Effect of body temperature on the cyclic fatigue resistance of the nickel–titanium endodontic instruments: A systematic review and meta-analysis of in vitro studies

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Abstract

Aim: The aim of this systematic review was to compare the effect of body temperature (I) on the cyclic fatigue resistance (O) of nickel–titanium (NiTi) endodontic instruments (P) to that of room temperature (C).

Methods: The study was registered in the PROSPERO database (CRD42020204286). A systematic search in PubMed, Scopus, Web of Science, Google Scholar, and OpenGrey was conducted in English until December 31, 2021. In vitro studies comparing the cyclic fatigue resistance of NiTi instruments at the body (35°C ± 2°C) and room temperature (20°C–25°C) were included. Eligible studies were evaluated for risk of bias and meta-analyzed to estimate the effects.

Results: Twenty-one studies out of 347 met the criteria for inclusion. The meta-analysis included six studies (n = 215) with comparative study parameters. The overall effect sizes (5.49; 95% confidence interval [CI]: 4.04–6.93) were significantly different (P < 0.001), indicating that the mean values at room temperature were significantly (P < 0.001) higher. The effect sizes for full rotary motion (standardized mean difference [SMD]: 4.80; 95% CI: 3.04–6.56) and reciprocating motion (SMD: 6.37; 95% CI: 3.63–9.11) were not significantly different (P = 0.346). Heterogeneity was high (I² = 94%). Sensitivity analysis revealed that the SMD values were not significantly different (P > 0.05) from the overall effect size, indicating that none of the studies had an effect on the overall effect size.

Conclusions: Within the limitation of the study, the cyclic fatigue resistance of heat-treated NiTi endodontic files is significantly reduced at body temperature when compared to room temperature. Cyclic fatigue testing should be conducted at simulated body temperature.

Keywords: Cyclic fatigue; dental instrument; endodontics; meta-analysis; nickel–titanium; root canal preparation/instrumentation; root canal therapy/instrumentation; temperature

INTRODUCTION

Nickel–titanium (NiTi) engine-driven instruments continue to be the mainstay in performing mechanical debridement and shaping during endodontic treatment. It has revolutionized the root canal preparation technique by decreasing operator fatigue, time, and procedural errors associated with manual instrumentation.[1] Despite the increased flexibility, a major concern related to their use is the possibility of intracanal separation. The reported incidence of separation is in the wide range of 0.4%–23%.[2] This is widely attributed to two mechanisms.

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One is torsional fatigue which occurs when the file’s tip is locked inside the canal while the main body or shaft of the file continues to rotate, exceeding the elastic limit.[3] The second is cyclic fatigue, which results from rotation around a curve with the consequence of repeated tension and compression of metal and, finally, work hardening followed by fracture.[4] Cyclic or flexural fatigue accounts for most fractured instruments during clinical use and has been studied extensively.[5] The various factors affecting the cyclic fatigue of a NiTi instrument include the instrument design, type of alloy, radius of curvature, angle of curvature, movement kinematics, and temperature.[6] Environmental or intracanal or body temperature is an important confounding factor that is least studied.[6] It is relevant since the metallurgy of NiTi alloys exhibits different behaviors at room or body temperature.[7] Earlier, most of the fatigue studies were performed at room temperature. Recently, many studies have reported the dramatic effect of body temperature on the cyclic fatigue resistance of NiTi instruments with a reported 300%–500% impact on their lifetime.[8-11] Hence, the present systematic review aimed to evaluate the effect of body temperature on the cyclic fatigue resistance of the NiTi endodontic instruments compared to room temperature. The objective was to determine how temperature affects the cyclic fatigue resistance of NiTi instruments and help the clinicians to learn more about the mechanical behavior of NiTi in clinical situations.

**METHODS**

**Protocol and registration**
The current review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 guidelines.[12] The review protocol was registered a priori in the PROSPERO database (CRD42020204286).

**Research question and eligibility criteria**
The PICOS acronym was used to devise the following question: What is the effect of body temperature (I) on the cyclic fatigue resistance (O) of NiTi endodontic instruments (P) when compared to room temperature (C) as measured by in vitro studies (S)?

