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# Knowledge-map Analysis of Ureteroscopy for Urolithiasis

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**Abstract:** The utilization of ureteroscopy (URS) for managing urolithiasis has garnered substantial global recognition. Nonetheless, bibliometric analyses focusing on URS in the context of urolithiasis treatment remain sparse. Therefore, we used bibliometrics to summarize the relevant literature in this field in recent years, in order to grasp the core research directions, capture the developmental frontiers, and provide valuable information for urologists to understand the research hotspots. In this study, we compiled the literature on URS and urinary stones from the Web of Science core database over the past two decades. In this study, we compiled literature about URS and urolithiasis from the Web of Science Core Collection spanning the past two decades. The assembled data were subsequently visualized and analyzed using CiteSpace and VOSviewer software. The findings revealed a total of 1,461 publications, with a consistent annual increase and a notable surge post-2010. The most frequently occurring keywords identified were "ureteroscopy" and "calculi". Olivier Traxer, a prominent figure from France, is recognized as a leading expert in the domain, particularly emphasizing the practical application of diverse techniques for the treatment and management of urinary stones. The Journal of Urology has disseminated the most pertinent literature in this area, with Turkey emerging as the most prolific contributor. Keyword analysis within this field has identified four primary research hotspots: the investigation of complications to mitigate treatment risks, the standardization of treatment protocols, the determination of treatment indications based on stone types, and the implementation of novel techniques in ureteroscopic lithotripsy.

Keywords: ureteroscopy, urolithiasis, bibliometric analysis, co-citation, visual analysis

#### Introduction

Urinary stones include kidney stones, ureteral stones, bladder stones, and urethral stones. This urologic condition is common worldwide, with a prevalence of 7–13% in North America, 5–9% in Europe, and 1–9% in Asia.<sup>1</sup> The prevalence and incidence of urolithiasis have been reported to be rising globally, posing a threat to human health.<sup>2,3</sup> Because of the current changes in the living environment and people's dietary habits, the prevalence of kidney stones has increased significantly, bringing a heavy burden to society.<sup>4,5</sup> The primary symptoms of urolithiasis include sudden onset of back pain or hematuria. If left untreated, it can lead to serious complications such as infection, hydronephrosis, acute kidney injury, renal failure, and uremia, thereby endangering the patient's health.<sup>6–8</sup>

Open surgery for urolithiasis is becoming less common, with three main treatment modalities now being utilized: extracorporeal shock wave lithotripsy (ESWL), ureteroscopy, and percutaneous nephrolithotomy (PNL). Retrograde intrarenal surgery (RIRS) and URS are recognized for treating stones smaller than 2 cm, with RIRS effectiveness for stones up to 3 cm recommended in the EAU guidelines. However, its success depends on the skill of the operator and often requires staged surgeries.<sup>9</sup> In comparison, ESWL is considered the least efficient method for treating stones.<sup>10,11</sup> Consequently, ureteroscopy has been extensively studied and widely used in the treatment of urolithiasis. Despite the efficiency of ureteroscopy, there is no bibliometric method available to analyze the publication trends of ureteroscopy in the treatment of urolithiasis through visual analysis.

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# **Materials and Methods**

#### **Research Methods**

Bibliometrics is a research methodology for describing and analyzing the dynamics and progress of a discipline or field of study based on literature, citations, and textual data, using mathematical methods for quantitative analysis.<sup>12</sup> De Bellis articulated the nature of bibliometrics, stating that its purpose is to analyze and identify patterns in the literature, such as the most productive authors, institutions, countries, and journals in scientific disciplines, trends in literary production over time, and collaborative networks.<sup>13</sup> According to Garfield, bibliometric studies are able to examine the history and structure of a field, the flow of information within the field, the impact of journals, and the citation status of publications over longer time scales.<sup>14</sup> The interpretations of bibliometrics by all of these individuals illustrate the unique role that bibliometrics as a methodology possesses when evaluating in the field of characterization.

Bibliometric research results include descriptive statistics and visual analysis. Descriptive statistics involve data such as authors, institutions, citations, and keywords, while visual analysis provides an intuitive representation of the data. Therefore, scholars often use it to assess research quality, identify future research directions, and provide new ideas for researchers, greatly improving scientific research efficiency. In this paper, we conduct bibliometric analysis using the visualization software VOSviewer and CiteSpace.

