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SYSTEMATIC REVIEW

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Intentional foraminal enlargement: a systematic review with bibliometric analysis

Ampliação foraminal intencional: uma revisão sistemática com análise bibliométrica

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ABSTRACT

Objective: The purpose of this systematic review with bibliometric analysis was to map the available scientific evidence on intentional foraminal enlargement (IFE) and explore publication trends. **Methods:** This review is in accordance with the PRISMA 2020 Statement and is registered on the Open Science Framework. Two independent reviewers carried out a comprehensive search of seven databases (PubMed/MEDLINE, Cochrane Library, Scopus, Embase, Web of Science, LILACS, and BBO) up to January 31st, 2022. Studies that investigated IFE were considered eligible, and the data were analyzed using the VOSViewer software. **Results:** The search identified a total of 55 IFE-related articles from 10 countries and 25 journals, with an increasing trend for publications over the last decade. The majority of evidence was based on laboratory assays (65.4%), followed by randomized clinical trials (18.1%) with follow-up periods of up to 2 months. The main clinical outcome evaluated was post-operative pain. The highest number of studies were carried out by the State University of Campinas, and published in the Journal of Endodontics. Also, studies with the highest level of evidence found that IFE resulted in greater post-operative pain in the initial days post-treatment. **Conclusion:** This systematic review with bibliometric analysis mapped the scientific progress and publication trends in the field of IFE, thus shedding light on gaps in the literature with the aim of guiding researchers to conduct more high-impact investigations by performing clinical studies evaluating rates of periapical repair and IFE treatment success using long-term observation periods.

KEYWORDS

Root canal preparation; Endodontics; Instrumentation; Systematic review; Bibliometrics.

RESUMO

Objetivo: O objetivo desta revisão sistemática com análise bibliométrica foi mapear as evidências científicas disponíveis sobre ampliação foraminal intencional (IFE) e explorar as tendências de publicação. **Métodos:** Esta revisão está de acordo com a declaração PRISMA 2020 e está registrada no Open Science Framework. Dois revisores independentes realizaram uma busca abrangente em sete bases de dados (PubMed/MEDLINE, Cochrane Library, Scopus, Embase, Web of Science, LILACS e BBO) até 31 de janeiro de 2022. Os estudos que investigaram IFE foram considerados elegíveis e os dados foram analisados usando o software VOSViewer. **Resultados:** A busca identificou um total de 55 artigos relacionados ao IFE provenientes de 10 países e 25 periódicos, com tendência crescente de publicações na última década. A maioria das evidências foi baseada em ensaios laboratoriais (65,4%), seguido de ensaios clínicos randomizados (18,1%) com períodos de follow-up de até 2 meses. O principal desfecho clínico avaliado foi a dor pós-operatória. O maior número de estudos foi realizado pela Universidade Estadual de Campinas e publicado no Journal of Endodontics. Estudos com os maiores níveis de evidência constataram que IFE resultou em maior dor pós-operatória nos primeiros dias pós-tratamento. **Conclusão:** Esta revisão sistemática com análise bibliométrica mapeou o progresso científico e as

tendências de publicação na área de IFE, lançando luz sobre lacunas na literatura com o objetivo de orientar pesquisadores a realizar investigações de maior impacto, realizando estudos clínicos avaliando taxas de reparo periapical e sucesso do tratamento usando essa técnica e com acompanhamento à longo prazo.

PALAVRAS-CHAVE

Preparo do canal radicular; Endodontia; Instrumentação; Revisão sistemática; Bibliometria.

INTRODUCTION

Successful periapical healing is one of the main expected outcomes of root canal treatment [1]. The key goals of root canal preparation include reducing bacterial levels and removing biofilm and inflamed and/or infected pulpal tissue [2] through the use of instruments that allow the preservation of healthy dental tissues and maintenance of the root canal morphology [3]. Therefore, effective cleaning and shaping of the apical third of the root canal is of paramount importance for endodontic treatment success due to the presence of apical ramifications and high prevalence of lateral canals, which can nurture bacterial biofilms, leading to persistent apical periodontitis [4,5]. Achieving and maintaining apical patency using a small caliber instrument is essential for effective infection control in this critical zone and, therefore, plays an important role in increasing the success rates of conventional endodontic treatments [6]. Intentional foraminal enlargement (IFE) involves widening of the apical foramen using a larger caliber instrument at the level of or through the apical foramen after the achievement of root canal patency [7]. The effects of instrumentation beyond the apex were primarily investigated in the 1970s with the purpose of increasing decontamination on the cemento-dentinal junction [8], and since then, several studies have shown that apical enlargement may assist in minimizing bacterial load, leading to more predictable long-term success following root canal treatment [9-12].

Prior to IFE shaping, establishment of a working length is clinically pertinent in order to effectively enlarge the apical foramen. Instrumentation of the canal to a length just short of the apex may fail to achieve effective enlargement of the apical foramen, while over-instrumentation can affect the periapical tissues by causing mechanical irritation or extrusion of debris, leading to mild post-operative pain [13]. Although some studies recommend a pre-determined working length that is 1.0 mm short of the apical foramen, others suggest one that extends up to or beyond the apical foramen itself in order to achieve improved debridement and disinfection of the apical portion of the root canal. This approach can also lead to more favorable outcomes [14-16], with previous studies reporting periapical healing rates of 96% [16,17]. In contrast, studies examining conventional instrumentation techniques (working length: 1.0 mm short of the apical foramen) reported a well-established success rate of 90-94% [16]. The authors explained this outcome by means of a classic study [15] which showed that the connective tissues of the periodontal ligament could proliferate and invaginate into the interior of the root canal in case of apical over-instrumentation, suggesting disinfection of the cementum canal and apical foramen. In recent decades, researchers have evaluated the effects of IFE shaping on the clinical outcomes of root canal treatment extensively, and bibliometric analyses of these studies could not only help map the available evidence and amplify perception, but also indirectly contribute to guiding future studies by analyzing the past, understanding the present, and preparing for the future in this field [18].

Bibliometric analysis is a popular systematic method used to evaluate research output by scrutinizing pertinent literature using mathematical and statistical approaches. It shows the historical development of research fields and evaluates the scientific research productivity of researchers, institutions, countries, and journals [19-25]. Moreover, by extracting relationships between articles, bibliometric mapping offers a method of quickly summarizing and visualizing the structure inherent to a set of publications. The resulting visualizations or maps can then be used to examine the history of scientific research in a specific field and also identify potential directions and collaboration opportunities for future research [26]. Therefore, the aim of this systematic review with bibliometric analysis was to map the available scientific evidence and evaluate the publication trends on IFE in order to highlight prominent research lines, researchers, institutions, and study designs while also investigating the scientific impact of this technique.

