

ORIGINAL RESEARCH

***In vitro* study of fracture resistance and color stability of 3D-printed, milled hybrid ceramic, milled PMMA and prefabricated zirconia crowns for restoration of primary incisors**

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Abstract

Background: The advancement of digital technology has expanded the options for pediatric dental restorations, offering more esthetic alternatives and optimizing tooth structure preservation. However, the mechanical properties of these emerging materials remain insufficiently investigated. This study evaluates the fracture resistance and color stability of 3D (Three-dimensional) - printed resin, milled hybrid ceramic, milled PMMA (Polymethyl Methacrylate) and prefabricated zirconia crowns in restoring primary incisors. **Methods:** An intact naturally exfoliated maxillary primary central incisor was collected and prepared for restoration. Digital impressions of the prepared incisor were taken, and resin dies were printed and used as supporting materials. Crowns were digitally fabricated using 3D-printed (RC), milled hybrid ceramic (HC), milled PMMA (PC) with thicknesses of 1 mm and prefabricated zirconia crowns (ZC) with the same thickness (n = 20 crowns/group) were prepared. After cementation using resin-modified glass ionomer cement, it was subjected to 1000 thermal cycles (5–55 °C). Fracture resistance was assessed using a universal testing machine with axial loading. Color stability was evaluated with a spectrophotometer after two weeks of immersion in orange juice and a carbonated beverage. Data were analyzed using one-way analysis of variance and *post hoc* tests ($\alpha = 0.05$). **Results:** All crowns exhibited fracture resistance above 400 N. A statistically significant difference was found between RC and ZC ($p = 0.0398$). The lowest value is in the RC group (433.1 ± 61.9 N), and the highest is in the ZC group (511 ± 65.0 N). No significant differences were observed among the other groups. RC exhibited the highest color change ($\Delta E = 5.4 \pm 0.6$), while HC, PC and ZC demonstrated better stability. **Conclusions:** 3D-printed resin, milled hybrid ceramic crowns and milled PMMA crowns demonstrated good fracture resistance and acceptable color stability for primary incisor restorations. These materials have potential clinical applications but require further *in vivo* studies to assess long-term effectiveness.

Keywords

CAD/CAM; Crown; 3D printed resin; Hybrid ceramic; PMMA; Zirconia; Fracture resistance; Color stability

1. Introduction

Primary teeth play an essential role in the oral health of children. The damage of an anterior primary tooth due to caries or trauma can result in significant clinical consequences, including compromised mastication, speech impairment, space loss for the proper eruption of permanent teeth and diminished esthetic appearance, potentially impacting a child's psychosocial development and overall oral function [1]. An increasing number of parents and children seek restoration with materials that closely resemble natural teeth in shape and color [2]. Full-coverage crowns, such as stainless-steel crowns (SSC), are

usually indicated for children at high risk of caries or when caries are detected on multiple [3]. The primary advantages of SSC are its high clinical success rate, low recurrent caries rate, affordability, thin structure and ease of clinical adjustment, thereby minimizing the reduction of natural tooth structure. However, many parents and pediatric patients are dissatisfied with the unesthetic metallic appearance of SSC crowns [4].

Prefabricated zirconia crowns have been widely used for restoring permanent teeth but are relatively new in pediatric dentistry, introduced in 2010. The advent of zirconia crowns provides a highly aesthetic solution and meets durability and biocompatibility requirements [5]. However, a drawback of

prefabricated zirconia crowns is that they cannot be adjusted like SSC crowns, requiring more tooth reduction to ensure proper fit, which may affect the success of the restoration [6].

The demand for integrating new technologies and materials in pediatric restorative dentistry to overcome the limitations of existing restorations is crucial. In recent years, the integration of digital impression technology (IOS), computer aided design-computer aided manufacturing (CAD-CAM) and 3D printing in dentistry has revolutionized dental restorations. Additive manufacturing, or 3D printing, involves building objects layer by layer based on digital designs. Common types used in dentistry include stereolithography (SLA), digital light processing (DLP) and fused deposition modeling (FDM). SLA and DLP are most frequently used for producing dental restorations due to their high resolution and material compatibility [7]. On the other hand, CAD designs virtual restorations from digital impressions, while CAM fabricates them using computer-controlled machines. Techniques like milling, grinding, and laser cutting are commonly used. CAD/CAM systems offer advantages such as high accuracy, faster workflows, no need for traditional impressions and improved restoration quality [8]. The advancement of digital technology optimizes examination, treatment planning and procedures while saving time and effort for both dentists and patients, reducing anxiety in children during dental treatments [9]. Furthermore, prosthetic design software and materials advancements have enabled minimally invasive restorations with greater precision than prefabricated options. As minimally invasive procedures remain a primary objective in pediatric restorative dentistry, digital dentistry—including CAD-CAM and 3D printing technology—is an effective tool to achieve this goal.