#### Data Sources

We used the Web of Science Core Collection as the data source to ensure the comprehensiveness and authority of the analyzed data, indexing SSCI, SCIE, CCRE, and IC. The search strategy was: TS=(ureteroscopic lithotripsy) OR TS= (retrograde intrarenal surgery) OR TS=(URS) OR TS=(URL) OR TS=(RIRS) AND TS=(urolithiasis) OR TS=(nephrolithiasis) OR TS=(ureterolithiasis) OR TS=(urinary calculi) OR TS=(kidney calculi) OR TS=(urinary bladder calculi) OR TS=(kidney stone) OR TS=(urostone) OR TS=(renal stone) OR TS=(urinary stone) OR TS=(ureteral stone) OR TS= (urinary bladder stone). We limited the literature type to reviews and articles and restricted the period from January 1, 2000, to December 31, 2023. The search included all languages and yielded 2,073 documents (Table 1). To ensure the quality and accuracy of the data, we also performed a data cleaning process by two reviewers, as shown in Figure 1.

# **Result and Descriptive Statistics**

#### Underlying Quantitative Information

The 1461 papers used in this study came from 1034 authors at 1699 institutions (organizations) in 68 countries, published in 126 journals, citing 11259 citations from 2029 journals.

Figure 2 shows the temporal distribution of papers published in the research field of ureteroscopy for urinary tract stones. Overall, the number of papers published in this field has gradually risen, experiencing an explosive growth period

Research Database	Web of WoSCC
Citation indexes Query formulation	SSCI, SCIE, CCR, IC (TS=(ureteroscopic lithotripsy)OR TS=(retrograde intrarenal surgery)OR TS=(URS)OR TS=(URL)OR TS=(RIRS))AND (TS=(urolithiasis)OR TS=(nephrolithiasis)OR TS=(ureterolithiasis)OR TS=(urinary calculi)OR TS=(kidney calculi)OR TS = (ureteral calculi)OR TS=(urinary bladder calculi) OR TS=(ureteral calculi)OR TS=(kidney stone)OR TS=(urostone)OR TS=(uroteral calculi)OR TS=(urinary bladder calculi) OR TS=(ureteral calculi)OR TS=(kidney stone)OR TS=(urostone)OR
	IS=(renal stone)OK IS=(urinary stone)OR IS=(ureteral stone)OR IS=(urinary bladder stone))
Type of articles	Articles and Reviews
Searching period	L January 2000 to 31 December 2023
Data collection	Export with full records and cite references in plain text format
Sample size	2072 publications including 1904 articles and 269 reviews
Sample Size	20/3 publications including root articles and 20/ reviews

Table I The Search Strategy of Web of WoSCC



Figure I Comprehensive search flow diagram.

after 2010 and stabilizing at more than 90 papers per year after 2015. This indicates that the research field has matured in recent years and continues to hold significant research value.

#### Bibliometric Analysis of the Co-authorship

The analysis of the authors allows us to identify the most influential and core authors currently active in the field. According to Price's Law, we determined that  $m = 0.749 \times \sqrt{n_{max}} \approx 5.08$ . This result indicates that authors in the field of ureteroscopy for the treatment of urinary stones with five or more publications are considered core authors, totaling 254 individuals. Figure 3 (A) Top 10 author H index. (B) Author article count shows the top 10 authors in the field regarding the H-index.

The most published author in this field is Olivier Traxer, with a total of 55 papers, and he is second in H-index. Meanwhile, Kemal Sarica and Bhaskar Somani published 30 and 27 articles, respectively. Remarkably, Glenn Michael Preminger, with only 18 publications, achieved the highest H-index. His high-quality contributions focus on developing treatment guidelines for urinary tract stones and guidance on minimally invasive treatments, primarily shockwave lithotripsy. Another notable author is Guohua Zeng, who, although not in the top ten for the number of articles, ranks fifth for contributions. His main research interests include minimally invasive surgical treatments for urinary tract stones, particularly minimally invasive percutaneous nephrolithotripsy, and ureteroscopic lithotripsy.



