Aus der Klinik für Orthopädie und Unfallchirurgie
der Medizinischen Fakultät Charité – Universitätsmedizin Berlin

DISSERTATION

Evaluation of periprosthetic joint infection using bibliometric and meta-analysis

zur Erlangung des akademischen Grades
Doctor medicinae (Dr. med.)

vorgelegt der Medizinischen Fakultät
Charité – Universitätsmedizin Berlin

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Datum der Promotion: 17.09.2021

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ABKÜRZUNGSVERZEICHNIS

AUC	Area under the curve
BCB	Blood culture bottle
CI	Confidence interval
CORR	Clinical Orthopaedics and Related Research
CRP	C-reactive protein
DOR	Diagnostic odds ratio
H	Histological examination
IDSA	Infectious Disease Society of America
JBJS	Journal of Bone and Joint Surgery
JOA	Journal of Arthroplasty
M	Microbiological examination
NA	Not available
NLR	Negative likelihood ratio
P	Presence sinus tract or purulence around the prosthesis
PCR	Polymerase chain reaction
PJI	Periprosthetic joint infection
PICO	Patients, intervention, control, outcome
PLR	Positive likelihood ratio
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	Prospective Register of Systematic Reviews
PT	Periprosthetic tissue
QUADAS-2	Quality Assessment of Diagnostic Accuracy Studies-2
SROC	Summarized receiver operating characteristic
TKA	Total knee arthroplasty
UK	United Kingdom
USA	United States of America
WoS	Web of Science

Abstrakt (DEUTSCH)

Ziele: Der weltweite Forschungsstand zur periprothetischen Gelenkinfektion (PJI) ist bis jetzt nicht gut abgebildet. Die vorliegende Arbeit beschreibt den aktuellen Stand der Forschung zur PJI mithilfe bibliometrischer Instrumente und der Metaanalyse und wurde in drei Studien aufgeteilt. Ziel der ersten Studie war es, den globalen klinischen Zustand von PJI aus verschiedenen Perspektiven zu analysieren, nämlich aus Sicht von Autoren, Institutionen, Ländern, Fachzeitschriften, am häufigsten zitierten Publikationen, aktuellen Themen und Forschungsbereichen. Die zweite Studie zielte darauf ab, die Merkmale der PJI-Metaanalyse anhand von Informationen zu Autor(en), Zitaten, Land, elektronischer Datenbank, Fachzeitschrift, Stichwörtern, Anzahl der Studien, Institution(en), Suchalgorithmus, Software und verschiedenen Forschungsthemen mithilfe einer bibliometrischen Methode zu bestimmen. In der dritten Studie wurde eine diagnostische Metaanalyse durchgeführt, um den Wert von periprothetischem Gewebe in automatisierten Blutkultursystemen für die Diagnose von PJI zu beurteilen.

Die Methoden: Themenbezogene Begriffe wurden in den Datenbanken von Web of Science (WoS), PubMed, Scopus, und Embase recherchiert. Zur Analyse der Ergebnisse wurden die folgenden Software-Tools verwendet: VOSviewer, SPSS, Microsoft Excel, EndNote X7 und Meta-Disc.

Die Ergebnisse: Die erste Studie zeigte, dass die Vereinigten Staaten von Amerika die größte Anzahl von Artikeln veröffentlichte. Das Journal of Arthroplasty (JOA) veröffentlichte die meisten Artikel zum Thema PJI, während die Wissenschaftszeitschriften Clinical Orthopaedics und Related Research am häufigsten zitiert wurden. Der Research Interest Score korrelierte positiv mit der Anzahl der Zitationen. Die zweite Studie zeigte, dass Scopus in der Metaanalyse von PJI relevantere Forschungen als PubMed und WoS beinhaltete. China zählte als das Land mit den meisten Beiträgen, während die Universität Bristol als das Institut mit den größten Beitrag galt. Das JOA veröffentlichte die größte Anzahl von Metaanalysen. Die am häufigsten verwendete Datenbank war Embase, gefolgt von MEDLINE und Cochrane Library. Die meisten Forschungsaktivitäten konzentrierten sich auf Hüft- und Knieinfektionen. Die beliebtesten Themen waren dabei der Alpha-Defensin-Test, der Einsatz von Antibiotika und intraartikuläre Steroidinjektionen. In der dritten Studie wurden vier Studien in die Metaanalyse einbezogen. Die gepoolte diagnostische Sensitivität und Spezifität von periprothetischem Gewebe in Blutkulturflaschen für PJI betrug 70 % bzw. 97 %. Die Fläche unter der Kurve betrug 0,9537.

Schlussfolgerungen: Keine einzelne Datenbank konnte alle einschlägigen Publikationen abdecken, deswegen ist die Recherche in mehreren Datenbanken der ideale bibliometrische Ansatz. Diagnosebezogene Artikel stellen die hochaktuellsten Themen der klinischen Forschung in PJI dar. Die Bibliometrie der Metaanalyse zeigte, dass Alpha-Defensin, Antibiotikaeinsatz und Steroidinjektionen die derzeit am häufigsten erwähnten Themen sind. Die Inokulation von periprothetischem Gewebe in Blutkulturflaschen erweist sich als zuverlässige Diagnosemethode für PJI.

Abstract (ENGLISCH)

Aims: The global state of research in periprosthetic joint infection (PJI) is not well described. The present thesis describes the current state of research involving PJI using bibliometric tools and meta-analysis and is divided into three parts. In the first study, the objective was to analyze the global clinical state in PJI from multiple perspectives, namely authors, institutions, countries, journals, most cited publications, hot topics, and research areas. The second study aimed to determine the characteristics of meta-analysis in PJI from information on author(s), citations, country, electronic database, journal, keywords, number of studies, institution(s), search algorithm, software, and subject information using a bibliometric method. In the third study, a diagnostic meta-analysis was performed to assess the value of periprosthetic tissue in automated blood culture systems for diagnosing PJI.

Methods: Subject-related terms were searched in the databases of Web of Science, PubMed, Scopus, and Embase. Software tools used to analyze the results were VOSviewer, SPSS, Microsoft Excel, EndNote X7, and Meta-Disc.

