

Research Article



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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Influence of autoclave sterilization procedures on the cyclic fatigue resistance of heat-treated nickel-titanium instruments: a systematic review

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ABSTRACT

Objectives: This systematic review evaluated the influence of autoclave sterilization procedures on the cyclic fatigue resistance of heat-treated nickel-titanium (NiTi) instruments.

Materials and Methods: A systematic search without restrictions was conducted in the following electronic databases: PubMed, Scopus, Web of Science, ScienceDirect, Cochrane, and Open Grey. The hand search was also performed in the main endodontic journals. The eligible studies were submitted to the methodological assessment and data extraction.







Results: From 203 abstracts, a total of 10 articles matched the eligible criteria. After reading the full articles, 2 were excluded because of the absence of the heat-treated instruments in the experimental design and 3 due to the lack of a control group using heat-treated instruments without autoclave sterilization. From the 5 included studies, 1 presented a low risk of bias, 3 presented moderate and 1 high risk. It was observed heterogeneous findings in the included studies, with autoclave sterilization cycles increasing, decreasing or not affecting the cyclic fatigue life of heat-treated NiTi instruments. However, the retrieved studies evaluating the cyclic fatigue resistance of endodontic instruments presented different protocols and assessing outcomes, this variability makes the findings less comparable within and also between groups and preclude the establishment of an unbiased scientific evidence base.

Conclusions: Considering the little scientific evidence and considerable risk of bias, it is still possible to conclude that autoclave sterilization procedures appear to influence the cyclic fatigue resistance of heat-treated NiTi instruments.

Keywords: Autoclave sterilization; Cyclic fatigue resistance; NiTi instruments; Systematic review

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INTRODUCTION

The use of nickel-titanium (NiTi) instruments in endodontic clinical procedures provided many advantages, such as faster set-up time, cutting efficiency, and canal centering ability compared to manual stainless steel files [1]. Despite these benefits, NiTi instruments appear to be vulnerable to deformations and/or fractures, which may contribute negatively to treatment prognosis [2]. To overcome these drawbacks, improvements in instrument design and the development of new NiTi alloys with superior mechanical properties have been proposed [1].

The nickel and titanium ratio of a conventional NiTi alloy is almost equiatomic, with approximately 56% and 44% of each element, respectively [3]. With these proportions, there are 2 temperature-dependent crystalline structures called austenite and martensite phases [4]. In the austenitic state, the NiTi alloy is rigid, hard and has superior superelastic properties, whereas in its martensitic state the NiTi alloy is soft, ductile, can be easily deformed and has the shape memory effect [2]. At room temperature, many files are in the martensitic state or at least below the austenite finish (Af) temperature, that is why they are still rather flexible [4-9]. Based on this information, several producers have developed special thermomechanical processing aiming to produce NiTi alloys, which mainly contain a stable martensitic phase under clinical conditions. Thus, several thermomechanical treatments have been suggested, such as the Control Memory (CM; Coltene, Cuyahoga Falls, OH, USA), the Blue Technology (Dentsply Tulsa Dental Specialties, Tulsa, OK, USA), and the Gold Technology (Dentsply Tulsa Dental Specialties). Within these treatments, instruments have demonstrated increased flexibility, resistance to fatigue, and capacity of self-centering in the canal during preparation [4-9].

NiTi instruments are generally used more than one single-use in clinical practice for different reasons. Therefore, sterilization procedures are necessary to avoid cross-contamination among patients [10]. Since NiTi properties are highly influenced by thermomechanical processing, the effects of additional heat retreatment promoted during autoclaving procedures can affect the mechanical properties of these instruments. This issue has been demonstrated in previously published studies that showed the influence of autoclave sterilization on the cyclic fatigue strength of NiTi instruments [7,9,11,12]. However, these findings remained controversial. Thus, a systematic review of the available literature using strict inclusion criteria could help to clarify the differences in the results of these studies. Therefore, the purpose of this systematic review was to answer the following question: “Do autoclave sterilization procedures influence the cyclic fatigue resistance of heat-treated NiTi instruments?”