2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021 2022 2023

Figure 2 Distribution of publications from 2000 to 2023.

Figure 4 illustrates the author collaboration network, where connecting lines indicate collaboration between authors. Table 2 lists the top ten authors by the number of publications and citations. The top five authors with the most published articles are Olivier Traxer (55), Kemal Sarica (30), B. Resorlu (27), B.K. Somani (27), and A. Unsal (23). The five most cited authors are C. Türk (438), M. Grasso (269), Olivier Traxer (255), and J.J.M.C.H. de la Rosette (200). From the analysis of published articles, Olivier Traxer focused on the practical application of various techniques in treating urinary stones<sup>15–17</sup> and managing the treatment process.<sup>18,19</sup>

#### Bibliometric Analysis of Journals

Articles, which we plotted as a network diagram (Figure 5) and listed the top 10 published journals in Table 3. This table shows that the Journal of Urology has the highest Impact Factor (IF) value of 5.9. In addition, the journals with higher Impact Factors, BJU International (2023 IF 3.7), Journal of Endourology (2023 IF 2.9), and World Journal of Urology (2023 IF 2.8), have more than 30 publications. Combined with the Journal Citation Reports (JCR) evaluation system's data, these journals are classified in Q1 and Q2. Table 4 lists the ten most cited journals. The Journal of Endourology has the highest number of citations with 6,556, followed by the Journal of Urology with 4,876 citations. It is not in the top ten in terms of the number of publications, it has an IF of 25.3 and a citation count of 2,782, indicating that this journal is extremely influential in the field.

#### Analysis of Top Countries and Institutions

The development of ureteroscopy for treating urinary tract stones is unevenly distributed worldwide. We analyzed publication data by country using VOSviewer software to identify countries with outstanding contributions. We visualized countries with more than five publications, as shown in Figure 6. The figure shows that the distribution of



(A):H-index

Figure 3 (A) Top 10 author H index. (B) Author article count.

publishing countries is skewed, with most papers from a few top countries. Table 5 lists the top 10 countries by number of publications and citations per paper. Analysis shows Turkish scholars contributed the most papers (305) with 6,340 citations. This is followed by China, with 297 papers but fewer citations. American scholars achieved the highest average citations per article, indicating that US research is the most recognized globally. They boast 9,663 citations from 281 papers, with an average citation count of 34.39.

Table 6 displays the top ten contributing institutions in ureteroscopy for urinary stones. Sorbonne University (30 citations), Duke University (28 citations), and the University of Michigan (28 citations) are the top three. Duke



Figure 4 Cooperation map of authors.

University has 2,180 citations, leading all other institutions, indicating its authoritative position in ureteroscopy for treating urinary tract stones. Further analysis of the collaborative network (Figure 7) shows the potential to expand global cross-institutional collaboration in ureteroscopy for urolithiasis, enhancing research outcomes and innovations.

# Visual Analysis and Discussion

#### Co-Occurrence Analysis on Keywords

Keywords from the paper were visualized and analyzed using VOSviewer software. We screened for keywords with a frequency of more than 40 occurrences and created a keyword density graph shown in Figure 8. Each word appears as a node, with larger nodes indicating higher frequency. Thus, the keyword density graph highlights research hotspots in the field. The graph shows that keywords such as calculus, ureteroscopy, ESWL, and retrograde intrarenal surgery are representative terms in this field. Table 7 lists the 20 most frequently occurring keywords. Among these, ureteroscopy, calculus, and renal stone were core keywords for our search. Keywords like flexible and laser indicate the significant

Rank	Author	Documents	Co-cited Author	Citations
I	Traxer, Olivier.	55	Türk, c	438
2	Sarica, kemal.	30	Grasso, m	269
3	Resorlu, b.	27	Preminger, Glenn	268
4	Somani, B.K.	27	Traxer, Olivier	255
5	Unsal, a.	23	De la rosette, jjmch	200
6	Atis, g.	20	Pearle, ms	196
7	Castellani, d.	18	Breda, a	194
8	Gauhar, vineet	18	Resorlu, b	193
9	Monga, manoj	18	Dindo, d	190
10	Preminger, Glenn	18	Assimos, dg	169