Results: In the first study, the United States of America was shown to publish the most papers. The Journal of Arthroplasty (JOA) published the most articles related to the topic PJI, and Clinical Orthopaedics and Related Research was the most highly cited journal. The Research Interest score was positively associated with citation counts. The second study demonstrated that Scopus covered more relevant research than PubMed and WoS in the meta-analysis of PJI. China provided the most contributions as a country, whereas the University of Bristol contributed most as an institute. The JOA published the greatest number of meta-analyses. Moreover, the most commonly used database was Embase, followed by MEDLINE and the Cochrane Library. Most investigators focused on hip and knee infection. The most popular topics were the alpha-defensin test, antibiotic use, and intra-articular steroid injections. In the third study, four studies were included in the meta-analysis. The pooled diagnostic sensitivity and specificity of periprosthetic tissue in blood culture bottles for PJI was 70% and 97%, respectively. The area under the curve was 0.9537.

Conclusions: The ideal bibliometric approach is the use of multiple databases for searching. No single database could cover all interrelated publications. Diagnosis-related articles are the hot topic of clinical research in PJI. Bibliometrics of the meta-analysis showed that alpha-defensin, antibiotic use, and steroid injections are currently the most popular topics. Inoculation of periprosthetic tissue in blood culture bottle was demonstrated to be a reliable diagnostic method for PJI.

Evaluation of periprosthetic joint infection using bibliometric and meta-analysis

1. Introduction

Arthroplasty is a routine surgical procedure performed by orthopaedic surgeons that greatly enhances the quality of life and joint functions of patients with joint disease [1]. However, complications after arthroplasty are of concern, especially infection. Periprosthetic joint infection (PJI) is a debilitating complication that occurs following joint replacement and is usually accompanied by multiple surgical procedures and a high mortality rate [2–4]. A previous report found that PJI has become a major cause of failure after knee arthroplasty and one of the top three reasons for revising total hip replacement [5]. An increasing number of scholars have focused on advances in the diagnosis and management of PJI [6–8]. Nonetheless, the global research trend in PJI has not yet been explored. Bibliometrics is a practical means of evaluating the characteristics and research direction of a topic through publications [9]. Despite multiple orthopaedic studies assessed using bibliometrics [10–12], bibliometrics of PJI has not yet been performed. In the current era of social media, an increasing number of scholars are reading, interacting, or commenting on publications online, with citations ceasing to be the single assessment indicator in academic articles [13]. The Research Interest score and Altmetric score are two networking tools used to assess the academic impact of publications. Regrettably, the correlation between these two network metrics and citations remains undiscovered. Therefore, the first study aimed to provide a clinical perspective on PJI and determined the relationship among network metrics, impact factor, publication year, and citations in the most cited articles.

Meta-analysis is a statistical approach that collects and analyses results from multiple studies to determine the perspective or relationship between variables. Published meta-analyses most likely indicate popular or controversial topics in a particular field [14,15]. To date, no research literature has utilized bibliometric studies in PJI meta-analyses. The choice of database and the search method used are crucial factors in bibliometrics and meta-analysis. Because of discrepancies in various databases, most bibliometric studies use a single database to analyse publications

[16,17]. Thus, such differences between various databases have remained unclear. Accordingly, the second study aimed to conduct a bibliometric study of the meta-analysis of PJI and determine the most appropriate database for bibliometric analysis.

Although tissue culture is a conventional method for bacterial detection in cases of PJI with somewhat suboptimal diagnostic accuracy, the sensitivity typically ranges from 61% to 75% [18–21]. A previous meta-analysis found that sonication fluid in blood culture bottles (BCBs) was more accurate than conventional media [22], whereas the diagnostic accuracy of periprosthetic tissue (PT) in BCBs was unknown. The purpose of the third study was to investigate the diagnostic value of PT in BCBs for PJI.

2. Matter and methodology

The WoS, PubMed, Scopus, and Embase electronic databases were used, and the search strategy of each study is depicted in **Table 1**. Two reviewers independently extracted and screened the data, and any discrepancies were adjudicated by the third investigator.

Name	Medical subject headings or text keywords	Timespan	Electronic databases (search results)
First study	"periprosthetic joint infection", "prosthetic joint infection"	From 1998 to 2018	WoS (3245)
Second study	"arthroplasty", "joint prosthesis", "joint replacement", "periprosthetic joint", "prosthetic joint", "infection", "infectious", "infected", "meta analysis", "meta-analysis"	From inception to December 2019	WoS/PubMed/Scopus (117)
Third study	"periprosthetic joint infection", "prosthetic joint infection", "orthopaedic implant", "infection", "tissue", "periprosthetic tissue", "blood culture vials", "blood culture bottles", "blood culture system"	From inception to October 2018	WoS/PubMed/Embase (4)

Table 1. Search strategy and results in each study.

2.1 First study (bibliometric analysis of clinical research and trends in PJI)

Information on PJI was exported from the WoS database, and fundamental research related to *in vitro* testing and animal experiments was excluded. Visualized coupling, co-citation, and co-occurrence analyses were performed using VOSviewer software (Leiden University, the Netherlands). Co-citation analysis occurs when two documents are referenced together in a third document [23]. Coupling analysis is based on the number of identical references between two documents [24]. Co-occurrence analysis is performed using all keywords to identify high-frequency subject terms and research directions [10].

Numerical results of the Research Interest score and Altmetric score were obtained from the internet. Logistic regression was performed to assess the relationships among altmetric tools, impact factor, publication year, and citations using SPSS software (IBM, SPSS, Chicago, IL, USA).

2.2 Second study (bibliometric study of meta-analysis publications from PJI)

All records from the databases were exported in text format. Microsoft Excel (Microsoft, Redmond, WI, USA) and EndNote X7 softwares (Thomson Reuters, USA) were used for bibliometrics. The following information was collected from PJI meta-analyses: author, citations, country, electronic database, impact factor, journal, keywords, number of studies, institution, search algorithm, software, subject information, title, and year of publication.