METHODS

Protocol registration

The current systematic review with bibliometric analysis was reported using a systematic review model based on the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA 2020) guidelines [27]. The protocol was registered on the Open Science Framework and can be accessed using the following web-link: https://osf.io/KMYGA.

Eligibility and exclusion criteria

Studies that investigated IFE shaping and were published in English, Portuguese, or Spanish were included in this analysis. No study design restrictions were applied.

The analysis excluded all studies that did not investigate enlargement of the apical foramen or those that evaluated teeth with immature roots or open apices. Moreover, editorials, letters, news articles, commentaries, perspectives, opinions, scientific blogs, or technical notes were also excluded.

Search strategy

A systematic search strategy was implemented using the following seven electronic databases: PubMed/Medline, The Cochrane Library, SciVerse Scopus, Embase, Web of Science, LILACS, and BBO. The specific keywords used to carry out the search were selected based on PubMed/Medline MeSH terms and were adjusted for the other databases (Table I). All relevant studies identified by the search strategy were imported into Mendeley (Elsevier, Amsterdam, NE) to allow removal of duplicates. Manual searching of the reference lists in the included studies was also carried out to identify any additional eligible studies. Where the publication was unavailable through the database, the corresponding author of the included study was contacted via e-mail to retrieve the study. A second reminder e-mail was sent after two weeks in case of no response, and the study was excluded from the analysis if it could not be accessed using this method.

Selection process

All studies identified by the systematic search strategy were imported into the web application Rayyan (Qatar Computing Research Institute, Doha, QA) [28], and the study titles and abstracts were screened by two blinded, independent reviewers (LPA and LPM). Studies that appeared relevant as well as those that were slightly ambiguous were selected for full-text analysis, and only those that clearly met the inclusion criteria were included in the final bibliometric analysis. Any disagreements between the two reviewers were resolved through discussion with a third independent reviewer (WLOR).

Data collection process

All data of interest from the included studies were tabulated and interpreted by two independent reviewers (LPA and LASF) using an Excel spreadsheet (Microsoft Corporation, Redmond, WA, USA), and these were also double-checked by a third reviewer (LPC). Parameters of interest included the annual number of published articles; frequency of authorship; institutional affiliations; geographic distribution; impact factor of publishing journals; study design; tooth groups; and working length used. The level of evidence (LoE) in each included study was determined based on previous evidence [29,30] and the key findings from studies with the highest LoE. No LoE was assigned to laboratory studies.

Bibliometric analysis

All included studies were imported into the Visualization of Similarities Viewer software (VOSViewer 1.6.8, Center for Science and Technology Studies, Leiden University, Leiden, Netherlands) in.RIS format to allow graphical analysis [31]. The minimum set of published articles was set to “1” to allow examination of co-authorship networks and keyword co-occurrences. The software works as a distance-based map where the terms are arranged into clusters shown as colored circles . The links between these clusters represent collaborations, while the thickness and distance show the strength of the bond between the terms.

The impact factors of journals with the highest number of publications on this topic were extracted from the Journal Citation Reports (JCRs) 2020 (Clarivate Analytics, Philadelphia, PA, USA). Journals that published IFE studies and were not listed on the JCRs were classified separately.