The commonly used CAD-CAM materials for dental restorations include Zirconia (Yttria-Stabilized Tetragonal Zirconia Polycrystals (Y-TZP)), Lithium Disilicate (Glass-Ceramic), Hybrid Ceramics (Resin-Nanoceramic Composites) and PMMA (Polymethyl Methacrylate) [10]. Hybrid ceramic and PMMA have emerged as viable alternatives to conventional restorative materials, offering significant advantages in mechanical properties, esthetics and minimally invasive preparation, making them suitable for pediatric dentistry. Hybrid ceramic is a composite material combining ceramic particles with a polymer-based matrix. This combination enhances flexibility, shock absorption and fracture resistance while maintaining high aesthetic quality [11]. The restoration of a primary molar using a hybrid ceramic block demonstrated excellent clinical performance, with no chipping, no discoloration and an optimal marginal fit [12]. Alternative CAD-CAM-milled material is PMMA block/dish, which presents a more homogeneous and structurally stable composition and enhanced flexural strength, contributing to improved mechanical performance compared to the conventional form of a powder-liquid system [13]. In permanent restorations, PMMA is commonly used as a provisional material. However, in pediatric dentistry, it is still selected for restoring primary teeth due to its ease of fabrication, acceptable esthetics and cost-effectiveness, making it particularly suitable for the limited lifespan of primary teeth [14, 15]. Moreover, one of the most recent advancements in digital dentistry centers around

3D printing technology, significantly impacting clinical practice. Crowns and bridges produced through 3D printing technology have exhibited adequate mechanical strength for intraoral use, making them suitable for temporary and long-term restorations [16]. 3D-printing resin consisting of photopolymerized liquid, Bis-EMA (Bisphenol A Ethoxylated Dimethacrylate), fiberglass, pyrogenic silica, catalysts and inhibitors, offering good flexibility and suitable mechanical properties [17]. Clinically, 3D-printable crowns for cariously treated primary molars presented a survival rate of 84% [18].

Both CAD-CAM and 3D printing technologies demonstrate significant potential for use in primary tooth restoration. However, there remains a lack of data comparing the mechanical and physical properties of digitally fabricated crowns and prefabricated zirconia crowns for primary incisors. Therefore, this study was designed to conduct an *in vitro* evaluation of the fracture resistance and color stability of four material groups used for primary incisor restorations: 3D-printed resin (RC), milled hybrid ceramic (HC), milled PMMA (PC) and prefabricated zirconia crowns (ZC). This study integrates fracture resistance testing and color stability analysis to evaluate mechanical performance and esthetic longevity comprehensively—key considerations in pediatric restorative dentistry. The utilization of advanced digital fabrication technologies, including CAD/CAM and 3D printing, underscores the clinical applicability of the findings, aligning with contemporary trends toward minimally invasive, cost-efficient and digitally driven treatment approaches for children. Here, we proposed the study with the null hypothesis that there was no statistically significant difference in fracture resistance of crowns for restoring primary incisors. Similarly, there was no statistically significant difference in color stability among crowns after immersion in staining solutions.

2. Materials and methods

2.1 Study design

Maxillary primary incisors were extracted due to the natural exfoliation process. Tooth preparation and sample fabrication with a 0.8–1 mm shoulder finish line at the cervical region, a 1 mm occlusal reduction, and a minimum of 1 mm axial wall thickness (Fig. 1A,B). A digital impression of the prepared teeth was taken using an intraoral scanner (3Shape TRIOS 3 Wireless, 3Shape Co., Copenhagen, Denmark), and resin dies (CURO; Ackuretta Technologies, Taipei, Taiwan) were printed using a 3D dental printer (SOL 3D Printer, Ackuretta Technologies, Taipei, Taiwan). Based on the scanned digital impression, a 1 mm thick 3D crown design was created using Exocad software (Exocad GmbH, Darmstadt, HE, Germany) (Fig. 1C,D, Table 1).