2.3 Third study (meta-analysis of PT in blood culture bottles for diagnosing PJI)

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was used to guide our methods for this meta-analysis [25].

2.3.1 Research question development

The following PICO (patients, intervention, control, outcome) format was applied: P, patients with prosthetic joint infection; I, the diagnostic test of PT in BCB; C, diagnostic standard; and O, sensitivity and specificity of PT in BCBs for diagnosing PJI.

2.3.2 Study selection and quality assessment

The inclusion criteria were as follows: (1) clear definition of PJI diagnostic criteria; (2) calculation of the numeric value of true-positive, true-negative, false-positive, and false-negative outcomes; and (3) publications in the English language. The exclusion criteria were as follows: (1) article type was a case report, system review, or comment; and (2) study was irrelevant to PT in BCBs, or data of diagnostic values were not available.

All of the identified studies were evaluated according to the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies-2) guidelines [26].

2.3.3 Statistical analysis

To assess the diagnostic value of PT in BCBs, the pooled sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR), and summarized receiver operating characteristic (SROC) curves were analysed using Meta-Disc software (version 1.4, Unit of Clinical Biostatistics team, Madrid, Spain) [27]. In the case of heterogeneity among the studies, the random-effects model was applied.

3. Results

According to the search strategy, the search results of each study are presented in **Table 1**.

3.1 First study (bibliometric analysis of clinical research and trends in PJI)

3.1.1 Countries and institutions

All clinically related data of PJI were derived from 58 countries (**Figure 1**), with the United States of America (USA; 1226) being the greatest contributor, followed by Germany (358) and the United Kingdom (UK; 298). Coupling analyses of the top three countries with the highest total link strength were the USA, Germany, and the UK.

Figure 1. Global distribution of clinical PJI research. The countries contributing to this field are indicated in blue. Most studies originated from Europe (n = 32), followed by Asia (n = 16) and the Americas (n = 9).

Of the top 10 most productive institutions, seven institutions were in the USA, whereas the remaining three were in Europe. The Rothman Institute published the most papers (245), followed by the Mayo Clinic (219).

3.1.2 Authors

The author with the greatest number of publications was Parvizi J (204), followed by Hanssen AD (85) and Osmon DR (77). Coupling analysis revealed the top three authors with the highest total link strengths were Parvizi J, Osmon DR, and Hanssen AD. Parvizi J was also the author with the highest total link strength in co-citation analysis, followed by Zimmerli W and Trampuz A.

3.1.3 Journals

Among 362 different journals, the *Journal of Arthroplasty* (JOA) had the largest number of publications (466), with an impact factor of 3.524. The journal with the highest impact factor was the *New England Journal of Medicine* (70.67), which accounted for six publications.

Coupling analysis and co-citation analysis showed the top three journals with the

greatest total link strengths to be JOA, *Clinical Orthopaedics and Related Research* (CORR), and the *Journal of Bone and Joint Surgery* (JBJS). The top journal in coupling analysis was JOA, whereas CORR was the top journal in co-citation analysis.

3.1.4 Top 50 most-cited publications

The 50 most cited articles were published in 14 journals. The first and second most-cited papers were from the *New England Journal of Medicine* [18,28]. JBJS had the greatest number of publications with 15, followed by *Clinical Infectious Diseases* and CORR, with seven articles each.

Multivariate analysis demonstrated no significant differences between the impact factor or the year and number of times cited ($P > 0.05$). Citations and Research Interest scores showed a positive correlation, while a negative correlation was observed between citations and the Altmetric Attention score. In the list of the most cited publications, Twitter was present on 16 occasions, and Facebook was present on seven occasions.

3.1.5 Hot topics and research areas

VOSviewer identified popular topics and research fields, and the identified keywords were divided into three groups: “diagnosis”, “treatment”, and “risk factor and prevention” (Figure 2). The most common keyword was “diagnosis” from 2010 to 2018, followed by “risk factor”.

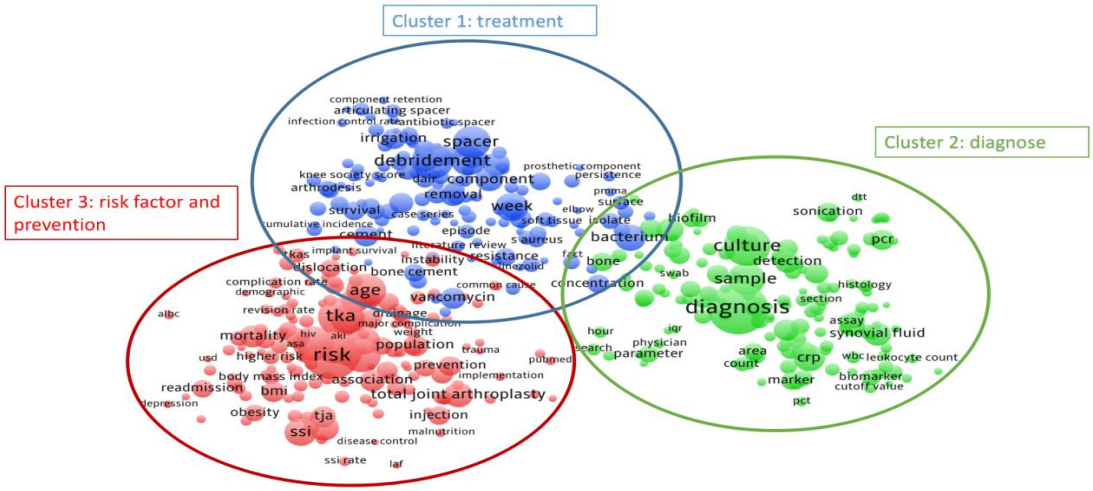

Figure 2. Co-occurrence analysis of PJI clinical studies**.** In the "diagnosis" cluster (green), the most commonly used keywords were culture, CRP (C-reactive protein), and synovial fluid culture, whereas the most frequently used keywords in the cluster "treatment" (blue) were spacer, debridement, and week. The primary keywords for the "risk factor and prevention" cluster (red) were complications, total knee arthroplasty (TKA), and age.