Table I. Search strategies

Search Terms	
Pubmed	
#3	Search #1 AND #2
#2	Seach (Foraminal Enlargement) OR (Apical Enlargement) OR (Root Canal Enlargement) OR (Apical Foramen) OR (Apical Diameter) OR (Foramen Size) OR (Diameter Enlargement) OR (Apex Enlargement) OR (Foramen Enlargement) OR (Apical Foramen Enlargement) OR (Overinstrumentation) OR (Overinstrumented) OR (Overinstrumented Foramen) OR (Overinstrumented Apical Foramen)
#1	Search (Tooth, Nonvital) OR (Tooth, nonvital) OR (Nonvital Tooth) OR (Tooth, Devitalized) OR (Devitalized Tooth) OR (Tooth, Pulpless) OR (Pulpless Tooth) OR (Teeth, Pulpless) OR (Pulpless Teeth) OR (Teeth, Devitalized) OR (Devitalized Teeth) OR (Teeth, Nonvital) OR (Nonvital Teeth) OR (Teeth, Endodontically-Treated) OR (Endodontically-Treated Teeth) OR (Teeth, Endodontically Treated) OR (Tooth, Endodontically-Treated) OR (Endodontically-Treated Tooth) OR (Tooth, Endodontically Treated) OR (Root canal therapy) OR (Canal Therapies, Root) OR (Canal Therapy, Root) OR (Root Canal Therapies) OR (Therapies, Root Canal) OR (Therapy, Root Canal) OR (Endodontics) OR (Endodontics) OR (Endodontology)
Embase	
#3	Search #1 AND #2
#2	Seach "Foraminal Enlargement" OR "Apical Enlargement" OR "Root Canal Enlargement" OR "Apical Foramen" OR "Apical Diameter" OR "Foramen Size" OR "Diameter Enlargement" OR "Apex Enlargement" OR "Foramen Enlargement" OR "Apical Foramen Enlargement" OR "Overinstrumentation" OR "Overinstrumented" OR "Overinstrumented Foramen" OR "Overinstrumented Apical Foramen"
#1	Search "Tooth, Nonvital" OR "Tooth, nonvital" OR "Nonvital Tooth" OR "Tooth, Devitalized" OR "Devitalized Tooth" OR "Tooth, Pulpless" OR "Pulpless Tooth" OR "Teeth, Pulpless" OR "Pulpless Teeth" OR "Teeth, Devitalized" OR "Devitalized Teeth" OR "Teeth, Nonvital" OR "Nonvital Teeth" OR "Teeth, Endodontically-Treated" OR "Endodontically-Treated Teeth" OR "Teeth, Endodontically Treated" OR "Tooth, Endodontically-Treated" OR "Endodontically-Treated Tooth" OR "Tooth, Endodontically Treated" OR "Root Canal Therapy" OR "Canal Therapies, Root" OR "Canal Therapy, Root" OR "Root Canal Therapies" OR "Therapies, Root Canal" OR "Therapy, Root Canal" OR "Endodontics" OR "Endodontics" OR "Endodontology"
Web of Science	
#3	Search #1 AND #2
#2	TS=((Foraminal Enlargement) OR (Apical Enlargement) OR (Root Canal Enlargement) OR (Apical Foramen) OR (Apical Diameter) OR (Foramen Size) OR (Diameter Enlargement) OR (Apex Enlargement) OR (Foramen Enlargement) OR (Apical Foramen Enlargement) OR (Overinstrumentation) OR (Overinstrumented) OR (Overinstrumented Foramen) OR (Overinstrumented Apical Foramen))
#1	TS=((Tooth, Nonvital) OR (Tooth, nonvital) OR (Nonvital Tooth) OR (Tooth, Devitalized) OR (Devitalized Tooth) OR (Tooth, Pulpless) OR (Pulpless Tooth) OR (Teeth, Pulpless) OR (Pulpless Teeth) OR (Teeth, Devitalized) OR (Devitalized Teeth) OR (Teeth, Nonvital) OR (Nonvital Teeth) OR (Teeth, Endodontically-Treated) OR (Endodontically-Treated Teeth) OR (Teeth, Endodontically Treated) OR (Tooth, Endodontically-Treated) OR (Endodontically-Treated Tooth) OR (Tooth, Endodontically Treated) OR (Root Canal Therapy) OR (Canal Therapies, Root) OR (Canal Therapy, Root) OR (Root Canal Therapies) OR (Therapies, Root Canal) OR (Therapy, Root Canal) OR (Endodontics) OR (Endodontics) OR (Endodontology))
SciVerse Scopus	
#3	Search #1 AND #2
#2	ALL ("Foraminal Enlargement") OR ("Apical Enlargement") OR ("Root Canal Enlargement") OR ("Apical Foramen") OR ("Apical Diameter") OR ("Foramen Size") OR ("Diameter Enlargement") OR ("Apex Enlargement") OR ("Foramen Enlargement") OR ("Apical Foramen Enlargement") OR ("Overinstrumentation") OR ("Overinstrumented") OR ("Overinstrumented Foramen") OR ("Overinstrumented Apical Foramen")
#1	ALL ("Tooth, Nonvital") OR ("Tooth, nonvital") OR ("Nonvital Tooth") OR ("Tooth, Devitalized") OR ("Devitalized Tooth") OR ("Tooth, Pulpless") OR ("Pulpless Tooth") OR ("Teeth, Pulpless") OR ("Pulpless Teeth") OR ("Teeth, Devitalized") OR ("Devitalized Teeth") OR ("Teeth, Nonvital") OR ("Nonvital Teeth") OR ("Teeth, Endodontically-Treated") OR ("Endodontically-Treated Teeth") OR ("Teeth, Endodontically Treated") OR ("Tooth, Endodontically-Treated") OR ("Endodontically-Treated Tooth") OR ("Tooth, Endodontically Treated") or ("Root Canal Therapy") OR ("Canal Therapies, Root") OR ("Canal Therapy, Root") OR ("Root Canal Therapies") OR ("Therapies, Root Canal") OR ("Therapy, Root Canal") OR ("Endodontics") OR ("Endodontics") OR ("Endodontology")
LILACS/BBO	
#3	Search #1 AND #2
#2	Search ((Foraminal Enlargement) OR (Apical Enlargement) OR (Root Canal Enlargement) OR (Apical Foramen) OR (Apical Diameter) OR (Foramen Size) OR (Diameter Enlargement) OR (Apex Enlargement) OR (Foramen Enlargement) OR (Apical Foramen Enlargement) OR (Overinstrumentation) OR (Overinstrumented) OR (Overinstrumented Foramen) OR (Overinstrumented Apical Foramen))
#1	Search ((Tooth, Nonvital) OR (Tooth, nonvital) OR (Nonvital Tooth) OR (Tooth, Devitalized) OR (Devitalized Tooth) OR (Tooth, Pulpless) OR (Pulpless Tooth) OR (Teeth, Pulpless) OR (Pulpless Teeth) OR (Teeth, Devitalized) OR (Devitalized Teeth) OR (Teeth, Nonvital) OR (Nonvital Teeth) OR (Teeth, Endodontically-Treated) OR (Endodontically-Treated Teeth) OR (Teeth, Endodontically Treated) OR (Tooth, Endodontically-Treated) OR (Endodontically-Treated Tooth) OR (Tooth, Endodontically Treated) OR (Root canal therapy) OR (Canal Therapies, Root) OR (Canal Therapy, Root) OR (Root Canal Therapies) OR (Therapies, Root Canal) OR (Therapy, Root Canal) OR (Endodontics) OR (Endodontics) OR (Endodontology))

RESULTS

Search strategy

The electronic search (terminated on January 31st, 2022) identified 8793 potentially relevant records. Figure 1 is a schematic flowchart that outlines the study selection process in accordance with the PRISMA 2020 Statement [27]. Removal of all duplicates left 5780 articles for title and abstract screening using the web application Rayyan (Qatar Computing Research Institute). Thereafter, 5679 studies were excluded as they did not meet the inclusion criteria, and full-text analysis was carried out on 102 studies. Of these, 45 studies were excluded as they evaluated enlargement short of the apical foramen or had missing information that could not be retrieved from the authors (n = 2). The remaining 55 articles fulfilled all inclusion criteria and were included in the bibliometric analysis.

Study characteristics

A total of 55 articles examining IFE were published in 25 journals over a period of 48 years. Of the 25 journals identified, 11 (44%) were indexed on the most recent version of the *Journal Citation Reports* (JCRs) and had their impact factors recorded (shown in Table II). The *Journal of Endodontics* had the maximum number of publications (n = 14) in this field [14,32-44], followed by the *International Endodontic Journal* with 9 published studies [45-51]. Those two journals also had the highest impact factors in the field of endodontics. The journal of *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* published 5 studies [7,8,15,52,53], while the *Journal of Applied Oral Science* and the *Australian Endodontic Journal* published 2 studies each [9,54-56]. Additionally, *Photodiagnosis and Photodynamic Therapy, BioMed Research International, Acta Odontologica Scandinavica, Clinical Oral Investigations, Quintessence International, and the Nigerian Journal of Clinical Practice* published one article each [16,57-61]. The remaining 17 studies [16,60-75] were published in 14 different journals that did not appear on any of the internationally relevant bibliographic lists or JCRs (Table III).

