, the studies reflect limited risk of bias due to quality of approach.

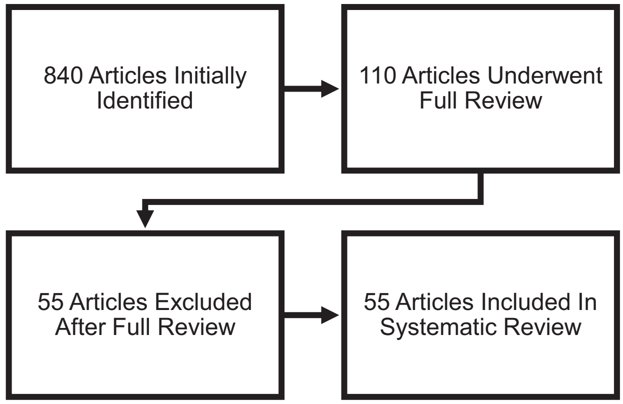

Fig. 1. PRISMA-P chart outlining the systematic review workflow.

The total number of patients in this systematic review is 5,517 with stand-alone ALIF conducted across 6,303 levels (see Table 3). The included studies spanned 31 years from 1988 through 2018. Mean subject age was 43.2. Weighted average patient fusion rate following stand-alone ALIF was 88.2% (range: 16.6%−100%, σ=15.2%, see Fig. 2). To examine the impact of small group sampling variance, the weighted average patient fusion rate following stand-alone ALIF in 42 studies with groups ≥50 subjects was 88.6% (range: 57.5%−99.0%, σ=9.57%, n=4798). The difference between fusion rates of all studies and those with larger group size was not significant (p>.05).

Fusion rate was assessed using radiographs in 65% of the included studies and 35% using CT scans. Mean radiological follow-up period was 27.4 months across all studies. Studies assessing fusion using CT scans had a fusion rate of 88.7% (n=2085). In studies utilizing radiographic approach for assessing fusion, fusion rate was 87.9% (n=3432). The difference between rates of fusion across the two fusion assessment approaches was not significant (p>.05; OR=1.08).

Fusion rate differences related to rhBMP-2 and graft utilization were observed between study group populations. Studies varied in their utilization of rhBMP-2. Weighted