- **Population**: NiTi endodontic instruments
- **Intervention**: Body temperature (35°C ± 2°C)
- **Comparison**: Room temperature (20°C–25°C).
- **Outcomes**: Cyclic fatigue resistance, i.e., the number of cycles to fracture (NCF) or time to fracture (TTF).
- **Studies**: In vitro studies.

Exclusion criteria included studies assessing cyclic fatigue resistance at temperatures other than those indicated above. In addition, abstracts, conference proceedings, reviews, and studies published in languages other than English were not selected. However, those translated into English were included.

**Information sources, search strategy, and selection process**
A search of the literature was conducted in three databases: PubMed (1964–2021), Scopus (1960–2021), and Web of Science (1980–2021) until December 31, 2021. Google Scholar (first 100 returns) and OpenGrey databases were searched electronically for unpublished manuscripts, research reports, doctoral dissertations, and other gray literature. The electronic search strategy was developed using the most cited descriptors in previous publications on this theme combining Medical Subject Heading terms and text words. For the database, the following terms were combined: “Body temperature,” “Temperature,” “Environmental temperature,” “Fatigue,” “Cyclic fatigue,” “Fatigue resistance,” “Flexural fatigue,” “Fracture resistance,” “Nickel titanium,” “Niti,” “Nitinol,” “Dental instruments,” “In” and “Rotary.” The Boolean operators “AND” and “OR” were applied to combine the terms and create a search strategy. The search strategies for each database are summarized in Supplementary Table 1. The search was expanded to include reference lists for screened studies and published reviews. The leading endodontic journals, including the Journal of Endodontics, the International Endodontic Journal, and the Australian Endodontic Journal, were manually searched. Duplicate articles were removed from the database using the Covidence tool (Melbourne, Australia). The selection of studies was performed using a two-stage screening process. This was accomplished by two independent reviewers (SS1 and SS2) screening the title and abstract for appropriate studies and reading the full text. The reasons for exclusion are documented in Supplementary Table 2. In the event of a disagreement, a third reviewer (AL) was consulted.

**Data collection and data items**
The following data were recorded in an Excel spreadsheet (Microsoft, Redmond, WA, USA) by the two independent reviewers: author, year of publication, instrument name, size, taper, type of alloy (conventional or heat-treated), sample size, motion type (full rotary or reciprocating), testing model (static or dynamic), angle of curvature, radius of curvature, distance from the tip, immersion media, rotational speed, insertion depth, insertion angle, material of artificial canal, inner diameter of the canal, and NCF or TTF at room and body temperatures [Table 1].