MATERIALS AND METHODS

The present systematic review was conducted following the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement [13]. In addition, it was also registered in the PROSPERO database (CRD42018096428).

Search strategy

The systematic search of the literature was conducted by 2 independent reviewers (M.Z. and T.K.S.F.) until March 2019 using the following databases: Medline, Scopus, and The Cochrane Library. The gray literature was consulted by OpenSIGLE. To complement the

searches, the references of the included studies were screened to find any additional study that did not appear in the database searches.

The systematic search strategy was based on the following Medical Subject Heading terms (MeSH) or Text Word (tw) in different combination: “NiTi,” “nickel-titanium,” “titanium nickelide*,” “nickelide,” “root canal therapy,” “dental instruments,” “instrument*,” “instrument*,” “rotatory,” “sterilization,” “autoclave,” “heat*,” “thermal*,” “fatigue,” “stress fracture,” “fracture resistance,” “resistance,” and “fracture strength.” The MeSH and tw were applied by combining the Boolean operators (OR, AND) for the searches. Appropriate modifications were performed in terms of adequate syntax rules of each database (**Table 1**).

The search was performed without any restrictions on the publication date. It was included only studies in the English language. To find additional studies, the electronic search was supplemented by a hand search of the reference lists from the articles included and alerts created in databases concerning the search strategy. An additional screening was performed in the references of the included studies and in specific journals, such as the *Journal of Endodontics* and in the *International Endodontic Journal* to find any additional study that did not appear in the searched databases.

Table 1. Search strategy in the databases

Database	Search strategy
PubMed	#1 (((NiTi[Title/Abstract]) OR Ni-Ti[Title/Abstract]) OR nickel-titanium[Title/Abstract]) OR titanium nickelide[Title/Abstract]) OR nickelide[Title/Abstract] #2 ((((((root canal therapy[MeSH Terms]) OR root canal therapy[Title/Abstract]) OR dental instruments[MeSH Terms]) OR dental instruments[Title/Abstract]) OR instrument*[Title/Abstract]) OR endodontic*[Title/Abstract]) OR rotatory[Title/Abstract]) #3 ((((((sterilization[MeSH Terms]) OR sterilization[Title/Abstract]) OR autoclave[Title/Abstract]) OR heat*[Title/Abstract]) OR termal*[Title/Abstract]) #4 ((((((fatigue[MeSH Terms]) OR fatigue[Title/Abstract]) OR stress fracture[MeSH Terms]) OR stress fracture[Title/Abstract]) OR fracture resistance[Title/Abstract]) OR resistance[Title/Abstract]) OR fracture strength[Title/Abstract]) #1 and #2 and #3 and #4
Scopus	#1 TITLE-ABS-KEY(NiTi) OR TITLE-ABS-KEY(Ni-Ti) OR TITLE-ABS-KEY(nickel-titanium) OR TITLE-ABS-KEY(titanium nickelide) OR TITLE-ABS-KEY(nickelide) #2 TITLE-ABS-KEY(root canal therapy) OR TITLE-ABS-KEY(dental instruments) OR TITLE-ABS-KEY(instrument*) OR TITLE-ABS-KEY(endodontic*) OR TITLE-ABS-KEY(rotatory) #3 TITLE-ABS-KEY(sterilization) OR TITLE-ABS-KEY(autoclave) OR TITLE-ABS-KEY(heat*) OR TITLE-ABS-KEY(termal*) #4 TITLE-ABS-KEY(fatigue) OR TITLE-ABS-KEY(stress fracture) OR TITLE-ABS-KEY(fracture resistance) OR TITLE-ABS-KEY(resistance) OR TITLE-ABS-KEY(fracture strength) #1 and #2 and #3 and #4
Web of Science	#1 TS=(“NiTi” OR “Ni-Ti” OR “nickel-titanium” OR “titanium nickelide*” OR “nickelide”) #2 TS=(“root canal therapy” OR “dental instruments” OR “instrument*” OR “instrument*” OR “rotatory”) #3 TS=(“sterilization” OR “autoclave” OR “heat*” OR “termal”) #4 TS=(“fatigue” OR “stress fracture” OR “fracture resistance” OR “resistance” OR “fracture strength”) #1 and #2 and #3 and #4
ScienceDirect	#1 TITLE-ABS-KEY(NiTi) OR TITLE-ABS-KEY(Ni-Ti) OR TITLE-ABS-KEY(nickel-titanium) OR TITLE-ABS-KEY(titanium nickelide) OR TITLE-ABS-KEY(nickelide) #2 TITLE-ABS-KEY(root canal therapy) OR TITLE-ABS-KEY(dental instruments) OR TITLE-ABS-KEY(instrument*) OR TITLE-ABS-KEY(endodontic*) OR TITLE-ABS-KEY(rotatory) #3 TITLE-ABS-KEY(sterilization) OR TITLE-ABS-KEY(autoclave) OR TITLE-ABS-KEY(heat*) OR TITLE-ABS-KEY(termal*) #4 TITLE-ABS-KEY(fatigue) OR TITLE-ABS-KEY(stress fracture) OR TITLE-ABS-KEY(fracture resistance) OR TITLE-ABS-KEY(resistance) OR TITLE-ABS-KEY(fracture strength) #1 and #2 and #3 and #4
Open Grey - SIGLE	#1 “NiTi” OR “Ni-Ti” OR “nickel-titanium” OR “titanium nickelide*” OR “nickelide” #2 “root canal therapy” OR “dental instruments” OR “instrument*” OR “instrument*” OR “rotatory” #3 “sterilization” OR “autoclave” OR “heat*” OR “termal” #4 “fatigue” OR “stress fracture” OR “fracture resistance” OR “resistance” OR “fracture strength” #1 and #2 and #3 and #4