Table 2
Characteristics of publications included in systematic review

Study	Design	ALIF subjects	Fusion rate	Age	Follow-up length	Graft type	rhBMP-2 use	Smoking status	WC status	Fusion analysis
Allain et al. 2014	Prospective	54	96.3%	57.1	12	Autograft	90.80%	30.8%	N/A	CT
Anjarwalla et al. 2006	Prospective	25	32.0%	45.0	60	Autograft	N/A	12.0%	36.0%	CT
Aunoble et al. 2006	Prospective	20	95.0%	39.0	24	Autograft	N/A	N/A	5.0%	X-ray
Behrbalk et al. 2013	Retrospective	25	90.6%	52.0	17	Allograft	100%	N/A	N/A	X-ray
Beutler and Peppelman 2003	Retrospective	104	97.0%	45.5	24	Autograft	N/A	N/A	N/A	CT
Bozzio et al. 2018	Retrospective	53	75.5%	37.8	12	Variable	100%	N/A	N/A	X-ray
Burkus et al. 2002	RCT	279	91.7%	42.8	24	Autograft	51.3%	N/A	33.7%	X-ray
Burkus et al. 2002	Prospective	43	83.7%	43.5	24	Autograft	52.2%	26.1%	26.1%	X-ray
Burkus et al. 2003	Prospective	679	91.1%	41.7	24	Autograft	38.1%	32.3%	33.1%	CT
Burkus et al. 2006	RCT	131	92.7%	41.5	24	Autograft	60.3%	32.8%	30.5%	X-ray
Chatha et al. 2014	Prospective	286	94.0%	N/A	24	Allograft	100%	N/A	28.0%	X-ray
Cheung et al. 2003	Retrospective	67	95.5%	31.0	168	Autograft	N/A	N/A	N/A	X-ray
Cho et al. 2010	Retrospective	28	85.7%	58.0	27	Autograft	N/A	N/A	N/A	X-ray
Choi et al. 2005	Retrospective	22	100.0%	46.0	35	Allograft	N/A	N/A	N/A	X-ray
Choi and Sung 2006	Retrospective	90	86.7%	53.0	27	Allograft	N/A	N/A	N/A	CT
Chung et al. 2003	Prospective	54	91.0%	49.5	24	Autograft	N/A	N/A	N/A	X-ray
Flouzat-Lachaniette et al. 2014	Retrospective	51	88.7%	59.0	12	Autograft	33.3%	23.5%	N/A	X-ray
Flouzat-Lachaniette et al. 2015	Retrospective	47	97.9%	64.0	36	Autograft	85.1%	12.8%	N/A	CT
Frantzides et al. 2006	Retrospective	24	100.0%	43.0	12	Autograft	37.5%	N/A	N/A	X-ray
Hironaka et al. 2013	Retrospective	142	90.1%	64.3	76	Autograft	N/A	N/A	N/A	X-ray
Ishihara et al. 2001	Prospective	23	83.0%	38.0	135	Autograft	N/A	N/A	N/A	X-ray
Kalb et al. 2016	Retrospective	231	99.0%	47.0	11	Allograft	100%	40.2%	N/A	CT
Kleeman et al. 2001	Prospective	21	100.0%	38.0	12	Allograft	100%	9.1%	55.0%	X-ray
Kuang et al. 2017	Retrospective	42	100.0%	52.9	24	Allograft	N/A	N/A	N/A	CT
Lammli et al. 2014	Retrospective	115	93.0%	43.0	24	Allograft	100%	33.1%	N/A	CT
Lee et al. 2017	Retrospective	26	69.2%	53.1	24	Allograft	N/A	N/A	N/A	X-ray
