Survival of different caries managements in children with autism and unaffected peers: a retrospective cohort study

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Abstract

Aim Dental caries is a common oral disease in children with special needs such as those with autism spectrum disorders (ASDs). The aim is to assess whether the type and survival of three caries management, conventional resin restorations (CR), ART technique (ART) and SDF application without caries removal (SDF), in primary teeth carried out at the Pediatric Dentistry Department of San Paolo Hospital (University of Milan) differed between children with ASDs and unaffected peers.

Methods Data from a convenience sample of children with and without ASDs, who have received dental care for caries in primary teeth from January 2019 to June 2022, were analysed. Medical history, age, sex, teeth treated, and type of treatment were collected from dental charts. Data on success and minor and major failures of each treatment were also collected. Two survival analysis were performed, one considering both major and minor failures, a second considering only major failures. Cox Proportional Hazards multivariate logistic models were run to assess factors associated with failures. The statistical significance was set at 5% ($p< 0.05$).

Results Overall, 233 conventional restorations, 136 ART restorations, and 78 SDF applications were analysed. A statistically significant difference was found in the prevalence of the three caries managements performed in the two cohorts of children ($p<0.01$); SDF was the most used in ASDs cohort (41.13%), while conventional treatment in unaffected cohort (52.13%). At 6-month follow-up, the success rate was found to be high (>86%) in both cohorts for all caries managements ($p>0.05$). At 12- and 18-month follow-ups, success rate of the three managements decreases, with no statistical differences between cohorts ($p>0.05$). In the cohort with ASDs, CR showing the higher number of successes ($p=0.02$ at 12 months; $p<0.01$ at 18 months). Considering major and minor failures together, treatment success was not associated with any of the variables considered in the ASDs cohort, while considering only major failures, treatment success was associated with caries severity ($p=0.01$).

Conclusion In children with autism, the different techniques for approaching caries lesions seem to have the same probability of success. Therefore, the choice of treatment should be patient-oriented rather than lesion-oriented. In unaffected children, the gold standard always seems to be traditional restorative treatment.

KEYWORDS Paediatric Dentistry, Public Health Dentistry, Dental Atraumatic Restorative Treatment, Silver Diamine Fluoride, Autism Spectrum Disorders.

Introduction

Dental caries in children is the most common oral disease worldwide, with significant negative effects on well-being [Campus et al., 2020; Pakkhesal et al., 2021]. It can cause pain, infection, difficulty eating or sleeping, and can disrupt school attendance. Children with caries may experience impaired weight gain and nutritional deficiencies [Ferrazzano et al., 2020b]. These problems are common in the general children population but even more prevalent in special needs patients [Desai et al., 2001; Purohit et al., 2010], in whom poor oral health can contribute to worsening their quality of life. However, these problems can be effectively managed through proper preventive strategies and dental treatments. Therefore, children at risk of caries or with caries lesions must have access to appropriate dental care [Kandiah et al., 2010].

Autism Spectrum Disorders (ASDs) are complex biological disorders that generally last for a person's entire life, characterized by challenges with social and communication impairments and by restricted and repetitive behaviours [American Psychiatric Association, 2013]. Although ASDs, does not have a direct effect on oral health, it is often associated with severe difficulties in performing oral hygiene procedures at home and preventive/therapeutic procedures at the dental chair, exposing affected individuals to an increased risk of oral diseases and dental caries in particular [Bagattoni et al., 2021]. Cavitated caries lesions are traditionally managed through the complete removal of decayed tissues and the placement of a composite resin restoration, even if in children, and in those with ASDs especially, it may be difficult to ensure optimal bonding conditions due to their poor cooperation [Melgar et al., 2017]. In recent years there has been a change in the way cavities, especially in primary teeth, are managed [Pitts et al., 2021] and conventional methods have been challenged by non/minimally invasive, as

the use of the Er:YAG Laser and the Hall technique, or biological approaches, which focus on modifying the biofilm to arrest cavity progression [Chua et al., 2023; Ricketts et al., 2013; Valenti et al., 2021]. Among the minimally invasive approaches, Atraumatic Restorative Treatment (ART) is an extensively studied technique which provides alternative restorative materials and less invasive intervention strategy [Holmgren and Frencken, 2009]. ART has demonstrated an ease of use compared to the traditional method, being less painful, and cost-effective, with similar success rate [Gao et al., 2003]. Glass Ionomer Cements (GICs), especially high-viscosity cements (HVGIC), are the restoration materials used for the ART concept. GICs are biocompatible, bioactive, release fluoride, and share similar thermal expansion and elasticity properties as dental tissues [Hahnel et al., 2017; Mustafa et al., 2020]. Furthermore, GICs have unique characteristics in that they bond directly to the dental tissue, becoming a true adhesive dental material. All these qualities make GICs particularly suitable for paediatric dental care, especially for younger or poorly cooperating children. Silver Diamine Fluoride (SDF) has been shown to be an effective biomedical approach to caries lesions as it impacts both the microbiota and hard tissues [Chibinski et al., 2017; Splieth et al., 2020]. SDF promotes enamel and dentin remineralization, reduces bacteria in the biofilm, and prevents collagen degradation, thus arresting cavity progression [Gao et al., 2021]. Applied at a concentration of 38% on cavitated primary teeth, SDF has shown comparable efficacy to GICs restorations, proving more effective than both no treatment and fluoride varnish in arresting lesion progression [Zaffarano et al., 2022]. Moreover, its ease of use in community settings is frequently reported, with a survival rate of treated teeth exceeding 75% [Raskin et al., 2021]. Non-invasive and minimally invasive caries approaches are low-cost, effective, and simple methods and can contribute to reducing fear and anxiety, particularly in special needs children, making them suitable and effective treatments for dental caries management.