**Study risk of bias assessment**
The methodological quality of the included research was determined using an adaption of a prior systematic review that included in vitro investigations.[13] The domains listed below were used: (1) sample standardization, (2) sample size calculation, (3) sample randomization, (4) single-operator, (5) blinding, (6) testing model standardization, and (7) appropriate statistical analysis.
| First author | Year | Instrument type | Type of alloy | Sample size | Type of motion | Rotational speed (rpm) | Size and taper | NCF at room temperature | NCF at body temperature |
|-------------|------|----------------|---------------|-------------|----------------|------------------------|---------------|------------------------|------------------------|
| Savitha, et al.: Temperature and cyclic fatigue resistance |  |  |  |  |  |  |  |  |  |
| Arians 2019 | EdgeSequel | Heat treated | 40 | Rotary | 500 | 20/0.04 | 252.5 (212-300.7) | 82.9 (71.1-96.8) |
| Sapphire |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| Vortex Blue |  | Heat treated | 40 | Rotary | 500 | 20/0.04 | 311.7 (270.7-359) | 93.9 (88.3-99.9) |
|  |  |  |  |  |  |  |  |  |  |
| Cardoso 2019 | HyFlex EDM | Heat treated | 40 | Rotary | 300 | 25/0.06 | 234.7 (209-263.6) | 83.2 (76-91.1) |
| TRU shape |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| De Vasconcelos 2016 | HyFlex CM | Heat treated | 40 | Rotary | 500 | 25/0.06 | 2986±412 | 487±96 |
| TRU Shape |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| Generali 2020 | Procidile | Heat treated | 40 | Rotary | 500 | 25/0.06 | 2986±412 | 487±96 |
| Reziflow |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| Huang 2017 | K3 | Heat treated | 40 | Rotary | 500 | 25/0.06 | 300.9±35.4 | 603.4±112.45 |
| K3XF |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| Ismail 2020 | WaveOne Gold | Heat treated | 40 | Reciprocating | 350 | 25/0.07 | 2209±42.1 | 102±29.1 |
| TFA |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| Keleş 2019 | Reciproc Blue | Heat treated | 40 | Reciprocating | 300 | 25/0.08 | 214.4±108.4 | 254.4±62.9 |
|  |  |  |  |  |  |  |  |  |  |
| La Rosa 2021 | F6 SkyTaper | Heat treated | 40 | Rotary | 300 | 25/0.06 | 275.9±47.9 | 253±27.7 |
|  |  |  |  |  |  |  |  |  |  |
| Plotino 2017 | PTU S1 | Heat treated | 30 | Rotary | 300 | 18/0.02 | 515±90.3 | 380±39.4 |
| PTG S1 |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| Plotino 2018 | Reciproc blue | Heat treated | 40 | Reciprocating | 300 | 25/0.08 | 941.1±48.22 | 1264.44±171.58 |
| Reciproc |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| Topcuoglu 2020 | HyFlex CM | Heat treated | 40 | Rotary | 500 | 25/0.6 | 5419±1179.85 | 2019±388.49 |
| One Curve |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| Vieira 2020 | Reciproc blue | Heat treated | 24 | Reciprocating | 300 | 25/0.06 | 18.06±3.93 | 6.73±1.29 |
| Vortex blue |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| Vieira 2021 | Reciproc blue | Heat treated | 24 | Reciprocating | 300 | 25/0.06 | 18.06±3.93 | 6.73±1.29 |
| X1 Blue |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| Dosanjh 2017 | ESX Files | Heat treated | 60 | Rotary | 500 | 25/0.04 | 7243 | 1675 |
| EdgeFile1 |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| Contd... |  |  |  |  |  |  |  |  |  |
Table 1: Contd...

| First author | Year | Instrument type | Type of alloy | Sample size | Type of motion | Rotational speed (rpm) | Size and taper | NCF at room temperature | NCF at body temperature |
|--------------|------|-----------------|---------------|-------------|------------------|------------------------|---------------|------------------------|------------------------|
| Alwafaz | 2018 | PTG F2 | Heat treated | 30 | Rotary | 300 | 25/0.08 | 1239.1±388.2 | 962.9±276.0 |
| Gundogar | 2019 | Reciproc Blue | Heat treated | 30 | Reciprocating | 300 | 25/0.08 | 7914±1266 | 1349±161 |
| Klymus | 2019 | X1 Blue | Heat treated | 30 | Reciprocating | 300 | 25/0.08 | 3067±278.9 | 1532.7±182.4 |
| Saeed | 2019 | HyFlex EDM | Heat treated | 30 | Rotary | 300 | 25/0.08 | 4685.3±726.39 | 297.8±58.8 |
| Staffoli | 2019 | OneShape | Conventional | 40 | Rotary | 300 | 25/0.06 | 473.8±83.4 | 295±46.5 |

First author Immersion medium Testing model Radius of curvature of the canal Angle of curvature of the canal Distance of center of curvature from instrument tip Material of the artificial canal Insertion angle Insertion depth (mm) Inner diameter of canal (mm)