3.2 Second study (bibliometric study of meta-analysis publications from PJI)

3.2.1 Database

Of all of the databases, Scopus contained the largest number of PJI meta-analysis studies. The combination of PubMed and Scopus covered all of the relevant research, while the Web of Science and PubMed groups had the most missed articles (Figures 3A and 3B).

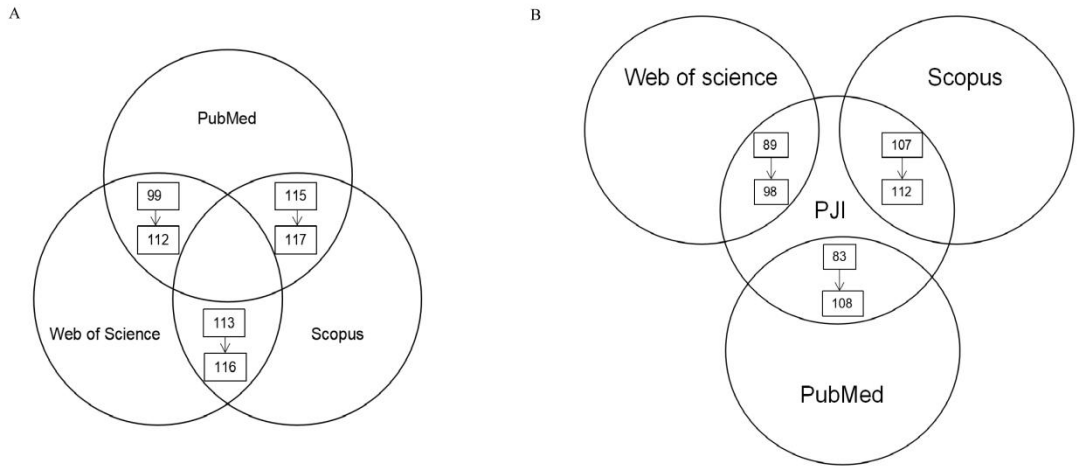

Figure 3 Number of PJI meta-analyses in combined (A) and single (B) databases (with or without search algorithms).

3.2.2 Countries and institutions

Nineteen countries and seventy-six institutions published PJI-related meta-analyses. The top three countries with the most contributions were China, the USA, and the UK. Fourteen organizations published more than one meta-analysis study, with half from

China. The University of Bristol in the UK had the largest number of meta-analyses (n = 11), followed by the Shanghai 6th People's Hospital in China (n = 8).

3.2.3 Authors

The number of collaborators in meta-analysis studies ranged from 2 to 37. The top three comprising the largest numbers of collaborative authors were four (n = 27), followed by six (n = 25) and five (n = 20). The author with the most first authorships was Kunutsor SK (n = 10), followed by Qu X (n = 3). Ten first authors had more than one publication, with half stemming from Chinese institutions.

3.2.4 Journals

Among 54 different journals, the top three journals with the most contributions were JOA (n = 15), JBJS (n = 8), and *PLoS ONE* (n = 7). From submission to acceptance, the *Journal of Clinical Medicine* (16 days) had the shortest acceptance time for all meta-analyses, followed by the *Journal of Computational and Theoretical Nanoscience* with 18 days.

3.2.5 Most-cited publications

One hundred three meta-analyses had citation information from Google Scholar, and 41 publications were referred to more than 20 times. The article “Antibiotic prophylaxis for wound infections in total joint arthroplasty: a systematic review” had the most citations (n = 264) [29], followed by the meta-analysis by Parvizi and coworkers (n = 235) [30].

3.2.6 Search algorithm and keywords

The topic of the search strategy can be categorized into five groups: PJI-related terms, diagnosis, prevention, risk factor, and outcome. The top five most widely used author keywords were PJI, meta-analysis, total knee arthroplasty, arthroplasty, and infection.

3.2.7 Database and software

In PJI meta-analyses, three databases were most commonly searched. The top three most commonly used databases were Embase, MEDLINE, and Cochrane Library. The Cochrane, Embase, and MEDLINE/PubMed groups (n = 10) were the most routinely searched databases, followed by Embase and MEDLINE (n = 6). STATA, REVMAN,

and Meta-Disc were the top three most widely used software programs.

3.2.8 Subject analysis

Surgical site information was found in 112 papers. The knee and hip were the most researched subjects, with more than 89 papers found. Ninety-eight diagnostic tests were analysed from 40 meta-analyses. No diagnostic test had sensitivity and specificity of 100%. Most studies focused on preoperative methods (n = 72), with synovial fluid alpha-defensin having the highest sensitivity among all of the preoperative examinations. Tissue culture was the most sensitive method in 14 reimplantation tests, whereas tissue polymerase chain reaction (PCR) was most sensitive in 12 intraoperative examinations. The most popular test used was joint fluid (n = 16), followed by diagnostic imaging (n = 10) and PT (n = 7).

Twenty-three meta-analyses described sixty-four PJI-related risk factors, whereas 17 meta-analyses showed nine preventive measures. The most popular topics were steroid injections and antibiotic use in risk factors and prevention. Of these topics, the majority were associated with the hip and the knee. From 26 contrastive studies, there was no significant difference detected among 13 comparison studies. Controversial issues included whether bone cement should be implemented in surgery, cement spacer type, and one- or two-stage exchange.

3.3 Third study (meta-analysis of PT in BCB for diagnosing PJI)

A total of 479 articles were identified following the database search. After excluding duplicates, 75 articles were screened via their abstracts. Following full article review, 14 papers were excluded because they were unrelated to the research topic or had a lack of available data [21,31–43]. Finally, four publications met the inclusion criteria and were included in the analysis (Figure 4) [44–47].