Lekovic et al. 2007	Retrospective	15	73.3%	57.5	31	Autograft	N/A	75.0%	N/A	X-ray
Li et al. 2010	Prospective	112	57.5%	41.7	24	Autograft	N/A	62.5%	N/A	X-ray
Liu et al. 2002	Retrospective	14	80.0%	45.5	6	Autograft	N/A	N/A	N/A	CT
Loguidice et al. 1988	Retrospective	85	75.0%	41.0	35	Autograft	N/A	N/A	66.0%	X-ray
Madan et al. 2003	Retrospective	51	92.1%	41.9	47	Autograft	N/A	56.9%	31.4%	X-ray
Malham et al. 2014	Prospective	131	96.9%	45.3	12	Allograft	100%	9.2%	N/A	CT
Mobbs et al. 2014	Prospective	110	93.6%	57.6	24	Allograft	N/A	17.3%	20.0%	X-ray
Newman and Grinstead 1992	Retrospective	36	88.9%	38.0	26	Autograft	N/A	N/A	33.3%	X-ray
Nishizawa and Fujimara 1997	Prospective	58	67.0%	53.0	24	Autograft	N/A	N/A	N/A	X-ray
Norotte and Barrios 2018	Prospective	65	95.4%	48.0	24	Allograft	N/A	N/A	N/A	X-ray
Pellise et al. 2002	Prospective	12	16.6%	36.5	37	Autograft	N/A	41.7%	N/A	CT
Penta and Fraser 1997	Retrospective	87	72.4%	48.0	120	Autograft	N/A	N/A	59.2%	X-ray
Pfeiffer et al. 1996	Retrospective	113	88.0%	42.7	28	Autograft	N/A	N/A	N/A	CT
Phan et al. 2017	Prospective	137	82.4%	56.7	12	Allograft	N/A	13.9%	17.5%	X-ray
Pineda et al. 1998	Prospective	831	87.3%	41.1	12	Autograft	N/A	N/A	N/A	X-ray
Rahn et al. 2010	Retrospective	37	75.0%	38.8	24	Autograft	N/A	45.9%	40.5%	CT
Rao et al. 2015	Prospective	125	94.4%	57.0	20	Allograft	N/A	17.6%	20.0%	X-ray
Rao et al. 2015	Prospective	27	91.0%	64.9	17	Allograft	100%	18.5%	14.8%	CT
Rao et al. 2017	Prospective	147	91.2%	57.3	6	Allograft	7.5%	11.6%	N/A	X-ray
Rauzzino et al. 1999	Retrospective	42	94.7%	44.5	14	Autograft	N/A	N/A	N/A	X-ray
Riouallon et al. 2013	Retrospective	65	90.8%	40.0	79	Autograft	N/A	N/A	N/A	X-ray
Sarwat et al. 2001	Prospective	43	93.0%	40.0	12	Allograft	N/A	N/A	N/A	CT
Sasso et al. 2004	RCT	140	77.1%	40.8	24	Autograft	N/A	32.2%	38.9%	CT
Satomi et al. 1992	Retrospective	27	92.6%	51.1	N/A	Autograft	N/A	N/A	N/A	X-ray
Schiffman et al. 2003	Retrospective	71	86.0%	43.4	12	Autograft	N/A	36.0%	96.0%	X-ray
Strube et al. 2012	Prospective	34	68.7%	51.6	41	Allograft	N/A	N/A	N/A	CT
Tiusanen et al. 1996	Retrospective	134	80.0%	30.1	63	Autograft	N/A	N/A	N/A	X-ray
Verbruggen et al. 2015	Prospective	38	84.0%	41.1	114	Autograft	N/A	N/A	N/A	X-ray
Wan et al. 2014	Retrospective	48	91.0%	56.3	24	Autograft	N/A	6.3%	N/A	X-ray

