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Clinical effectiveness of direct resin composite restorations bonded using one-step or two-step self-etch adhesive systems: A three-year multicenter study

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The purpose of this multicenter clinical study was to compare the mid-term clinical effectiveness of direct resin composite restorations using one-step or two-step self-etch adhesives (1-SEAs or 2-SEAs). In total, 352 restorations of class I–V cavities and non-carious cervical lesions in vital teeth (1-SEAs; 52 cases, 2-SEAs; 300 cases) were placed at nine university hospitals and evaluated according to the modified USPHS criteria at baseline, and after 1, 2, and 3 years. The recall rates were 86.6% (1 year), 80.1% (2 years), and 62.2% (3 years). Two restorations failed due to fracture during the follow-up, and there was no significant difference in survival rates between 1-SEAs (97.6%) and 2-SEAs (99.4%). However, 2-SEAs exhibited significantly lower occurrences of discoloration, marginal discoloration, fracture, and plaque retention. Moreover, the subjects reported a significantly lower postoperative hypersensitivity and higher overall satisfaction at all evaluation periods if 2-SEAs were used.

Keywords: Multicenter clinical study, Direct resin composite restorations, Self-etch adhesive system, Adhesion

INTRODUCTION

Direct resin composite restorations (DCRs) bonded using advanced adhesive materials have been widely accepted as a conservative option for caries treatment under the minimal intervention dentistry concept[1]. Besides the esthetic appearance of DCRs, their principal advantage is that sound dental tissues can be preserved because retention is provided by adhesive systems. The development of adhesives also ensured a sufficient long-term clinical effectiveness of DCRs, although the results are not consistent. Meta-analyses of clinical studies by Heintze *et al*. reported 10-year success rates of 95% for class III cavities[2], 90% for class IV cavities including midline diastema closures[2], and 92% for class I and class II cavities[3]. On the other hand, a systematic review by Kubo showed that outcomes are affected by several factors and concluded that at least 60% of resin composite restorations would survive more than 10 years[4]. Another review article reported a wide range of survival rates (53.4%–100%) in anterior DCRs with a follow-up time of at least 3 years[5].

To achieve the longevity of DCRs, the application of reliable adhesives is indispensable. Three-step etch-and-rinse adhesives (3-ERAs) and two-step self-etch adhesives (2-SEAs) are considered a gold standard as their clinical effectiveness was proven to be excellent in NCCLs[6]. The more recent generations of adhesives with a simplified

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application procedure, *i.e.*, one-step self-etch adhesives (1-SEAs), which are designed to simultaneously etch, prime, and bond the dental substrates, are favored by many clinicians due to the simplified application. However, compared to the previous generations, they were proven to be excessively hydrophilic, making the adhesive layer more susceptible to the absorption of water from both the humid oral environment and the intrinsically moist dentin[7]. Consequently, the adhesive layer formed using 1-SEAs is more prone to hydrolytic degradation in laboratory studies[8,9], and the bond durability of 1-SEAs was reported to be lower than that of multi-step adhesive systems[10].

As for the clinical effectiveness of 1-SEAs, they were found inefficient in NCCLs by a meta-analysis of clinical trials in 2005[11]. However, the follow-up meta-analysis in 2014[12] revealed that this was true only for strongly acidic 1-SEAs (pH<1.5) and concluded that the performance of mildly acidic 1-SEAs was comparable to multi-step adhesives. Among more recent reports, there was no significant difference between the clinical performance of the 1-SEA All-Bond Universal (Bisco, Schaumberg, IL, USA) and the 2-SEA Optibond XTR (Kerr, Orange, CA, USA) in class II cavities after 3 years[13]. Two other trials that compared the clinical effectiveness of the 3-ERA Optibond FL (Kerr) in NCCLs to the 1-SEA G-Bond (GC, Tokyo, Japan) after 9 years[14] and to Clearfil S3 Bond (Kuraray Noritake Dental, Tokyo, Japan) after 2 years[15] concluded that there was no significant difference between them in retention rate, but revealed more marginal defects in restorations bonded using the 1-SEAs.

Nevertheless, there are many 1-SEAs available in the market, and the clinical evidence is still relatively scarce. Therefore, the Japan Society for Adhesive Dentistry started a multicenter clinical trial to investigate the effectiveness of DCRs in carious lesions and NCCLs. Multicenter studies' advantage is that a large sample size of diverse subjects can be acquired within a short time[16]. The purpose of this multicenter trial was to investigate the short-term and mid-term clinical performance of DCRs bonded using self-etch adhesive systems (1-SEAs or 2-SEAs) over three years. The null hypothesis tested was that there would be no significant difference between 1-SEAs and 2-SEAs in survival rate or any of the evaluated parameters after one, two, and three years.