Table 2 The Top 10 Productive and Cited Authors



🔼 VOSviewer



impact of new laser technology and flexible instruments in ureteroscopic lithotripsy. Flexible ureteroscopes are now widely used to treat upper urinary tract stones, and URS has become the preferred treatment in many regions.<sup>20–22</sup> With rapid laser technology development, treatment options for surgeons are increasing, with many attempts to combine laser technology with flexible ureteroscopy for treating upper urinary tract stones.<sup>23–28</sup> Digital flexible scopes, using cutting-edge chip technology, have dramatically improved RIRS outcomes with high-quality visual images. Keywords like outcomes and effectiveness suggest that new ureteroscopic lithotripsy techniques aim to improve efficiency, a key clinical

Rank	Source	Publications	2023 IF	JCR	Citations
1	Journal of endourology	261	2.9	QI	6556
2	World journal of urology	115	2.8	Q2	2043
3	Urolithiasis	113	2.0	Q2	2008
4	Urology	106	2.1	Q2	3383
5	Journal of urology	62	5.9	QI	4876
6	Urologia internationalis	57	1.5	Q3	758
7	Urology journal	43	1.5	Q3	349
8	Bmc urology	39	1.7	Q3	402
9	Bju international	36	3.7	QI	1564
10	Archivos espanoles de urologia	33	0.6	Q4	86

Table 3 Top 10 Most-Articled Journals

Rank	Source	Citations	2023 IF	JCR
1	Journal of endourology	6556	2.9	QI
2	Journal of urology	4876	5.9	QI
3	Urology	3383	2.1	Q2
4	European urology	2782	25.3	QI
5	World journal of urology	2043	2.8	Q2
6	Urolithiasis	2008	2.0	Q2
7	Bju international	1564	1.7	Q3
8	Urologia internationalis	758	1.5	Q3
9	Urologic clinics of north america	433	2.4	Q2
10	Bmc urology	402	1.7	Q3

Table 4 Top	10 Most-Cited	Journals
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focus. Keywords like management and complications highlight the research focus on managing stone patients and postlithotripsy issues. For example, UAS use has been studied to enhance minimally invasive management of complex upper urinary tract disease.<sup>29</sup> Other studies compare different methods for higher stone-free rates.<sup>30</sup>

#### Evolution Analysis on Keywords

To explore research hotspots and focuses in the field, we can extract from the keywords. We first use Citespace to filter and extract keywords, visualizing their co-occurrence relationships. We further process the data for keyword evolution



Figure 6 Countries' cooperative ties.

VOSviewer

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Rank	Country	Documents	Citations	Average Citation
1	Turkey	305	6340	20.79
2	China	297	3842	12.94
3	USA	281	9663	34.39
4	Germany	88	2672	30.36
5	Italy	86	2100	24.42
6	England	83	2003	24.13
7	France	81	2072	25.58
8	South korea	67	923	13.78
9	India	63	1760	27.94
10	Japan	62	1455	23.47

 Table 5 Top 10 Productive Countries/Regions

 Table 6 Top 10 Productive Institutions

Rank	Organization	Documents	Citations
1	Sorbonne Univ	30	377
2	Duke Univ	28	2180
3	Univ Michigan	28	955
4	Guangzhou med Univ	27	483
5	Univ Hlth sci	23	106
6	Shanghai jiao tong Univ	20	300
7	Univ british columbia	20	212
8	Istanbul medeniyet Univ	18	251
9	Ankara Univ	17	546
10	Bozok Univ	17	212

analysis, which reveals research hotspots and helps understand the field's development. This led to the creation of a keyword time zone view (Figure 9). Each color bar in the figure represents a year (2000–2023); the size of nodes indicates frequency, and lines show co-occurrence relationships. The figure shows that high-frequency keywords are uniformly distributed across time zones, indicating constant development in the field. End keywords appear smaller due to their recent emergence and fewer citations, confirming ongoing development. The field has evolved from ureteroscopy and ESWL to laser lithotripsy, RIRS, and flexible ureteroscopy, staying at the forefront of technology application.<sup>31</sup> Over the past two decades, ureteroscopy has increasingly contributed to stone treatment, with the intensive application of novel techniques. ESWL has developed rapidly since 2000, mainly for proximal ureteral and intrarenal stones. As ureteroscopy and laser technology developed, ureteroscopic lithotripsy became the preferred treatment for small stones. From 2010 onwards, minimally invasive stone management became mainstream. Keywords like stone classification and clearance rate indicate a focus on efficient, safe treatment and reduced complications.<sup>32</sup>