Eligibility criteria of the studies

The eligibility criteria were formulated according to the “PICOS” (Population, Intervention, Comparison, Outcome, and Study design) strategy. It was selected studies that evaluated heat-treated NiTi instruments (P, population) submitted to autoclave sterilization (I, intervention), compared to no autoclave sterilization (C, comparison), which evaluated the cyclic fatigue resistance (O, outcome) in *in vitro* models (S, study design).

The final decision on the study selection was performed based on the full-text reading of the potentially eligible studies, and only studies that included adequate control groups without autoclave sterilization were included. Additionally, review articles, opinion articles, and letters were also excluded.

Screening and selection

The selection of studies was independently performed by 2 authors (M.Z. and T.K.S.F.) based on the title and abstract. When the title and abstract of the studies did not provide enough information to judge its inclusion or exclusion, the full articles were obtained. In cases of diverging judgment or any disagreement between examiners, the title/abstract was reexamined in consensus with a third examiner (E.J.N.L.S.). Then, the full texts of the studies that presented the potential to be included were evaluated and judged according to eligible criteria following the PICOS strategy. Articles that appeared in more than one database search were removed and only one was maintained.

Assessment of risk of bias

The methodological quality of the included studies was judged based on the adaptation of the quality assessment of a previous systematic review conducted considering *in vitro* studies [14]. The methodological quality assessment of the included studies was performed independently by the reviewers (M.Z. and T.K.S.F.). The following domains were used: 1) aleatorization of specimens; 2) standardization of samples; 3) standardization of autoclave sterilization procedures (time, temperature and pressure); 4) single-operator protocol execution; 5) sample size calculation; 6) blinding of fatigue test operator; and 7) correct statistical analysis carried out. In cases of disagreement between the examiners, a third examiner (E.J.N.L.S.) was consulted. The calculation of the power of the included studies was performed using the cyclic fatigue resistance means, standard deviations, and sample size for each group of instruments. The power analysis is a strategy that provides the effect size for the study considering the sample size. For this purpose, it was adopted a confidence interval of 95% and a 2-tailed test using OpenEpi 3.04.04 tool www.openepi.com software (Emory University, Atlanta, GA, USA).