MATERIALS AND METHODS

Study design/subject population

The ethical review board approved the clinical protocol of this project at each test center; Aichi Gakuin University (protocol No. 237), Nagasaki University (No. 1072), Nihon Dental University-School of Life Dentistry at Tokyo, and School of Life Dentistry at Niigata (No. NDU-T2010-43, ECNG-H-52), Nihon University (No. 2010), Osaka Dental University (No. 100716), Tohoku University (No. 22-10), Tokyo Medical and Dental University (No. 571), and Tsurumi University (No. 864). Patients visiting the test centers were invited to participate in the study if they fulfilled the inclusion criteria. The participants had to be between 20 and 65 years old, had a class I–V cavity or an NCCL in a vital tooth, and had to be physically and psychologically able to tolerate the DCR placement. The exclusion criteria included active periodontal or pulpal diseases, the use of a removable partial prosthesis, an ongoing orthodontic treatment, allergy to resin-based materials, pregnancy or nursing, and the absence of will to return for follow-up. Informed consent was obtained from each subject before the treatment.

The following data were registered for each subject: gender, age, and information about the frequency of tooth brushing, flossing, and snacking (Table 1). Then, a detailed clinical examination was performed by the operators, and the dental status was recorded. For every restoration, the following details were registered: the date of placement, tooth location, cavity type according to Black's classification of carious lesions, surface involved, margin location, information about antagonists and previous treatment of the tooth, if any (Table 2).

Clinical procedures

A total of 42 specialists in operative dentistry with more than five years of clinical experience participated in this study. The DCRs were placed at the nine centers mentioned above across Japan from September to December 2010. Cavities were opened using a high-speed air-turbine with a diamond bur, and carious tissues were removed using a low-speed micro-motor with round steel/stainless burs or spoon excavators. The operators were allowed to decide about using a rubber dam and a caries detecting dye solution. They also freely selected an adhesive system and a resin composite and used them according to manufacturers' instructions. The adhesives were applied without selective enamel etching. The resin composites were placed in increments less than 2 mm in thickness and light-cured using an LED or a halogen light-curing unit. The optional treatment procedures and their distribution in each group are listed in Table 3.

The evaluation of restorations

The evaluation was performed at baseline (1 month), after 1 year, 2 years, and 3 years according to the modified the United States Public Health Service (USPHS) criteria (Table 4). The following parameters were included: pulp vitality, retention, discoloration of restoration, marginal discoloration, fracture including marginal fracture, recurrence of caries, plaque retention (Silness-Löe Plaque Index), gum recession, postoperative hypersensitivity, and overall satisfaction of subjects such as food impaction, tongue feeling, and color match. The evaluation process was not blinded. Regular meetings of each university hospital's representatives were held to calibrate the evaluation methods by sharing clinical intraoral photographs. When a replacement or repair was necessary, the reasons and procedures were recorded.

The data obtained from the evaluation were

Table 1 Distribution of restorations according to the characteristics of the subjects in percentages

Characteristics		Subjects (*n*=352)	Restorations	
			1-SEA (*n*=52)	2-SEA (*n*=300)
Gender	Male	37.8 (101)	15.4 (8)	31.0 (93)
	Female	62.2 (251)	84.6 (44)	69.0 (207)
Age	20–29 years	21.9% (77)	21.2 (11)	22.0 (66)
	30–39 years	15.3% (54)	11.6 (6)	16.0 (48)
	40–49 years	18.2% (64)	21.2 (11)	17.7 (53)
	50–59 years	23.0% (81)	28.8 (15)	22.0 (66)
	<66 years	21.6% (76)	17.3 (9)	22.3 (67)
	mean	44.8±13.8	45.0±13.6	44.9±13.9
Tooth brushing per day	≥3 times	57.4 (202)	50.5 (26)	60.5 (176)
	2 times	39.8 (140)	44.6 (25)	36.9 (115)
	1 time	2.8 (10)	5.4 (1)	2.6 (9)
Daily flossing	Yes	59.1 (208)	50.0 (25)	61.8 (183)
	No	40.9 (144)	50.0 (27)	38.2 (117)
Frequency of snacking	Frequent	9.7 (34)	16.1 (8)	8.7 (26)
	Sometimes	63.0 (222)	51.8 (29)	64.3 (193)
	Seldom	25.0 (88)	30.4 (14)	24.7 (74)
	Never	2.3 (8)	1.8 (1)	2.3 (7)