#### **Co-Citation Analysis**

Co-citation analysis helps identify highly cited papers in the research field. We used VOSviewer to map co-citation relationships, and the final map of highly cited articles is shown in Figure 10. These papers form four clusters, corresponding to the four colors in the figure. The red clusters focus on studies related to complications, emphasizing risk factor reduction and safe management of stone patients. The green clusters focus on new technologies like laser lithotripsy and PCNL in urinary stone treatment. The blue clusters focus on clinical guidelines for urolithiasis management, emphasizing standardized treatment protocols. The yellow clusters involve comparative studies of treatments, focusing on identifying indications for ESWL, URS, and PCNL. The papers were analyzed for citations, and the five most highly cited are listed in Table 8. The five most highly cited papers all relate to urolithiasis management and complications. The most cited paper is by Dindo D, on classifying surgical complications, developed from studies at 10





centers worldwide. It has become a powerful tool for assessing surgical procedure quality globally.<sup>33</sup> The guideline on urinary stones, the second most cited, is a global authority on stone management. Traxer O's study on ureteral injuries from UAS in RIRS surgery is third. He concluded that visual evaluation of the ureter and preoperative double J stenting can significantly reduce severe ureteral injuries.<sup>34</sup>

#### Discussion

Ureteroscopic lithotripsy is a long and mature field. Over the decades, the attention it has received has not declined; instead, it has expanded into more and deeper areas of exploration as technology has advanced. This paper analyzes research in this field over the past two decades using VOSviewer and CiteSpace software. It reviews the development trends, core authors, high-yield countries and institutions, the most influential journals, and keyword clustering in this field, all based on bibliometric analysis.

By analyzing published papers, we learn that research in this field is gradually maturing. Additionally, the number of papers rises significantly every three years, indicating steady development in the field. Analysis of authors reveals a stable core group whose research drives the field forward. A leader in this field is Traxer Olivier, whose large number of publications and equally large number of citations illustrate the profound impact his work has had on the field. His most cited article is a study on intraoperative ureteral wall injury in RIRS (30), which provides very valuable value to the field. Other contributing authors, such as Glenn Michael Preminger and Zeng, guohua, have contributed to the minimally invasive treatment of stones in a variety of ways, guiding the standardization of clinical treatment of urolithiasis.



Figure 8 Map of keyword density.

At the country/region level, the largest number of articles originated from Turkey, consistent with previous findings of numerous Turkish authors. The United States is a central contributor, with a high number of articles and leading citation rates, indicating high quality. In contrast, although China has a similar number of articles, its low number of citations shows that Chinese research is not recognized by the West, which points out the important task for Chinese scholars to improve the quality of their research. Furthermore, the average citations per article in Germany and India are significant, indicating high research quality. The US collaborates closely with Turkey, China, Italy, and others, with its high-quality research gaining widespread recognition. When exploring this level of the institution, it can be seen that Duke Univ's citation count breaks ahead of the others, signaling France's important role in advancing the field of ureteroscopy for stone treatment. It also proves that French research has a wide resonance in the medical community. Meanwhile Sorbonne Univ and Univ Michigan are very productive and show that the US likewise holds a prominent position in the field.

We have visualized keywords in this article, including co-occurrence and evolution analysis. Flexible, laser, outcomes, efficiency, management, and complications are keywords that appear to represent an important core in the development of ureteroscopy for the treatment of urinary tract stones, and show the development of the field's history. The development of the field over the years has been diversified and integrated, with scholars constantly exploring new technologies, such as lasers and flexible ureteroscopy, and others focusing on the direction of surgical complications and postoperative management, and throughout the development of the field, scholars are pursuing standardized diagnosis and treatment of stone patients. The development of the field is not only in depth, but also in breadth. Scholars are no longer limited to the study of etiology or mechanism, but also take advantage of new methods of data collection and processing, trying to find more appropriate treatment of urinary tract stones and corresponding management of minimal complications.

