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journal homepage: www.elsevier.com/locate/jdsrZirconia bond strength durability following artificial aging: A systematic review and meta-analysis of in vitro studies[☆]Athanasios E. Rigos^a, Katia Sarafidou^b, Eleana Kontonasaki^{c,*}^a Resident, Graduate Prosthodontics, Texas A&M School of Dentistry, Dallas, TX, USA^b Postdoctoral Researcher, Department of Prosthodontics, School of Dentistry, Faculty of Health Sciences, Aristotle University of Thessaloniki, Greece^c Associate Professor, Department of Prosthodontics, School of Dentistry, Faculty of Health Sciences, Aristotle University of Thessaloniki, Greece

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ABSTRACT

The present study systematically reviewed the literature regarding the bond strength durability of zirconia ceramics to resin-based luting cements after application of different bonding protocols and aging conditions. Electronic searches in PubMed, Scopus, and Web of Science databases were performed for relevant literature published between January 1st 2015 and November 15th 2022. Ninety-three (93) English language in-vitro studies were included. The percentage of the mean bond strength change was recorded prior to and after artificial aging, and the weighted mean values and 95% confidence intervals were calculated. Bonding protocols were classified based on the combination of MDP/non-MDP containing cement/primer and surface pretreatment, as well as the level of artificial aging performed. Alumina sandblasting (SA) was identified as the most frequently used surface pre-treatment while an insufficient number of studies was identified for each category of alternative surface treatments. The combination of MDP cement with tribochemical silica coating (TSC) or SA yielded more durable results after aging, while the application of SA and TSC improved bond durability when a non-MDP cement and a non-MDP primer were used. TSC may lead to increased bond durability compared to SA, whereas MDP cements may act similarly when combined with SA or TSC.

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[☆] Scientific field of dental Science: Prosthodontics.

* Correspondence to: Department of Prosthodontics, School of Dentistry, Faculty of Health Sciences, Aristotle University of Thessaloniki, 54124, Greece.

E-mail address: kont@dent.auth.gr (E. Kontonasaki).

1. Introduction

Zirconia ceramics present the highest mechanical properties among all-ceramic materials used in dentistry and hence combine favorable esthetics with increased strength [1]. One of the major complications reported for zirconia restorations is loss of retention [2]. This has been attributed to the inability of zirconia ceramics to be roughened with the use of hydrofluoric acid (HF) because they don't contain silica [3], and thus the question of the appropriate bonding protocol has not been answered yet [4]. As an oxide that does not contain silica, zirconia requires different pre-treatment of the internal surface prior to cementation, compared to silica containing ceramics such as lithium disilicate.

The effect of several surface treatments, cements and primers on the bond strength of zirconia has been the topic of extensive research. In vitro studies have evaluated a wide range of different adhesive protocols but there is lack of evidence to support one of them in clinical practice. Nonetheless, alumina sandblasting (SA), tribochemical silica coating (TSC) and the use of MDP containing cements and primers have been proposed as more effective in achieving a strong bond [5,6]. However, there are still conflicting findings in terms of bond durability after artificial aging and/or water storage.

Several testing methods - shear, tensile, push-out bond strength tests and the Brazil nut method [7,8] - have been used to evaluate the bond strength of zirconia to luting cements. The present systematic review and meta-analysis aims to identify a correlation between the difference of the bond strength following artificial aging, such as water storage (WS) or thermal cycling (TC), and a particular surface treatment or luting cement by classifying studies based on the type of cement, primer or surface treatment. The primary goal was to identify whether the application of different bonding protocols - sandblasting surface pretreatment (SA), tribochemical silica coating (TSC), use of an MDP or non-MDP cement, use of an MDP or non-MDP primer - can yield durable bond strength after different types of thermal cycling. Although there is no ISO standard or other consensus in literature defining the term "durable bond", it is important, as a first step, to systematically investigate the percentage of change in bond strength after application of different bonding strategies and thermal cycling. Based on this, the purpose of this review and meta-analysis was to evaluate the bond strength change of zirconia ceramics to resin-based luting cements after the application of various bonding protocols and thermal cycling. The null hypothesis of the study was that the application of different bonding protocols and thermal cycling would not significantly affect the bond strength of zirconia ceramic to resin-based luting cements.

2. Materials and methods

The PRISMA (Preferred Items for Reporting Systematic Reviews and Meta-Analyses) search strategy was adopted for the conduction of the present systematic review. The question to be addressed was: 'Among different adhesive cementation protocols and pretreatment methods of zirconia ceramics to resin-based luting cements, which one ensures the least mean bond strength change after artificial aging?'

The PICO method was adopted to state the scope of the review accurately. Participants in the study included zirconia specimens, Interventions consisted of the zirconia surface treatment method and the luting cement used, Comparators comprised of the control group of each study (where control was considered the study group that was named control by the authors of each individual study) and the artificially aged groups, and Outcomes were considered the values of the Shear and Tensile Bond Strength. Three databases (PubMed, Scopus and Web of Science) were searched by two independent reviewers (TR and KS). The reference lists of all articles

that were selected for full text evaluation were also screened manually. The search terms were: ((monolithic zirconia) OR (zirconia) OR (YTZP) OR (Y-TZP) OR (YPSZ) OR (Y-PSZ)) AND ((luting cement) OR (cementation) OR (resin cement) OR (composite resin cement)) AND ((bond strength) OR (shear bond strength) OR (micro-shear bond strength) OR (tensile bond strength) OR (micro-tensile bond strength)) AND ((aging) OR (hydrothermal treatment) OR (water) OR (thermal cycling)).

Inclusion criteria were: in-vitro studies, studies in English language published between January 1st 2015 and November 2022, studies performing in-vitro shear or tensile bond strength test regardless of their micro- or macro- classification, studies reporting on zirconia specimens with a disc or block geometry, studies including a control group (baseline) of artificial aging with a performance time span of 0–7 days, studies performing artificial aging in water storage (37 °C) for a minimum of 6 months or thermal cycling, or a combination of the above mentioned protocols and studies containing groups with ≥ 5 samples. The following types of studies were excluded: systematic reviews, meta-analyses, clinical studies, studies testing zirconia abutments, studies evaluating indirect composite materials, repaired zirconia or orthodontic bracket bond strength, studies evaluating the bond strength of zirconia ceramics to dentin or enamel, studies including loading (chewing simulators), studies not stating the exact zirconia ceramic product or articles using commercially unavailable (experimental) zirconia, studies investigating glass infiltrated zirconia, zirconia reinforced lithium disilicate or other zirconia-based ceramics, studies not reporting numerical mean bond strength values with standard deviation, studies investigating the effects of saliva contamination, silicone disclosing materials or zirconia coloring on the bond strength. Since there is no standard risk of bias tool to assess the methodological quality of in-vitro studies to date, strict inclusion and exclusion criteria were applied. Disagreements among the reviewers (TR, KS) were resolved by discussion and then by consulting a third author (EK) for arbitration.

Data extraction was also undertaken independently to minimize the likelihood of error and in order to reduce bias. Extracted data were recorded in [supplementary Tables 1 and 2](#) as they were divided in shear bond strength studies and tensile bond strength studies respectively. Descriptive analysis was performed using the R statistical software. From all the included studies, mean and standard deviation values for the outcome of bond strength were extracted. Then, pooled mean difference and 95% confidence intervals were calculated for different factors: surface treatment (SA + no other surface treatment, SA + other surface treatment, TSC+ no other surface treatment, TSC + other surface treatments, no SA + no other surface treatment, SA + other surface treatments), aging (WS, TC < 10000, TC \geq 10000, WS + TC < 10000, WS + TC \geq 10000) and cement/primer combination (MDP cement + MDP primer, MDP cement + non-MDP primer, non-MDP cement + MDP primer, Non-MDP cement + non-MDP primer, MDP cement-no primer, Non-MDP cement-no primer). Moreover, the percentage of change in mean bond strength was calculated in each group with the same surface treatment, cement/primer combination and aging.

3. Results

The electronic search and hand search concluded in 1227 records, 1142 through the electronic search and 85 through manual search. After duplicates removed 536 articles were selected for screening, from which 354 abstracts were evaluated. Finally, 169 articles were subjected to full-text assessment. The excluded articles after full-text analysis and reasons for exclusion are given in [Table 1](#). Eventually, 93 studies fulfilled the inclusion criteria and were included in this review ([Fig. 1](#), [Supplementary tables 1 and 2](#)).

Table 1
Excluded studies after full-text evaluation and reasons for exclusion.

Not reporting arithmetic bond strength values		
da Silva 2021 [9]	Yang et al. 2020 [17]	Bielen et al. 2015 [24]
Lima et al. 2019 [10]	Al-Dobaiei et al. 2020 [18]	Kim 2019 [25]
Chen et al. 2017 [11]	Yang et al. 2018 [19]	Piest 2018 [26]
Aboushelib et al. 2018 [12]	Chen et al. 2019 [20]	Aggarwal et al. 2018 [27]
Lima et al. 2019 [13]	Vecchiato-Filho et al. 2017 [21]	Tsujimoto et al. 2017 [28]
Zhang et al. 2021 [14]	Xie et al. 2016 [22]	Khanlar et al. 2022 [29,30]
Tzanakakis et al. 2021 [15]	Yu 2021 [23]	Garcia et al. 2022 [31]
All specimens were subjected to aging, no non-aged control		
Steiner et al. 2019 [32]	Lümkemann et al. 2019 [37]	Alnassar et al. 2016 [42]
Yenisey et al. 2016 [33]	Pozzobona et al. 2015 [38]	Alnassar et al. 2017 [43]
Al-Harbi et al. 2016 [34]	Liebermann et al. 2018 [39]	Kaimal et al. 2017 [44]
Sousa et al. 2016 [35]	Kim et al. 2015 [40]	Fernandes Neto et al. 2022 [45]
	Vicente et al. 2016 [41]	Sriamporn et al. 2022 [46]
Not reporting arithmetic bond strength values for all groups		
Shafiei et al. 2019 [47]	Byeon et al. 2017 [48]	
No aging		
Chen et al. 2017 [49]	Qian et al. 2016 [54]	Nagaoka et al. 2017 [59]
Yu et al. 2019 [50]	Takahashi et al. 2018 [55]	Cho et al. 2017 [60]
Murakami et al. 2017 [51]	Özdemir et al. 2019 [56]	Chen et al. 2016 [61]
Şanlı et al. 2015 [52]	Llerena-Icochea et al. 2017 [57]	Wei et al. 2018 [62]
Noro et al. 2015 [53]	Park et al. 2017 [58]	Kim et al. 2022 [63]
Only median bond strength values reported (no mean values)		
Kim et al. 2016 [64]	Bömicke et al. 2016 [66]	
Samran et al. 2019 [65]	Sawada et al. 2016 [67]	
No standard deviations reported		
Diniz et al. 2019 [68]	Malgaj et al. 2019 [69]	
Zirconia product name not reported / experimental product		
Sathish et al. 2019 [70]	De Araujo Neto et al. 2022 [71]	Malgaj et al. 2021 [72]
Bonding to enamel or zirconia to zirconia		
Liu et al. 2016 [73]	Thammajaruk et al. 2021 [74]	
Not an original research paper		
Scribante et al. 2016 [75]		
Sample size < 5 specimens or not reporting sample size		
Akay et al. 2019 [76]	Gutierrez et al. 2020 [78]	Silva et al. 2016 [79]
Lee MH et al. 2021 [77]		
Layered with composite resin, not cemented with a luting cement		
Sarfaraz et al. 2020 [80]	Li et al. 2020 [81]	Ataol et al. 2018 [82]
Zirconia samples were bonded following artificial aging		
Moqbel NM et al. 2022 [83]		
Contaminated samples with saliva prior to bonding		
Rui L et al. 2021 [84]		

From the 93 studies, 73 reported results of shear tests and 20 from tensile tests, while one study reported results from both shear and tensile tests [85]. In the shear testing group mean bond strength ranged between 1.3 [86] and 60.64 MPa [87] for control groups, and between 0.00 [88,89] and 47.58 [87] for artificially aged groups. Furthermore, the number of specimens per group (n) ranged between n = 7 [90] and n = 20 samples [87,91–95]. Twenty (20) studies performing tensile testing were included in the present review (Supplementary Table 2). In 13 of them, specimens were fabricated with a bonding area of > 7 mm² and < 28 mm² [85,96–107], while in 7 of them the bonding area was < 2 mm² (microtensile) [108–114]. Mean bond strength ranged between 4.41 [115] and 90.88 MPa [112] for control groups, and between 0 [115] and 90.12 [112] for artificially aged groups. Furthermore, the number of specimens per group (n) in the 20 tensile bond strength test studies ranged between 5 and 30 samples.