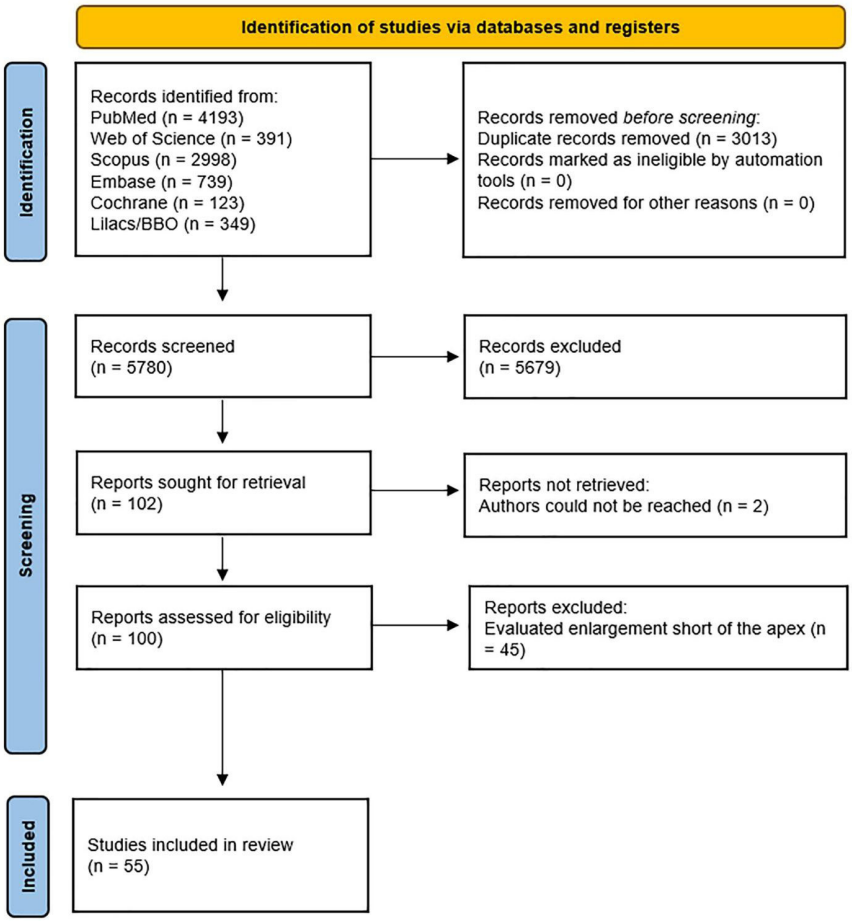


Figure 1 - Flowchart showing search strategy based on the PRISMA 2020 Statement.

Table II - The top journals based on the number of publications, impact factor (IF), as well as the subject category and ranking in the 2020 Journal Citation Reports (Clarivate Analytics) and journals' country of origin

Journal	Articles (n)	JCR® IF 2020	Journal category (ranking)	Country
Journal of Endodontics	14	4.171	Dentistry, Oral Surgery & Medicine (16/91) (Q1)	USA
International Endodontic Journal	9	5.264	Dentistry, Oral Surgery & Medicine (10/91) (Q1)	England
Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontology±	5	2.589	Dentistry, Oral Surgery & Medicine (44/91) (Q2)	USA
Journal of Applied Oral Science	2	2.698	Dentistry, Oral Surgery & Medicine (38/91) (Q1)	Brazil
Australian Endodontic Journal	2	1.659	Dentistry, Oral Surgery & Medicine (77/91) (Q4)	Australia
Photodiagnosis and Photodynamic Therapy	1	3.631	Oncology (144/242) (Q3)	Netherlands
Clinical Oral Investigations	1	3.573	Dentistry, Oral Surgery & Medicine (21/91) (Q1)	Germany
BioMed Research International	1	3.411	Biotechnology & Applied Microbiology (69/159) (Q2)	England
Acta Odontologica Scandinavica	1	2.331	Dentistry, Oral Surgery & Medicine (53/91) (Q3)	England
Quintessence International	1	1.677	Dentistry, Oral Surgery & Medicine (76/91) (Q4)	USA
Nigerian Journal of Clinical Practice	1	0.968	Medicine, General & Internal (136/169) (Q4)	India

± Journal was discontinued in 2011 and replaced by the Oral Surgery Oral Medicine Oral Pathology Oral Radiology journal.

Table III. Journals not ranked on any JCRs, number of articles published on each, and journals' country of origin

Journal	Articles	Country
Restorative Dentistry & Endodontics	1	Korea
Iranian Endodontic Journal	1	Iran
Chinese Journal of Dental Research	1	China
Journal of Clinical and Diagnostic Research	2	India
Indian Journal of Dental Research	1	India
European Journal of Dentistry	1	India
Endodontic Practice US	1	USA
Revista de Odontologia da UNESP	1	Brazil
Revista da Associação Paulista de Cirurgiões Dentistas	2	Brazil
Brazilian Journal of Oral Science	1	Brazil
Dental Press Endodontics	2	Brazil
achoBrazilian Dental Journal	1	Brazil
International Journal of Odontostomatology	1	Spain
The Bulletin of Tokyo Dental College	1	Japan

Of the 55 studies included in this analysis, 36 were laboratory-based; 10 were randomized controlled trials (RCTs) with LoE = 2; 1 was a systematic review of RCTs (LoE = 1); 1 was a systematic review and meta-analysis of *in vitro* studies; 2 were cohort studies (LoE = 2); 2 were case-control studies (LoE = 3); and 3 were narrative literature reviews (LoE = 5). Table IV summarizes the demographic data, study designs, working length, and citation analysis of the included studies, while Table V lists the key findings and instrumentation techniques used in studies with the highest levels of evidence. The RCTs evaluated post-operative pain over follow-up periods ranging between 1 and 30 days, while the observational studies aimed to examine periapical healing over follow-up periods ranging from 6 to 72 months.

Bibliometric analysis

Brazil had the highest number of publications (n = 34) globally, followed by Turkey and India (n = 4 each). Additionally, the United States and Lebanon published 3 articles each, Spain and Italy published 2 articles each, and Canada, Japan, and Sweden were tied at 1 publication each. Only one study was an international collaboration, and the vast majority of researchers that carried out studies in this field had not collaborated with other countries or institutions. This could likely be attributed to the fact that the majority of studies were laboratory-based with no need for external resources or advanced technology to perform tests.

Table IV - Demographic data, correspondent author's institution, study design, working length, and cites of each included article