Rank	Keyword	Frequency	Total
			Link Strength
I	Ureteroscopy	619	1919
2	Calculi	554	1792
3	Management	554	1902
4	Renal stone	529	1793
5	ESWL	429	1448
6	Retrograde intrarenal surgery	375	1315
7	Urolithiasis	372	1236
8	Lithotripsy	362	1173
9	Percutaneous nephrolithotomy	345	1313
10	Complications	315	1106
11	Flexible ureteroscopy	207	775
12	Ureteral calculi	198	606
13	Laser lithotripsy	181	686
14	Outcomes	143	657
15	Experience	132	576
16	Holmium laser	132	578
17	Laser	122	536
18	Efficacy	115	555
19	Ureterorenoscopy	113	496
20	Ureteroscopic lithotripsy	99	360

Table 7 High-Frequency Keywords in Research

Finally, we conducted a co-citation analysis to identify highly cited journals and papers, uncovering four key hotspots: reducing treatment complications, standardizing protocols, determining treatment indications for various stones, and applying new technologies in ureteroscopic lithotripsy. While the research direction remains consistent, new data

stone free rate ureteroscopic lithotripsy flexible ureterorenoscopy trend classification safety / ureteral access sheath rir risk factor laser efficacy impact retrograde intrarenal surgery surgerychildren clinical research office holmium laser ureterorenoscopy laser lithotripsy experience outcm ureteral calculi flexible ureteroscopy lithotrips percutaneous nephrolithotomy 2cm urolithiasis eswl enal stone complication calculi Commanagement ureteroscopy

Figure 9 Map of timezone view.



Figure 10 Co-citation of cited references.

processing methods, such as big data and artificial intelligence, offer clinicians fresh perspectives on urolithiasis. This study aims to guide future research in capturing development directions and focuses.

This study has limitations due to certain factors. The bibliometric approach requires researchers to analyze and interpret data, necessitating a comprehensive understanding of the field, which can introduce subjective bias. Additionally, the literature analysis software requires high data standards. This study only included journal articles from the Web of Science database's SSCI, SCIE, CCRE, and IC indexes, limiting the data analysis. However, we believe research on ureteroscopic lithotripsy will continue to develop, offering more areas to explore, making this study valuable for further investigation. Future studies should address data integrity and quality by integrating multiple databases for comprehensive screening. Additionally, engaging with scholars in ureteroscopic lithotripsy can deepen understanding, grasp cutting-edge developments, and minimize subjective analysis.

Rank	Cited Reference	Citations	Strength
I	Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey <sup>33</sup>	187	521
2	EAU Guidelines on Interventional Treatment for Urolithiasis <sup>32</sup>	181	408
3	Prospective evaluation and classification of ureteral wall injuries resulting from insertion of a ureteral access sheath during retrograde intrarenal surgery <sup>34</sup>	127	429
4	The clinical research office of the endourological society ureteroscopy global study: indications, complications, and outcomes in 11,885 patients <sup>35</sup>	104	250
5	2007 guideline for the management of ureteral calculi <sup>36</sup>	103	238

Table 8 Top 5 Most Important Publications in the Field

## Conclusions

The findings revealed a total of 1,461 publications, with a consistent annual increase and a notable surge post-2010. The most frequently occurring keywords identified were "ureteroscopy" and "calculi". Olivier Traxer, a prominent figure from France, is recognized as a leading expert in the domain, particularly emphasizing the practical application of diverse techniques for the treatment and management of urinary stones. The Journal of Urology has disseminated the most pertinent literature in this area, with Turkey emerging as the most prolific contributor. Keyword analysis within this field has identified four primary research hotspots: the investigation of complications to mitigate treatment risks, the standardization of treatment protocols, the determination of treatment indications based on stone types, and the implementation of novel techniques in ureteroscopic litho-tripsy. This study aims to highlight the core research directions for URS in urolithiasis, to grasp the frontiers of development, and to provide valuable information for urology researchers to understand research hotspots.

## **Ethics Declarations**

This study does not involve human and/or animal subjects, therefore it does not require approval from the institutional ethics review committee, nor does it require informed consent.

# **Data Sharing Statement**

Data will be made available on request.

# **Author Contributions**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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# Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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