Mean difference and 95% confidence intervals (95% CI) of bond strength are presented in Figs. 2–4 while the percentage of change is depicted in Tables 2 and 3.

The included studies were grouped according to surface treatment, aging protocol, and the cement/primer combination applied. Seven studies [88,89,105,115,154,157,177] included groups that presented instant debonding following aging and those groups were excluded from the pooled mean difference calculation. In general, the bond strength was significantly reduced by artificial aging in most groups, especially for aging protocols including a combination of WS and TC.

3.1. Shear group

In cases where SA was applied with no other surface pre-treatment (SA+NOST), 7 studies [137,147,148,160,161,162,171] in the shear test group showed no significant difference of bond strength after aging, while mean pooled difference of groups based on cement/primer combination showed significant differences in all groups (Fig. 2A, Table 2). Four of them presented increase [86,137,147,162]. When SA was used with additional surface pre-treatments (SA + OST), mean pooled difference showed significant changes in all groups, while only 1 study [171] showed no significant mean difference of bond strength after aging and (Fig. 2B). In this study, the combination of MDP cement + non-MDP primer was used. When no SA and no other surface treatment was applied (no SA+NOST), 6 studies from the shear test group showed no significant change in bond strength after aging and even increase (Fig. 2C) [85,122,123,143,162,169]. The combinations of MDP cement with MDP primer and Non-MDP cement with MDP primer showed negative mean pooled difference. In cases where treatments other than SA or TSC were used (no SA + OST) in the shear test group, 3 studies using a non-MDP cement + non-MDP primer [128,131] or non-MDP cement + no primer [130] presented a non-significant increase in the bond strength after aging (Fig. 2D). Groups from these studies showed increase in bond strength after aging.

In cases where TSC was applied only (TSC+NOST), 11 out of 23 studies in the shear test group showed no significant difference of the bond strength after aging (Fig. 3A, Table 2), while 2 studies

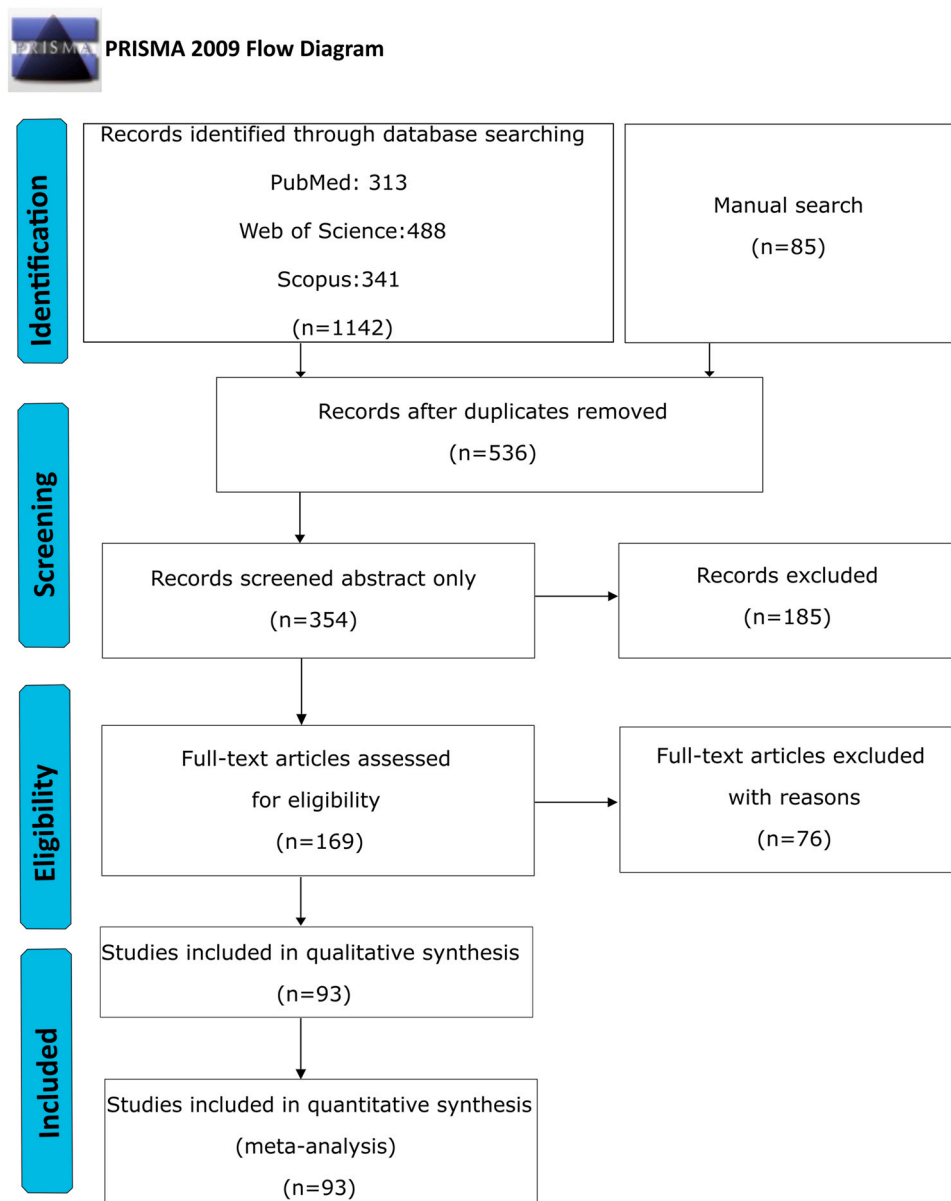


Fig. 1. PRISMA flow diagram.

[94,131] showed slight increase in bond strength. Mean pooled difference showed significant decrease in most of the cement/primer combination groups irrespectively of the aging process. In the study of Cadore-Rodriguez et al.[94], a significant increase was observed even after WS + TC \geq 10000 cycles. When TSC was used combined with other surface treatments, 1[91] out of 6 studies in the shear test group showed increase in bond strength after aging and three no significant difference [88,89,91] (Fig. 3B).

3.2. Tensile group

In cases where SA was applied with no other surface pre-treatment, all studies (20) in the tensile group showed decrease in strength after aging, with the least being observed in the study of Thammajarak et al.[178] [95%CI 0.76 (-7.74,9.26)] which included the combination of MDP cement + MDP primer (Fig. 4A). When SA was used with additional surface pre-treatments (SA+OST), all 2 [113,178] studies in the tensile test group showed significant mean pool difference of bond strength after aging (Fig. 4C).

When no surface treatment was applied (No SA+NOST), in the tensile group only 1[85] out of 14 study groups showed slight increase in bond strength and included the combination of MDP cement + no primer (Fig. 4B). The rest of the studies showed significant decrease in bond strength after aging. In cases where treatments other than SA or TSC were used (No SA+OST), in the tensile test group, all 3 studies presented significant decrease in bond strength (Fig. 4D)[102,110,111] In cases where TSC was applied only (TSC+NOST), 3 out of 8 study groups involved in the tensile test group showed no significant difference of the bond strength after aging (Fig. 4E), showing in fact slight increase after aging [MDP cement + non-MDP primer (2 studies)[85,109], non-MDP cement + non-MDP primer[85] (1 study).

3.3. Non-MDP cement and non-MDP primer

When non-MDP cement and non-MDP primer was used and no SA was applied in the shear group (No SA+NOST/ No SA+OST), the decrease of bond strength was < 63.3% in most of the studies, while 3 studies showed increase in bond strength [123,128,131] (Table 2).

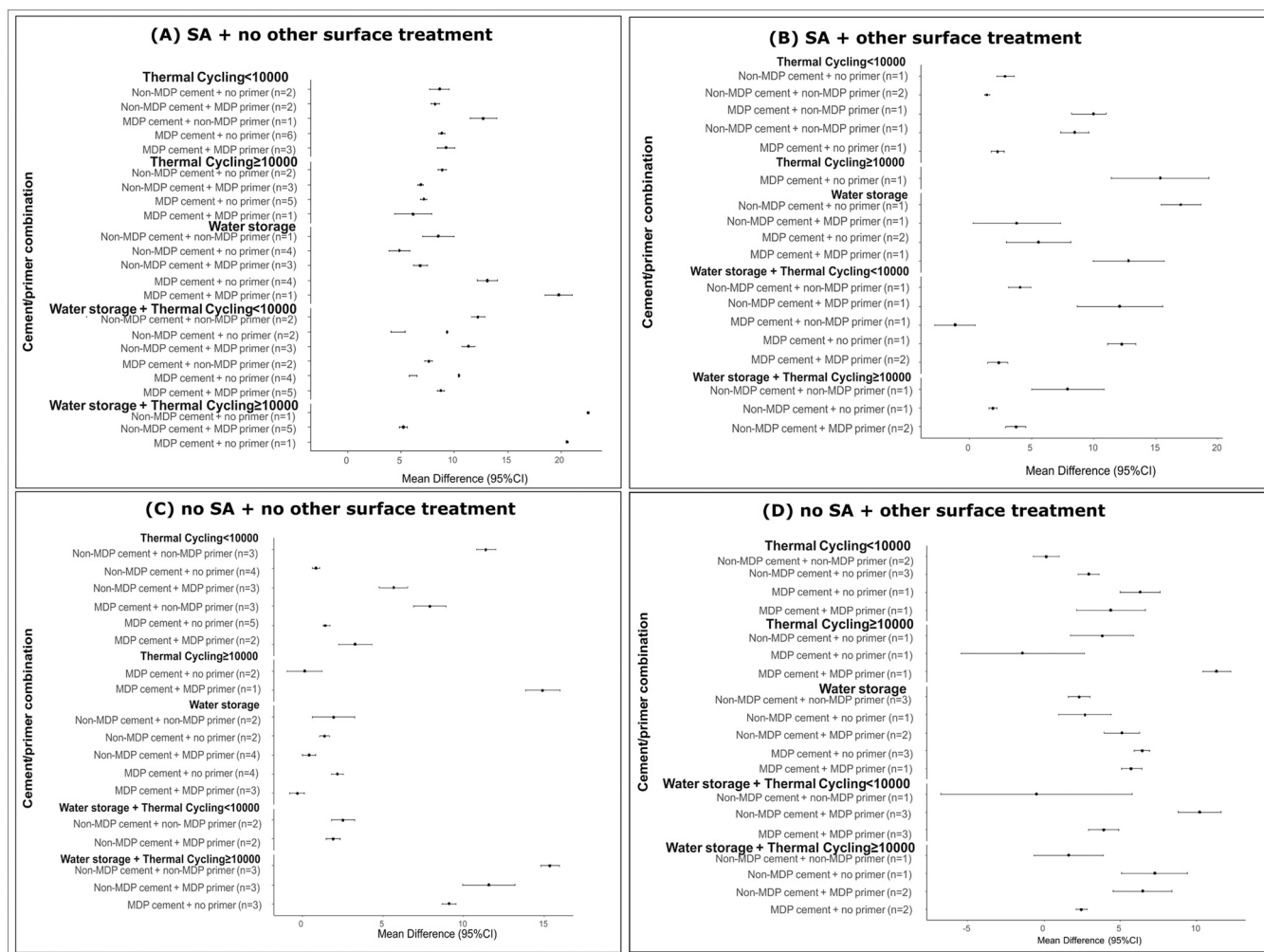


Fig. 2. Mean Difference of bond strength between control group and aging group from studies including shear tests for zirconia-resin bond strength evaluation. Classification was based on whether SA was applied or not in combination with or without other surface treatments and studies were grouped based on different cement/primer combinations. Error bars represent the 95% confidence intervals of mean difference. (A) SA + no other surface treatment, (B) SA + other surface treatment, (C) no SA + no other surface treatment, (D) no SA + other surface treatment.