- 3D-printed crowns (Saremco print CROWNTEC; SAREMCO Dental AG, Switzerland) were printed using the SOL 3D optical printer (Ackuretta Technologies Co., Taiwan) with DLP technology following the manufacturer's guidelines. The selected build angle was 45 degrees, and the layer thickness was 50 μm . After printing, crowns were immersed in 90% alcohol for 10 minutes, then cured under 580 nm wavelength light in a Curie device for 15 minutes.

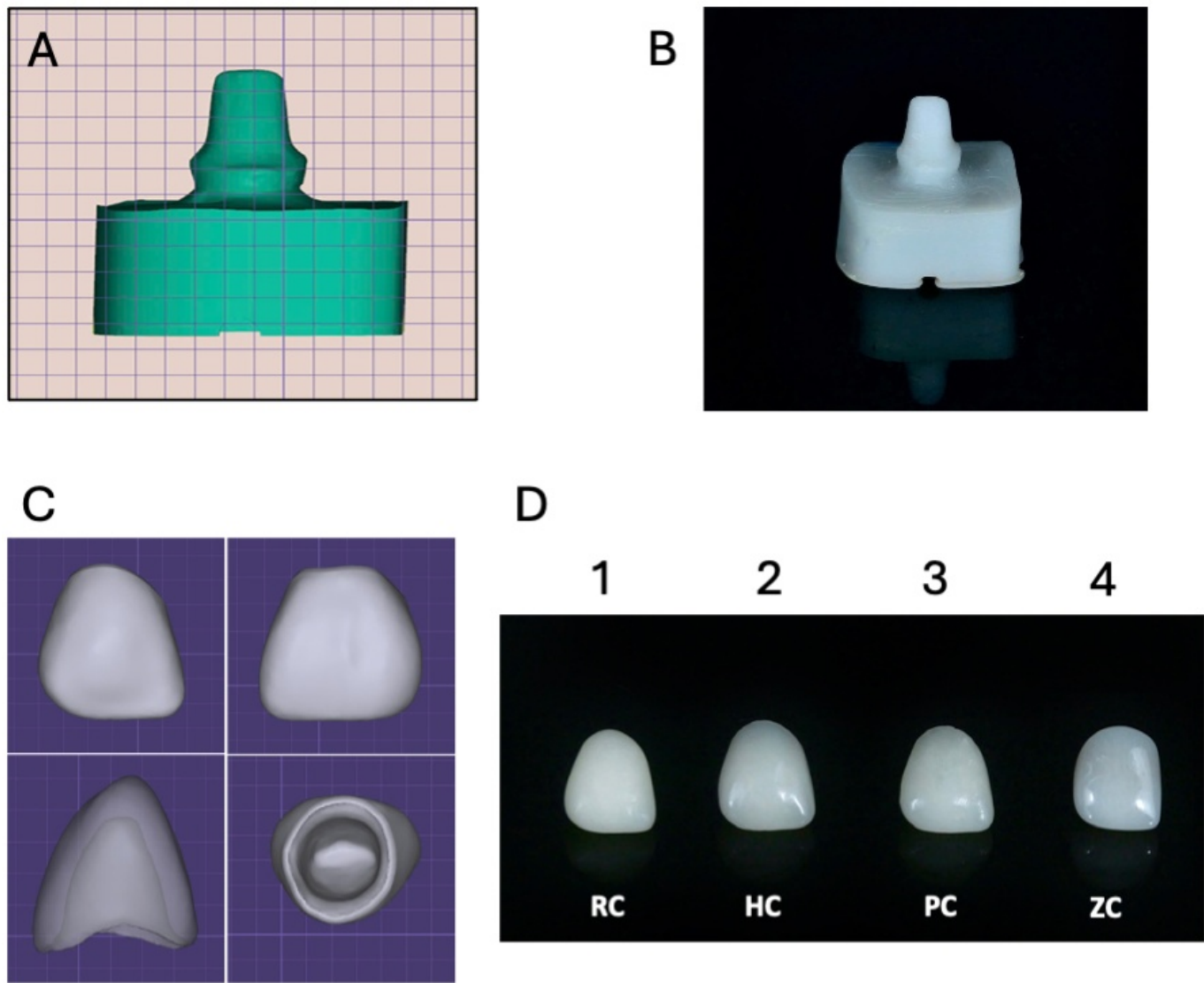


FIGURE 1. Core design and manufacturing. (A) 3D core design. (B) 3D printed cores. (C) 3D-designed crown. (D) Manufactured crowns, including (1) 3D-printed resin (RC); (2) milled hybrid ceramic (HC), (3) milled PMMA (PC) and (4) prefabricated zirconia crowns (ZC).