Table 2 Distribution of restorations according to the characteristics of the lesions in percentage

Characterization of lesions		Percentages and number of lesions			
		1-SEAs (*n*=52)	2-SEAs (*n*=300)	Total (*n*=352)	
Tooth type	Maxillary incisor	28.8% (15)	22.3% (68)	23.6% (83)	
	Maxillary canine	3.8% (2)	10.7% (32)	10.0% (34)	51.1% (180)
	Maxillary posterior	26.9% (14)	16.3% (49)	17.9% (63)	
	Mandibular incisor	3.8% (2)	13.3% (40)	11.9% (42)	
	Mandibular canine	0% (0)	7.0% (21)	6.0% (21)	48.9% (172)
	Mandibular posterior	36.5% (19)	30.0% (90)	31.0% (109)	
Class	Class I	9.6% (5)	17.0% (51)	15.9% (56)	
	Class II	40.4% (21)	27.7% (83)	29.5% (104)	
	Class III	15.4% (8)	13.7% (41)	13.9% (49)	
	Class IV	3.8% (2)	6.0% (18)	5.7% (20)	
	Class V&NCCLs	30.8% (16)	35.7% (107)	34.9% (123)	
Margin	Enamel	13.5% (7)	39.0% (117)	35.2% (124)	
	Dentin	1.9% (1)	0.7% (2)	0.9% (3)	
	Enamel and dentin	84.6% (44)	60.3% (181)	63.9% (225)	
Antagonist	Natural tooth	82.7% (43)	93.0% (279)	91.5% (322)	
	Metal	0% (0)	4.7% (14)	4.0% (14)	
	Ceramics	0% (0)	1.0% (3)	0.9% (3)	
	Composite resin	5.8% (3)	1.0% (3)	1.7% (6)	
	Denture tooth	11.5% (6)	0.3% (1)	2.0% (7)	
Existing restorations	None	63.5% (33)	70.7% (212)	69.6% (245)	
	Composite resin	15.4% (8)	21.7% (65)	20.7% (73)	
	Metal inlay/onlay	15.4% (8)	4.0% (12)	5.7% (20)	
	Amalgam	0% (0)	3.0% (9)	2.6% (9)	
	Glass ionomer cement	5.8% (3)	0.7% (2)	1.4% (5)	

statistically analyzed using the chi-square test or the Fisher's exact test at a significance level of 0.05 for comparing grade A with the combined grades B, C, and D. The Kaplan-Meier statistical method was used to estimate the survival of restorations bonded with 1-SEAs or 2-SEAs. The groups were compared using the log-rank test at a significance level of 0.05. The analyses were performed in SPSS Statistics 22 (IBM, Chicago, IL, USA).

Table 3 The distributions of the optional treatment procedures

Treatment procedures	1-SEAs (n=52)	2-SEAs (n=300)	Total
Rubber dam isolation	51.9% (27)	22.7% (68)	27.0% (95)
Caries detector dye	59.6% (31)	46.3% (139)	48.6% (171)
Only flowable resin composite	34.6% (18)	28.0% (84)	29.0% (102)

Table 4 Modified USPHS criteria for the evaluation of restorations

Pulp vitality	A: Vital B: Non-vital
Retention	A: Retention is present B: Tiny fracture and partial loss of retention (can be polished) C: Loss of retention (should be replaced)
Discoloration	A: No discoloration evident B: Slight staining (can be polished away) C: Obvious staining, cannot be polished away (should be repaired or replaced)
Marginal discoloration	A: No discoloration evident B: Slight staining (can be polished away) C: Obvious staining, cannot be polished away (should be repaired or replaced)
Fracture	A: No fracture B: Minor crack or chipping C: Moderate or severe break-down (should be repaired or replaced)
Recurrence of caries	A: No evidence of caries continuous along the margin B: Minor change but can be observed C: Caries evident continuous with the margin of the restoration (should be repaired or replaced)
Plaque retention (Silness-Löe Plaque Index)	A: Absence of microbial plaque B: Thin film of microbial plaque along the free gingival margin C: Moderate accumulation with plaque in the sulcus D: Large amount of plaque in sulcus
Gum recession	A: No recession B: Slight recession C: Severe recession
Postoperative hypersensitivity	A: No symptoms B: Slight sensitivity C: Moderate or severe sensitivity (should be repaired or replaced)
Overall satisfaction	A: Very satisfied B: Satisfied C: Unsatisfied D: Very unsatisfied