The primary aim of the present retrospective cohort study is to assess whether the type and survival of three different caries managements, conventional resin restorations, ART and SDF, in primary teeth carried out at the Pediatric Dentistry Department of San Paolo Hospital (University of Milan) differed between children with ASDs and unaffected peers. The null hypothesis tested is that there is no difference in the 12- and 18-month survivals of the three caries management strategies in children with ASDs and unaffected peers. The secondary objective is to compare the survival of the three caries management strategies regardless of the patient's underlying disease. Demographic and clinical characteristics of patients recorded at the first dental visit were also investigated as potential protective and/or risk factors for treatment failure.

Materials and Methods

Ethics

A retrospective cohort study was designed and approved by the Ethics committee Board of San Paolo Hospital, Milan, Italy approval number 546/2021. The study is a human observational study and as such conformed to STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) guidelines. The ethical principles stated in the Declaration of Helsinki were followed.

Study design

A retrospective cohort study was planned and carried out. The study involved a convenience sample of children with and without ASDs who have received dental care for caries in primary teeth at the Pediatric Dentistry Department of San Paolo Hospital (University of Milan) from January 2019 to June 2022. The primary outcome of the study was to assess whether the type and survival of three different caries managements, conventional restoration (CR), ART and SDF, differed between children with ASDs and unaffected peers. A secondary aim was to compare the survival rates of the three caries management techniques regardless of the patient's underlying disease. Inclusion criteria were children between the ages of 6 and 12 years with 1 or more proximal cavitated carious lesion in primary teeth with a score of 4 or 5 according to the International Caries Detection and Assessment System (ICDAS) [Ismail et al., 2007] treated with one of the three caries managements reported above, and a follow-up period of at least 12 months. The exclusion criteria were incomplete clinical records, treatments with less than 12-months of follow-up, dental care provided under sedation or general anaesthesia, and dental treatments carried out on children with systemic disorders beyond ASDs.

To obtain this sample, treatments performed until June 2022 were included so there was at least 12 months of follow-up. For treatments performed from January 2019 to June 2022, the treatment status was recorded until July 2023, when the data were analysed.

In order to comply with the Data Protection Act and to ensure patient anonymity, personal details, including hospital ID number, name, address and date of birth were not recorded. To each chart was assigned an unique identifier associated with a letter (A or B) to divide the patients into the two cohorts, patients with or without ASDs. A separate 'code sheet' was kept as a key, which links each unique identifier to the patients' hospital number held by one of the authors (M.A.), who is an hospital doctor and did not participate in data analysis. Without this list, data collection forms cannot be linked to specific patients. The key was destroyed when the analysis was complete. Data on medical history (any systemic diseases and presence of physical/psychological disabilities), age, sex, the tooth/teeth treated, and the type of treatment used (CR, ART or SDF) were collected. Finally, data on the possible failure of the treatment was also collected. For ART and CR, any partial or total loss of the restoration and the presence of secondary caries was considered a minor failure, whereas for the application of SDF, the enlargement of the lesion (assessed through the ICDAS classification) or the implementation of another management strategy (ART or CR) was considered a minor failure. For all caries management considered, the appearance of pulpal inflammatory signs, leading to tooth extraction or endodontic therapy, was considered a major failure [Santamaria et al., 2014]. All data collected, anamnestic, demographic, and treatment-related, were entered into an Excel spreadsheet (Microsoft® Excel 2023, Microsoft® Corp, Redmond, WA, USA) according to subject identification code.

Caries Management

According to San Paolo Hospital protocol, all children/parents/caregivers received oral hygiene instructions and dietary recommendations during the admission visit. A toothpaste with at least 1000 ppm of fluoride was also recommended. All dental procedures, including the first dental visit, caries treatment, and follow-ups, were performed by at least two post-graduate students in Pediatric Dentistry, with

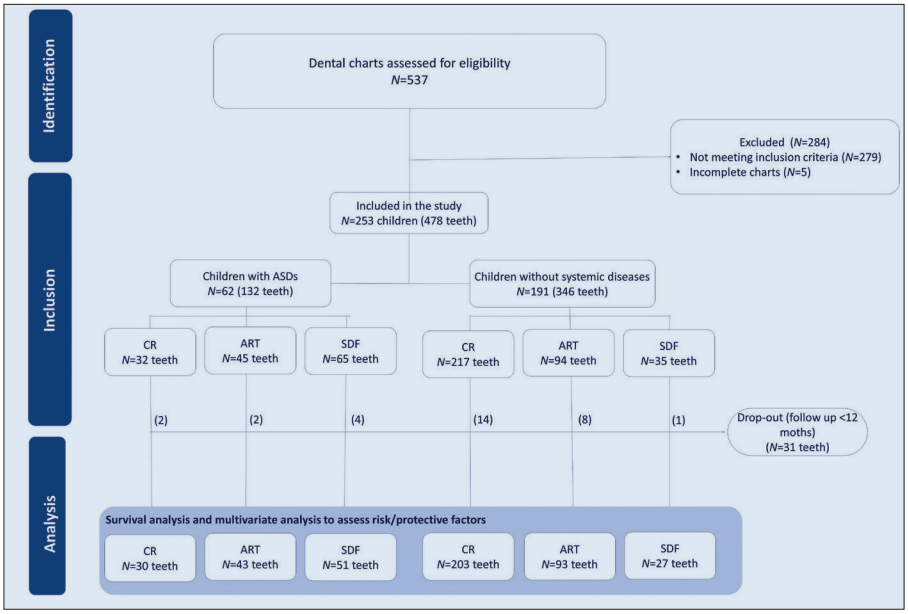

FIG. 1
Study flow-chart according to STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement.

at least one-year of training in children.