TABLE 1. Material used.

Material	Trade name	Composition	Shade	Manufacturer
3D printed resin	Resin Crowntec Saremco	Bis-EMA, fiberglass, pyrogenic silica, catalyst and inhibitor	A2	Saremco, Switzerland
Milled Hybrid ceramic	Shofu Block HC	Bis-EMA, UDMA particles, UDMA particles	A2	Shofu, Japan
Milled PMMA	Aidite Block PMMA	Polymethyl methacrylate, Inorganic fillers, fiber reinforcement	A2	Aidite, China
Zirconia	Prefabricated zirconia crowns	Zirconium dioxide, Yttria, Alumina, Silica, Pigments	A2	Shinhung, Korea

3D: Three-dimensional; PMMA: Polymethyl Methacrylate; Bis-EMA: Bisphenol A Ethoxylated Dimethacrylate; UDMA: Urethane Dimethacrylate.

- Milled hybrid ceramic crowns (SHOFU Block HC, Shofu Dental Cor., Japan) and milled PMMA crowns (Aidite PMMA CAD/CAM Block, Aidite Technology Co., China) were milled using the CORiTEC 350i five-axis milling machine (CORiTEC 350i, Imes-icore GmbH, Eiterfeld, HE, Germany). To ensure accuracy, calibration and tool replacement were performed before each milling cycle. After milling, the samples were carefully removed and refined using a rubber wheel. Prefabricated zirconia crowns (Shinhung Prefabricated Zirconia Crown, Shinhung Co., Korea) of appropriate size were selected and adjusted to fit the prepared dies.

After mixing it on a glass slab, all crowns were cemented onto the resin dies ($n = 20/\text{group}$) using resin-modified glass-ionomer cement (GC FujiCEM, GC Corporation, Japan). The cement was applied to fill all crowns, and a 5 kg load was applied to ensure complete seating of the crowns. After 30 minutes, excess cement was removed. The specimens were stored in distilled water at room temperature for 72 hours before testing.

2.2 Fracture resistance testing

The specimens underwent 1000 thermal cycles between 5 °C and 55 °C, with a dwell time of 30 seconds per cycle (Thermocycling Machine, University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam) [19]. A universal testing machine (Instron 5584; Instron Co., Norwood, MA, USA) was used to apply force at a 1 mm/min crosshead speed using a 3 mm-diameter steel tip directly onto the incisal edge of each crown (Fig. 2A,B). The compression load cell (2500 N) is used when the force is applied to the crown in a top-down direction, simulating the direct force applied to the occlusal surface of the crown. The force required to fracture each crown was recorded in Newtons (N) [20].

2.3 Color stability testing

The specimens were stored in a dark box to prevent external light reflection and immersed in orange juice (Twister Orange Juice, Suntory PepsiCo Co., Vietnam) for one week, followed by carbonated soft drinks (Coke) (Pepsi Carbonated Soft Drink, PepsiCo, USA) for another week. The solutions were refreshed every 12 hours, and the crown surfaces were brushed with toothpaste and a soft toothbrush every 12 hours (Fig. 2C,D). Color changes were measured using a spectrophotometer (LS171 Colorimeter; Shenzhen Linshang Technology Co., Shenzhen, Guangdong, China) and evaluated using the Commission Internationale de l'Eclairage (CIE) L , a , b (LAB) color system before and after 1 and 2 weeks of immersion.

On this scale, the values are defined as follows:

- L is used to assess an object's brightness. Black has a value of (0) L , and total light reflection has a value of (100) L .
- $(+a)$ measures the amount of red, while $(-a)$ measures the amount of green.
- $(+b)$ measures the amount of yellow, while $(-b)$ measures the amount of blue [21].

Color values were reassessed after two weeks using the LS171 Linshang spectrophotometer to measure L , a and b values:

The color variation (ΔE) was calculated using the following formula:

- ΔE represents the color variation.
- L , a and b are the color values after crown placement.
- After immersion in staining solutions for two weeks, $L1$, $a1$ and $b1$ are the color parameters.