RESULTS

In total, 352 restorations were placed in 226 subjects (59 males, 167 females; mean age 45.3±13.8 years) using 1-SEAs (52 cases) or 2-SEAs (300 cases) (Table 1). A similar number of restorations were placed in the maxilla (51.1%) and mandible (48.9%), but anterior restorations were prevailing in the maxilla, while more posterior restorations were placed in the mandible (Table 2). Class V cavities and NCCLs were most frequent (34.9%), followed by class II (29.5%) and class I (15.9%) (Table 2). All cavities had enamel margins except for three, whose margin was located entirely in dentin. In 30.4% of the cases, an existing restoration was replaced (Table 2).

The restorations were bonded using nine different self-etch adhesive systems —six 1-SEAs and three 2-SEAs (Table 5). As for the optional treatment procedures (Table 3), the operative field was isolated with a rubber dam in 27.0% of cases. A caries detector dye was used in 48.6% of cases. The operators who selected 1-SEAs used a rubber dam more often than those who chose 2-SEAs (Table 3). Twenty-nine percent of the cavities were restored only with the selected flowable composites.

The outcomes of the evaluation of the restorations are summarized in Table 6. The recall rates were 90.1% (1-SEAs) and 86.0% (2-SEAs) at 1 year, 96.2% (1-SEAs) and 77.3% (2-SEAs) at 2 years, and 80.8% (1-SEAs) and 59.0% (2-SEAs) at 3 year. The Kaplan-

Table 5 List of the adhesive systems and resin composites used in this study

Adhesive systems	pH	Compositions
One-step self-etch adhesive systems (1-SEAs)		
Adper Easy Bond (3M, St. Paul, MN, USA)	0.9	methacrylate phosphoric esters, Bis-GMA, HEMA, polyalcenoic acid, 1,6 hexanediol dimethacrylate, silica filler, CQ, stabilizers, water, ethanol
Adper Prompt L-Pop (3M)	0.9	methacrylate phosphoric esters, Bis-GMA, HEMA, polyalcenoic acid, CQ, stabilizers, water
BeautiBond (Shofu, Kyoto, Japan)	2.4	phosphoric acid monomer, carboxylic acid monomer, Bis-GMA, TEGDMA, water, acetone, initiator
Bond Force (Tokuyma Dental, Tokyo, Japan)	2.3	methacryloyloxyalkyl acid phosphate, HEMA, Bis-GMA, TEGDMA, glass filer, water, isopropyl alcohol, CQ
Clearfil Tri-S Bond (Kuraray Noritake Dental, Tokyo, Japan)	2.3	MDP, HEMA, Bis-GMA, silanated colloidal silica, water, ethanol,
G-Bond Plus (GC, Tokyo, Japan)	1.5	4-MET, phosphoric acid ester monomer, DMA, water, acetone, silica filler, photoinitiator
Two-step self-etch systems (2-SEAs)		
Clearfil SE Bond (Kuraray Noritake Dental)	2.1	Primer: MDP, HEMA, hydrophilic aliphatic dimethacrylate, water, dl-CQ, Bond: MDP, Bis-GMA, HEMA, Hydrophobic aliphatic dimethacrylate, dl-CQ, initiators, accelerators, silica
Clearfil Protect Bond (Kuraray Noritake Dental)	2.3	Primer: MDP, HEMA, MDPB, dimethacrylates, photoinitiator, water Bond: MDP, HEMA, dimethacrylates, photoinitiator, surface treated NaF, microfiller
Fluorobond II (Shofu)	2.3–2.4	Primer: ethanol, carboxylic acid monomer, phosphoric acid monomer, ethanol, initiator, water; Bond: S-PRG filler on fluoroboroaluminosilicate glass, UDMA, TEGDMA, HEMA, an initiator.
Resin composites	Flowable/Paste	Compositions
Beautifil (Shofu)	Paste	Bis-GMA, TEGDMA (6), aluminofluoro-borosilicate glass (75), Al_2O_3, PI
Beautifil Flow (Shofu)	Flowable	Bis-GMA, TEGDMA photoinitiator, fluoroboroaluminosilicate S-PRG
Clearfil AP-X (Kuraray Noritake Dental)	Paste	silanated barium glass filler, silanated silica filler, silanated colloidal silica
Estelite Sigma (Tokuyama Dental)	Paste	Bis-GMA, TEGDMA, Bis-MPEPP photoinitiator, silica–zirconia
Herculite XRV (Kerr, Orange, CA, USA)	Paste	Bis-GMA, UDMA, TEGDMA, barium glass filler, silica filler
MI Flow (GC, Japan)	Flowable	UDMA, Bis-MEPP, TEGDMA photoinitiator, silicon dioxide, strontium glass
Filtek Supreme Ultra Universal Restorative (3M)	Paste	Bis-GMA, UDMA, TEGDMA, PEGMA, Bis-EMA, zirconia, silica
Filtek Supreme Ultra Flowable Restorative (3M)	Flowable	Bis-GMA, TEGDMA, "Procrylat" resins, zirconia, ytterbium trifluoride