Similarly, in the tensile test group, the same group presented the lowest percentage of change. However, when SA was applied (SA+NOST and SA+OST), the decrease of bond strength was $\leq 50.9\%$ in five out of six studies for shear test [95,116,117,119,159] and below 42.2% in 4 out of 5 study groups for the tensile test (Tables 2 and 3) [96,100,107,114]. The decrease was more than double (83.4%) in the study of Elsayed et al., 2017[100], when they increased TC above 10000 cycles. Interestingly, the application of other surface treatments without SA (no SA+OST) resulted in low bond strength decrease, ranging from 7.1% to 23.7% in the shear test group[116,127,129], while in 2 studies an increase after aging was observed[128,131]. When TSC was applied with no other surface pre-treatment (TSC+NOST), all studies presented low bond strength decrease ($\leq 28.6\%$), for both shear (8 studies)[85,89,122,127,129,130,132,133,145] and tensile (3 studies)[108,111,114] test groups, while in 1 study in the tensile group[85], and in 1 study in the shear group[131] an increase in bond strength was recorded.

3.4. Non-MDP cement + No primer

Several studies investigated the bond strength before and after aging, with the application of non-MDP cement for bonding alone without primer (Table 2). A trend towards low mean pooled difference is observed irrespectively of the aging process when SA was

applied. When SA was used with no additional surface pre-treatment (SA+NOST), in 3[116,134,139]out of 8 studies in shear test and the 3 [103,104,108] studies in the tensile test groups revealed $\leq 42.3\%$ decrease of bond strength as a result of different aging processes, while 2 studies showed 82.4[136] and 96.8%[117] decrease in the shear group (Tables 2 and 3). In the samples where SA was not applied, great variation of the received percentage of change cannot give any conclusive result from both shear and tensile tests. This variation was evident also when OST or TSC was applied. In 1 study however[130], an increase (-6.1%) in bond strength was calculated for the specimens that were immersed in an aqueous suspension of aluminum nitride powder for 15 min at 75 °C, however not statistically significant compared with the non-aged group.

3.5. Non-MDP cement + MDP-primer

With the use of a non-MDP cement and an MDP-primer, SA application resulted in 8[94,117,136,139,146,148,149] out of 11 studies presenting bond strength change $\leq 39.6\%$ in the shear test group and $\leq 49.9\%$ in the 9 studies [96,100,101,104,105,107,109,110] included in the tensile test group (Tables 2 and 3). The great heterogeneity of the percentage of change values (-24.3 to 100%) in the specimens where SA was not applied, does not allow any conclusive result. When other treatments were applied without SA, 2 studies out of 8 that used

Table 2
Mean difference (95% CI) and % change of bond strength before and after aging in studies included in the shear test group.

Surface treatment	Study	Non-aging			Aging			Mean difference (95% CI)	% Change	
		Total No	Mean	SD	Total No	Mean	SD			
SA + NOST	WS	10	12.27	2.11	10	8.65	2.23	3.62 (1.72, 5.52)	30	
	WS+TC <10000	24	17.03	2.36	24	8.36	1.53	8.67 (7.94, 9.79)	50.9	
		120	22.20	4.85	120	14.09	4.61	8.11 (6.91, 9.30)	36.5	
	Pooled Mean Difference (95%CI)							6.14 (5.76, 6.51)		
	SA + OST	TC <10000	20	9.75	2.50	20	1.30	0.45	8.45 (7.34, 9.56)	86.7
		WS+TC <10000	30	10.72	1.15	30	6.65	2.23	4.07 (3.17, 4.97)	38
		WS+ TC ≥10000	11	20.50	4.30	11	12.60	2.40	7.90 (4.99,10.81)	38.5
		TC <10000	88	20.11	3.47	88	3.54	1.05	16.57 (15.82, 17.33)	82.4
	No SA + NOST	Rebholz-Zaribaf et al 2016[85]	15	12	4.2	15	4.4	1.7	7.60 (5.31, 9.89)	63.3
		Ramos 2020[121]	15	2.7	2	15	0.3	0.5	2.40 (1.36, 3.44)	88.9
Pooled Mean Difference (95%CI)							11.40 (10.81, 11.99)			
WS		10	4.35	1.44	10	2.38	1.67	1.97 (0.60, 3.34)	45.3	
Oliveira-Ogliari et al 2015[122]		20	14	8	20	12.4	5.4	1.60 (-2.63, 5.83)	11.4	
Pooled Mean Difference (95%CI)							1.94 (0.64, 3.24)			
WS+ TC <10000		30	10.8	5.37	30	12.1	3.53	-1.30 (-3.60, 1.00)	-12*	
Zhao et al 2022[124]		12	7.53	0.59	12	5.50	0.47	2.03 (1.60, 2.45)	26.9	
Pooled Mean Difference (95%CI)							2.53 (1.83, 3.24)			
WS+ TC ≥10000		12	18.6	4.4	12	2.4	1.2	16.20 (13.62, 18.78)	87.1	
No SA + OST	Noda et al 2017[125]	20	8.5	4.6	20	0.3	0.1	8.20 (6.18, 10.22)	96.5	
	Kim et al 2015[92]	60	29.97	1.32	60	13.97		16.00 (15.38, 16.62)	53.4	
	Pooled Mean Difference (95%CI)							15.36 (14.78, 15.94)		
	TC <10000	24	10.58	1.44	24	9.63	2.33	0.95 (-0.15, 2.04)	8.9	
	Lung et al 2015[127]	12	11.7	1.3	12	12.7	1.9	-1.00 (-2.30, 0.30)	-8.5*	
	Pooled Mean Difference (95%CI)							0.14 (-0.70, 0.98)		
	WS	24	10.58	1.44	24	9.06	1.48	1.52 (0.69, 2.35)	14.4	
	Lung et al 2015[127]	10	21.28	3.03	10	16.23	2.17	5.05 (2.74, 7.36)	23.7	
	Su et al 2021[116]	120	29.7	6.7	120	25.17	7.78	4.53 (2.69, 6.36)	15.2	
	Pooled Mean Difference (95%CI)							2.32 (1.60, 3.04)		
TSC + NOST	WS+ TC <10000	10	3.31	2.67	10	3.8	9.71	-0.49 (-6.73, 5.75)	-14.8*	
	WS+ TC ≥10000	30	22.45	5.2	30	20.85	3.7	1.60 (-0.68, 3.88)	71	
	TC <10000	8	15.93	1.17	8	12.6	2.17	3.33 (1.62, 5.04)	20.9	
	Lung et al 2015[127]	15	38.6	8	15	33.4	5.1	5.20 (0.40, 10.00)	13.5	
	Thammajaruk et al 2020[130]	30	10.15	4.55	30	7.25	4.4	2.90 (0.64, 5.16)	28.6	
	Rebholz-Zaribaf et al 2016[85]	12	10.2	1.2	12	12	1	-1.80 (-2.68, -0.92)	-17.6*	
	Pooled Mean Difference (95%CI)							-0.20 (-0.93, 0.53)		
	TC ≥10000	15	38.6	8	15	31.7	5.4	6.90 (2.02, 11.78)	17.9	
	WS	8	15.93	1.17	8	14.5	2.38	1.43 (-0.41, 3.27)	9	
	Pooled Mean Difference (95%CI)							5.13 (0.99, 9.27)		
TSC + OST	WS+ TC ≥10000	15	19.9	5.3	15	18.7	3.8	1.20 (-2.10, 4.50)	6	
	WS	30	14.33	1.17	30	13.67	1.53	0.67 (-0.02, 1.36)	4.7	
	Pooled Mean Difference (95%CI)							2.04 (0.36, 3.72)		
	WS+ TC <10000	10	31.9	4.6	10	22.8	3.5	9.10 (5.52, 12.68)	28.5	
	Wandscher et al 2016[129]	10	19.80	2.00	10	17.10	2.30	2.70 (0.81, 4.59)	13.6	
	Chen et al 2020[132]	20	15.8	7	20	2.8	2.3	13.00 (9.77, 16.23)	82.3	
	Pooled Mean Difference (95%CI)							0.98 (0.31, 1.64)		
	TC <10000	10	19.80	2.00	10	17.10	2.30	2.70 (0.81, 4.59)	13.6	
	WS+ TC <10000	20	15.8	7	20	2.8	2.3	13.00 (9.77, 16.23)	82.3	

(continued on next page)

Table 2 (continued)

Non-MDP cement + non-MDP primer		Aging		Non-aging		Aging		Mean difference		% Change			
Surface treatment	Study	Total No	Mean	SD	Total No	Mean	SD	Total No	Mean	SD	Mean difference (95% CI)	% Change	
Non-MDP cement + no primer Surface treatment	SA + NOST	TC <10000	12	20.5	8.39	12	14.5	3.27	6.00 (0.91, 11.09)	3.27	29.3	29.3	
													30
	Pooled Mean Difference (95%CI)		3.76 (2.59, 4.93)		3.90 (1.52, 6.28)		82.4						
	TC ≥10000	30	4.99	1.1	17.05	20	13.15	2.14	4.10 (3.58, 4.62)	2.14	22.9	22.9	
													Pooled Mean Difference (95%CI)
	WS	10	13.38	2.38	17.19	10	8.12	1.97	1.97	5.26 (3.35, 7.17)	1.97	39	39
	Lopes et al 2016[86]	12	14.60	4.90	16.00	12	16.00	4.80	-1.40 (-5.28, 2.48)	4.80	-9.6*	-9.6*	
													Soto Montero et al 2022[138]
	Pooled Mean Difference (95%CI)		9.55 (8.30, 10.80)		9.55 (8.30, 10.80)		20.1						
WS+ TC <10000	10	17.19	1.12	5.99	12	13.74	1.09	1.09	3.45 (2.48, 4.42)	1.09	20.1	20.1	
													12
Pooled Mean Difference (95%CI)		4.70 (4.04, 5.36)		4.70 (4.04, 5.36)		43.9							
SA + OST	TC <10000	12	6.6	1.1	18.33	30	3.7	0.6	2.90 (2.19, 3.61)	0.6	43.9	43.9	
													30
WS	11	2.4	0.5	11.91	11	0.5	0.1	1.90 (1.60, 2.20)	0.1	79.2	79.2		
												WS+ TC ≥10000	22
TC <10000	15	7.5	5.6	15	0	0	0	7.5	0	100	100		
												Lee et al 2015[142]	50
Lee et al 2015[140]	12	34.7	4.1	30	6.3	4.3	4.3	5.80 (3.39, 8.21)	4.3	47.9	47.9		
												Pooled Mean Difference (95%CI)	
WS	16	4.16	0.59	5.23	10	2.83	1.39	1.72	2.66 (1.29, 4.03)	1.72	50.9	50.9	
													Zhao L et al 2016[143]
Pooled Mean Difference (95%CI)		1.33 (1.03, 1.64)		1.33 (1.03, 1.64)		68.4							
No SA + OST	TC <10000	15	27.7	5.7	10.33	15	1.8	3.8	3.90 (1.65, 6.15)	3.8	68.4	68.4	
													15
Pooled Mean Difference (95%CI)		2.93 (2.23, 3.62)		2.93 (2.23, 3.62)		12.3							
No SA + OST	TC ≥10000	28	30.95	4.05	10.59	28	27.15	3.9	3.80 (1.72, 5.88)	3.9	12.3	12.3	
													10
WS	24	10.33	4.73	3.07	24	3.07	2.53	7.26 (5.12, 9.41)	2.53	70.3	70.3		
												WS+ TC ≥10000	15
TC <10000	8	10.2	5.1	8	9.1	4.4	1.10 (-3.57, 5.77)	10.8					
									WS+ TC ≥10000	15	18.2	6.1	15
Pooled Mean Difference (95%CI)		4.41 (1.32, 7.50)		4.41 (1.32, 7.50)		18.0 (15.42, 20.58)							
TSC + NOST	TC <10000	15	18.9	4.6	15	0.9	2.2	2.2	18.0 (15.42, 20.58)	2.2	95.2	95.2	
													15
Pooled Mean Difference (95%CI)		18.0 (15.42, 20.58)		18.0 (15.42, 20.58)		95.2							