$\Delta E > 3.3$ is an unacceptable color change visible to the naked eye [22].

$$\Delta E = [(L - L1)^2 + (a - a1)^2 + (b - b1)^2] 0.5.$$

2.4 Statistics analysis

Data were analyzed using SPSS 27.0 computer software (IBM Corp., Armonk, NY, USA). The measured variables are tested

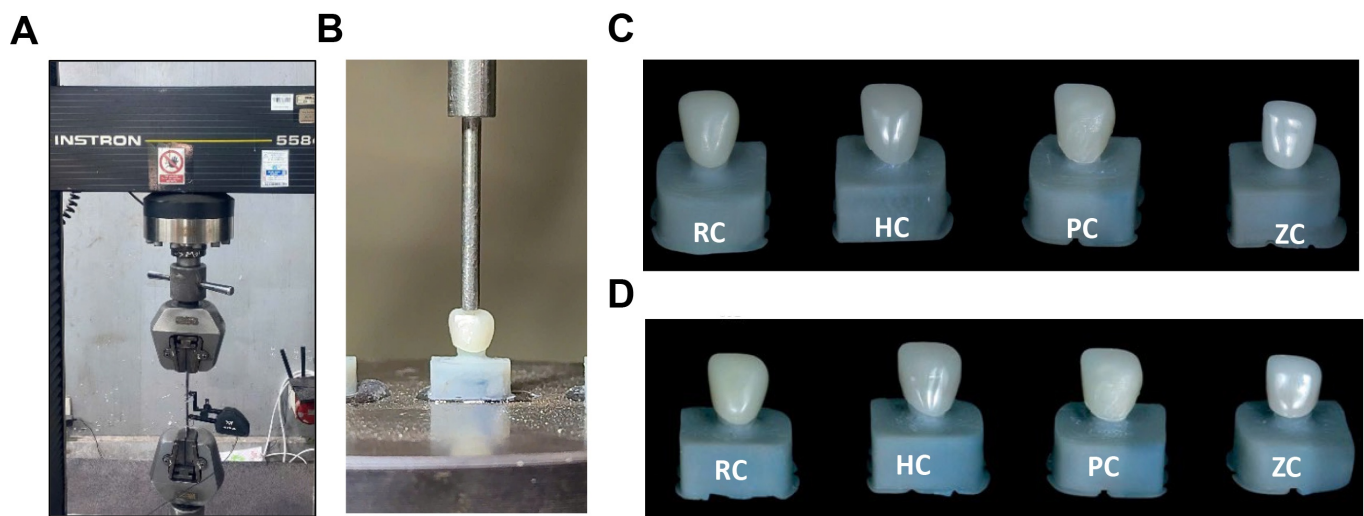


FIGURE 2. Fracture resistance test. (A) Universal Testing Machine setup for fracture resistance testing. (B) Fracture Resistance Testing. Color stability test. (C) Images of colored crowns at 7 days. (D) Images of colored crowns at 14 days. RC: 3D-printed resin; HC: milled hybrid ceramic; PC: milled PMMA; ZC: prefabricated zirconia.

for normal distribution by the Shapiro-Wilk test, while Levene's test tests the difference of variance. Data were compared between the groups using one-way and two-way Analysis of Variance (ANOVA) with a Tukey *post hoc* test. p value < 0.05 was considered to be statistically significant.

3. Results

3.1 Fracture resistance

The mean fracture resistance values and standard deviations for 3D-printed, milled hybrid ceramic, milled PMMA and prefabricated zirconia crowns were >400 N (433.1 ± 61.9 N, 487.3 ± 51.5 N, 483 ± 69.5 N and 511 ± 65.0 N, respectively). Multiple comparisons showed that only 3D-printed crowns differed from prefabricated zirconia crowns with $p = 0.0398$ (Fig. 3A; Table 2). No significance was found in other groups.

3.2 Color stability

Spectrophotometric analysis showed that after 7 days of drink soaking, 3D-printed crowns produced the highest change of ΔE (2.8 ± 0.9), then hybrid ceramic-milled, PMMA-milled and prefabricated zirconia crowns ΔE (1.8 ± 0.3 ; 1.1 ± 0.3 ; 0.8 ± 0.4 ; respectively). Although 3D-printed crown and milled hybrid ceramic ΔE groups were significantly different from the other groups, and there was no difference in PMMA-milled and prefabricated zirconia crowns ΔE , these ΔE values were less than the 3.3 threshold value of clinical recognition (Fig. 3B; Table 2).

After 14 days, only 3D-printed crowns had $\Delta E > 3.3$ and significantly differed from the other groups (5.4 ± 0.6). Milled hybrid ceramic and milled PMMA reached 3 ± 0.5 and 3 ± 0.3 , respectively, and were not significantly different. Especially, prefabricated zirconia crowns were 2.4 ± 0.4 and were significantly different from the other groups (Fig. 3C; Table 2). Multiple group comparisons revealed that all crowns changed color over time (Fig. 3D).