Abbreviations: MDP: 10-methacryloyloxydecyl dihydrogen phosphate, MDPB: methacryloyloxydodecylpyridinium bromide, HEMA: 2-hydroxyethyl methacrylate, 4-MET: 4-methacryloxyethyl trimellitic acid, CQ: camphorquinone, Bis-GMA: bisphenol A diglycidyl methacrylate, TEGDMA: triethyleneglycol dimethacrylate, UDMA: urethane dimethacrylate, Bis-EMA: ethoxylated bisphenol-A dimethacrylate, Bis-MPEPP: Bisphenol A bis(2-hydroxyethyl ether) dimethacrylate

Table 6 The outcomes of the evaluation of the restorations according to the modified USPHS criteria at baseline and recalls

Period		Baseline				1 year				2 years				3 years			
Recall rates	1-SEAs	100%				90.1%				96.2%				80.8%			
	2-SEAs	100%				86.0%				77.3%				59.0%			
Rating		A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D
Pulp vitality	1-SEAs	100 (52)	0% (0)	—	—	100% (47)	0% (0)	—	—	100% (50)	0% (0)	—	—	100% (42)	0% (0)	—	—
	2-SEAs	100 (300)	0% (0)	—	—	100% (258)	0% (0)	—	—	100% (232)	0% (0)	—	—	100% (177)	0% (0)	—	—
Retention	1-SEAs	100 (52)	0% (0)	0% (0)	—	100% (47)	0% (0)	0% (0)	—	100% (50)	0% (0)	0% (0)	—	100% (42)	0% (0)	0% (0)	—
	2-SEAs	100 (300)	0% (0)	0% (0)	—	100% (258)	0% (0)	0% (0)	—	99.1% (230)	0.9% (2)	0% (0)	—	99.4% (176)	0.6% (1)	0% (0)	—
Discoloration	1-SEAs	98.1% (51)	1.9% (1)	0% (0)	—	91.5% (43)	8.5% (4)	0% (0)	—	84.0% (42)	16.0% (8)	0% (0)	—	90.5% (38)	9.5% (4)	0% (0)	—
	2-SEAs	100 (300)	0% (0)	0% (0)	—	98.4% (254)	1.6% (4)	0% (0)	—	99.1% (230)	0.9% (2)	0% (0)	—	93.2% (165)	6.8% (12)	0% (0)	—
Marginal discoloration	1-SEAs	100 (52)	0% (0)	0% (0)	—	85.1% (40)	14.9% (7)	0% (0)	—	90.0% (45)	10.0% (5)	0% (0)	—	78.6% (33)	21.4% (9)	0% (0)	—
	2-SEAs	99.3% (298)	0.7% (2)	0% (0)	—	93.4% (241)	6.6% (17)	0% (0)	—	88.8% (215)	11.2% (17)	0% (0)	—	89.3% (158)	10.7% (19)	0% (0)	—
Fracture	1-SEAs	100 (52)	0% (0)	0% (0)	—	97.9% (46)	0% (0)	**2.1% (1)**	—	100% (50)	0% (0)	0% (0)	—	97.6% (41)	2.4% (1)	0% (0)	—
	2-SEAs	100 (300)	0% (0)	0% (0)	—	98.8% (255)	1.2% (3)	0% (0)	—	98.7% (229)	0.9% (2)	**0.4% (1)**	—	98.3% (174)	1.7% (3)	0% (0)	—
Secondary caries	1-SEAs	100 (52)	0% (0)	0% (0)	—	100% (47)	0% (0)	0% (0)	—	100% (50)	0% (0)	0% (0)	—	100% (42)	0% (0)	0% (0)	—
	2-SEAs	100 (300)	0% (0)	0% (0)	—	100 (258)	0% (0)	0% (0)	—	99.1% (230)	0.9% (2)	0% (0)	—	100% (177)	0% (0)	0% (0)	—
Plaque retention	1-SEAs	76.9% (40)	23.1% (12)	0% (0)	0% (0)	68.1% (32)	31.9% (15)	0% (0)	0% (0)	84.0% (42)	16.0% (8)	0% (0)	0% (0)	69.0% (29)	31.0% (13)	0% (0)	0% (0)
	2-SEAs	94.3% (283)	5.7% (17)	0% (0)	0% (0)	91.1% (235)	8.9% (23)	0% (0)	0% (0)	93.1% (216)	6.9% (16)	0% (0)	0% (0)	88.1% (156)	11.9% (21)	0% (0)	0% (0)
Gum recession	1-SEAs	100% (52)	0% (0)	0% (0)	—	100% (47)	0% (0)	0% (0)	—	100% (50)	0% (0)	0% (0)	—	97.6% (41)	2.4% (1)	0% (0)	—
	2-SEAs	100% (300)	0% (0)	0% (0)	—	98.1% (253)	1.9% (5)	0% (0)	—	99.6% (231)	0.4% (1)	0% (0)	—	100% (177)	0% (0)	0% (0)	—
Postoperative hypersensitivity	1-SEAs	92.3% (48)	7.7% (4)	0% (0)	—	85.1% (40)	14.9% (7)	0% (0)	—	96.0% (48)	4% (2)	0% (0)	—	95.2% (40)	4.8% (2)	0% (0)	—
	2-SEAs	99.3% (298)	0.7% (2)	0% (0)	—	99.2% (256)	0.8% (2)	0% (0)	—	99.6% (231)	0.4% (1)	0% (0)	—	99.4% (176)	0.6% (1)	0% (0)	—
Overall satisfaction	1-SEAs	38.5% (20)	59.6% (31)	1.9% (1)	0% (0)	38.3% (18)	61.7% (29)	0% (0)	0% (0)	16.0% (8)	84.0% (42)	0% (0)	0% (0)	23.8% (10)	76.2% (32)	0% (0)	0% (0)
	2-SEAs	85.3% (256)	14.7% (44)	0% (0)	0% (0)	77.5% (200)	22.5% (58)	0% (0)	0% (0)	80.6% (187)	19.4% (45)	0% (0)	0% (0)	84.2% (149)	15.8% (28)	0% (0)	0% (0)