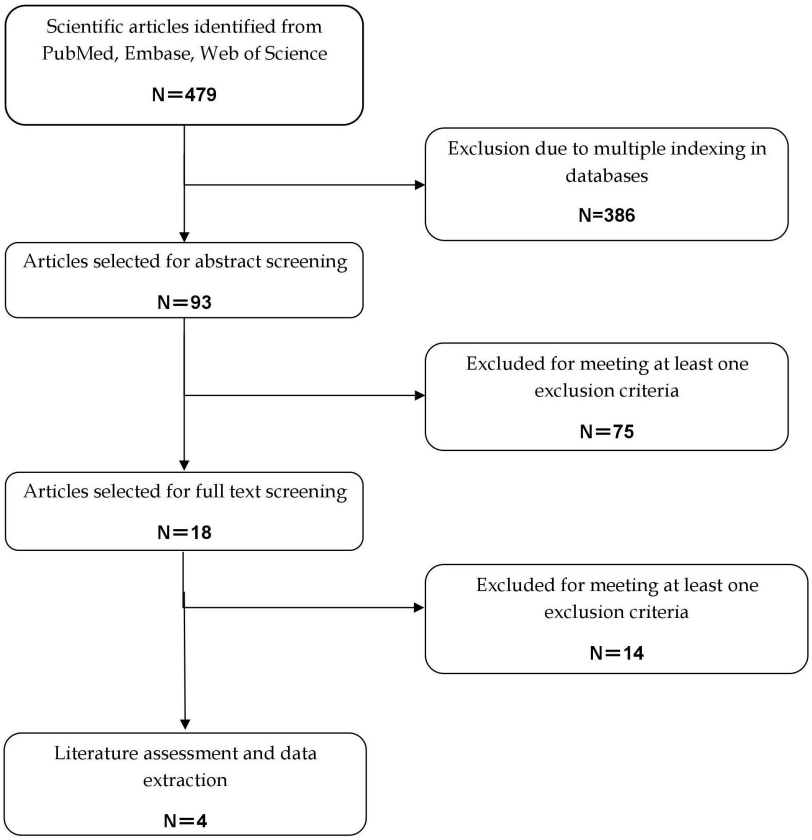

Figure 4. Flow diagram of the selection process for eligible studies

All of the eligible resources were prospective studies published between 2011 and 2018. Two studies were from the USA [44,45] with the remainder from the UK [46,47]. The surgical location encompassed the ankle, elbow, hip, knee, and shoulder. Antibiotic use was identified in three research papers (Table 2). Diagnostic results extracted from each study are summarized in Table 3. The QUADAS-2 tool demonstrated the high quality of each article.

First author	Year	Country	Study design	Surgical site	Received antibiotics	Diagnostic standard
Yan Q	2018	USA	Prospective study	Hip/knee/shoulder/elbow	Yes	IDSA
Minassian AM	2014	UK	Prospective study	Hip/ankle/shoulder	Yes	P, H, M
Hughes HC	2011	UK	Prospective study	Hip/knee	NA	H
Peel TN	2016	USA	Prospective study	Hip/knee/shoulder/elbow	Yes	IDSA

H, histological examination; **IDSA**, Infectious Disease Society of America; **M**, microbiological examination; **NA**, not available; **P**, presence of sinus tract or purulence around the prosthesis.

Table 2. Characteristics of four studies in the current meta-analysis for the diagnosis of PJI using BCB.

Reference	TP	FP	FN	TN
Yan Q	69	5	35	120
Yan Q	56	2	30	99
Yan Q	13	3	5	21
Minassian AM	66	3	13	240
Hughes HC	20	3	3	138
Peel TN	71	3	46	249

TP, True-positive; **FP**, False-positive; **FN,** False-negative; **TN,** True-negative.

Table 3. Diagnostic results in BCB for each study.

Based on the degree of heterogeneity, the random-effects model was utilized. The pooled analysis of the four studies revealed (Figure 5) a sensitivity of 0.70 (95% confidence interval [CI]: 0.66–0.75), specificity of 0.97 (95% CI 0.95–0.98), PLR of 20.98 (95% CI 11.52–38.20), NLR of 0.28 (95% CI 0.20–0.40), and DOR of 92.26 (95% CI 43.93–193.78). The AUC of SROC was 0.9537 (standard error, 0.0305).