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Table 2 (continued)

Surface treatment	Aging	Study	Non-aging		Aging		Mean difference		% Change	
			Total No	Mean	Total No	Mean	(95% CI)	SD		
Non-MDP cement + MDP primer Surface treatment	SA + NOST	TC <10000	Salem et al 2019[146]	24	9.67	24	7.11	2.57 (2.07, 3.06)	0.79	26.6
			Elgendy et al 2020[147]	20	18	20	5.95	12.05 (10.27, 13.83)	2.85	66.9
			<i>Pooled Mean Difference (95%CI)</i>					3.25 (2.77, 3.72)		
	TC ≥10000	WS	Yoshida et al 2018[148]	8	24.1	8	22.5	1.60 (0.07, 3.13)	1.7	6.6
			Pitta et al 2018[137]	40	31.62	40	22.7	8.92 (6.50, 11.35)	4.57	28.2
			Yang et al 2018[136]	120	12	120	10.63	1.37 (1.08, 1.66)	1.11	11.4
	WS	WS	<i>Pooled Mean Difference (95%CI)</i>				4.10 (3.58, 4.62)			
			Su et al 2021[116]	10	18.27	10	10.65	7.62 (5.31, 9.93)	2.01	42
			Lopes et al 2016[86]	48	5.97	48	5.68	0.30 (-0.54, 1.14)	1.90	5.0
	WS+TC <10000	WS+TC <10000	Darvizeh et al 2015[149]	18	21.4	18	15.1	6.30 (3.28, 9.32)	5.1	29
			<i>Pooled Mean Difference (95%CI)</i>				1.48 (0.69, 2.29)			
			Liu et al 2020[139]	10	22.38	10	20.11	2.27 (0.83, 3.71)	1.73	10.1
	WS+TC ≥10000	WS+TC ≥10000	Chuang et al 2017[117]	36	23.59	36	14.24	9.35 (8.26, 10.44)	1.47	39.6
			Ahn et al 2020[150]	10	25.66	10	15.03	10.63 (8.39, 12.87)	2.56	41.4
			<i>Pooled Mean Difference (95%CI)</i>				8.40 (7.58, 9.22)			
WS	TC <10000	Ishi et al 2015[151]	20	16.4	20	14.25	2.15 (0.44, 3.86)	2.6	13.1	
		Cadore-Rodriguez et al 2020[94]	20	28.15	20	19.69	8.46 (4.09, 12.83)	6.06	30.1	
		Rohr et al 2022[152]	24	11.75	24	1.75	10.00 (8.50, 11.50)	2.30	85.1	
WS	WS+TC <10000	Awad et al 2022[153]	16	19.33	16	7.48	11.85 (8.76, 14.94)	3.64	61.3	
		Yan et al 2021[154]	210	16.69	210	11.75	4.95 (4.55, 5.34)	1.85	29.6	
		<i>Pooled Mean Difference (95%CI)</i>				5.18 (4.81, 5.55)				
SA + OST	TC <10000	Darvizeh et al 2015[149]	18	29.1	18	25.3	3.80 (0.27, 7.33)	5.2	13.1	
		El-Wassefy 2021[155]	112	4.11	112	2.97	1.13 (0.92, 1.35)	0.84	27.5	
		Kang 2022[89]	40	18.98	40	12.00	6.98 (6.01, 7.94)	2.05	36.8	
No SA + NOST	TC <10000	<i>Pooled Mean Difference (95%CI)</i>				1.41 (1.20, 1.63)				
		Ahn et al 2020[150]	10	21.82	10	9.72	12.10 (8.70, 15.50)	0.75	55.5	
		Akazawa et al 2017[119]	22	18.35	22	15.55	2.80 (1.94, 3.66)	1.7	15.3	
WS	WS+TC <10000	Feitosa et al 2017[156]	15	27.8	15	11.09	16.71 (13.53, 19.89)	3.8	60.1	
		<i>Pooled Mean Difference (95%CI)</i>				3.74 (2.92, 4.57)				
		Yagawa et al 2018[120]	44	44.72	44	38.17	6.55 (5.14, 7.96)	3.17	14.6	
WS	WS+TC <10000	Rehholz-Zaribaf et al 2016[85]	45	14.1	45	8.63	5.47 (3.80, 7.13)	3.4	38.8	
		Mangione et al 2019[157]	10	6.9	10	2.3	4.60 (2.91, 6.29)	2.4	66.7	
		<i>Pooled Mean Difference (95%CI)</i>				5.67 (4.76, 6.57)				
WS	WS+TC <10000	Zhao et al 2016[143]	16	8.68	16	10.78	-2.10 (-2.64, -1.57)	0.9	-24.3*	
		Su et al 2021[116]	10	9.03	10	3.62	5.41 (3.93, 6.89)	1.74	59.9	
		Darvizeh et al 2015[149]	18	14.5	18	4.5	10.00 (8.21, 11.79)	3.2	69	
WS	WS+TC <10000	<i>Pooled Mean Difference (95%CI)</i>				-0.43 (-0.92, 0.05)				
		Pott et al 2016[123]	60	17.72	60	13.92	3.80 (2.08, 5.52)	5	21.4	
		Zhao et al 2022[124]	12	7.53	12	5.50	2.03 (1.60, 2.45)	0.47	26.9	
WS	WS+TC ≥10000	<i>Pooled Mean Difference (95%CI)</i>				1.92 (1.50, 2.33)				
		Noda et al 2017[125]	48	25.92	48	17.92	8.00 (5.96, 10.04)	4.2	30.9	
		Kim et al 2015[92]	60	31.97	60	19.43	12.53 (10.58, 14.49)	5.67	39.2	
WS	WS+TC ≥10000	Alegria Acevedo et al 2022[126]	60	29.97	60	13.97	16.00 (15.38, 16.62)	2.08	53.4	
		<i>Pooled Mean Difference (95%CI)</i>				11.56 (9.97, 13.17)				

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Table 2 (continued)

Non-MDP cement + non-MDP primer		Aging		Non-aging		Aging		Mean difference		% Change			
Surface treatment	Study	Total No	Mean	SD	Total No	Mean	SD	Total No	Mean	SD	(95% CI)		
No SA + OST	TC <10000 WS	10	5.7	1.4	10	0	0	10	0	0	5.7	100	
		10	14.39	2.23	10	9.56	1.88	10	9.56	1.88	4.83 (3.02, 6.64)	33.6	
	WS+TC <10000	54	28.47	3.63	54	23.17	4.43	54	23.17	4.43	5.30 (3.77, 6.83)	18.6	
		10	11.64	5.31	10	3.62	3.79	10	3.62	3.79	5.10 (3.94, 6.27)	68.9	
	WS+TC ≥10000	10	19.99	4.67	10	6.66	0.81	10	6.66	0.81	13.33 (10.39, 16.27)	66.7	
		20	9.8	3.9	20	0.3	0.4	20	0.3	0.4	9.50 (7.78, 11.22)	96.9	
	TSC + NOST	TC <10000 WS+TC ≥10000	30	22.55	7.49	30	15.1	5.38	30	15.1	5.38	10.18 (8.79, 11.58)	33
			40	29.09	5.89	40	23.17	4.91	40	23.17	4.91	7.45 (4.15, 10.75)	59.5
	TSC + OST	TC <10000 WS+TC <10000 WS+TC ≥10000	20	9.5	3.7	20	7.7	3.9	20	7.7	3.9	17.30 (16.29, 18.31)	18.9
			10	27.28	7.35	10	31.43	5.08	10	31.43	5.08	6.45 (4.52, 8.38)	-15.2*
MDP cement + no primer	Aging	10	25.80	4.60	10	24.20	3.40	10	24.20	3.40	1.80 (-0.56, 4.16)	6	
		15	8.2	2.2	15	10.4	4.9	15	10.4	4.9	1.60 (-1.02, 4.22)	-26.8*	
Surface treatment	Aging	15	29.7	9.4	15	16.4	9.4	15	16.4	9.4	-2.20 (-4.55, 0.15)	44.8	
		30	20.3	5.7	30	11.3	3.9	30	11.3	3.9	13.30 (6.57, 20.03)		
SA + NOST	TC <10000	60	15.18	2.4	60	8.33	1.71	60	8.33	1.71	Mean difference	% Change	
		185	38.16	5.06	185	34.92	6.8	185	34.92	6.8	(95% CI)		
TC ≥10000	Aging	240	13.18	2.87	240	9.72	2.79	240	9.72	2.79	6.85 (6.11, 7.60)	45.1	
		30	20.85	4.25	30	18.85	4.75	30	18.85	4.75	2.02 (4.46, 5.20)	5.3	
Surface treatment	Aging	9	26.26	1.33	9	25.22	1.38	9	25.22	1.38	3.56 (2.95, 3.96)	2.7	
		10	20.3	5.7	10	11.3	3.9	10	11.3	3.9	2.00 (-0.28, 4.28)	9.6	
SA + NOST	TC ≥10000	14	28.3	3.2	14	24.4	3.4	14	24.4	3.4	1.04 (-0.21, 2.29)	3.9	
		20	19.6	2.01	20	22.65	5.18	20	22.65	5.18	9.00 (4.72, 13.28)	44.3	
Surface treatment	Aging	60	13.73	1.06	60	12.11	1.12	60	12.11	1.12	4.07 (3.70, 4.44)	13.8	
		10	7.7	2.18	10	7.88	3.97	10	7.88	3.97	3.90 (1.45, 6.35)		
WS	Aging	20	20.12	4.64	20	6.28	1.35	20	6.28	1.35	-3.05 (-5.49, -0.61)	-15.6*	
		30	19.5	3.1	30	14.3	7.3	30	14.3	7.3	1.61 (1.22, 2.00)	11.7	
Surface treatment	Aging	28	28.3	3.2	28	19	5.05	28	19	5.05	-0.18 (-2.98, 2.63)	-2.3*	
		14	40.8	2.35	14	23.45	3.1	14	23.45	3.1	13.84 (11.72, 15.95)	68.8	
WS+TC <10000	Aging	10	14.30	5.5	10	22.10	2.20	10	22.10	2.20	1.90 (1.53, 2.27)		
		20	27.15	0.96	20	20.71	0.85	20	20.71	0.85	5.20 (2.36, 8.04)	27	
Surface treatment	Aging	10	5.5	1.1	10	0.06	0.04	10	0.06	0.04	9.30 (7.09, 11.51)	33	
		15	23.35	3.12	15	1.8	1.2	15	1.8	1.2	17.35 (15.31, 19.39)	43	
SA + OST	TC <1000 TC ≥1000 WS	30	8.75	2.07	30	5.64	0.76	30	5.64	0.76	-780 (-11.47, -4.13)	-54.5*	
		45	22.97	1.38	45	20.68	1.19	45	20.68	1.19	9.55 (8.30, 10.80)	23.7	
Surface treatment	Aging	10	20.47	6.2	10	5.13	1.21	10	5.13	1.21	6.44 (5.87, 7.00)	98.9	
		30	18.15	5.85	30	12.6	4.25	30	12.6	4.25	5.44 (4.76, 6.12)	92.3	
WS+TC <10000	Aging	30	19.26	4.28	30	3.08	0.7	30	3.08	0.7	21.55 (19.86, 23.24)	35.5	
		30	16.48	2.71	30	4.24	1.64	30	4.24	1.64	3.11 (2.32, 3.90)		
Surface treatment	Aging	30	16.48	2.71	30	4.24	1.64	30	4.24	1.64	6.14 (5.76, 6.51)	101	
		30	16.48	2.71	30	4.24	1.64	30	4.24	1.64	15.34 (11.42, 19.26)	74.9	
WS+TC <10000	Aging	30	19.26	4.28	30	3.08	0.7	30	3.08	0.7	5.55 (2.96, 8.14)	30.6	
		30	16.48	2.71	30	4.24	1.64	30	4.24	1.64	16.18 (14.63, 17.74)	84	
Surface treatment	Aging	30	16.48	2.71	30	4.24	1.64	30	4.24	1.64	13.38 (12.04, 14.70)		
		30	16.48	2.71	30	4.24	1.64	30	4.24	1.64	12.24 (11.11, 13.37)	74.3	