Prospective, prospective cohort study; RCT, randomized control trial; Retrospective, retrospective cohort study; WC Status, workers compensation status. Follow-up length reported in mean months.

Table 3
Risk of bias assessment using the Newcastle-Ottawa Scale.

Study	Selection	Comparability	Outcome	Total	Risk of bias rating
Allain et al. 2014	4	2	3	9	Low
Anjarwalla et al. 2006	3	2	3	8	Low
Aunoble et al. 2006	3	1	3	7	Medium
Behrbalk et al. 2013	3	2	3	8	Low
Beutler and Peppelman 2003	4	2	3	9	Low
Bozzio et al. 2018	4	2	3	9	Low
Burkus et al. 2002	3	2	3	8	Low
Burkus et al. 2002_2	3	2	3	8	Low
Burkus et al. 2003	3	2	3	8	Low
Burkus et al. 2006	3	2	3	8	Low
Chatha et al. 2014	3	2	3	8	Low
Cheung et al. 2003	4	2	3	9	Low
Cho et al. 2010	3	1	3	7	Medium
Choi et al. 2005	3	1	3	7	Medium
Choi and Sung 2006	4	1	3	8	Low
Chung et al. 2003	4	2	3	9	Low
Flouzat-Lachaniette et al. 2014	3	2	3	8	Low
Flouzat-Lachaniette et al. 2015	3	2	3	8	Low
Frantzides et al. 2006	3	1	3	7	Medium
Hironaka et al. 2013	3	1	3	7	Medium
Ishihara et al. 2001	3	2	3	8	Low
Kalb et al. 2016	3	1	2	6	Medium
Kleeman et al. 2001	3	2	3	8	Low
Kuang et al. 2017	3	2	3	8	Low
Lammli et al. 2014	3	1	3	7	Medium
Lee et al. 2017	3	2	3	8	Low
Lekovic et al. 2007	4	2	3	9	Low
Li et al. 2010	3	2	3	8	Low
Liu et al. 2002	3	2	2	7	Medium
Loguidice et al. 1988	3	2	3	8	Low
Madan et al. 2003	3	1	3	7	Medium
Malham et al. 2014	4	2	3	9	Low
Mobbs et al. 2014	3	2	3	8	Low
Newman and Grinstead 1992	3	2	3	8	Low
Nishizawa and Fujimara 1997	4	2	3	9	Low
Norotte and Barrios 2018	4	2	3	9	Low
Pellise et al. 2002	3	2	3	8	Low
Penta and Fraser 1997	3	2	3	8	Low
Pfeiffer et al. 1996	4	1	3	8	Low
Phan et al. 2017	3	2	3	8	Low
Pineda et al. 1998	4	2	3	9	Low
Rahn et al. 2010	3	2	3	8	Low
Rao et al. 2015	3	1	3	7	Medium
Rao et al. 2015_2	3	2	3	8	Low
Rao et al. 2017	3	2	2	7	Medium
Rauzzino et al. 1999	3	1	3	7	Medium
Riouallon et al. 2013	4	1	3	8	Low
Sarwat et al. 2001	3	2	3	8	Low
Sasso et al. 2004	3	2	3	8	Low
Satomi et al. 1992	3	2	3	8	Low
Schiffman et al. 2003	3	2	3	8	Low
Strube et al. 2012	3	2	3	8	Low
Tiusanen et al. 1996	4	2	3	9	Low
Verbruggen et al. 2015	3	1	3	7	Medium
Wan et al. 2014	3	1	3	7	Medium