The domains reported in the included studies were classified as ‘+’ to register low risk of bias and ‘-’ to register high risk of bias and ‘?’ to register unclear parameter. The articles were classified as low risk of bias if 6 or more domains were assigned as low (+), a moderate risk of bias if 4 or 5 domains were assigned as low, and a high risk of bias if only 3 or fewer domains were assigned as low. The authors were contacted via e-mail to provide eventual missing information about the included studies. Studies that were not possible to recover the missing information for the correct judgment, after at least 2 attempts to contact the authors via e-mail, were assigned as unclear.

Data extraction

The examiners (M.Z. and T.K.S.F.) performed the independent data extraction of the included articles. The information related to the details of the included studies (first author, year, and country), instruments and brands, sample size, angles, and radii of curvature of simulated canals, model set up, groups and sterilization cycle, and main statistical results were extracted.

RESULTS

Study selection

An overall of 203 studies was retrieved. The title and abstract reading resulted in 10 studies [4,7,9-12,15-18] that matched the eligibility criteria. No additional study was included after the manual search of the references of these 10 studies. After reading the full text of these studies, 2 were excluded because heat-treated instruments were not used [8,18], and 3 studies due to the lack of a control group without autoclave sterilization [10,11,15]. Therefore, after the removal of duplicates, the systematic databases search resulted in 5 studies [4,7,9,12,16], as demonstrated in the flow diagram (Figure 1).

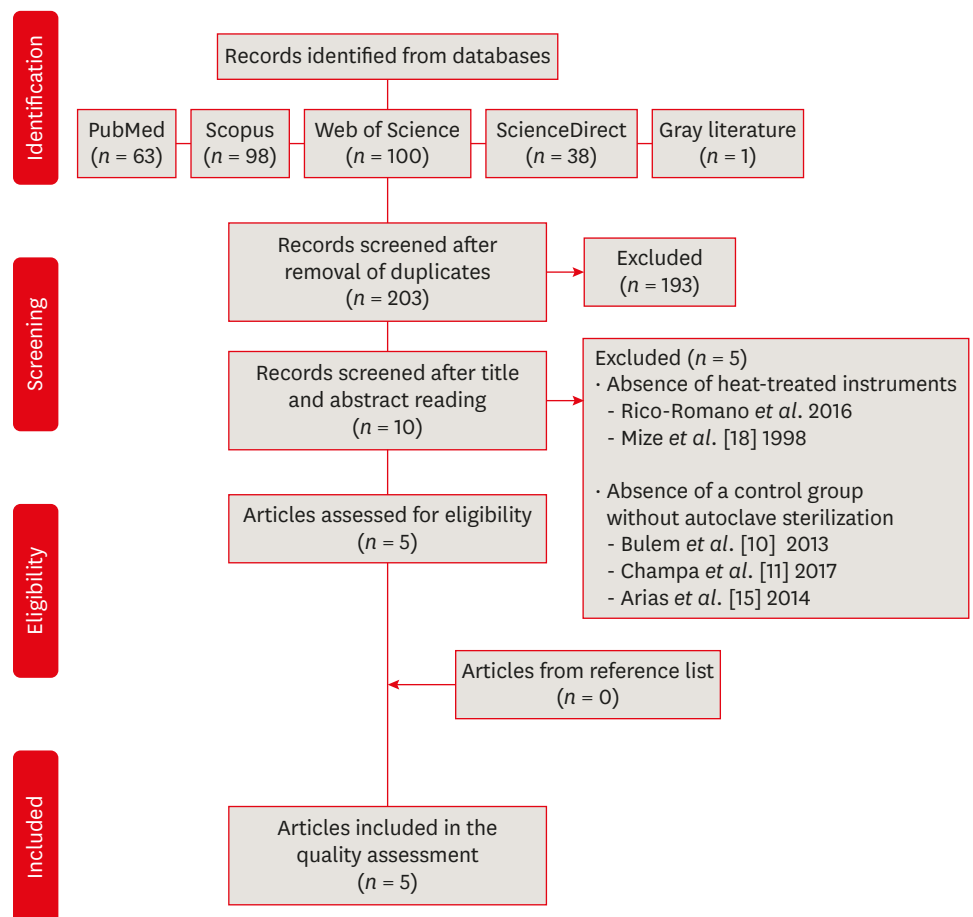


Figure 1. Flow diagram showing the process of identifying, screening and reasons for the exclusion of the studies.