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Table 2 (continued)

Surface treatment	Non-MDP cement + non-MDP primer		Aging		Non-aging		Aging		Mean difference		% Change	
	Surface treatment	Study	Total No	Mean	SD	Total No	Mean	SD	Total No	Mean		SD
No SA + NOST	TC <10000	Gomes et al 2015[88]	15	6.8	3.4	15	1.5	2.6	5.30 (3.13, 7.47)	77.9		
		Lee et al 2015[142]	20	3.4	0.58	20	2.51	0.47	0.89 (0.56, 1.22)	26.2		
		Le et al 2018[158]	185	19.62	4.78	185	12.3	6.4	7.32 (6.17, 8.47)	37.3		
		Moon et al 2016[159]	10	6.7	1.95	10	3	1.12	3.70 (2.31, 5.09)	55.2		
		Rehholz-Zaribaf et al 2016[85]	15	5.7	1.7	15	9.7	3.4	-4.00 (-5.92, -2.08)	-70.2*		
		Pooled Mean Difference (95%CI)										
		Saade et al 2020[144]		14	10.4	7.2	14	6.2	3.1	4.20 (0.09, 8.31)	40.4	
		Pardo et al 2016[162]		10	5.97	0.41	10	6.11	1.77	-0.14 (-1.26, 0.99)	-2.3*	
		Pooled Mean Difference (95%CI)										
		Zhao et al 2016[143]		8	5.84	0.54	8	5.42	0.5	0.42 (-0.09, 0.93)	7.2	
WS		De Mendonca et al 2019[164]	30	11.5	3.8	30	7.35	2.65	4.15 (2.49, 5.81)	36.1		
		Negreiros et al 2021[168]	20	5.7	1.15	20	2.05	0.35	3.65 (3.12, 4.18)	64		
		Saade et al 2020[144]	28	10.4	7.2	28	1.4	1.8	9.00 (6.25, 11.75)	86.5		
		Pooled Mean Difference (95%CI)										
		Liu et al 2015[169]		10	3.87	1.17	10	3.81	1.07	0.06 (-0.92, 1.04)	1.6	
		Kwon et al 2020[160]		20	6.2	1.4	20	0.95	0.35	5.25 (4.62, 5.88)	84.7	
		Le et al 2018[158]		185	19.62	4.78	185	0.94	1.2	18.68 (17.97, 19.39)	95.2	
		Pooled Mean Difference (95%CI)										
		Gomes et al 2015[88]**		15	6.9	2	15	0	0	6.9	100	
		Le et al 2018[158]		185	23.04	5.46	185	16.74	7.44	6.30 (4.97, 7.63)	27.3	
WS+ TC ≥10000		Thammajaruk et al 2020[130]	15	27.0	5.2	15	29.1	6	-1.40 (-5.42, 2.62)	-5.1*		
		De Mendonca et al 2019[164]	30	11.3	4.25	30	7.4	4	3.90 (1.81, 5.99)	34.5		
		Negreiros et al 2021[168]	40	9.18	1.65	40	2.9	0.55	6.28 (5.74, 6.81)	68.4		
		Saade et al 2020[144]	56	30.95	4.05	56	20.17	6.45	10.78 (0.97, 4.39)	34.8		
		Pooled Mean Difference (95%CI)										
		Liu et al 2015[169]		90	4.96	1.4	90	4.67	1.24	0.29 (-0.10, 0.68)	5.8	
		Le et al 2018[158]		185	23.04	5.46	185	5.74	4.36	17.30 (16.29, 18.31)	75.1	
		Pooled Mean Difference (95%CI)										
		Re et al 2015[93]		40	16.55	1.82	40	8.29	1.23	8.26 (7.58, 8.93)	50	
		Gomes et al 2015[88]		15	15.8	4.8	15	15.3	5.8	0.50 (-3.31, 4.31)	3.2	
TSC + NOST		Pooled Mean Difference (95%CI)										
		Pardo et al 2016[162]		10	8.78	1.92	10	9.53	2.78	-0.75 (-2.84, 1.34)	8.5	
		Gomes et al 2015[88]		15	11.1	3.8	15	9.9	3.5	1.20 (-1.41, 3.81)	10.8	
		Pooled Mean Difference (95%CI)										
		Paschoalino et al 2019[170]		14	13.40	2.52	14	4.34	1.74	9.06 (7.46, 10.66)	67.6	
		Zaia et al 2016[171]		12	5.74	1.32	12	5.61	1.89	0.13 (-1.17, 1.43)	2.3	
		Cao et al 2022[172]		66	10.34	1.37	66	7.55	1.45	2.79 (2.30, 3.27)	26.9	
		Pooled Mean Difference (95%CI)										
		Paschoalino et al 2019[170]		28	14.15	2.58	28	4.18	1.20	9.97 (8.19, 11.02)	70.5	
		Zaia et al 2016[171]		12	6.55	2.27	12	7.7	1.82	-1.15 (-2.80, 0.50)	-17.6*	
No SA + NOST		Akazawa et al 2017[119]	11	20.5	4.3	11	12.6	2.4	7.90 (4.99, 10.81)	38.5		
		Rehholz-Zaribaf et al 2016[85]	15	10.3	4.8	15	14	4.9	-3.70 (-7.17, -0.23)	-35.9*		
		Hjerppe et al 2021[173]	10	21.8	4.2	10	7.4	5.4	14.40 (10.16, 18.64)	66.1		
		Paschoalino et al 2019[170]	7	10.5	1.42	7	1.86	0.3	8.64 (7.56, 9.72)	82.3		
		Pooled Mean Difference (95%CI)										
		Rehholz-Zaribaf et al 2016[85]		30	12.9	3.55	30	12.85	4.15	0.05 (-1.90, 2.00)	0.4	
		Hjerppe et al 2021[173]		10	22.5	4.2	10	5.9	4.1	16.60 (12.96, 20.24)	73.8	
		Pooled Mean Difference (95%CI)										
		Gomes et al 2015[88]		15	11.1	3.8	15	9.9	3.5	1.20 (-1.41, 3.81)	10.8	
		Pooled Mean Difference (95%CI)										

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Table 2 (continued)

Non-MDP cement + non-MDP primer		Study		Non-aging		Aging		Mean difference		% Change		
Surface treatment	Aging	Mean	SD	Total No	Mean	SD	Total No	Mean	SD	Mean difference (95% CI)	% Change	
MDP cement + MDP primer												
Surface treatment												
Aging												
SA + NOST	TC <10000	Salem et al 2019[146]	16.47	1.5	12	12.52	1.34	12	12.52	1.34	3.95 (2.81, 5.09)	24
		Elgendy et al 2020[147]	22.9	6.4	10	23.2	5.6	10	23.2	5.6	-0.30 (-5.57, 4.97)	-1.3 *
		Hyerpe et al 2021[173]	19.5	6.9	10	2.4	1.5	10	2.4	1.5	17.10 (12.72, 21.48)	87.7
	<i>Pooled Mean Difference (95%CI)</i>											
	TC ≥10000	Yoshida et al 2018[148]	24.3	1.9	8	23.7	2.6	8	23.7	2.6	0.60 (-1.63, 2.83)	2.5
		Negreiros et al 2017 [90]	39.5	2.7	14	21.3	1.55	14	21.3	1.55	18.20 (16.57, 19.83)	46
		Liu et al 2020[139]	24.35	1.45	10	13.84	1.02	10	13.84	1.02	10.51 (9.41, 11.61)	43.2
	WS+ TC <10000	Cheung et al 2015[165]	10.2	1.3	10	8.2	0.9	10	8.2	0.9	2.00 (1.02, 2.98)	19.6
		Alvim HC et al 2018[174]	16.1	6	10	9.73	4.75	10	9.73	4.75	6.37 (1.63,11.11)	39.6
		Ahn et al 2020 [150]	16.62	0.9	10	14.37	0.93	10	14.37	0.93	2.25 (1.45, 3.05)	13.5
	<i>Pooled Mean Difference (95%CI)</i>											
	SA + OST	WS	Cao et al 2022[172]	13.07	1.73	44	9.62	1.69	44	9.62	1.69	3.45 (2.73, 4.16)
Sanal et al 2020[141]			16.3	8.04	30	3.5	0.59	30	3.5	0.59	3.93 (3.50, 4.36)	78.6
Cheung et al 2015[165]			9.2	1.3	20	7	1.35	20	7	1.35	12.81 (9.92, 15.69)	23.9
<i>Pooled Mean Difference (95%CI)</i>												
No SA + NOST	TC <10000	Ahn et al 2020 [150]	12.89	2.34	10	9.39	2.33	10	9.39	2.33	3.50 (1.45, 5.55)	27.2
		Rehholz-Zaribaf et al 2016[85]	11.63	2.9	45	9.63	3.13	45	9.63	3.13	2.00 (0.75, 3.25)	17.2
		Mangione et al 2019 [157]	8.2	1.9	10	2.2	2.2	10	2.2	2.2	6.00 (4.20, 7.80)	73.2
<i>Pooled Mean Difference (95%CI)</i>												
No SA + OST	TC ≥10000	Liu et al 2015 [175]	16.8	2.4	24	1.9	1.1	24	1.9	1.1	14.90 (13.84, 15.96)	88.7
		Zhao et al 2016 [143]	5.73	0.74	8	11.36	0.61	8	11.36	0.61	-5.63 (-6.29, -4.97)	-98.3*
		Negreiros et al 2021 [168]	6.35	1.25	20	2.4	0.65	20	2.4	0.65	3.95 (3.333, 4.570)	62.2
No SA + OST	WS	Emamieh et al 2019 [176]	24.47	4.28	28	17.13	6.84	28	17.13	6.84	7.34 (4.35, 10.34)	30
		Monteiro 2022 [177]	15.67	4.53	90	9.50	3.87	90	9.50	3.87	6.17 (4.94, 7.40)	39.4
		<i>Pooled Mean Difference (95%CI)</i>										
No SA + OST	TC <1000	Mangione et al 2019 [157][130]	5.7	2.9	10	1.3	2.2	10	1.3	2.2	0.44 (0.02, 0.86)	77.2
		Liu et al 2015 [175]	22.2	3.43	72	10.87	2.01	72	10.87	2.01	11.33 (10.41, 12.25)	51.1
		Negreiros et al 2021[168]	10.77	1.98	40	5.05	0.77	40	5.05	0.77	5.72 (5.07, 6.38)	53.1
No SA + OST	WS+TC <10000	Cheung et al 2015[165]	10.9	1.65	20	8.5	1.9	20	8.5	1.9	2.40 (1.30, 3.50)	22
		Alvim et al 2018[174]	17.31	7.84	10	2.14	1.7	10	2.14	1.7	15.17 (10.20, 20.14)	87.6
		Ahn J et al 2020 [150]	12.62	3.82	10	4.14	0.61	10	4.14	0.61	8.48 (6.08, 10.88)	67.2
<i>Pooled Mean Difference (95%CI)</i>												
TSC + NOST	WS+TC ≥10000	Feitosa et al 2017[156]	22.55	7.49	30	15.1	5.38	30	15.1	5.38	7.45 (4.15, 10.75)	33
		Liu et al 2015[175]	25.1	2.7	24	11.9	1.9	24	11.9	1.9	13.20 (11.88, 14.52)	52.6
		Alvim HC et al 2018[174]	14.36	3.14	10	3.81	3.94	10	3.81	3.94	10.55 (7.43, 13.67)	73.5