| First author | Immersion medium | Testing model | Radius of curvature of the canal | Angle of curvature of the canal | Distance of center of curvature from instrument tip | Material of the artificial canal | Insertion angle | Insertion depth (mm) | Inner diameter of canal (mm) |
|--------------|-----------------|---------------|-------------------------------|-------------------------------|--------------------------------|--------------------------------|---------------|------------------|-----------------------------|
| Arias | Deionized water | Static | 3 | 60 | 4.5 | Stainless steel | - | - | - |
| Arias | Water | Static | 3 | 60 | 5 | Stainless steel | - | - | 1.5 |
| Cardoso | Water | Static | 5 | 90 | 5 | Stainless steel | - | - | - |
| De | Water | Static | 3 | 60 | 4.5 | Stainless steel | - | 19 | - |
| Vasconcelos | Water | Static | 5 | 60 | 5 | Stainless steel | 0 | 16 | - |
| Huang | Water | Dynamic | 5 | 60 | - | Stainless steel | - | - | - |
| Ismail | Water | Static | 2 | 60 | - | Stainless steel | - | 19 | 1.5 |
| Keleş | Water | Static | 5 | 60 | 5 | Stainless steel | - | - | 1.5 |
| La Rosa | Water | Static | 5 | 60 | - | Stainless steel | 0 | - | - |
| La Rosa | Water | Static | 3 | 60 | 5 | Stainless steel | 20 | - | - |
| Plotino | 5% Naocl | Static | 5 | 60 | - | Stainless steel | - | - | - |
| Plotino | Water | Static | 5 | 60 | 6 | Stainless steel | - | - | - |
| Topcuoglo | Water | Dynamic | 5 | 60 | 8 | - | - | 18 | - |
| Vieira | Water | Dynamic | 5 | 60 | 5 | Stainless steel | - | 17 | - |
| Vieira | Water | Static | 5 | 60 | 5 | Stainless steel | - | - | 1.5 |
| Dosanjh | Water | Static | 5 | 60 | - | Stainless steel | - | - | 1.5 |
| Alwafaz | Water | Static | 5 | 60 | 5 | Stainless steel | - | - | 1.5 |
| Gundogar | Water | Static | 5 | 60 | 5 | Stainless steel | - | - | 1.5 |
| Klymus | Water | Static | 5 | 60 | 5 | Stainless steel | - | - | - |
| Saeed | Water | Static | 5 | 60 | 5 | Stainless steel | - | - | 1.5 |
| Staffoli | Water | Static | 5 | 60 | 5 | Stainless steel | - | - | 16 | - |

*TTF, *Included in meta-analysis. PTU: ProTaper Universal, PTG: ProTaper Gold, PTN: ProTaper next, TFA: Twisted File Adaptive, NCF: Number of cycles to fracture
RESULTS

Study selection
Figure 1 presents a flowchart of the systematic review process. A total of 21 studies met the criteria for inclusion.\[14-34\]

Characteristics of instrument types
The studies examined a total of 29 instruments, nine of which were made of conventional NiTi alloy and eight of which were reciprocating systems. The size of the instrument tip ranged from #20 to #40; however, the majority of studies utilized size #25. In addition, the taper and speed of rotation varied between studies [Table 1].

Characteristics of study design
The studies revealed differences in the test model type, radius of curvature, angle of curvature, and immersion media.\[14-34\] The distance of the curvature from the tip, the fit of the instrument, angle of insertion, and length of the instrument inserted were not mentioned in all the studies [Table 1].

| First author          | Year | Sample standardization | Sample size calculation | Sample randomization | Single operator | Blinding | Standardization of testing model | Statistical test | Grading |
|-----------------------|------|------------------------|-------------------------|---------------------|----------------|----------|----------------------------------|-----------------|---------|
| Arias et al\[14\]     | 2019 | -                      | -                       | -                   | -              | +        | +                                | +               | High    |
| Arias et al\[15\]     | 2018 | -                      | -                       | -                   | -              | +        | +                                | +               | High    |
| Cardoso et al\[16\]   | 2019 | +                      | -                       | -                   | -              | +        | +                                | +               | Moderate |
| De Vasconcelos et al\[17\] | 2016 | -                      | -                       | -                   | -              | -        | -                                | +               | High    |
| Generali et al\[18\]  | 2020 | +                      | +                       | -                   | -              | -        | -                                | +               | Moderate |
| Huang et al\[19\]     | 2017 | -                      | -                       | -                   | -              | +        | +                                | -               | High    |
| Ismail et al\[20\]    | 2020 | +                      | +                       | -                   | -              | -        | +                                | +               | Moderate |
| Keleş et al\[21\]     | 2019 | +                      | +                       | -                   | -              | -        | -                                | +               | Moderate |
| La Rosa et al\[22\]   | 2021 | +                      | +                       | -                   | -              | +        | +                                | +               | Moderate |
| La Rosa et al\[23\]   | 2021 | +                      | +                       | -                   | -              | -        | -                                | +               | Moderate |
| Plotino et al\[24\]   | 2017 | +                      | -                       | -                   | -              | -        | +                                | +               | Moderate |
| Plotino et al\[25\]   | 2018 | +                      | -                       | -                   | -              | +        | +                                | +               | Moderate |
| Topçuoğlu et al\[26\] | 2020 | +                      | +                       | -                   | -              | -        | +                                | +               | Moderate |
| Vieira et al\[27\]    | 2020 | +                      | +                       | -                   | -              | +        | +                                | +               | Moderate |
| Vieira et al\[28\]    | 2021 | +                      | +                       | -                   | -              | -        | +                                | +               | Moderate |
| Dosanjh et al\[29\]   | 2017 | -                      | +                       | +                   | -              | -        | -                                | +               | High    |
| Alifawaz et al\[30\]  | 2018 | +                      | -                       | -                   | -              | -        | +                                | +               | Moderate |
| Gündoğar et al\[31\]  | 2019 | +                      | -                       | -                   | -              | -        | +                                | +               | Moderate |
| Klymus et al\[32\]    | 2019 | +                      | -                       | -                   | -              | -        | -                                | +               | Moderate |
| Saeed and Rafea\[33\] | 2019 | +                      | -                       | -                   | -              | +        | +                                | +               | High    |
| Staffelli et al\[34\] | 2019 | +                      | +                       | -                   | -              | -        | +                                | +               | Moderate |

