

Systematic Review

Percutaneous Endoscopic Debridement and Drainage for Spinal Infection: Systemic Review and Meta-Analysis

Yi Mao, MM, Yang Li, MD, and Xingang Cui, MD

From: Shandong Provincial Hospital, Shandong University, Shandong Province, China

Address Correspondence: Xingang Cui, MD Shandong Provincial Hospital, Shandong University 9677 Jingshi Rd. Jinan, Shandong 250000, China E-mail: spine2014@163.com

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Background: Percutaneous endoscopic debridement and drainage (PEDD) has played a vital role in the management of spinal infection; however, limited PEDD results are available to date.

Objectives: The purpose of this systematic review is to examine the existing literature, to give an objective estimate of the outcomes of PEDD using a meta-analytical approach.

Study Design: Meta-analysis and systematic review of retrospective single-arm studies.

Methods: A comprehensive online review was performed in MEDLINE, EMBASE, PubMed, Web of Science, and Cochrane databases from 1980 to October 2018. Eligible studies included the single-arm studies that mentioned PEDD in the management of spinal infection. Pooled event rates for positive bacteria culture, pain control satisfaction, and reoperation were estimated. The complications of PEDD were also recorded.

Results: Nine single-arm PEDD articles (158 patients) were included. The pooled event rate was 82% (95% CI: 75%-88%) for positive bacteria culture, 81% (95% CI: 73%-87%) for pain control satisfaction, and 21% (95% CI: 15%-29%) for reoperation. There are few complications reported in the literature that included transient paresthesia in the affected lumbar segment and local kyphosis.

Limitations: First, all included studies were retrospective series with inherent methodological limitations. Second, the sample size and the number of studies that were found to be eligible was small. In addition, all included studies are single-arm, and further studies are necessary in large randomized controlled trials on comparing the efficacy of conservative therapy, PEDD, and open surgical intervention.

Conclusions: PEDD not only has a high rate of causative-pathogen identification, but also provides satisfactory clinical outcome. Early PEDD intervention in spinal infection is encouraging; however, further studies in large randomized controlled trials on comparing the efficacy of conservative therapy, PEDD, and open surgical intervention are necessary.

Key words: Percutaneous endoscopic debridement and drainage, spinal infection, meta-analysis

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Currently, the incidence of spinal infection is rising (1) as a consequence of longer life expectancy for patients with chronic debilitating diseases, immunocompromise, human immunodeficiency virus, intravenous drug use, and recent spinal surgery (2,3).

Treatment strategies of spinal infection still remain

controversial. Conservative cases seem to be followed by mechanical back pain more often than surgical cases and develop more deformity long term (4). However, surgical intervention is always associated with more complications (5,6), although overall mortality is lower in operated patients (1). Percutaneous endoscopic de-

bridement and drainage (PEDD), which is coupled with less complications and satisfactory clinical outcome, provides a minimally invasive surgical choice for the treatment of spinal infection (7-12).

The purpose of this manuscript is to use a meta-analytic approach to provide surgeons with an objective estimate of the outcomes of PEDD in the management of spinal infection.

METHODS

Search Strategy

We performed a comprehensive search for published relevant studies on PEDD in the treatment of spinal infection in MEDLINE, EMBASE, PubMed, Web of Science, and Cochrane databases. Since percutaneous endoscopic discectomy was first employed for treating lumbar disc herniation in the early 1980s (13), the articles from 1980 to October 2018 were searched.

The following key terms were included in our searches: "spinal infection," "spondylodiscitis," "spondylitis," "diskitis," "vertebral osteomyelitis," "spondylodiskitis," "epidural abscess," "paravertebral infection," "endoscopy," "endoscope," and "endoscopic." These keywords searched with various combinations of the operators "AND," "NOT," and "OR." We also chose references cited in the articles and relevant review articles to identify additional studies.

Selection of Studies

Two review authors (YM and YL) independently examined all titles and abstracts that met our search terms and reviewed full publications, when necessary. The full texts of all potentially relevant studies were also assessed by 2 reviewers, if necessary. If no agreement could be reached, a third reviewer (XC) made the final decision. We also included observational studies (nonrandomized controlled clinical trials, cohort studies, case-control studies, and retrospective patient series) for an effectiveness analysis.