Risk of bias

The results of the methodological quality of the included studies are described in **Figure 2**. From the 5 included studies, 1 presented low risk of bias [4], 3 presented moderate [7,9,12], and 1 high risk [16]. All studies standardized the included samples, the autoclave sterilization cycle, and the test design. The power analysis of the included studies resulted in satisfactory effect size for 3 studies [9,12,16].

Characteristics of included studies

The information related to the 5 included studies is shown in **Table 2**. The 5 studies performed *in vitro* cyclic fatigue tests using heat-treated instruments. All included studies compared new unsterilized instruments with new, but autoclaved instruments. The number of autoclaving cycles varied from 1 to 10 cycles. All studies were performed using static cyclic fatigue assays. The testing jig varied in the angle of curvature (60° to 90°) and in the radii of curvature (3 mm to 5 mm).

Outcomes of the cyclic fatigue life

Due to the high heterogeneity among instruments brands, methods, and applied techniques to measure the outcomes of the cyclic fatigue life, it was not possible to standardize the outcome data and conduct a meta-analysis. Therefore, in the current systematic review, a descriptive analysis was carried out, and the main relevant findings are reported in **Table 2**.

The findings resulted from the included studies were varied, with autoclave sterilization cycles increasing [7,9,12], decreasing [4,16] or not affecting [4,7,9,16] the cyclic fatigue life of heat-treated NiTi instruments.

	Aleatorization of specimens	Standardization of samples	Standardization of autoclavation procedures	Single-operator protocol execution	Sample size calculation	Blinding of the operator of the testing machine	Statistical analysis
Hilfer <i>et al.</i> [16] 2011	?	+	+	?	-	?	+
Özyürek <i>et al.</i> [12] 2017	+	+	+	?	-	?	+
Pedullà <i>et al.</i> [4] 2018	+	+	+	+	-	+	+
Plotino <i>et al.</i> [7] 2012	+	+	+	+	-	-	+
Zhao <i>et al.</i> [9] 2016	+	+	+	?	-	?	+

Figure 2. Methodological quality assessment of the included studies.