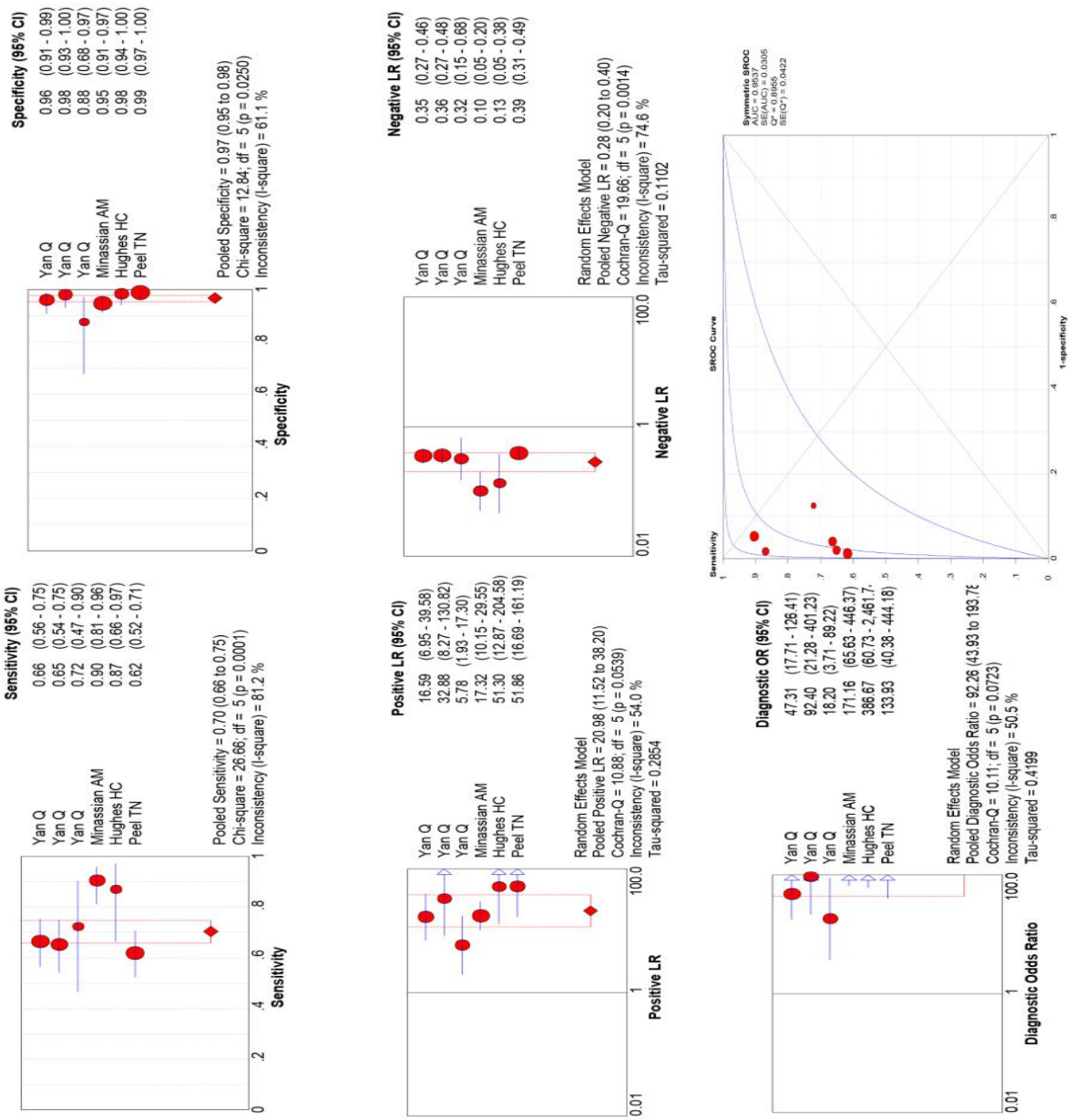

Figure 5. Pooled diagnostic parameters of PT BCB

4. Discussion

The first bibliometric study of clinically based PJI demonstrated the contribution of 58 countries. Organizations and scholars from the USA showed a significantly higher impact than those from other countries. The journals JOA, CORR, and JBJS were found to pay the most attention to clinical studies focusing on PJI. Coupling and co-citation analysis indicated that articles published in the JOA were most related to the topic. Furthermore, CORR had the strongest academic impact. The journal with

the highest impact factor was the *New England Journal of Medicine*, with publications ranking in the first and second positions for the most-cited papers [18,28]. Multivariate analysis of the top 50 most-cited PJI research articles indicated a positive correlation between citation counts and the Research Interest score, with the Research Interest score potentially a supplementary indicator aiding scholars in assessing articles. Information from the Altmetric website found that most PJI researchers used Twitter instead of Facebook to share knowledge. A recent study also showed that the use of Twitter in scholarly communication is more frequent [48]. Three major themes emerged in PJI clinical research based on the keyword results: “diagnosis”, “treatment”, and “risk factor and prevention”. The most frequently used keyword between 2010 and 2018 was “diagnosis”, potentially implying that diagnosis-related publications were simply more popular.

The second bibliometric study presents 117 PJI meta-analyses from three databases (PubMed, Scopus, and Web of Science). Interestingly, no single database was able to cover all of the relevant publications. Scopus had the greatest number of meta-analyses on PJI; however, only the combination of Scopus and PubMed covered all of these databases' results. A multiple database search was superior to the use of a single database. Most research groups used three databases for searches. Embase, MEDLINE, and Cochrane were the most commonly used databases, either alone or in combination. The available search algorithm was exported to provide scholars with a guide for further literature searches and study designs. The current research found China to be the most active country in meta-analyses of PJI. Furthermore, the University of Bristol in the UK had the largest number of publications in this area. Our first study showed that the diagnosis of PJI was a popular topic during the investigated years. In contrast, the second bibliometric study exported all of the diagnostic meta-analyses to further aid scholars in providing insight into the diagnostic methods and clinical value in PJI. Our observations suggest that joint fluid samples are most commonly used in diagnostic meta-analyses. Furthermore, the most researched test was synovial fluid alpha-defensin, with the greatest sensitivity for PJI diagnosis [49]. Tissue PCR and tissue culture were the most sensitive intraoperative and reimplantation tests, respectively [50,51]. Since no single test could achieve an ideal result, new diagnostic methods require further improvement and development. Concerning the subject, most of the research has focused on preventative measures of

the effect of systemic or local antibiotic use and whether steroid injections pose a risk factor for PJI. The top three most controversial topics were cement use, cement spacer type, and one- or two-stage exchange arthroplasty.

In the third study, a meta-analysis determined that PT in BCBs had high diagnostic value for PJI, with sensitivity of 70% and specificity of 97%. PT in BCB appears to be a better method than conventional tissue culture. Previous research has found that the sensitivity of PT in BCBs is higher than that of direct solid media, cooked meat broth, and fastidious anaerobic broth (87% *vs*. 39%, 83%, and 57%, respectively) [47]. A prospective cohort study found that PT in BCBs was not only more sensitive than traditional culture media of aerobic and anaerobic agars and thioglycolate culture but also had a faster time for the detection and identification of microorganisms [44]. Minassian et al. [46] also supported the thesis that the PT in BCBs could rapidly detect microorganisms, the majority within three days. In general, most research has shown that the sensitivity of traditional tissue is lower than that of sonicated fluid in the diagnosis of PJI, particularly in samples collected after antibiotic treatment [18]. However, the use of PT in BCBs is likely to result in better diagnostic accuracy. Yan et al. [45] reported that there was no statistically significant difference in sensitivity between PT in BCBs and sonicate fluid culture in patients who received antimicrobial therapy (71.1 *vs.* 76.3%, respectively. $P = 0.41$), with 27 positive cultures in PT in BCBs and 29 in sonicate fluid. The Infectious Diseases Society of America guidelines recommend that five or six periprosthetic specimens be collected during revision arthroplasty [7]. Nevertheless, using the BCB method, Peel and colleagues [41] observed that the greatest diagnostic accuracy was observed when using three PTs. In contrast, conventional PT culture techniques require four tissue samples, hence demonstrating the suitability and superiority of PT in BCBs. In an additional study from Peel et al. [36], a further advantage of PT in BCBs over conventional techniques was described, with enhanced work efficiency. The automatic PT BCB system could reduce the total staff time by a mean of 60.1%.