Author and year	Country	Institution	Study design	Working length	Cites
Seltzer et al., 1973 [8]	United States	Temple University	In vivo	2mm beyond the apical foramen	59
Holland et al., 1979 [53]	Brazil	São Paulo State University	In vivo	2mm beyond the apical foramen	45
Bergenholtz et al., 1979 [37]	Sweden	University of Gothenburg	Case-control study	Apical foramen	142
Benatti et al., 1985 [14]	Brazil	State University of Campinas	In vivo	2mm beyond the apical foramen	28
Morse et al., 1987 [52]	United States	Temple University	Randomized Clinical Trial	Beyond apical foramen towards the center of periapical lesions	34
Souza-Filho et al., 1987 [15]	Brazil	State University of Campinas	In vivo	2mm beyond the apical foramen	60
Ricucci, 1998 [45]	Italy	Private practice	Literature Review	-	356
Ricucci, 1998 [4]	Italy	Private practice	In vivo	1mm beyond the apical foramen	632
Adorno et al., 2009 [49]	Japan	Tokyo Medical and Dental University	In vitro	Apical foramen	109
Borlina et al., 2010 [7]	Brazil	São Paulo State University	In vivo	Apical foramen	57
Endo & Soares, 2011 [73]	Brazil	State University of Campinas	In vitro	1mm beyond the apical foramen	4
Lima et al., 2012 [72]	Brazil	State University of Campinas	In vitro	1mm beyond the apical foramen	4
Marinho et al., 2012 [9]	Brazil	State University of Campinas	In vitro	Apical foramen	45
Silva et al., 2013 [43]	Brazil	Rio de Janeiro State University, and State University of Campinas	Randomized Clinical Trial	Apical foramen	69
Liu et al., 2014 [62]	China	Xuzhou Stomatological Hospital	In vitro	1mm beyond the apical foramen	6
Silva et al., 2014 [67]	Brazil	Grande Rio University	In vitro	1mm beyond the apical foramen	6
Yadav et al., 2014 [70]	India	All India Institute of Medical Sciences	In vitro	Apical foramen	-
Çapar et al., 2015 [39]	Turkey	İzmir Katip Çelebi University	In vitro	Apical foramen	59
Teixeira et al., 2015 [46]	Brazil	Rio de Janeiro State University	In vitro	Apical foramen	24
Bourreau et al., 2015 [71]	Brazil	São Leopoldo Mandic University	Randomized Clinical Trial	1mm beyond the apical foramen	5
Silvestrin et al., 2016 [60]	United States	Loma Linda University	In vitro	Apical foramen	8
Silva et al., 2016 [63]	Brazil	Grande Rio University	In vitro	1mm beyond the apical foramen	17
Charara et al., 2016 [36]	Canada	University of Toronto	In vitro	1mm beyond the apical foramen	56
Saini et al., 2016 [48]	India	Institute of Dental Sciences Rohtak	Randomized Clinical Trial	Apical foramen	12
Jyotsna et al., 2016 [74]	India	Sri Sai College of Dental Surgery	In vitro	Apical foramen	7
Ferrari et al., 2016 [65]	Brazil	São Paulo State University	Literature Review	-	
Silva et al., 2016 [76]	Brazil	Grande Rio University	In vitro	Apical foramen	15
Cruz et al., 2016 [41]	Brazil	São Leopoldo Mandic University	Randomized Clinical Trial	Apical foramen	36
Santos et al., 2017 [35]	Brazil	São Leopoldo Mandic University	In vitro	1mm beyond the apical foramen	8
Yammine et al., 2017 [77]	Lebanon	Lebanese University	In vitro	1.5mm beyond the apical foramen	7
Borges-Silva et al., 2017 [42]	Brazil	Fluminense Federal University	Systematic Review	Apical foramen	11
Yaylali et al., 2017 [38]	Turkey	Isparta Military Hospital	Randomized Clinical Trial	Apical foramen	23
Bucchi et al., 2017 [57]	Spain	University of Barcelona	In vitro	0.5mm beyond the apical foramen	11
Frota et al., 2018 [54]	Brazil	Federal University of Ceará	In vitro	1mm beyond the apical foramen	15
Tarallo et al., 2018 [75]	Brazil	São Paulo State University	In vitro	1mm beyond the apical foramen	-
Watanabe et al., 2018 [69]	Brazil	Federal University of Pará	In vitro	1mm beyond the apical foramen	1
Jara et al., 2018 [50]	Brazil	Pontifical Catholic University of Rio Grande do Sul	In vivo	Apical foramen	12
Marion et al., 2019 [66]	Brazil	Federal University of Mato Grosso do Sul	Literature Review	-	-
Brandão et al., 2019 [59]	Brazil	Bahian School of Medicine and Public Health	In vivo	Apical foramen	5
Albuquerque et al., 2020 [56]	Brazil	São Leopoldo Mandic University	In vitro	1mm beyond the apical foramen	-
Eyüboğlu et al., 2020 [16]	Turkey	Istanbul Medipol University	Cohort study	Apical foramen	-
Bourreau et al., 2020 [17]	Brazil	State University of Campinas	Case-control study	1mm beyond the apical foramen	-
Daou et al., 2020 [40]	Lebanon	Saint Joseph University of Beirut	In vitro	Apical foramen	-
Vieira et al., 2020 [44]	Brazil	Federal University of Espirito Santo	In vitro	1mm beyond the apical foramen	-
Bucchi et al., 2020 [57]	Spain	University of Barcelona	In vitro	0.5mm beyond the apical foramen	-
Kurnaz, 2020 [58]	Turkey	Kutahya Health Sciences University	Randomized Clinical Trial	Apical foramen	1
Aggarwal et al., 2021 [34]	India	Indian Institute of Technology	In vitro	1mm beyond the apical foramen	-
Vivacqua et al., 2021 [32]	Brazil	University of São Paulo	In vitro	1mm beyond the apical foramen	-
Belladonna et al., 2021 [47]	Brazil	Fluminense Federal University	In vitro	1mm beyond the apical foramen	-
Machado et al., 2021 [55]	Brazil	Pontifical Catholic University of Paraná	Cohort study	2mm beyond the apical foramen	-
Portela et al., 2021 [33]	Brazil	São Leopoldo Mandic University	Randomized Clinical Trial	Apical foramen	-
Yammine et al., 2021 [64]	Lebanon	Lebanese University	In vitro	1.5mm beyond the apical foramen	-
Machado et al., 2021 [68]	Brazil	Regional University of Blumenau	Systematic Review	Apical foramen	-
Souza et al., 2021 [61]	Brazil	University of Passo Fundo	Randomized Clinical Trial	1mm beyond the apical foramen	
Guimarães et al., 2021 [51]	Brazil	Fluminense Federal University	Randomized Clinical Trial	Apical foramen	-

Table V - Level of evidence provided, instrumentation technique used, and main findings of the included studies