Table 2. Tested instruments, testing conditions and main results

Study	Heat-treated instruments and brand	Sample size (No.)/ power analysis	Angles and radii of curvature of simulated canals	Model setup	Groups and sterilization cycle	Results
Pedullà et al. [4], 2018	Twisted Files 25/.06 (SybronEndo, Orange, CA, USA) and HyFlex CM 25/.06 (ColteneWhaledent, Cuyahoga Falls, OH, USA)	15/power: 1 time autoclaved; Hyflex CM: 27.38%; Twisted File: 59.16%; Mean: 43.25%; 3 times autoclaved; HyFlex CM: 93.76%; Twisted File: 100%; Mean: 96.88%	60° angle 5-mm radii of curvature	Static	- Control group (non-sterilized) and experimental groups (autoclaved 1 or 3 times). - Cycle of autoclave sterilization was performed at a temperature of 134°C for 17 minutes.	No cyclic fatigue difference was found between the control and both autoclave groups of Hyflex CM ($p > 0.05$). Twisted Files autoclaved 3 times had significantly lower resistance to cyclic fatigue than new ones ($p < 0.05$). No differences were observed between one cycle sterilization and new ones ($p > 0.05$).
Hilfer et al. [16], 2011	GT Series X files 20/.06 and 20/.04 (Dentsply Tulsa Dental Specialties, Tulsa, OK, USA) and Twisted Files 25/.06 and 25/.04 (SybronEndo, Orange, CA, USA)	20/power: GT 20/.04: 2.13%; GT 20/.06: 70.14%; Twisted File 25/.06: 40.24%; Mean: 37.50%	90° angle 5-mm radii of curvature	Static	- Control group (non-sterilized) and experimental groups (autoclaved 1 time). - Cycle of autoclave sterilization was performed at a 132°C for 6 min (30–35 psi).	Autoclave sterilization conditions did not significantly affect the cyclic fatigue behavior of GT Series X (20/.04 and 20/.06) or the (25/.04) Twisted Files ($p > 0.05$). However, a statistically significant decrease in Twisted File (25/.06) cycles to failure after autoclaving was observed ($p < 0.05$).
Plotino et al. [7], 2012	Vortex 40/.04 (Dentsply-Tulsa, Tulsa, OK, USA) and K3XF 40/.04 (SybronEndo, Orange, CA, USA)	12/power: K3: 9.83%; Mtwo: 71.4%; Vortex: 11.22%; K3XF: 33.98%; Mean: 15.54%	60° angle 5-mm radii of curvature	Static	- Control group (non-sterilized) and experimental group (autoclaved 10 times). - The sterilized instruments were subjected to 10 cycles of autoclave sterilization and each cycle was performed at a temperature of 134°C for a duration of 35 min (including 20 min of sterilization and 15 minutes for drying).	K3XF autoclaved 10 times had significantly higher resistance to cyclic fatigue than new ones ($p < 0.05$). No cyclic fatigue difference was found between new and autoclaved Vortex instruments ($p > 0.05$).
Özyürek et al. [12], 2017	ProTaper Next 25/.06 (Dentsply Maillefer, Ballaigues, Switzerland) and ProTaper Gold 25/.08 (Dentsply Maillefer, Ballaigues, Switzerland)	20/power: ProTaper Gold: 95.73%; ProTaper Next: 85.14%; ProTaper Universal: 5.34%; Mean: 62.07%	60° angle 5-mm radii of curvature	Static	- Control group (non-sterilized) and experimental group (autoclaved 10 times). - Each autoclave sterilization process was performed for 18 minutes under 30 psi of pressure at 134°C and then dried for 30 min.	Both ProTaper Next and ProTaper Gold autoclaved 10 times had significantly higher resistance to cyclic fatigue than new ones ($p < 0.05$).
Zhao et al. [9], 2016	HyFlex CM 30/.06 (Coltene Whaledent, Cuyahoga Falls, OH, USA), Twisted Files 30/.06 (SybronEndo, Orange, CA, USA) and K3XF 30/.06 (SybronEndo, Orange, CA, USA)	20/power: HyFlex CM: 97.61%; Twisted Files: 1.96%; K3XF: 80.73%; K3: 6.99%; Race: 2.54%; Mean: 37.96%	60° angle 3-mm radii of curvature	Static	- Control group (non-sterilized) and experimental group (autoclaved 10 times). - Each cycle was performed including sterilization at 134°C, with a pressure of 30 psi, for 20 min and then drying for 15 min.	HyFlex CM and K3XF autoclaved 10 times had significantly higher resistance to cyclic fatigue than new ones ($p < 0.05$). No differences were observed between Twisted File instruments autoclaved or not ($p > 0.05$).

DISCUSSION

The assessment of the cyclic fatigue life of NiTi instruments is a frequently studied topic in endodontics, as it is considered the main reason of instrument fracture during clinical use [5,6,19]. This type of fracture is more prevalent in curved root canals. It occurs due to metal fatigue because the instrument rotates freely at the curvature without binding so that the compressive and tensile stresses are concentrated at the point of maximum flexure until the fracture occurs [19,20].

Several methodologies, using different devices, have been proposed to assess the cyclic fatigue resistance of NiTi instruments. The majority of the studies tested instruments confined in a glass or metal tube, in a grooved block-and-rod assembly, or in a sloped metal block [21]. However, it is important to emphasize that there are no specifications or international standards for the evaluation of this property in endodontics, which may explain the large variation in results. This lack of standardization was one of the major challenges of this study and can explain the variety of results. Therefore, the seek for a standardized methodology to evaluate the cyclic fatigue resistance is necessary.