Observations are in percent (the numbers of cases). The three restorations which failed due to fracture or severe discoloration (highlighted in bold) were intraorally repaired. The statistical analyses compared A with B, C, and D in total. The shaded cells represent groups that showed a significant difference between 1-SEAs and 2-SEAs ($p<0.05$).

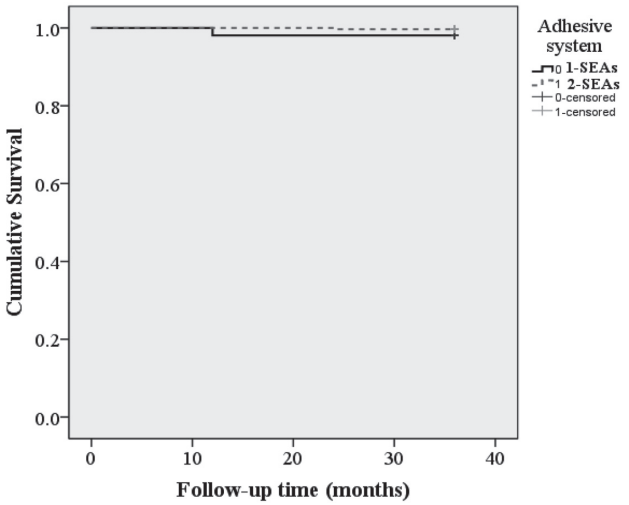

Fig. 1 The Kaplan-Meier survival curves.
One failure was observed in each group and the cumulative survival of restorations bonded with 1-SEAs (97.6%) was not significantly different from those bonded with 2-SEAs (99.4%).