*Negative values means that specimens in non-aging group have lower mean bond strength than those in the aging group.** study is excluded from the pooled mean difference.
NOST: No Other Surface Treatment; OST: Other Surface Treatment

Table 3
Mean difference (95% CI) and % change of bond strength before and after aging in studies included in the tensile test group.

Surface treatment	Non-aging			Aging			Mean difference (95% CI)	% Change	
	Study	Total No	SD	Study	Total No	SD			
SA + NOST	TC <10000	Elsayed et al 2017 [100]	16	6.65	14.85	16	4.30	9.50 (5.62, 13.38)	39.0
		Madrigal et al 2021 [107]	16	4.90	19.35	16	3.80	2.35 (-0.69, 5.39)	10.8
TC ≥10000	Pooled Mean Difference (95%CI)	Elsayed et al 2017 [100]	16	6.65	4.05	16	1.70	5.07 (2.68, 7.46)	83.4
		Wille et al 2017 [96]	8	0.80	14.10	8	2.40	20.30 (16.94, 23.66)	42.2
WS+ TC <10000	Pooled Mean Difference (95%CI)	Lenz et al 2017 [96]	30	6.30	21.60	30	1.66	0.40 (-2.90, 3.70)	1.8
		Lenz et al 2021 [114]	30	6.30	22.00	30	1.66	0.40 (-2.90, 3.70)	1.8
No SA+ NOST	TC <10000	Pooled Mean Difference (95%CI)	15	6.50	6.00	15	5.00	8.13 (6.58, 9.67)	41.7
		Rebholz-Zaribaf et al 2016 [85]	15	6.50	6.00	15	5.00	4.30 (0.15, 8.45)	41.7
TSC + NOST	WS+ TC ≥10000	Yoshida et al 2020 [103]	16	2.35	9.25	16	1.45	13.65 (12.29, 15.00)	59.6
		Thammajaruk et al 2018 [111]	20	15.68	80.56	20	17.12	4.54 (-5.63, 14.71)	5.3
WS+ TC ≥10000	Pooled Mean Difference (95%CI)	Rebholz-Zaribaf et al 2016 [85]	30	4.20	9.15	30	3.50	-0.35 (-2.31, 1.61)	-4.0*
		Thammajaruk et al 2018 [111]	20	15.68	70.45	20	19.85	-0.18 (-2.10, 1.75)	17.2
Non-MDP cement + no primer	WS	Lenz et al 2021 [114]	30	8.2	20.95	30	6.2	4.75 (1.07, 8.43)	18.5
		Ebeid 2018 [105]	8	3.70	15.70	8	5.40	7.40 (2.86, 11.94)	32
SA+ NOST	WS+ TC <10000	Abu Rujia et al 2019 [108]	5	2.28	17.87	5	1.66	3.27 (0.80, 5.74)	15.5
		Yoshida et al 2020 [103]	16	3.40	31.85	16	2.80	6.50 (4.34, 8.66)	16.9
No SA+ NOST	TC <10000	Passia et al 2016 [104]	16	6.80	18.60	16	6.35	13.65 (9.09, 18.21)	42.3
		Pooled Mean Difference (95%CI)	20	1.10	5.10	20	0.50	7.81 (5.86, 9.76)	70.7
WS+ TC <10000	Pooled Mean Difference (95%CI)	Sakrana et al 2017 [110]	20	1.80	5.00	20	2.75	12.30 (11.77, 12.83)	20.0
		Rebholz-Zaribaf et al 2016 [85]	30	1.80	5.00	30	2.75	1.25 (0.07, 2.43)	20.0
No SA+ OST	WS+ TC ≥10000	Abu Rujia et al 2019 [108]	15	2.75	23.07	15	1.65	10.44 (9.96, 10.92)	26.6
		Yoshida et al 2020 [103]	16	2.35	9.25	16	1.45	8.35 (6.73, 9.98)	59.6
TC ≥10000	Pooled Mean Difference (95%CI)	Sakrana et al 2017 [110]	40	1.30	38.75	40	0.95	13.65 (12.29, 15.00)	9.7
		Thammajaruk et al 2018 [111]	20	10.22	79.43	20	14.60	4.15 (3.65, 4.65)	8.9
Thammajaruk et al 2018 [111]	Pooled Mean Difference (95%CI)	Thammajaruk et al 2018 [111]	20	10.22	72.00	20	16.27	7.75 (-0.06, 15.56)	17.4
		Thammajaruk et al 2018 [111]	20	10.22	72.00	20	16.27	4.17 (3.67, 4.66)	17.4

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Table 3 (continued)

Surface treatment	Non-MDP cement + non-MDP primer				Study	Non-aging			Aging			Mean difference (95% CI)	% Change
	Aging	WS+ TC <10000	WS+ TC ≥10000	TC <10000		Total No	Mean	SD	Total No	Mean	SD		
TSC + NOST					Abu Rujia et al 2019 [108]	5	23.11	2.60	5	16.80	2.02	6.31 (3.42, 9.20)	27.3
Non-MDP cement + MDP primer Surface treatment													
SA + NOST					Study	Non-aging Total No	Mean	SD	Aging Total No	Mean	SD	Mean difference (95% CI)	% Change
					Elsayed et al 2017 [100]	24	44.07	8.07	24	40.90	10.57	3.17 (-2.15, 8.49)	7.2
					Sakrana et al 2017 [110]	20	43.70	1.70	20	38.50	1.20	5.20 (4.29, 6.11)	11.9
					Madrigal et al 2021 [107]	16	33.95	6.00	16	32.30	4.35	1.65 (-1.98, 5.28)	4.9
					Koko et al 2020 [101]	25	30.30	5.24	25	15.52	3.48	14.78 (12.31, 17.25)	48.8
					Pooled Mean Difference (95%CI)								
					Elsayed et al 2017 [100]	24	44.07	8.07	24	31.87	7.57	6.04 (5.21, 6.86)	22.7
					Ruales-Carrera et al 2019 [109]	60	18.63	4.74	60	17.58	4.95	1.04 (-0.70, 2.78)	5.6
					Pooled Mean Difference (95%CI)								
					Wille et al 2017 [96]	8	31.10	3.50	8	25.20	2.90	2.53 (0.91, 4.14)	19
					Passia et al 2016 [104]	16	38.50	6.30	16	19.30	3.45	19.20 (15.68, 22.72)	49.9
					Ebeid et al 2018 [105]	8	22.20	3.60	8	17.20	5.10	5.00 (0.67, 9.33)	22.5
					Pooled Mean Difference (95%CI)								
					Yoshida et al 2021 [97]	20	23.90	2.65	20	17.45	1.20	13.54 (10.81, 16.27)	27
					Reboliz-Zaribaf et al 2016 [85]	45	16.37	4.57	45	15.10	4.83	1.27 (-0.68, 3.21)	7.7
					Pooled Mean Difference (95%CI)								
					Ruales-Carrera et al 2019 [109]	54	7.93	4.61	56	5.01	2.96	4.89 (3.82, 5.96)	36.8
					Ebeid et al 2018 [105]**	8	12.7	2.2	8	0	0	2.91 (1.46, 4.37)	100
MDP cement + no primer Surface treatment													
SA+ NOST					Study	Non-aging Total No	Mean	SD	Aging Total No	Mean	SD	Mean difference (95% CI)	% Change
					Halliman et al 2016 [102]	16	38.85	6.25	16	35.30	10.25	3.55 (-2.33, 9.43)	9.1
					Al-Akhalil et al 2021 [106]	50	35.00	6.66	50	31.06	6.24	3.94 (1.41, 6.47)	11.3
					Pooled Mean Difference (95%CI)								
					Passia et al 2016 [104]	8	35.00	6.30	8	23.50	11.60	3.88 (1.56, 6.20)	32.9
					Sakrana et al 2020 [113]	30	25.10	6.00	30	19.17	3.87	11.50 (2.35, 20.65)	23.6
					Guers et al 2019 [98]	76	42.92	4.97	76	37.70	6.90	5.93 (3.38, 8.49)	12.2
					Pooled Mean Difference (95%CI)								
					Sakrana et al 2020 [113]	60	23.28	5.23	60	17.50	5.00	5.64 (4.13, 7.15)	24.8

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Table 3 (continued)

Non-MDP cement + non-MDP primer		Non-aging		Aging		Mean difference (95% CI)		% Change		
Surface treatment	Study	Total No	Mean	SD	Total No	Mean	SD	Mean difference (95% CI)	% Change	
No SA+ NOST	Rebholz-Zaribaf et al 2016 [85]	TC <10000	7.20	2.70	15	9.70	3.40	-2.50 (-4.70, -0.30)	-34.7*	
		TC ≥10000	24.55	7.60	16	10.75	6.35	13.80 (8.95, 18.65)	56.2	
		TC ≥10000	26.60	7.24	56	12.64	6.59	13.96 (11.39, 16.52)	52.5	
MDP cement + non-MDP primer	Study	Non-aging Total No	Mean	SD	Aging Total No	Mean	SD	Mean difference (95% CI)	% Change	
		80	10.81	2.22	8	2.52	1.00	8.29 (7.76, 8.82)	76.7	
		30	23.47	6.00	30	13.63	4.20	9.83 (7.21, 12.45)	41.9	
		60	24.25	4.40	60	19.52	4.65	4.73 (3.11, 6.35)	19.5	
		15	4.40	3.80	15	3.30	2.50	1.10 (-1.20, 3.40)	25	
		30	12.40	2.60	30	12.45	2.95	-0.05 (-1.46, 1.36)	-0.4*	
TSC + NOST	Ruales-Carrera et al 2019 [109]	TC ≥10000	13.26	4.74	60	15.06	3.98	-1.80 (-3.37, -0.23)	-13.2*	
		MDP cement + MDP primer								
		TC <10000	90.88	17.41	20	90.12	8.54	0.76 (-7.74, 9.26)	0.8	
SA + NOST	Thammajaruk et al 2019 [112]	TC <10000	90.88	17.41	20	80.29	23.37	10.59 (-2.18, 23.36)	11.7	
		TC ≥10000	16.27	3.50	80	10.12	2.66	6.15 (5.23, 7.07)	37.8	
		TC <10000	37.57	9.9	20	24.05	3.06	13.52 (8.98, 18.06)	36	
SA + OST	Thammajaruk et al 2019 [112]	TC ≥10000	37.57	9.9	20	13.43	7.93	24.14 (18.58, 29.70)	64.3	
		TC <10000	23.58	1.92	40	19.52	1.58	4.05 (3.28, 4.82)	17.2	
		TC <10000	13.03	3.10	45	12.33	3.40	0.70 (-0.64, 2.04)	5.4	
Rebholz-Zaribaf et al 2016 [85]		Pooled Mean Difference (95%CI)						3.22 (2.55, 3.89)		