The eligibility criteria of the included articles were: 1) those that mentioned percutaneous endoscopic surgery for the treatment of spinal infection; 2) a retrospective study, prospective study, cohort study, regardless of sample size; 3) sufficient reported data for extraction and calculation of a recurrence rate with 95% confidential interval (CI); 4) in the case of duplicate publication, the most recent or largest study was selected; 5) publications were excluded if the patients

underwent thoracoscopic or laparoscopic surgeries, and publications were also excluded if they were review articles, comments, case reports, letters, animal trials, or cadaveric studies; and 6) the language of the included studies was limited to English.

Quality of Data Assessment

Although the included studies were limited by their retrospective design, all were considered to be of high methodological quality, according to Newcastle-Ottawa Scale criteria (14). Using a star rating system (range: 0-9 stars), each study was independently judged by 2 authors (YM and YL).

Data Extraction

Two reviewers (YM and YL) independently extracted the data of included studies and reached consensus on each item. Data included: 1) authors' names and nationality, publication time, study design, follow-up time, recruitment period, and journal title of each included study; 2) sample size and patient demographic characteristics including age and gender; and 3) the clinical outcome measurement including the length of bacteria culture, operation time, visual analog scale (VAS) or Oswestry Disability Index (ODI) scores, C-reactive protein, elevated erythrocyte sedimentation rate preoperation and postoperation, complications, and reoperation (included re-PEDD and open surgery). These extracted data were rechecked by reviewer XC.

Data Analysis

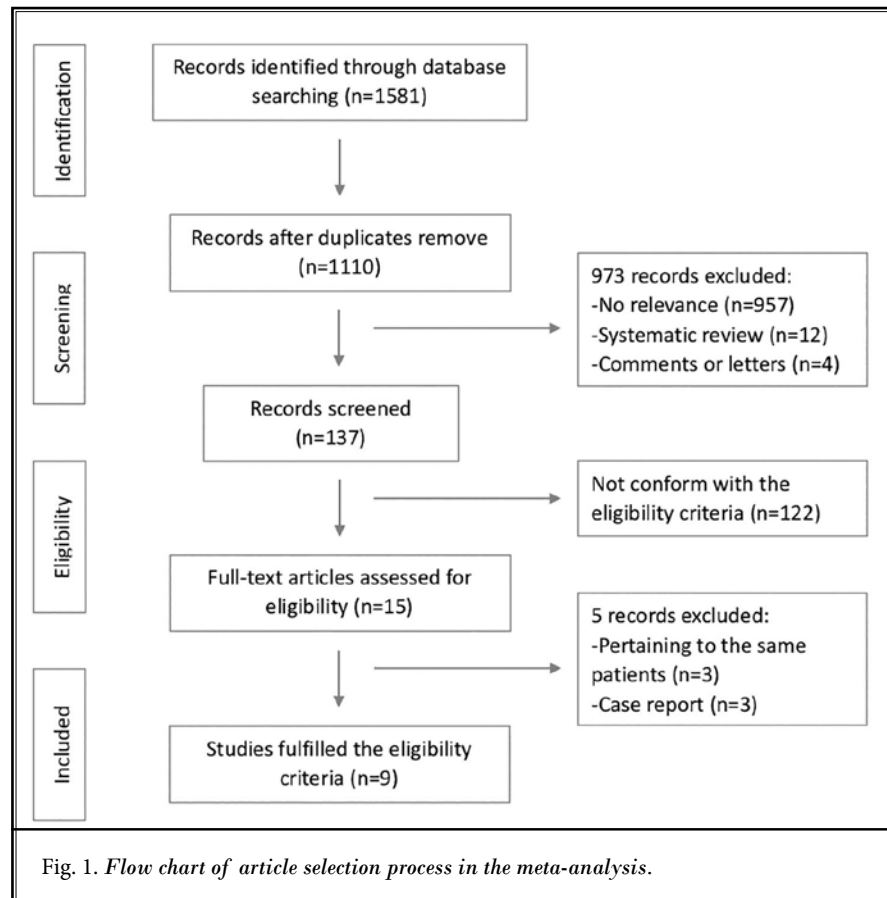
A meta-analysis was conducted by using R software version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria) for all extracted data. The Cochran Q statistic and the I^2 test were used to assess study heterogeneity. When a significant Q test ($P < 0.10$) or $I^2 > 50\%$ indicated heterogeneity across studies, the DerSimonian and Laird method random effects model was used for meta-analysis, otherwise the Mantel-Haenszel method fixed-effects model was used.