4. Discussion

The null hypothesis for fracture resistance was rejected in the present study as a significant difference was found between 3D-printed resin and prefabricated zirconia crowns ($p = 0.0398$). Similarly, the null hypothesis for color stability was rejected due to significant differences observed, particularly evident in the 3D-printed resin group compared to other tested materials ($\Delta E > 3.3$) after 14 days. One of the pediatric dentists' key objectives is the demand for highly aesthetic restora-

tions for primary incisors. Therefore, selecting a restorative material that meets the requirements of effectiveness, cost-efficiency and personalization is essential. The chosen material should ensure functionality and proper adaptation and help shorten treatment time while simplifying clinical procedures. Digital dentistry, including CAD-CAM and 3D printing technologies, has emerged as a key strategy in achieving these goals. However, few studies have compared these digitally fabricated crowns with prefabricated zirconia crowns. Our study addresses this gap by providing comparative data to support evidence-based material selection in primary anterior restorations.

Based on the above criteria, four materials were selected for this study. Under standardized conditions specifically for primary anterior teeth, it also integrates fracture resistance and color stability assessments, reflecting key clinical concerns in pediatric restorative treatment. Aging conditions and simulated real-life exposures (orange juice and cola) were applied, providing more clinically relevant data. Furthermore, the findings help clarify the clinical suitability of digitally fabricated materials for primary teeth, which are increasingly being adopted in modern pediatric dentistry, and provide scientific evidence to support clinicians in making material choices for pediatric care. Thus, the study confirms some known characteristics and fills critical gaps in comparative data and clinical applicability.

This study used resin models as dental dies instead of natural teeth, as in other *in vitro* studies. This was done to minimize variations between natural teeth since each extracted dry tooth has different fracture resistance depending on its anatomical structure and enamel thickness. Additionally, the elastic modulus of resin dies closely resembles that of natural teeth (1.5 to 5.0 GPa), which is close to the value of natural teeth, suitable for *in-vitro* studies and allowing for a more clinically relevant simulation [23]. Furthermore, customized restorations were fabricated to ensure compatibility with the prepared teeth, overcoming the disadvantages of prefabricated restorations. This prevents improper sizing, minimizes excessive tooth reduction, and shortens the treatment duration. Personalized restorations also provide better marginal adaptation and retention. The crowns were not subjected to final polishing after fabrication to maintain standardization and consistency across all test specimens.

Fracture resistance is critical in determining the clinical longevity of full-coverage crowns. The results indicated that prefabricated zirconia crowns, milled hybrid ceramic crowns and milled PMMA crowns demonstrated greater fracture re-

TABLE 2. Testing results of fracture resistance and color stability among different groups.

Group	Material	Mean ($\pm$ SD) Fracture resistance (N)	Mean ($\pm$ SD) ΔE (7 d)	Mean ($\pm$ SD) ΔE (14 d)
RC	3D printed resin	433.1 ± 61.9	2.8 ± 0.9	5.4 ± 0.6
HC	Milled Hybrid ceramic	487.3 ± 51.5	1.8 ± 0.3	3.0 ± 0.5
PC	Milled PMMA	483.0 ± 69.5	1.1 ± 0.3	3.0 ± 0.3
ZC	Zirconia	511.0 ± 65.0	0.8 ± 0.4	2.4 ± 0.4

RC: 3D-printed resin; HC: milled hybrid ceramic; PC: milled PMMA; ZC: prefabricated zirconia crowns; SD: standard deviation; ΔE : color variation; PMMA: Polymethyl Methacrylate; 3D: three-dimensional.