Risk of bias in studies
Table 2 contains a detailed information addressing the RoB in the selected studies. The RoB was evaluated as moderate to high overall.

Meta-analysis
Because of the heterogeneity among the study design and instrument types, it was decided not to perform a meta-analysis on overall data. To ensure homogeneity, the meta-analysis included only those studies that matched the following criteria:

- Heat-treated files
- Tip size of 25
- Static stainless steel model
- Angle of curvature = 60°
- Radius of curvature = 5 mm
- Water as an immersion media
- Cyclic fatigue expressed in NCF.

Six studies were included,\[29-34\] examining 10 different instrument types, including the ProTaper Gold (Dentsply Sirona, Charlotte, NC, USA), EdgeFile (EdgeEndo, Albuquerque, NM), Vortex Blue (Dentsply Sirona, Charlotte, NC, USA), Reciproc Blue (VDW, Munich, Germany), HyFlex EDM (Coltene, Cuyahoga Falls, OH, USA), WaveOne Gold (Dentsply Sirona, Charlotte, NC, USA), Twisted File Adaptive (TFA) (SybronEndo, CA, USA), X1 Blue (MK Life, Porto Alegre, RS, Brazil), 2Shape (MicroMega, Besancon, France), and One Curve (MicroMega, Besancon, France). Three of these systems were reciprocating while one had an adaptive (rotation–reciprocating) motion. The TFA changes to a reciprocating mode when engaging dentin or stress. As a result, it was considered under reciprocating subgroup during the meta-analysis [Table 1].
Statistical analysis
STATA version 16.0 (Stata Corp, College Station, Texas, 77845, USA) software was used to carry the meta-analysis to assess whether the mean differences at 20°C and 37°C across the studies were statistically significant. The standardized mean difference (SMD) was calculated using Hedges' g bias correction and was taken as effect size with 95% confidence interval (CI). The fixed-effect model using the inverse-variance method and the random-effect model using the restricted maximum likelihood method were estimated. The heterogeneity was tested across the studies using the I²-statistics using DerSimonian–Laird estimator for τ². I²-statistics of >50% was considered as significant heterogeneity. The publication bias was assessed using the funnel plot and Begg–Egger regression test. Since two motions (rotary and reciprocating) were adopted, a subgroup analysis was carried out. To assess the consistency of the results, sensitivity analysis was performed by the method of leaving one out study. A meta-regression of SMD on the other study variables available was performed to find out significant contributing factors.