*Negative values means that specimens in non-aging group have lower mean bond strength than those in the aging group. **study is excluded from the pooled mean difference NOST. No Other Surface Treatment, OST: Other Surface Treatment

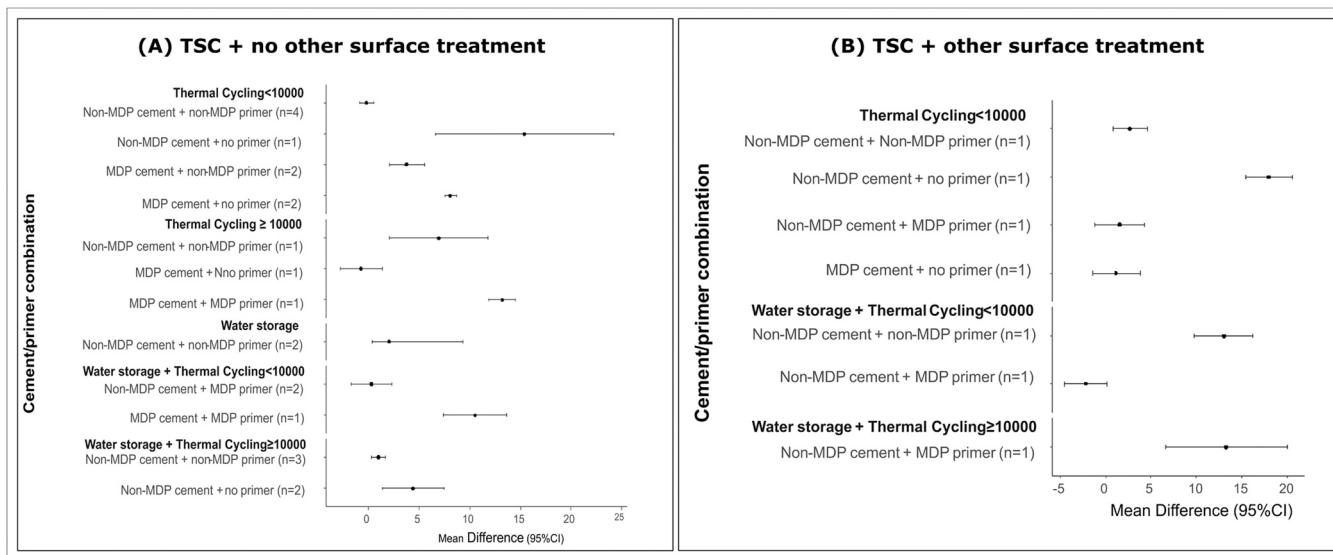


Fig. 3. Mean Difference of bond strength between control group and aging group from studies including shear tests for zirconia-resin bond strength evaluation. Classification was based on whether TSC was applied or not in combination with or without other surface treatments and studies were grouped based on different cement/primer combinations. Error bars represent the 95% confidence intervals of mean difference. (A) TSC + no other surface treatment, (B) TSC + other surface treatment.

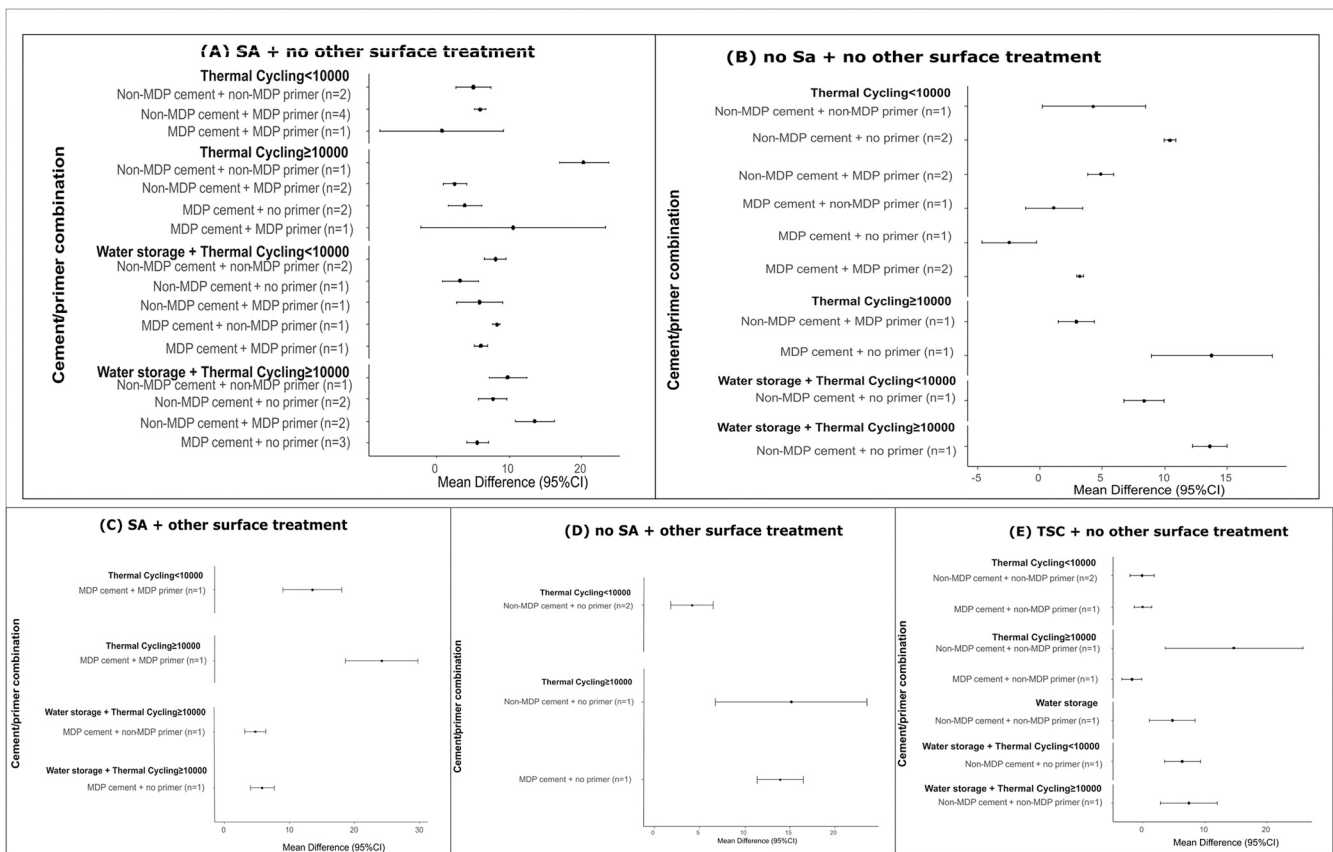


Fig. 4. Mean Difference of bond strength between control group and aging group from studies including tensile tests for zirconia-resin bond strength evaluation. Classification was based on whether SA or TSC was applied or not in combination with or without other surface treatments and studies were grouped based on different cement/primer combinations. Vertical line indicates no difference between the two groups. Error bars represent the 95% confidence intervals of mean difference. (A) SA + no other surface treatment, (B) SA + other surface treatment, (C) no SA + no other surface treatment, (D) no SA + other surface treatment, (E) TSC + no other surface treatment.

immersion in Zr/Si suspension and Zr/Si primer resulted in slightly lower decrease, one 33.6% [116] by the use of a porous silica-zirconia coating and another 18.6% [149] after in-situ nano-silica deposition and bioglass or alumina abrasion respectively. Regarding TSC, the limited number of studies and the variation among their results does not allow any conclusive result.

3.6. MDP cement+ No primer

When MDP cement was used alone without any primer and no SA was applied, the decrease of bond strength ranged from 1.6% to 100% in 19 out of 22 groups using shear test, where 3 [85,130,162] reported an increase after aging, while in the tensile group, two study groups presented a 56.2% and a 52.5% decrease respectively [82,102], and another [85] a 34.7% increase (Tables 2 and 3). When only SA was applied (SA+NOST), decrease of bond strength $\leq 45.1\%$ was observed in most of the studies in the shear group, and $\leq 32.9\%$ in all 5 studies in the tensile group, while 3 [163,165,166] studies in the shear group presented decrease ranging from 68.8% to 98.9% and 3 studies [137,138,162] an increase ranging from 2.3% to 54.5%. When SA was combined with other surface treatments, a bond strength decrease was observed ranging from 10.1 to 74.9 for both shear and tensile groups. The application of surface treatments other than SA or TSC, could not show a distinct trend, due to large variation in the included studies. When TSC was applied with no other surface treatment (TSC+NOST), 3 studies in the shear group [88,93,162] presented a low decrease (3.2–8.5%) and one study [93] a 50% decrease.

3.7. MDP cement + non-MDP primer

The combination MDP cement + non-MDP primer was investigated in a few studies conducting shear or tensile tests, with either SA or TSC pre-treatments alone, without being able to yield any conclusive result for the benefit of this specific combination, because a great variation was recorded among the different studies, irrespectively of the aging protocol applied (Tables 2 and 3).

3.8. MDP cement + MDP primer

Ten studies evaluated the combination of MDP cement + MDP primer by shear test, in zirconia specimens after SA and bond strength change varied from -1.3 – 87.7% (Table 2). Most studies presented a decrease up to 46%, one study [173] presented a decrease of 87.7% and another study that test a bioactive cement [147] demonstrated an increase of 1.3%. Low values of bond strength decrease were observed for SA in the study of Thammajaruk et al., 2019 [112] with tensile test (0.8% after TC < 10,000 cycles and 11.7% after TC ≥ 10000 cycles) (Table 3). When no SA was applied, great variation was observed in the mean bond strength percentage of change (-98.3 to 88.7%). This cement/primer combination was used with TSC pre-treatment in only 2 studies, showing decrease in bond strength from 52.6% [175] and 73.5% [174].

Regarding the application of OST, different results were observed whether they were combined or no with SA. In the shear sample groups in which an alternative surface treatment was performed alone, samples which were cemented with non-MDP cement and without MDP primer presented a tendency for low percentage of bond strength change (up to 23.7%) or even increase. These surface treatments included silica coating [127,131], silica-zirconia coating [116], in situ silica nanoparticle surface deposition [122], silica surface infiltration [128] and tribochemical glass-ceramic coating [129]. On the other hand, when SA was performed in combination with an alternative surface treatment, the bond strength change was higher when a non-MDP cement and a non-MDP primer were used [118,119] and when a non-MDP cement and no primer were use [119,140,141].

When MDP cement and MDP primer were used, samples did not present any significant difference whether the alternative surface treatment was combined with SA [119,141,150,156,165] or it was performed alone [150,156,157,165,168,174,175]. Data were not as favorable for specimens without SA that were cemented with a non-MDP cement and an MDP primer was used, as other surface treatments did not seem to result in a durable bond [91,128,150,157]. Thus, the combination of an alternative surface treatment with non MDP primers and cements seems to provide a more stable bond compared to the use of an MDP primer instead.