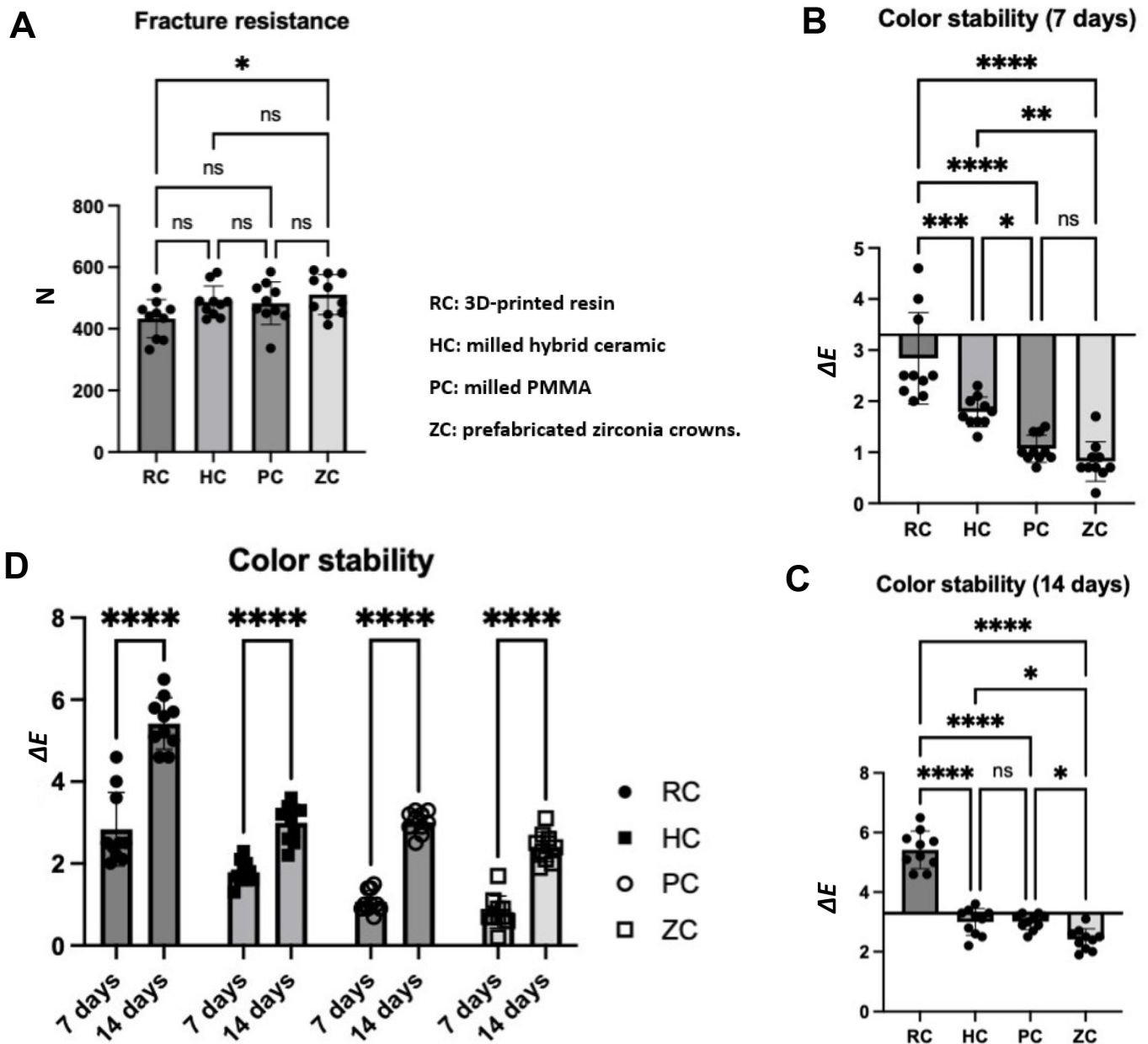


FIGURE 3. Comparison of fracture resistance and color stability (ΔE) between material groups. (A) Fracture resistance comparison between groups. (B) Color stability comparison at 7 days. (C) Color stability comparison at 14 days. (D) Two-way ANOVA comparison of the color stability test. Statistical significance is denoted as * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$, ns (non-significant). Group: (1) 3D-printed resin (RC), (2) milled hybrid ceramic (HC), (3) milled PMMA (PC) and (4) prefabricated zirconia crowns (ZC). ΔE : color variation.

sistance than 3D-printed ones. According to Denry *et al.* [24] (2008), the stable crystalline structure of zirconia, reinforced by transformation toughening, enhances its strength and durability. HC crowns contain dispersed ceramic fillers within a polymer matrix, balancing fracture resistance and material flexibility [11]. Milled PMMA is reinforced with fibers, enhancing its uniform microstructure, improving crack resistance and increasing load-bearing capacity more effectively [25]. In contrast, 3D-printed resin crowns have lower fracture resistance due to the inferior mechanical properties of 3D-printed polymers, which often exhibit incomplete polymerization and micro-porosities, reducing load-bearing capacity and increasing susceptibility to fractures [26]. A recent study