The Newcastle-Ottawa Scale (NOS) assessment of studies involves scoring three key dimensions: selection (0−4 points), comparability (0−2 points), and outcome (0−3 points). Total scores are tabulated on a scale of 0−9 points and assigned an overall risk of bias rating. Higher scores are associated with less risk of bias. Low risk was assigned to scores 8 and 9, moderate risk of bias was assigned to scores 4−7, and high risk of bias was assigned to scores 0−3. Studies with overlapping names were differentiated by power with the smaller of two studies labeled "_2" in each case.

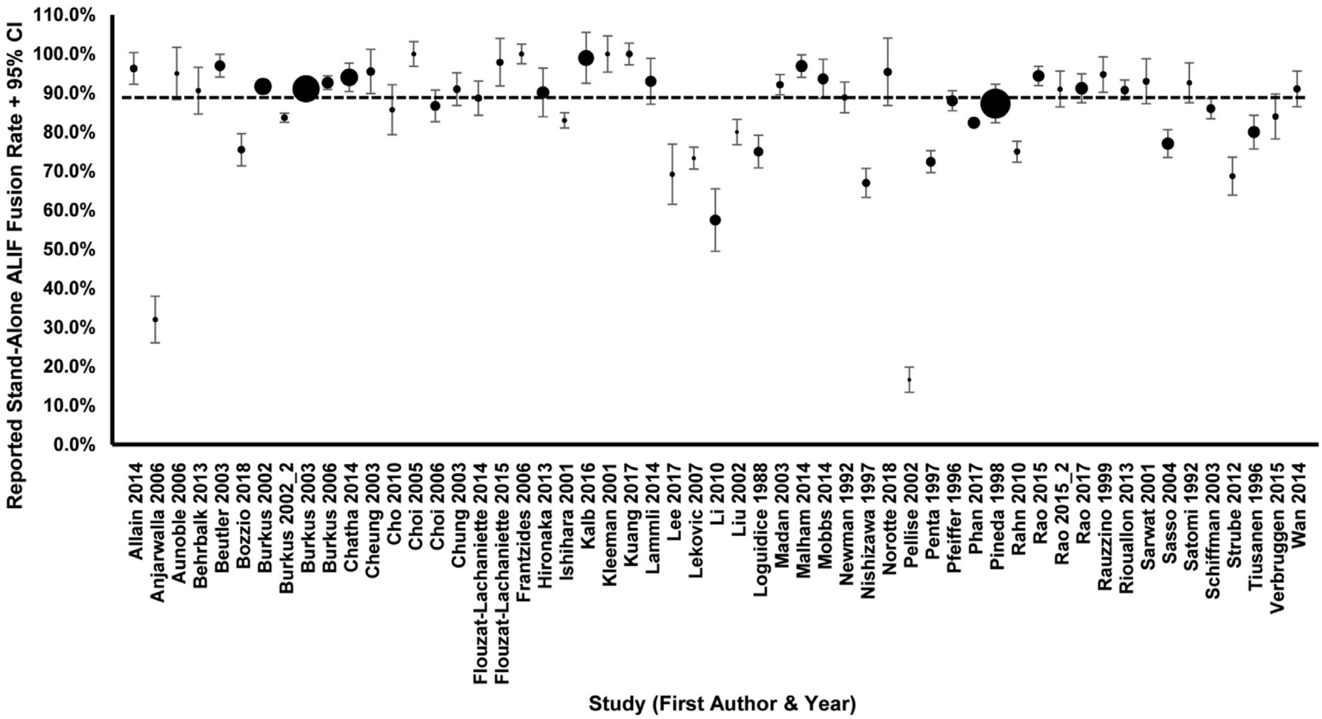

Fig. 2. Forest plot of reported mean stand-alone ALIF fusion rates with 95% confidence intervals.

mean fusion rate for subjects in the eight rhBMP-2 study groups was 94.4% (n=889) compared with 84.8% (n=3102) in 38 study groups without rhBMP-2 used. This difference was not significant (p=.106; OR=3.02). Studies also varied with respect to the utilization of autograft versus allograft. Weighted mean fusion rate for subjects in the nine allograft studies without rhBMP-2 was 88.5% (n=734) compared with 84.4% (n=2,446) in 29 study groups with autograft. This difference was not significant (p>.05; OR=1.42).

Fusion rate differences related to subject smoking status and workers compensation (WC) status were observed between studies at the group level. Of the studies included in this review, we noted that no single paper reported stand-alone ALIF fusion rate specifically for smokers or WC patients. To elucidate the impact of smoking and positive WC status on fusion rate indirectly, we examined cohort fusion rate differences between studies that reported significantly higher prevalence of smokers and WC patients. This was observed when each demographic was split by a 50% prevalence threshold (p<.0001). Three groups which included 50% or more smokers had a weighted average fusion rate of 68.8% (n=178) compared with 81.8% (n=2382) in 21 groups that had less than 50% smokers (p>.05; OR=.49). Four groups that included 50% or more patients with positive WC status had a weighted average fusion rate of 79.1% (n=264) compared with 89.4% (n=2126) in 15 groups that had less than 50% patients with positive WC status (p>.05; OR=.45). Fusion rate differences between these cohorts are not significant.

Surgical fusion approach for stand-alone ALIF was also examined for trends (see Table 4). Only seven of the included papers described a stand-alone ALIF surgical approach with allogenic bone dowels and none were published using this approach after 2007. Stand-alone ALIF with interbody cage placement was the most frequently used surgical approach (73%). Supplemental utilization of an anterior fixation plate device was described in 16% of studies and yielded a fusion rate of 94.2%. Newer zero-profile interbody implants with integrated anterior spacers were used in 29% of the included studies and reported a fusion rate of 89.2%.

Table 4
Fusion rate by stand-alone ALIF definition

Stand-alone ALIF definition	Studies	Subjects	Fusion rate
Bone dowels	5	239	88.5%
Bone dowels+cortical blocks	2	172	73.7%
Cages	18	2693	86.7%
Cages+anterior plate	7	813	95.2%
Cage (zero-profile)	14	867	88.7%
Cage (zero-profile)+anterior plate	1	115	93.0%
Cortical blocks	1	67	95.5%
Cortical blocks+anterior plate	1	113	88.0%
Cortical blocks+wire	3	128	81.1%
Other	3	310	87.8%
Total	55	5517	88.2%

Other = did not clearly define stand-alone ALIF definition used.