In general, the additional zirconia surface treatments were performed uniquely in the individual studies that utilized them, except for selective infiltration etching [144,165], Nd:YAG laser irradiation [166,169] and non-thermal plasma etching [150,168,174] which were utilized in different studies. Additional surface treatments included argon plasma with or without SA [164], ceramic glaze vitrification [156], CO₂ laser [166], immersion in Si/ Zr primer [149], use of a paste liner with or without HF [165] and silica-based epitaxial transition film formation [161]. Experimental silica coated aluminum oxide particles [94], Bioglass 45S5 particles abrasion [149], slurry coating with silica particles 6.5–8.1 mm (at pre-sintered phase) [175], coating with feldspathic ceramic powder and leucite glass ceramic powder of 45 μm [129], zirconia particle abrasion [102], alumina coating through aluminum nitride suspension [111] are some other surface modifications prior to bonding. Er,Cr:YSGG [144] and Er:YAG [88] laser irradiation etching were other laser treatments that were used. Also, TSC 110 μm [118,119,171] and HF [140,158,175] etching were performed additionally to SA. Other treatments included the immersion in different chemical solutions such as Si₃N₄ and Si₃N₄ -NaOH solution [127], 37% H₃PO₄ [125,157], piranha solution (H₂SO₄:H₂O₂ = 3:1) [102], CH₂Cl₂ and hot etching solution 37% HCl [110].

4. Discussion

Based on the correlations established from the present meta-analysis, the null hypothesis has been rejected as there were several statistical associations established between the surface pre-treatment, MDP content of the cement and primer used as well as the level of artificial aging. The study evaluated the mean bond strength change between resin cements and zirconia ceramics after thermal cycling, as derived from in vitro studies. It is important to estimate the bond strength change of zirconia ceramics to resin-based luting cements in water aging environments after the application of different adhesive protocols to verify their efficiency in bond durability. Immediate bond strength evaluation after cementation has limited clinical significance, as the intraoral conditions may lead to debonding of the restoration, if the bonding interface is not able to withstand its integrity in the wet oral environment. In the present review, all studies selected included at least one non-aged control group. Previous reviews have not rejected studies without non-aged control groups [3,6,179].

Studies that performed shear or tensile bond strength testing were considered for inclusion, as these testing methods are the most widely used for bond strength testing [180]. In addition, ISO (Dentistry – Polymer-based luting materials containing adhesive components, TECHNICAL SPECIFICATION ISO/TS 16506) declares that the standard deviation in that type of test is usually high, so we decided to include studies with at least 5 specimens per group to accommodate this issue. The main surface treatments evaluated, were SA and TSC coating since those pre-treatment methods present the highest amount of existing evidence of efficacy, while they are also mostly accessible to clinicians [181]. Other methods that have been evaluated in in vitro studies were classified as additional surface pre-treatments. In the included studies bonding procedures took place either by curing a resin cement cylinder on the zirconia surface, or

by cementing a metallic or composite rod on the zirconia surface with the use of a resin cement. Studies that bonded zirconia to human or animal dental tissues were excluded, since cohesive failures of dentin or enamel during bond strength testing have been reported [182].

The included studies in the present review were grouped according to the pre-treatment method applied and the artificial aging protocol. In most of the subgroups the number of the included studies did not lead to conclusive results according to descriptive statistics, due to the small number of studies applying the same protocols. However, the evaluation of pooled mean difference and percentage of change in values implicated a tendency for better results in groups where MDP-containing products were used, as well as TSC when compared to SA. Most of the other various applied pre-treatment methods, did not have a significant impact except the different methods that led to the development of a silica layer. This can be attributed to the greater resistance to hydrolysis of siloxane bonds formed between silanol groups of organo-silane and the developed silica layer on zirconia surface [122].

In the shear group, the use of an MDP cement combined with a non-MDP primer followed by surface pre-treatment with either SA or TSC (with no other surface treatment), led to a lower percentage of change in bond strength values after thermal cycling. In the group where no SA was applied, alternative surface treatments or MDP primer application or MDP cement bonding, yielded the lowest percentages of bond strength reduction. Similarly, low percentages of bond strength change were observed in the group where TSC was performed without further surface treatment but following the application of a non-MDP primer and eventually cemented with a non-MDP cement. Thus, it can be assumed that a simplified cementation method where no mechanical surface treatment is used, or alternatively TSC is performed solely, stable bond strength values may be achieved. This is partly in disagreement with the previous meta-analysis of Inokoshi et al. [183] who concluded that the combination of a mechanical surface treatment with chemical steps is of critical value. Nonetheless, the application of TSC prior to cementation with an MDP cement leads to a reduced percentage of change in the bond strength, according to the present study. This is in agreement with the meta-analysis by Thammajaruk et al. [6].

In the tensile group, where SA was performed followed by the application of an MDP primer and cementation with a non-MDP cement, a reduced percentage of bond strength reduction was observed compared to the respective group in which a non-MDP primer was used. The remaining groups of studies were of insufficient number and have not allowed similar observations as in the shear group. In a recent systematic review, Quigley et al. [181] suggested that SA combined with MDP cement should be in the first line of action for zirconia bonding. This is in agreement with the present study, as derived especially from tensile tests, where low percentages of change were observed in all studies (maximum 32.9% in one study) despite the intense and prolonged aging process (either $TC \geq 10000$ or $WS + TC \geq 10000$). In the tensile group, the bond strength appears to be more severely affected when aging protocol combines WS and TC, compared to TC solely. This should be taken into consideration since restorations have to adequately function in an aqueous milieu in the oral cavity.

Finally, it should be mentioned that in the present study the tensile and shear bond strength investigations were not divided into micro and macro types of testing as opposed to a recent meta-analysis and authors acknowledge that this remains one of the studies limitations [6]. There is insufficient literature clarifying which surface area may alter the testing type from micro to macro. It has been reported that a decreased bonding area reduces cement defects in the bonded interface and hence ensures a minimum number of pre-test bond failures and this may affect the results of a study depending on the bonded area [184]. Further classification based on

micro or macro testing method was abandoned because this would reduce the amount of data available for every individual variable studied, although this parameter could have an impact on the pooled results. In spite of the increased popularity of the “micro” bond strength tests and the criticism endured by the conventional tensile and shear methods, the number of articles using “macro” tests published in recent years remains high, meaning that a lot of the available data on dental adhesion still comes from mechanical tests performed in specimens with large bonded areas. As during chewing, all adhesive interfaces are subjected to both shear and tensile forces, all applied methods can be useful in predicting the bond strength of zirconia to resin.

Clinical studies establish one of the highest levels of scientific evidence. However, it is difficult or impossible to attribute a restoration's loss of retention solely to its adhesion protocol because other factors such as tooth preparation or chewing forces may significantly affect the restoration's resistance and retention as well as the magnitude of the forces that tend to displace the restoration [185,186]. The importance of a correct tooth preparation remains fundamental but with a rising predilection of clinicians for less destructive preparations and maximum hard tissue preservation, the importance of factors affecting restoration survival and success leans more towards the adhesive protocol [187,188].

Since zirconia is a polycrystalline material, the matter of adequate and durable bonding remains unsolved. During the conduction of the present systematic review many different studies were found in literature with regards to the most promising bonding protocol. Investigators have performed various innovative methods – such as piranha solution etching [156], laser pre-treatment [88,144,166,169], silica coating [122,128,131,139], ceramic glaze vitrification [156] – which reveals the ongoing wish of the dental community to answer this crucial scientific question. At the same time, most studies included an artificial aging protocol when testing ceramic materials. However, despite ISO guidelines (ISO 4049:2009, ISO 29022:2013), there is no established aging protocol, which leads to results that cannot be easily compared. In the present study, articles were subgrouped, in order to better analyze the results, in those performing an artificial aging protocol with less than 10,000 thermal cycles or with > 10000 cycles. Gale and Darvell [189] postulated that approximately 10,000 thermal cycles correspond to 1 year of clinical function, so 10,000 cycles can be a convenient threshold based on that. Furthermore, a lot of studies now use a higher number of cycles, and the 10,000 threshold helped to have good homogeneity of the groups. Additionally, control groups included water storage from 0 to 7 days. This selection was based on previous literature. According to the study of Blumer et al. [190], at least 1 day of water storage at 37 °C should be performed prior to TC of resin cements to allow adequate conversion rate and curing. In addition, according to Carek et al. [191], various resin cements present a significant degree of conversion during their first 7 days post-cure and this period seems to be critical to determine their flexural strength and modulus as these properties tend to increase during the first 28 days. Aguiar et al. [192], reported that resin cement micro-hardness increases during the first 7 days following curing, regardless of curing time and conditions. Finally, the classic articles by Mitchell et al. [193], and Knoblock et al. [194], use the 7-day period post-cure as a landmark for the determination of the mechanical properties of resin cements. Thus, in our study we opted to choose the 7-day period following curing of the cements as the baseline period, during which the cements are most likely to have achieved their full mechanical strength. Finally, the cut-off of 6 months was set as there is evidence from literature that after 6 months the hydrolytic stability of MDP-based primer is being significantly reduced [195,196]. Furthermore, alumina sandblasting and tribochemical silica coating remain the pre-treatment methods most widely applied. However, differences in particle size in both treatments may yield different

effects on the bond strength. Due to the limited number of studies it was not possible to compare these effects in the present review, suggesting one limitation. Similarly, the aging protocols applied in the included studies varied and involved only thermal cycling, without the effect of mastication loading. Additionally, different types of zirconia ceramics with different composition and crystalline phases, were used in the included studies, a factor that may have influenced bond strength and durability. Thus, the results of this investigation should be considered under those limitations. Power analysis was not performed for the individual studies that fulfilled the inclusion criteria. This parameter determines the statistical reliability of the included study itself, although the majority of the studies do not perform power analysis. Future systematic reviews and meta-analyses should consider this in their inclusion criteria for in-vitro studies.

The use of silane in zirconia bonding protocols that include a silicization step is fundamental, and not having taken it into consideration in a review dealing with this topic is a limitation. However, the following findings from the present study are clear and should be pointed out in this review. In the shear test group, Campos et al., 2016 [128] compared the use of Monobond Plus and Monobond S, on infiltrated specimens, and found that even though prior to aging Monobond Plus achieved higher bond strength values, following TC of 6000 both primers achieved similar bond strength levels. In the study of Akazawa et al., 2017 [119], a combination of MDP and silane provided the best adhesion values, while zirconia specimens that were submerged in a suspension containing zirconia and silica prior to sintering, presented over 30% higher bond strength values following WS when a silane primer was applied compared to when an MDP primer was applied. In the study of Dal Piva et al., 2019 [91], following TC, MDP primer combined with silane, achieved bond strength values that were at least 3.7 times higher compared to silane primer alone, when these were applied on TSC treated zirconia surface. On the contrary, in the tensile group, no studies were identified that could attribute any similar comparisons between MDP primers and silane primers on TSC treated surfaces.

Finally, studies evaluating the durability of bond strength are the most appropriate when determining the most successful protocol for clinical use. The percentages of bond strength change may be a useful method to compare the effect of aging on bond strength durability. An in-vitro study with a uniform methodology evaluating the different groups of bonding protocols, as they were classified in the present study, may enlighten the question of which bonding protocol offers the most durable bond strength.

5. Conclusions

Within the limitations of the included studies that were not equally distributed to different combinations of surface pre-treatments and cementation protocols, the following conclusions may be drawn: 1. When non-MDP cement and non-MDP primer are used, SA and TSC should be performed, while TSC seems to provide more durable bond compared with SA. 2. The use of MDP primer alone does not seem to provide a clear benefit on the bond durability from in vitro studies, but its combination with SA provides a lower decrease in bond strength after aging. 3. When MDP cement is used alone, a durable bond cannot be guaranteed, unless other surface treatments such as SA or TSC are applied. 4. There is no clear evidence of an additional benefit when combining an MDP cement with an MDP primer. 5. The combination of an MDP cement with TSC may yield more durable results after aging.

Conflict of interest

The authors have no conflicts of interests directly relevant to the content of this article.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jdsr.2023.04.002.

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