Funnel plots and the Egger's regression test were used to assess for potential publication bias in our meta-analysis. If publication bias was suspected, visual assessment of cumulative forest plots as well as the Classic and Orwin's fail-safe N tests were used for further assessment. If significant publication bias was found, the Duval and Tweedie trim and fill method was used to adjust for the possible bias.

RESULTS

Eligible Studies and Characteristics of Studies

Among 1,581 retrieved searched articles, 9 single-arm PEDD articles (7-11,15-18) were with a total of 158 included patients (Fig. 1). All of the 9 studies were retrospective. The sample size ranged from 4 to 41, with a median of 16. The follow-up of all included studies ranged from 1 to 92 months. The mean age of patients at surgery ranged from 46 to 70.4 years. Among all included studies, 4 articles were from Taiwan, China, and 2 were from Japan. The remaining 3 were from mainland China, South Korea, and India. All relevant information listed and other general characteristics of the included articles were recorded (Appendix 1).



Study Quality

The results of our Newcastle-Ottawa Scale assessment yielded 3 studies with 6 stars and 6 studies with 7 stars.

Meta-Analysis of Postoperative Outcomes

Bacteria Culture

The pooled positive bacteria culture rate was 82%, with 95% CI of 75% to 88% in a fixed-effect model. A total of 149 patients were assessed for this outcome and recruited from 8 included articles. No methodological heterogeneity among the

studies ($I^2 = 0$; $P = 0.78$) was observed (Fig. 2A). No serious publication bias was observed in the funnel plot (Fig. 2B).

Pain Control

The VAS ≤ 3 or ODI ≤ 50 at last postoperative follow-up was considered as satisfactory pain control. No pain score was used in the articles, however, patient satisfaction with pain was mentioned and was also included in the study. Finally, 5 articles were scored with VAS, one with ODI, and one article mentioned patient satisfaction with pain. Finally, 7 included articles and 134 patients were selected into the single-arm meta-analysis. The pooled pain control satisfaction rate was 81%, with 95% CI of 73% to 87% in a fixed-effect model. No methodological heterogeneity among the studies ($I^2 = 0$; $P = 0.70$) was observed (Fig. 3A). No serious publication bias was observed in the funnel plot after using the trim and fill method (Fig. 3B).

Reoperation

The pooled reoperation rate was 21%, with 95% CI of 15% to 29% in a fixed-effect model, and 19%, with 95% CI of 12% to 29% in a random-effect model. A total of 158 patients were assessed for this outcome and recruited from 9 included articles. No methodological heterogeneity among the studies ($I^2 = 30\%$; $P = 0.17$) was observed (Fig. 4A).

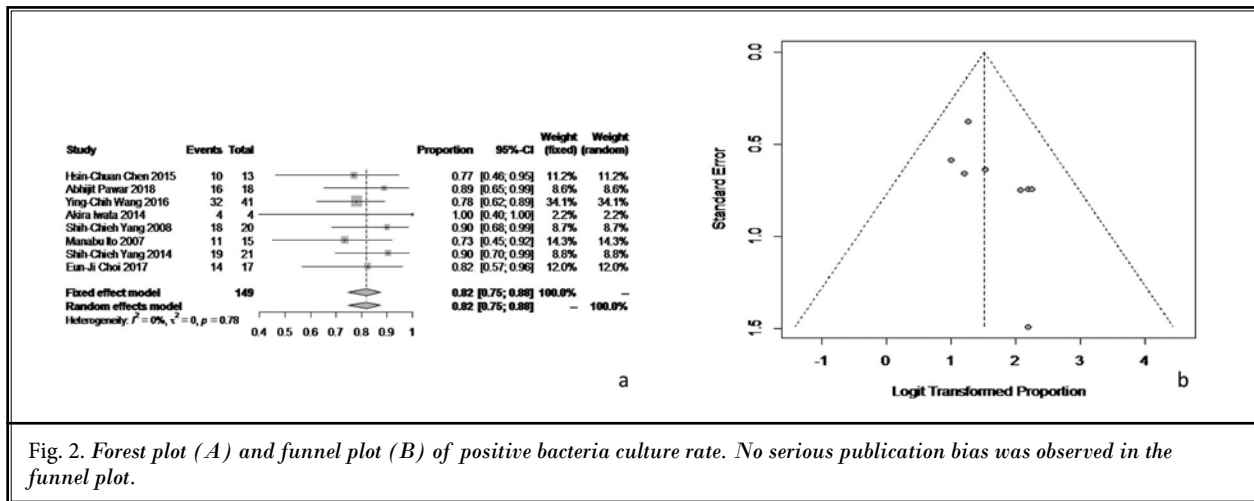


Fig. 2. Forest plot (A) and funnel plot (B) of positive bacteria culture rate. No serious publication bias was observed in the funnel plot.