There were several potential limitations of the present thesis. First, the first bibliometric analysis was performed using the single database of WoS; therefore, literature from other databases is potentially absent. In the bibliometrics of the meta-analysis of PJI, we further found that the optimal method for bibliometrics was to use multiple databases for searches. Next, the second study presented the results of

the PJI meta-analysis from diagnostic methods, risk factors, prevention measures and contrastive studies, while the potential heterogeneity in each meta-analysis was not considered. Third, the first and second bibliometric analyses focused on clinical research and meta-analysis; however, the comprehensive analysis still requires further exploration. Fourth, the protocol for the present meta-analysis was not registered on the Prospective Register of Systematic Reviews (PROSPERO). Fifth, the meta-analyses only screened previous publications in English, with some potentially relevant studies likely missed. Finally, the diagnostic value of PT in BCBs was found to hold great potential for the diagnosis of PJI and better microbial detection than conventional tissue culture. Since the number of eligible studies was limited, further research is required to confirm our findings.

5. Conclusions

No single database could cover all related articles, and the best form of bibliometric analysis is the use of multiple databases for the search process. The USA and China made the greatest contributions to clinical research and meta-analysis, respectively. The bibliometric analysis of clinical studies established the most popular topic within PJI to be diagnosis, and meta-analysis presented the subjects of the alpha-defensin test, antibiotic use, and intra-articular steroid injections to be the most popular topics. PT in BCBs appears to be a promising tool for the diagnosis of PJI. Further studies should be conducted to demonstrate the current diagnostic meta-analysis results.

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Eidesstattliche Versicherung

„Ich, Cheng Li, versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema: “Evaluation of periprosthetic joint infection using bibliometric and meta-analysis” selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe.

Alle Stellen, die wörtlich oder dem Sinne nach auf Publikationen oder Vorträgen anderer Autoren beruhen, sind als solche in korrekter Zitierung (siehe „Uniform Requirements for Manuscripts (URM)“ des ICMJE -*www.**icmje**.org*) kenntlich gemacht. Die Abschnitte zu Methodik (insbesondere praktische Arbeiten, Laborbestimmungen, statistische Aufarbeitung) und Resultaten (insbesondere Abbildungen, Graphiken und Tabellen) entsprechen den URM (s.o) und werden von mir verantwortet.

Meine Anteile an den ausgewählten Publikationen entsprechen denen, die in der untenstehenden gemeinsamen Erklärung mit dem Betreuer, angegeben sind. Sämtliche Publikationen, die aus dieser Dissertation hervorgegangen sind und bei denen ich Autor bin, entsprechen den URM (s.o) und werden von mir verantwortet.

Die Bedeutung dieser eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unwahren eidesstattlichen Versicherung (§156,161 des Strafgesetzbuches) sind mir bekannt und bewusst.“

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Ort, Datum Unterschrift

Anteilserklärung

Cheng Li hatte folgenden Anteil an den folgenden Publikationen:

Publikation 1:

Li C, Ojeda-Thies C, Renz N, Margaryan D, Perka C, Trampuz A. The global state of clinical research and trends in periprosthetic joint infection: A bibliometric analysis. Int J Infect Dis. 2020;S1201-9712(20)30320-9.

Contribution Detail: Cheng Li proposed the design, performed the literature search and literature selection from the Web of Science database, and collected Research Interest scores from ResearchGate (https://www.researchgate.net/) and Altmetric scores using the Altmetric bookmarklet (https://www.altmetric.com). He identified relevant articles and presented a flowchart of the study inclusion process (Figure 1). In addition, he summarized the data (Tables 1–7, 9, and 10), was involved in multivariate statistical analysis (SPSS), In addition, he used Microsoft Excel and VOSviewer to analyze data from Web of Science, and presented data as figures. Further, he wrote the manuscript independently and modified the revision paper.

Publikation 2:

Li C, Ojeda-Thies C, Xu C, Trampuz A. Meta-analysis in periprosthetic joint infection: a global bibliometric analysis. J Orthop Surg Res. 2020;15(1):251. Published 2020 Jul 10.

Contribution Detail: Cheng Li conceived and designed the presented idea, participated in the data information search and screening from PubMed, Scopus, and Web of Science, .extracted study results (title, author, year of publication, country, institution, journal, keywords, citations, state of the manuscript, language, number of studies, impact factor, software, database, search algorithm, and subject information), and performed bibliometric analysis using Microsoft Excel and EndNote X7. In addition, he created all figures and tables in the manuscript. Further, he wrote the paper and modified the revised manuscript.

Publikation 3:

Li C, Ojeda-Thies C, Trampuz A. Culture of periprosthetic tissue in blood culture bottles for diagnosing periprosthetic joint infection. BMC Musculoskelet Disord. 2019;20: 299.

Contribution Detail: Cheng Li drafted the study protocol, performed the database search, extracted study results (first author, year of publication, country, enrollment period, number of total cases and infected cases, location, whether to use antibiotics, diagnostic criteria or method, number of tissue samples, antibiotic treatment before sample collection, incubation time, sensitivity and specificity of tissue culture), and summarized data in tables and figures. He identified relevant articles, presented a flowchart in Figure 1, assessed the quality of included studies using the QUADAS-2 tool, and performed and presented the analysis (Figure 2), In addition, he analyzed the sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio and summary receiver operating characteristic of included studies with Meta-Disc software, depicting the results in figures (3–8). Cheng Li drafted and revised the manuscript.

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Unterschrift, Datum und Stempel des betreuenden Hochschullehrers

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Unterschrift des Doktoranden/der Doktorandin

Ausgewählte Publikationen

Publikation 1:

Li C, Ojeda-Thies C, Renz N, Margaryan D, Perka C, Trampuz A.

The global state of clinical research and trends in periprosthetic joint infection: A bibliometric analysis

Int J Infect Dis. 2020;S1201-9712(20)30320-9.

DOI: https://doi.org/10.1016/j.ijid.2020.05.014

First authorship.