Conventional Restorations (CR)

The recommended protocol in the Pediatric Dental Department includes, after local anaesthesia, opening the cavity with a high-speed handpiece and diamond bur and removing the infected and affected dentine using a slow handpiece and/or an excavator. Automatrix (Dentsply Sirona, Charlotte, NC, USA) and a wedge (Interdental Wedge, Kerr, Biogglo, Switzerland) are used, and a restoration with composite resin (Filtek Z250, 3M, ESPE, USA) is realized under cotton roll isolation and continuous aspiration or rubber dam [Santamaria et al., 2014].

ART

The treatment includes caries removal using small (EXC153/4), medium (EXC131/2), and larger (EXC129/0) size spoon excavators corresponding to sizes 1, 1.4, and 1.7 mm, respectively (Hu-Friedy Mfg. Co., LLC, Chicago, Illinois, United States). If an enamel roof is present, the 14/14 off-angle axe (CP14/14), also from (Hu-Friedy Mfg. Co., LLC, Chicago, Illinois, USA), is used to widen the opening to accommodate the excavator for proper removal of the carious tissue. Selective removal of carious dentine tissue is applied, and the cavity is restored with GC Fuji IX ART (GC Corporation, Tokyo, Japan). No local anaesthesia is usually performed.

SDF

SDF protocol provides for the opening of the caries lesion, if it is partially closed, with a high-speed bur to remove overhanging enamel, making the lesion accessible for plaque removal. No carious dentine is removed from the pulpal wall, and no local anaesthesia is placed. Silver Diamine Fluoride (Riva Star, SDI Limited, Australia) is applied to the cavity according to product instructions. A second application is performed one month after the first.

Data collection and statistical analysis

The following data recorded at the first dental visit were retrieved from the dental charts and imputed into a Microsoft Excel® 2023 spreadsheet (Microsoft Corporation, Washington, USA): sex, age, number of primary and permanent teeth affected by caries, and presence of systemic diseases. Location of the affected tooth (upper-anterior, upper-posterior, lower-anterior and lower-posterior), type and date of caries management undergone, and presence of minor or major failures during the follow-up period were also collected. If a failure event was recorded, the follow-up period was interrupted and no subsequent change of status from minor to major failure was recorded.

Means, standard deviations and skewness were calculated for continuous variables. Survival was analysed at 6-, 12- and 18-months; the overall survival summarized results from the entire observation period, including all teeth with at least 12 months of observation. Two types of survival analysis were performed, the first considering both major and minor failures as a "failure event" and the second considering only major failures as a "failure event". The Kaplan–Meier estimator was endorsed to estimate the survival fraction of teeth during the follow-up period for the two cohorts according to the three caries managements, and the log-rank test compared the survival curves. Cox Proportional Hazards multivariate logistic models were run to assess factors associated with failures in the two cohorts examined. Estimates are reported in the hazard ratio (HR) and their respective 95% confidence interval (95%CI). Statistical analysis was performed using STATA/BE® 18.0 for MAC (Statacorp, USA). For all statistical analyses, the statistical significance was set at 5% ($p< 0.05$).

Results

Overall, the dental charts of 537 children who received dental treatment for caries in primary teeth at the Pediatric Dental Department of San Paolo Hospital from January 2019 to June 2022 were evaluated, and 253 were considered eligible for this retrospective cohort study, 62 from children with ASDs and 191 from unaffected peers. A total of 478 treatments were retrieved, of which 132 were performed in children with ASDs and 346 in unaffected children. As the follow-up period of 31 treatments was shorter than 12 months, these treatments were excluded, and data analysis was performed on 447 treatments, of which 124 were carried out in children with ASDs and 323 in unaffected peers (Fig.

		ASDs	Unaffected	p	Total sample
Children variables		*(N=62)*	*(N=191)*		*(N=253)*
Sex	N (%)				
Female		17 (27.42)	76 (39.79)	0.11	93 (37.15)
Male		45 (72.58)	115 (60.21)		160 (63.24)
Age	Mean (SD)	7.59 (1.06)	8.02 (1.33)	0.06	7.89 (1.29)
	Median	7.16	7.85		7.63
	Range	6.07 - 9.85	6.04 - 11.88		6.04-11.88
	95% CI	[7.28-7.85]	[7.79-8.23]		[7.71-8.07]
N of caries teeth	Mean (SD)	1.95 (1.32)	1.69 (1.04)	0.31	1.75 (1.12)
	Median	1.00	1.00		1.00
	Range	1.00 - 6.00	1.00 - 7.00		1.00-7.00
	95% CI	[1.62-2.28]	[1.54-1.82]		[1.62-1.89]
Teeth variables		*(N=124)*	*(N=323)*		*(N=447)*
Tooth position	N (%)				
Upper anterior		6 (4.84)	7 (2.17)	0.38	13 (2.91)
Upper posterior		63 (50.81)	172 (53.25)		235 (52.57)
Lower anterior		2 (1.61)	3 (0.93)		5 (1.12)
Lower posterior		53 (42.74)	141 (43.65)		194 (43.40)
Treatment					
CR		30 (24.19)	203 (62.85)	<0.01	233 (52.13)
ART		43 (34.68)	93 (28.79)		136 (30.43)
SDF		51 (41.13)	27 (8.36)		78 (17.45)

ASDs: Autism Spectrum Disorders; N: number; SD: Standard Deviation; CI: Confidence Interval; CR: Composite Restoration; ART: Atraumatic Restoration Treatment; SDF: Silver Diamine Fluoride.

TABLE 1 Characteristics of the sample examined.