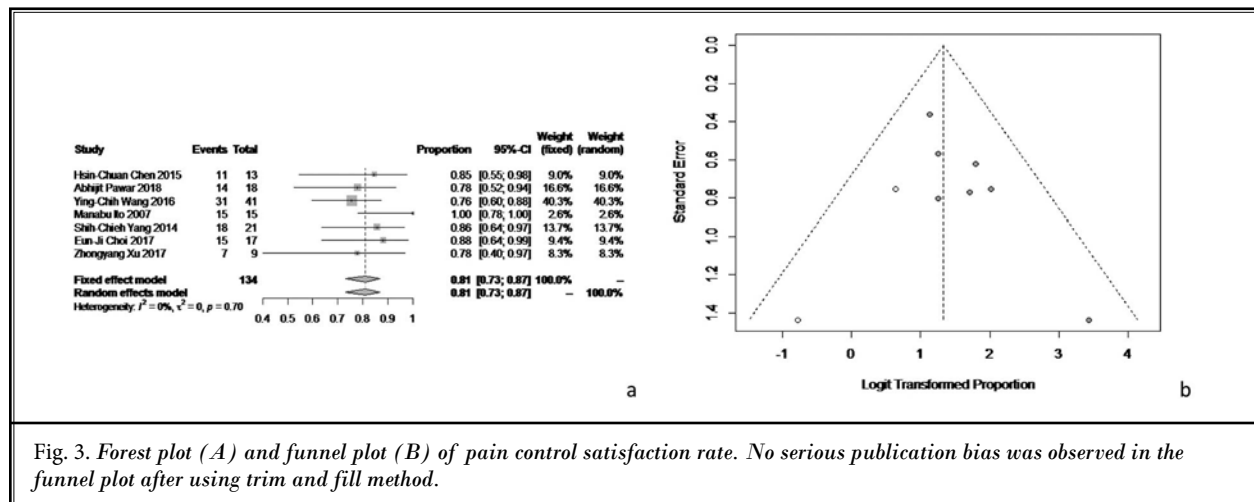


Fig. 3. Forest plot (A) and funnel plot (B) of pain control satisfaction rate. No serious publication bias was observed in the funnel plot after using trim and fill method.

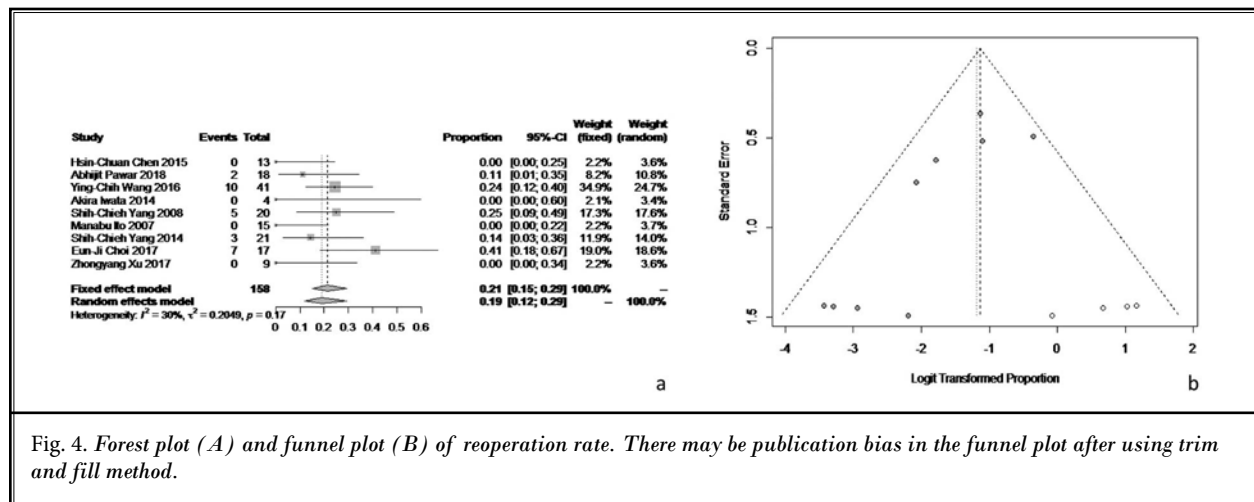


Fig. 4. Forest plot (A) and funnel plot (B) of reoperation rate. There may be publication bias in the funnel plot after using trim and fill method.