Impact Factor: 3.202

Rank in Category (INFECTIOUS DISEASES): 38 of 93

Quartile in Category: Q2

Publikation 2:

Li C, Ojeda-Thies C, Xu C, Trampuz A.

Meta-analysis in periprosthetic joint infection: a global bibliometric analysis

J Orthop Surg Res. 2020;15(1):251. Published 2020 Jul 10.

DOI: https://doi.org/10.1186/s13018-020-01757-9

First authorship.

Impact Factor: 1.777

Rank in Category (ORTHOPEDICS): 46 of 82

Quartile in Category: Q3

Publikation 3:

Li C, Ojeda-Thies C, Trampuz A.

Culture of periprosthetic tissue in blood culture bottles for diagnosing periprosthetic joint infection

BMC Musculoskelet Disord. 2019;20: 299.

DOI: https://doi.org/10.1186/s12891-019-2683-0

First authorship.

Impact Factor: 2.002

Rank in Category (ORTHOPEDICS): 44 of 82

Quartile in Category: Q3

Lebenslauf

My curriculum vitae does not appear in the electronic version of my paper for reasons of data protection.

Komplette Publikationsliste

Article list (first author):

1. **Li C**, Renz N, Trampuz A. et al. The value of conventional radiographs for diagnosing internal fixation-associated infection. BMC Musculoskelet Disord 22, 411 (2021). https://doi.org/10.1186/s12891-021-04170-3 (IF:1.879)

2. **Li C**, Cheng Y, Li Z, Margaryan D, Perka C, Trampuz A. The Pertinent Literature of Enhanced Recovery after Surgery Programs: A Bibliometric Approach. Medicina. 2021; 57(2):172. https://doi.org/10.3390/medicina57020172 (IF:1.205)

3. **Li C**, Margaryan D, Ojeda-Thies C. et al. Meta-analysis of serum and/or plasma D-dimer in the diagnosis of periprosthetic joint infection. J Orthop Surg Res 15, 298 (2020). https://doi.org/10.1186/s13018-020-01808-1 (IF:1.777)

4. **Li C**, Ojeda-Thies C, Renz N, Margaryan D, Perka C, Trampuz A. The global state of clinical research and trends in periprosthetic joint infection: A bibliometric analysis. Int J Infect Dis. 2020;S1201-9712(20)30320-9. doi:10.1016/j.ijid.2020.05.014 (IF:3.202)

5. **Li C**, Ojeda-Thies C, Xu C, Trampuz A. Meta-analysis in periprosthetic joint infection: a global bibliometric analysis. J Orthop Surg Res. 2020;15(1):251. Published 2020 Jul 10. doi:10.1186/s13018-020-01757-9 (IF:1.777)

6. **Li C**, Renz N, Trampuz A, Ojeda-Thies C. Twenty common errors in the diagnosis and treatment of periprosthetic joint infection. Int Orthop. 2019. doi:10.1007/s00264-019-04426-7 (IF: 2.384)

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8. **Li C**, Renz N, Trampuz A. Management of Periprosthetic Joint Infection. Hip Pelvis. 2018;30: 138–146.

9. **Li C**, Renz N, Thies CO, Trampuz A. Meta-analysis of sonicate fluid in blood culture bottles for diagnosing periprosthetic joint infection. J Bone Jt Infect. 2018;3: 273–279.

10. **Li C**, Trampuz A. 口袋指南：德国骨折术后内置物相关感染的诊疗指(Pocket Guide to

11. Diagnosis and Treatment of implant-associated infections after fracture fixation). 中华创伤骨科杂志,2020,22 (05): 375-378. DOI: 10.3760/cma.j.cn115530-20191113-00411.(Article in Chinese)

12. **Li C**, Trampuz A. 人工关节置换术后假体周围感染的临床诊断(Clinical diagnosis of periprosthetic joint infection after joint replacement). 中华关节外科杂志(电子版),2019,13(06):715-723.(Article in Chinese)

13. **Li C**, Trampuz A. 关节穿刺在假体周围感染诊断及治疗中的应用与意义 (Application and significance of joint puncture in the diagnosis and treatment of periprosthetic joint infection).中国组织工程研究,2019,23(36):5868-5874.(Article in Chinese)

14. **Li C**, Renz N, Trampuz A. 超声裂解法在诊断假体周围感染的应用(The application of sonication in diagnosis of periprosthetic joint infection). 实用骨科杂志,2019,25(08):724-728.(Article in Chinese)

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Book list:

Zhang XL, Wang KZ, Parvizi J, Gehrke T. Prosthetic Joint Infection—Practice and Considerations. Shanghai Scientific & Technical Publishers; 2019.

Chapter 10: New Progress in Etiological Diagnosis

Chapter 11: Diagnosis process--Practice and Considerations

Chapter 12: PJI Diagnosis--European Experience

Danksagung

I would first like to extend my sincere gratitude to my first supervisor, Prof. Dr. Andrej Trampuz, for guiding my research and supporting the project as well as for providing me with opportunities to present, participate in writing the book on periprosthetic joint infection, and demonstrate my research in international meetings.

I would also like to thank my second supervisor PD Dr. Serafeim Tsitsilonis for providing me with the opportunity to take part in clinical practice and for instructing me patiently.

Furthermore, I would like to express my sincere thanks to Dr. Cristina Ojeda-Thies, who taught me so many skills from preparing manuscripts to responding to reviewers of revision articles during the entire publishing process of our papers. Also, I would like to thank Dr. Sandra Kamhieh-Milz and Dr. Nora Renz for helping me to improve the manuscript quality and useful suggestions. Mrs. Sabrina Cabric is greatly appreciated for her assistance with data collection.

I am very grateful to Ms. Franziska Grimm, Zhonghua Helmke, and Pamela Glowacki from the Charité International Welcome Center in helping me to better integrate in Germany, especially living and studying.

My sincere thanks also go to the support from the China Scholarship Council, PRO-IMPLANT FOUNDATION, German Research Foundation, and the Open Access Publication Fund of Charité - Universitätsmedizin Berlin.

Finally, I express my very profound gratitude to my parents, who provided me with their unconditional support and encouragement whenever needed.