Meier survival curves are presented in Fig 1. During the follow-up period, two restorations failed: restoration fractures were observed after 1 year in a class I cavity (1-SEA, BeautiBond, and Beautifil Flow Plus) and after 2 years in a class II cavity (2-SEA, Clearfil SE Bond, and Herculite XRV). Thus, the 3-year survival rates of 1-SEAs and 2-SEAs were 97.6% and 99.4%, respectively. The log-rank test revealed that there was no significant difference between 1-SEAs and 2-SEAs (p=0.157). 2-SEAs exhibited a significantly lower occurrence of discoloration, marginal discoloration, fracture (except after 2 years), and plaque retention. Among them, plaque retention was observed most commonly (3 years: 1-SEAs: 31.0%, 2-SEAs: 11.9%), followed by marginal discoloration (3 years: 1-SEA: 21.4%, 2-SEA: 10.2%) and the discoloration of the restorations (3 years: 1-SEA: 9.5%, 2-SEA: 6.8%). A correlation was found between these factors (plaque retention, marginal discoloration, and the discoloration of the restoration) in individual cases. Loss of vitality or retention was not observed in any case, as well as secondary caries. A slight gum recession was observed in a few cases. As for the parameters evaluated by the subjects, a significantly lower occurrence of postoperative hypersensitivity was observed with 2-SEAs at any evaluation periods, and the use of 2-SEAs also resulted in a significantly higher overall satisfaction compared to 1-SEAs throughout the evaluation period.

DISCUSSION

Due to the rapid development of resin composites and adhesive systems, materials are often quickly replaced by their successors. These rapid transitions make a thorough clinical evaluation of the materials very complicated. In this aspect, multicenter clinical research is a powerful tool because it enables a large sample size to be acquired within a short period. To our knowledge, there are few multicenter studies to investigate the clinical effectiveness of DCRs so far. Therefore, this project aimed at conducting a prospective multicenter clinical trial to evaluate the clinical effectiveness of DCRs using adhesives and resin composites, which were newly marketed or popular at the time the study began. Although some of them are no longer available, this study provides evidence for materials that have not been tested in previous clinical studies[2-5,12,17], such as BeautiBond, Bond Force, Beautifil, Beautifil Flow, Estelite Sigma, or MI Flow. Besides, this study covered a wide range of cavity types, including class III and IV, for which limited information about the clinical performance of DCRs bonded with self-etch adhesives is available. A mid-term clinical study may have limited relevance for the long-term durability of restorations but remains useful in excluding materials with deficient properties. Unfortunately, the recall rate was relatively low (62.2% in total after 3 years), which can be seen as a limitation of this study as well as subjects of the only university hospital, non-controlled isolation method, and non-blinded evaluation by operators themselves.

Only two failures were observed in this study, and the survival rate after 3 years did not change significantly from the baseline. There was also no significant difference in the 3-year survival rate between 1-SEAs and 2-SEAs. The present results corroborate the high success rates of a 2-SEA (100%)[18] and a 1-SEA (>90%)[19] after 3 years reported in previous studies and imply that the mid-term reliability of contemporary 1-SEAs is comparable to multi-step self-etch adhesive systems. Since high acidity has been previously reported to have a negative effect on the clinical performance of both 1-SEAs and 2-SEAs[12], the survival rate of 1-SEAs in this study may be higher than previously reported because the operators mostly chose the more recently developed mildly acidic 1-SEAs, although the strongly acidic Adper Easy Bond and Adper Prompt L-Pop were used in some cases as well. All 2-SEAs were mildly acidic, and the results with Clearfil SE Bond and Clearfil Protect Bond confirmed the excellent results reported in the systematic review[12]. However, there were significant differences between them in discoloration, marginal discoloration, fracture, plaque retention, hypersensitivity, and overall satisfaction between 1-SEAs and 2-SEAs. Therefore, the null hypothesis tested in this study was partially rejected.

As for postoperative hypersensitivity, its significantly higher occurrence was reported by the subjects throughout the evaluation period with 1-SEAs. This might be because the sealing ability of 2-SEA is generally better compared to 1-SEAs, as reported by a study using optical coherence tomography[20]. The subjects' overall satisfaction (including food impaction, color matching, and tongue feeling) was significantly higher with 2-SEAs from the baseline. This difference may be associated with difficult situations requiring rubber dam isolation

or limited chair time, leading the operators to choose 1-SEAs. We speculate that in such cases, less attention was paid to shade taking which may have resulted in shade mismatching, an occlusal adjustment which may have resulted in a fracture, finishing which may have resulted in marginal discoloration and plaque retention, or polishing which may have resulted in uncomfortable tongue feeling or discoloration.