Author and year	LoE	Instrumentation technique used to enlarge the apical foramen	Main findings of the included studies
Systematic Review and Meta-Analyses			
Borges-Silva et al., 2017 [42]	1	Not aplicable	Intentional enlargement of the apical foramen resulted in greater post-operative pain in the initial days after treatment.
Machado et al., 2021 [55]	1	Not aplicable	Intentional foraminal enlargement did not result in extrusion of a larger quantity of debris from extracted human teeth with fully formed apices.
Randomized Clinical Trials			
Morse et al., 1987 [52] *Follow-up period: 1 day to 2 months* *Outcomes evaluated: Flare-up, swelling, and post-operative pain*	2	Manual stainless steel files were used to over-instrument the apex until the center of the periapical lesion.	Periapical instrumentation did not result in any statistically significant differences with regard to flare-ups, swelling, pain, and post-operative complications when compared to intra-canal instrumentation.
Silva et al., 2013 [43] *Follow-up period: 3 days* *Outcomes evaluated: Post-operative pain*	2	Manual stainless steel files up to three sizes larger than the first apical binding file used at the apical foramen.	The foraminal enlargement and non-enlargement techniques resulted in the same degree of post-operative pain and need for analgesic medication.
Bourreau et al., 2015 [71] *Follow-up period: 1 day* *Outcomes evaluated: Post-operative pain*	2	Rotary file (Mtwo system; VDW, Bayerwaldstraße Munich, Germany) numbers 10/.04, 15/.05, 20/.06 and 25/.06 were used 1mm beyond the apical foramen.	Different auxiliary chemical substances had no effect on post-operative pain when performing foraminal enlargement.
Saini et al., 2016 [48] *Follow-up period: 7 days* *Outcomes evaluated: Post-operative pain*	2	Manual stainless steel files up to three sizes larger than the first apical binding file used at the apical foramen.	Enlargement of the apical foramen during root canal treatment increased the incidence and intensity of post-operative pain.
Cruz et al., 2016 [41] *Follow-up period: 7 days* *Outcomes evaluated: Post-operative pain*	2	A Reciproc R40 file (VDW) was used to enlarge the apical foramen at the working length.	Foraminal enlargement resulted in a low incidence of pain. Patients who underwent IFE reported mild pain after 24 hours when compared to the control group, although these differences ceased to exist after 72 hours and one week.
Yaylali et al., 2017 [38] *Follow-up period: 7 days* *Outcomes evaluated: Post-operative pain*	2	Rotary file (ProTaper Next; Dentsply Maillefer®, Ballaigues, Switzerland) numbers 17/.04 and 25/.06 were used to enlarge the apical foramen at the working length.	Foraminal enlargement with a continuous rotary system caused more post-operative pain in the first two days.
Kurnaz et al., 2020 [58] *Follow-up period: 7 days* *Outcomes evaluated: Post-operative pain*	2	Rotary file (ProTaper Next; Dentsply Maillefer®, Ballaigues, Switzerland) numbers 17/.04, 25/.06, 30/.075, and 40/0.6 were used to enlarge the apical foramen at the working length in the rotary group. A WaveOne (Dentsply Maillefer®) reciprocating file 40/.08 was used at the working length in the reciprocating group.	Foraminal enlargement created by reciprocating instruments was associated with greater post-operative pain compared to rotary systems in the 2-day follow-up period after endodontic treatment,
Portela et al., 2021 [33] *Follow-up period: 1 day to 7 days* *Outcomes evaluated: Post-operative pain*	2	Reciprocating files (WaveOne Gold Primary; Dentsply Maillefer®) were used to enlarge the apical foramen at the working length.	Foraminal enlargement was associated with higher levels of filling material extrusion and pain 24 hours post-operatively.
Souza et al., 2021 [61] *Follow-up period: 1 day to 7 days* *Outcomes evaluated: Post-operative pain*	2	Reciprocating files (WaveOne Gold Primary; Dentsply Maillefer®) were used up to 1mm beyond the apical foramen.	Apical limitation of instrumentation and photodynamic therapy of lower molars with asymptomatic apical periodontitis had no influence on post-operative pain.
Guimarães et al., 2021 [51] *Follow-up period: 1 day to 30 days* *Outcomes evaluated: Post-operative pain*	2	Reciprocating files (Reciproc R40 or R50; VDW) were used to enlarge the apical foramen at the working length	Photo-biomodulation had no significant effect on post-operative pain, tenderness, edema, or the use of analgesics after root canal treatment with foraminal enlargement
Cohort studies			
Eyüboğlu et al., 2020 [16] *Follow-up period: 48 to 72 months* *Outcomes evaluated: Periapical healing*	2	Rotary file (Revo-S System; Micro-Méga, Besançon, France) numbers 35/.06 and 40/0.6 were used to enlarge the apical foramen at the working length.	After a mean follow-up period of 60 months, single-visit root canal treatments with apical enlargement on teeth with necrotic pulp tissue provided favorable outcomes, with a healing rate of 96.7%.
Machado et al., 2021 [68] *Follow-up period: 3 days* *Outcomes evaluated: Post-operative pain*	2	Rotary file (Profile 04 system; Dentsply Maillefer®) numbers 30/.04 through 60.04 (depending on the initial foramen size) were used to enlarge the apical foramen at the working length.	Low incidence and degree of post-operative pain observed after performing endodontic treatment with large intentional foraminal enlargement on necrotic teeth.

Table V - Continued...

Author and year	LoE	Instrumentation technique used to enlarge the apical foramen	Main findings of the included studies
		Case-control studies	
Bergenholtz et al., 1979 [37] *Follow-up period: 2 years* *Outcomes evaluated: Periapical healing*	3	Instrumentation technique not reported by the authors	Root canals that were over-instrumented were at a higher risk of being over-filled and, thus, exhibited lower frequency of complete periapical healing.
Bourreau et al., 2020 [17] *Follow-up period: 6 to 12 months* *Outcomes evaluated: Periapical healing*	3	Rotary file (Mtwo system; VDW) numbers 10/.04, 15/.05, 20/.06 and 25/.06 were used 1mm beyond the apical foramen.	Root canal treatment and re-treatment with apical enlargement performed in a single visit resulted in a favorable prognosis with regard to periapical repair over a follow-up period of 6 months to 1 year. The complete success rate was 73.6% and the acceptable success rate was 96%.
		Literature reviews	
Ricucci, 1998 [45]	5	Not aplicable	All valid prognosis studies confirm the practice of homogeneous obturation up to a length just short of the apex in order to achieve the highest success rate of 90±94%
Ferrari et al., 2016 [65]	5	Not aplicable	No solid scientific evidence in support of the use of intentional foraminal enlargement. The literature reviewed in this study reiterated that this approach posed both local and systemic risks to the patient
Marion et al., 2019 [66]	5	Not aplicable	The advantages of apical third enlargement and foramen extension for endodontic treatment predictability are evident. However, further randomized clinical trials should evaluate the success rates of this approach.

The first publication in this field appeared in 1973 [1], with exponential growth in terms of publications per year only happening much later in 2009 (Figure 2a), reflecting an increased awareness of this field of research among the scientific community. An increasing trend over time was observed, with the maximum number of publications (n = 9) occurring in 2021, followed by 2020 (n = 7). Although assessment of LoE was not possible for several studies due to their study designs, only 2 studies out of those that could be evaluated were found to have the highest LoE and were published in the *Journal of Endodontics* and the *Australian Endodontic Journal*. Citation analysis demonstrates the level of influence that articles have in the scientific community, and our analysis found that the top 3 most cited articles had been referenced 632, 356, and 142 times (Table IV). Evaluation of citation metrics was not possible for some of the included studies as these journals did not provide bibliographic indexes.