Results of the meta-analysis
Fourteen groups (8 groups with rotary motion and 6 groups with reciprocating motion) were evaluated in six studies with two arms (20°C–25°C and 35 ± 2°C). A total of 215 instruments per arm consisting of 140 with rotary motion and 75 with reciprocating motion were studied. All the 14 groups demonstrated that the effect sizes were significantly different, indicating that the SMD was significantly (P < 0.001) higher in the 20°C arm [Figure 1]. The overall effect size for the fixed-effect model was 2.99 (95% CI: 2.66–3.33) and for the random-effect model was 5.49 (95% CI: 4.04–6.93) [Figure 2]. Heterogeneity (I²-statistics = 94%) was very high, and it was highly significant (P < 0.001) between the studies. Since the heterogeneity was more than the threshold level (50%), subsequent analyses were restricted to the random-effect model. Subgroup analysis by motion showed that the overall effect size for full rotary motion (SMD: 4.80; 95% CI: 3.04–6.56) and reciprocating motion (SMD: 6.37; 95% CI: 3.63–9.11) did not differ significantly (P = 0.346) [Figure 2]. Sensitivity analysis by leaving out one study was carried out to determine the influence of any particular study on the outcome [Supplementary Table 3]. The SMD values did not differ significantly (P > 0.05) from the overall effect size by leaving one particular study, confirming that none of the studies influenced the overall effect size.
Funnel plot analysis indicated the presence of high publication bias as evident by an asymmetric pattern of the effective size. Further, the intercept of the Beg–Egger regression was highly significant ($P < 0.001$), confirming the presence of publication bias [Supplementary Figure 1]. To assess the possible influencing factors for the high heterogeneity level, a meta-regression analysis was carried out by considering the taper size as the covariate. The testing of the regression coefficient of taper size was not statistically significant ($P = 0.461$), implying that the taper size was not a significant influencing factor toward the high heterogeneity level.

**DISCUSSION**

The relative proportion and characteristic of the microstructural phases in a NiTi instrument determine its mechanical behavior.\[35\] The alloy can be classified into two distinct temperature-dependent crystallographic phases: martensite (low-temperature phase) and austenite (high temperature or parent phase), each with its own distinct set of properties.\[7\] When heated, martensite NiTi transforms into austenite. The austenite start temperature is when this phenomenon begins ($A_s$). The temperature at which it is complete is referred to as the austenite finish temperature ($A_f$). When austenite NiTi is cooled to a specific temperature, it transforms into martensite. Similarly, martensite start temperature ($M_s$) and martensite finish temperature ($M_f$) exist.\[35\] The transformation temperatures have a substantial effect on the mechanical characteristics and behavior of NiTi, which can be varied during the production process by minor compositional changes, impurity additions, and heat treatments.\[37\] The $A_f$ temperature of the vast majority of heat-treated files is clearly above body temperature. CM wire, M-wire, and conventional SE NiTi wire have an $A_f$ of approximately 55°C, 50°C, and 16°–31°C, respectively.\[36\] During root canal preparation, the average intracanal temperature is 35.1°C, comparable to body temperature.\[38\] Thus, conventional NiTi files are predominantly in the austenite phase at or below intracanal temperature, whereas heat-treated files are predominantly in the martensite/R-phase/hybrid phase at intracanal temperature.

The bulk material properties primarily determine fatigue life. A hybrid (austenite–martensite) microstructure containing a trace of martensite is more likely to be fatigue resistant than a completely austenitic microstructure. This is often explained by martensite’s stronger resistance to fatigue crack growth than stable austenite. The fatigue crack propagation speed of austenitic structures is significantly faster than that of martensite structures at the same stress intensity level. In addition, due to the energy absorption properties of its twinned phase structure, the martensitic phase transformation exhibits exceptional damping characteristics.\[39\]

In cyclic fatigue studies, environmental temperature is a crucial confounding variable. Numerous investigations have established a considerable effect of ambient temperature on the cyclic fatigue resistance of NiTi endodontic instruments since NiTi alloys behave differently depending on their metallurgical properties.\[8-11\] Thus, compared to room temperature, the current systematic review studied the influence of body temperature on the cyclic fatigue resistance of NiTi devices. The studies that examined the effect of various temperatures ($−20°C$ to $60°C$) were excluded, as cooled or heated irrigant solutions...
rapidly equilibrate to body temperature inside the root canal.\textsuperscript{[6]} The included 21 studies demonstrated notable heterogeneity in the test model type, curvature radius, angle of curvature, immersion media, and instrument features. The present review demonstrates the importance of developing an international standard for validating a device for cyclic fatigue testing of NiTi rotary endodontic instruments. In an ideal scenario, it would enable the testing of all instruments with a precise trajectory in terms of radius and angle of curvature, fit, and angle of insertion, among other characteristics, allowing the comparison of different instruments.\textsuperscript{[4]}