Even though the simplification of restorative procedures has been one of the main goals of dental research and adhesives systems with fewer application steps have been gaining popularity, the specialists involved in this study selected 2-SEAs in 85.2% of cases, *i.e.*, approximately six times as often as 1-SEAs (14.8%). The tendency could be due to the limited available evidence regarding the longevity of the 1-SEAs compared to the well-proven 2-SEAs. Akimoto *et al*. reported a 100% 10-year success rate of DCRs for Class I-V cavities bonded with the 2-SEA Clearfil Liner Bond II[21], and Peumans *et al*. reported an 86% 13-year success rate of DCRs in NCCLs bonded with its successor, the 2-SEA Clearfil SE Bond[6]. 2-SEAs also exhibit higher bond strengths and durability in laboratory studies. In contrast, the performance of 1-SEAs might be compromised by their excessive hydrophilicity which makes them prone to hydrolytic degradation. Besides that, the adhesive layers of 1-SEAs are thinner compared to 2-SEAs, which increases their susceptibility to the inhibition of polymerization by oxygen and decreases their stress-absorbing ability[22]. Another factor that could contribute to the choice of 2-SEAs could be that dentists working at university hospitals in Japan are not under time pressure, so they do not tend to reduce the number of adhesive application steps. A survey conducted by the Japanese Association for Dental Sciences revealed that dentists working in hospitals spent more time on restorative treatments than dentists working in private clinics[23].

During the 3-year follow-up, two DCRs failed due to a fracture of the composite (1×1-SEA, 1×2-SEA), but they were successfully directly repaired using a resin composite. Reparability is one of the advantages of DCRs[24], and intra-oral repair is recommended instead of replacement for its minimal biological and financial cost[25,26]. There was no failure due to secondary caries in this study which contributed to the high survival rates. One of the factors could be that the restorations were placed under ideal conditions, *i.e.,* by specialists in operative dentistry in a university setting[27]. The specialists have a large experience with caries removal even without a caries detector dye. They are also familiar with the mechanisms of bonding to tooth substrates and used to the handling and application procedures of adhesive systems. Apart from that, subjects willing to join the study were probably highly motivated and in a low caries risk, which is known to affect the longevity of dental restorations positively[28]. The mean frequency of tooth brushing was 2.6 times/day, 59.1% of the subjects flossed daily, and most subjects ate only sometimes or seldom between meals.

Marginal discoloration increased over the follow-up period with both types of adhesives. Given their mild acidity, the demineralizing effect on enamel could be insufficient, compromising their adhesion to enamel[29,30] and increasing the susceptibility to discoloration. Additional selective enamel etching could prevent this with phosphoric acid, which was proved to effectively reduce marginal discoloration[6]. The discoloration of the restorations may be related to the chemical degradation of the resin composites, change of surface roughness by tooth brushing, and the subjects' eating and drinking habits. The discoloration was observed only in 1 restoration at baseline, but the incidence gradually increased over the follow-up period (1-SEAs; 9.5%, 2-SEAs; 6.8% at 3 years).

The overall success of DCRs can be affected by numerous factors. Some of them were examined in this study, but the number of failures was low, so a longer follow-up period would probably be necessary to observe their effect. It can only be concluded that rubber dam isolation did not affect the survival of DCRs, which agrees with some previous studies[31-33]. In this study, a rubber dam was only used in 27.0% of cases, while the others were isolated with cotton rolls and suction. This can also be attributed to the expertise of the specialists in operative dentistry. However, a rubber dam is certainly important in restorative treatments because it improves the treatment field's visualization through the retraction of soft tissues in the operating field, prevents contamination and accidental ingestion/aspiration of drugs and equipment, and protects soft tissues reduces mental stress of subjects, *etc.*[34] Among other factors, there is no doubt that restoration success is influenced by material, subject, and operator factors, especially for relatively technique sensitive DCRs[35].

CONCLUSIONS

The three-year multicenter clinical trial demonstrated the excellent mid-term clinical performance of DCRs bonded using self-etch adhesive systems. There were no significant differences between DCRs bonded with 1-SEAs and 2-SEAs in the survival rates. However, DCRs bonded with 2-SEAs outperformed those bonded with 1-SEAs in discoloration, marginal discoloration, fracture, plaque retention, postoperative hypersensitivity, and overall satisfaction. A further follow-up is necessary to determine long-term effectiveness.

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CONFLICT OF INTEREST

The authors received no financial support and declare no potential conflicts of interest for this article's authorship or publication.

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