1). The included caries managements were 233 conventional restorations, 136 ART restorations, and 78 SDF applications.

The mean age of the children considered in this retrospective cohort study was 7.89±1.29, with no difference between cohorts (p<0.05); the majority were male in both cohorts (ASDs=72.58%, Unaffected=60.20%). The mean number of caries teeth per subject was 1.75±1.12, ranging from 1 to 7 lesions with no difference between the two cohorts (p>0.05). Most treated teeth were in the upper posterior (43.40%) and lower posterior (52.57%) areas, with no difference between the two cohorts (p>0.05). A statistically significant difference was found in the prevalence of the three caries managements performed in the two cohorts of children (p<0.01). In the cohort with ASDs, the application of SDF was the most used caries management (41.13%), while among the unaffected children, conventional treatment was the most applied (62.85%) (Table 1).

For treatments performed from January 2019 to June 2022, the survival was recorded until data analysis, thus ranging from 0 to 50 months (Table 2, Table 3).

Teeth location did not differ between the two cohorts for each caries management considered (p>0.05) (Table 2). At 6-month follow-up, the success rate was found to be high (>86%) in both cohorts for all caries managements, with no difference when comparing the number of successes and major/minor failures (p>0.05). At 12- and 18-month follow-ups, success rate of the three managements decreased, especially for ART and SDF, but no difference between the two cohorts was observed (p>0.05) (Table 2). In the cohort with ASDs, the success rate was found to be high (>76%) for all caries managements at 6- and 12-month follow-ups, decreasing at 18 months, with CR showing a higher number of successes compared to the other two types of caries managements (p=0.02 at 12 months; p<0.01 at 18 months) (Table 3). In the Unaffected cohort, the success rate was found to be high for all caries managements at 6- and 12-month follow-ups (>80%), decreasing at 18-month follow-up with CR showing a higher number of successes (p=0.02 at 12 months and 18 months). Considering the overall success rate of the three managements in the total sample, it decreases at the 18-month follow-up from the previous evaluations; the worst performance was registered for teeth treated with SDF (success=55.00%), and a significant difference between managements was found (p<0.01) with CR resulting in the most successful treatment (Table 3). The overall successes, considering the entire follow-up period, are more optimistic than those recorded at 18 months as they also include teeth classified as successes with an observation period ranging from 12 to 17 months.

When considering both major and minor failures as a "failure event", no statistically significant difference was found in the survival rate of the three caries managements during the follow-up period in both cohorts (Figure 2a). When considering only major failures as a "failure event" (Figure

	ASDs	Unaffected		ASDs	Unaffected		ASDs	Unaffected	
	(N=30)	(N=203)		(N=43)	(N=93)		(N=51)	(N=27)	
Variable	N (%)		p	N (%)		p	N (%)		*p*
Tooth location	**CR** *(N=233)*			**ART** *(N=136)*			**SDF** *(N=78)*		
Upper posterior	16 (53.33)	94 (46.31)	0.05	10 (23.26)	39 (41.94)	0.06	27 (52.94)	8 (29.63)	0.11
Upper anterior	3 (10.0)	3 (1.48)		2 (4.65)	3 (3.23)		1 (1.96)	1 (3.70)	
Lower anterior	0 (0.0)	3 (1.48)		1 (2.33)	0 (0.00)		1 (1.96)	0 (0.00)	
Lower posterior	11 (36.67)	103 (50.74)		30 (69.77)	51 (54.84)		22 (43.14)	18 (66.67)	
Survival at 6-mo.									
Major failure	1 (3.33)	2 (0.99)	0.49	3 (6.98)	1 (1.08)	0.19	6 (11.76)	2 (7.41)	0.71
Minor failure	2 (6.67)	13 (6.40)		3 (6.98)	9 (9.68)		-	-	
Success	27 (90.00)	188 (92.61)		37 (86.05)	83 (89.25)		45 (88.24)	25 (92.59)	
Survival at 12-mo.									
Major failure	2 (6.67)	5 (2.46)	0.24	4 (9.3)	6 (6.45)	0.82	11 (21.57)	3 (11.11)	0.36
Minor failure	3 (10.00)	15 (7.39)		6 (13.95)	12 (12.90)		-	-	
Success	25 (83.33)	183 (90.15)		33 (76.74)	75 (80.65)		40 (78.43)	24 (88.89)	
Survival at 18-mo.	**CR** *(N=160)*			**ART** *(N=95)*			**SDF** *(N=40)*		
Major failure	2 (7.69)	8 (5.97)	0.78	5 (15.15)	7 (11.29)	0.86	12 (54.55)	5 (27.78)	0.14
Minor failure	4 (15.38)	19 (14.18)		7 (21.21)	14 (22.58)		0 (0.00)	1 (5.56)	
Success	20 (76.92)	107 (79.85)		21 (63.64)	41 (66.13)		10 (45.45)	12 (66.67)	
Overall survival	**CR** *(N=233)*			**ART** *(N=136)*			**SDF** *(N=78)*		
Major failure	1 (3.33)	2 (0.99)	0.40	5 (11.63)	6 (6.45)	0.52	12 (23.53)	5 (18.52)	0.37
Minor failure	2 (6.67)	13 (6.40)		7 (16.28)	13 (13.98)		0 (0.00)	1 (3.70)	
Success	24 (80.00)	176 (86.70)		31 (72.09)	74 (79.57)		39 (76.47)	21 (77.78)	
	Mean±SD (Range)			Mean±SD (Range)			Mean±SD (Range)		
	25.77±13.55	21.05±11.94	0.07	20.77±13.86	19.57±11.68	0.78	13.55±6.31	15.44±5.95	0.08
	(3-50)	(0-50)		(2-50)	(1-45)		(0-38)	(1-27)	

ASDs: Autism Spectrum Disorders; N: number; mo.: months; SD: Standard Deviation; CI: Confidence Interval; CR: Composite Restoration; ART: Atraumatic Restoration Treatment; SDF: Silver Diamine Fluoride.