Six studies were selected with similar study designs, instrument characteristics, and outcome measures to achieve homogeneity.\textsuperscript{[29-34]} A meta-analysis was performed, which discovered that the cyclic fatigue resistance of heat-treated NiTi endodontic instruments is significantly reduced at body temperature. This can be attributed to the alloy transitioning to the austenitic phase in heat-treated instruments. At room temperature, the various heat-treated files are martensitic and transform to a more austenitic state at body temperature, resulting in a mixed martensitic, \textit{R} phase, and austenitic structure. The martensitic to austenitic conversion is not complete at body temperature, but a considerable proportion is already austenitic. However, the crystal lattice of conventional NiTi instruments is almost identical at room and body temperatures; nevertheless, literature reports that fatigue resistance is reduced, albeit slightly.\textsuperscript{[17]} This implies that additional unidentified factors may play a role that warrants further investigation. In addition to alloy, the cyclic fatigue of an endodontic instrument is also affected by the instrument’s working kinematics (rotary and reciprocating) and diameter.\textsuperscript{[90,41]} Hence, a subgroup analysis was conducted using the motion type. Even though the effect size for the reciprocating motion was higher than the rotary motion, the difference was not statistically significant.

The primary limitation of this meta-analysis was the high degree of heterogeneity attributed to the different instrument brands and designs. The instruments all had the same tip size (#25). However, the tapers ranged from 2\% to 8\%. Previous research has demonstrated that instruments with a narrower taper exhibit greater cyclic fatigue resistance.\textsuperscript{[32]} As a result, the taper size was tested as a covariate in a meta-regression analysis and found to have no significant effect on the effect size, implying that other variables may have contributed to the high heterogeneity. Each of the heat-treated alloys included in the meta-analysis has a different phase transformation temperature, contributing to the heterogeneity. Given that temperature is the focus of the included studies, the methods used to maintain the temperature during testing varied widely, including using a thermocouple or a hotplate and ice. Again, various study design parameters such as the distance of curvature from the tip, the instrument’s fit, and the angle of insertion were not mentioned in all studies and could not be retrieved. In addition, most studies demonstrated a high or moderate RoB. Sensitivity analysis was used to determine the effect of omitting one study on the outcome. However, none of the studies affected the overall effect size. High publication bias was also a limitation, indicating that there may be a bias toward publishing only positive effects or due to language bias.

The current review’s strength was that, despite discovering significant variation in cyclic fatigue testing models, it attempted a meta-analysis by including studies with comparable parameters. In this regard, this is the first systematic review to investigate the effect of body temperature on the cyclic fatigue resistance of NiTi endodontic instruments.

**CONCLUSIONS**

Within the limitations of this systematic review, the overall effect size was significantly higher at room temperature, indicating that the cycle fatigue resistance of heat treated NiTi instruments decreases significantly at body temperature compared to room temperature. As a result, future cyclic fatigue testing should be performed at a simulated body temperature that resembles the intracanal environment.

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**Conflicts of interest**
There are no conflicts of interest.

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Supplementary Figure 1: Funnel plot analysis revealing publication bias

Supplementary Table 2: List and reason of excluded studies after full text reading

| Study            | Reason                                                                 |
|------------------|------------------------------------------------------------------------|
| Grande et al. (2017) | Different temperature (+20°C and -20°C)                                |
| Shen et al. (2018)  | Exact NCF values not available                                        |
| Arslan et al. (2020) | Different temperature (saline irrigation at +4°C and room temperature) |
| Elsewify et al. (2020) | No comparative room temperature group                                 |
| Shen et al. (2012)  | Different study setting (fatigue behavior under various medium)        |
| Keskin et al. (2021) | Different study setting (cyclic fatigue resistance of different instruments) |
| Scott et al. (2019) | Different study setting (cyclic fatigue resistance of reciprocating instruments) |
| Alghamdi et al. (2020) | Different study setting (effect of 5 different curvature locations on the fatigue resistance) |