In this systematic review, all studies assessed the cyclic fatigue resistance of NiTi instruments at room temperature [4,7,9,12,16]. However, the intracanal temperature at which the instruments are used during clinical root canal preparation is around 31°C–35°C [7,22]. Recently, few studies have demonstrated that environmental temperature may drastically affect the cyclic fatigue resistance of NiTi instruments [23–25]. Therefore, future studies should be performed considering the simulation of environmental temperature when evaluating the influence of autoclave sterilization in the cyclic fatigue resistance of NiTi instruments.

During clinical practice, it is common to reuse NiTi instruments. These instruments are more prone to fracture to cyclic fatigue as they are used several times; therefore, more susceptible to tensile and compressive stresses. Besides that, the choice to reuse instruments makes the sterilization process necessary to prevent cross infections [26]. Also, clinicians use pre-determined sets of NiTi files, and some of them may be not used in a specific root canal treatment, requiring autoclave sterilization before reuse. Several studies have shown the effects of sterilization procedures on the mechanical properties of NiTi instruments, such as cyclic fatigue [7,16,18,26,27]. Moreover, it has been suggested that NiTi properties are related to the thermomechanical processing history of the product [28], and additional heat treatment during autoclavation procedures might have a direct influence on instrument properties [4,7,9,12,16, 29].

The present study aimed to systematically review the effects of autoclave sterilization procedures on the cyclic fatigue resistance of heat-treated NiTi instruments. After the search, a total of 10 studies matched the inclusion criteria [4,7,9–12,15–18]. However, after a complete reading of them, only 5 were included in this systematic review [4,7,9,12,16]. Overall, this systematic review presented a moderate risk of bias, since most of the studies were classified as moderate risk of bias [7,9,12] and only one was classified as high risk [16]. The major concern of all included studies was the absence of a sample size calculation. In addition, Plotino *et al.* [7] presented the domain “blinding of the operator of test machine” as high risk of bias since the blinding was not performed. All included studies were classified as low risk of bias for the domains: “standardization of sample,” “standardization of autoclavation procedures,” and “statistical analysis.” The power analysis can be applied before and after

experiment tests. In this review, it was applied as a post-hoc analysis that was performed to judge if the sample size of the included studies were powerful. In this sense, the power analysis demonstrated a satisfactory effect size for the 5 studies. Plotino *et al.* [7] presented the lowest effect size and Pedullà *et al.* [4] the highest.

Hilfer *et al.* [16] showed that autoclavation procedures did not significantly affect the cyclic fatigue resistance of GT series X (Dentsply Tulsa Dental Specialties) (both 20/0.04 and 20/0.06) or Twisted Files (TF; SybronEndo, Orange, CA) (25/0.04) instruments. However, TF (25/0.06) presented significantly lower mean cycles to failure after autoclavation. Plotino *et al.* [7] tested the effect of autoclave sterilization on the cyclic fatigue resistance of K3 (SybronEndo), Mtwo (VDW, Munich, Germany), Vortex (Dentsply Tulsa Dental Specialties), and K3XF (SybronEndo) instruments and concluded that repeated cycles of autoclave sterilization did not influence the mechanical properties of NiTi instruments except for the K3XF files, which demonstrated a significant increase in its cyclic fatigue resistance. The results from Zhao *et al.* [9] showed that HyFlex CM (Coltene Whaledent), TF and K3XF instruments, which are composed of new thermal-treated alloy, were more resistant to fatigue failure than Race (FKG Dentaire, La-Chaux-de-Fonds, Switzerland) and K3; autoclaving extended the cyclic fatigue life of HyFlex CM and K3XF instruments, but did not affect the cyclic fatigue life of TF. Özyürek *et al.* [12] concluded that ProTaper Gold (Dentsply Maillefer, Ballaigues, Switzerland) instruments, made of a new gold alloy, were more resistant to cyclic fatigue than ProTaper Next (Dentsply Maillefer) and ProTaper Universal (Dentsply Maillefer). Autoclaving increased the cyclic fatigue resistance of ProTaper Next and ProTaper Gold instruments [12]. Pedullà *et al.* [4] showed no differences in the cyclic fatigue life of new, and 1 or 3 times autoclaved Hyflex CM and new or 1 autoclaved cycle TF instruments; however, TF instruments autoclaved 3 times showed poor results when compared to new ones. Analyzing these results, GT Series, HyFlex CM, K3XF, ProTaper Gold, and ProTaper Next showed an improvement on the cyclic fatigue resistance after autoclaving protocols. This trend is mainly observed in studies that performed a large number of cycles of sterilization (10 cycles) [7,9,12], which leads us to believe that few cycles of sterilization are not able to promote significant modifications in the mechanical behavior of these instruments. However, in 2 studies [4,16], autoclaved TF instruments demonstrated lower cyclic fatigue resistance when compared to non-autoclaved ones. The decrease in the cyclic fatigue resistance of TF instruments indicates that repeated sterilization procedures could negatively influence TF mechanical properties, leading to instrument fracture. Although TF is heat-treated instruments, they undergo a twisting process during their manufacture. On the contrary, the other instruments evaluated in the included studies of this systematic review are heat-treated instruments manufactured by grinding. Therefore, the difference in the manufacturing process (twisting X grinding) might be related to general observations previously discussed in the present study. Future studies should be performed evaluating this issue. Recently, Shen *et al.* [30] demonstrated that austenite start and Af temperatures play an important role in fatigue resistance in different temperatures. For this reason, a table summarizing the properties of heat-treated instruments used in the studies included in this systematic review was included (**Table 3**) [23,31-40]. However, no consistent conclusion could be reached after analyzing these characteristics.