The funnel plot after using the trim and fill method of the reoperation rate indicated possible mild publication bias (Fig. 4B), which may also be caused by the small sample size or the different parameters and methods in different studies. The sensitivity analysis was performed to determine the robustness of the overall treatment effects because of the small sample size in the included studies. After eliminating the included studies one by one, the sensitivity analysis of reoperation rate was 21%, with 95% CI of 15% to 29%, which demonstrated the stability of the analysis results (Table 1).

Complications

There are too few articles that reported the complications to carry out a meta-analysis. Yang et al (12) reported 3 patients with transient paresthesia in the affected lumbar segment. The other complication referred to in the studies (7,15,19) was local kyphosis. Chen et al (7) reported one of 13 patients had a kyphotic change > 10° at last postoperative follow-up. Ito et al (15) reported 9 of 15 patients had kyphotic deformity, and local kyphosis ranged from 2° to 25° with an average of 12°. Fu et al (19) counted the local kyphosis angle of all 6 patients, which ranged from -15° to 10° (average, 1°).

Table 2 summarizes the outcomes of the single-arm studies.

DISCUSSION

This single-arm meta-analyses yield 9 studies with 158 patients who underwent PEDD. The important findings of these analyses were that the pooled event rate of positive bacteria culture, pain control satisfaction, and reoperation was 82%, 81%, and 21%, respectively. We also concluded that PEDD that accompanied few complications was relatively safe.

Treatment strategies of spinal infection still remain controversial. Conservative cases seem to be followed by mechanical back pain more often than surgical cases and develop more deformity long term (4).

Table 1. *The sensitivity analysis of reoperation rate.*

Trial	Proportion	95% CI	Tau ²	I ²
Omitting Chen et al (7)	0.2226	0.1576-0.3047	0.1533	26.6%
Omitting Pawar et al (8)	0.2269	0.1590-0.3129	0.2200	32.20%
Omitting Wang et al (9)	0.2003	0.1294-0.2968	0.3757	37.40%
Omitting Iwata et al (10)	0.2181	0.1541-0.2991	0.2494	37.10%
Omitting Yang et al (11)	0.2079	0.1418-0.2943	0.3283	38.20%
Omitting Ito et al (15)	0.2232	0.1580-0.3055	0.1356	24.30%
Omitting Yang et al (16)	0.2263	0.1574-0.3141	0.2656	35.10%
Omitting Choi et al (17)	0.1800	0.1209-0.2595	0.0015	0.30%
Omitting Xu and Zheng (18)	0.2211	0.1564-0.3029	0.1926	31.30%
Pooled estimate	0.2148	0.1522-0.2942	0.2049	30.50%

Table 2. *Outcomes summary of included single-arm studies.*

Pooled Event Rate	Number of Studies	Patients	Percentage	95% CI	Heterogeneity
Positive bacteria culture	8	149	0.82	0.75-0.88	I ² = 0; P = 0.78
Pain control Satisfaction	7	134	0.81	0.73-0.87	I ² = 0; P = 0.70
Reoperation	9	158	0.21	0.15-0.29	I ² = 30%; P = 0.17

However, surgical intervention is always associated with more complications, although overall mortality is lower in operated patients (1). PEDD, which is coupled with less complications and satisfactory clinical outcome, provides a minimally invasive surgical choice for the treatment of spinal infection (7-12).