Discussion

Studies that met the inclusion criteria for this systematic review indicate that stand-alone ALIF surgery generally has a high fusion rate. Shift in ALIF surgical approaches utilizing interbody cage implants with anterior plating and screws have led to increased fusion rates. Anterior plate and zero-profile cage use yields high rates of fusion. Positive smoking or WC status cohorts have lower fusion rates that are not statistically significant. Fusion rate between studies utilizing autograft have similar fusion rates to studies utilizing allograft. Utilization of rhBMP-2 during stand-alone ALIF surgery may ensure successful fusion outcomes when treating patients at elevated risk for poor outcomes.

Although not always measured in the included studies, the relationship between fusion rate and overall rate of significant complications may help triangulate the risk-benefit of stand-alone ALIF surgery. A recent systematic review estimated that the clinical complication rate is approximately 21.5% regardless of presurgical comorbidities. In this same review, adverse surgical events including revision, removal, additional fixation, and reoperation were conducted at a rate of 9.6% [13].

The use of rhBMP-2 did not result in a statistically significant increase in fusion rate for stand-alone ALIF procedures. However, utilization of rhBMP-2 for lumbar spine surgery, in general, has been shown to result in complications including vertebral osteolysis, development of antibodies targeting rhBMP-2, postoperative radiculitis and nerve injury, as well as ectopic and heterotopic bone growth. The United States Food and Drug Administration has been particularly concerned with the association of retrograde ejaculation and cancer for rhBMP-2 use. Several retrospective studies have examined the Food and Drug Administration concern regarding rates of retrograde ejaculation symptoms in men following ALIF surgery and report inconsistent findings [14]. High product cost, complication risk, and increased length of stay associated with rhBMP-2 may lend itself to be more beneficial in prevention of nonfusion-related sequela such as pseudoarthroses and extended downstream treatment costs when treating smokers, WC patients, and those with chronic comorbidities [15,16].

Autograft appears to have similar fusion rates when compared with allograft when used in stand-alone ALIF. Autograft utilization has generally been regarded as standard of care during spine surgery despite reported complication rates as high as 25%. Substitution with allograft has been associated with slower incorporation rates and fusion development, disease transmission risk, and higher cost [17]. Benefits of using allograft include decrease in surgical time, blood loss, and complication rates. However, the literature on allograft utilization in lumbar spine surgery appears to be heterogeneous in terms of span of surgical procedures examined, levels of fusion, and range of conditions treated [18]. Additionally, while randomized control trial (RCT) studies focused on comparing fusion rate outcomes of autograft versus allograft these studies have limited sample size and low power which has limited their ability to identify potential fusion rate and/or functional outcome differences [19]. There remains a need for RCTs to further examine the efficacy of autograft versus allograft in stand-alone ALIF cases.

Approximately 65% of all included studies used radiographs whereas the remaining 35% used a CT approach. Of the 55 studies included in this review, 30 studies reported ≥90.0% fusion rates. Among the 30 studies with high reported fusion rates, 70% used radiographs whereas the remaining 30% used a CT approach. Fusion rate is more likely to be over-reported in studies with a single radiologist involved with examining radiograph data instead of multiple radiologists reviewing CT data [20]. However, it is difficult to justify utilization of CT for fusion rate measurement given the significant variance of radiation dosage between the two diagnostic scans in scenarios when a patient has positive functional outcomes and positive surgical fusion outcome confirmation via radiograph.

Positive smoking status and WC status was not uniformly indicated across the included studies. As a significant source of confounding, the number of patients who were both smokers and were involved with WC claims was not indicated in any of the studies fully reviewed. Therefore, the relationship between positive smoking and WC status as well as fusion rate is subject to confounding and cannot be elucidated entirely based on the studies included in this review. Two recent papers have examined stand-alone ALIF outcomes for patients with positive smoking status and observed significant association of pseudoarthrosis development among the smokers included in the study [21,22]. Fusion rate of the WC population following stand-alone ALIF has also been examined, however association of positive WC status with pseudoarthrosis has not been observed with significance [23,24]. Further research in this area is needed to determine appropriate mitigation strategies for these patient populations to ensure high fusion rate and predictable positive functional outcomes. Similarly, patient comorbidities, prior spine surgery, utilization of NSAIDs before, during, and after surgery may be other confounding variables worth considering.