The overall evidence quality of this systematic review is moderate and should be interpreted with caution. The included studies had significant heterogeneity in their methodology because they used a great variety of cyclic fatigue set-ups, variations in angles and radii of curvature of simulated canals, and autoclave sterilization protocols. Moreover, several

Table 3. Included instruments and its characteristics

Included instruments	NiTi alloy	As temperature (°C)	Af temperature (°C)	Reference
Twisted Files	R-phase alloy	37.9	58.3	Aminsobhani <i>et al.</i> [31], 2016
		12.0	51.7	Shim <i>et al.</i> [32], 2017
Hyflex CM	Controlled memory alloy	22.2	32.4	Iacono <i>et al.</i> [33], 2017
		11.8	39.7	Shim <i>et al.</i> [32], 2017
		21.5	43.5	de Vasconcelos <i>et al.</i> [23], 2016
		20.1	51.4	Shen <i>et al.</i> [34], 2013
GT Series X files	M-wire alloy	-	-	No data published
Profile Vortex	M-wire alloy	-7.7	50.4	Shen <i>et al.</i> [35], 2011
		29.0	43.4	Braga <i>et al.</i> [36], 2014
		28.1	53.1	Shen <i>et al.</i> [37], 2015
		0.08	53.8	Tsujimoto <i>et al.</i> [38], 2014
		0.02	51.7	Shen <i>et al.</i> [39], 2012
K3XF	R-phase alloy	-5.5	24.8	Shen <i>et al.</i> [34], 2013
		-4.8	27.0	Tsujimoto <i>et al.</i> [38], 2014
ProTaper Next	M-wire alloy	37.8	54.1	Aminsobhani <i>et al.</i> [31], 2016
ProTaper Gold	Gold alloy	-	50.1	Hieawy <i>et al.</i> [40], 2015

As, austenite start; Af, austenite finish.

commercial brands of instruments with most varied NiTi alloys were evaluated - each alloy can have its transitional temperatures and the percentage phases of the alloy affected in a different way [9]. Thus, it was hard to perform cross-study comparisons due to the lack of uniformity in methodologies and evaluation criteria. This systematic review highlighted that available studies assessing cyclic fatigue resistance of endodontic instruments have different protocols and evaluating outcomes, which make them less comparable within and between groups and preclude the establishment of an unbiased scientific evidence base.

CONCLUSIONS

Although the available scientific evidence base is short and at considerable risk of bias, it is still possible to conclude that autoclave sterilization procedures appear to influence the cyclic fatigue resistance of heat-treated NiTi instruments.

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