TABLE 2 Comparison of the two cohorts of children in relation to successes and minor and major failures obtained with each caries management.

2b), no statistically significant difference was found in the survival rate of different caries managements in the cohort with ASDs, while in the Unaffected cohort, a statistically significant difference between CR, ART and SDF (Logrank test p=0.01) and between CR and SDF (Logrank test p<0.01) was found. No statistically significant difference was found between ART and SDF, as well as between ART and CR. In both failure scenarios, the survival curves for each caries management were lower in the ASDs cohort than in the Unaffected cohort.

When considering only major and minor failures as a 'failure event' in the total sample (Figure 3a), a statistically significant difference was found in the survival rate between CR, ART and SDF (Logrank test p=0.02), between CR and ART (Logrank test p=0.01) and between CR and SDF (Logrank test p=0.03), while no statistically significant difference was found between ART and SDF. Considering only major failures as a 'failure event' (Figure 3b), a statistically significant difference in the survival rate was found between CR, ART and SDF (Logrank test p<0.01), between CR and SDF (Logrank test p<0.01) and between ART and SDF (Logrank test p=0.01), while no statistically significant difference was found between CR and ART.

In the multivariate analysis (Table 4), if considering both major and minor failures as a "failure event", treatment success was not associated with any of the variables considered in the ASDs cohort, while it was associated with the age of the children in the Unaffected cohort, with greater success rate if caries management was performed in older subjects (p<0.01). Considering only major failures as a "failure event", treatment success was associated with the number of decayed teeth in the ASDs cohort (p=0.01) and with the type of caries management in the Unaffected cohort, with lower success rate obtained with SDF and higher with CR (p<0.01).

Discussion

The present clinical cohort study focused on three different caries management strategies (conventional restoration with composite resin, ART technique and application of SDF without caries removal) used for the treatment of caries in primary teeth, performed in two cohorts of children, one with Autism Spectrum Disorders and a second without disabilities. The analysis included 253 eligible dental records from 62 children with ASDs and 191 unaffected peers. The distribution of caries management strategies exhibited noteworthy variations between the two cohorts. In the cohort with ASDs, the application of Silver Diamine Fluoride was the most employed method (41.13%), while conventional treatment was predominant in the unaffected cohort (62.85%), results that reject the null hypothesis. This discrepancy in treatment preferences raises questions about the factors influencing decision-making processes in the management of dental

	ASDs *(N=124 teeth)*				**Unaffected** *(N=323 teeth)*				**Total** *(N=447 teeth)*			
Variable	N (%)			*p*	N (%)			*p*	N (%)			*p*
Tooth location	**CR** *(N=30)*	**ART** *(N=43)*	**SDF** *(N=51)*		**CR** *(N=203)*	**ART** *(N=93)*	**SDF** *(N=27)*		**CR** *(N=233)*	**ART** *(N=136)*	**SDF** *(N=78)*	
Upper posterior	16	10	27	0.01	94	39	8	0.38	110	49	35	0.47
	(53.33)	(23.26)	(52.94)		(46.31)	(41.94)	(29.63)		(47.21)	(36.03)	(44.87)	
Upper anterior	3	2	1		3	3	1		6	5	2	
	(10.00)	(4.65)	(1.96)		(1.48)	(3.23)	(3.70)		(2.58)	(3.68)	(2.56)	
Lower anterior	0	1	1		3	0	0		3	1	1	
	(0.00)	(2.33)	(1.96)		(1.48)	(0.00)	(0.00)		(1.29)	(0.74)	(1.28)	
Lower posterior	11	30	22		103	51	18		114	81	40	
	(36.67)	(69.77)	(43.14)		(50.74)	(54.84)	(66.67)		(48.93)	(59.56)	(51.28)	
Survival at 6-mo.												
Major failure	1	3	6	0.21	2	1	2	0.08	3	4	8	<0.01
	(3.33)	(6.98)	(11.76)		(0.99)	(1.08)	(7.41)		(1.29)	(2.94)	(10.26)	
Minor failure	2	3	0		13	9	0		15	12	0	
	(6.67)	(6.98)	(0.00)		(6.40)	(9.68)	(0.00)		(6.44)	(8.82)	(0.00)	
Success	27	37	45		188	83	25		215	120	70	
	(90.00)	(86.05)	(88.24)		(92.61)	(89.25)	(92.59)		(92.27)	(88.24)	(89.74)	
Survival at 12-mo.												
Major failure	2	4	11	0.02	5	6	3	0.02	7	10	14	<0.01
	(6.67)	(9.30)	(21.57)		(2.46)	(6.45)	(11.11)		(3.00)	(7.35)	(17.95)	
Minor failure	3	6	0		15	12	0		18	18	0	
	(10.00)	(13.95)	(0.00)		(7.39)	(12.90)	(0.00)		(7.73)	(13.24)	(0.00)	
Success	25	33	40		183	75	24		208	108	64	
	(83.33)	(76.74)	(78.43)		(90.15)	(80.65)	(88.89)		(89.27)	(79.41)	(82.05)	
Survival at 18-mo.	**CR** *(N=26)*	**ART** *(N=33)*	**SDF** *(N=22)*		**CR** *(N=134)*	**ART** *(N=62)*	**SDF** *(N=18)*		**CR** *(N=160)*	**ART** *(N=95)*	**SDF** *(N=40)*	
Major failure	2	5	12	<0.01	8	7	5	0.02	10	12	17	<0.01
	(7.69)	(15.15)	(54.55)		(5.97)	(11.29)	(27.78)		(6.25)	(12.63)	(42.50)	
Minor failure	4	7	0		19	14	1		23	21	1	
	(15.38)	(21.21)	(0.00)		(14.18)	(22.58)	(5.56)		(14.38)	(22.11)	(2.50)	
Success	20	21	10		107	41	12		127	62	22	
	(76.92)	(63.64)	(45.45)		(79.85)	(66.13)	(66.67)		(79.38)	(65.26)	(55.00)	
Overall survival	**CR** *(N=30)*	**ART** *(N=43)*	**SDF** *(N=51)*		**CR** *(N=203)*	**ART** *(N=93)*	**SDF** *(N=27)*		**CR** *(N=233)*	**ART** *(N=136)*	**SDF** *(N=78)*	
Major failure	2	5	12	0.01	8	6	5	0.03	10	11	17	<0.01
	(6.67)	(11.63)	(23.53)		(3.94)	(6.45)	(18.52)		(4.29)	(8.09)	(21.79)	
Minor failure	4	7	0		19	13	1		23	20	1	
	(13.33)	(16.28)	(0.00)		(9.36)	(13.98)	(3.70)		(9.87)	(14.71)	(1.28)	
Success	24	31	39		176	74	21		200	105	60	
	(80.00)	(72.09)	(76.47)		(86.70)	(79.57)	(77.78)		(85.84)	(77.21)	(76.92)	
	Mean±SD (Range)				Mean±SD (Range)				Mean±SD (Range)			
	25.77	20.77	13.55	<0.01	21.05	19.57	15.44	0.09	21.66	19.95	14.21	<0.01
	±13.55	±13.86	±6.31		±11.94	±11.68	±5.95		±2.23	±12.37	±6.21	
	(3-50)	(2-50)	(0-38)		(0-50)	(1-45)	(1-27)		(0-50)	(1-50)	(0-38)	