NCF: Number of cycles to fracture

Supplementary Table 1: Search strategy for each database

| Database     | Search strategy                                                                                                                                 |
|--------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| PubMed       | (((body temperature[MeSH Terms]) OR (“temperature”[MeSH Terms]) OR (Intracanal temperature[Title/Abstract])) OR (Environmental temperature[Title/Abstract]) AND (((“fatigue”[MeSH Terms]) OR (cyclic fatigue[Title/Abstract]) OR (fatigue resistance[Title/Abstract]) OR (fracture resistance[Title/Abstract]) OR (flexural fatigue[Title/Abstract]) AND ((((( nickel?titanium[Title/Abstract]) OR (nickel titanium[Title/Abstract]) OR (NITI[Title/Abstract]) OR (niti[Title/Abstract]) OR (nitinol[Title/Abstract]) OR (rotary[Title/Abstract]) OR (“dental instruments”[MeSH Terms]) OR (instrument[Title/Abstract]) AND TITLE-ABS-KEY (“fatigue”) OR (“cyclicfatigue”) OR (“flexuralfatigue”) OR (“fatigueresistance”) OR (“resistance”)) AND TITLE-ABS-KEY (“temperature”) OR (“bodytemperature”) OR (“canaltemperature”) OR (“environmentaltemperature”)) AND TITLE-ABS-KEY (“rootcanal”) OR (“endodontic”) OR (“preparation”))) AND (LIMIT-TO (LANGUAGE,”English”))) |
| Scopus       | (TITLE-ABS-KEY (“NiTi”) OR (“nickletitanium”) OR (“niti”) OR (“rotary”) OR (“instrument”) ) AND TITLE-ABS-KEY (“fatigue”) OR (“cyclicfatigue”) OR (“flexuralfatigue”) OR (“fatigueresistance”) OR (“resistance”)) AND TITLE-ABS-KEY (“temperature”) OR (“bodytemperature”) OR (“canaltemperature”) OR (“environmentaltemperature”)) AND TITLE-ABS-KEY (“rootcanal”) OR (“endodontic”) OR (“preparation”))) AND (LIMIT-TO (LANGUAGE,”English”))) |
| Web of science | TS=(body temperature OR temperature OR canal temperature OR environmental temperature) AND (fatigue OR cyclic fatigue OR flexural fatigue OR fatigue resistance OR fracture resistance) AND (nickel titanium OR NiTi OR niti OR nitinol OR rotary OR instrument OR dental instruments) AND (root canal OR endodontic OR preparation) AND LANGUAGE: (English) INDEXES=SCI-EXPANDED TIMESPAN=All years |
## Supplementary Table 3: Sensitivity analysis

| Study omitted          | SMD     | 95% confidence limits | Percentage weight |
|------------------------|---------|-----------------------|-------------------|
|                        | Lower   | Upper     |                   |
| Alfawaz et al., 2018   | 5.91    | 4.40      | 7.42             | 91.5          |
| Dosanjh et al., 2017   | 5.72    | 4.09      | 7.36             | 77.9          |
| Dosanjh et al., 2017A  | 5.83    | 4.14      | 7.52             | 72.9          |
| Gundogar et al., 2019  | 5.34    | 3.87      | 6.81             | 96.5          |
| Gundogar et al., 2019A | 5.26    | 3.81      | 6.71             | 99.1          |
| Gundogar et al., 2019B | 5.27    | 3.82      | 6.72             | 98.8          |
| Gundogar et al., 2019C | 5.45    | 3.95      | 6.95             | 92.9          |
| Klymus et al., 2019A   | 5.25    | 3.80      | 6.71             | 98.3          |
| Klymus et al., 2019B   | 5.33    | 3.86      | 6.80             | 96.2          |
| Klymus et al., 2019C   | 5.87    | 4.29      | 7.44             | 84.28         |
| Saeed et al., 2019     | 5.92    | 4.39      | 7.44             | 89.5          |
| Saeed et al., 2019A    | 5.06    | 3.66      | 6.47             | 99.8          |
| Saeed et al., 2019B    | 5.27    | 3.81      | 6.73             | 97.8          |
| Staffoli et al., 2019C | 5.40    | 3.92      | 6.87             | 95.2          |
| Overall effect         | 5.49    | 4.04      | 6.93             | 100           |

SMD: Standardized mean difference