There have been several attempts to treat spinal infections using minimally invasive surgical techniques. Valls et al (20) reported the technique of needle biopsy for vertebral infections in 1984. Yu et al (21) treated osteomyelitis by percutaneous suction aspiration in 2 patients. Staatz et al (22) published the technique of computed tomography (CT)-guided percutaneous catheter drainage in the management of spondylodiscitis abscesses. Then, there was a flood of new technologies including percutaneous transpedicular automated nucleotomy for debridement (23,24), percutaneous transpedicular discectomy and drainage (25,26), and percutaneous drainage and continuous irrigation (27,28). These have been approved as relatively efficient and safe procedures in the management of spinal infection; however, these procedures lack intraoperative virtual images monitoring for debridement of the lesion site. Since percutaneous endoscopic discectomy was first employed for treating uncomplicated herniated discs in the early 1980s (13), numerous minimally invasive percutaneous endoscopic procedures for lumbar

disc herniation have been developed. Several surgeons attempted to apply percutaneous endoscopic surgery to the management of spinal infections (15,19,29).

The diagnosis of spinal infection is usually delayed before finding a specific neurologic deficit because its onset of symptoms and signs, such as back pain and fever, are insidious and nonspecific (17). Early detection of causative organism is of important significance for the diagnosis and treatment of spinal infection. The most reliable tests for finding the causative organism are histologic examination and cultures of the samples taken from the infection sites. CT-guided biopsy is a less invasive procedure used to obtain specimens for pathogen identification; however, the rate of pathogen identification varies from 30% to 47% in most of these studies (11,30-33). Yang et al (11) compared the diagnostic value of CT guidance with that of endoscope guidance in 52 patients with suspected infectious spondylitis and found that causative bacteria were identified more frequently with percutaneous endoscopy than in CT-guided biopsy (90% vs. 47%). In our study, the positive bacteria culture rate of PEDD was 82%, well above that of CT-guided biopsy, its basic anastomotic with the Yang et al (11) research. Direct endoscopic observation makes possible the direct collection of sufficient amounts of samples from the infected region for a better possible diagnosis of the causative organism (12). Moreover,

PEDD can effectively eliminate the infected tissues and curette the bony end plates to enhance blood flow at the site of infection, which makes the infiltration of antibiotics to the infected areas more efficient (9,10,12). Therefore, a good clinical result is achieved.

To the best of our knowledge, this study is the first review of the efficacy of PEDD in the management of spinal infection. However, there are several limitations. First, all included studies were retrospective series with inherent methodological limitations. Second, the sample size and the number of studies that were found to be eligible was small. In addition, all included studies are single-arm, and further studies are necessary in large randomized controlled trials on comparing the efficacy of conservative therapy, PEDD, and open surgical intervention.

CONCLUSIONS

This systematic review provides evidence that PEDD not only has a high rate of causative-pathogen identification, but also provides satisfactory clinical outcome. Early PEDD intervention in spinal infection is encouraging; however, further studies in large randomized controlled trials on comparing the efficacy of conservative therapy, PEDD, and open surgical intervention are necessary.

Appendix 1. Characteristics of the included studies.

Trial	No. of total patients	Male/Female	Age (years)	Country	Recruitment period	No. of positive bacteria culture patients	No. of patients with satisfactory pain control	operation time (minutes)	Study design	No. of reoperation patients	Follow-up (months)
Hsin-Chuan Chen 2015	13	5/8	65.6	Taiwan China	October 2006 to March 2014	10	11	NR	Retrospective Study	0	42.5
Abhijit Pawar 2018	18	6/12	46	India	May 2015 to May 2017	16	14	52	Retrospective Study	2	17
Ying-Chieh Wang 2016	41	29/12	55.2	Taiwan China	August 2002 to August 2012	32	31	NR	Retrospective Study	10	24
Akira Iwata 2014	4	4/0	59.8	Japan	January 2001 to December 2009	4	NR	44	Retrospective Study	0	42.5
Shih-Chieh Yang 2008	20	12/8	63	Taiwan China	January 2001 to January 2006	18	NR	NR	Retrospective Study	5	36.8
Manabu Ito 2007	15	10/5	60	Japan	NR	11	15	58	Retrospective Study	0	24.6
Shih-Chieh Yang 2014	21	14/7	56.5	Taiwan China	January 2006 to December 2010	19	18	NR	Retrospective Study	3	43.1
Eun-Ji Choi 2017	17	11/6	70.4	Korea	November 2008 to November 2015	14	15	NR	Retrospective Study	3	3
Zhongyang Xu 2017	9	5/4	64.4	China	August 2014 to December 2016	NR	7	NR	Retrospective Study	0	1

Abbreviation: No. = number, NR = not reported

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