ASDs: Autism Spectrum Disorders; N: number; mo.: months; SD: Standard Deviation; CI: Confidence Interval; CR: Composite Restoration; ART: Atraumatic Restoration Treatment; SDF: Silver Diamine Fluoride.

TABLE 3 Comparison of successes and minor and major failures obtained with the different caries managements within each cohort of children.

caries in children with ASDs, who are often less cooperative at the dental chair compared to their unaffected peers [Delli et al., 2013; Ferrazzano et al., 2020a]. The observed variation in treatment preferences aligns with the limited existing literature[Corridore et al., 2020; Hu et al., 2020; Zerman et al., 2022]. Previous studies have suggested that children with ASDs may have unique challenges and sensory sensitivities that influence treatment acceptance [Kuhaneck and Chisholm, 2012; Stein et al., 2011]. This is consistent with the higher utilization of SDF in the ASDs cohort, possibly due to its non-invasive nature compared to conventional restorations, which may be better tolerated by children with ASDs.

The survival analysis over a follow-up period ranging from a minimum of 12 to a maximum of 50 months provided

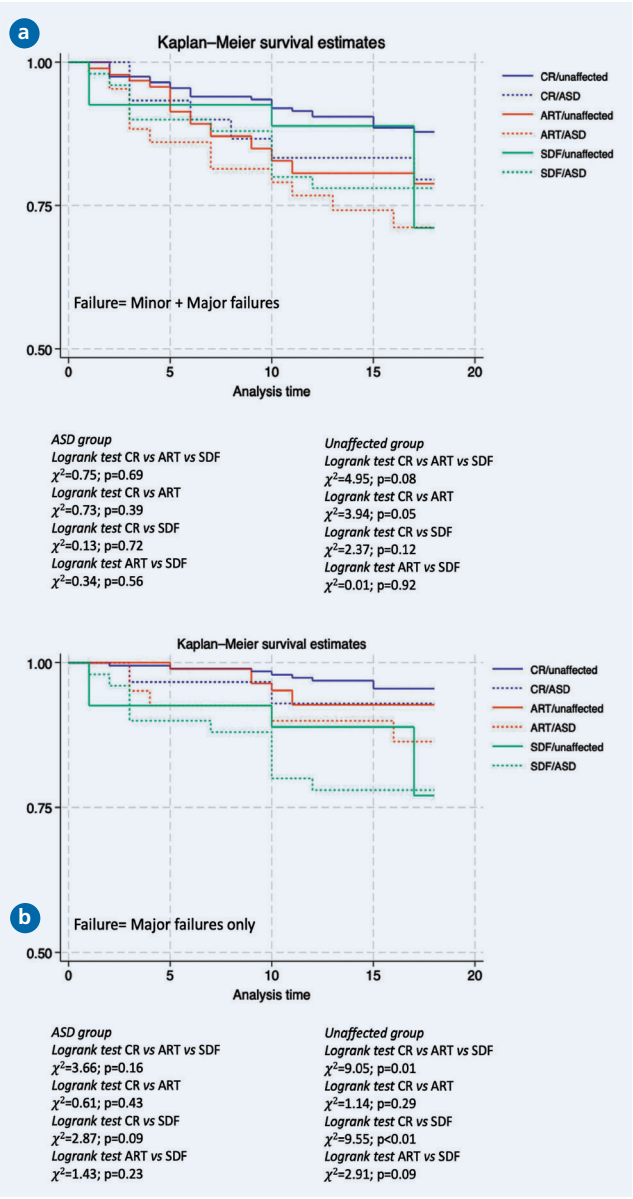

FIG.2 Kaplan Meier survival curves illustrating the survival fraction of each caries management during the follow-up period for each cohort with log-rank test. Both major and minor failures were considered as a "failure event" **(a)**; only major failures were considered as a "failure event" **(b)**.