Clinical adjacent segment disease (ASD) pathology is a significant complication resulting in degenerative changes to the vertebral disc either above or below a fused spinal segment due to changes in mechanical load. When reported, relatively low rates of ASD development (19.1%) are expected with stand-alone ALIF after 24 months which is comparable to what has been observed with alternative lumbar interbody fusion approaches [25]. Fusion rate for patients that develop ASD following stand-alone ALIF ranges between 80.0% and 100% but was reported in studies with small sample sizes [25,26]. Follow-up studies with higher power are necessary to understanding the relationship between ASD development and fusion rate following stand-alone ALIF.

Inconsistent measurement of pain, patient satisfaction, and functional outcome scores of patients was observed across the included papers in this review. Score changes may have an association with fusion rate results in stand-alone ALIF surgery but this could not be examined in detail. When reported, high rates of successful surgical fusion did not appear to associate with patient satisfaction. During postdischarge follow-up communication, 89% of patients reported that they would reconsider their decision to have their ALIF procedure [27]. Another study reported that approximately 27% of patients would choose to not have another ALIF procedure [28]. Carefully curating surgical and nonsurgical treatment options appropriate to patients' needs and clearly presenting options with all potential risks related to negative outcomes may help improve postoperative patient satisfaction rates.

Based on evidence in current literature, stand-alone ALIF surgery yields an overall high rate of surgical fusion within 12 to 24 months. Stand-alone ALIF surgical approaches have increased in sophistication over the last thirty years. Of the included studies in this systematic review, there was a shift away from allogenic bone dowel placement and towards approaches associated with higher fusion including utilization of interbody cage implants in combination with zero-profile screw placement and/or anterior plates. Literature describing considerations for autograft versus allograft utilization reflects a low level of evidence. Utilization of rhBMP-2 during stand-alone ALIF surgery may ensure high rates of fusion among patients with chronic comorbidities or positive smoking or WC status.

References

[1] Capener N. Spondylolisthesis. Br J Surg 1932;19:374–86.

[2] Burns BH. An operation for spondylolisthesis. Lancet 1933;1:1233.

[3] Kalb S, Perez-Orribo L, Kalani MYS, Synder LA, Martirosyan NL, Burns K, et al. The influence of common medical conditions on the outcome of anterior lumbar interbody fusion. Clin Spine Surg 2016;29:285–90.

[4] Dennis S, Watkins R, Landaker S, Dillin W, Springer D. Comparison of disc space heights after anterior lumbar interbody fusion. Spine 1989;14:876–8.

[5] Phan K, Xu J, Scherman DB, Rao PJ, Mobbs RJ. Anterior lumbar interbody fusion with and without an "Access Surgeon": a systematic review and meta-analysis. Spine 2017;42:592–601.

[6] Zhang JI, Poffyn B, Sys G, Uyttendaele D. Are stand-alone cages sufficient for anterior lumbar interbody fusion? Orthop Surg 2012;4:11–4.

[7] Choi KC, Ryu KS, Lee SH, Kim YH, Lee SJ, Park CK. Biomechanical comparison of anterior lumbar interbody fusion: stand-alone interbody cage versus interbody cage with pedicle screw fixation—a finite element analysis. BMC Musculoskelet Disord 2013;14:220.

[8] Assem Y, Pelletier MH, Mobbs RJ, Phan K, Walsh WR. Anterior lumbar interbody fusion integrated screw cages: intrinsic load generation, subsidence, and torsional stability. Orthop Surg 2017;9:191–7.

[9] Kornblum MB, Turner AW, Cornwall GB, Zatushevsky MA, Phillips FM. Biomechanical evaluation of stand-alone lumbar polyether-ether-ketone interbody cage with integrated screws. Spine J 2013;13:77–84.

[10] Pradhan BB, Nassar JA, Delamarter RB, Wang JC. J Spinal Disord Tech 2002;15:355–61.