reported that 3D-printed resin has a flexural strength ranging from 90–150 MPa, lower than hybrid ceramic (150–250 MPa) and Zirconia (>900 MPa) [27]. However, all experimental materials showed fracture resistance exceeding 400 N, above the average occlusal forces in the anterior region of pediatric patients from the primary to permanent dentition stages. The average bite force in the early primary dentition stage is 176 N, increasing to 240 N in the late primary stage, 289 N in the early mixed dentition stage and 433 N in the late mixed dentition stage [28]. Therefore, based on the study results, ZC, HC and PC crowns demonstrate potential as suitable options for primary anterior tooth restorations while also meeting the high occlusal load demands in the posterior region. Mean-

while, RC crowns can still be effectively utilized for primary anterior tooth restorations, optimizing cost and fabrication time. Although all tested crowns exhibited fracture resistance exceeding the average bite force in primary teeth, further research is needed to evaluate their wear resistance, flexural strength, and long-term biocompatibility. Additionally, long-term clinical studies are required to accurately assess each crown type's longevity and clinical performance under real-world conditions. Regarding color stability, spectrophotometric analysis after two weeks of immersion showed that the RC group exhibited the most significant color changes ($\Delta E = 5.4 \pm 0.6$), which were visually perceptible, indicating poor stain resistance. In contrast, HC, PC and ZC groups maintained their color better. This can be attributed to the pigment-absorbing nature of 3D-printed resin, as its polymer structure is susceptible to environmental factors, especially exposure to pigmented foods and beverages. On the other hand, zirconia has a highly water-resistant and stain-resistant surface, preserving aesthetics over time [29, 30]. Moreover, HC exhibits better stain resistance than 3D-printing resin but is less resistant than zirconia due to its polymer content [31]. Another study found that 3D-printed resin initially has high translucency, but its polymer matrix absorbs water, leading to gradual color changes [32]. In this study, 3D-printed resin crowns showed unacceptable color changes. However, this level of discoloration may still be clinically acceptable for primary tooth restorations. Although all four groups exhibited a statistically significant color change after 14 days, only the 3D-printed crowns demonstrated a color change exceeding the perceptibility threshold within the same period. Therefore, future studies should consider extending the observation period beyond 14 days to determine whether the remaining groups reach the perceptible color change threshold. The null hypothesis was rejected as there was a significant difference among the tested groups.

This study was conducted under *in vitro* conditions, which may not fully replicate the oral cavity's complex physiological and mechanical environment, such as the presence of saliva. Additionally, color stability was assessed after immersion in orange juice and Pepsi; however, these solutions do not fully represent the variety of dietary exposures commonly encountered in pediatric patients. The 14-day testing period also poses a limitation, as it does not reflect the long-term performance of the materials under real clinical conditions.

Future research should focus on long-term *in vivo* studies to evaluate the fracture resistance, wear resistance, and color stability of materials under real-world conditions, as well as their biocompatibility and patient satisfaction. Additionally, exploring the improvement of the mechanical properties of materials and investigating the cost-effectiveness and workflow optimization of digital technologies in pediatric restorative dentistry are essential. These studies would offer valuable insights into these materials' clinical relevance and applicability for primary dental restorations, ultimately enhancing treatment outcomes and advancing pediatric dental care.

5. Conclusions

3D-printed resin, milled hybrid ceramic crowns, and milled PMMA demonstrated good fracture resistance and acceptable color stability for primary incisors. These crowns may be suitable treatment options for primary anterior teeth, with promising clinical performance warranting further *in vivo* studies. Despite its promising findings, this study was limited by its *in vitro* design and short observation period. Further long-term clinical trials are necessary to confirm these materials' clinical relevance and performance under real-world conditions.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

AUTHOR CONTRIBUTIONS

VNTN, TQK—Study conception and design; Acquisition of data and analysis; Drafting of the manuscript; Critical revision. VNTN, TQK, NHT—Design implementation; Data acquisition; Critical revision. NHT, NCNH, HTH—Acquisition of data; Critical revision. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study used extracted maxillary primary incisors that were collected anonymously after natural exfoliation. According to institutional guidelines and common ethical standards, when biological samples are non-identifiable and collected without linking to patient data, informed consent may be exempted. We have confirmed with our institutional ethics committee that informed consent was not required in this case. The study was approved by the Research Ethics Committee of the University of Medicine and Pharmacy at Ho Chi Minh City under approval number 1830/ĐHYD-HĐĐĐ, dated 08 June 2024.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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