valuable insights into the effectiveness of different caries management strategies. The hierarchy of treatment success (CR > ART > SDF) observed in the current study is consistent with existing literature [Abdellatif et al., 2021; Raggio et al., 2013; Vargas et al., 2020; Vollú et al., 2019]. However, the specific success rates and the observed reduction in survival curves for teeth managed with SDF over time warrant further investigation and comparison with studies that have evaluated the long-term effectiveness of SDF in paediatric populations [Raskin et al., 2021]. One factor to consider for SDF higher feature is that the protocol currently implemented at the Pediatric Dentistry Department of San Paolo Hospital (University of Milan) provides for two applications of the solution one month apart, whereas current evidence suggests repeated applications every six months to increase the success rate [Zaffarano et al., 2022].

The initial 6-month follow-up revealed a high success rate (>86%) for all treatments, with no significant differences in success and failure rates in both cohorts. However, at 12- and 18-month follow-ups, a decline in success rates was observed across all management types, particularly for Atraumatic Restorative Treatment and SDF.

When comparing the overall success rates among different management strategies, CR proved to be the most successful, followed by ART and SDF. These findings partially align with existing literature but highlight the need for individualized approaches based on patient characteristics [Chisini et al., 2018; Frencken, 2017; Santamaria et al., 2014; Tirupathi et al., 2019; Yunus et al., 2021].

The overall results are more optimistic than those at 18 months as they also count teeth with a follow-up ranging between 12 and 17 months, which are classified as successes. Unfortunately, it was not possible to follow-up all teeth for more than 12 months evaluating any change in status also because the Covid-19 pandemic has not only reduced the number of treatments but also the regular follow-up visits [Faccini et al., 2020; Farronato et al., 2020; Üstün et al., 2021].

Survival curve analyses revealed that, while no significant differences were observed in the cohort with ASDs among the different caries managements, the unaffected cohort exhibited distinctions in CR, ART, and SDF survival rates. In particular, the curves for teeth managed with SDF showed the greatest survival reduction over time, a result consistent with what has already been reported in the literature [Zaffarano et al., 2022].

Multivariate analysis identified age as a significant factor for treatment success in the unaffected cohort, with older subjects demonstrating greater success. This association resonates with findings from a previous study [Melgar et al., 2017], suggesting that older children may exhibit better cooperation and understanding during dental procedures. However, the lack of a similar association in the ASDs cohort underscores the complexity of factors influencing treatment outcomes in children with ASDs, possibly including individualized behavioural approaches, sensory considerations and new strategy as virtual reality [Cirio et al., 2022; Delli et al., 2013; Pagano et al., 2022]. In this cohort, treatment success was not associated with any of the considered variables when both major and minor failures were considered. However, when assessing only major failures, the number of decayed teeth, recorded at the first dental examination, emerged as a significant factor, suggesting a potential impact of disease severity on treatment outcomes. This finding aligns with broader literature indicating that the severity of dental caries may affect the success of various treatment modalities [Melgar et al., 2017].

In summary, although the current study provides valuable insights into the caries management in children with ASDs, further research, and comparative analyses are needed to validate and contextualize these findings. Collaborative efforts between multiple research centers could provide a more comprehensive understanding of the complexities involved in paediatric dental care, particularly for children with neurodevelopmental disorders such as ASDs.

The overarching conclusion from the current study, emphasizing the need for individualized approaches in managing dental care for children with ASDs, is consistent with the evolving paradigm in paediatric dentistry. Tailoring