[11] Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015;350:g7647.

[12] Rajaee SS, Bae HW, Kanim LE, Delamarter RB. Spinal fusion in the United States: analysis of trends from 1998 to 2008. Spine 2012;37:67–76.

[13] Giang G, Mobbs R, Phan S, Tran TM, Phan K. Evaluating outcomes of stand-alone anterior lumbar interbody fusion: a systematic review. World Neurosurg 2017;104:259–71.

[14] Tannoury CA, An HS. Complications with the use of bone morphogenetic protein 2 (BMP-2) in spine surgery. Spine J 2014;14:552–9.

[15] Hustedt JW, Blizzard DJ. The controversy surrounding bone morphogenetic proteins in the spine: a review of current research. Yale J Biol Med 2014;87:549–61.

[16] Ghogawala Z, Whitmore RG, Watters 3rd WC, Sharan A, Mummaneni PV, Dailey AT, et al. Guideline update for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 3: assessment of economic outcome. J Neurosurg Spine 2014;21:14–22.

[17] Thalgott JS, Giuffre JM, Klezl Z, Timlin M. Anterior lumbar interbody fusion with titanium mesh cages, coralline hydroxyapatite, and demineralized bone matrix as part of a circumferential fusion. Spine J 2002;2:63–9.

[18] Buser Z, Brodke DS, Youssef JA, Rometsch E, Park JB, Yoon ST, et al. Allograft versus demineralized bone matrix in instrumented and noninstrumented lumbar fusion: a systematic review. Global Spine J 2018;8:396–412.

[19] Tuchman A, Brodke DS, Youssef JA, Meisel HJ, Dettori JR, Park JB, et al. Iliac crest bone graft versus local autograft or allograft for lumbar spinal fusion: a systematic review. Global Spine J 2016;6:592–606.

[20] Choudhri TF, Mummaneni PV, Dhall SS, Eck JC, Groff MW, Ghogawala Z, et al. Guideline update for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 4: radiographic assessment of fusion status. J Neurosurg Spine 2014;21:23–30.

[21] Phan K, Fadhil M, Chang N, Giang G, Gragnaniello C, Mobbs RJ. Effect of smoking status on successful arthrodesis, clinical outcome, and complications after anterior lumbar interbody fusion (ALIF). World Neurosurg 2018;110:e998–e1003.

[22] Kalb S, Perez-Orribo L, Kalani MY, Snyder LA, Martirosyan NL, Burns K, et al. The influence of common medical conditions on the outcome of anterior lumbar interbody fusion. Clin Spine Surg 2016;29:285–90.

[23] Phan K, Davies S, Rao PJ, Mobbs RJ. Worker's compensation status and outcomes following anterior lumbar interbody fusion: prospective observational study. World Neurosurg 2017;103:680–5.

[24] Penta M, Fraser RD. Anterior lumbar interbody fusion. A minimum 10-year follow-up. Spine 1997;22:2429–34.

[25] Flouzat-Lachaniette CH, Ratte L, Poignard A, Auregan JC, Queinnec S, Hernigou P, Allain J. Minimally invasive anterior lumbar interbody fusion for adult degenerative scoliosis with 1 or 2 dislocated levels. J Neurosurg Spine 2015;23:739–46.

[26] Rao PJ, Loganathan A, Yeung V, Mobbs RJ. Outcomes of anterior lumbar interbody fusion surgery based on indication: a prospective study. Neurosurgery 2015;76:7–23.

[27] Pinson H, Hallaert G, Herregodts P, Everaert K, Couvreur T, Caemaert J, et al. Outcome of anterior lumbar interbody fusion: a retrospective study of clinical and radiologic parameters. World Neurosurg 2017;103:772–9.

[28] Verbruggen D, Tampere T, Uyttendaele D, Sys G, Poffyn B. Long-term follow-up of the anterior lumbar interbody fusion procedure. Acta Orthop Belg 2015;81:546–52.