A total of 223 researchers appeared as authors or co-authors in the included publications, and only 2 researchers (Silva, EJNL; Zaia, AA) had collaborated in more than 4 publications, appearing as authors or co-authors in 7 and 5 studies, respectively. Figure 2b shows the 20 researchers with the highest number of publications in this field. Emmanuel JNL da Silva, Ricardo Machado, Cristina Bucchi, Marcelle LS Bourreau, Salwa D Yammine, and Domenico Ricucci appeared as first authors on the most number of articles published (n = 2 each).The co-authorship network map (Figure 3a) showed that Emmanuel João Nogueira Leal da Silva had the highest number of links (n = 37), followed by Alexandre Augusto Zaia (n = 20), and Augusto Shoji Kato and Carlos Eduardo da Silveira Bueno (n = 18 each). Analysis of the corresponding author's research institutions showed that the State University of Campinas led publication growth with a total of 7 studies, followed by São Leopoldo Mandic University (n = 5 studies) and São Paulo State University (n = 4 studies). Figure 2c is a graphical representation of the academic institutions with more than one published article.

The papers included in this study used a total of 247 keywords, of which 219 were connected items. The most commonly used keyword was "root canal preparation" (n = 19 studies), while those with the most robust link strengths were "root canal preparation" (n = 150 links) and "tooth apex" (n = 116 links). Figure 3b shows a density map of the co-occurrence analysis containing keyword terms. The central terms and those represented in warmer tones appeared more often and exhibited stronger connections with the other terms as a whole.

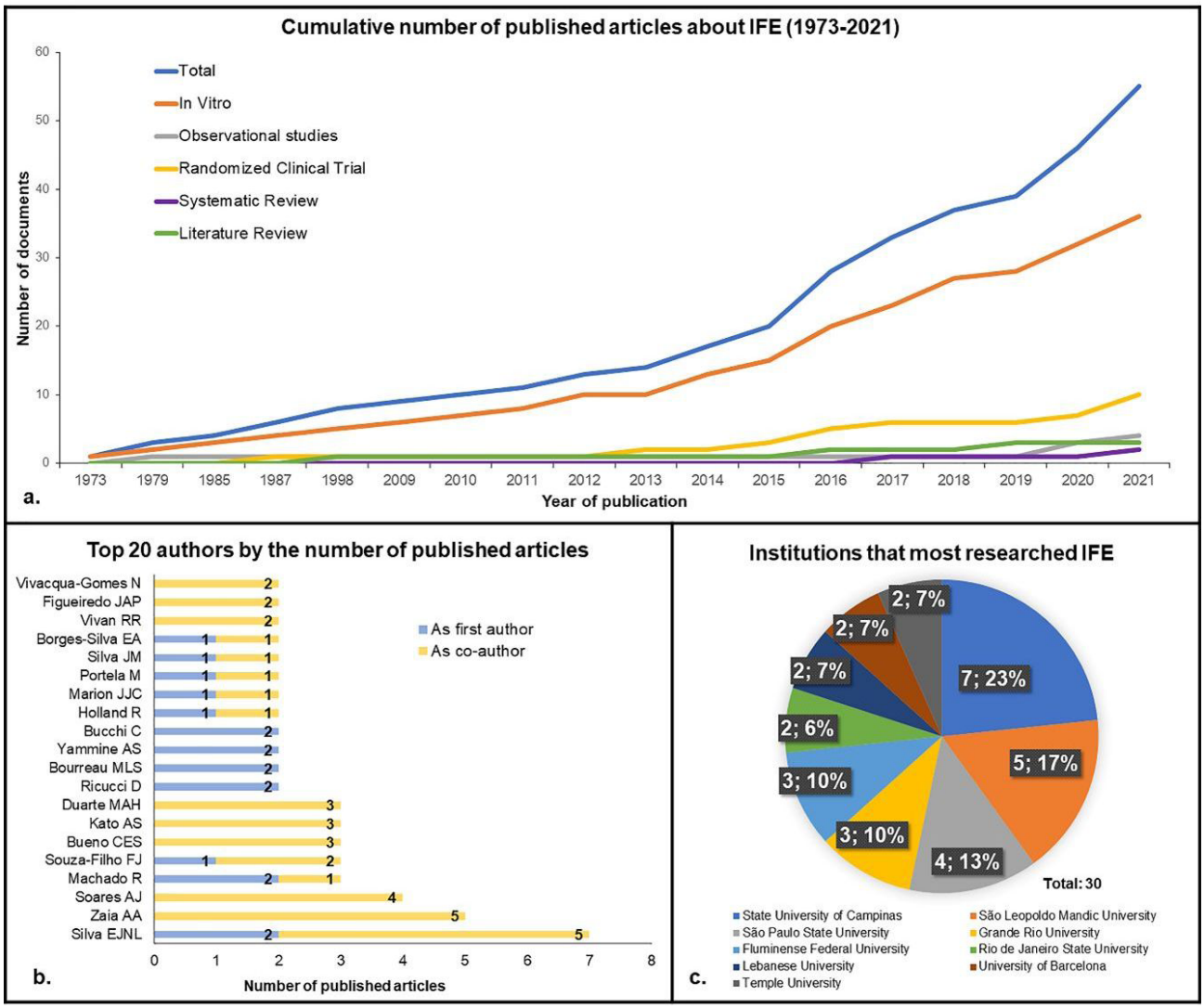


Figure 2 - 2a: Cumulative number of published articles on IFE in the period 1973-2021; 2b: Top 20 authors by the number of published articles; and 2c: Graphical representation of academic institutions with more than one published article on IFE.

DISCUSSION

To the best of our knowledge, the current bibliometric analysis is the first of its kind to evaluate the evolution of endodontic research in the field of IFE shaping. Although several bibliometric studies with distinct scopes in endodontics [20-23,25] have been published recently, none of them focused on IFE, and an in-depth analysis of this field may help summarize the available evidence and guide future studies. The current study identified 55 articles, all of which were published in journals focusing on endodontics, and these were classified into 6 different categories based on the methodological study design used. Descriptive analyses and bibliometric mapping of several parameters including author contribution, countries, journals, citations, and keywords was carried out in order to identify any trends in research over time and enable visualization of areas requiring methodological improvements [31].