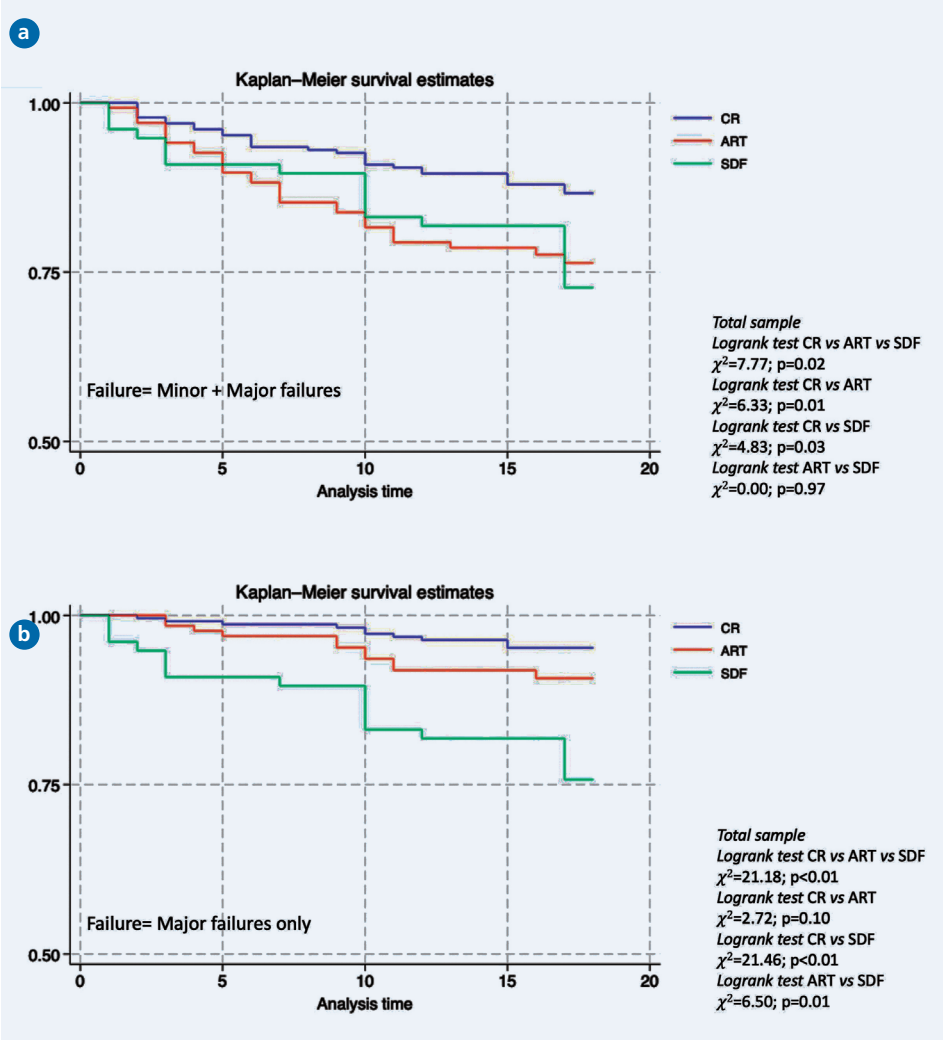

FIG.3 Kaplan Meier survival curves illustrating the survival fraction of each caries management during the follow-up period in the total sample with log-rank test. Both major and minor failures were considered as a "failure event" **(a)**; only major failures were considered as a "failure event" **(b)**.

interventions to each child's unique needs and characteristics is increasingly recognized as crucial for optimizing outcomes [El Khatib et al., 2014; Zerman et al., 2022].

The main limitation of the present study is its retrospective design, which does not allow controlling for several variables that may have influenced the results. However, having analysed a reality of care makes it possible to evaluate the effectiveness of the care provided and to carry out a reassessment to improve the quality of day-to-day care, especially for the care offered to special needs patients such as children with ASDs. Despite the limitations of the study design, the present study represents the first investigation to assess the survival of traditional restorative therapy, ART and SDF in a cohort of children with autism, comparing it with one of unaffected peers.

Conclusion

The study results shed light on the nuances of caries management in children with ASDs compared to their unaffected peers. The observed differences in treatment preferences, success rates, and factors that may influence them highlight the importance of personalized approaches to address the unique needs of children with ASDs in dental care. Further research is needed to investigate deeper the specific factors that contribute to treatment outcomes in this population and to develop evidence-based guidelines to optimize the dental care of children with ASDs.

Ethical approval and consent to participate

The study was approved by the Ethics Committee Board of San Paolo Hospital, Milan, Italy approval number 546/2021. The study is a human observational study and as such was conformed to STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) guidelines. All performed procedures were in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments. Informed consent was obtained from all subjects involved in the survey.

Availability of data and materials

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

Competing interests

The authors declare no competing interests in relation to the present study.

Author contributions

MGC and GMT contributed to conception and design of

Cox regression with Breslow method for ties					
ASDs Failure=Major + Minor failures					
N of teeth=123; N of failures=29; Time at risk=2.36; Log likelihood=-132.24; LR 2(4) =6.18; p=0.18					
	Hazard Ratio	Standard Error	z	p	95% Confidence Interval
Tooth location	1.28	0.19	1.69	0.09	[0.96;1.70]
Treatment	0.87	0.23	-0.53	0.60	[0.51;1.48]
N of decayed teeth	1.22	0.16	1.59	0.11	[0.95;1.57]
Age	1.07	0.13	0.51	0.61	[0.83;1.37]
Unaffected *Failure=Major + Minor failures*					
N of teeth=320; N of failures=49; Time at risk=6.51; Log likelihood=-264.64; LR 2(4) =21.34; p<0.01					
	Hazard Ratio	Standard Error	z	p	95% Confidence Interval
Tooth location	0.85	0.84	-1.64	0.10	[0.70;1.03]
Treatment	1.49	0.33	1.82	0.07	[0.97;2.31]
N of decayed teeth	0.82	0.10	-1.61	0.11	[0.64;1.04]
Age	0.70	0.07	-3.62	<0.01	[0.58;0.85]
ASDs *Failure=Major failures only*					
N of teeth=123; N of failures=18; Time at risk=2.36; Log likelihood=-79.14; LR 2(4) =10.59; p=0.03					
	Hazard Ratio	Standard Error	z	p	95% Confidence Interval
Tooth location	0.98	0.17	-0.08	0.93	[0.71;1.37]
Treatment	1.17	0.44	0.42	0.67	[0.56;2.45]
N of decayed teeth	1.52	0.26	2.47	0.01	[1.09;2.13]
Age	1.09	0.19	0.51	0.61	[0.77;1.55]
Unaffected *Failure=Major failures only*					
N of teeth=320; N of failures=19; Time at risk=6.51; Log likelihood=-101.42; LR 2(4) =10.21; p=0.04					
	Hazard Ratio	Standard Error	z	p	95% Confidence Interval
Tooth location	0.89	0.14	-0.75	0.45	[0.65;1.22]
Treatment	2.60	0.88	2.80	<0.01	[1.33;5.08]
N of decayed teeth	0.68	0.15	-1.71	0.08	[0.43;1.06]
Age	0.90	0.13	-0.68	0.49	[0.67;1.20]

ASDs: Autism Spectrum Disorders; N: number.

TABLE 4 Cox multiple logistic regression estimates of failure at tooth level in each cohort of children both considering major and minor failures as a "failure event" and only major failures as a "failure event".

the study. SC, CS and AM organized the data collection. ACI and CS performed the analyses. GMT, ACI, SC and CS wrote the frst draft of the manuscript and MGC and GC revised it critically for important intellectual content. All authors approved the submitted version of the manuscript.

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