IFE instrumentation attempts to reduce microbial levels to those more favorable to wound healing and periapical repair, with previous studies reporting satisfactory outcomes with this treatment modality [16,17]. However, our findings showed a lack of consensus among the included studies with regard to the ideal IFE working length in order to achieve the best risk-benefit balance. The majority of clinical trials evaluated IFE at the "0.0" reading of the apex locator, while the laboratory assays evaluated it at a working length extending to 1mm beyond the apical foramen (Table IV). This difference between study designs should be further investigated in clinical trials since performing IFE with a working length beyond the apical foramen could have histological repercussions

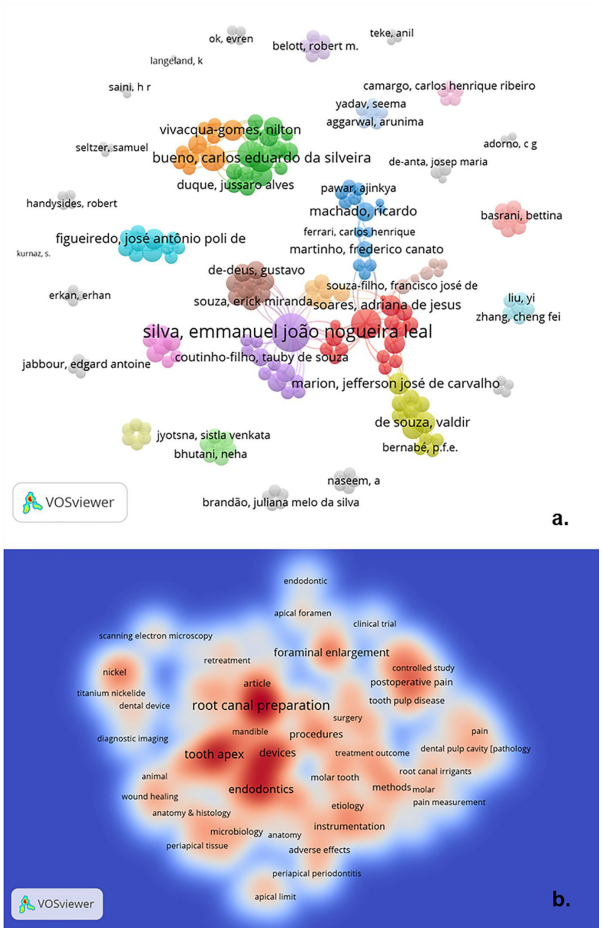


Figure 3 - 3a: Co-authorship network map analysis; and 3b: Density map of the most commonly used keywords based on co-occurrence analysis.

and impact clinical outcomes. Clinical studies also reported several limitations associated with the IFE procedure, including an increase in post-operative pain [38,41,42,48,58] and a higher risk of complications caused by extrusion of irrigation substances, dentinal debris, or endodontic filling materials when performing root canal treatment [56]. One RCT [71] investigated the effects of different chemical auxiliary substances used to irrigate the root canals on post-operative pain after IFE and found no differences between 5.25% sodium hypochlorite and 2% chlorhexidine gel [71]. Another RCT evaluated the effects of photo-biomodulation as an additional approach to controlling post-operative complications after IFE and reported no significant differences in post-operative pain, tenderness, edema, or the use of analgesics after root canal treatment with IFE [51,61]. The *in vitro* studies found no differences in foraminal deformation [35,40,54,67] or formation of apical dentinal microcracks [34,44,47] as long as thermally treated NiTi files were used to perform the IFE.

Highlighting the contributions of the most distinguished researchers toward the development of a specific field may help guide other scientists in their investigations, thus allowing further advancement of existing scientific knowledge [78]. Citation analysis is commonly performed during bibliometric analyses to evaluate the scientific relevance of a publication [79]. The current study found that a systematic review and meta-analysis of RCTs, which had the highest LoE, had only 11 citations, while the median citation for the 10 other RCTs included in this study was 19. Additionally, the majority of IFE studies were carried out in Brazilian institutions, and this was in contrast to other dental bibliometric findings that reported the highest number of studies occurring in American institutions [23,80].

The majority of publications included in this study were laboratory assays, followed by RCTs, and this was also in contrast to previous bibliometric analyses in the field of regenerative endodontics which found that the majority of published studies were case reports, review articles, or *in vitro* studies [20]. Evidence based dentistry has a hierarchy of scientific evidence based on the study design used, and this ranges from the most biased to the least biased. *In vitro* studies usually represent initial investigations and are considered to be the basis of the hierarchy as the complex biology of human beings is not completely evaluated, which compromises the results for clinical extrapolations [81]. RCTs are typically considered to produce the highest levels of evidence as they usually compare different interventions by controlling for factors that could influence the outcomes of interest. Figure 2a demonstrates the ascension of scientific evidence through the years, with an increase in the publication of RCTs aiming to answer questions that cannot be addressed through laboratory tests since 2012. The 10 RCTs included in this study focused mainly on post-operative pain outcomes, leaving a persistent gap in scientific knowledge regarding the long-term success rates of this approach. The few observational studies exploring this only [16,17] evaluated periapical healing up to a follow-up period of 6 to 72 months, preventing extrapolation of long-term clinical outcomes. The publication trends in IFE studies indicate that more RCTs evaluating different clinical outcomes with long-term observations are likely to arise in the future.

The key limitation of this study was the difficulty associated with retrieving articles that were not available on the searched databases. The corresponding authors of 6 studies were contacted via e-mail, of which only 4 responded and provided us with the relevant articles. This problem may be overcome in the future by applying different contact strategies, such as communication with the corresponding authors through social media networks; however, this non-traditional approach has yet to be tested [82]. A previous bibliometric review in the field of endodontics [20] reported difficulties with handling the VOSViewer software as it labeled all the items in a map without data overlapping due to the high number of articles analyzed. Although the current study found an increasing trend in the publication of scientific research examining IFE, thus generating relevant insight into the topic, future studies should focus on the clinical success rates of this technique using long-term follow-up. Moreover, post-operative outcomes such as pain, periapical healing, and tooth survival rate should also be considered, and fundamental studies examining the histological repercussions of using different working lengths to perform IFE should be carried out in order to fully understand the advantages of this clinical approach.

CONCLUSION

The current systematic review with bibliometric analysis mapped and discussed the scientific progress and publication trends in the field of IFE. The findings showed an increasing trend in publications over the last decade, and also highlighted gaps in scientific evidence with the aim of guiding researchers to conduct more high-impact investigations by performing clinical studies evaluating rates of periapical repair and IFE treatment success using long-term observation periods.

Author's Contributions

LPA, ELRS: Conceptualization. LPA, WLOR, LMP: Methodology. LPA: Formal Analysis, Investigation, Writing – Original Draft Preparation. WLOR: Validation. WLOR, LPC: Visualization. WLOR, NSF, ELRS: Writing – Review & Editing. LPC, LMP, LASF: Data Curation. LPC, LMP, LASF, ELRS: Investigation. LASF: Software analysis. NSF, ELRS: Supervision; Project Administration.

Conflict of Interest

The authors have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.

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Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subjects.

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